Commission of the European Communities

radiation protection

Radiation protection research and training programme 1990-91

Catalogue of contracts

Report

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Preface:

The Community Radiation Protection Research and Training Programme was initiated in the framework of the EURATOM TREATY almost 30 years ago. During this time it has undergone major changes in adapting itself to new research needs in relation to the changing demands of radiation protection policies and practices and to new applications of ionizing radiation. The present catalogue of contracts which presents a complete overview of the 1990-1991 Radiation Protection Programme bears witness to this.

The Commission now favours multi-partner contracts which allow an even better integration of the work of different institutes into a common goal. Although, due to administrative reasons, a few individual contracts still exist, from a scientific management point of view all contracts are co-ordinated in a multi-national structure. Experience with this structure has been very satisfactory, and all scientists have eagerly taken the opportunity provided for the close cooperation which avoids duplication of effort and results in a better integration of Community research. It should also be noted that Sweden now participates as a full member in the activities of the Programme.

Training in radiation protection, now a matter of great urgency in view of the pending retirement of many senior scientists, has been substantially expanded in the current Programme, extended to several levels of knowledge and adapted to various target groups.

The scientific structure of the 1990-1991 Programme is also new and emphasizes the main goals of radiation research as well as their interdependence and the need for multi-disciplinary approaches to solve the problems. Accordingly, the Programme is divided into three large sectors as follows:

A) Human Exposure to Radiation and Radioactivity
   1) Measurement of Radiation Dose and its Interpretation.
   2) Transfer and Behaviour of Radionuclides in the Environment.

B) Consequences of Radiation Exposure to Man; their Assessment, Prevention and Treatment
   1) Stochastic Effects of Radiation.
   2) Non-stochastic Effects of Radiation.
   3) Radiation effects on the developing organism.

C) Risks and Management of Radiation Exposure
   1) Assessment of human exposure and risks.
   2) Optimization and Management of Radiation Protection.

Indeed, several of the most urgent problems of radiation protection demand a multi-disciplinary approach involving more than one of the above sectors. To give some examples:

- risks from exposure to low doses and at low dose rates, the most frequent type of exposure, cannot be assessed directly but require an extrapolation of information from high to low dose/low dose rate exposure. This is based on a concerted approach involving microdosimetric, molecular, cellular, animal and epidemiological investigations on induction of radiation-induced cancer, genetic damage and other effects.

- radon in homes represents the principal radiation exposure of man. In view of the recommendations which are to be issued and the remedial actions which will have to be taken to control radon exposure, one must obtain a better understanding of the ways by which radon and its daughter nuclides enter the human environment and from there into the lung, and of their effects on radiosensitive pulmonary structures. A co-operative approach is being taken in the Community, together with the USA, to execute existing, and plan new epidemiological studies on lung cancer after radon exposure.

- medical diagnostic radiology of patients represents the most important man-made source of radiation exposure and should be reduced as far as possible without deterioration of image quality and diagnostic information. Recent pilot research on quality control and dose reduction revealed the potential of dose- and cost-saving measures which can be taken. Expert systems for quality and dose control are developed to allow the scientific results to be introduced into everyday practice.

- in view of new stricter dose limits, radiological protection at the workplace must be optimized basing management procedures on improved scientific information. In this respect, comprehensive statistics of human exposure from different sources, including natural and medical ones, are being obtained. The monitoring of workers for external and internal exposure under realistic working conditions is being further developed with respect to accuracy and sensitivity. Among others, new and improved instrumentation and procedures are being developed and further research on the metabolism of radionuclides is being carried out to improve the detection of low levels of internal contamination.

- the Chernobyl accident has emphasized the need for an integrated nuclear emergency management system. Probabilistic approaches will now be finalised and will be applied in the near future. The different modules of accident consequence analysis must now be integrated with the monitoring systems, and real-time emergency management systems are being further developed on a Community level. Moreover, the scientific development of countermeasures to treat accident victims or to deal with contamination in the near, intermediate and far fields of a nuclear accident are being intensified within the co-operative groups of scientists from the Community. Such countermeasures must be based on a reliable assessment of the dynamic behaviour of radionuclides in the environment.

The studies carried out in the Programme will continue to provide:

- the scientific basis for the continued updating the Community directives for the "Basic Safety Standards for the Health Protection of the General Public and Workers against the Dangers of Ionizing Radiation" and the scientific background for the continued evolution of radiation protection concepts and practices,

- the scientific knowledge to evaluate possible carcinogenic and genetic effects and risks from exposure to low doses and low dose rates of radiation of different qualities arising from natural radiation, medical diagnostic radiology, and nuclear and other industrial activities,

- the methodologies to assess risks from radiation accidents as well as the rationales and techniques for the implementation of monitoring and countermeasures to prevent or

reduce the consequences of such accidents to man and the environment,

- the incentive and support for co-operation between scientists in Member States, and the training of young scientists indispensable for maintaining radiation protection competence in the Community,
- the efficient use and dissemination of scientific knowledge in radiation protection.

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Director DG XI.A
Nuclear Safety, Industry and
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Head of Unit DG XII.D.3
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RESEARCH CONTRACTS MANAGEMENT AND SCIENTIFIC DATA

A HUMAN EXPOSURE TO RADIATION AND RADIOACTIVITY

A1 MEASUREMENT OF RADIATION DOSE AND ITS INTERPRETATION

A1 Measurement of radiation dose and its interpretation

Contract Bi6-026 Collaboration on research and development concerned with the methodology and data in radiation dosimetry.

Coordinator EURADOS-CENDOS
European Dosimetry Group
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Total Contribution by the Commission: 77 kECU
24 months from 1/01/90 to 31/12/91

Participating Scientists

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77 kECU

Description of research work:

Collaboration on Research and Development concerned with the Methodology and Data of Radiation Dosimetry (EURADOS = European Radiation Dosimetry Group)

Objectives:

1. The stimulation of collaborative developments and research into methods and techniques for the evaluation of exposures to and risks of ionising radiations.
2. The harmonisation of collaborative developments and researching radiation exposures by means of intercomparisons, workshops, seminars and by active collaboration.
3. The collection and evaluation of physical data relevant to the assessment of the biological effects of ionising radiations and to the assessment of the occupational and environmental exposures of the populations of the European Communities.

Programme:

The collaboration is implemented or organised by Working Groups on the following topics:

Working Group 2: Skin Dosimetry

Objectives:

The evaluation of dose to the skin, in particular from exposure to beta and low energy photon radiations, and the development of appropriate methods for its measurement and assessment.

Programme:

Theoretical and experimental study of hot particle dosimetry.

Intercomparison of extrapolation chambers.

Collaboration with EULEP on biological effectiveness and depth of sensitive layers in the skin.

Study of methods for skin dose-rate measurements.

Study of the importance of weakly penetrating radiations in nuclear workplaces.

Collaboration with the CEC and Nuclear Energy Board, Dublin, in organising a workshop on skin dosimetry.

Working Group 4: Numerical Dosimetry

Objectives:

To disseminate information about computer programmes for numerical dosimetry.

Programme:

Intercomparison of calculated response functions for Bonner spheres.

Study of the use of voxel phantoms for external and internal dosimetry.

Collection and computation of radiation albedos from phantoms and people.

Theoretical and computational support for Working Groups 7 and 10.

Working Group 6: Assessment of Internal Dose

Objectives:

The preparation of guidance on the interpretation of monitoring data relating to internal exposures of radiation workers and the implementation of ICRP recommendations on this topics within Europe.

Programme:

An intercomparison of assessments of five cases of internal contamination by nine laboratories will be published as a CEC report with appendices on methods. A shortened version will be published in Radiation Protection dosimetry.

A metabolic study using stable isotopes will be coordinated by a member of the Working Group.

A study contract to define the basis for a European Registry of dose assessments, autopsy data and metabolic models will be completed.

A joint task group with EULEP will be set up to produce respiratory tract models. These models will relate intakes of radioactivity by workers to organ doses. An experimental programme will be proposed.

Working Group 7: Radiation Spectrometry in Working Environments

Objectives:

The determination of dose equivalent quantities in mixed photon:Neutron fields is still a problem due to the strong energy dependence of the dose equivalent response of commonly used neutron monitors. Sufficient accuracy is only achieved if instruments or detector systems with spectrometric properties are employed.

The main objectives of the proposed committee are therefore:

- discussion of the properties of various portable photon/neutron spectrometers including their calibration procedures
- intercomparison the various spectrometer systems by performing measurements in well specified radiation fields or working environments
- investigation of the use of spectrometric measurements in the interpretation of individual dosemeter readings for the assessment of organ absorbed doses and dose equivalent.

Programme:

All spectrometric systems will be included in the proposed programme:

Justification for the use of spectrometers in radiation protection practice (non-ideal energy response of area and personnel dosemeters).

Comparison of the properties of realised portable neutron/photon spectrometers (ranges of operation in energy, fluence or dose rate, n/γ-discrimination, evaluation of the spectral fluence, instabilities, uncertainties, limitations).

Calibration procedures (calculation and experimental calibration of the energy response, traceability, reproducibility).

Intercomparison of spectrometer properties.

Recommendations for the use of spectrometers.

Application: spectrometry in working environments.

Working Group 8: Development of Individual Dosemeters for External Penetrating Radiations

Objectives:

The objectives of the group would be to develop and improve techniques for the individual dosimetry of penetrating radiations.

Programme:

Intercomparison of neutron dosemeters based on track-etch techniques

Development of neutron detectors for electronic dosemeters

Intercomparisons of electronic dosemeters

Working Group 9: Criticality Accident Dosimetry

Objectives:

The objectives of the group are to provide training int he operation of criticality accident dosimetry systems and to improve the methods of interpretation in terms of relevant dosimetric quantities.

Programme:

Spectrometry and dosimetry of the Silene reactor system

Organisation of international intercomparisons

Correlation of physical and biological dosimetry systems

Present state of criticality dosimetry systems

Working Group 10: Basic Physical Data and Characteristics of Radiation Protection Instruments

Objectives:

The collection and assessment of basic physical data relevant to the biological effects of ionising radiations and to the development of instrumentation for dosimetry in radiation protection and radiobiology.

Programme:

Mean energy required to create an ion pair, W-value:

Critical evaluation of available W-values for charged particles in different gases currently used (CH_4 and C_3H_8 based TE gas, C_4H_{10}, Ar-CO_2).

Recommendation of W-values to be used for calibration purposes and assessment of average W-values for photons and neutrons with regard to the gas mixtures used and cavity size; investigation of the accuracy achievable in absorbed dose measurements, considering in particular the case of non-homogenous detectors.

Alternative approaches to assess and improve the knowledge of W-values and average W-values.

Electrical discharge processes in gas cavity detectors

Assessment of electron-molecule cross sections and related swarm parameters (drift velocities, diffusion and ionisation coefficients); investigation of the application of these calculations to the gas mixtures and detectors currently used and their limitation.

Investigation of gas gain properties, space charge effects with regard to low and high LET particles and counter geometry of proportional counters and to compare the results of theoretical and experimental investigations.

Gas detectors for experimental investigation of energy deposition in small sites
Evaluation of the suitability of proportional counter to simulate sites in the order of or smaller than 100 nm diameter.

Study of new generation of detectors (e.g. digital chamber, multi-wire drift chamber) for nanometer dimensions.

A1 Measurement of radiation dose and its interpretation

Contract Bi6-322 Quantities, units and measurement techniques for ionizing radiation.

Coordinator ICRU
International Commission for Radiation Units and Measurements
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Total Contribution by the Commission: 75 kECU
24 months from 1/01/90 to 31/12/91

Participating Scientists

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Description of research work:

The International Commission on Radiation Units and Measurements (ICRU), since its inception in 1925, has had as its principal objective the development of internationally acceptable recommendations in terms of:

(1) Quantities and units of radiation and radioactivity,

(2) Procedures suitable for the measurement and application of these quantities in radiation protection as well as in clinical radiology and radiobiology,

(3) Physical data needed in the application of these procedures, the use of which tends to assure uniformity in reporting.

The ICRU considers and makes recommendations on quantities, units and measurement techniques appropriate for the field of radiation protection. In this connection, its work is carried out in close cooperation with the International Commission on Radiological Protection (ICRP). Also, it should be noted that much of the ICRU's work in the field of clinical radiology is conceived to lead to a direct and considerable dose reduction for the patient.

The ICRU endeavours to collect and evaluate the most recent data and information pertinent to the problems of radiation measurement and dosimetry and to recommend the most acceptable values for current use.

The Commission's recommendations are kept under continuous review in order to keep abreast of the rapidly expanding uses of radiation and also to provide answers to urgent questions.

The program of the ICRU is regularly adapted to meet newly identified needs. However, the work is illustrated by the following examples of topics on which work is currently underway:

(1) measurement of dose equivalent,

(2) phantoms for protection, therapy, and diagnosis,

(3) absorbed dose standards for photon irradiation and their dissemination,

(4) stopping powers for heavy ions, and

(5) fundamental quantities and units.

Recently released is ICRU Report No. 45, Clinical Neutron Dosimetry--Part I: Determination of Absorbed Dose in a Patient Treated by External Beams of Fast Neutrons.

New work has been initiated on (1) clinical neutron dosimetry: specification of radiation quality, (2) hyperthermia, (3) in situ gamma spectrometry in the environment and (4) proton therapy.

A11 Development and implementation of standards and procedures linked to the concepts of dose equivalent quantities for both external and internal exposure

Contract Bi6-347a The implementation of the operational dose quantities into radiation protection dosimetry (NRPB Association).

Coordinator NRPB
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Total Contribution by the Commission: 240 kECU
24 months from 1/04/90 to 31/03/92

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Description of research work:

Aim and Objectives

The overall aim of the project is to develop reliable methods to measure the spectral and angular distribution of external radiation in the workplace and to use the results to estimate effective dose equivalent.

At present, techniques for measuring neutron spectra in the workplace are well developed and measurements will be made at various nuclear installations. For photons, NRPB has designed a straight-forward method to obtain spectral and angular information using Geiger-Müller detectors. Alternative methods of obtaining such information will be investigated, using sodium iodide and germanium detectors. These devices will be used for measurements in the workplace, and calculational methods will be developed to use these measurements to estimate effective dose equivalent from external photon radiations. Calculations and experimental measurements will be extended to other irradiation geometries for the evaluation of the response of personal dosemeters. The implications of such measurements for personal dosimetry will be investigated and the correspondence between operational dose-equivalents quantities and effective dose equivalent will be evaluated.

NRPB (GB)

NRPB will coordinate this project, which deals with methods of measurement of the spectral and angular distribution of external radiations in the workplace and draws on experimental investigations and photon transport calculations by the Monte Carlo method. It will provide the expertise and facilities to develop reliable methods for measuring the spectral and spatial distributions. The implications of such measurements for personal dosimetry will be considered, including their utility in making estimates of worker doses.

In collaboration with the UKAEA, ENEA and CEA, NRPB will evaluate various methods to obtain spectral and angular information on external radiations and examine ways in which the data obtained can be used to estimate effective dose equivalent. The NRPB secondary standard calibration laboratory will be used to test various measurement techniques before they are used in the workplace. At present, the techniques for measuring neutron radiation spectra in the workplace are relatively well developed, so efforts will be concentrated on evaluating methods to measure the spatial and spectral distributions of photon radiations. Furthermore, the feasibility of obtaining useful spectral information for beta radiation in the workplace will be investigated.

UKAEA (GB)

UKAEA Harwell Laboratory will provide theoretical and computational input in order to:

(1) evaluate the general limitations of devices which rely on filtration, detector response and collimation to provide simple energy and angular information;

(2) interpret the data from experimental devices relying on filtration, detector response and collimation;

(3) evaluate the use of photon energy detectors (NaI and Ge) with appropriate collimation, to determine the photon energy and angular distributions;

(4) develop techniques to unfold the energy and angular distributions from the measured pulse height distributions in support of the experimental work.

Harwell Laboratory has produced a fully mobile neutron spectrometer, which has been used in various environments, including within a PWR containment building. It is proposed that operational improvements be made to the spectrometry system and that neutron spectra be measured at a number of locations provisionally identified as:

(1) at the Silene reactor near Dijon, with various shields, as will be required for the proposed International Criticality Accident Dosimetry Intercomparison;

(2) at the NPL Laboratory near London, using a $^{252}Cf/D_20$ moderator source and thick target p-Li source and moderator assembly, which are proposed as international benchmark standard fields;

(3) in nuclear plants in Europe, in collaboration with others able to make measurements with tissue equivalent proportional counters (TEPCs) and dosemeter survey instruments and measurements of angular distribution. Where possible, measurements of photon energy and angular spectra will also be made using the instruments developed at the time.

ENEA (IT)

The ENEA Dosimetry Laboratory will perform experimental investigations and photon transport calculations using the Monte Carlo method. Calculations will be made of backscatter photon spectra on the surface of different types of phantoms. In addition, the influence of air will be investigated. The calculations will be performed for all X and gamma ISO reference radiation beams and for other radiation qualities employed for routine calibrations. Plane parallel photon beams with normal incidence will be simulated.

Calculations will be made of correction factors related to each type of phantom for calibration in terms of the ICRU quantities. Different kinds of individual dosimeters currently in use will be considered, as will the energy and angular responses of each dosimeter. Experimental determinations of the correction factors previously calculated for the different kinds of personal dosemeters will be pursued.

The calculations and the experimental measurements will be extended to other irradiation geometries for the evaluation of angular distribution factors. Dosimetric intercomparisons will be held with the other participants in the research program so as to verify the calibration data and procedures adopted for the project.

CEA (FR)

The CEA will investigate appropriate methods for calibrating personal dosemeters and the implications of energy spectra and spatial distribution measurements for personal dosimetry. An experimental programme of irradiations of personal dosemeters will be carried out and compared with results from computations at ENEA using Monte Carlo methods. Various phantoms will be used for the irradiations and a comprehensive series of measurements will be carried out with photons in the ISO series and at various angles of incidence. The results will be analyzed and compared with calculations, in order to determine the backscatter spectra at the surface of phantoms and any special correction factors required for the shape and composition of the phantom. The influence of angular incidence of irradiation will also be examined.

Most personal dosimetry services irradiate dosemeter for calibration purposes free in air. This enables several dosemeters to be irradiated at the same time, thereby ensuring that reliable calibration factors can be derived. This is not so easy when phantoms are used for calibrations, particularly the spherical phantoms recommended by ICRU. The results will therefore be analyzed to establish calibration factors for personal dosemeters, both in the presence and absence of phantoms, appropriate for use in various photon fields which exist in the workplace.

A12 Radiation measurement and instrumentation for individual and area dosimetry

Contract Bi7-020 Study and development of an individual electronic neutron dosemeter.

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Total Contribution by the Commission: 246 kECU
24 months 1/11/90 to 31/10/92

Participating Scientists

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18 kECU

Description of research work:

The aim of this contract is to develop a macroelectronic dosemeter which will be compared with optimized HECE, ECE and CE track etch dosemeters. LEPOFI (Limoges) and SIDR (Fontenay-aux-Roses) work on the electronic system; ENEA (Roma), NPD (Tessaloniki) and SFR (Barcelona) are concerned with dosemeters based on track etching.

In the first year of the contract, each group will work with its own dosemeter in order to optimize its system. Calculations and experiments with monoenergetic neutron beams (normal incidence) will be done and γ contributions on diodes will be calculated. LEPOFI and SIDR will work in permanent collaboration for electronic system. At the end of this phase joint irradiations will be done on the accelerator of SIDR-CEA (energy 2.3 MeV) and results of the five groups will be intercompared.

In the second year, the next following problems will be treated by theoretical calculations:

- Study of angular and energy response,

- n-γ discrimination,

- background

- low doses and low dose rates.

Then new intercomparisons will be realized in reference neutron fields and well known practical fields which the coordinator will identify.

Université de Limoges (F)

The following work will be carried out:

- From October 1990 to spring of 1991, the existing electronic dosemeter will be improved . Its components will be characterized and parameters of the diodes which must be measured during experiments for damaging studies will be defined. Then the response will be compared with that of SIDR system for the same neutron irradiations.

The response of the dosemeter to monoenergetic neutron and γ radiations will be calculated. Several problems are to be solved: choice of a calculation method, sensor modelization and development of a computer code.

- During the second step (up to October 92), the experimental response to monoenergetic neutron and γ beams will be studied. Several parameters will be considered :
- The sensor parameter: diode and converter characteristics,
- beam characteristics: energy, incidence and dose rate of the radiations.

Comparison with previous calculations will be done. If possible the response to realistic neutron spectra will be calculated and compared with experimental results.

ENEA (I)

The solution of the complex problem of personal neutron dosimetry is becoming far-reaching specially in view of the new ICRP recommendations which will decrease the personal dose limits and increase the quality factor.
In this particular project, attempts will be made to exploit a new electrochemical etching procedure of track detectors for the development of a new neutron dosemeter with sufficiently high sensitivity.

In the first year of the project, it will be demonstrated how this new electrochemically etching HECE allows to exploit the advantageous characteristics of both the spark counter and the conventional electrochemical etching, and to overcome all the limitations of these two techniques.

Different types of detectors will be analyzed such as polycarbonate and cellulose derivatives with thicknesses in the range between 10 and 30 μm.
The principal goal of the two years project is to gather sufficient information for the choice of a suitable track detector for thin film electrochemical etching.

Once the most suitable detector has been found, systematic investigations will be started in order to analyse the neutron detector response.

University of Thessaloniki (GR)

The detection system consists of a thin layer of ^{6}Li (about 2μm) evaporated directly on CR - 39 surface (which is the detector). The radiator could act at the same time as moderator for neutrons. So, we want at the same time proton recoils as well as alpha particles coming from ^{6}Li (n,a) reaction.

FIRST YEAR (with neutron of an energy of 2,5 MeV) :

1 - Study of the system response as function of the removed thickness layer, in order to obtain saturation. In this region proton recoils can be counted at the same time with alpha particles.
2 - Study of (V_g t) as a function of neutron energy.
3 - Study of the radiator moderator thickness for which the maximum of tracks is obtained. In this condition protonic equilibrium begins to be destroyed but there are sufficient alpha particles.
4 - Study of χ_{max} (thickness) as a function of neutron energy.

SECOND YEAR :

5 - For (V_{gt}), χ_{max}, the angular response will be studied.
6 - Angular response as a function of neutron energy will be investigated.
7 - The steps 1 - 2 - 3 - 4 - 5 - 6 - will be realized for various neutron doses.

CEA - IPSN (F)

FIRST YEAR :

The diodes will be tested electrically with regard to IV characteristic, the background, capacity and the depleted zone (4 months).
The thickness of the radiation and the optimum boron implementation will be chosen (2 months).
This will be followed by testing of the detection system and its calibration (6 months). This includes investigation of background, linearity, photon (X and γ) response and response to an external source of alpha particles.

SECOND YEAR :

The detection system will be investigated in order to characterize the energy response, differential response (double diode), detection threshold and linearity with dose rate (3 months).

Furthermore, the angular response and the long term stability will be studied (3 months).

Universidad Autónoma de Barcelona (ES)

FIRST YEAR :

- The response (tracks cm^{-2} μSv^{-1}) of a fast neutron dosemeter, composed of a polyethylene radiator and CR 39 plastic detector to monoenergetic and neutron sources at different incident angles will be calculated.
- The etching conditions for plates of 500 μm (electrochemical etching) will be optimized.
- The theoretical calculation will be compared with experimental results obtained of last CENDOS experiments (April 1990).

SECOND YEAR :

- CR 39 will be characterized in order to envisage a samples selection with a corresponding background improvement.

- Experimental study of angular response as a function of dose (CENDOS experiences programmed in 1991) will be carried out.
- Thermoluminescent materials for which the response of thermal neutrons is well known will be studied.

A12 Radiation measurement and instrumentation for individual and area dosimetry

Contract Bi7-025 Use of the variance-covariance method in radiation protection.

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Total Contribution by the Commission: 135 kECU
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Description of research work:

Reductions of the dose limits in radiation protection and changes of the quality factor for densely ionizing radiations will require increased precision in area monitoring and in personal dosimetry. Tissue equivalent proportional counters are increasingly employed for this purpose. However, their routine use in radiation protection requires the variance-covariance method which is an extension of the pulse height determination in two ways: it is not restricted to radiation fields of extremely low dose rate and, unlike the variance methods, it is applicable in the time-varying radiation fields that are frequently encountered in radiation protection practice.

Universität München (D)

Implementation of the Variance-Covariance Method for Radiation-Protection Dosimetry

In previous research, tissue equivalent proportional counters have been developed that are suitable for variance-covariance measurements of energy imparted. These detectors will be improved; the volume will be decreased to extend the range of applicability to higher dose rates, and the two detectors will be combined to a twin detector in a common housing. This will provide a more compact instrument which is particularly suitable for applications in inhomogeneous radiation fields and which will guarantee that both detectors be subject to the same dose rate. The electronic system for signal processing will utilize a pair of electrometer amplifiers that integrate the detector current in feedback capacitors.

The voltage at the capacitors is digitized by a single ADC which contains two separate sample and hold stages. The data are stored in a PC. The performance of the improved system will be assessed in pulsed photon, electron and in neutron fields.

The development of a practical, portable system will necessitate a sealed detector housing without linkage to a gas-flow system. The same stage of the work will be directed towards the miniaturization of the electronic components.

A theoretical and numerical analysis of the possibilities and limitations of the variance-covariance method with regard to various perturbing or interfering factors will parallel the practical implementation. These theoretical investigations will include a comparison of the experimental data to the results of radiation transport computations.

Univ. Arhus Hospital (DK)

Application of the Variance-Covariance Method to Characterize the Quality of X-Ray Beams in Diagnostic Radiology.

The previous research, equipment for the variance-covariance method has been developed. Two commercially available detectors are used. The signals from the detectors are amplified and sent through two linear stretchers before they enter a multi-function data acquisition board with sample and hold capabilities for further processing. Results have been obtained so far therapy radiation beams.

In the new research programme, the equipment will be further developed and modified for measurements in radiological X-ray beams. This will be a further development of the variance-covariance method. The design of more suitable and reliable detectors is necessary and the method needs to be compared with conventional methods. The measuring technique needs to be extended, to make it possible to measure pulsed with widths of multi-seconds rather than microseconds; and to allow measurements also in "continuous" radiation fields. The relation between detector sensitivity and electronic amplification needs to be optimized, and a simplification of the instrumentation will be required before it is employed in practical radiation protection applications.

In the second step of the programme, the method will then be applied to characterize the beam quality, and to serve as a quality assurance method that contributes further to current efforts to optimize dose reduction in diagnostic radiology.

NIRP (S)

Photon-Dosimetry Procedures in Terms of the Variance-Covariance Method.

In X-ray beams with half-value layers less than a few mm Cu the ranges of the electrons released by photons become less than the width of the gas cavity of the detector. The Bragg-Gray condition will then not apply. However, by reducing the gas pressure inside the detector so that mean chord lengths of about 1 μm are simulated, one can achieve the condition that the electrons cross the gas cavity. By calibrating such a detector in a cobalt-60 γ beam and deriving an absorbed dose gas cavity calibration factor, one can make the chamber usable in conventional X-ray beams with the same formalism as in high energy photon beams. This procedure will be tested in X-ray beams with HVL between 2.2 mm Al and 2.5 mm Cu. Using the variance-covariance method y_D can be determined in a phantom and possible corrections for changes in beam quality between air and phantom will be investigated, as well as the possibility of relating the quantities to microdosimetric parameters.

For the variance-covariance measurements electrometers with either capacitor or resistor in the feed back circuit will be used. The two different solutions will be compared.

A12 Radiation measurement and instrumentation for individual and area dosimetry

Contract Bi7-027 The measurement of environmental gamma doses

Coordinator Risø National Laboratory
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Total Contribution by the Commission: 183 kECU
24 months from 1/06/90 to 31/05/92

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Description of research work:

The ambient background radiation is typically measured by active high-pressure ionisation chambers, plastic scintillators, GM counters, proportional counters and passive TL dosemeters. To ensure that measurements of the environmental photon radiation can be made with sufficient accuracy, it is necessary to determine the response of the monitoring instruments and dosemeters, e.g. to cosmic and terrestrial radiation, and to take into account the inherent instrument (dosemeter) background. Calibration also poses problems since it is usually not possible to use a calibration facility within which the dose rate is low enough to permit calibration of the instruments and dosemeters at the level to be measured.

The intention is to improve calibration methods at low dose rates with the scope of recommending internationally standardised procedures to obtain reliable and comparable measurement results of the ambient background radiation. Instrument calibration studies will include free-field and shadow-shield calibrations where ground albedo, air build-up and room scatter components for a variety of source-detector geometries will be calculated using Monte Carlo calculations.

Collimated beam calibrations and the determination of instrument linearity, angle - and temperature dependence and inherent background will be performed in the Asse salt mine facility (925 m depth) having an ultra-low radiation background. The energy response will be determined including the measurements of 4 MeV and 6 MeV photons.

Environmental monitoring based on TL dosemeters will be improved by introducing a new evaluation method based on numerical analysis of the TL glow curve. This method has proved to be useful especially in assessing the individual dosemeter background from the same readout from which the radiation dose is evaluated.

Emphasis will be laid on long term measurements of the ambient radiation around a nuclear installation to assess how environmental monitors and TL dosemeters respond to small variations of the background radiation and how to differentiate between natural and man made radiation.

WORK PROGRAMME

A) Calibration experiments and field measurements.

Risø National Laboratory will mainly evaluate practical calibration methods and perform field experiments with the aim of standardising instrument readings and studying the responses of different detector types.

The following experiments and evaluations are planned:

- Performing free-field calibration experiments using low-active certificated ^{137}Cs, ^{60}Co, and ^{226}Ra gamma sources. Determination of different detector responses by Monte Carlo calculations (MCNP code) with special regard to ground scatter components and taking into account the energy responses of the individual detector.
- Performing indoor shadow-shield calibration experiments using a low-active certificated ^{137}Cs gamma source. Determination of different detector responses by Monte Carlo calculations (MCNP code) with special regard to room scatter contributions and taking into account the energy responses of the individual detector.
- Establishment of free-field irradiation facilities to assess how different environmental monitors respond to small elevations of the ambient radiation by exposing them to radiation from low-active artificial gamma sources introduced into the natural environment.
- Measurement of terrestrial and cosmic radiation components at different field sites and on board boat at sea respectively with emphasis on determining the responses to the cosmic radiation for the individual detector type.
- Under a subcontract agreed between Risø and Dr. I.M.G. Thompson, UK, field measurements will be carried out at a site nearby the Hinkley Point Nuclear Power Station in UK to assess how accurately environmental monitors and TL dosemeters left unattended over prolonged periods can measure the small dose rates arising from routine releases of ^{41}Ar, and their variation with time.

B) Measurements in an ultra-low radiation environment.

Physikalisch-Technische Bundesanstalt (PTB), will mainly carry out investigations of instrument properties in a measurement laboratory recently established at 925 m depth in the Asse salt-mine having an ultra-low environmental radiation background of about 1 nGy/h. The investigations will include the testing of representative new types of proportional counters, GM counters, high pressure ionisation chambers and plastic scintillators and the following instrument characteristics will be intensively studied:

- Inherent instrument background
- Linearity of the instrument response
- Energy dependence of the instrument response in the energy range of 60 keV to 1250 keV
- Angular dependence of the instrument response at a photon energy of 661 keV (Cs-137 source)
- Temperature dependence of the instrument response

The following facilities will be installed:

- A collimated beam set-up for measuring energy response, using low-active ^{241}Am, ^{57}Co, ^{137}Cs, and ^{60}Co gamma sources.
- Set-up using different calibrated low-active ^{137}Cs sources to determine instrument linearity at low dose rates.
- An additional lead shielding for measuring the inherent background of different instruments.
- A turntable for measuring the angular dependence of the instrument response using the collimated beam set-up.
- Environments for measuring the temperature dependence of the instrument readings within a temperature range of 25°C to about 40°C.

As part of the energy dependence studies, accelerator facilities at PTB will be used to further assess the instrument responses at 4 MeV and 6 MeV photons, respectively.

C) Improvement of TL methods for environmental monitoring

Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT) will mainly contribute with the development of new practical TL evaluation methods for environmental monitoring to be incorporated into routine procedures.

The aim is to improve thermoluminescence dosimetry for assessing ambient dose rates especially regarding reliability and operational characteristics by developing new evaluation methods based on numerical analysis of the TL glow curve. Under laboratory conditions, these methods (in particular a simplified method, especially adapted for low measurements) have so far proved their usefulness, arising mainly from its ability to individually estimate the background contributions in the same read out from which the radiation dose is evaluated. Other important advantages of these methods arise from the possibility of establishing quality criteria intrinsic to the TL measurements, that allow to identify and eventually discard results produced by anomalous glow curves, originated e.g. by the presence of contaminants or by faulty readouts.

The project has the further purpose of establishing new TL evaluation methods for the determination of environmental doses in real field conditions working with commonly used TL materials. From experience previously gained, improvements of the measurement quality and the lower detetable level are expected.

Some of the operational characteristics of the TL materials relevant for long term environmental monitoring will be tested in the facilities and sites provided by RISø and PTB, trying to incorporate TLDs into the common work programme, in order to effectively compare dosimetric data obtained by TLDs with those obtained by active non integrating systems. Emphasis will be laid on monitoring with TLDs the ultra-low radiation level in the Asse salt mine facility also with the aim of assessing the intrinsic dosemeter background.

A12 Radiation measurement and instrumentation for individual and area dosimetry

Contract Bi7-028 Dosimetry of beta and low-energy photon radiation using extrapolation chambers and thin solid state dosimeters.

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Total Contribution by the Commission: 154 kECU
24 months from 1/08/90 to 31/07/92

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Description of research work:

Objectives

For accurate dosimetry of beta and low-energy photon radiations, a large number of specific requirements on measurement techniques have to be defined and appropriate calibration facilities realised because of the low penetrability of these radiations. This project is aimed at identifying

such requirements and realising facilities to measure doses due to weakly penetrating radiations with greater accuracy and consistency than is possible at present.

The work of the contract comprises the following main objectives:

- Establishment of a regimen for ß-calibrations based on extended area sources that comply with ISO series 2 specifications;
- Study and refine the extrapolation chamber measurement technique for beta dosimetry;
- Characterisation of beta radiation fields in terms of the directional dose equivalent rate, $H'(d,\alpha°)$;
- Development and characterisation of thin solid state dosemeters for beta radiation;
- Development of dosimetry of low-energy photon radiation.

Programme of work

For experimental work and for many routine calibrations ß-ray sources are needed with energies and activities resulting in dose rates outside the range of sources in ISO series 1 which are commercially available. This study will therefore be directed to the development and realisation of beta ray calibration facilities based on extended area sources that would conform to series 2 reference beta radiation specified by the ISO. The study will centre around two different source constructions: circular sources, 42 mm in diameter, now in use at CEA laboratories in France and square source, 40 mm x 40 mm, used at the NRPB in the UK. Sources incorporating beta emitting nuclides with maximum energies ranging from 0.156 MeV (^{14}C) to 3.54 MeV ($^{106}Ru/^{106}Rh$) constructed accordingly will be acquired jointly by the participating laboratories (CEN Grenoble, CEA Fontenay aux Roses, NRPB and Risø).

Appropriate holders for practical use with calibration set up will be designed and constructed (CEA/FAR, NRPB). The homogeneity of radiation fields and residual maximum beta energy at various calibration distances will be measured and the usefulness of beam-flattening filters will be investigated.

Various experiments will be conducted with a view to establishing a common regimen for the extrapolation chamber measurement of absorbed dose rate to tissue due to beta radiation at different depths in tissue and for different angles of incidence, $D_t(d;\alpha°)$(CEA/FAR, CEN Gren., NRPB, Risø). The influence of different design parameters of extrapolation chamber on the results will be investigated, for example, the effect of collecting electrode area (CEN, Gren.) and the thickness of entrance window (Risø). Sources will be interchanged between the four participating laboratories with a view to comparing results obtained with the different designs of extrapolation chamber and that of measurement techniques used by the laboratories (CEA/FAR, CEN Gren., NRPB, Risø).

Having established a common regimen for the extrapolation chamber measurements (among the participating laboratories) the main thrust will be directed to characterising radiation fields from the sources (both circular and square construction incorporating ^{14}C, ^{147}Pm, ^{204}Tl, $^{90}Sr/^{90}Y$ and $^{106}Ru/^{106}Rh$ nuclides) in terms of directional dose equivalent rate, $H'(d;\alpha°)$ by measuring the absorbed dose rate to tissue at different depths in tissue and for different angles of radiation incidence, $D_t(d;\alpha°)$ (CEN Gren., CEA/FAR, NRPB, Risø). Particular attention will be given to the evaluation of factors, to convert from absorbed dose rate to tissue at a depth of 0.07 mm and for normal incidence of radiation, $D_t(0.07;0°)$, to absorbed dose rate to tissue at the same depth in tissue but different angles of radiation incidence, $D_t(0.07;\alpha°)$. The data obtained will be compared with similar data obtained for other types of source construction, e.g. the PTB-Büchler secondary standard point sources.

For individual monitoring for weakly penetrating radiation there is a need for thin tissue-equivalent detectors with relatively high sensitivity. Highly sensitive TL materials, e.g. MgB_4O_7:Dy, LiF:Mg,Cu,P and $Li_2B_4O_7$:Cu (Risø) and TSEE detectors based on LiF and BeO (CEA/FAR, CEN Gren.) will be studied with a view to their application in individual monitoring of weakly penetrating radiation.

The results of extrapolation chamber measurements will be used as bench-mark for determining the response of detectors developed.

The part of the programme concerned with dosimetry of low-energy photons, (energies below 15 keV) will commence during the second year of the contract. A facility for generating low-energy X rays will be established at CEA, Fontenay-aux-Roses and measurements with extrapolation chamber will be initiated to determine coefficients to convert from air kerma to directional dose equivalent, $H'(0.07;\alpha°)$. The facility will be used for the development and characterisation of thin solid state dosemeters for application into the dosimetry of low-energy photons. The response of detectors for different angles of radiation incidence will also be investigated.

Univ. Sciences Technol. Languedoc and Universidad Autónoma de Barcelona

A new laser heating TL reader will be built, developed, tested and adapted to ß-dosimetry. This work will include, partially, the optimisation of adapted thermoluminescent dosemeters. The dosimetry response with respect to the filter-support-detector arrangement will be investigated. Part of the existing experience deals with the concepts of dosemeter and of TLD readers for radiation metrology of low energy radiations. The skills and the tools accumulated during the past few years will be applied to the measure of low energy ß and γ rays.

The use of laser heating allows very short reading times; the limitation is the heat propagation in the TLD material; one of the advantages is a high intensity signal. Compared to conventional readers, laser heating allows a gain of one hundred or more for both the reading time (in the range of few miliseconds) and in the signal intensity. A few readers are available in the laboratories; one of them is dedicated to small size (22 x 22 x 0.1 mm^2) dosemeters. The first feasibility experiments were performed on a reader not specially designed for high sensitivity. In this system, the data acquisition and processing is realized by an old version of a desk computer and the whole concept of the system must therefore be improved.

In the first months a new reader adapted to ß-dosimetry will be designed and built. This will include:

1. A control of the experiment: positioning the dosemeters, heating control and command, and remote configuration of the various apparatus.

2. A data acquisition and processing software and system.

3. New dosemeters adapted to laser heating and to ß-dosimetry. This operation will be carried out by adjusting the dosemeter-filter-support assembly.

4. A comparison of the performances of the laser system with those of a conventional reader.

Universität Giessen

Is intended to optimize TSEE emitting BeO thin films for the requirements of ß and skin dosimetry.

1.Improvement of the detector geometry

In order to diminish the previously observed oversensitivity of BeO thin film detectors to ^{90}Sr it is necessary to reduce the height of their side wall. Detectors of various side wall heights shall be tested, which will be ordered from the Staatliches Materialprüfungsamt in Dortmund (FRG). For the further investigations 100 additional detectors of the best geometry will be made available. Some of them will also be supplied to the CEA institutes in Fontenay-aux-Roses and in Grenoble for comparative measurements.

2.Test of the reproducibility of the dose responses

The short-term and long-term reproducibility of the dose response during repetitive TSEE measurements will be tested for exposures to $+^{90}Sr/^{90}Y$ and to ^{60}Co. Irradiated BeO thin film detectors will also be stored in water prior to dose readout.

3.Covering foils

Various tissue equivalent light absorbing covering materials of a thickness of 7 mg cm^{-2} will be tested with respect to the correspondence between TSEE response and conversion factors F (0.07;) for exposures to a $^{90}Sr/^{90}Y$ source at different angles of radiation incidence. Additionally, a combination of black polycarbonate and Hostaphan will be used.

4.Optimised dosemeter badge

Experiments with former badges indicated that the TSEE response is strongly disturbed at higher angles of ß-radiation incidence if the front plate of the badge overlaps with the detector side walls. For this reason a badge shall be designed and tested, where even at the side walls only the covering foil is at the top of the detector. The badge includes a second detector, which is covered by 3 mm of tissue equivalent material for the measurement of $H_p(3)$.

5.Comparison with the results obtained by extrapolation chambers for different ß-sources

Exposures to calibrated ß-sources at different angles of radiation incidence will be carried out by the CEA institute in Fontenay-aux-Roses. The TSEE results will be compared to those by extrapolation chamber measurements in Fontenay-aux-Roses.

6.Determination of the ratio ß/γ of the dosemeter sensitivity

^{60}Co irradiations to the same BeO thin film detectors as used for 3. and 5. will give information about the ratio ß/γ of the dosemeter sensitivity.

A12 Radiation measurement and instrumentation for individual and area dosimetry

Contract Bi7-030 The use of microdosimetric methods for the determination of dose equivalent quantities and of basic data for dosimetry.

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Total Contribution by the Commission: 436 kECU
24 months from 1/05/90 to 30/04/92

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Description of research work:

Introduction:

The partner laboratories will perform work to develop different types of dose equivalent meters for radiation protection dosimetry in neutron-photon fields. The methods used include low pressure tissue-equivalent proportional counters and high pressure ionisation chambers as area monitors, and a semiconductor type detector as individual dosemeter. The research is aimed at the implementation of these techniques for various tasks in practical radiation protection work. The technical development of these instruments will be combined with experimental and theoretical investigations necessary to improve their performance.

Measurements will be performed in reference photon and neutron fields in order to compare the dose equivalent response of the dosemeters. Neutron fields in the energy range from thermal up to 20MeV will be produced among the partner laboratories. Neutron energies above 20 MeV will be investigated in collaboration with high energy accelerator facilities (Paul Scherrer Institute, Villigen, Ch; Cyclotron CYCLONE, UCL, Louvain-la-Neuve, Belg.). The determination of basic physical characteristics of the beams will be an important part of the work, in particular the knowledge of photon and neutron fluences will enable the comparison of experimental and theoretical data.

The dosemeters developed will also be tested in radiation environments of practical relevance for radiation protection (nuclear power plants, research reactors, physical and medical accelerators) which will enable the operational characteristics of the instruments in routine conditions to be verified.

Basic physical data of relevance for neutron dosimetry will be obtained (fluence-to-kerma conversion factors, average W-values, gas-to-wall dose conversion factors) for neutron energies above 20 MeV for which theoretical data are inaccurate and experimental data are scarce.

Basic characteristics of radiation protection instruments (electrical discharge in gas, cavity theory, semiconductor properties) will be investigated on theoretical and experimental bases. These studies will contribute towards a better knowledge of the detector properties and to extend their range of applicability for ionising radiation dosimetry and microdosimetry, with practical consequences for the development and optimisation of dose equivalent meters. This work will be performed in collaboration with Working Committee 10 of EURADOS-CENDOS.

Ambient dose equivalent meters:

Low pressure tissue-equivalent proportional counters (TEPC) have been shown to provide solutions for practical dosimetry problems in area monitoring of mixed neutron-photon fields. Prototype instruments have shown the feasibility of such monitors in the form of portable survey meters. Using the combination of cavity chamber principles and single registration of pulse height, TEPC provide simultaneously dose- and diagnostic information in terms of photon and neutron dose components and the related mean quality factors. At neutron energies below several hundred keV, however, the ambient dose equivalent response of a TEPC is considerably too low.

Based on the experience gained with the prototype "HANDI" (Homburg Area Neutron Dosimeter) and during the TEPC intercomparison carried out at PTB Braunschweig by EURADOS, Uni. Homburg will perform additional work to optimize the performance of TEPC at low neutron energies using as parameters the counting gas mixture, the simulated diameter and the counter geometry. Measurements will be made in low energy neutron fields produced at PTB. The optimisation of the quality factor algorithm used will be investigated based on the research performed at KFA Jülich to unfold biological response functions of lineal energy for various biological endpoints. In collaboration with the Bundesminister für Umwelt, Naturschutz und Reaktorsicherheit (FRG), several copies of the HANDI system will be built to be used at different institutes for radiation protection survey work.

High pressure ionisation chambers (HPC) systems might provide an alternative to TEPC instruments as dose equivalent meters in mixed fields. The experimental and signal processing system is less complex and HPC provide a better spatial resolution without loosing sensitivity. The characteristics of ionisation chambers measured as a function of gas pressure indeed demonstrated that an increased sensitivity is obtained at elevated pressures with various filling gases. The amount of initial recombination as well as the pressure dependence of the reading at fixed voltages can be used to determine radiation quality. Based on the experience gained using TE HPC filled with methane and Al HPC filled with argon with neutrons of energy ranging between 0.9 and 15 MeV, TNO Rijswijk will investigate the pressure dependence of the reading of TE and Al HPC filled with hydrogen-rich gases and argon as a function of collecting potential. Experiments will be performed in the neutron fields produced at TNO and PTB and are planned in high energy beams.

The use of the reference field at PTB in particular will facilitate the correlation of the results obtained with HPC to the field properties as well as to the results obtained using different dose equivalent meters.

Individual dose equivalent meters:

Semiconductors are attractive materials for developing individual dose equivalent meters in mixed fields. Modern semiconductor devices, like memory chips used in computer technology, are well known to be sensitive to radiation. The sensitive volumes in such chips are junctions between differently doped areas of the basic semiconductor material and can be approximated as cylindrical volumes with micrometer dimensions. The effect due to an ionising particle crossing a junction can be measured in the form of a pulse height proportional to the charge of the ions produced, or as a detectable change of information in a memory cell. Applying pulse mode analysis similarly as with proportional counters, pulse height spectra can be used to derive radiation quality parameters. KFA Jülich will develop an individual dosemeter based on semiconductor devices. The information available from the literature will be analyzed and experiments are planned to select the most suitable type of semiconductor device to be used. Due to their design and level of integration, indeed, semiconductors present variable sensitivities to radiation. KFA will test prototype instruments. Intercomparisons with the other systems developed within the framework of the contract will be carried out in various photon and neutron fields.

The calibration of individual dosemeters and the determination of their dose equivalent response represent essential tasks prior to their application in radiation protection practical work. This problem will be investigated by KFA Jülich within the project of developing a semiconductor type individual dosemeter. PTB Braunschweig will investigate the applicability of using the TEPC as a transfer device for dose equivalent quantities, in particular as a reference instrument for the "field calibration" of individual dosemeters. The information available from TEPC measurements will be improved by combining time-of-flight (TOF) techniques with TEPC. Furthermore the influence of phantoms on the TEPC response will be studied on theoretical basis using neutron transport calculations. The extensive calculations performed will provide important information for the optimisation of free parameters for field radiation protection instruments.

Basic data for neutron dosimetry:

Fluence-to-kerma conversion factors in tissues, tissue-substitute plastics and their components represent relevant quantities for neutron dosimetry in radiation protection. Kerma is calculated from the cross sections and the kinematics of nuclear reactions. For neutron energies above 14 MeV, however, neutron cross section data are inaccurate and nuclear reaction models for the interaction of neutrons with light nuclei are inadequate. In this energy range experiments to determine kerma are therefore needed. High energy neutrons are encountered in the vicinity of particle accelerators used for high energy physics research and medical applications.

The determination of kerma factors requires the measurement of the absolute values of the kerma and the neutron fluence for mono-energetic neutrons. Uni. Homburg has performed measurements of kerma in A-150 TE plastic and in carbon for neutrons up to 20 MeV at PTB using proportional counter techniques. These experiments will be continued in the energy range between 20 and 60 MeV using the quasi- monocinetic neutron beams produced at PSI (Ch.). PTB Braunschweig will measure the neutron fluence and spectral fluence for the same beams with an NE213 scintillation detector and a recoil proton telescope. These techniques will be modified and their applicability will be extended to this high neutron energy region. In addition different computer codes will be used to improve the efficiency of the measuring devices. In parallel, TOF techniques with microdosimetric counters will be used in order to discriminate the contamination of the beams by neutrons with energies lower than the nominal energy. Within this programme, PTB Braunschweig and Uni. Homburg will provide basic data for neutron dosimetry such as average W-values and gas-to-wall conversion factors for by combining experimental ion yield distributions and calculated energy deposition spectra.

Basic characteristics of radiation protection instrumentation:

Low pressure proportional counters (LPC) have become indispensable instruments for neutron dosimetry research, and the application of TEPC and HPC in radiation protection increases. A better knowledge of electrical discharge processes in gas detectors and of the application of the cavity theory is therefore desirable. Uni. Toulouse will contribute towards basic understanding and quantification of gas amplification and various quantities characteristic of electron displacement in the cavities of LPC. The framework of this project is the determination of electron-molecule cross sections and modelling calculations for the motion of electrons and ions inside the counters. Indeed, if the motion of charged particle is qualitatively rather well understood, no rigorous and quantitative study has been made. In particular, due to the lack of adequate cross section data, the gas mixtures of interest for microdosimetry purposes could not be considered. Based on the electron-molecule cross sections obtained, swarm parameters (ionisation and diffusion coefficients) and gas amplification will be derived taking into account the gas quality and counter geometry. This study will provide basic information for the construction and optimisation of area monitors based on TEPC and for the development of individual dosemeter based on the same principles.

To complete the basic approach adopted by Uni. Toulouse, the experimental data collected in Homburg and PTB with TEPC as well as those from energy deposition calculation will be used to interpret the results for "real detectors". This study will also contribute towards a better interpretation of the results obtained by TNO Rijswijk using HPC on the basis of cavity size effects and of the recombination theory.

A12 Radiation measurement and instrumentation for individual and area dosimetry

Contract Bi7-031 Determination and realisation of calibration fields for neutron protection dosimetry as derived from spectra encountered in routine surveillance.

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Total Contribution by the Commission: 327 kECU
24 months from 1/07/90 to 30/06/92

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Description of research work:

Objective and Research Programme

The objective of this collaborative project is to produce, in the laboratory, a few well characterised neutron fields that replicate typical spectral neutron fluence distributions encountered in radiation protection practice. These fields are needed for the calibration of neutron area and personnel dosemeters which generally do not have the energy response required to determine dose equivalent quantities. The project consists of four distinct parts, namely

- the measurement of the spectral neutron fluence typically encountered in practice,
- the preparation of a catalogue of all measured spectra in an agreed format including the calculation of relevant dose equivalent quantities and the response of commonly used neutron dosemeters
- the inspection of this catalogue in order to extract a few representative spectra and their expansion in terms of the calibration spectra already available or, if necessary, newly defined ones and finally

- the computational prediction of configurations consisting of the usual neutron sources (accelerator, reactor or radionuclide based) and appropriate moderators in order to produce these reference fields in the laboratory.

Four European laboratories, well experienced in the field of neutron metrology and dosimetry, will cooperate in this project. Spectrometric measurements will be performed independently by each laboratory, chiefly in their own country. Setting up and analysis of the catalogue, however, require a close cooperation.

Contribution of the collaborating laboratories

1. Physikalisch-Technische Bundesanstalt (PTB), F.R.G.

The PTB will contribute to almost all parts of the project, namely by:

- measurement of the spectral fluence in working areas wherever possible in the F.R.G. and where neutrons may make a considerable contribution to the dose equivalent,
- collection and preparation of the measured spectra for the catalogue and their analysis in terms of dosimetric quantities and responses of commonly used dosemeters,
- systematic search for a few representative reference fields and/or mathematical expansion of these spectra in terms of the calibration fields available or newly defined ones, and finally
- numerical investigation of moderator assemblies at accelerator-based or radionuclide neutron sources which may replicate these fields in the laboratory for calibration purposes.

The PTB also intends to participate with the set of Bonner spheres, proton recoil proportional counters and an NE213 liquid scintillation detector in the intercomparison planned to be performed at the Cadarache facility.

2. National Physical Laboratory (NPL), U.K.

Before any attempt can be made to produce 'realistic' fields, considerable preliminary work is needed to identify and characterise the types of neutron fields to which radiation workers are exposed. The first part of the project will thus involve establishing a data base of the fields encountered in the nuclear industry. This must be based on actual measurements of neutron spectra and dose-equivalent rates. A number of measurements are now available, and it is our intention to gather together existing information, from all sources worldwide, in a unified representation.

Other participants intend to carry out further spectrum measurements, NPL will contribute with data already measured in the UK, but will concentrate mainly on producing the data base, evaluating the spectra in this data base, and producing the catalogue. In addition to the spectral distribution of the neutron fluence, this will include estimates of dose-equivalent quantities and instrument responses in these fields. These will be obtained by folding dose-equivalent conversion factors and instrument responses over the spectral distributions. It is intended to store the information on a computerised data base so that it may be continually updated. The catalogue will provide a presentation of this data at a particular point in time. It may turn out that there are such a large number and variety of neutron spectra in the nuclear industry, with no significant similarity in terms of fluence distribution, that the overall project may need to be re-evaluated. However, the catalogue will still be an extremely valuable reference for all interested in neutron dosimetry for radiation workers.

3. Commissariat a l'Energie Atomique (CEA), Fr.

The contribution of CEA/DPT/SIDR to the project comprises:

- improvements of the spectrometric devices, namely proton-recoil and multi-sphere spectrometers, and of the unfolding codes.
- the collection of spectral data at the sites and facilities in France where there is a risk of neutron radiation in order to prepare an extensive catalogue of realistic spectra.

- application of a general neutron-photon transport code (MCNP) to determine the optimized set-up (geometry, material ....) of an irradiation facility (C.E.N. - Cadarache).
- preparation of this irradiation facility for a comparison exercise of the spectrometric techniques used by the participants.

4. Gesellschaft für Strahlen- und Umweltforschung (GSF), FRG

Within the framework of the project, the GSF will compile a catalogue of neutron spectra which are observed in occupational areas of nuclear power facilities, fuel cycle plants and research areas.

This catalogue will primarily be used for the calculation of integral responses of dosemeters and of integral parameters of the neutron fields. It could also be the basis for neutron model fields which are planned to be installed at the partner institutes if a reasonable array of neutron sources and moderators can be found to simulate realistic exposure conditions.

The GSF will contribute with data which have been and will be measured by means of the Bonner sphere technique in areas where there is a relevant neutron contribution to the radiation field. Up to now, the data available have been analyzed only as regards integral parameters of the neutron fields. In this project the spectra analysis will be performed on the basis of suitable and tested unfolding codes and recently re-determined Bonner sphere response matrices. Special emphasis will be placed in the influence of the first guess spectra on the final spectral and integral results.

A12 Radiation measurement and instrumentation for individual and area dosimetry

Contract Bi7-051 Dosimetry and spectrometry measurements of the leakage radiation fields from the SILENE reactor with various shields (study contract)

Coordinator CEA - FAR
Commissariat à l'Energie Atomique - CEN de Fontenay-aux-Roses
Av. G.Leclerc 60-68, BP-6
F-92265 Fontenay-aux-Roses
Tel: 1-46548585

Total Contribution by the Commission: 20 kECU
12 months from 1/06/90 to 31/05/91

Participating Scientists

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1 Dr. R. Medioni
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Tel. 1-46547539
20 kECU

2 Dr. H.J. Delafield
Radiation Dosimetry Department
Environmental Research Division
AEA Environmental and Energy
Building 364, Harwell Lab.
GB-0X11 0RA Oxon
Tel. 235-434099

Description of research work:

I - GENERAL AIM OF THE CONTRACT -

The aim of this programme of work is to establish reference dosimetry and spectrometry measurements for the leakage radiation fields available from the French SILENE reactor using shields of different materials. The characterisation of these radiation fields is required before their use for a proposed EURADOS-CENDOS international intercomparison, in cooperation with the IAEA, of the criticality accident dosimetry systems used in European and other laboratories.

The initial objective is to make spectrometry and dosimetry measurements, at one reference location and to define the uniformity of the radiation field around the source, as a feasibility study for the criticality accident dosimetry intercomparison.

The ultimate objective is to propose the full protocol for an international intercomparison of criticality accident dosimetry systems. This is required for the training of staff in the specialist measurement techniques employed, for the evaluation and development of dose assessment procedures and to ensure compatibility of such systems within the CEC.

The study contract will be undertaken in consultation with other EURADOS-CENDOS Committee-9 European Laboratories.

II - CEA - FONTENAY-AUX-ROSES CONTRIBUTION -

The IPSN-DPT-SIDR Laboratory, will take the lead in establishing liaison with the Service de Recherches en Sûreté et Criticité, Institut de Protection et de Sûreté Nucléaire, who operate the SILENE reactor at Valduc. The IPSN-DPT-SIDR Laboratory will also undertake neutron and gamma-ray dosimetry measurements at the SILENE reactor.

Measurements of the neutron field will be made at a reference location with tissue equivalent ionisation chambers and at different points within the irradiation hall using activation detectors and fission chambers. Then, using well established models, neutron spectra and kerma will be derived from the measurements and compared with definitive measurements made with the recoil spectrometry system. Gamma-ray doses will be measured using thermoluminescent dosemeters and Geiger Muller counters.

These measurements will be made at the "bench mark" reference locations and extended as necessary to establish the uniformity of the field around the SILENE reactor.

III - UKAEA - HARWELL CONTRIBUTION -

Harwell have developed a transportable high-resolution neutron spectrometer for research applications based on a set of three small spherical proportional counters (type SP2) filled with hydrogen. These counters cover the neutron energy range from about 50 keV to 1.5 MeV, above which energy an alpha-recoil proportional counter has been developed to extend measurements up to about 15 MeV. The spectrometry system, has neutron energy and fluence calibrations traceable to the National Physical Laboratory UK.

The system, which covers the neutron energy range giving rise to the principal component of neutron dose from the SILENE leakage spectra, will be used to make a definitive spectrum measurement at a reference location for the shielded reactor. Neutron kerma will be derived directly from the measured fluence spectra. Multi-sphere measurements made with the assistance of the NPL, UK, or resonance activation detector measurements will be used, to estimate neutron kerma below 50 keV.

IV - WORK PROGRAMME -

In June and November 1990, it is intended that the complimentary dosimetry techniques offered by Fontenay-aux-Roses and Harwell Laboratories should be used to make reference dosimetry and neutron spectrometry measurements for the SILENE leakage radiation field with the reactor shielded. These measurements will be repeated in 1991 for a second field, with the reactor unshielded, under another study contract.

The full intercomparison could be planned for 1992.

This work will be undertaken under the DG XII programme, but is a requirement for the proposed international intercomparison of criticality accident dosimetry systems to be undertaken under DG XI.

A13 Derivation of organ doses and effective dose equivalents

Contract Bi7-021 Calculation and measurement of doses from particulate radioactive source.

Coordinator Nuclear Electric
Berkeley Nuclear Laboratories
GB-GL13 9PB Berkeley, Glos.
Tel: 453-812489

Total Contribution by the Commission: 100 kECU
24 months from 1/09/90 to 31/08/92

Participating Scientists

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1 Dr. M.W. Charles
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60 kECU

2 Dr. Y. Herbaut
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29 kECU

3 Dr. J.P. Patau
Université de Toulouse III
Biophysique Pharmaceutique
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11 kECU

Description of research work:

There is an increasing awareness of the importance, particularly in the USA, of the dosimetry of radioactive particles ('hot particles', microscopic, high activity radioactive particulates) which commonly arise in reactor operations from neutron activation product debris and fissioned fuel contamination and in hospital and other industrial situations where such sources present a potential skin hazard. Current methods of calculating doses from particulates use semi-empirical beta depth dose data such as those of Cross which are based on semi-infinite, tissue geometries and cannot be easily applied to real geometries and high atomic number particles. This project will provide improved and validated methods of calculations of dose from radioactive particulates

The NCRP and ICRP have recently provided recommendations for limiting the occupational exposure of the skin from radioactive particulates. Their deliberations relied upon the interpretation of animal studies which used a range of radiation sources (including particles) for which detailed dosimetry was limited and for which no low energy beta source data were available. This work will provide improved dosimetry and a supply of well characterised Co-60 particle sources for related CEC animal skin studies (CEC BI7-0041).

This project will produce beta emitting radioactive particulates by neutron activation (Radiological Protection Branch, Nuclear Electric plc at Berkeley Nuclear Laboratories, BNL) and measure the radiation doses using TLD, extrapolation chamber, (BNL & Commissariat a l'Energie Atomique, Centre d'Etudes Nucleaires de Grenoble, CENG) and radio-chromic dye film (BNL).

A Monte Carlo computer code, suitable for PC use, will be developed to predict doses from the specific designs of source used (Department of Biophysique and Pharmaceutique, Tolouse University, TU) and these will be compared with measurements and the simplified empirical calculation methods currently in wide use. Such a programm will be useful to the scientific and health physics community at large. Experiments using cobalt-60 particles will initially be used because of the important practical relevance of this radionuclide to the nuclear industry, but can be extended to include fission products.

Pure cobalt particles will be produced with diameters of about 100, 500, and 1000 microns and mounted on ultra-pure aluminium supports. Neutron activation will be used to produce individual Co-60 particle activities with maximum values of about 0.1 mCi (5 MBq). Doses will be measured over various areas and at various depths (using tissue-type plastic absorbers) relevant to epidermal and dermal target cells in the skin (10-700 microns).

The extrapolation chambers will be based on the original Failla extrapolation chamber (BNL) the Far Western (CENG) and Bohm chambers (BNL & CENG).

Target dates:

1990-91: Production of smallest low activity Co-60 sources. Extrapolation chamber and radio-chromic dye film measurements. Initial development of a Monte Carlo code and comparison with initial dosimetry data.

1991-92: Comparison of measurements for larger, higher activity sources with theory. Refinement of MC code and comparison with semi-empirical methods.

1992- : Extension of studies to other neutron activation and fission product particle sources.

The results of this work will enable potential skin doses, and their hazards, from practical radioactive particles to be calculated more reliably. The data will also help to interpret the results of skin radiobiology studies (CEC BI7-0041) and aid their application to practical particle exposure situations. This work is carried out under the auspices of EURADOS committee 2. The related radiobiology studies form part of the current programme of EULEP.

Radiation Biophysics Group, Radiological Protection Branch,
Berkeley Nuclear Laboratories, Nuclear Electric plc, England

The Radiation Biophysics Group within the Radiological Protection Branch of Nuclear Electric plc will be responsible, as well as for coordination, for the production of idealised Co-60 beta particle sources which will be made available to CEA CEN Grenoble for parallel dosimetry studies using extrapolation chamber, thermoluminescent and radio-chromic dye techniques. At BNL an automated computer controlled extrapolation chamber with interchangeable electrodes will be used together with ultra-thin LiF TL dosemeters and radio-chromic dye films. These will provide central axis depth doses as well as average doses over various areas and depths for comparison with Monte Carlo calculations (University of Tolouse). Comparison will also be made with empirical computer codes and beta dose tabulations currently in use in Europe and the USA.

The Radiation Biophysics Group have been involved for several years with the handling, characterisation and dosimetry of radioactive particles arising in the nuclear power industry. We have considerable experience of radioactive source production and beta dosimetry in the context of personal dosimetry and skin radiobiology studies. Laboratory facilities include scanning electron microscopy and X-ray microanalysis/image analysis, GeLi gamma spectrometry, TL and extrapolation chamber equipment, a Magiscan image analysis system and a range of standard radiation sources. The work of this group has been extensively published and presented at CEC workshops. This work is carried out under the auspices of a EURADOS committee on skin dosimetry and surface contamination. The related skin radiobiology studies form part of the current programme of EULEP.

This project is part of an established coordinated collaborative skin radiobiology and biological dosimetry programme which has been supported by Nuclear Electric plc (previously the Central Electricity Generating Board, CEGB) for several years.

Centre d'Etudes Nucleaires de Grenoble, CEA, France

At Grenoble dose rates from radioactive particulates associated with nuclear reactors and reprocessing plant operations will be measured using equivalent extrapolation chambers with various sized collection electrodes (1-3 cm) for various depths between 20-700 μm. The measurements amy also be performed with TLD stacks or ultra-thin dosemeters, using tissue type plastic absorbers. Initially, in the period 1990-91, the radioactive sources will be Co-60 particles mounted on an ultra-pure aluminium block and fixed with low atomic number adhesive and thin aluminium foil. This will be constructed by RPB with a maximum activity of 0.1 mCi. This work will be extended in future years to consider fission product sources such as neutron fissioned enriched uranium-235 particles or other neutron activation beta sources.

In radiation protection work risks occur because of the very small distances between skin and source. In several recent studies we have determined the response of radiation protection instruments in an homogeneous irradiation. A common radiological protection problem is to interpret readings from instruments calibrated in terms of uniform irradiation when they are subject to the non-uniform irradiation from particle sources. This work should help to provide basic data and radiation sources which can be used in such interpretations.

The laboratory has performed dosimetric studies for several years in beta dosimetry and has designed an extrapolation chamber and a set-up system to simulate extended beta sources by using a point source. The laboratory has the function as 'Service de Metrologie Habilite du Bureau National de Metrologie' in the frame of ionising rays and has to calibrate radiation protection devices. The Laboratory is engaged in two EURADOS working groups of Committee I & II.

Universite Toulouse III - Biophysique Pharmaceutique

The University of Tolouse will produce Monte Carlo computer codes providing radiation dose distributions in some materials irradiated by beta particles emitted out of a sphere (particles). Initially the radionuclide considered will be Co-60 but subsequent evaluations will include fission product sources. An homogeneous distribution of the radionuclide within the sphere bulk will be assumed. The transport of beta particles will be simulated through the whole system: sphere (taking account of self absorption); tissue type adhesive; aluminium protective film; dosimetric medium. The latter will be in case 1: tissue equivalent plastic and in case 2: homogeneous mixture of LiF/teflon. The aluminium base and dosimetric medium will be assumed infinitely thick. In case 1 the doses will be calculated in a set of nested discs centred on a common point O. In case 2 the doses will be calculated in each of the coaxial discs of a stack, the first being adjacent to the aluminium slice.

The programme will be performed so that the user will be free to fix on the following values:- sphere radius, aluminium slice depth, energy spectrum of beta particles; in case 1 from distance O to the aluminium slice, number of nested discs, radius and thickness of each disc: in case 2: number of stacked discs, radius and number of the discs. The electron transport simulation will be based on a step by step slowing down using for each step path length (Landau) and deflection (Goudsmit & Saunderson) distributions. A separate processing of inelastic collisions producing secondary electrons will be made on the basis of Moller cross sections. The transport of secondary electrons, Auger electrons included, will be simulated. The photon transport, if necessary, will be simulated taking into account relevant interactions.

Monte Carlo codes will be written in FORTRAN 77 and able to run on PC-AT compatibles with 20Mb hard disc. A fast maths co-processor will be recommended. The computer codes will be circulated on floppy disc among every partner during the validation time. A users guide will be written.

A14 Assessment of internal exposure

Contract Bi6-341 Radionuclide transfer factor for human milk (study contract)

Coordinator Istituto Superiore di Sanità
Viale Regina Elena 299
I-00161 Roma
Tel: 6-4990339

Total Contribution by the Commission: 30 kECU
18 months from 1/10/89 to 31/03/91

Participating Scientists

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1 Prof. Dr. G. Campos-Venuti
Istituto Superiore di Sanità
Physics Laboratory
Viale Regina Elena 299
I-00161 Roma
Tel. 6-4990/0039
30 kECU

Description of research work:

From May 1986 till the end of 1988 a research on human milk contamination in Rome and in the Latium District has been conducted. About 80 milk samples have been collected - each from 5 - 15 nursing mothers in the first week after delivery - and analyzed by gamma spectrometry. Caesium 137 and caesium 134 concentration and, during the first period, iodine 131 concentration, measured in the above mentioned areas, were much lower in human than in cow's milk. The effective dose equivalents calculated for infants born at the end of April 1986 and in the following months were negligible (1, 2, 3).

In order to extend the significance of the research, a new research program (in collaboration with a staff of physicians from maternal hospital in Northern Italy) has been developed. Its main aims are:

1) to investigate the diets of pregnant and nursing women (on which up to now no satisfactory data exist) in order to assess the caesium transfer factor from food to maternal milk;

2) to evaluate the caesium concentration in the milk of single women of the same area, in order to assess the range of variation due to different diets or metabolic factors;

3) to compare the caesium concentration in the first week milk with that of first and second month milk, due to their different composition.

Regarding the comparison of caesium concentration in milk of different lactating periods, about 15 nursing mothers will be selected. Each one will collect 15 ml of milk on the 4th, 30th and 60th day after delivery.

At the end of collection the milk collected on these three occasions will be mixed to obtain three samples.

The milk of "lost persons" will be excluded. Control samples will be collected from three groups of mothers on their 4th day after delivery, the same days the group under study effects the collection, in order to measure the variation of caesium concentration with time.

As far as the diet investigation and the caesium variation range assessment, 50 women will be involved, in order to be sure to have data at least for 30 cases. The women will be selected among those who follow the respiratory autogeny training course before delivery. In a first oral interview the amount of food (milk, meat, vegetables, etc.) usually eaten will be quantified. The women will also receive a series of forms, regarding the type of food eaten, to be filled in each day for a week every month, during the last months of pregnancy and of the beginning of lactation.Furthermore they will be asked to collect 15 ml of milk each day from the 10th to the 40th day after delivery.

At the same time a selection of the main food distributed in the area will be collected.

All the maternal milk food samples will be gamma measured with high purity Ge spectrometers. The transfer factor of caesium from food to human milk will be calculated. However it is well known that the result will contain high uncertainty due to the difficulty in obtaining an exact evaluation of the caesium content in diet and, eventually,to the variability of metabolic factors.

Once significant data regarding the diet of pregnant and nursing mothers have been obtained, the caesium transfer factor will be evaluated :

1) comparing human milk data of that area (measured during 1986 and 1987 by this research group) with the food contamination data of the same area (collected by the local health authorities during the same period);

2) using the food and human milk contamination data of the Latium District, after checking the possible differences in local diet.

In 1990, when the strontium measurements will be set up, an assessment of strontium transfer factor could also be made.

A14 Assessment of internal exposure

Contract Bi6-347b The calculation of doses from intakes of radionuclides by inhalation or ingestion; implementation of the operational dose quantities into radiation protection dosimetry (NRPB Association).

Coordinator NRPB
National Radiological Protection Board
GB-OX11 ORQ Chilton, Didcot
Tel: 235-831600/2227

Total Contribution by the Commission: 384 kECU
24 months from 1/04/90 to 31/03/92

Participating Scientists

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1 Dr. M.R. Bailey
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50 kECU

2 Dr. G.M. Kendall
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40 kECU

3 Dr. W. Stahlhofen
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100 kECU

4 Dr. M. Roy
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B.P. 6
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Tel. 1-46548591
65 kECU

5 Dr. G. Patrick
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Radiobiology Unit
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30 kECU

6 Prof Dr. A. Kaul
Bundesamt für Strahlenschutz
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82 kECU

7 Prof.Dr. D.M. Taylor
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17 kECU

Description of research work:

Knowledge of the doses to different body organs following intakes of radionuclides is an essential component in the control of occupational exposures. Similar data are needed in assessing the consequences of accidental and routine releases from nuclear installations, the estimation of doses from weapons fall-out and radionuclides of natural origin, and in nuclear medicine.

There is a continuing requirement for the development of more realistic and comprehensive dose-intake models to improve radiation protection standards; ensure that measures taken are cost-effective; allay public fears; and answer informed critics. This requires the continuous review of relevant biokinetic data, identification of parameters for which further experimental work is needed, and the conduct of suitably-designed experimental studies.

Inhalation is the main route of radionuclide intake for workers and, through the inhalation of radon decay products, for the general public. This project therefore places particular emphasis on this route of intake. It will address uncertainties in existing models, and contribute to the provision of more comprehensive and realistic models to relate intakes by inhalation to organ doses and monitoring results for workers, and to calculate the distribution of doses among the general population. Although inhalation has been extensively studied, and significant advances made, important gaps in knowledge remain. Most human inhalation studies have been conducted on healthy men. There are few data on submicron particles, and major uncertainties about clearance kinetics in each region of the respiratory tract. Volunteer studies will be conducted to quantify parameters for the human respiratory tract. Studies of total and regional deposition will focus on submicron particles, and on inter-subject differences due to age, health status and airway dimensions. Complementary studies will be performed of flow and deposition in physical and computer models of airways, and of deposition in human airway casts. Clearance of material from each part of the respiratory tract will be studied. Special attention will be paid to possible slow clearance from the bronchial tree, thought to be the most radiosensitive area. Theoretical and empirical models will be developed to calculate, for different types of subject, regional deposition; radionuclide clearance rates to other organs; and doses to respiratory tract tissues.

Ingestion is often the main route of intake for the public following environmental releases. Improved methods will be developed for calculating doses from intakes by both inhalation and ingestion, for a very wide range of radionuclides.

The contributions of the laboratories participating in this project are outlined below.

National Radiological Protection Board, Chilton, UK.

Improved models for respiratory tract clearance and dosimetry of inhaled radionuclides will be developed. Initially, work will focus on development and implementation of the new ICRP lung model.

The kinetics of clearance of inhaled particles from the human nasal passage will be measured. Mono-disperse radio-labelled particles in the approximate size range 0.5 - 20 μm aerodynamic diameter will be inhaled by volunteers, and the pattern of retention and clearance followed.

Improved methods for calculating doses from intakes of radionuclides by inhalation and ingestion, applicable to a very wide range of radionuclides will be developed. This will involve assessment of biokinetic studies in the literature, conducting biokinetic experiments, and carrying out intercomparisons of results of dose-per-unit-intake calculations with other laboratories.

Gesellschaft für Strahlen- und Umweltforschung, Institut für Biophysikalische Strahlenforschung, Frankfurt, FRG

The convective transport mechanisms in the human respiratory tract will be studied. An improved computer program to evaluate the results of bolus dispersion experiments will be developed. Bolus dispersion will be studied in models of airways. The effect of morphological and physiological parameters on bolus dispersion will be studied in humans.

Particle deposition in the human respiratory tract will be studied. Deposition mechanisms will be investigated in models of airways. Preparations will be made to measure regional deposition of ultra-fine particles in humans.

An improved statistical and algebraic model will be developed to calculate regional deposition according to respiratory and aerosol parameters. An existing model will be updated as new experimental data are obtained and will be extended to subgroups of the population.

Human tracheobronchial clearance will be investigated by measuring lung retention of radio-labelled particles inhaled as a bolus.

Lung clearance in humans will be investigated using magnetometery. Further work will be conducted on interpretation of the measurements. The technique will be applied to investigate particle uptake by macrophages and to measure long-term particle clearance.

Commissariat à l'Énergie Atomique, Institute de Protection et de Sûrété Nucléaire, Fontenay-aux-Roses, France

Measurements will be made of total respiratory tract deposition, in healthy adults and children, of particles in the size range 0.5 - 6 μm aerodynamic diameter.

Measurements will be made of nasal deposition, in healthy adults and children, of inhaled particles in the size range 0.5 - 6 μm aerodynamic diameter, inhaled by mouth.

Further studies of total deposition will be conducted on subjects with impaired lung function. Further studies of nasal deposition will be conducted on subjects from various non-caucasian ethnic groups, and subjects with rhinitis.

Medical Research Council Radiobiology Unit, Chilton, UK

Animal studies will be conducted, to investigate slow clearance from large airways, of particles administered mainly by inhalation. Initial studies in the F-344 rat will be extended to make comparisons with other species.

Studies will be conducted of the functional morphology of respiratory tract epithelium in man and laboratory animals. Measurements will be made of the surface density of ciliated cells.

Bundesgesundheitsamt, München, FRG

Biokinetic data for selected elements will be collected. To avoid subjective decisions in deriving recommended values of biokinetic parameters from several reports, the data will be tabulated and assessed according to uniform criteria.

Detailed computer models will be used to investigate the effects on organ doses and Annual Limits on Intake of varying biokinetic parameters over the observed ranges. The biokinetic parameters will be identified which are of primary importance for doses and Annual Limits on Intake, and for which further experimental work is needed.

Kernforschungszentrum, Karlsruhe, FRG

The aim of this programme is to contribute to the important and urgent task of making new calculations of committed dose equivalent/unit intake for internally deposited radionuclides for adults and children of different ages. This work is necessitated by the changes in tissue weighting factors, approaches to dose calculation and a reduction in the dose limits for workers from 50 mSv to an average of 20 mSv per annum which will be recommended by the International Commission on Radiological Protection early in 1991. The proposed work will fall into two areas:

a) A critical review of the biokinetic models used by ICRP in Publication 30 for the individual elements. Approximately 30 elements are being considered by a Task Group of ICRP which is concerned with age-dependent dosimetry, leaving the biokinetic parameters for some 60 elements to be reviewed in the present work.

Where significant new information has become available in the 10 to 20 years which have passed since the ICRP Publication 30 models were developed, new biokinetic models will be proposed. Where information for individual elements within groups of chemically related elements, such as the lanthanide or actinide series, remains sparse an attempt will be made to develop generic biokinetic models for such groups of elements. This work will be carried out in close collaboration with ICRP Committee 2.

b) The new, or confirmed, biokinetic models will be used in the revision of ICRP Publication 30 which will be carried out over the next few years, but a more immediate task will be to use the models, as well as the revised ICRP tissue weighting factors and dose calculation methods to update the EULEP Computer Programme "DOSELIB" which is a programme providing rapid, age-related dosimetric information for some 50 of the most important radionuclides. This aspect of the work will be carried out with the collaboration of scientist from the German Federal Radiation Protection Bureau (Bundesamt für Strahlenschutz).

A14 Assessment of internal exposure

Contract Bi7-024 The assessment of internal dose: The establishment of registries of dose assessment, autopsy data and models (study contract)

Coordinator AEA Technology
Charles II Street 11
GB-SW1Y 4QP London
Tel: 1-9305454

Total Contribution by the Commission: 40 kECU
18 months from 30/04/90 to 31/10/91

Participating Scientists

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Environment and Energy
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Tel. 235-434075
40 kECU

Description of research work:

1. INTRODUCTION

This contract is designed to establish the basis for setting up three registries:

(i) A European Registry of Internal Dose Assessments (ERIDA) using information obtained by individual laboratories in each European laboratories and obtained from the literature.

(ii) A European Registry of Autopsy Data (ERAD) using information obtained by individual laboratories in each European country.

(iii) A European registry of mathematical models used for Internal Dosimetry (ERMID) in European laboratories and in the literature.

The study contract will be used to establish protocols, in consultation with other Eurados-Cendos committee 6 (E-C6) European laboratories and with the US Uranium and Transuranium Registries, in order to produce compatible databases for ultimate exchange of information. An intercomparison of dose assessment methods, organised by E-C6, is already underway and will form the basis of the protocols. The ultimate objective is to ensure compatibility of internal dose records within Europe in the context of 1992.

2. PARTICIPATING LABORATORIES

AEA Environment and Energy, Harwell Laboratory, UK are coordinating the contract and will study task (i) above: with NRPB, Chilton, UK studying task (ii) and CEA, Fontenay-aux-Roses, France, studying task (iii). Other members of committee 6 of Eurados-Cendos from Denmark, France, Germany, Italy, Spain and the UK will provide ideas and critisms of the protocols produced. Also, corresponding members throughout the world, particularly at Hanford in the USA, will be involved.

3. DETAILS OF THE CONTRACT

ICRP models exist from which internal dose assessments are be made. Intercomparisons of assessment methods have been made in the UK and have been extended to other European laboratories in 1989. Formal autopsy registries exist only in the USA although extensive measurements of autopsy material are made in Europe. The assessments on man and autopsy data need to be brought together to confirm or modify the mathematical models.

It is intended that detailed protocols will be prepared for the 3 European Registries on Internal Dose Assessments (ERIDA): Autopsy Data (ERAD): and Models for Internal Dosimetry (ERMID) for discussion by E-C6. These protocols will be used to provide the basis for a database for use under a new contract. The Registries will provide a pool of information on a database which can be accessed through computer networks by authorised users in Europe when they wish to make an internal dose assessment. The data contained in the registries will enable comparisons to be made with predictions based on knowledge of intakes and mathematical models to obtain a better understanding of metabolic behaviour of radionuclides in man. Existing information will be reviewed on assessments, autopsy material and models. This will include a review of autopsy analysis methods in Europe.This should be completed in 1990 and then detailed protocols will be proposed (compatible with those in the USA) and discussed in E-C6 in order to make a detailed proposal to set up the registries.

The registries can be used to run assessment intercomparisons between European laboratories on a regular basis. There will be close collaboration with laboratories in France, Germany, Italy, Spain, UK etc and particularly with EULEP through an agreed coordinated programme organised by EULEP and Eurados-Cendos. In the context of the single European Market in 1992, it is important that dose records for radiation workers are compatible in all EC countries. The objective of this contract is to establish models for use in Europe and ultimately to have them accepted by the ICRP and the IAEA. This will ensure that internal doses measured in each European country can be used with confidence in another and that all information is available on a database to assist in dose assessments when similar cases arise in another country and so reduce the costs of dose assessments.

3.1 European Registry of Internal Dose Assessments (ERIDA)

This project will be implemented by AEA Environment and Energy at Harwell Laboratory, UK, and will establish the protocols for a registry of internal dose assessments in Europe. A protocol for comparing internal dose assessments has been established and will be used to extend the UK intercomparison to European Laboratories. The first stage of this intercomparison should be completed in early 1990 and will then form the basis for preparing a protocol for ERIDA. It is intended that a detailed protocol will be devised and discussed at Eurados-Cendos committee 6 and be circulated to corresponding members. The basis of the protocol for ERIDA will include:

(I) details of the initiating event:
(II) Information on PAS, chemical form, particle size, etc:
(III) body monitoring data:
(IV) bioassay data:
(V) methodology used in calculations:
(VI) results of the assessment.

The basic purpose of this Registry is to provide a pool of information on a database which can be accessed, initially through computer networks, so that any assessment of an unusual nuclide can be made with knowledge of possible techniques available. It is intended that this practical experience of man's exposure be fed into ICRP Model Registry (ERMID) in project 3.

The basis of setting up ERIDA will be in place by 1991 with a view to starting full operation with a CEC contract. ERIDA can also be used to run regular internal dose assessment intercomparisons to ensure that dose records are transferable across national boundaries.

Close collaboration through the EULEP Committee on International. Dosimetry & standardisation will be maintained in order to obtain the relevant animal data.

3.2 European Registry of Autopsy Data (ERAD)

This project will be implemented by NRPB, Chilton, UK and will establish the basis for the collection, collation and dissemination of information relating to the accumulation in human tissues of radionuclides with long effective half-lives in the body.

The only formal autopsy registries that exist are those in the USA. In 1980, the Los Alamos Scientific Laboratory established an autopsy analysis programme for occupationally-exposed workers. The main purpose was to validate the estimates of body content based on urine bioassay. Subsequently, the study was extended to include non-occupationally exposed subjects. The arrangements for cases of occupational exposure were put on a more formal basis in 1988 with the establishment of the United States Transuranium Registry (USTR).

Information on autopsies performed in the UK has contributed to the USTR. The United States Uranium Registry (USUR) tissue programme was initiated in 1978. Analyses of autopsy tissues are performed in Europe on both occupationally-exposed persons and members of the public. Results may be published in scientific literature, but there is no formal mechanism for collecting and collating these results. The UK has agreed to set up a study of human metabolic data of those occupationally exposed to radionuclides based upon existing autopsy data and future material. The UK approach will be considered in its wider application to Europe and for exchange of information with the USTR and USUR.

The objectives are:

(I) to establish a protocol for a European registry of radionuclide contents of human tissues at autopsy:

(II) to determine the likely availability of autopsy data within the member states, bearing in mind potential difficulties arising from legal and confidential considerations:

(III) to investigate the possibility of extending the registry to include other Western European countries that are not presently members of the European Community:

(IV) to establish a basis for exchange of information with the US registries, to make proposals to the CEC for the setting-up and management of a European registry.

The establishment of a European registry will provide a focal point for the acquisition of information about long-lived radionuclides in human tissues. The data contained in the registry would enable comparisons to be made with predictions based on knowledge of intakes and standard models of human exposure. The results of such comparisons, in turn, enable improvements to be made to the models. Better knowledge of the behaviour of radioactive material in the human body will lead to improved standards of protection for both workers and the general public.

A review will be carried out of the feasibility of conducting autopsy analyses within the Member States of the Community and in other European countries. The radionuclides of importance will be determined and guidelines will be drawn up concerning the types and amounts of tissue required, the most suitable methods of analysis and the presentation of the analytical data. Consideration will be given to the extent of supplementary information that needs to be recorded concerning the type of exposure. Consultation with those responsible for the US registries will take place so as to ensure. as far as possible compatibility of information. These tasks will be completed by 1991 so that a proposal for the setting up and management of the registry an be submitted to CEC for funding.

3.3 European Registry of Models for Internal Dosimetry (ERMID)

This project will be implemented by the CEA,Fontenay-aux-Roses, France and will examine the basic for establishing a database of mathematical models. The models, used for internal dose assessments in europe, are based upon the recommendations of the International Commission on Radiological

Protection particularly ICRP30 (in all its parts) ICRP48 and ICRP54. Data for many radionuclides is based upon animal studies and it has been shown that these models do not necessarily represent human metabolism. It is vital in accurate dose assessments, to provide appropriate mathematical models based upon actual measurements on humans through in-vivo monitoring: bioassay measurements of urine, faeces, blood, etc; comparison with personal air samples for lung intake or with measurements at wound sites; and ultimately comparison with autopsy data. It is important to consider the latest information on human anatomy and physiology and the routes of entry of radioactivity into the body.

Although directed to improve dose assessments in radiation workers, these models should provide basic information on human metabolism. Thus the practical experience from ERIDA and ERAD will be fed into the mathematical models which will be applied to environmental exposure of members of the public. The intention is to provide a basis for the selection of models by the end of 1991 after which a new contract will be proposed to provide a database of such models for use within Europe. Coordination with other relevant CEC projects will be achieved via Eurados-Cendos and EULEP with particularly close collaboration with the study of stable isotope metabolism supported by the CEC and coordinated through E-C6.

4. CONCLUSIONS

The whole project will be coordinated through Eurados-Cendos Committee 6 with representation of countries within the CEC and corresponding members from other European countries, Japan and USA, where registries already exist.

A14 Assessment of internal exposure

Contract Bi7-029 Assessment of internal dose from radionuclides using stable isotope tracer techniques in man.

Coordinator GSF
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Total Contribution by the Commission: 337 kECU
24 months from 1/05/90 to 30/04/92

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Description of research work:

The limits for the intake of radionuclides as recommended by the International Commission on Radiological Protection (IRCP) are calculated on the basis of the metabolic data and dosimetric models given in ICRP Publication 30. Much of the information on the behaviour of the radionuclides in the body is derived from animal studies and broad assumptions are made where information is lacking. There are, however, no generally accepted criteria for extrapolating animal data to man. Furthermore, IRCP Publication 30 refers exclusively to occupationally exposed adult persons. IRCP does not recommend the use of these data and models for calculating doses for members of the public. There is therefore a continuing and accepted need for more realistic human metabolic data, especially with respect to the variability of dose values for non-standard, non-occupational conditions (variability with valency state and chemical form of the radionuclides, food constituents, age dependency).

The common way by which metabolic data in humans are obtained is either from measurements after accidental exposure or from experimental studies where radioactive nuclides are used as tracers. Human studies with radioactive tracers, however, while very valuable, are becoming increasingly restricted to perform, especially when healthy persons or even children are involved. A promising possibility of undertaking metabolic studies in man seems to be use of isotopically enriched stable elements as tracers.

This project aims to obtain biokinetic data in humans by a novel stable isotope approach and to assess radiation doses for several relevant radionuclides for which the current state of knowledge is poor. The elements identified are Sr, Ce, Ba, Ru, Te, Zr, Pu and higher actinides. Whereas Sr, Ce, Ba, Te and Zr can be studied by substituting the radioactive nuclides by stable isotopes of the same element as tracers, for Pu and the higher actinides stable analogues will be used as surrogates. Promising candidates are Eu, Gd, and Yb as analogues for Am and Cm respectively, whereas Hf may be considered as Pu analogue.

The goals of this project require the collaboration of several laboratories to contribute with their special expertise and experience in the different aspects involved.

Gesellschaft f. Strahlen- und Umweltforschung (GSF) Frankfurt/Main

The contribution from GSF Frankfurt is to provide metabolic data for certain radionuclides by stable isotope tracer investigations in man. A major part of this work is to evaluate the variability of uptake and metabolism for non-standard conditions.

Intestinal absorption of strontium in man from oral test doses in water and complete meals will be measured. Equivalency of extrinsic and intrinsic labelling for strontium absorption measurements in man is to be proven. Internal strontium kinetics will be evaluated by following plasma strontium concentrations after oral and intravenous administration, and determination of strontium excretion patterns.

The variability of intestinal tellurium uptake in man due to its valency state and chemical form, and absorption from intrinsically labelled vegetable material will be evaluated.

Measurement techniques for hafnium, tellurium and ruthenium in biological samples will be developed and optimized before use for metabolic studies in human subjects.

GSF Frankfurt will coordinate the project.

University of Milano

As shown in the general description of the project, the main task of the University of Milano will be the quantitative measurement of trace stable isotopes (Ce, Ru, Zr, Te) in biological tissues and the subsequent application to biokinetic studies. The analytical technique will be nuclear activation, in particular by means of charged particles beams. Our group has a large experience in the field of trace element analysis by means of proton induced activation. The main used facility will be the cyclotron of the Joint Research Centre - ISPRA. A special rotating irradiation chamber to activate 30 samples at a time is already installed. To measure the gamma decay spectra we have 2 Ge detectors, one equipped with an anti Compton shield. By start of this research project we will have a clean room for the treatment of samples in controlled atmosphere and a new laboratory equipped for radiochemical treatments. For the development and optimization of the analytical technique we plan to design a new irradiation chamber for the measurement of short living (some hours) activation products. Moreover we plan to develop appropriate procedures for radiochemical treatments in order to significantly decrease the detection limits.

Harwell Laboratory

In this laboratory, many studies have been carried out in which radio-tracers have been used to assess human uptake of stable species such as lead, cadmium and arsenic, and radioactive species such as radium and plutonium.

Recently, a new mass spectrometric technique became available which enabled stable isotope techniques to be used with human subjects, with a potentially rapid measurement time compared with traditional thermal ionisation mass spectrometric procedures. The reduced measurement time per sample analyzed enables quite large isotope uptake studies to be carried out at a relatively modest cost. The technique, inductively coupled plasma-mass spectrometry (ICP-MS), achieves measurement precessions that are better than those achievable with neutron activation techniques, but poorer than those usually attained with thermal ionisation MS.

Work carried out thus far in this laboratory using ICP-MS, and funded by the UK Department of Health, has concentrated on strontium, as an analogue for Sr90. Two human uptake studies have been carried out. The first was a demonstration experiment, in which blood and urine isotope ratios were measured for a period following the ingestion of 2 mg of Sr86 by two adult males. The second involved a larger group of subjects, in order to assess the variability of uptake with sex and age.

In the current research programme, these studies with strontium will be extended to children, and the equivalency assessed of extrinsic and intrinsic labelling. The kinetics of excretion after oral and intravenous administration will also be examined. The use of stable isotopes of barium, and of hafnium and rare earths as actinide analogues, will be validated with animal studies, and measurement procedures for the human samples developed prior to human uptake experiments with these isotopes.

Kernforschungszentrum Karlsruhe

The contribution of Kernforschungszentrum Karlsruhe is concerned with the biochemical validation of selected lanthanide or other elements as surrogates for the actinides plutonium, americium and curium which could be used for metabolic studies in human subjects. An essential part of this validation is to establish that the chosen surrogate exhibits essentially similar biochemical and biological behaviour to that of the actinide it is to mimic. Since protein binding, especially binding to the iron-transport protein transferrin, appears to play an important role in the transport, cellular uptake and deposition of actinide elements, an important part of this study is the investigation of the interactions of europium, gadolinium and ytterbium, as potential surrogates for trivalent actinides, with transferrin and with liver proteins in vivo and in vitro. Similar studies with tetravalent hafnium as an analogue of plutonium, which have been in progress for some time, will be extended. In order to compare the biokinetics and bio-distribution of europium and gadolinium with the data already available for americium and curium a small series of animal studies will be performed in rats.

Gesellschaft f. Strahlen- und Umweltforschung (GSF) Neuherberg

The participant is working since 1978 on problems of internal dosimetry especially concerning the derivation of age-dependent dose conversion factors. It is the major part of his scientific work to develop, improve and apply models describing the dynamics of biological systems. This work is partly done for the design of experiments concerning radio-ecologic problems and the measurement of biokinetic parameters of radionuclides in animals and humans. The tasks and contributions of GSF Neuherberg to the project are the following:

- review of the available data base for the elements relevant for the project;
- planning of the experimental design within the limits of the measuring techniques, thus especially defining the kind of samples selected, the necessary frequencies of sampling after administration and the temporal pattern of sampling in order to prepare an optimal evaluation;
- evaluation of the measured data, aiming to develop or to improve biokinetic models suitable for dosimetric purposes;
- calculation of dose conversion factors for the relevant radionuclides for members of the general public taking into account the important dependencies on age and on chemical characteristics as far as investigated experimentally.

A2 TRANSFER AND BEHAVIOUR OF RADIONUCLIDES IN THE ENVIRONMENT

A2 Transfer and behaviour of radionuclides in the environment

Contract Bi6-052 Promotion of formation and exchange of information in radioecology (International Union of Radioecologists).

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Total Contribution by the Commission: 65 kECU
24 months from 1/01/90 to 31/12/91

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Description of research work:

The proposals aims to promote:

1) Cooperation and the exchange of information between radioecologists in particular Soviet Scientists and those from countries outside EC and from countries which are not associated with the Radiation Protection Research Programme, in order to stimulate interactions that would increase our understanding of Radioecology problems;

2) Training of young scientists will be emphasized in the IUR new programme, in particular a summer school will be organized in 1990 (Mol).

3) IUR will develop a curriculum for a basic course in Radioecology

4) Furthermore IUR will play various roles in the field of informing the Public, i.e., "Information packages" and individual experience of IUR members previously involved in this difficult area etc...

The main goals for the IUR Working Groups in the framework of the present proposal are:

1) to identify and review problems in the field of radioecology,

2) to provide input to training of young scientists,

3) to assist in the development of a curriculum for a basic course in radioecology.

- It is important to remember that the IUR in its various activities should be concerned primarily with Radioecology in both basic and applied areas.

- Where appropriate, such activities can involve matters relating to Radiation Protection especially in the context of Ecology. But IUR should not become involved in proper scientific research and in questions that are best handled by the appropriate scientific disciplines, such as, for example, Meteorology, Botany, Physiology, etc...

PROGRAMME 1990 - 1991

A) General Objectives:

1) Promotion of Exchange of Information and Cooperation between Seniors Scientists

- The main task of IUR is to review problems and stimulate interactions that would increase our understanding of radioecology problems. It is not the purpose of IUR to solve them.
- IUR could encourage and underwrite special trips or visits of Seniors Scientists for the purpose of improving research collaboration at international level.

2) Promotion of the Formation of young Scientists

- The creation of a Summer School
- IUR will help to develop a curriculum for a basic course in Radioecology.

3) Promotion of the Information of the Scientific Community

- It is recognized that there is a lack of communication between people working on radioactive pollution problems and those working on non-radioactive pollution problems.
- IUR should promote, in conjunction with other Organizations, Workshops, Seminars ... that deal with the use and implications of radionuclides behaviour in the environment for understanding and dealing with environmental behaviour questions of other pollutants.

4) Promotion of the information of the Public

- Various possible roles of IUR in this field are suggested: "Information Packages", Inventory of individual experience of IUR Members previously involved in this difficult area etc...

5) Contribution of IUR to International Programme

- Review of the actual situation:

  + IAEA-CRPVAMP: (C.Myttenaere is WG Leader on Terrestrial Environment) - Global dose assessment for the various Pathways in the Marine Environment (A.Aarkrog is Chairman; H.Dahlgaard is IUR Representative).

  ++SCOPE-RADPATH: follow-up of the SCOPE-ENUWAR (R.Kirchmann is IUR Representative in the Scientific Advisory Committee);

  +++BIOMOVS: this programme will end in 1990.

- IUR will encourage continuing interaction with IAEA and SCOPE; the support to BIOMOVS will be reviewed taking into account that there is a strong connection with the VAMP Programme.

6) Development of Cooperation with the Soviet Scientists

- IUR will continue encouraging Soviet Scientists to participate in Working Group meetings
- Several contacts are under way in order to increase this cooperation.

B. Implementation

The main goals for the IUR Working Groups will be:

1) to identify and review problems in the field of radioecology

2) to improve research collaboration at an international level,

3) to promote the utilization of radioecological methodology in studying non radioactive pollution problems,

4) to cooperate to the development a curriculum for a basic course in radioecology.

In the new CEC Radiation Protection Programme, the cooperation between the European countries is very important. When such groups of European Laboratories have been established it is important to assure contacts and exchange of information between those groups and other European and especially non European Scientists in the same fields. The WG under IUR can act as an international forum for such contacts.

The Working group "Radioecology of Continental Waters" (Leader: L.Foulquier) will continue the inventory and the updating of informations in this field, to feed a data bank on the Transfer Factors in Continental Waters ecosystems which will allow the comparison of the behaviour of the major radionuclides in different natural conditions.

The Working Group "Marine Radioecology" (Leader: H.Dahlgaard) will arrange meetings aiming at improving interdisciplinary contacts which must aim at being beneficial to radioecology as well as related fields such as oceanography and metal pollution. A few titles of such meetings are suggested as examples: - "Review of Kd and CF and the effects of environmental parameters - Sampler intercomparison results for sediments, water and particles - Experimental marine radioecology: field comparability, reproducibility, goals and justification.

The Working Group "Plant-Animal transfer" (Leader: J.Van den Hoek) will continue to focuse on the discussion of the data produced by the various laboratories participating in order to identify the lack of knowledge in this field. The conclusion will serve as background to promote research by the relevant teams of scientists on the identified needs of complementary knowledge.

The Working Group "Soil-to-Plant Transfer Factors" (Leader: M.Frissel) until now focused its activities almost only to the contamination of crops. Numerous problems remain to be solved and challenging tasks to be performed. A way to approach this is to create, within the Working Group, different task Groups.

An overview of available data for Soil-to-Plant Transfer Factors shows that there is a considerable lack of data for mediterranean and tropical products.

For mediterranean products, emphasis may be on the southern CEC countries, cooperation may be via CEC sponsored contracts. For tropical countries another approach is required. It might be possible to create such a Group cooperating in the IAEA.

The collection of data within the framework of the counter-measures programme will continue. The exchange of ideas and experiences has to be increased in this important area.

The validation of the Transfer Models (Leader: G.Linsley) remains one of the main objectives of the IUR activities: the participation of IUR, as organization, to various international Programmes such as BIOMOVS and VAMP will continue. This will allow the identification of the needs of data for particular compartments in various ecosystems and suggestions for implementation of additional research will be made.

A21 Environmental behaviour of radionuclides in situations meriting particular attention for long-term behaviour or post-accident conditions

Contract Bi7-008 Modelling the transport of radionuclides through the freshwater environment

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Total Contribution by the Commission: 482 kECU
24 months from 1/5/90 to 30/4/92

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Description of research work:

Introduction.

Although models of radionuclide transport through the aquatic environment are becoming more sophisticated, they still remain site-specific in their application. Models developed for a specific river or lake system require considerable reworking and calibration in order to be made applicable to other sites. Major causes for this lack of portability are the variability of the adsorption coefficients (K) and concentration factors (CF) used as lumped parameters in all models. Both parameters can vary by 3-4 orders of magnitude between sites. In a similar way the dominance of different processes in both the catchment and the lake or river varies from site to site in an, as yet, unpredictable way. By studying the transport of several radionuclides, but mainly radiocaesium, in aquatic systems we hope to increase our understanding of the general properties of K , CF and process dominance and develop more portable models. The groups will focus on: the chemical processes underlying adsorption onto particles; the effects of water chemistry and the ecology of aquatic organisms on the uptake, storage and excretion of radionuclides; the relative importance of some newly identified pathways of radionuclides from catchment to water to sediments; processes of remobilisation in sediments and at the seawater/ freshwater interface.

Adsorption coefficients.

Chemical properties of sediments and particulate material from several sites throughout Europe (IFE, LNETI, ENEA, LBR) will be measured and compared with the results of clay mineral masking techniques (ULe) to assess the relative importance of illite in the adsorption of radiocaesium. K factors will be described in terms of underlying theory.

Concentration factors.

Models of fish growth and feeding habits (IFE, CEN, LNETI) will be combined with physiological information on the intake pathways, storage and excretion of individual radionuclides in different forms (LBR) and in competition with other trace metals (RUCA). Complementary physiological work on algal uptake of radionuclides will be undertaken by LBR and EMU and on bacterially mediated uptake and release of radionuclides by ULi.

Transport processes.

Major differences in the run-off rate of radiocaesium from clay rich and clay deficient, organic catchments will be studied in order to elucidate the storage medium on the latter and the physical chemistry of the loss processes (IFE, LNETI, ULE in collaboration with the University of Linkoping, Sweden). The chemical studies of the properties dictating the magnitude of K_d will be extended to try and clarify the importance of organic matter, particularly algal material, as a transporter of radionuclides from the water column to the sediments.

Remobilisation.

Processes driving the release of radiocaesium from sediments will be studied by the analysis of pore water and adsorbed caesium concentrations in cores from several sites (IFE, ENEA, ECN, ULe) using very sensitive counting facilities (ECN). The release of radionuclides at the freshwater/ seawater interface will also be studied (Ule, ENEA, LBR) in order to test recent theories of remobilisation under these circumstances (ULe, ENEA, LBR).

Modelling.

Where advances in understanding can be described mathematically they will be incorporated into existing models (IFE, CEN).

A21 Environmental behaviour of radionuclides in situations meriting particular attention for long-term behaviour or post-accident conditions

Contract Bi7-042 Radioecology of transuranics in the marine environment.

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Total Contribution by the Commission: 314 kECU
24 months from 1/11/90 to 31/10/92

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Description of research work:

The aim of this project, is to improve and refine our understanding of the behaviour of plutonium, americium and other long-lived radionuclides in the marine environment. The study will embrace five distinct marine zones namely, the Irish sea, the Channel and the Seine Estuary, the Almanzora river bed/mouth and adjacent shelf, the Gulf of Taranto and the Ligurian Sea. Although these domains differ widely in their physical oceanography, many of the fundamental process governing the behaviour of transuranics and other long-lived nuclides are common to them all and, as such, are the main focus of the work proposed below. A feature of this collaboration is the application of compatible and, in some case, identical analytical techniques to the study of physical and chemical speciation, dispersion, sediment transport and organic complexation of transuranium nuclides under a wide range of marine (and riverine) conditions. It has been agreed that the programmes of the participating laboratories will be closely coordinated with the aim of enhancing the value and universality of the results obtained.

University College Dublin (UCD)

The behaviour of plutonium and americium in the western Irish Sea and the mechanisms of transfer from the source (the Sellafield outfall together with local sedimentary deposits) to possible sinks such as the large mud bank in the western Irish Sea and estuaries along the NE coast of Ireland, will be examined in detail at UCD. Five questions, in particular, will be addressed:

(1) What are the dominant chemical species of plutonium and americium governing its bio-geo-chemical interactions in the western irish Sea?

(2) What fraction of the released plutonium and americium is actually transported with the water and at the same velocity to middle-field, i.e., the western Irish Sea?

(3) What are the effective transit times for plutonium and americium released from Sellafield to the western irish Sea zone and what are the residence times of these elements once they reach this zone?

(4) How significant is the role of (Irish) east cost estuaries in the entrapment of plutonium and americium?

(5) What is the present geographical distribution of plutonium and americium around the Irish coastline and how closely does the radiometric data correlate with water circulation patterns and sea fronts in the vicinity of Ireland?

Centro de Investigaciones Energéticas Medioambientales y Tecnológicas (CIEMAT)

The basic objectives and relevant activities of the CIEMAT programme are as follows

(1) To study the migration of plutonium and americium along the Almanzora river bed/mouth close to Palomares. Activities for this objectives will include sampling of surface sediments in both river bed. Plutonium and americium analyses will be made in these samples and other relevant parameters such as grain size, mineralogical composition, etc., will be determined.

(2) To trace the plutonium and americium contamination along the continental shelf. Activities will involve sampling and plutonium and americium analyses of sediment cores taken in the area of 25 m depth and in the area of 50-100 m depth. It is also hoped, in collaboration with the other project participants, to determine plutonium and americium in the water column, suspended matter (especially in the water-sediment interface) and biological samples.

(3) To differentiate the contribution of fallout plutonium and americium from the contribution due to the accident. Activities involving the determination of plutonium isotopic ratios will be carried out. In addition, the contribution of Cs-137 from Chernobyl in this marine environment will be determined.

(4) To establish the chronology of sediment deposition. Unsupported Pb-210 determinations will be made in order to achieve this objective.

Commissariat à l'Energie Atomique (CEA)

The objectives of the laboratory of Marine Radioecology are as follows :

(1) To estimate the transit time of particulates and associated transuranics in La Manche.

(2) To study, experimentally, the mechanisms of complexation of americium and its analogues, the rate earths, with organic ligands in zones of high concentration, and to assess the consequences in bio-availability terms.

(3) To evaluate the well-established principle of analogy with other rare earths/transuranics.

(4) To complete certain studies which have been carried out on the Irish Sea, by the measurement of stable rare earths in sediment banks.

The successful realisation of the above objectives should lead to a better understanding of (a) sedimentary transport processes and (b) the complexation of transuranics by organic matter in aqueous media.

Centro Richerche Energia Ambiente S. Teresa (ENEA)

The objective of the ENEA programme is to identify, trace and quantity some of the environmental and biogeochemical processes that affect the fate of radionuclides in the specific marine environments. The project focuses on the understanding the cycling of transuranic and other long-lived radionuclides in the lower part of the rivers, their deltas and in the coastal environment.

A22 Natural radioactivity in the environment and its pathways to man

Contract Bi7-006 Behaviour of Polonium-210 and Lead-210 in European marine environments. Application of bioindicators.

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Total Contribution by the Commission: 158 kECU
24 months from 1/06/90 to 31/05/92

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Description of research work:

INTRODUCTION.

The radiation dose to man from the marine environment is dominated by the consumption of fishery products. The radionuclide ^{210}Po has an important part in this. ^{210}Po ($T_{½}$ 138 days) is a daughter of ^{210}Pb ($T_{½}$ 21 year). Both these natural radionuclides belong to the ^{238}U series, which has several other daughters amongst which is ^{226}Ra. Locally large quantities of these radionuclides are released into the coastal environment by non-nuclear industries (e.g. in phosphogypsum effluents of phosphorus industries). In contrast to the knowledge of artificial radionuclides and of ^{226}Ra, little is known about the behaviour of ^{210}Po and ^{210}Pb in marine ecosystems.

The study has the general aim to obtain insight into the effects of such industries on the activity levels and distribution of ^{210}Po and ^{210}Pb in abiotic components and bioindicators, both in adjacent estuaries and in nearby coastal areas. An additional aim is to apply the obtained insight in the development of a model to predict ^{210}Po and ^{210}Pb distribution and levels.

The four participants of the contract cover a wide geographical range. Depending on the situation and expertise each participant directs his research to certain parts of the chain : emission, dissolution/sorption, distribution/accumulation in the abiotic environment, coupled with modelling and with the effects on potential bioindicators. Doing this in a coordinated joint study will yield a more complete insight into the chain from emission to effect and into geographical differences.

DESCRIPTION OF THE PROJECT.

The study encompasses the Westerschelde estuary in the Netherlands, the Seine estuary in France and the Tagus estuary in Portugal. A link will be established to the data obtained in 1989 on the Rhine estuary (CEC project BI6- 0328-NL). In each of these estuaries large quantities of ^{210}Po and ^{210}Pb are emitted by local phosphate industries. In addition, natural levels will be studied in a Portuguese river/estuary free from industrial ^{210}Po emissions.

The effluents of the Dutch phosphate industries will be studied in laboratory experiments, in order to identify the characteristics determining the behaviour of ^{210}Po and ^{210}Pb after emission (RIVM). A sampling programme of water and bottom sediment of the Westerschelde and the adjacent North Sea coast with analyses of ^{210}Po and ^{210}Pb will be executed. Particular attention will be given to possible distribution pathways of industrial effluents and to seasonal, hydrological and biological effects (NIOZ). The data and information obtained will be used to develop a model to predict ^{210}Po and ^{210}Pb levels in the Westerschelde (RIVM).

In the Seine estuary and the nearby Northern coast, a detailed study will be made of the ^{210}Po and ^{210}Pb levels in the mussel Mytilus edulis to characterise its potential use as a bio-indicator. Special attention will be given to the geographical and seasonal variation in these waters and to bottom sediments. Laboratory experiments will be executed with M. edulis to study the evolution of its ^{210}Po level in correlation with sudden or regular contamination of water and/or suspended matter, the quality of seawater, and to determine the characteristics of Po and Pb metabolism by M. edulis (CEA).

In Portugal a river/estuary, on which no industrial ^{210}Po emissions take place, will be studied to establish the natural background levels of this environment and their variation. In the Tagus estuary and the adjacent coast the focus will be on the distribution of ^{210}Po and ^{210}Pb discharged by the phosphorus industry. The major emphasis will be on abiotic materials and to a lesser extend on bioindicators (LNETI).

Conclusions of general applicability will be drawn and location specific differences will be identified from the data and the conclusions of the five estuaries. This will give new inputs both to future generic and location specific modelling, as to the direction of future research (RIVM, NIOZ, CEA, LNETI).

By coordinating these studies, a more complete insight in the total chain will be obtained and geographical differences will be identified. General characteristics of Po and Pb behaviour and the effects of industrial emissions will be identified from the research-data of the five estuaries. Attention will be given to location specific differences in the behaviour of Po and Pb. All this will give new inputs to future generic and location specific modelling, as to the direction of future research. (RIVM, NIOZ, CEA, LNETI).

A23 Influence of speciation, chemical modification, changes in physico-chemical properties and biological conversion

Contract Bi6-339 Biogeochemical pathways of artificial radionuclides (study contract)

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Total Contribution by the Commission: 30 kECU
36 months from 1/01/89 to 31/12/91

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Description of research work:

The RADPATH project was initiated two years ago under the auspices of the Scientific Committee on Problems of the Environment (SCOPE), which is a standing committee of the International Council of Scientific Unions (ICSU). The project is examining the present status of knowledge concerning the environmental pathways of artificial radionuclides following releases from the nuclear fuel cycle, reactor accidents, spillages or detonation of nuclear weapons. As it is recognised that man-made radionuclides contain a very wide range of chemicals elements, and consequently exhibit a variety of behaviour patterns, the RADPATH programme is focusing on the more abundant and toxic isotopes. The project also has a broader significance as knowledge from the study of radionuclide pathways provides valuable insight into those of stable elements. RADPATHS's overall programme is directed by a Scientific Advisory Committee (SAC), chaired by Sir Frederick Warner, with co-ordination through an office at the University of Essex, U.K. Members of the S.A.C. include members of the following organizations: Soviet Academy of Sciences, U.S.S.R.; International Union of Radioecologists (IUR), Belgium; Commissariat à l'Energie Atomique (CEA), France; Bhabha Atomic Research Centre, India; Nagoya National Hospital, Japan and Lawrence Livermore National Laboratory (LLNL), USA.

The subject is being addressed primarily by environmental compartment and pathway (comprising three principal areas: atmospheric, terrestrial and aquatic), and only secondarily by nuclide. With regard to atmospheric pathways, besides identifying sources of atmospheric radioactivity and physico-chemical forms, processes, environmental measurements and modelling are being considered. This work is being co-ordinated through members of LLNL (U.S.A.) with contributions from members of: Bhabha Atomic Centre, India; National Institute of Radiological Sciences, Japan; Studsvik Nuclear, Sweden and various other U.K. and Soviet institutes and organizations. Studies of terrestrial pathways, co-ordinated through I.U.R., (Belgium), are concerned with identifying sources of radionuclides and their behaviour in various ecosystems (namely forests, agricultural and semi-natural). Collaborators include: members of Associated Nuclear Services and Institute of Terrestrial Ecology, U.K.; Lawrence Livermore and Los Alamos

National Laboratories, U.S.A. and various laboratories in Holland, Belgium, Denmark and U.S.S.R. After consideration of the major chemical, physical and biological processes in the marine environment, the aquatic section is involved with examining radionuclides in fresh waters, estuaries, shelf seas, semi-enclosed basins and the deep ocean. This work is being co-ordinated via CEA (France) with contributors from several U.K. and Soviet institutes and academies; Risø National Laboratory, Denmark and the Federal Maritime and Hydrographic Agency, Germany. Factors affecting radionuclides in the urban environment, including elucidation of suspension and removal processes and retention behaviour, are being assessed by the University of Lancaster, U.K., with collaboration of other U.K. and Danish institutes and laboratories. Finally, analysis of dosimetry and environmental effects is being co-ordinated by scientists from the Ministry of Agriculture, Fisheries and Food, U.K., with assistance from Soviet Academies of Science and the University of Tokyo, Japan.

A23 Influence of speciation, chemical modification, changes in physico-chemical properties and biological conversion

Contract Bi6-345 Transfer and conversion mechanisms of H-3 and C-14 compounds in the local environment.

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Total Contribution by the Commission: 55 kECU
24 months from 1/01/90 to 31/12/91

Participating Scientists

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Description of research work:

Fusion test reactors and associated tritium handling facilities as well as first-generation fusion plants will contain large inventories of tritium fuel, mainly in highly mobile forms (eg, HT and HTO). The safety analysis and licensing of these facilities require the availability of dynamic models to predict the environmental behaviour and impact of hypothetical tritium releases. Especially in the case of accidental short-term releases to the atmosphere, it is important to know the time history of the resulting local dose to evaluate risks and to prepare counter-measures. Furthermore and most important, in the design phase of a new technology like fusion, thorough knowledge on its environmental consequences provides the opportunity to incorporate passive safety into the practical realization, before the first tritium fueled reactor starts operation.

The evaluation of the recent experimental field releases in France and Canada has identified tritium remission from soil and vegetation after deposition from a primary plume of HT or HTO as a key process in tritium behaviour of higher relevancy dose. The remission rate determines the early dose from inhalation and skin absorption, the formation of HTO pools in the soil-plant system and the tritium clearance from the local environment. However, no model exists as yet, to predict remission rates on the basis of general or site-specific parameters.

Research in this project is focusing on the investigation and establishment of key relationships between the remission rate and soil physical as well as meteorological parameters, like soil texture, moisture content, temperature, wind-speed and air- HTO/H_2O contents. This is done with help of a wind-tunnel/soil-column arrangement equipped with a unit to control defined steady or dynamic conditions. The relevant relationships are evaluated from selected single-parameter studies.

The experimental results obtained so far under steady meteorological conditions with homogeneously labelled soils show that the remission rate is much higher immediately after deposition and decreases faster during the first few hours than derived from low time-resolution measurements during the field releases. Furthermore, HTO remission is principally not coupled to H_2O evaporation, though evaporation conditions may also be favourable for tritium remission

because of energy reasons. This independence of HTO and H_2O transports across the air-soil interface confirms the findings of the previous study on HTO deposition from air to soil.

After the establishment of principal relationships it is planned to proceed towards more realistic conditions with respect to HTO soil profiles resulting from actual deposition processes and with respect to dynamic meteorological sequences.

A23 Influence of speciation, chemical modification, changes in physico-chemical properties and biological conversion

Contract Bi7-011 The bio-availability of long-lived radionuclides in relation to their physico-chemical form in soils

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Total Contribution by the Commission: 190 kECU
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Description of research work:

INTRODUCTION

A disturbing feature of soil-to-plant transfer data is their variability, which is attributed to a variety of soil and plant properties depending on the radio-element studied. In order to reliably assess radionuclide migration in soils or their availability to crops, it is important that mechanisms of radionuclide complexation (immobilization and remobilization) and movement from soil to soil water and thence to plant root be as fully understood as possible. Soil characteristics indeed affect the availability of a nuclide, as well as the efficiency of the uptake process. In the case of caesium for example, the number of specific sites and the levels of K and NH_4 regulate the caesium concentration in the soil solution, and the soil solution root transfer process is regulated by the K and NH_4 levels in the solution. A separate analysis of these effects may allow a better prognosis to be made on the transfer expected and on the effectiveness of actions meant to reduce translocation.

DESCRIPTION OF THE PROJECT

The ongoing study deals with each of the two aspects of the behaviour of radionuclides in soil/plant systems, i.e. chemical speciation in soil systems and efficiency of the uptake process.

1. First of all, speciation of caesium (and of some transuranics) in soil systems is studied in relation to major chemical characteristics of the soils (such as soil solution conductivity, K and NH_4 -levels). this speciation study concerns both naturally and artificially labelled soils, and accentuates the quantification of chemical forms in soil and soil solution. Recently developed methodology to characterize soils and to study speciation is improved and applied. A variety of specific methods are used.

Porous ceramic cups are used by NRPB to isolate the soil liquid phase in a number of UKAE's existing, well-characterized sites in Cumbria, and also in the lysimeters at NRPB. In laboratory experiments RIVM uses immiscible liquid displacement for the isolation of soil solutions. Ultra-filtration and chromatographic techniques will be used by NRPB and RIVM to investigate the association of radionuclides with different molecular size fractions in soil and soil solution and to monitor time dependent changes in radionuclide speciation. These data can then be related to Cumbrian studies on seasonal trends in radiocaesium (and some transuranic) levels in bulk vegetation, being conducted by UKAEA and NRPB.

In order to produce meaningful distribution coefficients, NRPB conducts batch equilibrium experiments under conditions representative of the in situ situation. By studying soil solution and its associated radio-labelled soils as liquid and soil phases, the effects of various treatments and ad- and desorption can be determined under laboratory conditions before pursuing expensive field experiments. KUL accentuates the quantitative characterization of a broad range of soils in terms of soil chemical parameters, which regulate the specific interception potential and the K and NH_4 levels, with particular attention being given to reversibility aspects and aging effects. As a result, it will be possible to estimate the effect of amendments on radiocaesium availability in problem soils.

2. The first part in which chemical form studied is complimented with experiments in the field, and in phytotron on the bio-accumulation of caesium (and of some transuranics). The effects on transfer along the soil/soil solution/plant pathway are studied under controlled conditions in phytotron by RIVM and KUL, and validated with references to field observations made by UKAEA and NRPB on upland soils from Cumbria. RIVM, KUL and UKAEA further compare the uptake of plants from soils with the uptake from nutrient solutions in order to better distinguish between soil-specific and plant-specific phenomena. The samples on which chemical analyses are performed, are divided from the soil systems used in these experiments. The radionuclide of main interest is Cs-137, although some experiments on transuranics are planned as well. The time trend in the immobilization and remobilization of radiocontaminants is studied throughout the growing period in order to explain changes in transfer and to extend the information derived from the detailed soils studies.

3. The final goal will be a generalized description of the relationship between the concentration and species of a radionuclide present upon the solid phase of the soil, in both the liquid phase and in biota.

A24 The behaviour of accidentally released radionuclides, evaluation of the reliability of transfer parameters and experimental studies

Contract Bi7-018 Factors affecting radiocaesium transfer to ruminants.

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Total Contribution by the Commission: 557 kECU
24 months from 1/4/90 to 31/3/92

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Description of research work:

Recent reviews of the transfer of radiocaesium to ruminants after the Chernobyl accident have shown that there are a number of animal and dietary factors which may effect the transfer of radiocaesium. However, there is insufficient information available on the importance of these factors to enable predictive models to take them into account. Similarly, few attempts have been made to understand the relationship between radiocaesium levels in animal feed and tissues in terms of metabolic processes and mechanisms. Such an understanding may help to improve the effectiveness of countermeasures applied after environmental releases of nuclides. This 2 year research programme investigates some of these factors. The participants work in 10 laboratories in 7 different countries spread throughout western Europe and Scandinavia.

Although a limited number of experiments using cattle will be conducted, the sheep is being used as the 'model' ruminant since it is universally important throughout EEC and Scandinavian countries, easy to handle and relatively inexpensive to use in large numbers. However, in subsequent years we hope to extend studies of factors which we have found to be comparatively important for sheep to other ruminants.

EXPERIMENTAL APPROACH

The transfer of radiocaesium from feed to animal products is commonly described using the transfer coefficient, defined as the fraction of an animals daily intake of radiocaesium which is transferred to a kilogram of tissue (or litre of milk) at equilibrium. However, estimation of valid transfer coefficients are in many cases impossible, since equilibrium cannot always be achieved.

A major factor which leads to differences in transfer coefficients values for milk and meat from various dietary sources is the extent of uptake of a radionuclide across the gut wall. A more direct approach to compare the effect of various factors on tissue levels is to estimate absorption directly. Tissue levels can then be predicted without the need for equilibrium concentrations to be established. Many previous radiological studies have determined the apparent absorption of radiocaesium (ie the difference between faecal output and dietary intake of radiocaesium). However, such studies will underestimate the absorption of radiocaesium because faeces contains unabsorbed radiocaesium and absorbed radiocaesium which has been secreted in the digestive tract from the blood stream (endogenously excreted radiocaesium). In some of this programme estimates of the true absorption coefficient (TA) will be made where:

$$TA = \frac{RI - RF + REF}{RI}$$

and RI = Radiocaesium intake
RF = Radiocaesium output in faeces
REF = Endogenously excreted radiocaesium in faeces.

This is a means of measuring differences in the transfer of radiocaesium across the gut wall from different sources and under a variety of dietary and animal conditions. The technique involves infusing ^{134}Cs into the jugular vein whilst simultaneously feeding a diet contaminated with ^{137}Cs. In the blood stream ^{134}Cs and ^{137}Cs should behave in an identical manner, therefore faecal endogenous secretion of ^{137}Cs can be calculated from the faeces: urine ratio of ^{134}Cs. The true absorption coefficient can then be calculated using the equation above. Since equilibrium tissue concentrations are not needed the method has the advantage that studies are considerably shorter than those needed for accurate determination of tissue transfer coefficients.

PHYSIOLOGICAL FACTORS AFFECTING TRANSFER

1. Age (ITE/MLURI)

The transfer coefficient for radiocaesium to the tissues of lambs is generally accepted to be in the order of 2 times higher than that to adult sheep. However the rate of change in transfer with increasing age is not known and has been identified as an area in which more information is required.

Previous studies have often used lambs between 3 - 5 months of age. However, lambs are slaughtered for human consumption throughout Europe at ages ranging from 3 - >8 months. As part of this programme the uptake by different aged lambs will be estimated using the true absorption coefficient (as described above) and also the activity in tissues after 14 days of administration. Seven groups of c.8 to 52 wks old lambs, housed in metabolism cages, will be used.

2. Breed (all participants in sheep experiments)

Sheep, like other domestic animals, have been bred to fulfil a variety of different needs. The effect of breed on the transfer of radiocaesium to sheep has not previously been studied. Since the production of milk or meat, relative to body size, varies in different breeds it can be expected that the relative transfers of radiocaesium to milk or meat will also differ. The transfer of radiocaesium will be measured in the breeds of sheep already being used in the other parts of the programme. This will include sheep bred for a wide range of purposes eg Boutsiko (Greek sheep used for commercial milk production); Suffolk and Texel (northern European sheep bred for high meat production); Scottish Blackface (bred specifically for upland environments) and will ensure that the results from the other parts of the proposal can be compared.

3. Stage of lactation (Ioannina Univ.)

The concentration of some nutrients in milk is greatest during the later stages of lactation. The transfer of radiocaesium to the milk of sheep used for commercial milk production (Boutsiko - Greece) will be studied throughout a complete lactation.

DIETARY FACTORS AFFECTING TRANSFER

1. Feed characteristics (ITE/MLURI, S.C.K./C.E.N. ENEA-DISP, Ioannina Univ.)

Currently transfer models take no account of the vegetation species ingested. Most experiments which have been used to provide data for models have been performed indoors using "grassy" vegetation or commercially prepared isotope. Initially, experiments will be conducted to determine the extreme effects of feed characteristics, so that we can use models developed in the project (see below) to estimate the overall sensitivity to this factor. The transfer of radiocaesium from a range of environmentally contaminated species (including Calluna vulgaris and upland grass species), artificially contaminated feed crops (alfalfa; maize; rye-grass; and hay) will be investigated. The effect on the transfer of radiocaesium of drying, ensilaging, freezing and diluting with uncontaminated feeds will also be assessed. The digestibilities, nutrient and stable element composition of the feeds will be measured to determine their effect.

2. Soil ingestion (ENEA-DISP/Ioannina Univ.) and adhesion (ITE/, S,C,K./C,E,N, NEB, ENEA-DISP, Ioannina Univ.)

Although generally neglected in predictive models, in some situations ingested soil (which has been shown to be an available source of some trace elements) is a potentially important source of radionuclides, especially where soil:plant transfers are low. ITE have shown that during winter months soil contamination may account for up to 92% of ^{137}Cs and 62% of $^{239/240}Pu$ present in vegetation samples.

The importance of ingested soil as a source of radiocaesium to grazing animals will be assessed at sites in most of the participant countries covering a range of agricultural practices, soil types, climatic conditions and pastures types. Soil contamination of vegetation will be determined by comparing the ratio of titanium in soil and vegetation. The availability of radiocaesium associated with ingested soil will be assessed by indoor feeding trials, using a range of environmentally contaminated or experimental soils. A range of soil characteristics will also be measured to assess if any differences

will be assessed by indoor feeding trials, using a range of environmentally contaminated or experimental soils. A range of soil characteristics will also be measured to assess if any differences in availability are correlated with specific soil characteristics.

BEHAVIOUR OF RADIOCAESIUM IN THE GUT & TISSUES OF RUMINANTS

(MLURI/TEAGASC/Nottingham Univ.)

In a simple interpretation the process of transfer can be divided into absorption from the gut, transport within the body and turnover within individual organs (ie uptake, storage and removal).

Preliminary evidence suggests that absorption of radiocaesium from the gut may be the main factor responsible for the variation in transfer coefficient values found; after absorption radiocaesium appears to behave similarly irrespective of the dietary form.

Initial studies in this area will be performed using both sheep and cattle; empirical data has indicated that radiocaesium transfer to milk and body tissues is approximately an order of magnitude greater for sheep than for cattle. This study will determine if this difference is associated with gut processes and will help test the validity of using data obtained for sheep in predictive models for cattle. Two studies will be conducted on both cattle and sheep:

(i) an experiment to compare the true absorption of radiocaesium from the same source by both cattle and sheep;

(ii) a study to determine the sites of absorption and secretion throughout the digestive tract. The latter study will be performed twice, whilst the animals are being fed either a highly or poorly digestible diet, to determine the effect that changes in gut metabolism caused by different diets may have on the absorption of radiocaesium. A knowledge of the sites of absorption and resecretion of radiocaesium into the digestive tract should enable us to establish if countermeasures can be adapted to increase the rate of loss of radiocaesium from contaminated animals. Preliminary studies (Nottingham) will be conducted to investigate the biological mechanisms influencing the rates of accumulation and loss of radiocaesium by individual tissues.

MODELLING

(Ioannina Univ., Nottingham Univ.)

Both participants have developed compartment models describing the radiocaesium transport within sheep which are undergoing detailed assessment and validation. These models will be modified according to the experimental results that we obtain and will be combined to produce a predictive tool.

The models will be used to assess the relative importance of various factors which may affect the uptake of radiocaesium by animals. We shall thereby identify the most important factors affecting radiocaesium activity concentrations in ruminants and highlight areas which merit further investigation.

In parallel to these conventional, empirical compartment models, a more mechanistically based model will be developed. This will enable us to develop a clearer understanding of the underlying Cs metabolism. For instance, rates of tissue turnover, relative sizes of tissue pools and the gut passage time of various types of food could be used in an attempt to determine the rates of transfer between compartments on physiological grounds for comparison with empirical results. Once developed, this mechanistic model will provide a means whereby the results obtained for sheep could be extended to other ruminants.

A25 The role of retention and release of radionuclides in natural ecosystems and in marginal agricultural areas

Contract Bi7-009 Deposition of radionuclides on tree canopies and their subsequent fate.

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Total Contribution by the Commission: 280 kECU
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80 kECU

Description of research work:

Very few data are available on the deposition of radionuclides onto tree canopies and their subsequent biogeochemical pathways within forest ecosystems. However, the Chernobyl accident has highlighted the importance of such ecosystems and their possible contribution to the ultimate dose to man. The objectives of the programme are to produce data by field and laboratory investigations on the deposition and uptake of aerially deposited radionuclides into forest ecosystems and their subsequent fate, with a view to validating and refining models which are currently being developed on transfer within such ecosystems and their dependency on geographical location. This will lead to a substantially greater understanding of the mechanisms of wet and dry deposition of radionuclides in tree canopies and provide information on the amounts of radioactivity which will reach the soil in long-term, as a result of processes such as leaching, resuspension, weathering of leaf surfaces, translocation and leaf-fall.

Characterised radionuclides or surrogates in the form of aerosols and droplets will be applied to tree canopies in the field and laboratory studies. Aerosols containing radionuclides in the physico-chemical form arising in an accident will be simulated. These and other types of aerosol will be applied to the foliage of various species under controlled aerodynamic conditions in a wind tunnel and/or in the field. Wet deposition studies will be performed using a rain simulator. A complementary study will be carried out in the field measuring interception by spruce of natural aerosols and precipitation.

Loss of radionuclides will be measured in both the field and laboratory, and weathering half-lives, resuspension, foliar absorption, translocation and leaching quantified. Comparative investigations will be carried out between Mediterranean and North European woodlands, with emphasis on the dynamics of radionuclide pathways in different ecosystem compartments, e.g. litter and soils. Data from all the studies will be used to validate and refine mathematical models for radionuclide transfer after wet or dry deposition. Interlaboratory comparisons will aim at a high level of quality assurance.

The research programme is divided between 4 groups in the following way :

Imperial College (ICST) are undertaking controlled wet and dry deposition studies using a rain simulator and wind tunnel followed by measurements of field loss processes, including resuspension.

CEA, Fontenay are studying the same processes but under field conditions and also undertaking mathematical modelling of the transfer processes involved in a forest ecosystem.

UCL, Louvain are using aerosols generated in a simulated reactor accident system to study the physico-chemical effects on deposition together with the effect of leaf surface characteristics on interception and retention. Field studies of natural aerosols deposited in N. European and Mediterranean forest canopies enable geographical effects to be studied.

University of Barcelona are studying pathways of radionuclides in Mediterranean forest ecosystems both in the field and laboratory and these results will be compared with those of UCL, Louvain.

Details of the individual programmes are given below :

Imperial College : controlled dry and wet deposition studies make use of a wind tunnel (with associated anemometry for wind speed and turbulence measurements) and an aerosol laboratory (with aerosol production facilities, aerosol characterisation apparatus and a chamber for contaminating plant material on a small scale), together with a rain simulator with controlled droplet size and terminal velocity. Deposition velocities will be measured initially and the subsequent fate of the deposited aerosols will be quantified with respect to weathering, wash-off and wind induced resuspension using the same facilities.

In the first place Norway Spruce (Picea abies) will be used and another tree species later (e.g. Evergreen Oak - Quercus ilex) and Scots Pine (Pinus sylvestris) which are characteristic of Mediterranean sites. It is not possible to contaminate mature trees in the wind tunnel but these will be simulated by arranging closely cut shoots and/or potted seedlings to resemble the tree canopy as closely as possible. It may also be possible to use grafted material from mature trees. Initial deposition studies will use Cs, either in soluble or insoluble form (as a radionuclide or its surrogate) with a range of particle sizes between 1 to 10 μm. Deposition velocities and interception factors will be calculated. After deposition the subsequent fate of the aerosols will be studied under both wet and dry conditions and a total budget produced for the radionuclide deposited. Different conditions will be simulated by transferring whole seedlings contaminated in the wind tunnel to

(a) glass house with no wind or rain
(b) glass house with wet deposition using the rain simulator
(c) the field where the plants are exposed to wind and rain and
(d) the field with a transparent cover so that they are subjected to wind but no rain.

The ecological half life for the radionuclide can then be determined and results compared with the other laboratories. A similar programme will be carried out using seedlings contaminated with different applications of simulated contaminated rain. In addition studies will be made of resuspension of aerosols from tree foliage using a facility in the wind tunnel for producing controlled (measurable) guts of wind.

CEA, Fontenay (Dr. Y. Belot): most of the deposition data which can be used in predicting the radiological consequences of an accident have been acquired for short vegetation of grassland areas and are not relevant to tall vegetation of the forested areas in which nuclear plants can be established. Moreover, little is known about the translocation of nuclides in trees, although such information is needed for decision about countermeasures. The proposed studies are the following:

(1) Field studies :
Determination of aerosols deposition on undisturbed canopy components (bare and leaf bearing twigs) of conifer and deciduous species. This will be performed by exposing the canopy components to monodisperse particles of caesium iodide or fluorescent dye, and determining uptake velocities as a function of the size of particles and velocity of wind.

Evaluation of the interception by canopy components of water falling in the form of rain, low cloud droplets, mist and fog. Study of water uptake from the liquid water deposited at leaf surface as a function of plant species, age of leaves and water potential in the leaves. Study of the role of the water absorbed by leaves as a vehicle of the penetration of caesium into the plant.

(2) Mathematical modelling :
A multi-layered model will be developed to describe the transfer of radionuclides to forest canopies through uptake or interception by canopy components.

The model will calculate the velocity of the deposition of a pollutant to the canopy, the characteristics of the pollutant and the properties of canopy components as measured from the above field experiments.

UCL, Louvain (Dr. C. Ronneau) : the accident of Chernobyl showed that forest ecosystems act as powerful filters and accumulators of airborne radioactivity. Up to now, very few data have been acquired concerning the interception and retention of aerosols (radioactive or not) by woody species.

It is of great importance to precisely define the biogeochemistry cycle of the main long-lived radionuclides in forest ecosystems, in order to determine the impact of an accidental release of radioactivity by a reactor. In the case of a reactor accident, aerosols are emitted as a consequence of core fusion : the behaviour of the radionuclides which are linked to these aerosols depends on the physicochemical characteristics and this is the case during the atmospheric transport (coagulation, maturation, reaction with atmospheric trace gases), during the deposition phase (granulometry) and during the phase of transfer towards plant material (solubility, adsorption on terrigenous material). The study includes different aspects, all linked to the aforementioned phenomena :

- by means of a laboratory simulator, reproduction of conditions likely to be encountered in a damaged reactor core and production of radioactive aerosols which are studied by physicochemical (non destructive) methods ESCA, XRF, (electron microprobe, Mossbauer spectroscopy). The deposition behaviour of the aerosols is studied on different plant surfaces.
- identification of the phenomena which determine the interception and the retention of the radionuclides by a forest cover; analysis of the physicochemical properties of aerosols collected "in situ"; sampling on the tower of DONON (47 m Vosges, France:impactors, filters and rain gauges are placed in and above the canopy of a spruce stand). The physicochemical determinations include neutron activation analysis of the sampled material.
- sampling of plant material in temperate forests and analyses of surface properties of collected leaves in conjunction with their retention properties of natural aerosols (by electron microscope and microprobe). Study of these aerosols in relation with their capacity of adsorbing radiocaesium; sampling of the abiotic layer on leave surfaces (airborne terrigenous material retained by leaves), study of the sorption properties of this layer towards radioactive caesium associated with elements from the corium. Determination of the ecological half-life of radiocaesium, determination of the importance of its translocation as a function of the growing season and of the meteorological conditions. Study of the fixation of the aerosols (produced by the simulator) by forest soils. Study of the biodegradability of contaminated plant material; release of the radiocontaminants to the lower layers of the soil.

- study of the relative importance of direct and indirect contamination of plant (trees) in the case of a reactor accident. The study is performed by double-labelling under controlled conditions.

University of Barcelona (Dr. G. Rauret) : this study consists of an evaluation of the effect of the special dry conditions of Mediterranean forest regions on the interception of radionuclides, in particular caesium, compared with a temperate forest. Of particular importance are the role of dry deposition, the high rates of organic matter decomposition and the low rates of soil leaching.
With these aims the work consists on two aspects :

(1) The study of the properties of the aerosols sampled in an experimental Mediterranean forest, which is equipped with field instrumentation. This study consists of microscopic and physico-chemical analyses as well as radiochemical characterisation. Study of the relationship between the characteristics of the foliar surface of two mediterranean species and the aerosol retention. With this purpose the surface properties of different types of leaves are also being studied.

(2) A detailed study of the radiocaesium distribution in different forest ecosystems in order to ascertain the influence the distribution of factors such as type of soil and vegetation. These ecosystems are selected from the information obtained in previous studies carried out in Catalonia (NE Spain) and are located in restricted zones. previous studies show the importance of the organic layers in the mobility of radiocaesium in soil-plant systems. To discriminate the influence of the soil and vegetation factors in the dynamics of radiocaesium, a detailed and replicated sampling of the organic layers and on the first centimetres of the soil is carried out.

A25 The role of retention and release of radionuclides in natural ecosystems and in marginal agricultural areas

Contract Bi7-016 Behaviour of Cs and Sr in natural ecosystems and the potential radiation exposure of their extensive use.

Coordinator Bundesamt für Strahlenschutz
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Total Contribution by the Commission: 340 kECU
24 months from 1/04/90 to 31/03/92

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Description of research work:

The Chernobyl accident led to an enormous amount of measurements of ^{134}Cs and ^{137}Cs activities in e. g. wild berries and mushrooms. These data, which are varying widely are helpful for evaluating actual radiation exposure to man, but they are of no help in understanding the

behaviour of radionuclides in forest ecosystems. The project "Cycling of radiocaesium and strontium in natural ecosystems" investigates the fate of radiocaesium and strontium 90 in natural ecosystems in Belgium, Germany, Sweden, and Italy, in order to improve the knowledge of the cycling mechanisms and the understanding of their short and long term behaviour.

Seven laboratories from Belgium, Italy, Sweden, and Germany are involved in this research project. The investigations take place in different forests sites in their countries. For joint investigations, boreal forests in Sweden and beech forests in the Italian Alps have been chosen.

The experimental strategy is focusing on the fate of radiocaesium and strontium 90 after their deposition in forest ecosystems. One major point is the uptake of caesium and strontium from soil to plants. Until now, it is not completely understood, why the uptake rates of caesium in natural ecosystems are significantly higher than on agriculturally used areas. Natural ecosystems are characterized by undisturbed soils with organic and mineral horizons. In a first step, the distribution of radiocaesium and strontium 90 within the different layers are measured. To improve the knowledge of the plant availability, soil parameters like nutrient concentration, exchange capacity, kd-values, etc. are determined. Additionally, plant parameters as mycelium and rooting depths, potassium and calcium distribution within the plants are analyzed. The importance of various parameters on the transfer of caesium and strontium will be analyzed by statistical methods.

The plant-herbivore interactions are analyzed by a special programme on moose. Moose meat contributes to about 5 - 10% of the average meat consumption in Sweden and is therefore of radiological interest. To obtain the radionuclide intake rate, the migration of single moose is observed during the year as well as their seasonal consumption habits. Later they are shot and caesium 134 and 137 activities in meat are measured. The correlation of radiocaesium and potassium intake rates will be tested.

For long term considerations, the loss of radionuclides from the ecosystems by migration and run-off is analyzed. Further studies are concerned with the distribution of caesium and strontium within the ecosystems, the antagonisms of caesium and potassium as well as strontium and calcium, etc.

To test how the caesium 134 and 137 activity in forest ecosystems is reflected in human populations, whole body activities are measured in groups, which preferably consume mushrooms, wild berries, and moose meat. Their results will be compared with measurements of persons whose consumption rates of these products are low.

The natural ecosystems will be modelled at least on three levels : in a first step, different equations for each transfer will be tested on their reliabilities. In a second step the distribution and cycling of caesium and strontium within the whole system under short term and long term aspects will be described. On the third level, the potential radiation exposure of man by the extensive use of natural ecosystems will be calculated.

A25 The role of retention and release of radionuclides in natural ecosystems and in marginal agricultural areas

Contract Bi7-044 Radioecology of semi-natural ecosystems.

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Total Contribution by the Commission: 265 kECU
24 months from 1/07/90 to 30/06/92

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Description of research work:

Member States of the European Community have suffered fall-out both as a result of nuclear weapons testing and again following the Chernobyl accident. Radiocaesium from both these sources is present in soils in measurable amounts and is available for transfer to vegetation and herbage and onwards to man. Work in progress indicates that radiocaesium of Chernobyl origin has remained available for recycling in upland ecosystems for a longer period of time than was predicted by models available at the time of the Chernobyl accident. These models were largely based on data from studies of radionuclide movement in lowland agricultural ecosystems. Current work has also shown that radiocaesium concentrations in different species, from the same habitat, can vary by an order of magnitude. This could be due to the physical composition of the plant, or to specific physiological factors.

The levels of radiocaesium present in upland vegetation and herbage are therefore often enhanced when compared to those grown on mineral-rich lowland soils. Forest and upland ecosystems are also the natural habitat for domestic and wild animals such as sheep, red deer, moose and reindeer, and so a direct pathway into human food chains can be identified.

The mechanisms of recycling and transfer in these ecosystems are poorly understood, and the necessary data with which existing models can be revised or new models developed are not available. The research projects described in the following sections have been formulated with a view to using similar techniques to evaluate a number of different ecosystems where elevated levels of radiocaesium activity have already been identified, both in plant species and in grazing animals. Soil characteristics, plant composition, plant physiology and biological activity will all be examined and their effect on soil-plant transfers in acidic soils assessed. In addition, the seasonal variation in dietary composition of grazing animals and the subsequent effect on their radionuclide burden will be evaluated. Where appropriate, critical groups will be identified and annual dose commitments evaluated. All data collected will be made available for modelling purposes.

The proposal involves work on blanket bogs and montane peatlands (Ireland), upland heaths (UK), Northern Boreal forests (Sweden) and more extreme habitats as found in the Faeroe Islands (Denmark). A contrasting Mediterranean ecosystem grazed by sheep has recently been included in the programme.

2.1 Nuclear Energy Board, Ireland

Following the Chernobyl accident in May 1986, deposition of radiocaesium throughout Ireland was in the range 0.5-21.7 $kBqm^{-2}$ with a national weighted mean of 4.9 $kBqm^{-2}$. Some of the highest deposition took place in upland areas extensively grazed by sheep and characterised by poor quality acidic soils from which an enhanced uptake of radiocaesium to vegetation has previously been observed.

Studies will be undertaken at four such upland sites where elevated levels of radiocaesium (above 1500 Bq/kg) have been recorded in lambs since 1987 and both soil-plant and plant-animal transfer mechanisms will be evaluated. The main aspects of the work are:

(a) Soil sampling to 40 cm to ascertain the vertical migration of caesium of both Chernobyl and weapons origin

(b) Role of soil characteristics in determining uptake to different vegetation species

(c) Dietary evaluation by means of biomass measurements using exclusion frames and by faecal analysis

(d) Evaluation of the role of soil water in soil-plant transfer in organic soils

(e) Identification of bioindicators of radiocaesium contamination for use in any future accident situations.

The Nuclear Energy Board will also act as co-ordinator and will arrange a number of intercomparison exercises to ensure uniformity of sampling and measurement by all participants.

2.2 Risø National Laboratory, Denmark

Risø National Laboratory's contribution to the project is a comparative study of the radioecology in Faroese semi-natural ecosystems of ^{137}Cs from global fallout and of radiocaesium (^{134}Cs and ^{137}Cs) from the Chernobyl accident.

Risø has since 1962 studied the concentrations of ^{137}Cs (and ^{90}Sr) in systematic collected samples of precipitation, milk, herbage, potatoes, lamb and drinking water from the Faroe Islands. These time series of radionuclide concentrations in environmental samples make it possible to estimate effective environmental half lives of ^{137}Cs (and ^{90}Sr) in a semi-natural ecosystem such as the Faroese.

Information on environmental half lives is necessary for the prediction of future levels of contamination in a given environment and thus for the calculation of dose commitments from food consumption. After the Chernobyl accident, it has become possible to estimate effective half lives of the radiocaesium from Chernobyl and compare the results with those obtained from global fallout. It is a general observation that environmental half lives of products from semi-natural ecosystems are longer than those observed in agricultural environments. It furthermore appears that the environmental half lives of Chernobyl derived ^{137}Cs are shorter that those of global fallout ^{137}Cs; this has at least been the case in the first 4 year period after the Chernobyl accident. Both observations should be taken into consideration when the doses from the Chernobyl accident are estimated. Finally it is the intention to compare transfer factors from soil to vegetation, milk and lamb for radiocaesium in the Faroese environment with those obtained from Ireland, U.K., Sweden and Greece, in order to throw light on the variability between semi-natural ecosystems with respect to transfer of radiocaesium.

2.3 ITE Merlewood Research Station, England

The contribution to the programme will involve work on upland heaths which are characteristic of Western Europe. In Great Britain, at least, these areas have received considerable fallout from the Chernobyl accident. They are grazed by sheep and wild animals such as deer and grouse, which are taken as a crop, and present a direct pathway back to man. The site for the main investigations has been chosen as a high deposition area at Loch Laggan, Scotland with subsidiary sites in New Galloway, Scotland and at Ennerdale in the English Lake District. The work programme consists of:

a) The collection and analysis of vegetation and soils from the sites, gamma spectrometry on all samples plus physical and chemical analysis of all samples. This will enable the distribution of radionuclides and their movement to be described.

b) The determination of biological activity by infra-red gas analysis to see if this affects the availability of radiocaesium for plant uptake.

c) A laboratory experiment to investigate the effect of transpiration rate on radiocaesium uptake. This will help answering the question as to whether the movement is merely mass flow or if other physiological factors come into play. Depending on results this work may be extended.

d) Intercomparison studies both at the level of laboratory analysis and the collection of plant species common to all participating countries.

e) Providing information on the consumption of material and the levels of radiocaesium in animals. This data will come from previous research carried out by ITE Merlewood.

2.4 Swedish University of Agricultural Sciences

The aim of the study is to obtain a deeper understanding of the behaviour of radiocaesium in the forest ecosystem in the central part of Sweden. The transfer of ^{137}Cs from soil to plant as well as plant to animal will be studied. The study area is located 40 km from Uppsala where the deposition of ^{137}Cs is about 40.000 Bq m^{-2}. The forest is mainly conifers intermixed with some deciduous trees. The ^{137}Cs activity concentrations in game animal-moose and roe-deer have been studied since 1986. Up to now there seems to be no decrease in the ^{137}Cs activity concentrations in these animals. The mean ^{137}Cs activity concentrations in moose (n about 250) were 760 Bq kg^{-1} in 1986, 660 in 1987, 800 in 1988 and 740 in 1989. Roe-deer show very large seasonal variations with the highest levels during August-September with a mean of 8.000 Bq kg^{-1} in 1988. Intake of fungi seems to be the main reason to this large seasonal variations. The ^{137}Cs activity concentrations in plant samples have also been rather similar during the 5 vegetation periods after the Chernobyl accident. There has been a significant decrease in bilberry and lingonberry but in most other plants the levels are still rather similar to those found in 1986. The highest levels are found in fungi with a mean of more than 50.000 Bq kg^{-2} (dw). Among higher plants species belonging to the Ericacea family have the highest levels. Heather for example show about 12.000 Bq kg^{-1}.

The ^{137}Cs activity is found in the upper part of the soil profile where as much as 95% can be found in the upper 5 cm. Studies of the plant availability of radiocaesium in the system are in progress.

2.5 Aristotlean University of Thessaloniki, Greece

The work being undertaken in Greece is a study of the behaviour of radiocaesium in an unmanaged peat area grazed by sheep and both soil-plant and plant-animal studies will be undertaken. This site is in marked contrast to the Atlantic ecosystems being studied by the other participants. The data produced can also be compared with a highly cultivated basin sedge peatland site where the soil-plant transfer of radiocaesium has previously been investigated.

A26 Development of countermeasures to reduce the contamination in the environment and to impede its transfer to man

Contract Bi6-325 Rehabilitation of soil and surface after an accident (RESSAC)
Bi6-122 (CEA Association)

Coordinator CEA - Cadarache
Commissariat à l'Energie Atomique - CEN de Cadarache
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Total Contribution by the Commission: 882 kECU
24 months from 1/01/89 to 31/12/90 (500 kECU)
12 months from 1/01/91 to 31/12/91 (202 kECU + 1 Commission staff)
Associated research (180 kECU)
Participating Scientists

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Associated Research:

Contract Bi6-326
Design and development of a skim and burial plough for reclamation of contaminated land
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Risø National Laboratory
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65 kECU

Contract Bi6-327
Study of the transfer of accidentally released radionuclides in agricultural products with the aim of developing appropriate countermeasures
Dr. R. Kirchmann
Faculté Sci. Agronomiques Gembloux
Unité de Physique et Chimie Phys.
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Tel. 81-611576
50 kECU

Contract Bi6-329
Chemical treatments to reduce the transfer of caesium radioisotopes to the human food chain after a serious nuclear accident
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65 kECU

BI6-325

Description of research work:

The purpose of this program is to develop countermeasure which facilitate a return to normal living conditions in an area affected by a major nuclear accident. These actions should make it possible to reduce both external exposition due to the deposit of radioactive products and internal exposition due to suspension of these products in the atmosphere and subsequent contamination of the food chain.

Research work is divided in three main chapters: Analytical studies are conducted in order to drive parameters of transfer models, in situ studies allow to investigate the implementation of counter measures in the field, and global studies will be a simulation of an accidental release on a large laboratory scale.

Analytical studies

Soil-plant transfer factors are studied for caesium, strontium, ruthenium and tellure, using different types of soils and crops. For the two first radionuclides a mathematical expression of the transfer factor as a function of the soil characteristics and crop was derived. Work is under progress for the two other elements.

A computer code enabling the calculation of the migration of radionuclides in the soils was written and it is now operational.

In situ studies

The vegetation could intercept a great part of the deposits. Field studies conducted with non radioactive dry aerosols enabled to determine interception factors for more than ten crops (wheat, corn, sunflower, potatoes, grass, salad, beans, peas, beets, Brussels sprouts...) at different growth stages.

The efficiency of farm machinery used to remove the crops out their normal operation range was determined, as well as the resuspension induced by working on contaminated material.

Global studies

Large size lysimeters (soil monoliths of 7 to 8 m3) have been designed. The first prototype was sampled and the regulation system of soil water contents performs in a satisfactory manner.

These lysimeters will be contaminated by a device producing a source term representative of accidental conditions. It is the POLYR furnace, able to increase the temperature of a blend of elements to a temperature of 3000°C. This device is now operational.

The lysimeters and the POLYR furnace will be placed in a special building which construction should begin in the first months of 1991.

Work to be carried under the CEA association

Analytical studies

The soil to plant transfer factors will be determined more precisely for ruthenium and tellurium using aerosol deposition from the real term produced by the POLYR furnace.

Other work will be done on the use of decontaminating nets using superior plants or algae in association with a cohesive matrix like a plastic film.

Future studies will be directed to sod sowing also using rhizome chips and sod harvest on different soil types in collaboration with commercial sod producer. Furthermore, possibilities on critical uses and application as well as the transformation of the existing machines will be investigated.

Finally, field efficiency experiments with stable tracers will be performed and, if possible, trials in radioactively contaminated country sites will be prepared and carried out.

The use of polysaccharides in order to adsorb radioactive products, thus making them unavailable for plants will be investigated.

In situ studies

Wet deposition will be considered. Some experience has already been gathered on the simulation of rain and the granulometry of droplets; actually droplets between 0.5 and 2.0 mm diameter can be controlled and produced. Further studies are directed to the full simulation of rain taking into account droplet diameter plus density, rainfall velocity necessary for the bursting effect of droplets, pH, temperature, wind speed and terminal speed of rain, and the intermittence of rainfall.

As defoliation experiments are cannot be realised in situ, they were done in a tunnel.

Defoliation should be done with non-toxic agents in order to save the plants and trees. In 1990 defoliation tests have been made with thinning hormones (abscission hormones) normally used in agriculture for better fruit production.

Defoliation experiences are foreseen using alpha-Naphthyl acetic acid.

A feasibility study of the decontamination of fresh and dry biomass by aerobic and anaerobic degradation has been carried out.

So far the best conditions were found to be the anaerobic ones resulting in relatively high Cs and Sr dissolution and hence decontamination of the solid biomass. Therefore, in future experiments only anaerobic conditions will be considered and pursued.

Global studies

More lysimeters will be sampled in France and in other European countries.

The POLYR contaminating device will be used in preliminary contamination experiments. A new more powerful furnace facility was set up which will permit temperatures higher than 3000°C. Its final implementation will be in the new RESSAC building.

The RESSAC building will be constructed.

The building characteristics are the following:

For the greenhouse, the temperature will be regulated within 2°C with the following extreme:

- if temperature outside is -5°C, the maximum temperature inside is +18°C
- if temperature outside is +35°C, the minimum temperature inside is +12°C

In any case, the lowest temperature is +2°C. The hygrometry will be regulated within 10%. All the regulation will be computed referring to a climatic databank.

ASSOCIATED RESEARCHS

BI6-326 Risφ National Laboratory

Background and objectives

A considerable reduction in dose rate from contaminated arable land can be achieved by deep ploughing. The disadvantage of this practice is that less fertile subsoil is brought to the surface to replace topsoil. A better plough would be one which removes the contaminated (~ 5 cm) layer and buries it beneath some 50 cm of soil without inverting the (~ 5-50 cm) horizon. Such a plough is not available at present. The object of this project, therefore is to develop a plough to skim-off the topmost 5 cm soil and place it beneath a non inverted soil layer. Apart from the radiation in dose-rate, the contamination will then be much less available for uptake by plants.

A small-scale prototype plough (about 1/10) was built and tested in the field. The results were encouraging and based on this prototype a full-scale version was built and tested but the results were disappointing. The top soil did not fall to the bottom of the furrow. A modified version also failed to meet requirements; the front of the furrow was too high and the soil fell over the shield and partially filled the bottom of the furrow before the topsoil could be placed there.

A much modified version of the plough has now been built and is ready for testing.

Future Work Programme

The latest version of the plough will be tested in October of this year. Should visual inspection indicate that the plough is performing reasonably well the true performance will be assessed by spreading a tracer on the soil surface, ploughing and then determining the vertical distribution profile.

Comment

As expected, the construction of a "skim and burial plough" is proving to be very difficult although considerable progress has been made.

Although the original objective may prove difficult to achieve in the short-term we are probably close to producing a plough which bring about a considerable reduction in radiation levels with only limited loss in soil fertility.

BI6-327 Faculté Sciences Agronomiques Gembloux

The objective of the study is to define the countermeasures to be applied in order to improve the radiological quality of agricultural products after a major nuclear accident at a NPP (PWR type).

In order to reach this goal, one should consider two main phases:

1. Identification of sensitive soils and agricultural products in the near and intermediate fields; experiments on the behaviour of the radionuclides (Cs, Sr released from the simulated PWR source-term) in the soil-plant-animal food-chain transfer;

2. Experimental research to define the parameters and the methods to reduce the transfer along the soil-plant-animal food-chain and to investigate the possible use of industrial process to reduce the level of radioactivity in the end products of the plant and animal production.

The project is of co-operative nature among all Belgian laboratories interested in this field in particular:

- The Faculty of Agricultural Sciences (Gembloux) (Various research units);
- The Belgian Nuclear Establishment (CEN-SCK Biology Department);
- The University of Liège (Lab. of Radioecology).

There is also a close co-operation with the SERE/CEN Cadarache and co-ordination with other countries through the IUR Working Groups.

2. Identification of sensitive soils and crops

2.1. Methodology

The identification of the sensitive soils and crops from the radio-ecological point of view lies on the confrontation on the one hand of the results of the soils and agricultural products surveys, and on the other hand of the soil-to-plant transfer factors.

Theses surveys were realised on the Belgian territory; in a radius of 15 km around the NPP of Tihange, Chooz, Doel. For each of them, it was proceeded as follows.

a. The soils classification requires the knowledge of the parameters that influence the transfer of radionuclides from soils to plants.
The most important of them (texture, hydric conditions, presence of lime), as far as agricultural ecosystems are concerned, are taken into account in the Belgian Soil Map published by I.G.N.
So gathering the cartographic units, six soil types, based on these three parameters, were retained.

b. The question of the agricultural products was achieved according to two ways.
The first one is a statistic one. It was carried out by counting in each commune around the relevant sites, the areas devoted to specific crops (grass, cereals, root fowls, sheep). The original documents are provided by agricultural statistics of the belgian I.N.S.
The second one was performed by using remote sensing (Landsat image) which allowed to localize the agricultural areas but also to compare these ones with the soil map produced at the same scale.

c. That stage allows the determination, in each point around the NPP, of the soil-plant association. Then the superposition with transfer factors was made, in function of the qualitative and quantitative results of the surveys. The transfer factors values used were provided by the data bank worked out by the IUR's Working group on soil-to-plant transfer factors.

3. Soil-to-plant and plant-to-animal experiment

3.1. Aim of the experiment

The experiment is designed to investigate the consequences in a pasture ecosystem of the deposition of radioactive aerosols released after a nuclear accident. It considers two important aspects of the fate of the deposited radioactivity: on the one hand, the transfer from contaminated grass to cow's milk (CEN/SCK, Mol) and, on the other hand, the migration of the radionuclides in a specific soil and their transfer to newly growing vegetation (FSA, Gembloux).

The fate and behaviour of the radionuclides released as particles (availability for milk transfer, availability for soil-to-plant transfer and mobility in soils) is being compared with that of soluble forms. This work can be considered as preliminary phase, prior to studies on countermeasures to reduce the radio-contamination in pastures in products from animals grazing on these sites.

3.2. Material and methods

a. Plant and soil material

Surface horizons of soil (mat layer) with standing vegetation were collected at Dion (near Beauraing and Chooz) by the FSA (Faculté des Sciences Agronomiques) Gembloux during March. These soils, from an old permanent pasture, are representative of the region. They are stony loamy soils with a schistous charge (FAO classification: eutric cambisols). The stony loamy phase is 40 to 80 cm deep and lies directly on the bedrock. The pedologic characteristics (pH, granulometry, CEC, ...) of this soil were determined on samples taken at various depths (up to 25 cm).

12 mat layers (100 x 70 cm), about 10 cm thick, were placed in polyethylene trays (100 x 70 x 24 cm). laterally and underneath sustained by a wooden frame. The mat was laid on glass-wool and white sand to reach a total height of 20 cm. The plastic trays were provided with an exhaust at their bottom to allow percolation of the water through the soil. These soils were stored at Mol (CEN/SCK) until use.

b. Radionuclides used and minimum activities needed for each month of contamination

Two elements were chosen in relation to their importance after an accidental release of radioactivity from a nuclear power plant :Caesium and Strontium

Caesium: ^{134}Cs about 1 MBq on vegetation
Strontium: ^{85}Sr about 1 Mbq on vegetation

The estimation of the activity for Cs is based on the results of a previous experiment on cow with CSCl; the activity for Sr has been deduced taking into account its gastro-intestinal absorption relative to that of Cs but without correction for differences in counting efficiency.

BI6-329 Universitá di Piacenza

The project includes two plots: one regarding the agrochemical aspects and the other the zootechnics aspects.

Agrochemical aspects (Responsible: S. Silva)

When a serious nuclear accident occurs the radioactive fallout that concerns the aerial parts of the vegetation is transferred to the fruits and may involve a serious risk for human health. The destruction of the crops is certainly a drastic and antieconomical remedy. Therefore it is useful to search for right remedies to reduce foods contamination. In this research the possibility has been studied to reduce the radiocesium transfer to the edible parts of some plants by means of foliar fertilizations with potassic salts. Three plants species, barley, wheat and tomato arfe considered.

Zootechnics aspects (Responsible: V. Cappa)

The general aim of the research is to study the possible ways to reduce the radiocaesium transfer to meat and milk from feeding contaminated feeds to livestock. For this scope in the first year trials Ammonium Iron (III) Hexacinoferrate (II), hereafter indicated as AFCF, was administered in two equal portions during the morning and evening feeding at the rate of 0.33g /head/day and 5 g/head/day respectively to growing sheep and milking cows who received radiocaesium contaminated hay from Chernobyl accident. The results obtained show that AFCF is an efficacious product to reduce radiocaesium transfer to meat and milk.

The second year researches are programmed with three main scopes:

1) to study whether higher doses of AFCF would further reduce radiocaesium transfer to meat from feeding contaminated feeds;

2) to study the effect of AFCF administration once a day instead of twice a day on radiocaesium transfer to meat and milk from feeding contaminated feeds to ruminants as one administration requires less labour particularly for grazing animals;

3) to find out other efficacious products that can reduce radiocaesium transfer to meat and milk from feeding contaminated materials to ruminants.

In order to attain the above mentioned objectives two trials, one with sheep and the other with milking cows were programmed.

SHEEP TRIAL

For the trial 10 adult female Sarda sheep were bought and were fed with radiocaesium "uncontaminated" hay pellets supplemented with concentrates containing minerals and vitamins. After two weeks the animals were subdivided into 5 groups of two animals each and four groups received radiocaesium contaminated hay pellets from Chernobyl accident at the rate of $50g/kg^{0.75}$ l.w.in two equal meals administered in the morning and in the evening for 20 days. The total radioactivity of the hay pellets was about 4725 Bq/kg (615 and 4110 Bq from ^{134}Cs and ^{137}Cs respectively). Besides the hay pellets, group 1 received 200 g/head/day of pelleted concentrate feed containing 1 g of AFCF in two equal meals as hay pellets; group 2 received the same concentrate at the same rate but in one meal during the morning feeding; group 3 received 250 g/head/day of pelleted concentrate containing 50 g bentonite administered in two equal meals as the group 1; group 4 received 200 g/head/day of normal concentrate without AFCF or bentonite in two meals, while the group 5 continued to receive the "uncontaminated" feeds as before.

COW TRIAL

Eight milking Friesian cows of our Institute were subdivided into 4 groups of two animals each (one with high and the other with low milk production), All animals received the same type of ration consisting corn silage, hay and pelleted concentrates but supplied according to milk production. All 8 animals received 40 g of soybean meal artificially contaminated with ^{134}Cs (provided by the Institut de Protection et de Surete Nucleaire, Cadarache) in two equal meals administered in the morning and in the evening for 14 days. The total radioactivity received by each animal was about 4500 Bq/day. Besides the contaminated soybean meal, group 1 received 5 g/head/day of AFCF in two equal meals as soybean meal; group 2 received the same amount of AFCF but in one meal in the morning; group 3 received 300 g/head/day of bentonite in two equal meals as the group 1, while the group 4 received neither AFCF nor bentonite. Daily doses of contaminated soybean meal, AFCF and bentonite were mixed respectively to 360, 200 and 1000 g of normal concentrate and pelleted which substituted equal amount of normal concentrate in the ration of the animals in the respective groups.

Total milk production for each animal was measured daily and milk samples were collected before the start of feeding contaminated soybean meal and during the feeding for measuring the radioactivity.

A26 Development of countermeasures to reduce the contamination in the environment and to impede its transfer to man

Contract Bi7-046 Transfer of accidentally released radionuclides in agricultural systems (TARRAS)

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Total Contribution by the Commission: 432 kECU
24 months from 1/06/90 to 31/05/92

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Description of research work:

INTRODUCTION

The assessment of the radiological consequences of an accident in a nuclear plant rely on the quantification of several processes in the transfer of radionuclides along the food chain. This is particularly important in the case of a contamination of a large area where the doses will be mainly influenced by the deposition and transfer processes as well as the ingestion pathways.

The response to the Chernobyl accident has demonstrated that certain known processes and parameters such as the change in time of radionuclide availability, the dynamic behaviour of deposited activity and the influence of food processing on the radionuclide content in food, need to be investigated more accurately. These facts confirm the need for new experimental evidences to quantify the relevant processes with a source term as close as possible to real accidental conditions.

The use of reliable parameters and accurate description of processes are essential for the pre-accident assessment modelling, have serious implications on the establishment of the derived intervention levels and for the implementation of protective measures designed to mitigate the radiological consequences of an eventual accident.

The aim of this project is to contribute to the reliability of radiological assessment methods and to establish sound scientific bases to be used in the design of post-accident countermeasures. Three main aspects will be considered in the project:

- A simulated accidental source term will be used and the behaviour of aerosol deposits containing Sr, Cs and Ag isotopes will be followed in some European soil-crop systems.
- The extent of radionuclide transfer rates trough the food chain as modified by well established food processing techniques will be studied for Sr, Cs, Co and Ru.
- A study of specific mediterranean data and environmental factors aimed to an identification of the relevant differential characteristics and lack of appropriate data for the dose evaluation in southern Europe.

These studies are intended to be complementary with other CEC funded projects such as the RESSAC and COSYMA programs and consequently special attention will be paid to the coordination with other related projects.

WORK PROGRAM AND OBJECTIVES

The behaviour of radioactive aerosol deposits will be studied using a source term as similar as possible to accidental conditions. To achieve this objective CEN-CEA Cadarache has developed a particle generating system. Some of the relevant radionuclides in nuclear accidents and 12 other elements present in the reactor core will be volatilized by heating at high temperature (3000° C).

These particles will be characterized and the physico-chemical processes involved in their deposition on typical crops will be studied.

The research will start with lettuce (Lactuca sativa) one of the most universal plants in vegetable gardens and wheat (Triticum aestivum) one of the most important cereals in Europe.

Two types of soil will be used, a French one and a Spanish one. Both types of soils where chosen taking into account the fact that they will also be used in the CEC RESSAC Program.

The fractions intercepted by plants, adhered to leaves, directly absorbed, as well as the dynamics of leaf wash-out, root uptake, migration in soil and speciation will be studied in different growth stages of the lettuce plants. The soil-plant dynamics, the activity transfer to mature grain will be described for wheat sown in soil contaminated by aerosol deposits.

The factors that modify the radionuclide content in food processing and the potential contribution of those factors for dose control in the event of an accident will also be studied. Radionuclides and/or stable elements to be analyzed include Cs, Sr, Co and Ru.

The processes to be studied include freezing, drying, canning, milling, juice extraction, dairy processing and normal culinary operations. In Britain, vegetables to be studied are potatoes, carrots, peas, brussels sprouts and mushrooms. Wheat (milling) will also be included. In 1991, oil production from rapeseed and fruit juice extraction (apple and blackcurrant) will be studied. In France, studies will be made on the processing of haricot beans, tomato and grape juice, salad vegetables, sugar beet, rice and olive oil. In both Britain and France, some dairy products will be examined, including milk, fats, cheese, and powders of milk and whey.

Finally, the project will include a study on the specific mediterranean data that will be compared with currently used generic parameters and the relevant data that are lacking will be identified. Additionally some relevant soil/plant transfer factors for Sr and Cs isotopes will be obtained.

PARTICIPANTS

PRYMA/CIEMAT (D.Cancio): Coordination of the whole project. Derivation of transfer parameters from experimental data and application to a dynamic model. Comparison of those parameters with currently available parameters and models. Collaboration with the experimental work in Cadarache.

CEA/IPSN/CADARACHE (G.Deville): Production and characterization of aerosols for the contamination of soils and plants. Study of the behaviour of the deposits on plants.

UNIVERSITY OF BARCELONA (G.Rauret): Characterization of soils, mineral balance in plants, chemical speciation of radionuclides in soils and plants.

HARWELL/UKAEA (Dr.Cawse): Supply and characterization of agricultural raw materials (from soils of regions with known radiological burdens, additionally labelled if necessary). Measurement of radionuclides and relevant stable elements in raw materials and processed food.

UNIVERSITY OF READING (A.Grandison): Analysis of British factory food processes. Study of the radionuclide content in food products, before and after standard industrial food processing, and experiments in pilot plants.

CEA/IPSN (C.Colle): Analysis of the main food processing procedures in the French industry. Study of radionuclides in some French products before and after industrial food processing.

PRYMA/CIEMAT (J.Gutierrez): Study of agricultural production, diet and transfer factors in the mediterranean area. Assessment of the differential characteristics relevant for the dose evaluation procedures.

WORKING PLAN

A) Experimental aerosol-radionuclide transfer

Sampling of soils in Spain ("Terra rosa") and France (alluvial soil). Physicochemical characterization. Lettuce planting and onset of cultivation. Preparation of the blend of elements to be burnt in the furnace. Sampling of the particles produced by CEN/Cadarache.

Soils #1 and #2 with mature lettuce plants are contaminated. Analysis of wash-out and interception in mature lettuce samples. Analysis of samples in Barcelona.

Wheat is sown. Soil contamination shots #3 and #4. Study of soil-plant concentration factors in two kinds of soils. The contamination of roots, stem, leaves and seeds will be studied.

Lettuce is sown. Shots #5 and #6. Study of soil-plant concentration factors in two kinds of soils. The contamination of roots, stem, leaves and seeds will be studied.

Study of samples #3, #4, #5 and #6. Preparation of the report from the previous experiments.

Analysis of samples #3 and #4 is completed.

Shots #7 and #8. Contamination of lettuce in two kinds of soils. Investigation of the interception capacity of lettuce.

Analysis of samples #7 and #8.

Shots #9 and #10. If reproducibility in the aerosol has been achieved, young lettuce will be contaminated in order to measure their capacity of interception. If no reproducibility is achieved, tree different growth stages will be contaminated, in order to measure their respective interception capabilities.

Analysis of shots #9 and #10.

Analysis of results, data analysis and modelization. Preparation of the report, theoretical conclusions. Comparison with parameters used by models. Identification of future research needs.

B) Food processing parameters:

a) HARWELL: Control of cultivation and provision of crops with relatively high concentrations of Cs-137 and K-40 to be processed in pilot facilities at Reading University.

Identification of the most important processes that modify the concentration of radionuclides in food (in coordination with Reading). Sub-samples of the prepared food will be stored, enabling eventual analyses of other isotope concentrations such as uranium and thorium.

b) READING: 70% of the effort in Reading will be devoted to measurements using the pilot facilities. Identification of the most important processes that modify the concentrations of radionuclides in food, using products from regions having relatively high concentrations of radionuclides.

c) CEN/Cadarache: Non-specific consumption products, as vegetables, rice, fruits, oils and dairy products will be studied in order to characterize the effect of industrial processes.

C) Mediterranean Characteristics and Data

Bibliographic research on usual cultivation, production, consumption diets, and differential characteristics in Spanish mediterranean areas.

Sampling of characteristic Spanish soils and crops. Measurements. Soil/plant transfer factors for selected crops.

Analysis of the results. Assessment of the relative importance of crops, included exported quantities. Evaluation of food consumption and dose. Comparison with other regions.

B CONSEQUENCES OF RADIATION EXPOSURE TO MAN; THEIR ASSESSMENT, PREVENTION AND TREATMENT

B1 STOCHASTIC EFFECTS OF RADIATION

B11 Interpretation of low dose and low dose rate effects with the help of microdosimetry

Contract Bi7-032 Biophysical models for the effectiveness of different radiations.

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Total Contribution by the Commission: 319 kECU
24 months from 1/05/90 to 30/04/92

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Description of research work:

1. Introduction

This project does experimental and theoretical research towards a better understanding of the biological radiation actions of different radiation fields with particular emphasis on low doses and low dose rates. It aims at an improvement of our present knowledge on somatic and genetic radiation risks of man and to help develop radiation protection instrumentation measuring the characteristic properties with regard to these endpoints in mixed radiation fields. In addition, the combined action of radiation and chemicals (also of those prevalent in the environment) will be investigated on a mechanistic level. This goal shall be reached by the development of new models based on

- the improvement of biophysical track structure calculations for relevant radiation fields (photons, neutrons, electrons, ions) in particular by introducing structured cell geometry, condensed state cross sections, time dependency, and chemical and biological reactions; various codes of other authors will be compared in critical bench mark calculations;

- the analysis of such physical-chemical-biological track structures will be improved using new cluster algorithms and by testing biophysical models developed by participants 3 and 4.

- selective radiation biological experiments with soft X-rays and UV-photons will be performed, as well as with alpha-particles and gamma-rays; the biological systems will include appropriate transformational and inactivation assays, etc.

The usefulness of a better understanding of radiation effects on members of the public has often been described in the radiation protection literature. This understanding is necessary also to improve the protection of workers and the public in the ALARA-sense of the IRCP, where over-estimations of radiation risks might lead e.g. to a not optimum allocation of large resources.

Collaboration is foreseen with other projects working on the improvements of dosimeters and on biological radiation effects.

2. Overview on Sub-Tasks

Partner 1 (GSF) will improve the physical track structure codes for fast electrons, photons, neutrons, protons, alpha particles and HZE ions encountered in space, he will introduce complex geometry describing structured targets and condensed state cross sections for the DNA and other relevant biological molecules.

Partner 2 (CPA) will improve the cross sections for slow electrons and apply a different approach to condensed state cross sections (to permit a sensitivity study), he will be the leading partner in the intercomparison of results from various other track structure codes in a benchmark and validation study, and he is responsible for the introduction of the chemical reactions in the common code.

Partner 3 (MRC) will analyse dedicated track structures calculations to test and improve his biophysical model for radiation actions of different fields, he will accumulate for the comparison of theory and experiment selected radiobiological data from the literature and will perform own experiments with soft X-rays, alpha particles, etc. using appropriate combinations of genetic, chromosomal, transformational and inactivation assays.

Partner 4 (RIVM) will analyse results from dedicated track structure calculations in the framework of his DNA damage model, will try to make a sensitivity analysis of model parameters to understand their significance and the influence of different irradiation conditions. He will investigate the interaction of radiation with other DNA damaging agents to better understand the influence of such agents on the effects of low radiation doses. He will experimentally study effects of UV´ radiation of different wavelengths and the interaction with damage from gamma irradiation. The predictions of models of partners 3 and 4 will be compared.
All partners finally will try to derive conclusions regarding the quantification of stochastic risks at low doses and dose rates.

GSF

GSF will mainly contribute to this project the improvement of biophysical track structure codes and help in the interpretation of cellular radiation action models developed by the partners MRC and RIVM.

The track structure codes developed in the framework of the previous CEC programme will be improved by taking into account also the recombination in the fields of ions, introduction of complex geometry routines on a μm to cm level as well as on the atomic level, extending the cross section base for heavy charged particles above and below the present energy range as well as for high energy electrons. GSF will also participate in the validation study to be coordinated by partner CPA. GSF will use its expertise in the analysis of somatic radiation risks to improve the present knowledge in this field based on the outcomes of the biophysical modelling work on cellular levels by partners MRC and RIVM.

CPA

In this project the CEA continues to improve simulation transport codes and develop new ones to get inchoate distribution from low energy (eV to 10 keV) electrons and photons and time-space distributions of all chemical species set in motion following or during the irradiation, while the GSF codes are needed to obtain the inchoate distributions. Data obtained together are then used by participants MRC and RIVM. According to the objectives, calculations and results will be discussed and reoriented, when necessary.

During this and last years the CPA has set up computer codes to obtain the complete transport of electrons and the chemical evolution of species created during the slowing down of one particle in liquid water giving the radiolytic species distributions: e_{aq}, $^{\cdot}OH$, H_3O, $^{+}H_2O_2$, H_2, in a four coordinates system: x,y,z,t for each species. These data will then be used by participant MCR as input to calculate and form a data set of energy deposition and species distributions in 1-100 nm volumes. With participant RIVM the data will also be used to calculate the efficiency of the production of DNA strand breaks as a function of various parameters: incident energy, species, time.

Using the concept of "clusters" developed for our chemical code we shall try to determine the continuous background yields of species during irradiation as a function of the dose rate, taking into account overlapping of tracks and species reactions in time and space up to tens of seconds.

The model permits the addition of solutes able to react with the irradiated system species allowing, for instance, a study of the oxygen effect. We shall introduce various scavengers to theoretically test the radio-sensibility and furnish the obtained distributions to radiobiologists or radiotherapists.

Simulation codes will be improved by comparison with other experimental or theoretical work. We shall do intercomparisons of results obtained with other existing codes in the world, for instance, those of GSF, Kaplan (USSR), Turner (USA), Ito (Japan), Zaider (USA), Waibel (RFA), and Berger (USA).

MRC

The MRC will compare the microscopic features of tracks of diverse radiations with their observed effectiveness in producing biological changes, in order to assess what physical properties of tracks may be primarily responsible for their stochastic biological effects and to use controlled variations in track structure as a fine probe of the subcellular mechanisms of radiation action. This will include

a) analysis of statistically representative tracks generated by existing Monte Carlo track structure codes of participants GSF and CPA in the project. This will allow comparison between a wide range of different radiations (including electrons, X-rays, protons, α-particles and neutrons) and between the different Monte Carlo codes. Comparison with different codes will be extended further by limited analyses of tracks obtained from the Oak Ridge code of Hamm et al. and possibly other codes if available.

b) selective accumulation of radiobiological data in mammalian cellular systems, by experiment and from the literature, which allow systematic comparison of biological effectiveness with particular features of radiation tracks. These radiations will be selected for their analytical precision, their suitability as well-defined probes of microscopic features and their practical relevance. Ultrasoft X-rays will be used because of their precision as intracellular microscopic probes and because of the large contribution from electron track-ends in all low-LET radiations. Slow α-particles (some MeV) will also be used because of their well-defined tracks, with dominant high-LET characteristics, and also their practical relevance to emissions from natural and artificial radionuclides in the environment. Other radiations will be included for reference and comparison. Biological systems will include appropriated combinations of genetic, chromosomals, transformational and inactivations assays of stochastic effects in a variety of mammalian cell types, including human and rodent fibroblasts, lymphocytes and haemopoetic multipotent cells in established and primary cultures.

c) comparison of the results of the track structures analyses with the radiobiological data to identify track features which may be of critical importance in determining biological mechanisms. Our studies have pointed to the prime importance of highly localized clusters of initial physical damage. Consequences of our modelling studies, based on track analyses and radiobiological data, will be compared with other modelling approaches, particularly those of participant RIVM.

RIVM

The aim of the RIVM contribution is to continue the development of a comprehensive biophysical model for the analysis and interpretation of radiation biological effects on the basis of energy deposition in a specific molecular target.

The work will consist of both a theoretical and an experimental part. The theoretical approach will involve the improvement of an analytic track structure model to characterize the spatial energy deposition at nanometer dimensions for different types of radiation. This model will be used to analytically calculate the probability of inducing DNA damage and to relate this damage to cellular effects. A sensitivity analysis of the model parameters will be made to understand their significance for the magnitude of the effect and the influence of different radiation conditions. The results will be compared with those of the models of GSF and CPA and with the analysis of MRC.

In addition we will deal with the analysis of the interaction of radiation with other DNA damaging agents. This analysis of combined effects at the cellular level will be used to provide a better understanding of the combined dose-effect relationship and the influence of other agents on the radiation effects at low doses.

The experimental approach will study the cellular effect of ionizing radiation in combination with different wave lengths of UV radiation. Results from work in the current contract indicate that interaction occurs between 254 nm UV and gamma-radiation which appears to be independent of time between the two radiations and their sequence. It is known that 340 nm UV induces a different type of DNA damage than 254 nm UV, and that this damage behaves similarly to ionizing radiation induced damage. Comparison of the effects and interaction of the different types of radiation should provide insight in the mathematical from of the dose-effect relationships, and the role of repair on the shape of the dose-effect relationship.

B11 Interpretation of low dose and low dose rate effects with the help of microdosimetry

Contract Bi7-040 Specification of radiation quality at the nanometer level.

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Total Contribution by the Commission: 176 kECU
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Description of research work:

Research concerning the best way of specify radiation quality for radiobiology and radiation protection by physical parameter expressing the track structure-target structure relation remains a central task of microdosimetry. Since both molecular biology and radiobiological analysis (track segment method) suggest critical target sizes of few nanometre cellular radiation effects, the imperfection of present microdosimetric simulation of volumes in the micrometer range have become evident. For all ionizing particles or particle configuration (e.g. Auger cascade) which produce a high concentration of deposited energy on the nanometer scale, but having ranges much smaller than the micrometer dimensions, the spatial resolution of present microdosimetric detectors is inadequate. The project has four main aims.

1. Track structure studies for nanometer targets

Aim: to establish the approximated constancy of the delta-ray contribution to the energy deposition fluctuation in a nanometer target. To establish the constancy of the radio of restricted LET to linear primary ionisation.

Track structure studies, based on computer simulation, recent cross section and adequate statistical concepts such as distribution parameters, pattern recognition and target modelling, will provide the physical basis for validation of the proposed quantities linear primary ionisation or restricted LET. The phenomenon of O-ray cutoff at manometer target boundaries will need further study and the proposed close correlation of these quantities with lineal energy in simulated nanometer volumes will have to be substantiated. The work will include update cross-sections and genomic target structure.

2. Biological validation of the best suited parameter

Aim: to select bench-mark sets of survival, chromosome aberration and molecular lesion data to test and confirm the ability of linear primary ionisation and restricted LET to determine their variation with radiation quality.
The ultimate decision concerning the suitability of the new radiation quality parameters must be provided by their ability to predict the dependence of radiobiological yields on radiation quality. This work, already started by the cooperation groups in promoting linear primary ionisation or restricted LET, needs further effort in broadening the biological data base and stepping forward from retrospective analysis to predictive approach.

3. Experimental studies of associate detector systems

Aim: to measure the ionisation pattern around charged particles tracks and study a portable device able to simulate T.E. volumes of few tens of nanometers in size.

The actual experimental studies, which aim to determine the lowest simulation limit of slow ions as probes to explore the avalanche characteristics of single-wire and field-grid TEPC. A tissue-equivalent multi-step parallel plate avalanche chamber will be manufactured to measure single ionisations in order to study the correlation between primary ionisation and restricted LET. The possibility to manufacture a small cylindrical avalanche chamber will be studied. In parallel with the gas-filled detectors, a feasibility study will be carried out with the object of simulating the biological response to radiations in nanometer dimensions in condensed phase detectors. The optimum method will be selected, guided by the biological analysis, and work will begin on a device.

4. Quantification of indirect action from single tracks.

Aim: to conduct an experimental study of the yield and spatial distribution of paramagnetic free radicals formed in the wake of individual tracks by measurement of relaxation time and using ESR technique. To compare the experimental results with the predictions of a simplified theoretical model of biological effectiveness .

ESR measurements will be used to explore the spatial distribution, mean life times and reaction rates of free radicals generated by charged particle tracks in nucleic acids, proteins, aminoacids from cell cultures and possibly whole tissues. Measurement of radical density is based upon the dependence of the saturation value of microwave magnetic fields upon the spinspin relaxation time. The possibility of adapting simplified theoretical methods, developed for enzyme inactivation by indirect action, will be explored in an attempt to obtain a more meaningful model of radiation action for radiation protection purposes.

Collaboration schedule

Although the collaborators will support each other mutually by the exchange of theoretical and experimental data, the collaboration main lines will be the following.

Göttingen-Neuherberg	for the track studies.
St. Andrews-Göttingen	for the biological validation
Legnaro-St.Andrews-Neuherberg	for the experimental studies.
Rome-St.Andrews	for the interpretation of the indirect action studies.

B12 Repair and modification of genetic damage and individual radiosensitivity

Contract Bi6-099 Late somatic effects of ionizing radiation on the mammalian organism.

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Total Contribution by the Commission: 444 kECU
24 months from 1/01/90 to 31/12/91

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Description of research work:

The objective of the European Late Effects Project Group (EULEP) is to improve the understanding of late biological effects of exposure to ionizing radiation. Its work consists of the standardization and development of methodology in the member institutions, the co-ordination and promotion of co-operative research by means of task groups, and the organization of training activities, workshops and symposia. Twenty-three laboratories are currently participating in this work. In addition, EULEP has also developed useful links with certain laboratories outside the European Communities.

1. Standardization and development of methodology

The Committee of External Radiation Dosimetry and Techniques is conducting a series of inter-laboratory comparisons of X-ray dosimetry for whole-body irradiation of mice. It is also concerned with physical aspects of total body irradiation in man.
The Committee of Internal Radiation Dosimetry and Techniques is developing co-ordination and standardization in relation to those task groups (see below) which work on different aspects of the dosimetry of radionuclides in the body.
The Committee of Pathology continues to organize slide seminars in an on-going review of different areas of histopathology relevant to the study of late effects. The EULEP Pathology Atlas is being extended by the addition of new sections.
The Committee of Cell and Molecular Biology is mainly concerned with the introduction and standardization of new techniques in molecular biology that are relevant to the development of the Radiation Protection Programme.

2. Co-ordination and promotion of co-operative research

The co-ordination of collaborative research work between the member institutions is organized by means of 15 task groups. Their on-going work is summarized briefly as follows:

Molecular approach to the study of radiation-induced osteosarcoma. This group is engaged on a study of the pathogenesis of radiation-induced cancer at the molecular level. The osteosarcoma studies are highly relevant for man, extending through work on in vitro transformation to tumour histopathology.

Cell and molecular studies on radiation-induced haemopoietic neoplasias. The programme is devoted mainly to studies of myeloid leukaemia in the mouse, at the molecular and chromosomal level. Relationships are sought between specific lesions of chromosomes in leukaemic cells and the possible activation of genes resulting from these which may be concerned with leukaemogenesis itself.

Cell biology of haemopoietic tissues. The work of this group complements that of the previous one, in studies of cells from experimental leukaemia and lymphoma. The role of lymphokines after irradiation, during leukaemogenesis in vivo and also in vitro, is being investigated; other studies are concerned with certain cell membrane receptors in these cell types.

Cellular basis of late vascular changes in the areas at risk in the irradiated brain. Long-term studies have been conducted on damage to small blood vessels in the brain after irradiation; these have included work on regional blood flow, morphology and morphometry of vascular damage, as well as ultrastructural studies. New work is being undertaken on the possible alleviation of this type of damage by treatment with a certain type of drug.

Radiation effects on the heart. New studies by this group are concerned with a comparison of different methods for assessing effects on cardiac function in the rat. This will lead to new work on the correlation of functional and morphological changes in the heart after irradiation.

Effects of irradiation on pre-implantation mouse embryos. Effects of irradiation on very early stages of embryonic development include a variety of end-points such as cell cycle block, chromosome aberrations and biochemical effects; late effects include the study of malformations which can be seen in some strains of mouse.

Effects of radiation on the development of the central nervous system. The aim of this task group is to assess radiation-induced damage to the foetal CNS by means of animal experimental models. A number of related end-points have been studied, including structural defects in the developing brain, atrophy and cell depletion in different regions, lectin-binding sites on neuroblasts in several regions of the embryonic brain and behavioral studies on young mice which have been irradiated in utero.

Radiation-induced carcinogenesis in the liver. Co-operative studies are being undertaken on life shortening and tumour incidence, particularly in the liver, after irradiation with X-rays, gamma-rays and neutrons. The effect of age on mouse liver carcinogenesis is also being studied following combined treatment with radiation and diethylnitrosamine. Related cellular and molecular studies are also being undertaken.

The remaining task groups are all concerned with the dosimetry and effects of internally incorporated radionuclides:

Interspecies comparison of lung clearance. Comparisons are being made of the clearance of inhaled particles from the lungs of different species, with special emphasis on the rate at which particles can dissolve in the lung. In vivo experiments are being complemented by studies of alveolar macrophages in vitro. The aim is to understand how best to extrapolate lung clearance data from animal experiments to man.

Deposition and clearance of inhaled particles in the human respiratory tract. This group is concerned with the development of models of lung clearance in man which are used to assess the risk of carcinogenesis from inhaled radionuclides. Much of the work is concerned with the interpretation of data from human volunteer studies.

The reduction of risk of late effects from incorporated radionuclides. These co-ordinated studies are concerned with the overall effect and mode of action of treatment with chelating agents designed to enhance the elimination of radionuclides from the body. Special interest attaches to work on new chelating agents which are under development.

Stem cell studies after contamination with α-emitters. Co-ordinated studies are designed to investigate the effects of α-emitting bone-seeking radionuclides on target cells in mouse bone marrow. The objective is to detect early changes in primitive haemopoietic and osteo-progenitor cells in the development of leukaemia and bone tumours. The sensitivity of stem cells in different parts of the bone marrow is being studied. Other studies concern the effects of α-emitters on the micro-environment of stem cells in the marrow. This has been shown to be important both in the development of leukaemia and possibly also of osteosarcoma.

Metabolism, dosimetry and effects of bone-seeking radionuclides. Long-term studies are being co-ordinated on the metabolism, spatial distribution and toxicity of various α- emitting radionuclides. The biological effects studied have included leukaemia, lymphoma and osteosarcoma. Effects of the protraction of the α-dose have been studied and large-scale studies are under way on the effects of low doses. Work is now included on patient follow-up after treatment with ^{224}Ra in patients with ankylosing spondylitis.

Foetal dosimetry and effects of incorporated radionuclides. There is increasing concern regarding the risk to the developing embryo and foetus following the release of radionuclides into the environment. There are no generally accepted models for calculating relevant tissue doses and only limited information on the radiosensitivity of tissues in the foetus and newborn. Accordingly, studies are being co-ordinated on radionuclide distribution and retention in the foetus and newborn animal, on the effects of incorporated radionuclides and on dosimetric models.

Retention and absorption of ingested radionuclides and irradiation of gastro-intestinal tract. The gastro-intestinal tract of the neonate has been considered to be at a special risk from ingested radioactivity. Work has been undertaken on the extrapolation of animal data to man, in the light of notable species differences, e.g. in the retention of plutonium in the neonatal intestine. The possibility of uptake of ingested particulate material into lymphoid tissue of the intestine has also been studied. Finally, there are human volunteer studies on the measurement of intestinal absorption of neptunium and curium, as well as polonium in different chemical forms. The objective of these studies is to determine the availability of radionuclides in the food chain for intestinal absorption.

3. Training Activities

EULEP is taking steps to promote the training of young radiobiologists. High priority continues to be attached to the support of scientific exchange visits between laboratories for the purpose of acquiring technical expertise. EULEP has organised special training courses, e.g. in the fundamentals of molecular biology, in order to promote the introduction of new methodologies into member laboratories.

An investigation is also being made into the teaching of radiation biology throughout the European Community. Efforts to promote teaching in this area are under consideration, in the face of a decline in the number of academic institutions providing courses on this important subject.

B12 Repair and modification of genetic damage and individual radiosensitivity

Contract Bi7-022 Individual radiosensitivity and its relation to colo-rectal cancer

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Total Contribution by the Commission: 190 kECU
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Description of research work:

Aim of the study

In human populations, heterozygote carriers for the gene of familial adenomatosis polyposis coli (APC), mapped on chromosome 5, are highly predisposed to form polyps and subsequently adenocarcinomas of the colon.

This process of carcinogenesis is not simple. Several other genomic alterations are usually involved, and a susceptibility of these individuals to various mutagenes is suspected. A study is developed to look for an eventual chromosomal instability of the patients, in lymphocytes and epithelial cells from polyps and adenocarcinomas. In addition, studies on radiation sensitivity of the lymphocytes are conducted by comparing, in the same families, affected and non affected relatives, using cytogenetic and molecular techniques.

Material and methods

1. Ascertainment of the cases and characterisation

Patients are first ascertained on clinical criteria, in various specialised consultations and clinics of the Paris region. When an APC syndrome is suspected, a familial analysis is performed, and a pedigree established. Then, blood samples of members of the family are obtained. Aliquots of these samples are used for DNA extraction. DNA is cut by different restriction enzymes permitting the detection of polymorphisms, with tested markers located on both sides of the APC gene. Then, using Southern's technique, the haplotype of the chromosomal segment 5q21-q22 is established for each individual.

The 2 haplotypes of each individual are compared with those of their relatives to determine which one is associated with the disease and to localise the mutant gene. This part of the work is performed by the group of Gilles Thomas at the Institut Curie (Paris).

2. Cytogenetic analysis

They are developed in several directions:

(a) Characterization of "spontaneous" chromosomal anomalies in blood lymphocytes. After molecular confirmation of the status of the patients, heterozygote carriers are selected. Short term cultures are developed and 100 R-banded metaphases are analyzed per patient. Each suspected anomaly leads to the establishment of the karyotype. Metaphases from synchronized cultures are also analyzed to detect eventual constitutional microdeletion of chromosome 5.

The same study is developed on patients ascertained for colorectal cancer but without FAP syndrome to obtain a control group.

(b) Cytogenetic study of benign and malignant tumours. Polyps and adenocarcinomas are dissected and cell suspensions are cultured for a short term to obtain metaphases. The karyotypes of polyps and adenocarcinomas from APC and non APC patients are compared.

(c) Effect of radiation on blood lymphocytes. An aliquot of the blood from APC patients and relatives is irradiated by X-rays very soon after sampling in Paris. The blood samples are sent to Louvain where short term cultures are developed. Cell kinetics are studied using a BrdU incorporation technique and the chromosomal lesions of cells exposed to 0, 0.2 and 2 Gy irradiation are scored and compared in APC patients and relatives and in cancer patients without APC syndrome. The clastogenic effect of radiation during G2-phase will be studied in a second step.

Points (a) and (b) are developed in Paris (URA 620 CNRS, Institut Curie) coordinating the research. Point (c) is developed in Louvain by the TEMU Laboratory.

3.DNA breakage analysis

Blood samples from APC patients are irradiated by X-rays at doses of 0.2, 1 and 2 Gy. DNA breaks are analyzed using fluorometric analysis of DNA unwinding (FADN) method. The role of DNA repair systems and in particular the activity of poly (ADP-ribose) polymerase is studied in relation to the production of DNA breaks and the kinetics of DNA repair.

The part played by active oxygen species through modulation of endogenous levels of catalase activity and usage of OH scavengers is also studied. This part of the work, performed on blood samples obtained locally, is developed by the department of Genetics of UNL (Lisbon). Another study will be done by the same group on lymphoblastoid cell lines from APC patients developed at the Institut Curie (Paris).

Progress achieved

A few months after the beginning of the contract, the groups involved have started the accumulation of biological material. Several families in which the APC gene is segregating have been identified and blood samples were obtained. Pedigrees indicating the haplotypes of family members could be constructed, after analysis of their restriction polymorphism. The chromosome studies on non irradiated lymphocytes are being developed on 8 APC patients and 10 cancer non APC patients.

Irradiated blood samples from 3 families were sent to Louvain and scoring of radiation induced rearrangements could start. Cell lines of APC patients are being developed.

B12 Repair and modification of genetic damage and individual radiosensitivity

Contract Bi7-026 The genetic and biochemical basis of human DNA repair and radiosensitivity

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Total Contribution by the Commission: 380 kECU
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Description of research work:

The project aims at understanding the basis of radiation sensitivity in humans and the underlying role of DNA repair. Such knowledge is important for assessing relative radiation risk from one individual to another because people do not all respond equally to radiation. Much of this proposal is concerned with hereditary differences in radiosensitivity due to homozygous effects of DNA repair and related genes, but heterozygous effects are now recognized and, because of their high frequency in the population may be more important in practical terms. The development of more sensitive and advanced techniques for determining radiosensitivity within the normal range is important and will be pursued. The collaborating laboratories will further develop the isolation and characterization of radiosensitive and DNA repair defective mutants and will continue the cloning of relevant genes following the successful cloning of the first human DNA repair gene during the last contract.

We shall also investigate what aspects of DNA sequence or chromosomal organisation are important in determining reparability of DNA damage.

The project carried out in the Department of Radiation Genetics and Chemical Mutagenesis in Leiden is aimed to elucidate the relationship between initial DNA damage, DNA repair and mutagenesis. Research efforts during recent years have enable us to study both mutation and repair in the same endogenous locus i.e. the HPRT gene in various repair deficient cell lines. In this context we will investigate the repair of radiation damage in defined chromatin regions from normal and repair deficient cells, determine mutation spectra in normal and mutagen sensitive cell lines, and isolate and characterize the repair deficient mutants which are essential for these studies. Until now investigations aimed to study the relationship between DNA repair and mutations, are based on removal of DNA damage from the genome overall. However, there is increasing evidence that DNA damage in some domains of the eukaryotic genome is processed more efficiently than in others, and that such heterogeneity in repair would result in corresponding differences in biological responses. Mutagenesis for example could be influenced to a variety of degrees depending primarily on the extent of repair of a particular region of the genome. In this project we will study the repair of radiation induced DNA damage in transcriptionally active and inactive chromatin domains, both at the level of DNA loops associated with the nuclear matrix, and in defined DNA fragments of genes. Of particular interest is the role of transcription in DNA repair. Modulation of transcription of a given locus will provide direct insight in the role of transcription in DNA repair, but detailed analysis warrants an in vitro repair system designed to study the role of chromatin structure in DNA repair. The repair analysis will include the HPRT gene, which is the target gene of the molecular analysis of mutations. Genetic changes at the DNA sequence level will be determined in the endogenous HPRT gene using the polymerase chain reaction. Numbers and types of mutations will be correlated to efficiencies of repair of different types of DNA damage in this gene in different repair deficient and proficient cell lines. For a complete and detailed analysis of the relationship between DNA repair and mutagenesis it is essential to have a large variety of mutagen sensitive cell lines at our disposal. For this purpose, as well as for cloning of repair genes, we will expand our collection of mutagen sensitive cell lines. Cell lines of interest already available for cloning human repair genes, include two groups of mutagen sensitive mutants which show phenotypic homology with either Ataxia telangiectasia or Fanconi's anaemia.

The project carried out at the MRC Cell Mutation Unit in Sussex can be summarized as follows:

(a) New techniques for measuring radiosensitivity.

Conventional cellular assessments of radiosensitivity involve the measurement of the effect of radiation on the ability of skin fibroblasts to produce colonies. We are now using a similar approach with peripheral blood lymphocytes, which takes advantage of our ability to clone the majority of the T-cell population. In addition we are developing the biophysical method of Singh et al. (Expl. Cell Res. 175 (1988) 184-191) in which cells are lysed in agarose and then subjected to an electric field. Under these conditions the DNA streams out as a "comet tail". The size of the tail gives a measure of DNA damage. The technique is rapid and requires cells from only a few microlitres of blood.

The cloning and biophysical techniques are being used to measure variations in radiosensitivity in the population, and within an individual, to assess differences between cell types, as well as temporal variations in radiosensitivity.

(b) Cloning of DNA repair genes.

1. A search is being carried out, using pulse-field gel electrophoresis, for deletions in chromosome 11q22 in A-T cell strains. At least one A-T gene is known to be located in this area.

2. The human gene which corrects the hamster xrs mutants is being localised by microcell-mediated chromosome transfer. This is the first stage to cloning the gene.

3. Genes governing the radiation response of the fission yeast, Schizosaccharomyces pombe, are being cloned by their ability to complement the defect in radiation-sensitive mutants. The cloned gene are being sequenced and compared with similar genes in Saccharomyces cerevisiae. Conserved regions will be used to probe human DNA libraries in order to isolate the corresponding human genes.

The Department of Cell Biology and Genetics of the Erasmus University Rotterdam concentrates on the isolation of genes controlling nucleotide excision repair, a process which is deficient in the cells of xeroderma pigmentosum (XP) patients. ERCC-1 was the first of a series of such genes

isolated by our Dutch group. This human gene corrects ultraviolet light sensitive Chinese Hamster Ovary (CHO) mutant cells of complementation group 1. ERCC-1 is very likely not (yet) encountered as a mutated gene in the in total 8 complementation groups of XP. In addition to ERCC-1 we recently isolated also the human excision repair genes ERCC-3 and ERCC-6. ERCC-3 corrects specifically the excision repair defect of CHO mutants of complementation group 3, ERCC-6 those of complementation group 6. Microinjection experiments of the ERCC-3 cDNA in fibroblasts of various XP complementation groups indicated that this gene is involved in XP complementation group B, which at the same time displays the clinical symptoms of another human repair disorder Cockayne's Syndrome (CS). This finding reveals for the first time overlap between rodent and human excision deficient mutants and represents the first gene involved in XP as well as CS. Analysis of the excision repair genes cloned thus far has revealed a striking evolutionary sequence conservation at the protein level. The human ERCC-1 gene product is homologous to the yeast excision repair protein RAD10 and harbors - in addition - domains with significant similarity to parts of the E.coli uvr A and C polypeptides. The ERCC-3 also has a strongly homologous yeast equivalent, that was unknown until now, but has been traced back using the human gene as probe.

We performed also an evolutionary walk in the opposite direction from yeast, via intermediate organisms to man, using the RAD6 gene (in collaboration with Dr. P. Reynolds, S. and L. Prakash, Rochester). This gene specifies a histone specific, ubiquitin conjugating enzyme and is involved in post-replication repair, a process thought to be affected in XP-variant patients.

These cloned genes provide a good basis for unravelling the functioning and impact of these repair processes in man.

This work is performed by collaborating institutes in the Medical Genetics Centre South-West Netherlands (MGC).

The project carried out at the Institut Curie - Biologie can be summarized as follows:

Fanconi's anaemia (FA) has in common with the other inherited diseases studied by the other laboratories of the group:

a) an abnormal processing of induced DNA lesions (in the case of FA, the fate of DNA interstrand cross-links and of certain types of bulky monoadducts is altered);

b) the predisposition to cancer and c) a high spontaneous and induced chromosomal instability. At the Institut Curie, we are contributing to the common project along the following lines.

1. Having established that FA cells from genetic complementation group A are more affected in terms of DNA repair than cells from group B, we are trying to determine if there is a correlation between the genetic groups and the severity of the FA disease. Particular attention is given to the bone-marrow failure in differentiation.

2. We have demonstrated this year that FA cells show reduced mutation induction at the HPRT and at the Na+/K ATPase (OUA) loci compared to normal. This suggests that FA cells are defective in an error-prone repair pathway and that lesions are chanelled via a recombinational process. In order to test this possibility, the molecular nature of spontaneous and induced mutants ($6\text{-}TG^R$) is examined. The detection of DNA lesions in vitro being established, we are attempting within the suitable genetic probes to detect the same lesions in vivo.

3. Complementation of the FA defect by co-cultivation with FA-like mouse mutants and by DNA transfection. Molecular cloning of the complementing DNA sequences. Characterization of a complementing diffusible factor responsible for complementation by co-cultivation.

4. Chromosomal breaks at low doses of ionizing radiations as analyzed by pulse field electrophoresis and steps of DNA repair in individual chromosome. Use of the YAC system.

At the MRC Radiobiology Unit in Chilton studies will be carried out in three related areas:

(1) The use of recombinant DNA molecules, damaged at specific sites with radiation or radiomimetic agents, to examine the importance of different types of damage in producing gene inactivation. In particular the ability of nuclear extracts from human cells to repair (or misrepair) damage will be examined, using molecular (gel electrophoresis/Southern analysis) and biological (gene expression) methods. Initially, 'model' DNA breaks of various types as generated by restriction enzymes

(overlapping termini; blunt termini; mismatched termini; etc.) will be used, since these can be produced at unique sites which can be analyzed in detail following repair. Cell extracts will be from normal or radiosensitive lines; the normal lines will be used to assess ability to repair different types of breaks, while the radiosensitive lines (including ataxia-telangiectasia; A-T) will be used to assess the extent to which DNA break repair/misrepair is involved in their sensitivities.

(2) The cellular and genetic characterization of radiosensitive mutants of mammalian cells. Recently-isolated radiosensitive mutants will be examined for complementation by fusion to A-T cells and normal human lymphocytes, to establish their genetic similarities and to identify the human chromosome(s) complementing the phenotypes of new mutants. In addition, radiobiological experiments with these mutants will be continued to assess their ability to recover from damage under low-dose-rate irradiation conditions, which seems to relate to repair competence for DNA double-strand breaks.

(3) Analysis of the molecular nature of large deletions in a defined mammalian gene (hprt). Deletions will be examined in two ways: (a) using cytogenetic analysis in combination with pulsed field gel electrophoresis to find the sizes of the deletions and to locate flanking markers, and (b) by the isolation of sequences at which the gene has broken to give the deletions. A series of hamster cell mutants have already been characterized as far as the position of the deletion breakpoints, but we are isolating similar mutants from primary human fibroblasts for which a large panel of informative probes are becoming available. Southern analysis followed by variations on the polymerase chain reaction will be used to locate and isolate breakpoints for sequencing.

B13 Cellular, molecular and animal studies to determine the risk of stochastic somatic effects of radiation with respect to low dose, low dose rate and radiation quality

Contracts Bi6-225/166/223/146/171 Evaluation of the frequencies of chromosomal aberrations induced in human blood lymphocytes by low doses of neutrons.

Coordinator NRPB
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Total Contribution by the Commission: 135 kECU
24 months from 1/01/90 to 31/12/91

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Description of research work:

A study, funded by CEC, was set up essentially to study the effects of low X ray doses using cells from 4 subjects and the results (Lloyd et al, Int. J. Radiat. Biol. 53, 4, 1988) were compatible with a possible threshold at doses less than 20 mGy. This was later extended (still to be published) to blood from a further 20 subjects. Despite large numbers of cells being analyzed the statistical uncertainties on the data were fairly large. Nevertheless a similar conclusion of a threshold could still be drawn. If the low dose response is really linear as has been the usual assumption in radiobiology, it is remarkable that three studies have all shown, albeit each non-significantly, evidence for a low dose plateau in response and a reduction below the control value at 10 mGy or less.

The present project forms an extension of this work to obtain data using low doses of high LET radiation. Samples of blood from 4 subjects will be irradiated at the Fast Neutron Facility at the Reactor Centre Petten, The Netherlands. Expertise from NRPB, together with the staff at the Reactor Centre will be used in the dosimetry. Eight doses (0, 0.25, 0.5, 0.8, 1.25, 2.5, 12.5 and 62.5 mGy) will be used and the incident neutrons have a mean energy of 1.0 MeV. The irradiated samples will be taken to Leiden for culturing for metaphase preparations using a standard protocol. Many replicate slides will be prepared, coded and distributed between the six participating laboratories for microscope analysis. After scoring the data will be decoded and evaluated by statistical programs at NRPB.

B13 Cellular, molecular and animal studies to determine the risk of stochastic somatic effects of radiation with respect to low dose, low dose rate and radiation quality

Contract Bi6-338 Cytological follow-up of individuals exposed in the Goiania (Brazil) accident (study contract)

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Description of research work:

In an accident involving the destruction of a ^{137}Cs source (1325 Ci) in Goiania, Brazil in September 1987, several individuals were exposed to gamma radiation, mainly externally and some internally. In collaboration with the Institute of Radiation Protection and Dosimetry (IRD), Rio de Janeiro, we have made dose estimaties for exposed individuals by biological dosimetry using the frequencies of chromosomal aberrations.

There are 32 individuals exposed to radiation doses of 0.5 Gy to 7.0 Gy, of these three had mainly internal exposure. The present study is aimed at following up this exposed population in collaboration with IRD in Rio. The following parameters will be studied:

1. Frequency of unstable chromosome aberrations and micronuclei as well as their statistical distribution will be determined periodically (every four months) in individuals exposed to 0.5 Gy and above.

2. Frequency of stable aberrations will be followed by banding techniques in the same population.

3. Mutations in the HPRT locus will be determined in these individuals and if enough blood samples become available, mutants will be isolated and cloned for further sequencing of the mutants.

4. Mutant frequency in 3 different loci of the beta chain of haemoglobin will be measured in these individuals with parallel controls.

The determination of mutant frequencies will be made once a year.

B13 Cellular, molecular and animal studies to determine the risk of stochastic somatic effects of radiation with respect to low dose, low dose rate and radiation quality

Contract Bi7-023 Evaluation of existing and development of new human epithelial cell transformation systems and determination of their potential in radiation protection studies.

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Total Contribution by the Commission: 158 kECU
24 months from 1/01/90 to 31/12/91

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Description of research work:

INTRODUCTION

There is a need for a relevant in vitro assay for studying cell transformation of human cells. In this way the molecular mechanisms and dose response relationships of carcinogenesis in humans can be studied. As about 85-90% of human tumours are of epithelial origin, it is important to utilise cultures of normal human diploid epithelial cells in transformation studies. The systems which have been most extensively studied to date employ the:

BHK 21 line of Syrian hamster kidney cells (DiMayorca et al, 1973, Styles, 1977)

Primary Syrian hamster embryo cells (Berwald & Sachs, 1963, Pienta et al, 1977)

BALB/C 3T3 mouse fibroblast cell line (Aaronsen & Todaro, 1968, DiPaolo et al, 1972)

C3H 10T1/2 mouse fibroblast cell line (Reznikoff et al, 1973 a.b)

However, extrapolation from one species to another may not be valid and C3H 1OT1/2 cells for example, are aneuploid and cannot be considered normal. Rodent fibroblasts behave differently from human cells in culture, exhibit spontaneous chromosome rearrangements and form permanent cell lines. The background transformation frequency assessed from experiments on fibroblastic lines and ability of agents to transform are apparently quite different for rodent cells and human cells. Human cells exhibit chromosome stability and do not spontaneously transform in culture.

Recent improvements in cell culture methodology have seen the development of human epithelial cell cultures. These systems have now been used for carcinogenesis investigations (Harris, 1987). Cultured human keratinocytes have been established using feeder layers of irradiated 3T3 fibroblasts and have been exploited to study cell growth and differentiation. Rather than using feeder layers, collagen coated dishes have also permitted epithelial cell attachment and growth. Using similar methods, epithelial cultures from human prostate, endothelium, mammary tissue, bronchial epithelium and cervical epithelium have been established (reviewed in Reznikoff, Swaminathan & Verna, 1986). They exhibit similar patterns of behaviour undergoing senescence after 35-50 doublings, not transforming spontaneously, have a stable diploid chromosome component and retain the biochemical and morphological characteristics of the differentiated epithelial cells from the tissue of origin. The problem of senescence can be overcome by treating with SV40 or an origin defective mutant of SV40 cloned into a plasmid. In this way, lines have been developed which can be passaged. They do not form tumours in nude mice but can be cloned in soft agar. Transformation of such human cells in vitro has been reported however, the endpoint utilised is often ill-defined. Probably the best accepted criteria for demonstration of transformation is growth of malignant clones in nude mice. However, not all primary human tumours grow in nude mice so a negative result is not necessarily conclusive, following SV40 treatment cells are usually non-tumorigenic in nude mice but can be passaged invitro. Thus it has been suggested that increased growth potential and subsequent ability to escape growth crisis may be useful markers.

Studies on human epithelial systems, reviewed at the recent Dublin workshop on Cell Transformation, revealed that the most promising approach to the investigation of oncogenic transformation in human systems was to utilise lines that had been immortalised but were not tumorigenic. Several of these lines have now been developed from different tissues. The most promising of these are the SV40 immortalised human urothelial cell line, SV-HUC-1, developed by Reznikoff and the HPV 16 or 18 immortalized lines which can be developed routinely using the technique developed by DiPaolo from the transformation zone of the human cervix. This system has the advantage of being immortalised by human virus rather than SV40, although there is considerable variation from line to line, and the system is technically more difficult. The third promising human system is the immortalised keratinocyte line (HaCat) developed by Boukamp et al. This line arose spontaneously in normal keratinocyte cultures from a subject with skin carcinoma.

Overall Aims:

It is proposed to collaborate on a systematic study of radiation induced oncogenic transformation using these different human epithelial cell lines.
It has proved extremely difficult to transform primary cultures of normal human epithelial cells and thus this approach provides the next logical step in developing a full understanding of radiation-induced transformation of human epithelial cells It must not be forgotten, however, that initiation of transformation by radiation is a problem urgently in need of investigation. Much effort has gone into this field and with little success - for reviews see Mothersill, Seymour & Moriarty (1988); Seymour & Mothersill (1988) and Mothersill & Seymour (1989). The adoption of useful systems from the chemical carcinogenesis field may be profitable, eg the system developed by Thomassen et al (1983) for rat tracheal epithelium might adapt well to human epithelium or the human buccal cell system of Grafstrom & Harris (1989) which shows enhanced proliferation in response to chemical carcinogens. Enhanced proliferation of epithelial and endothelial cells in mixed cell type outgrowths from primary explants has been detected by Mothersill, Cusack & Seymour (Rad. Environ. Biophys., 1990) and Mothersill & Seymour (1989). The problem with initiation studies is that unless immortalisation is achieved, the meaning of the changes is hard to establish.

One of the main problems is defining the role of ionising radiation in oncogenic transformation is that radiation induces different types of lesion in DNA in exposed cells. It has now been shown that exposure of permeabilised cells to type II restriction endonuclease which induce double-strand breaks in DNA at specific sites leads to chromosomal aberrations, mutations and cell death (Bryant, 1984; 1988). Recently it has been shown that oncogenic transformation also occurs as a result of this treatment (Bryant & Riches, 1989; Yang & Tobias, 1989). Thus it may be possible to shed more light on the basic molecular mechanism of oncogenic transformation using this approach.

Specific Objectives:

(1) To compare available human transformation systems in terms of their ability to address radiation protection problems particularly radiation quality and low dose rate effects.

(2) To attempt to develop new human epithelial systems capable of looking at initiation of carcinogenic damage, particularly by target specific radionuclides on the target organ in culture.

Objectives for each Partner:

(A) Radiobiology Research Laboratories, Dublin:

(1) To establish the HPV transfected cervical epithelial system developed by DiPaolo and later the HaCat cell line developed at DKFZ, Heidelberg, in the laboratory and to assess the feasibility of obtaining radiation dose response data.

(2) To use these systems in experiments designed in collaboration with the St. Andrews group to evaluate the transformation frequencies resulting from exposure to low dose and low dose rate irradiation and to radiations of different qualities.

(3) To continue to develop primary cultures of human cells and to screen these for their response to radiation by examining a large number of endpoints which are associated with transformed cells.

(4) In collaboration with Dr. Pertusa, Valencia University, to quantify morphological changes resulting from irradiation of primary cultures of normal cells, specifically alterations in nuclear size and shape and in nucleus cytoplasm ratio and to measure relative frequencies of different cell types within the cultures after various doses.

(5) To investigate specific transformation associated genetic aberrations in interphase nuclei after irradiation using in situ hybridisation and chromosome painting techniques and in collaboration with Dr Pertusa (Valencia) and Dr. Hopman (Nijmegen) to quantify these changes with respect to dose, dose rate and radiation quality.

St. Andrews University:

(1) Measurement of the dose-response relationship for cell killing for the human urothelial cell line (SV-HUC-1).

(2) Measurement of the dose-response relationship for cell killing from primary cultures of urothelial cells using the outgrowth technique established by Mothersill & Seymour.

(3) Investigate the transformation frequency per surviving cell in the human urothelial cell line (SV-HUV-1) using a focus forming assay.

(4) Investigate the chromosomal responses following irradiation of the human urothelial cell line (S-HUC-1) and compare this with 10T1/2 cells and primary cultures of human urothelial cells.

(5) Investigate DNA damage and repair using the neutral elution technique using the human urothelial cells and 10T1/2 cells for comparison.

(6) Establish new epithelial lines from human urothelium by transfection with SV40 fragments

University of Valencia:

The role of our laboratory in the present project will be the quantification, by using advanced image analysis techniques, of the experiments carried out for the other laboratories participating in the project. Since our laboratory is also involved in neutron irradiation experiments with Portugal (Dpt. Energía e Engenharía Nuclears del Laboratorio Nacional de Engenharía e Tecnología Industrial, Lisbon, LNETI), it is envisaged that neutron experiments for the other contractors will be performed by us.

Samples shall be studied using two different techniques, morphometry and densitometry, in order to achieve the proper quantification of proliferation and outgrowth from experiments performed by the other partners. Moreover, additional information will be obtained with respect to the morphology of the cells and this will allow the proper characterisation of the cell lines used in the experiments. By using densitometric analysis of the samples, a proper and fast quantification of the cytochemical and/or immunocytochemical reactions will be provided . The quantification of in situ hybridisation autoradiographics and chromogenic patterns can also be undertaken.

The advantages of the use of a computerised system for image analysis are obvious. These modern techniques allow the user an easier measurement of very different parameters like percentage of outgrowth, number of cells in a given area, nucleoplasmic relation of every single cell, quantitative evaluation of autoradiographics, or the more complicated measurement of the optical density in the cells, all of them very useful for the biologists and nearly impossible to be performed by any other system.

B13 Cellular, molecular and animal studies to determine the risk of stochastic somatic effects of radiation with respect to low dose, low dose rate and radiation quality

Contract Bi7-033 Cellular and molecular studies on radiation quality: A comparison between genetically relevant damage and cell inactivation.

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Total Contribution by the Commission: 190 kECU
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Description of research work:

In the last ten years, heavy charged particles have been used in radiobiological experiments more extensively than before. This development has basically two reasons: the increasing use of these particles in radiotherapy and radioprotection problems of manned space flights.

In radiotherapy, approximately ten thousand patients have been treated with charged particles (mostly protons) with extraordinary success. Because of the better dose distribution and the increased relative biological efficiency at the end of the particle range, a strong trend is visible toward a treatment with heavier ions like carbon or neon ions.

At Chiba, Japan, a dedicated medical heavy ion synchrotron (Himac) is under construction with a cost of approximately 300 million dollars. From a joint collaboration between the Heidelberg University, the cancer research centre and GSI, a proposal for the medical use of the SIS accelerator has been submitted to the German government. Finally, a proposal for the European Light Ion Medical Accelerator, "EULIMA", has been submitted to the Commission of the European Community to develop a hospital based reliable heavy ion accelerator which, later on, could be located at various sites in Europe.

In manned space flights outside the shielding of the magnetosphere of the earth which are proposed by NASA and ESA, the heavy component of cosmic radiation pose a major risk for the health of the astronauts. In the case of the solar flare, lethal doses of protons can be reached even in short excursions outside the space craft. For long term space flights the risk of cancer induction is also important because the highly energetic heavy ions cannot be shielded very efficiently by the spacecraft and the radiation risk is accumulating with time, ie over the duration of the flight.

In both cases, radiotherapy and radioprotection in space, more information is needed on the inactivation process caused by the particle radiation where the data for lighter ions are scarce. But almost no information exists on the genetic risk caused by heavy charged particles.

In addition, no theoretical approach exists which allows to calculate the biological effects with sufficient accuracy. In previous experiments, the inactivation process of mammalian cells has been studied extensively with low energetic heavy ions (Ne-U) at the Unilac Darmstadt but only a very limited number of experiments with lighter ion (H to C) exists. The compilation of these experiments yielded some essential differences between the common adopted LET dependence from RBE. First, the maximum of RBE which occurs at 100 keV/µm for He-ion is shifted to higher LET values for the heavier ions. Secondly, an independent RBE-curve has been found for each atomic number. In the proposed experiment, the RBE-LET relationship will be studied for inactivation using the lighter ions, ie from proton to iron in great detail. In addition, the cell cycle dependence of the radiosensitivity will be measured for a representative combination of atomic numbers and energies. In contrast to x-ray exposure, where a radioresistant phase exists at the end of the S-phase, heavy ion exposure yields the most resistant phase at G1 and early S-phase. An extended study should yield the LET and energy dependence of this inverted cell cycle response.

Chromosome aberrations represent genetic mutations which are visible on mitosis after the first cell cycle. They are frequently used as an indicator of a mutative activity. Chromosome aberrations following particle exposure have been studied mostly for lighter ions. Chromosome aberrations induced by the heavy charged particles exhibit some specific features which are different from the induction by sparsely ionizing radiation. First, heavy ion induced aberrations exhibit a different distribution among the types of aberrations. Due to the high local and correlated density of ionization in a particle track, it is possible to induce chromosome type aberrations like isobreaks even in G2 phase cells with a high frequency. In x-ray induced chromosome aberrations, the number of break events is nearly balanced by the incidences of exchange events. This does not hold in the case of heavy ion exposure where the exchange figures are less frequent than the breaks. In addition, the complexity of the chromosome aberration increases with increasing LET values and also with decreasing particle energy. Finally, the radiation induced perturbation in cell cycle is different from those observed after x-ray exposure. These differences increase the difficulties in the analysis of the heavy ion induced chromosome damage. However, chromosome aberrations are one of the few exceptions where the radiation induced effects exhibit not only a quantitative difference, but also a qualitative difference between radiations of different quality.

Because both effects, the induction of chromosome aberrations as well as the inactivation process, are based on the generation of severe DNA lesions, it is mandatory to study the induction of DNA lesions for instance single and double strand breaks in parallel using the same type of radiation.

Most of the data on DNA strand breaks are obtained from extracellular DNA like ΦX174 or SV40 DNA which has been exposed in different buffer solutions. Only a few data exist on measurement of breaks of chromosomal DNA of mammalian cells. In both cases intra- and extracellular DNA, the induction probability exhibited a very similar functional dependence on LET. However, in the cellular DNA data large differences in the repair time has been observed depending on LET and energy of particle used. This has been interpreted as a higher complexity of DNA damage for high LET particles as for instance a double strand break combined with the loss of a few base pair at both strands or strand breaks which are associated with crosslinks to the nuclear protein.

However, the molecular nature of the very slowly restoring breaks has not been explored. In order to gain more molecular information, DNA damage of genetically well known plasmid sequences inserted in mammalian cells should be studied in greater detail and also new methods in gentechnology should be used to analyse induced DNA damage. In the proposed experiments both approaches will be started and used to analyse the complexity of particle induced DNA damage.

In summary, the radiobiological effects of charged particles like protons or heavier ions are of great importance for the development of heavy particle radiotherapy as well as for the estimation of the radiation risk in manned space flights. Because a unique theory of the RBE does not exist up to now, the radiobiological effects of the particle radiation has to be measured in detail. The proposed experiments aim to gain more insight into the biological efficiency of lighter ions at different biological levels for the induction and repair of DNA strand breaks of both chromosomal and plasmid DNA.

GSI Darmstadt

The GSI Biophysics group will concentrate on three different topics: chromosome aberrations, inactivation and induction and repair of strand breaks.

Induction of chromosome aberrations:

In recent experiments using V79 Chinese hamster cells, the analysis of chromosome damage demonstrates that the response of cells exposed to heavy ions differs quite largely from those observed after x-ray irradiation.

1. A particular type of chromosome damage, the partial or complete disintegration of chromosomes is only observed after heavy ion exposure. This damage can be attributed to the high local energy deposition of charged particles.

2. Heavy ions induce predominantly breaks and acentric fragments, whereas exchanges of chromosome parts are rare events. This is in clear contrast to x-ray irradiation where breaks and acentric fragments are less frequent than exchange-type aberrations.

3. After heavy ion exposure, significant perturbations in the cell cycle progression are observed. Whereas x-ray irradiation only prolongs cell transition through late S- and G2/M-phase, heavy ion irradiation leads to drastic delays in all cell cycle stages.

   However, there are large variations in the cell cycle delay of individual cells. Therefore, cells reaching mitosis at a definite time after irradiation belong to different generations.

Cell cycle and inactivation:

The radiosensitivity of mammalian cells is influenced by their phase during the cell cycle. This variation in sensitivity is highest for x-rays. Measurements with lighter ions with high energy (low LET) showed a diminished cell cycle response.

However, the maxima and minima of radiosensitivity are still located at the same position in the cell cycle. First measurement with heavy ions at low energies (high LET) could not confirm this tendency. Whereas for x-rays, radiosensitivity is high in G1 and lowest during the S-phase, for high LET particles it is lowest in G1 and tends to increase during the cell cycle.

Induction and repair of DNA breaks:

The double strand break (DSB) is believed to be the major lesion involved in radiation induced chromosomal aberrations and cell death. However, measurement of DNA DSBs shows technical limitations especially at low radiation doses.

Therefore, we are developing a new experimental approach to study the induction and repair of DSBs in mammalian cells applying improved pulsed field gel techniques.

NRC Demokritos

Proton beams produced by the Tandem Van de Graaff Accelerator of the National Research Centre for Natural Sciences (N.R.C.P.S. "Demokritos") and particles from an Am-241 source will be used to research the spatial dependence of sublesions forming events related to the radiobiological damage of the genetic apparatus of mammalian cells. It is proposed to study the effects of protons and α particles on DNA single strand breaks (SSB) and DNA double strand breaks (DSB) and the frequency of induced chromosome aberrations and base analogue resistance mutations in mammalian cell cultures in conjunction with their survival and repair phenomena.

DNA breaks and base analogue resistance mutations will be measured in parallel in SV supercoiled plasmids of known genetic constitutions. DNA breaks can be traced with high resolution in radiation exposed plasmids due to their transition from supercoiled to circular (with SSB) and linear (with DSB) form. Expression of induced mutations are also expressed with higher frequency in plasmid transformed mammalian cells than mutation in the eucaryotic carrier.

The relationship between SSB and DSB will be studied in parallel with work using DNA thermal transition spectrophotometry and reverse phase chromatography. A computational program already developed in our laboratory permits the estimation of T_M points with high accuracy while reverse phase chromatography permits the estimation of physicochemical parameters delta G (free energy), delta H (enthalpy) and delta S (entropy) which are related to the formation and breakage of hydrogen bonds nearby to SSB on different polynucleotide chains, the generally accepted hypothesis for the derivation of DSB from SSB.

Recent unpublished work in our laboratory indicates a good agreement between radiation effected changes in the thermal transition point and the DSB breaks as they are measured by neutral elution techniques. The use of more than one technique in measuring different endpoints of radiation effects restricts the danger of methodology artifacts. The use of variety of endpoints permits the study of the interrelationship between different sections of the genetic apparatus and the assessment of the relative efficiency of each one as a parameter for radiation damage and risk estimation in conjunction with problems associated with spatial and time dependence.

Collaboration Leiden and NRPB

The aim of the project is to use the heavy ion accelerator at GSI Darmstadt to irradiate thin specimens of human blood with ions of nearly constant LET and to examine the lymphocytes for induced chromosomal damage.

Physical measurements on the beam will be made mainly by GSI staff with some input from NRPB. The particles to be used are 3 Helium-4 ions in the energy range of 20-60 MeV and 3 Carbon-12 ions in the range 100-200 MeV. A range of doses will be used commencing at 50 mGy and extending possibly up to 5 Gy depending on the particles.

Sample holders each containing 70 µl of blood, 100 µm thick, will be irradiated and several replicates pooled to provide enough cells for culturing.
Cells will be cultured in Darmstadt for NRPB and Leiden staff and slides taken back to both laboratories for microscope scoring. In addition to conventional aberrations in first division metaphases some irradiated specimens will be processed for examining initial breaks in prematurely condensed chromosomes. This will be done by Leiden staff.

The aberration data will be analyzed by NRPB and used to test models that attempt to explain how biological effectiveness varies with radiation quality. In addition to conventional chromosomal aberrations in the first division metaphases, one set of irradiated lymphocytes will be processed for examining the initial chromosomal breaks by the technique of premature chromosome condensation (PCC) by the Leiden group. Comparison of PCC data with the mitotic data will be made which will give an estimate of interphase death. In addition, influence of inhibitors of DNA repair (cytosine arabionoside, 3 aminobenzamide) on the yield of aberrations induced by accelerated charged particles, will be studied. It is also proposed to check whether this high LET radiation, in contrast to x-rays, would induce sister chromatid exchanges in treated lymphocytes.

B13 Cellular, molecular and animal studies to determine the risk of stochastic somatic effects of radiation with respect to low dose, low dose rate and radiation quality

Contract Bi7-034 Radiation induced processes in mammalian cells: principles of response modification and involvement in carcinogenesis.

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Total Contribution by the Commission: 327 kECU
24 months from 1/06/90 to 31/05/92

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Description of research work:

INTRODUCTION

Current risk estimates for the effects of radiation are based on the assumption of linear dose-response relationships. Whether the assumption is justified is a question of considerable importance for public health considerations. This new proposal suggests to explore the existence and mechanisms of "response modification". The term response modification should include all processes that are induced by radiation, and that influence the subsequent fate of the cell and organism (other operational terms for the same processes are "UV-response" and "stress response".

This program consists of a collaboration between a number of European laboratories that have made several contributions to the study of stress responses in bacterial and mammalian cells. Devoret is one of the pioneers in bacterial SOS genetics, a system that serves as a model for the mammalian stress response. Rommelaere, Sarasin and Van der Eb were among the first to detect the stress responses of Enhanced Reactivation and Enhanced Mutagenesis in mammalian cells, whereas Bertazzoni has joined the field of radiation-induced responses more recently, concentrating primarily on hereditary disorders characterized by chromosomal fragility and tumour-prones.

In the present proposal, Devoret's group is focusing on the characterization of a recA-like protein in mammalian cells. In E.coli the recA protein plays a key role in protecting the genetic material against deleterious effects of radiation, and it seems likely that the mammalian homolog of this protein has a comparable function. The groups of Rommelaere and Van der Eb are investigating the phenomenon of radiation-induced Enhanced Reactivation (ER). Within this context, Rommelaere is concentrating primarily on the mechanism of induction of ER, whereas Van der Eb is studying abnormal ER responses in cells from certain cancer-prone genetic diseases. In the same framework Sarasin's groups is developing systems to quantify radiation-induced gene amplification and to study the underlying mechanism of this phenomenon. Finally, the group of Bertazzoni is investigating spontaneous and radiation-induced chromosome fragility phenomena, as well as the role of poly(ADP) ribosylation in the cellular response to radiation damage. Several of the groups of this joint research program are collaborating with P. Herrlich's and P. van de Putte's laboratories, which have made important contributions to the discovery of UV-inducibility of genes and the isolation of new classes of UV-inducible genes. Collaboration also exists with J.W.I.M. Simons' laboratory on mutagenesis in mammalian cells.

MECHANISMS OF RADIATION-INDUCED CARCINOGENESIS (A.J. van der Eb)

Induction of in vitro cell transformation by radiation

The objective of this study is to determine the contribution of ionizing radiation or UV-light to the process of (radiation-induced) carcinogenesis. Since oncogenic transformation is a multistep process requiring alterations in at least 2 complementing oncogenes (e.g. ras and myc), we will use as starting material cultures of primary cells that already express one activated oncogene but are not yet oncogenically transformed. This will make it possible to use lower (and thus, more realistic) radiation doses than when the cells are still completely normal. Since established cell lines are not suitable for such studies as they are often already oncogenic when a single activated oncogene is introduced, we will employ primary cell cultures derived from mice transgenic for an activated oncogene, ideally a ras-like oncogene or a myc-like oncogene. The specific question we will ask is whether the radiation treatment (X-ray or UV) can cause complete tumorigenic transformation of such cells and if so, which (complementing) oncogene has been activated by the radiation treatment. It should be noted that the modes of activation of different oncogenes are quite diverse. For example, ras is activated by a point mutation, but myc activation usually requires DNA rearrangements. The following types of mice are now available: mice transgenic for the pim-1 oncogene and mice transgenic for the polyoma large T antigen. In addition, we hope to be able to use a mouse in which one allele of the p53 gene (a tumour suppressor gene) is "knocked out" (collaboration with Dr. A.Berns (Amsterdam) and Prof.F. Cuzin (Nice)).

Inducible repair processes in human cancer prone syndromes

The SOS-responses studied in this laboratory include Enhanced Reactivation (ER) and Enhanced Mutagenesis (EM). Recently, we have noted that the ER phenomenon was absent in certain Xeroderma pigmentosum (XP) skin fibroblast strains, whereas EM was normally expressed in these cells. It then turned out that these ER$^-$ cells were derived from XP patients which uncharacteristically lacked tumours in sunlight-exposed skin areas, suggesting that the ER response may somehow be related to the process of cancer induction. This was confirmed by the observation that ER was super-induced in skin fibroblasts from hereditary cancer prone syndromes, e.g. Wilm's tumour (WT), Polyposis coli (PC), Dysplastic naevus syndrome (DNS).

These studies are presently being extended to other cancer prone syndromes. In addition, cells from UV-sensitive but not cancer-prone diseases will be investigated (Trichothiodystrophy; TTD).

Subsequent work will focus on the identification of molecular defects correlating with the abnormal ER responses such as defects in the induction of expression of UV-inducible genes. Genes that will be considered first are e.g. metallothioneine, HSP70, jun, fos. If genes are found that show abnormal UV-inducibility in conjunction with abnormal ER, the mechanism responsible for the abnormal UV-response will be investigated.

RADIATION-INDUCED RESPONSES IN NORMAL CELLS AND CELLS FROM CANCER-PRONE PATIENTS (A. Sarasin).

In order to look for the induction of cellular responses by radiation, we have constructed and used several shuttle vectors specific for this purpose. Particularly, we have developed the episomal Epstein-Barr virus-based shuttle vectors which contain both the EBV-replication origin necessary for replication and maintenance in human cells, and pBR plasmid replication origin for growth and selection in bacteria. Some of these shuttle vectors also contain the SV40 replication origin allowing an SV40-mode of replication in the presence of the SV40 T antigen, expressed from an inducible promoter. Several human cell lines (293, MRC5, xeroderma pigmentosum strains) have been established and selected for stable episomal replication of these vectors. Treatment of host cells with very low doses of UV-radiation which cannot produce any photolesion in the vectors, is able to induce a high level of DNA amplification of episomal vectors. The preliminary data show that we have developed an interesting system to detect and analyse the inducing signal leading to DNA amplification in mammalian cells. Indeed, it is interesting to note here that most human cancers are associated with oncogene amplification, the mechanism of which is still unknown.

A second part of our research program is focused on the study of cancer-prone diseases and particularly on the role of radiation on skin tumours. We have been working with UV-induced skin tumours in xeroderma pigmentosum patients (XP). XP is a DNA repair-deficient syndrome leading to a very high cancer incidence. We found oncogene activation in some epitheliomas isolated from these patients. Our goal is, therefore, to directly determine which DNA lesion is the mutagenic one, by comparing mutation spectra found in model systems and in human activated oncogenes. Indeed, by studying basal-cell carcinoma, squamous-cell carcinoma and melanoma from XP patients we found already a high level of ras gene activation due to point mutations at codons 12,13 or 61. All these mutations were located opposite pyrimidine-pyrimidine sequences. These sequences are known to be mutational hot spots in all living systems where they have been studied. Therefore, we can already say that UV-induced mutations found in UV-induced skin tumours from XP patients are probably due to unrepaired photolesions. Interestingly, high levels of oncogene amplification are also found in XP tumours, probably also due to unrepaired DNA lesions as suggested by our work described in the first part. Experiments in progress will provide information on the role of DNA lesions in inducing cellular stress leading to genomic rearrangements and modifications.

IDENTIFICATION OF A REC-A-LIKE PROTEIN IN MAMMALIAN CELLS (R. Devoret)

We have shown during the beginning of this contract that some proteins of several mammalian species share antigenic determinants with E.coli recA protein. Here we describe KIN17, a mouse cDNA fragment 601 nucleotides long, that codes for the polypeptide expressing the strongest immunoreactive recA epitope.

Sequence analysis of *KIN17* cDNA reveals a recA-like epitope and a homeo domain motif.

KIN17 cDNA codes for a polypeptide kin17 of 200 amino acids. The polypeptide has a short region of significant homology to recA protein. Fifteen out of 39 recA amino acids (between 309 and 347) are identical to kin17 amino acids (between 87 and 125). Furthermore, among the recA amino acids between 315 and 327, 8 are identical to kin17 amino acids between 93 and 105. Since this region of recA protein encompasses a major antigenic determinant, it accounts for the strong immunoreactivity displayed by kin17 protein.

More important, kin17 protein has a motif, LELEK, conserved in the helix 1 of most homeodomain containing proteins. In kin17, this motif is located immediately upstream of the putative recA homologous epitope. This region of kin17 also displays a significant homology with an N-*myc* motif known to be located in the leucine zipper region of N-*myc* (between the second and the third leucine residues).

Preferential neural location of *KIN17* transcripts in the mouse.

We found a KIN17 mRNA band of about 1.9 Kb in mouse cells derived from an interior pituitary tumour (AtT-20) as well as in rat cells derived from an insulinoma (RIN). Yet we failed to detect by Northern blotting any KIN17 transcripts in the total RNA extracted from mouse embryos or from the liver of an adult mouse. However, KIN17 transcripts were detected in 12-day old mouse embryo RNA by using RT-PCR. There is a low level of KIN17 mRNA in mouse embryos.

The *KIN17* gene identified in rodent and in human cells.

By hybridizing KIN17 cDNA with restriction-digested genomic DNAs of mouse, rat and human cells, we detected a KIN17 sequence in these cells. KIN17 gene sequences appear to be highly conserved in mammals.

MODULATION OF GENE EXPRESSION IN IRRADIATED AND RADIATION-TRANSFORMED HUMAN CELLS. (J. Rommelaere)

Our program aims at defining short- and long-term effects of radiation on the expression of cellular genes related to the initiation or maintenance of malignant transformation.

Investigation of radio-induced mechanisms.

Exposure of eukaryotic cells to radiation induces several distinct cellular responses, including the enhanced reactivation (ER) and mutagenesis (EM) of damaged viruses.

a) analysis of the mechanism of induction.
We shall investigate whether factors secreted by irradiated cell cultures can mimic radiation by triggering ER and EM of DNA viruses (H-1; HSV-1) in unirradiated cells. In parallel we shall determine whether the overexpression of proteins (fos, myc, jun) are able to induce ER and EM in the absence of radiation (in collaboration with Van der Eb and Herrlich).

b) molecular study of induced recovery process (ER)
In order to test whether a component of ER of damaged virus may consist of an increase in viral gene expression, the levels of mature viral transcripts and synthesis of viral proteins will be compared in irradiated/unirradiated cells. Interferon and/or interferon-induced genes can act synergistically with radiation for the induction of ER. Therefore we shall compare the expression of interferon-induced genes in both irradiated and untreated cells.

Identification and characterization of radio-induced cellular functions associated with neoplastic transformation.

Parvoviruses proved to be good indicators of inducible functions expressed by mammalian cells. Normal human cells are resistant to parvovirus H-1 while they become susceptible once transformed by radiation. Evidence indicates that radiation affects the expression of cellular factors involved in the replication and/or expression of parvoviral DNA. Parvoviral probes will be used to identify these factors in normal and radiation-transformed cells.

Molecular analysis of a putative defect of radiation-induced processes associated with a cancer-prone syndrome.

Cells from patients with ataxia telangiectasia (AT) were found to be proficient in ER of the double-stranded (DS) DNA virus (HSV-1) but deficient in both the ER of the single-stranded (SS) DNA virus (H-1) and the EM of both types of viruses. In order to test whether the failure is due to a conditional process related to replication of damaged DNA, the conversion of damaged SS to DS viral DNA will be analyzed in preirradiated or untreated AT and normal cells.

STUDY OF FUNCTIONS INVOLVED IN THE RESPONSE TO MUTAGENS AND IN THE POLY-ADP-RIBOSYLATION OF PROTEINS IN MAMMALIAN CELLS (U. Bertazzoni)

This study is performed using mutant cell lines defective in DNA repair processes. The research work in progress concerns the localization on human chromosomes of the genes that are able to complement the repair defect in two UV-sensitive Chinese hamster mutant cell lines (CHO4PV, CHO7PV), representing two new complementation groups. To this purpose hybrids obtained by fusing rodent mutant cells with normal human lymphocytes are characterised for UV sensitivity and human chromosome content. UV-sensitivity is analyzed by measuring survival after UV-irradiation; human chromosomes are recognized by in situ hybridization with total human DNA and are identified by banding procedures. Eighteen hybrids obtained by fusing CHO7PV with human cells have so far been analyzed and human chromosome 7 exhibits the strongest correlation with recovery of repair ability in the CHO7PV mutant. To confirm the involvement of this chromosome in the complementation of the defect of CHO7PV cells, the characterization of subclones of different hybrids is in progress. As far as natural mutants are concerned, we are analyzing the spontaneous and induced chromosome fragility and the occurrence of cytogenetically mutant clones in cultures of normal fibroblasts from individuals homozygous or heterozygous for xeroderma pigmentosum mutations.

The nuclear enzyme poly(ADP-ribose)polymerase, activated by DNA breaks, modifies chromosomal proteins and plays a key role in DNA repair. We have studied the non-histone proteins which are modified by ADP-ribosylation in HeLa cells in physiological conditions. We have focused our attention on a protein of 170 kDa, possibly corresponding to DNA topoisomerase II. To demonstrate that ADP-ribosylation of topoisomerase II is indeed occurring in HeLa cells, the enzyme was immuno-precipitated and further analyzed with a monoclonal antibody. By using affinity chromatography on a boronate column, a single 170 kDa immunoreactive peptide was isolated which was found to be ADP-ribosylated topoisomerase II. The pattern of ADP-ribosylation of nuclear proteins was followed after treatment of cells with DNA-damaging agents and the observed enhancement was directly related to autoribosylation of poly(ADP-ribose)polymerase whereas no further modification of topoisomerase II was observed. We have previously demonstrated the involvement of ADP-ribosylation in rat liver carcinogenesis by analyzing the level of the enzyme during initiation, promotion and progression steps of neoplastic transformation. We are now analyzing the expression of the poly(AD-ribose)polymerase gene by using a specific cDNA rat probe. The level of mRNA for the enzyme is determined in regenerating rat liver and in different model systems for hepatocarcinogenesis.

CONSTRUCTION AND THE USE OF EUKARYOTIC CELL LINES FOR THE ASSESSMENT OF RADIATION INDUCED ALTERATIONS LEADING TO NEW PHENOTYPES (H. Thomou-Politi)

Description of research work:

One way to approach the practical problems of human exposure to radiation, such as radiation protection or radiation therapy, is by extrapolating from molecular studies to the doses and dose-rates relevant in human exposure. More data using more advanced biological systems are needed towards this goal. Mutagenesis and mutation analysis of mammalian genes has been an active field of research by both conventional and recombinant DNA techniques. These studies indicate that ionizing radiation, brings about large deletions and rearrangements. In addition, "foreign" genes integrated into the mammalian genome by transfection, are more mutagenic, confer higher frequencies of mutants per rad than "native" mammalian genes (1,5), thus improving the sensitivity range of bioresponse to radiation.

We propose to develop indicator cell lines that would respond to low levels of radiation, not affecting cell survival by producing quantitative signals indicative of new defined phenotypes. Our approach will be the construction of stably transformed cell lines either with Bovine Papiloma Virus vectors, particularly the pBMT3X vector carrying the mouse and human metallotheionein genes that confer resistance to cadmium or with the SupF plasmid carrying cDNA of the human CD2 gene expressing the T11 surface antigen responsible for binding sheep erythrocytes and forming rosettes.

Our future approach will be the construction of transformed or co-transformed cell lines that would produce signals indicative of new defined phenotypes.

More specifically, we will attempt to:

1. Demonstrate by Southern hybridization analysis the location of the plasmid on the chromosome(s) of the cell. For this, we are going to use as probe either the intact pBMT3X vector or parts of it (with emphasis to metallotheionein gene) after digestion of the plasmid with appropriate restriction endonuclease.

2. Insert the SupF plasmid carrying the cDNA of the CD2 gene (gift from Dr. B. Seed) responsible for T11 cell surface antigen binding sheep erythrocytes, either as a cotransformant with the pBMT3x or alone and construct stably transformed cell lines by transfection, able to titrate radiation effects by counting the loss of defined phenotype, i.e. of rosette formation ability of the irradiated cells.

B13 Cellular, molecular and animal studies to determine the risk of stochastic somatic effects of radiation with respect to low dose, low dose rate and radiation quality

Contracts Bi7-035/6-004/6-075 Methodology for the analysis of radiation carcinogenesis studies and application to ongoing experiments.

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Total Contribution by the Commission: 420 kECU
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Contract Bi6-075

Description of research work:

Large scale animal experiments at various European institutes have been undertaken in the past decade. The information from different laboratories can be meaningfully combined if the experimental procedures and the pathology are closely coordinated and similar requirements apply to the design of an experiment with regard to animal numbers, dose groups and other factors and also to the methods of statistical analysis which need to be defined at the outset of the experiments. It is accordingly necessary to develop standards of experimental planning and methods of statistical analysis in animal experiments. Analysis of the tumour induction data reveals differences, which may be partly explained by a diversion of the cohorts under study, but are also believed to result from the employed analysis methods. In particular the different mathematical models, e.g. the parametric Weibull model (Broerse et al. 1986) versus the non-parametric proportional hazards model (Kellerer and Chmelevsky 1982), have been under discussion. The analysis approach of both the single dose, fractionated and protracted experiments, either with or without drugs, is also not resolved. The control group appears to play a crucial role in the analysis approach. A unified approach to the analysis of experimental data of animal carcinogenic studies will be the aim of this contract. To this aim a framework will be laid down for the analysis of dose-effect relationships in a concorded way for the existing data in Europe.

The results of the work will be assembled in a laboratory handbook and accompanying software. Essential points will be:

- A set of rules and recommendations concerning the choice of the animal strains, the number of animals required in an experiment and their distributions into groups with different doses and time schedules, and the necessity of control groups.
- A set of rules defining the conduct of an experiment to ensure comparability and repeatability of the results. Special emphasis will be on the necessity of correct randomization.
- Recommendations on the coordination of the pathology and on the recording of tumours (This can largely draw on work performed by EULEP, but needs to include conventions on data recording for exchange of results).
- A set of rules on the extent of data and their format which permit efficient exchange between laboratories for comparison of results.

An extensive section, that is central to the project, will deal with the models to be used in the analysis, and with the methods and algorithms to be applied. A computer program will be developed under this contract, encompassing the multi-institutional approaches to the analysis of dose-effect relationships. The department of Clinical Oncology of the Academic Hospital Leiden supports the project through the coordination of the proposed methodological approaches and the associated software development for the comprehensive analysis program. This program is produced in such a way that it can be distributed among the various European institutes, that are involved in carcinogenic studies. Extensive development of the computer program has already taken place in 1988-1989, as supported by the CEC under a previous contract nr. BI 6-D-219-NL.

A number of consecutive programs on induction of mammary cancer in different rat strains have been performed at the Radiobiological Institute TNO and the Institute for Experimental Gerontology TNO. A total number of more than 10.000 animals have been included in these experiments.In addition the incidence of both stochastic and non-stochastic effects in a group of rhesus monkeys irradiated with X-ray and fission neutrons continues to be followed. The incidence of malignancy in the irradiated group is considerably higher than in controls although many of the animals are still alive. Routine examination of the animals for the occurrence of tumours and cataracts will be carried out and complete necropsy will be made on the death of the animals. Data from this study will be made available for detailed statistical analysis. In view of a deviation in the work program of the TNO Institute the analysis of the tumour induction results is performed at the Department of Clinical Oncology at Leiden.

In the framework of this research proposal the group at GSF will be particularly involved in the definition of data requirements and of guidelines for the statistical analysis of animal data. This will be done in close collaboration with the groups at AZ Leiden, CEA-FAR, TNO, and the University of Würzburg. In addition computer programs will be prepared, which will accompany the laboratory handbook drafted for this project.

In the statistical analyses of animal data it is important to use appropriate methods that need to be selected according to the detrimental effect induced by the neoplasms, i.e. one must apply different algorithms for directly observable tumours and for tumours that are observed incidentally. Accordingly computer programs will be prepared for the analysis observed in the different possible contexts, i.e. lethal and non-lethal neoplasms. Although it has not been common in analyses of animal data to use non-parametric methods such approaches will gain importance. They are particularly advantageous for experiments with large numbers of animals.

Relevant algorithms have been used in the past years and they will need to be developed further to provide a choice between several analytical models (e.g. Weibull models or log-normal models). They will also need to be easily applicable by biologists, who are not necessarily experts in data analysis. This part of the work will be done in collaboration with the group at AZ Leiden.

Large experiments with Sprague-Dawley rats, performed at CEA-FAR or at Razes, which are already finished or close to termination will be analyzed jointly by the group at GSF and the University of Würzburg. The experiments include groups of animals which received total body irradiation of fission neutrons or of ^{60}Co gamma-rays at low doses. Another series of experiments include groups of animals which inhaled radon daughters with total exposure in the range from 20 to 1000 WLM.
The present analyses as well as the analyses of similar experiments at TNO (total body irradiation with low doses of neutrons or ^{60}Co gamma-rays) will be performed with the same methods which are explained and described in this research proposal. The comparison of the results in terms of RBE of neutrons, of time and dose dependencies for the most important neoplasms will be the contribution in the preparation of the presently discussed joint European animal experiments.

The part of the cooperative project to be performed by the department of Pathology of the IVVO-TNO is:

1. Histopathological examinations of about 420 irradiated and control rats for the occurrence of neoplastic and non-neoplastic lesions. This will be done for the various experimental groups and rat strains. It will be indicated whether a specific lesion is considered to be lethal, probably lethal, nonlethal or probably nonlethal.

2. In order to allow comparison of pathology data derived from different laboratories, IVVO-TNO will cooperate with the pathologists of the other participating laboratories to standardize: nomenclature of diagnostic entries, diagnostic criteria, tissues and number of slides per tissue examined. Before data from different laboratories can be brought into a common data base one has to be certain that the findings are inter-comparable and not related to differences between participating laboratories or individual pathologists.
   For the majority of lesions inter-laboratory differences with respect to nomenclature or diagnostic criteria can be solved relatively easily. For some lesions however, boundaries between diagnostic entities are rather vague and this necessitates slide review by a panel of pathologists of the cooperating laboratories (possibly reinforced by experienced rodent pathologists of the EULEP Pathology Committee).
   Such slide review sessions will remain necessary even after complying with internationally accepted guidelines for nomenclature and diagnostic criteria as presented in the ILSI monographs, EULEP Atlas, WHO publications on mouse and rat tumour pathology, International Society of Toxicologic Pathology (in preparation) and other publications in the international literature. It is planned to inventarize the areas where slide review by a panel of experienced rodent pathologists will be necessary.

Radiobiological concepts do not support that carcinogenesis by particles such as high LET neutrons be dependant on dose-rate, however very few animal experiments have been carried out at low doses

and low dose-rates and the point still needs to be clarified. Moreover it is well accepted that carcinogenesis occurs through oncogene activation, and there is some evidence that the density of cells with activated oncogens is as key issue for clonal expansion of precancerous cells. Therefore non linearity may be expected at low doses and low dose rates, even if hits in target cells have a dose rate independent probability of oncogene switching on.

In a previous series of experiments at CEA-FAR we have exposed 300 Sprague Dawley rats, 2.5 month old, to 16 mGy delivered by fission neutrons in 10 hours, and we have compared total incidence of cancers to that observed in 500 control rats. The rate of sarcomas shifted from 8.9% in controls to 19% in exposed rats and the rate of carcinomas was found to increase from 7.1% to 14%. Both increases were significant.

Our aim is to reproduce this experiment with 300 rats exposed to the same dose and 50 rats exposed to 80 mGy delivered in 10000 hours, which will reduce the dose rate by a factor of 1000, compared to the previous exposure schedule. These animals will be compared to 500 sham irradiated rats.

Such a protocol at low dose-rate implies aging of the animals during exposure. We shall complete the experiment by estimating the effect of aging in 75 rats 2.5 month old and 75 rats 9 month old exposed to 80 mGy delivered in a few hours. Our previous series of 150 young rats exposed to 80 mGy delivered in 10 hours resulted in an attributable excess of 18 carcinomas and 36 sarcomas.

At the present time a new circular facility has been built, suitable for continuous long term exposure of animals. A 15 mg ^{252}Cf source is being sealed and will be introduced in its plastic shielding. Exposure of animals will be launched October 1990.

BI6-004

Description of research work:

The present contract is a prolongation of the one expired in 1989. Therefore, the research programme follows the previous one and is intended to provide information useful to enlarge our knowledge and understanding of the biological action of radiation and so to tackle specialised problems relevant in the context of radiological protection. Shortly, the general aims of the work carried out in this contract are the study of the shape of the dose-effect relationship at low radiation doses, also in terms of interaction mechanisms and the influence of dose rate and radiation quality, as well as of important biological parameters for well identified endpoints in vivo and in vitro.

This purpose responds to the main objective of radiation protection, that is to achieve and maintain appropriate safe conditions for justified activities involving human exposure. Such a goal rests on the possibility of establishing unambiguous correlations between the physical quantities characterising the irradiation and the susceptibility of biological tissues and organs to biological effects of major severity.

In this context, it is widely recognised that animal studies are a very important tool concerning the study of the biological consequences of exposure to radiation and, in particular, the mechanisms of radiation induced carcinogenesis. They often represent the only reliable source of information related to important aspects of the biological response to radiation in vivo, as the shape of the dose-effect relationships at low doses, the influence of radiation quality and the time modalities of the dose administration. Recent studies have indicated a concordance of relative risk estimates for the induction of some cancer types between humans and mice, suggesting that extrapolation between species can be considered, and have encouraged further studies in this direction. Fast neutrons represent a particularly important problem, as, in the present situation, no useful estimate of RBE can be obtained from available human data of cancer mortality. Further more, they pose special important questions, some of which may have far reaching radiation protection implications. Among these, the variation of carcinogenic and mutagenic effectiveness consequent to a protraction of exposure deserves particular attention. Differences in RBE for tumour induction in various organs and tissues also call for careful consideration.

The present programme uses low doses of different radiation qualities and various modes of irradiation on different experimental model systems for suitable endpoints including life-shortening and tumour induction in experimental animals. In particular, in order to obtain further evidence on the enhanced effectiveness of prolongated low neutron dose exposures (low dose-rate or fractionation), the present activity includes as a substantial part an experimental in vivo study of the carcinogenic effect of fractionate doses of fission neutrons and, for comparison, also of X-rays on long-living BC3F1 male mice. This study is carried out on about 2000 animals, subdivided into 16 groups, given each five equal daily dose fractions, corresponding to cumulative doses of 2.5 to 70 cGy for fission neutrons from the reactor RSV TAPIRO and 25 to 300 Cgy for X-rays. Follow-up of the irradiated and the control animals for their entire life span is presently in progress. Soon after spontaneous death a complete autopsy is performed. The necropsy includes a complete external and internal gross examination. Tissue masses as well as sections of the major organs are taken and processed for histological analysis. Experimental data are being analyzed both with respect to life span shortening and cancer induction. Data treatment will include the correction for competitive risks and the analysis in terms of cumulative mortality, death-rates for specific causes, and trend. A comparison will be carried out with data for acute exposure of BC3F1 mice at comparable doses of the same radiation qualities, for critical endpoints such as the life-span shortening and the induction of malignant lymphoma and myeloid leukaemia.

Upon completion of these experiments further work is planned on experimental animals:

A- To investigate the induction of leukaemia in CBA/Cne male and female mice after acute and fractionated doses of fission neutrons, with the aim of obtaining further evidence on the influence of sex and the interstrains difference on the induction of a characteristic tumour by different qualities of radiation.

B- To study the influence of hormonal unbalance caused by irradiation on the incidence of ovarian tumours in CBA/Cne female mice.

In vitro studies of neoplastic transformation induced by radiation and chemicals have widely been carried out using different cell lines. In particular, the C3H1OT1/2 mouse embryo fibroblast system provides a very useful tool for these studies, since it allows a closely quantitative determination of the dose-effect relationships for this end point. Recently, this system has yielded very interesting information on the effect of radiation dose-rate. Data for sparsely ionizing radiation are abundant, generally showing that dose fractionation or protracted exposure produce a lower transformation frequency than acute doses. As far as densely ionizing is concerned, the information is more limited and sometimes controversial. Particular interest have recently raised the results of experiments with fission neutrons, which indicated an enhanced transforming potential of fractionated doses or low dose rates in the dose range of O to 1 Gy, in comparison to single acute exposures.

A series of experiments using C3H1OT1/2 cells are on their way. Cells are inoculated at low density 48 to 72 hours prior to irradiation with fission neutrons from the fast reactor RSV TAPIRO (average neutron energy 0.4 MeV) or with X rays from a deep therapy machine at Casaccia, and with mono-energetic neutrons from the Van de Graaff accelerator of the TNO Center at Rijswijk. Neutron doses are either single acute or fractionated. Dose fractionation follows a five fraction protocol, with equal doses delivered at 24 hour intervals. Following an incubation period of 6 weeks with weekly refeedings, transformed foci are identified by morphological criteria. Only type II and III foci are scored as transformants. The partial results obtained so far are for fission neutrons and show that:

A- The survival curves after fission neutron irradiation are very nearly exponential for both acute and fractionated exposures and there is no appreciable effect of dose fractionation.

B- Dose fractionation does not modify significantly the transformation rate compared to acute irradiation.

C- Fission neutrons are more effective than X rays both to inactivate and to transform C3H1OT1/2 cells at all neutron doses of this experiment (up to about 1 Gy). In this dose region, cell transformation frequency,is very nearly linear with the dose for exposure either to neutrons or X rays.

D- Maximum values of fission neutron RBE relative to X rays determined from survival and transformation data are in the region of 15 to 20, and are in close agreement with those obtained by other laboratories.

B13 Cellular, molecular and animal studies to determine the risk of stochastic somatic effects of radiation with respect to low dose, low dose rate and radiation quality

Contract Bi7-036 Molecular and cellular effects of protons, deuterons and alpha-particles.

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Description of research work:

INTRODUCTION

It has been well established experimentally in many biological systems that radiations of high linear energy transfer (LET), such as alpha-particles and neutrons, have greater biological effectiveness than the same absorbed dose of low-LET radiations, such as gamma-rays or X-rays. The high-LET radiations of greatest practical relevance to workers and the public are neutrons and alpha-particles with LET values in the range 10-300 keV/μm. Neutrons of < 5MeV produce proton recoils in the irradiated tissue with LET's of 10-90 keV/μm, while alpha-particles from natural and artificial radionuclides have LETs of 80-300 keV/μm.
It has been difficult to carry out systematic investigations of the quantitative dependence of relative biological effectiveness (RBE) with LET of such protons and alpha-particles because of the very short ranges of these charged particles. Similar LETs can be obtained with much higher velocity heavier ions which have much larger ranges, but the track structures of these differ greatly from those of protons and alpha-particles so RBEs obtained from them are less directly relevant. Among the few systematic studies for slow ions of these LETs are in vitro studies of Barendsen (cell inactivation), Cox et al. (cell inactivation and mutation) and Bird et al. (cell inactivation). The Barendsen data, in particular, are widely used to interpret radiobiological

effects of high-LET radiations including neutrons and alpha-particles. For example, the recent ICRU/ICRP task group on the quality factor in radiation protection recommended that quality factor should be defined as a function of lineal energy (rather than LET) with the form and parameters of essential elements of the function, most notably the saturation term, being based solely on Barendsen's data for alpha-particles. This is due to the findings of Barendsen and others, that RBE rises to a peak at LET's 100-200 keV/μm and then declines quite rapidly. It is implicitly assumed that differences in biological effectiveness of protons and alpha-particles of the same lineal energy, or the same LET, are negligible.

This assumption implies that possible differences between their track structures at the sub-micrometer level are not sufficiently large to be of biological significance. However, Belli et al. showed that at low doses, protons may be considerably the more effective particles for cell inactivation in the region 10-30 keV/μm, with their effectiveness per unit dose rising rapidly in this region rather like the well-established rise in effectiveness of alpha-particles at much higher LETs. Some confirmation is provided by experiments carried out in Greece by Perris et al. who found similar RBEs for protons of 10 keV/μm. Essential features of the results have been recently confirmed and extended in independent experiments in the U.K. at Mount Vernon and in collaborative experiments at Harwell. In addition, Belli et al. have preliminary data on induction of mutation which appear to show a similar phenomenon.

It is therefore important to investigate the generality of this phenomenon, its extension to deuterons of yet higher LET, its possible dependence on the dose-rate, and its causes in terms of the microscopic track structure.

GENERAL AIMS OF THE RESEARCH

Objectives of the project are to:

(1) measure the effectiveness of low doses of protons in inducing HGPRT- mutations, as a function of LET;

(2) measure the initial production of DNA double strand breaks in cells irradiated with protons, as a function of LET;

(3) establish a beam line for irradiation of cell monolayers with deuterons to extend to higher LETs that is practically possible with protons;

(4) measure the effectiveness of deuterons for cell inactivation or mutation, as a function of LET;

(5) start comparative experiments with low energy alpha-particle radionuclide sources at different dose-rates;

(6) analyse the microscopic track structure of the radiations to seek features which correlate with their observed biological effectiveness.

CONTRIBUTIONS OF THE DIFFERENT PARTICIPATING LABORATORIES

Contribution of the Legnaro Laboratories

The contribution of the Legnaro research group, in this project, will be the following:

- study, design and set-up of a new apparatus installed at the CN accelerator for cell irradiation with deuterons, with remote controlled multi-sample holder and temperature;
- study, design and construction of many small size systems for cell irradiation with alpha sources during incubation. These systems will be used to study low dose-rate effects;
- maintenance of cultured mammalian cells and their irradiation using both the already existing proton beam line facility and the ones under development;
- cooperation with ISS for cell irradiation and survival and mutation experiments.

Contribution of the MRC Radiobiology Unit, Chilton

The MRC will generate, by Monte Carlo methods, simulated tracks of the radiations at the level of the individual atomic interactions along the path of the particle and all its secondaries. In this way the microscopic features can be examined in detail over dimensions of > 1nm. Track features will be sought which correlate with the relative effectiveness of the radiations at low doses and attempts will be made to define regions (of, for example, distance and local energy deposition) within which these features may have biological relevance. The calculations will extend to other low-mass charged particles, such as deuterons, because these should provide additional valuable experimental comparisons and constraints, and also to regions of particle energy not readily open to biological experiments but nevertheless of practical importance in radiation protection. Comparisons will also be made with other common radiations.

In this way the track simulations should assist in fundamental interpretation of the experimental results being obtained with the charged particles, in assessing the practical implications and in guiding future experiments.

Contribution of the Istituto Superiore di Sanitá, Rome

The ISS group will carry out at Legnaro, in collaboration with the local group, a more detailed study on the RBE for mutation at low doses as a function of the proton's LET. The mutation frequency at the HGPRT locus will be determined by the 6-thioguanine resistance test on the same cell line (V79-753B) used for cell survival to ensure consistent comparison of the two endpoints. The RBE (at low doses) versus LET for cell inactivation and mutation induced by deuterons will be then determined. Deuterons will be considered since their microscopic track structure should be virtually identical to that of protons of the same velocity, but deuteron range is substantially greater permitting experiments at higher LETs than those allowed with protons. The ISS will also determine the initial yield of dsb produced by the same beams by means of the neutral gradient sedimentation technique. The K-SDS DNA precipitation technique also will be tried since it would be readily performed in the same area where irradiation will take place. The ISS will analyse the experimental data, including the fittings necessary to obtain the initial slopes of the survival and mutation curves.

Contribution of Gray Laboratory at Northwood

In common with the results of recent studies we have found that the RBE's for protons in the 17-32 keV μm^{-1} range are unexpectedly high compared with the earlier data of Barendsen and coworkers for deuterons and helium ions. These findings are of significance in respect of hazards of exposures to neutrons and α-particles. The Barendsen data have been used in estimating the dependence of the quality factor upon conventional microdosimetric parameters. The more recent proton RBE values demonstrate a substantial departure from the Barendsen data and support the view that very fine details of track structure have a significant influence on biological effectiveness. They therefore also have important implications for mechanisms of radiation action in relation to track structure. Work at the Gray Laboratory will extend these studies to higher LET's using deuterons in place of protons because of their greater range but almost equivalent track structure, also to include studies at low doses and low dose rates. Irradiation with α-particles or $^3He^{++}$ ions will be included. Cell survival and DNA double-strand breaks will be determined over similar dose ranges, both by filter elution and by pulsed-field gel electrophoresis methods. Irradiations will be carried out under oxic and hypoxic conditions. The lethality and repair of DSB induced at various LET will be compared with a view to relating the molecular mechanisms to differences in the micro-distributions of DNA damage determined by Monte Carlo track-structure simulations (MRC-RBU, Harwell).

B13 Cellular, molecular and animal studies to determine the risk of stochastic somatic effects of radiation with respect to low dose, low dose rate and radiation quality

Contract Bi7-037 Cellular and molecular mechanisms of radiation-induced myeloid leukaemia in the mouse.

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Total Contribution by the Commission: 200 kECU
24 months from 1/10/90 to 30/09/92

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Description of research work:

Introduction

Acute myeloid leukemia (AML) may be induced in mice by a single acute dose of X-irradiation. Rearrangements/deletions of chromosome 2 might be an initiating event, causally associated with deregulation of the interleukin-1 beta gene and loss of the developmentally important homeobox gene cluster.

However, other factors most probably play also a role in the general process, which might involve the participation of proviral, proto-oncogene or growth factor genes.

The experimental approaches aimed towards identifying events that may precede the overt AML are the following :

1. Phenotypic characterisation of the leukaemic myeloid cells, after generation of monoclonal antibodies;
2. Cytogenetic analysis with particular emphasis on chromosome 2;
3. Characterisation of growth factor and growth factor receptor activities/responses;
4. Search for a possible indirect (perhaps virally mediated) mechanism;
5. Molecular studies on the possible involvement of growth factor/receptor and proto-oncogene sequences.

Contribution of NRPB, Biomedical Effects Department, Chilton, U.K. (Dr. R. Cox).

1. To gain further information on the relationship between radiation-induced chromosome 2 changes in irradiated CBA/H haemopoietic cells and those which characterise radiation-induced murine acute myeloid leukemia (statistical concordance between chromosome 2 breakpoints in AMLs and similar events in irradiated haemopoietic cells).
2. To analyze the structure of the chromosome 2 F sub-region encoding the haemopoietic cytokine genes interleukin-1 alpha and beta (linkage and orientation of the genes as established by pulse field gel electrophoresis; their DNA methylation patterns).
3. To investigate the single copy radiosensitivity of chromosome 2.
4. To investigate the chromosome 2 radiosensitivity in other mouse strains.
5. To study DNA sequence losses from chromosome 2 in AMLs.
6. To explore the relationship between chromosome 2 radiosensitive sites and telomeric regions.

Contribution of CEN-SCK, Unit of Biology, Mol, Belgium (M. Janowski).

1. Preparative work : liquid nitrogen storage of bone marrow, circulating while blood cells, spleen and testis (control) of individual CBA/H mice, at various times after irradiation with one single 3 Gy X-ray dose (groups of 6 animals at 4, 12, 20, 28, 36, 44, 52, 60, 68 and 76 weeks) and at the time overt leukemia; determining the optimal conditions to amplify the exons 1 and 2 of the H-, K- and N-ras genes with the polymerase chain reaction (PCR); assessing nucleotide sequencing of molecular clones derived from the PCR products as a method to detect sequence modifications in the ras genes; improving the oligonucleotide mismatch hybridisation technique in order to detect straightforward specific (oncogenic) mutations in the ras genes.
2. Search for novel recombinant retroviral genomes first in AML DNA, then at various times after irradiation (novel recombinant proviruses exist in radiation-induced mouse thymic lymphomas).
3. Search for ras mutations first in AML DNA, then at various times after irradiation (ras mutations exist in human MLs).
4. Search for elevated myb gene expression, a marker for AML.
5. Search for growth factor (IL-1 and IL-6) expression and receptors in AMLs (expression in ML cell lines was yet observed).
6. Experimental inhibition of growth factor expression by decreasing the number of receptors with vitamin A derivates.

B13 Cellular, molecular and animal studies to determine the risk of stochastic somatic effects of radiation with respect to low dose, low dose rate and radiation quality

Contract Bi7-038 Automated detection of radiation induced chromosome aberrations by slit-scan flow cytometry.

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Total Contribution by the Commission: 230 kECU
24 months from 1/08/90 to 31/07/92

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Description of research work:

The aims of this contract are to develop techniques for the rapid assessment of chromosome aberrations for the purpose of evaluating possible occupational or accidental exposures of human individuals or groups. Protection and intervention measures must be based on dose assessments which are at least partly based on biological methods applied to individuals.

Investigations will be carried out at the Laboratory for Radiobiology of the University of Amsterdam to develop a method for the rapid analysis by automated techniques of karyotype abnormalities in large numbers of cells using slit-scanning of fluorescent chromosomes in suspensions prepared from irradiated cells.

In the slit-scan flow cytometer the morphology of each chromosome is analyzed separately through the time dependent registration of the fluorescence signal as the chromosome passes through a strongly focused laser beam. Chromosome profiles are characterised by the centromeres that appear as dips in the pulse shapes. Normal chromosomes produce only one centromere dip. Dicentric chromosomes, the most commonly registered type of radiation-induced aberration, show two dips. Using high speed electronics the centromeres are detected and counted in real-time i.e. during the passage of the chromosome through the flow cytometer. Thus it is possible to activate the cell sorter module incorporated in the system to collect abnormal chromosomes for fixation on microscope slides. These chromosomes are then available for examination by centromere and telomere counting, using visual and automated microscopy techniques. This check is necessary to distinguish chromosome aggregates and other artefacts from chromosome aberrations induced by radiation.

Chromosome suspensions prepared from cultured cells, irradiated in the G_1-phase of the cell cycle will be scored for the frequency of dicentric chromosomes by slit-scan flow karyotyping and by microscopy analysis. Cells from the same cultures will be plated for the analysis of cloning capacity as a test for cell survival. Dose-effect relations for these endpoints will be analyzed in various cell lines with different radiation sensitivities. At a later stage of the project, human lymphocytes irradiated in vitro or in vivo will be cultured for the preparation of chromosome suspensions and analysis by slit-scan-flow karyotyping.

Immunofluorescence labelling of human chromosome centromeres in suspension and the detection of centromere fluorescence coupled with chromosome DNA measurements has been demonstrated at the MRC Human Genetics Unit at Edinburgh. DNA probes for centromere and telomere sequences are currently available and work on cloning human telomeres is in progress. The use of a probe recognising sequences at the X-chromosome centromere, together with in situ hybridisation has led to improvements in the manual and atomic detection of fragile X-chromosomes in metaphase slide preparations. Experience has been gained recently in mapping telomeric repeat sequences chromosomes using similar techniques.

The positive identification of aberrant chromosomes by flow cytometry will enhance the sensitivity of the slit-scan procedure considerably. Fluorescent markers of both the centromeres and telomeres of each chromosome will provide information on chromosome morphology, which could clearly separate true dicentric chromosomes from artefacts, both in slit-scan flow cytometry analysis and in microscope slide analysis.

Experiments will be directed at the fluorescent labelling of isolated chromosomes using CREST antibodies and in situ hybridised DNA probes specific to chromosome centromeres or telomeres. The labelling techniques will be quantitatively monitored on slides by image analysis methods. Conventional flow cytometry equipment for the measurement of labelled chromosome fluorescence will be used to evaluate the performance of each labelling technique before being tested on the slit-scanning flow cytometer.

The aim of project at the Gesellschaft für Strahlen und Umweltforschung at Munich is to develop an automated micronucleus (MN) assay applied specifically to human lymphocytes, using flow cytometry. A flow cytometer technique has already established for determining the number of MN per cell nucleus by measuring number and DNA content of isolated MN and cell nucleus in irradiated mammalian cell cultures. Doses as low as 0.1 Gy can rapidly and with good statistical precision be detected. In this project a modification of this technique will be applied to human lymphocytes. Several problems have to be solved :

- MN must be clearly distinguished from blood cell debris and unspecific background during flow cytometric analysis;

- The cell cycle of stimulated lymphocytes has to be analyzed since the frequency of MN depends on the number of cell divisions after treatment.

The development and practical application of an automated MN assay depends on experience in microscopic scoring of MN. In principle the experimental approach for the project is to evaluate

the precision and sensitivity of automatic MN Scoring by microscopic analysis. A comparison of data sets derived with both scoring procedures provides the possibility to eliminate false positive and negative results of flow cytometric analysis. In addition, representative dose response curves for dicentrics and acentrics are available for several radiation qualities to study the correspondence between data on chromosomal aberrations and MN incidence.

It is planned to extend the current investigations in the following directions :

1 - Establishment of dose-effect curves for chromatin texture assay (CTA) of in vitro exposed human lymphocytes. The experiments shall also elucidate the role of varying chromatin texture during the cell cycle on damage expression and compare the effect efficiency with the chromosomal and micronucleus test.

2 - Establishment of dose-effect curves for CTA in whole body exposed mice. The experiments shall also elucidate the kinetics of damage expression during lymphopoieses.

3 - Investigation of the possible application of CTA for human exposure monitoring. A screening programme is planned with radiotherapy patients carefully selected with respect to clinical status and exposure conditions.

B13 Cellular, molecular and animal studies to determine the risk of stochastic somatic effects of radiation with respect to low dose, low dose rate and radiation quality

Contract Bi7-039 Studies on basic and applied aspects of radiation-induced chromosomal aberrations in human cells

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Total Contribution by the Commission: 531 kECU
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Description of research work:

Introduction:

Chromosomal aberration is considered to be one of the important biological effects arising as the consequence of exposure to ionizing radiation to man. In case of radiation accidents, chromosome aberration frequencies in peripheral blood lymphocytes are used to estimate absorbed radiation dose. Chromosomal aberrations in germ cells and somatic cells are associated with congenital malformations in newborns and neoplasms respectively. Thus, understanding of the mechanisms of induction of DNA lesions and formation of chromosomal aberrations is very important. Though the radiation induced DNA double strand break is considered to be the probable DNA lesion leading to chromosomal aberration, factors such as, dose rate, chromatin configuration at the time of irradiation, the DNA repair mechanisms that operate and the influence of cell cycle on the type and frequency of aberrations are not well understood. In addition, the influence of low doses and dose rates on the induction of chromosomal aberrations and other biological effects needs further investigations. The basis for the so called "adaptive response" following low doses of radiation needs to be understood. This project, involving 15 European laboratories aims at elucidating the relative role of the above factors on the yield of radiation induced chromosomal aberrations in mammalian cells.

(A) Radiation induced DNA lesions and chromosomal aberrations:

(1) G0/G1 human lymphocytes and G1 mammalian fibroblasts (Leiden, Stockholm NIRP):

Human blood samples or isolated lymphocytes will be irradiated with X-rays or fast neutrons (1 MeV) and the frequencies and distribution of aberrations will be studied (University of Leiden). For evaluation of immediate yields of aberrations, the technique of premature chromosome condensation (PCC) will be employed. PCC technique will allow us to estimate the repair kinetics of chromosome breaks after neutron irradiation (Leiden). Similar experiments have already been carried out in lymphocytes irradiated with X-rays. For efficient detection of dicentrics in PCCs, reaction with antibodies against kinetochore proteins or in situ hybridization with biotinylated centromere specific DNA sequences will be employed (Leiden).

Measurements of DNA double strand breaks and their repair following both high and low LET radiations will be carried out (Stockholm University 1).

The assumption that the formation of reciprocal translocations and dicentrics occurs in equal proportions (1 : 1) will be re-examined using immunological staining technique following in situ hybridization with individual human chromosome DNA libraries. This technique will allow detection of translocations very efficiently (Leiden). Molecular mechanisms of induction of aberrations will be explored by X-irradiation of lymphocytes/fibroblasts followed by electroporation of cells in the presence of enzymes (Leiden). With this method, we can introduce large molecules into the cells. The enzymes to be used include, Neurospora endonuclease, Micrococcus endonuclease etc. These enzymes will either convert DNA single strand breaks (SSBs) to double strand breaks (DSBs) or create SSBs at the site of radiation induced base damage. Quantification of the aberrations (Leiden) and strand breaks (Stockholm 1) will enable us to estimate the relative contribution of different types of lesions to the formation of aberrations. Comparison of induction and distribution of aberrations induced by X-rays (random lesions), restriction endonuclease (random, but depending on the sequences) and DNAse 1 (non-random) in human lymphocytes/fibroblasts in dormant vs transcriptionally active stages will be made (Leiden).

(2) G2 human/mammalian fibroblasts (St Andrews, Harwell):

Elucidation of the molecular mechanism of conversion of primary radiation damage (DNA DSBs) into G2 chromatid deletions and exchanges will be studied (St Andrews). This will include (a) study of kinetics of formation of chromatid deletions and exchanges in G2 stage of cell lines of different radiosensitivities under extended G2 conditions (lowered temperature). Chinese hamster xrs, irs (radiosensitive) and normal parental lines, normal human, radiosensitive ataxia telangiectasia and radioresistant glioma cell lines will be used. G2 aberrations will be scored in metaphases selected by mitotic shake off following 30' colcemide exposure (St Andrews). Manipulation of G2 response of radiosensitive cell lines (xrs, irs,AT) using purified nuclear extracts from normal human and Chinese hamster cells will be made. These extracts purified by gel chromatography, DNA affinity and electrophoretic methods, will be used to treat X-irradiated and porated G2 cells which will be assayed for aberrations in metaphase. Parallel experiments will be performed using neutral elution to measure the induction and repair of DSBs in cells exposed to X-rays or to porated cells exposed to X-rays and cell extracts (St Andrews).

In view of the fact that target population (G2 cells) has not uniform sensitivity for the production of chromatid-type aberrations by ionizing radiations, the observed frequencies fluctuate with sampling time and are subjected to considerable modification by treatment induced cell kinetic perturbations. To overcome these problems a BrdU cell marking method has been developed (Harwell) which enables one to concentrate scoring on cohorts of cells that were at recognizable developmental stages at the time of treatment. This allows valid comparisons between treatments.

The absence of an unique chromatid aberration frequency to set against dose implies that a "meaningful" dose response curve cannot be obtained by a standard single sampling time method. Cohort analysis, by providing comparable cell samples at each dose, irrespective of cell perturbation should overcome this. Attempts will be made to investigate some aspects of mitotic delay to back up some on-going theoretical studies (Harwell). BrdU cell marking will also be used to investigate the nature of observed chromatid "breaks" (discontinuities) and their relation to intra-arm intrachanges within G2 and S phases of cell cycle. Radiations of different qualities will be used in order to throw additional light on the existing various hypotheses of origin (Harwell).

(B) Adaptive response for radiation induced chromosomal aberrations (Rome, Sevilla, Harwell, Julich):

An initial small dose of radiation (adaptive dose) to human lymphocytes in G1 has been found to reduce the frequencies of aberrations induced by a subsequent high dose of radiation (challenging dose) in G2. (University of Rome). This phenomenon has been termed as "adaptive response"(AR).

AR has been found to be induced by low doses of X-rays, beta rays (Rome, Leiden). Inter individual variation for adaptive response has been reported (Rome, Leiden). It is proposed to study the causes for this variability to see whether this condition depends on transient physiological parameters or some stable constitutional traits determined genetically (Rome). Experiments will be repeated on lymphocytes of some donors already investigated and their families (Rome). Further, AR to clastogenic lesions induced to challenging doses of known chemical mutagens will be studied (Rome).

Since peroxides yield transient radical species, similar to those generated by ionizing radiation, it is proposed to carry out experiments using human lymphocytes to study the effectiveness of low doses of hydrogen peroxide (conditioning dose) on the yield of chromosomal aberrations by a subsequent (challenging dose) treatment with X-rays (Sevilla). In addition to chromosomal damage (different kinds of aberrations and micronuclei in cytochalasin blocked binucleated cells), cell proliferation will also be determined by analyzing mitotic indices as well as BrdU incorporation patterns (Sevilla).

For detailed analysis of adaptive response which rests heavily upon chromatid aberration scores for its validation, cohort analysis (by BrdU pulse labelling) will allow one to determine with considerable precision, where cells were at the time of exposure to adaptation and challenge doses and to base frequency comparisons at similar cell mixes (Harwell). Cellular AR response studies will be extended to in vivo (mouse) system (Julich). Cellular response will be studied by studying an enzyme, thymidine kinase (known to be prone to radical attacks) and DNA strand breaks by fluorometric analysis of unwinding of DNA from mouse bone marrow cells. (Julich).

(C) Studies on the effects of low doses and dose rates (Stockholm 2, Leiden, Uppsala):

Though it is generally assumed that with low dose/low dose rates the cancer risk is 2 to 10 times lower than cancer risk coefficients at high dose/dose rates (UNSCEAR, 1988, BIER V,1990), a few observations with both radiation and chemical exposure indicate that low doses/dose rates may be more effective than expected from linear extrapolation of doses at high dose/dose rate. Experiments are planned to study the mechanisms by which dose rates can influence the risk with the purpose of ultimately reducing the uncertainty of risk estimates at low doses and dose rates (Stockholm 2). It is proposed that supralinearity and sublinearity at low doses/dose rates can be obtained through induction of enzymes for "error-free" or "error-prone" repair of DNA lesions. As a general indicator of inducibility of enzymes, the inhibitory action of 2-mercaptoethylamine (MEA) on induction will be utilized in experiments with fractionated dose (one inducing and one challenging fraction) or with varied dose rates,i.e., dose delivered in ~1 minute compared to few hours (Stockholm 2). Induced mutations (HPRT) and chromosomal aberrations in cultivated mammalian cells will be studied (Stockholm 2 and Leiden). Mutants will be studied by PCR technique to characterise the nature of mutagenic event (point mutation vs deletion).

The frequencies of micronuclei will be measured in cells in culture (thyroid hormone responsive and non responsive) following pulse or continuous labelling with 125 - Iodine (Uppsala). Appearance of micronuclei will be determined in erythrocytes of fishes following incorporation of 125 iodine in the form of IrdU, or binding to chromatin by 125 I-T3 or by uptake of 137 Cs. The types of treatments will be adjusted to deliver low doses at low dose rates (Uppsala).

(D) G2 sensitivity to high LET (Viterbo):

I. Objectives of the project:

to irradiate blood in vitro with high LET irradiation to examine the influence of different classes of DNA repair inhibitors on the induction of chromosomal aberrations in the G2 phase of the cell cycle.

1. To irradiate with different doses 5,11,15 and 30 cGy of fission neutrons (0.4 MeV average energy) human lymphocytes in vitro and post treat with hydroxyurea(HU), arabinofuranosilcytosin (ara C) and caffeine.

2.To analyze the data for:

a) interindividual variation.

b) effect of the different classes of DNA repair inhibitors on the yield of chromosomal aberrations.

(E) Studies using the HPRT locus as a tester gene:

The estimate of the carcinogenic risk associated with exposure to low doses of ionizing radiations is generally based on the extrapolation of the results of exposures at high doses, but it largely depends on various hypotheses concerning the form of the dose-response curve. In this project, we want to set up the HPRT-clonal assay (Albertini, 1982) to study *in vivo* induced human mutants. Because this method allows selection of living mutant cells, characterization of mutation should be possible. Therefore, with this technique, we want:

1) to investigate the dose-response relationship for different well documented low doses of ionizing radiations in patients treated by Curietherapy (gamma rays of the ^{137}Cs, 0.662 Mev) and for whom a calculation of the irradiation dose received by the lymphocytes can be done.

2) a) set up an alternative method to the autoradiographic technique of Albertini. This method is based on the incorporation of 5-BrdU followed by a differential staining *Fluorescence plus Giesma* of the DNA cells which are HPRT$^-$ (Ostrovsky, 1987). Our goal is to establish, from samples obtained in similar conditions, a correlation between frequency and type of chromosomal aberrations and the production of HPRT mutations estimated by the staining intensities of the interphase nuclei.

b) to validate this technique in routine and to increase its sensitivity by the observation of a very high number of cells per individual using a computerized system of image analysis (SAMBA).

3) to determine the molecular nature of the induced mutations to establish the quantitative and qualitative relationship between the exposure and the damage.

4) to extend the former applications to people professionally exposed to an irradiation risk as in radiotherapy and nuclear medicine laboratories.

(F) Aberrations in G_0 and G_2 normal and tumour human cells:

In the first part of this project, premature chromosome condensation (PCC) will be used to measure directly induction and repair of chromatid damage in normal and tumour cells in an attempt to elucidate the mechanisms underlying the phenomenon of G_2 radiosensitivity fluctuations. Particular emphasis will be given to investigate whether the phenomenon is only expressed by cells that had passed the G_2 block transition point at the time of irradiation, and whether chromatin conformation changes are involved in its expression. Experiments similar to those at the cytogenetic level will also be carried out at the DNA level and induction and repair of DNA dsb will be measured using pulsed-field electrophoresis. In the second part, experiments complementary to those carried out in the previous funding period (BI6-E-206-GR) will be conducted for the development of a biological dosimeter for the early assessment of radiation-injury and the establishment of absorbed dose estimates in accidental overexposures. For this purpose, chromosomal aberrations scored in C-banded lymphocyte PCCs will be used.

(G) Sensitivity of lymphocytes from babies and juveniles:

Lymphocytes taken from newly born babies and 12 month old juveniles will be irradiated with 0.5 and 1.0 Gy of gamma radiation after stimulation in the G_2 phase of the cell cycle. Chromatid aberrations arising in the cells will be scored and the sensitivity of the children to radiation will be evaluated as a function of age. Comparisons will also be made with sensitivity of healthy adults and measurements will also be made of the chromosome aberrations induced in the lymphocytes when irradiated prior to stimulation in the G_0 phase of the cell cycle

B13 Cellular, molecular and animal studies to determine the risk of stochastic somatic effects of radiation with respect to low dose, low dose rate and radiation quality

Contract Bi7-043 Measurement of transformation of C3H 10T 1/2 cells by low doses of ionizing radiation.

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Total Contribution by the Commission: 458 kECU
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Description of research work:

Introduction:

The principal risk from low doses of ionising radiation is the induction of cancer. At present, the risks of developing specific types of cancer are based on predictions made by methods which have not been validated at occupational radiation doses. At such low doses the use of animal models to study dose response relationships for cancer becomes prohibitively expensive. Cell transformation in vitro offers an alternative approach, however, only one system, the C3H 10T½ assay, provides the relatively high precision required for measurements at low doses.

Even with this assay the sensitivity is low, consequently a collaborative effort involving several laboratories is necessary to measure effects at 10 mGy. A joint venture between AEA, Harwell;

GSF, Frankfurt; Nuclear Electric, Berkeley and the Universities of Milan and Wurzburg has been established to carry out such a programme with the following objectives:

1: To standardise the C3H 10T½ cell transformation assay between European laboratories to ensure comparability of results.

2: To establish the shape of the dose-response relationships for survival and transformation of 10T½ cells exposed to a range of radiation qualities down to 10 mGy.

Progress.

Initial discussions revealed several differences in the assay procedures used by the participating laboratories:

Comparative evaluation of scoring transformants.

As a first step towards harmonising the assay procedures each lab contributed a selection of culture vessels containing transformed foci from previous experiments. The vessels were then circulated around the laboratories and each laboratory independently recorded the number of foci they considered to be transformed. A comparison between the scores revealed some differences but overall there was good agreement. On the basis of round-table discussions the criteria for defining a transformed focus was further refined and the criteria for identifying transformants standardised between the participating laboratories.

Inter-comparison of experimental protocols.

A comparison of the standard procedures used by the different labs showed some minor differences but it is not clear whether these affect the final transformation frequency. At this stage, no attempt has been made to derive and impose a consensus standard procedure for the assay, However, certain additional steps have been taken to harmonise the technical procedures used by the different laboratories. In particular, the plating density of viable cells at the beginning of a transformation experiment has, initially, been set to 3-5 cells cm^{-2}, and a common method of staining the monolayer at the end of the experiment has been adopted.

Multi-centre measurement of transformation frequency.

In order to establish whether other differences in technique influence the outcome of a transformation experiment 10T½ cells irradiated at one laboratory will be shipped to the other participants who will then perform a transformation assay according to their normal procedures. Preliminary studies on the optimum method of shipping the cells, by the University of Wurzburg and Berkeley, revealed that they travelled best at 0°C in an ice-water mixture. Using this procedure, recovery was high and the plating efficiency was unaffected by 48 hr in transit. Freezing in liquid nitrogen followed by shipping on dry ice was unsatisfactory; recovery was poor and the plating efficiency was reduced by approximately 50%, irradiated and unirradiated cells being affected to the same extent.

Future objectives.

Having established the feasibility of shipping irradiated cells between the participants with no loss of viability 10T½ cells will be irradiated with 5 Gy-rays at one centre and shipped to each participant along with appropriate controls. Each participant will initiate a transformation assay from the cells in parallel with a transformation assay using their own cells as an internal control. The results will be reviewed and, if necessary the experimental procedures revised to achieve greater uniformity. If the results are in reasonable agreement, (i.e. no significant difference between the labs so the results can be pooled), the procedure will be repeated for a dose of 1 Gy and subsequently in steps to lower doses, the final target being 10 mGy.

B14 Assessment of genetic risks in man

Contracts Bi6-156/6-143/6-166/6-069/6-077/7-048/7-052 Radiation-induced genetic effects in germ cells of mammals

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Total Contribution by the Commission: 458 kECU
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Description of research work:

An estimation of the genetic risk resulting from an increased mutation rate due to radiation exposure in man must be based on experimental results in animals. As in any extrapolation, that estimate will have a higher likelihood of accuracy which is based on experimental results most

closely reflecting the situation to be estimated. For an estimate of the genetic risk in man, a number of **in vivo** mammalian germ cell mutation tests have been developed, including methods to screen for recessive coat color mutations at specific loci, dominant cataract mutations, enzyme change or activity mutations at selected loci and chromosome aberrations.

Mutations in mice and hamsters after split-dose exposure (GSF Neuherberg)

Two methods are available to estimate the human radiation genetic risk: The direct approach estimates the frequency of induced dominant deleterious mutations in man based on experimental results in the mouse for induced dominant mutations. An estimation of the frequency of induced chromosomal aberrations is extrapolated from a combination of mouse and primate data. The second approach, the indirect method, estimates the frequency of dominant deleterious mutations in man based on the estimated doubling dose determined in the mouse for recessive specific locus mutations or for a combination of mouse data for the most relevant genetic endpoints.

Both extrapolation procedures require the assumption that there are no species differences in the sensitivity to radiation mutation induction. The indirect approach requires the additional assumption that the doubling dose estimated in the mouse for induced specific locus mutations is representative for other genetic endpoints.

In humans, epidemiological results to estimate the genetic risk due to radiation exposure are available for the offspring of exposed survivors of the atomic bombings at Hiroshima and Nagasaki. Traits scored were embryonic mortality, juvenile mortality, juvenile cancer, reciprocal translocation, enzyme charge or enzyme activity alteration, and sex chromosome aneuploidy. The probability of observing an increased mutation rate in the exposed group was low since the human data base was meagre by animal experimentation standards due to a low parental generation exposure and a small population size. Despite these limitations Neel and co-workers have estimated the radiation doubling dose in man, defined as that dose of radiation which induces as many mutations as occur spontaneously per generation.

The doubling dose estimate in man was five times the doubling dose estimate for mouse recessive specific locus mutation rate data. This discrepancy has precipitated a controversy in which Neel and co-workers suggest a species difference in the sensitivity to radiation induced mutation rate.

By contrast it should be emphasized that the man-mouse mutation rate comparison is confounded by:

a) statistical variability of observations for low dose, small population size in humans,
b) differences in the genetic endpoints scored in man and mouse.

Thus, the source of the differences observed in the radiation doubling dose estimated in man and mouse might not reside in a species difference in the sensitivity to radiation induction of mutation but to the above confounding factors. Only reliable experimental data can resolve this controversy. To this end we have developed a multiple genetic endpoint mutation test protocol to determine the induced mutation rate for recessive specific locus alleles, dominant cataract alleles and enzyme charge or activity alleles in the same experimental animals. Results provide a systematic comparison of the induced mutation rate for different genetic endpoints in the mouse. Further, we have established an experimental procedure to screen for dominant cataract mutations in the two mammalian species, Mus musculus and Mesocricetus auratus. Preliminary results indicate no species differences in the sensitivity to mutation induction. In contrast, a difference for the various genetic endpoints tested in the mouse was observed in the sensitivity to mutation induction. More importantly, the estimated radiation doubling dose for induced dominant cataract mutations was four times the radiation doubling dose for induced recessive specific locus mutations. Together, these results suggest the differences in the radiation doubling dose estimated in man and mouse may be due to the genetic endpoints employed. Finally, the induction of a mutation is dependent on the interaction of the rate at which primary DNA lesions are induced with the rate at which DNA lesions are repaired or misrepaired. It may be safely stated that for every organism, including man, which has been characterized adequately, genetically determined deficiencies have been identified for DNA repair capability.

An adequate characterization of the mouse for DNA repair capability is imperative for two reasons. First, at present almost all **in vivo** germ cell mutagenicity data are based on the treatment of a single genotype, (101xC3H)F_1 hybrid mice. Should this genotype be inordinately deficient or proficient in DNA repair capability, it would render mutagenesis experimental results carried out with this genotype as not representative. Second, the identification of genetic variability for DNA repair capability in the mouse would provide the mutational variants with which to study the DNA repair process in germ cells of mammals. To date comparative results are available for irradiated (101xC3H)F_1 hybrid mice as well as the inbred strains BALB/c and DBA/2, and no differences in the sensitivity to irradiation induced mutation rate have been demonstrated. Experiments are still in progress with strain AKR.

Sensitivity to radiation induced cell killing is widely discrepant in the oocytes of mouse and man and suggests the mouse to be a poor model for radiation genetic effects following radiation exposure to women. The question remains if these differences in the sensitivity of oocytes to radiation induced cell killing are correlated with a difference in the sensitivity to radiation induced oocyte killing to be the cell membrane (Dobson et al., Environ. Mut. 5, 498, 1983).

For the contract period 1990-91, in the mouse and hamster the dominant cataract and enzyme activity mutation rate group is to be extended until mutations are recovered for both genetic endpoints in both species to provide a more accurate estimation of the spontaneous mutation rate. These data are critical in estimating the radiation doubling dose for these endpoints in germ cells of mammals. The mutation rate following 2+2 Gy spermatogonial exposure will be determined for dominant cataract and enzyme activity alleles in mouse and hamster as well as experiments to measure the radiation induced mutation rate in oocytes for both genetic endpoints in both species.

Factors affecting the yield of mutations from spermatogonial stem cells of mammals (MRC Chilton)

Assessment of the genetic risks to man of exposure to radiation is very largely dependent upon experimental work in the mouse and is based upon the assumption that man and mouse have equal sensitivities to mutation induction, and that factors modifying the mutation response in the two species are similar. It has long been recognised that the spermatogonial stem cells of various laboratory species vary in their sensitivity to translocation-induction by radiation and we have recently shown that male mice of the 101/H inbred strain give lower translocation yields than the standard C3H/HeH x 101/H hybrid following a range of X-ray doses. A variety of factors influencing the translocation and specific locus mutation response of mouse spermatogonial stem cells have also been identified using the hybrid animals.

The aims of the present work are:

1) to investigate the specific locus mutation response of the stem cells of 101/H mice to 24h fractionated (3 + 3 Gy) and single (6 Gy) X-irradiation;
2) to investigate the sensitivity of the stem cells of other inbred strains to cell killing and genetic damage and examine the genetic bases of the strain differences and
3) examine further the sensitivity of mouse spermatogonial stem cells in different stages of the cell cycle to mutation induction.

Experimental studies on non-disjunction in the mouse (MRC Chilton)

Non-disjunction is known to contribute significantly to the genetic load in man but the causal factors are not well understood. Numerous cytogenetic tests for non-disjunction in the mouse have been devised but they demand skilled expertise and are handicapped by the low spontaneous frequency of non-disjunction in this species. We have recently developed a system of genetic (complimentation) tests using Robertsonian translocations in tester animals to detect non-disjunctional or loss events in chromosomally normal mice. The method has the advantage over cytogenetic approaches of detecting events involving selected, whole chromosomes and can be conducted without the need for skilled personnel. Several chromosomes have been investigated using this approach. The aim of the present project is to complete ongoing studies upon chromosomes 11 and 13 loss following X-irradiation of male and female germ cells using the Rb tester and mono-brachial homology tester methods.

Radiation-induced genetic damage in mouse oocytes (MRC Chilton)

This project is a continuation of Contract No. B16-E-173-UK (Dr C Tease), Karyotypic analysis of spontaneous and radiation-induced chromosome anomalies in mouse foetuses, which has been combined with BI6-E-143-UK.

The aim of the present work is to examine further the various factors that influence the response of mouse oocytes to radiation-induced genetic damage. Such information should prove of value when using data from female mice for human genetic risk estimations.

Firstly, the influence of mouse strain on oocyte radiosensitivity is being investigated. Two inbred strains, C3H/HeH and 101/H, are being used initially; information from F_1 hybrid females between these strains is already available for comparison. The animals are being given either 2 or 4 Gy of X-rays and the effect of the treatment is being assessed by analysis of metaphase I stage oocytes for chromosome aberrations.

Secondly, induced loss of chromosome 19 is being examined using a genetic complementation test. Female mice are being given 1 Gy of X-rays a few hours prior to ovulation; germ cells are known to be extremely radiosensitive at this point of development. The induced incidence of chromosome 19 loss can be estimated from the frequency of genetically marked offspring resulting from complementation. This information will be useful for :

(i) assessing the importance of chromosome size as a factor influencing induced genetic damage;
(ii) comparing the radiosensitivities of oocyte at different stages of follicle development;
(iii) determining the relative sensitivities of different assays to detect radiation-induced genetic damage in oocytes.

Translocation in spermatogonia of Rhesus monkeys (Univ. Leiden)

The induction of structural chromosomal changes forms a significant portion of the genetic damage produced by ionising radiation. For human risk estimates one has to extrapolate from experiments with laboratory animals such as the mouse, and, to a limited extent, primates, to the human situation. During 1990 different aspects of translocation induction in spermatogonial stem cells were studied. In the rhesus monkey (Macaca mulatta) the effects of combined treatments with FSH (54 I.U./ kg/week) and X-rays (1 Gy) were examined. A nonsignificant decrease of 30% in the frequency of induced translocations was recorded for follicle-stimulating hormone (FSH) pretreated animals. Comparison of these translocation data with studies on cell killing in the same monkeys show that the ratio between the probabilities that radiation induced basic lesions kill a cell or produce translocations is about 10 : 1. This value of 10 is very similar to that observed for the mouse or calculated on theoretical grounds.

All data so far obtained in the rhesus monkey (dose-effect relationship, dose-rate effect, the effect of radiation quality, etc.) suggest that testicular repopulation after radiation damage in rhesus monkeys is mainly responsible for the observed differences between mouse and monkey. There is also evidence available that the recovery of radiation damage in the rhesus monkey is comparable to that seen in steel (Sl) and dominant spotting (W) mutations in the mouse. Preliminary data obtained by us point to a recovery of translocations from 3 Gy irradiated $W^v/+$ (viable allele of dominant spotting) and Sl^{con}/Sl^{con} (contrasted allele of steel) male mice which is comparable to the low frequencies observed in the rhesus monkey.

Genetic damage in oocytes of Guinea pigs (CEN/SCK)

Introduction

Research has suggested that the guinea-pig may constitute a particularly useful model for studying the effects of radiation on the female germ cells, in connection with the risks of radiation for human germ cells.

The project will consist in a contribution to an evaluation of the radio-sensitivity of the oocytes of the guinea-pig. Several parameters can be used to assess the radio-sensitivity of the germ cells: the project will concentrate on long-term reproductive effects and on cytogenetic effects.

Description of the studies to be performed

In these experiments, irradiation will be performed during intra--uterine life, early post-natal life or adult life, in order to compare the radiosensitivities of oocytes at different stages. Two doses of X-rays will be delivered, according to the results of a preliminary study. 6 and 12 months after treatment, exposed females will be mated with untreated males and the fertility of the animals will be followed. 3-4 weeks after the second mating, females will be killed and, in pregnant animals, the number of corpora lutea, live and dead embryos will be counted and the percentage yield of dominant lethal mutations will be calculated. In each experimental group some ovaries will be fixed for histological examination in order to determine the effects of treatment on oocyte killing.

Simultaneously with the long-term reproductive study, a method will be developed for culturing the guinea-pig oocytes and for obtaining preparations of their metaphase I and metaphase II chromosomes. This will be followed by investigations on the induction by radiation of translocations in the female germ cells of this species. The guinea-pig differs from other rodents in that the ovary of the post-natal animal contains two different populations of oocytes at diplotene. A "large" oocyte comparable to that of other mammals and a "contracted" type, which predominates as the animal ages. The sensitivities of these two cell types of resting oocytes to the induction of translocations by radiation will be evaluated and compared.

Induction of genetic damage in embryonal development and its transmission to new-born (Univ. Essen)

General Aim

The project aims at a better understanding of radiation risk during early pregnancy, a period for which virtually nothing is known with regard to radiation risk for the human embryo. As development during the preimplantation stage is similar in almost all mammals (including man), one cell mouse embryos in vitro and in vivo will be exposed to different radiation qualities (neutrons, X-rays, ß-rays) in different cell cycle stages. The following endpoints will be studied:

a) Chromosomal aberrations in the first, second and third mitosis after exposure.

b) The number of micronuclei in the first, second and third interphase after exposure.

c) The type and frequency of teratogenic effects on day 19 of gestation.

Marked differences in radiation sensitivity of the various cell cycle phases of the one cell stage have been observed. After neutron or X-ray exposure, the number of chromosomal aberrations increased already in the first mitosis after radiation; this was different for radiation exposure due to ß-rays from ^{3}H-arginine or ^{3}H-thymidine, because a rise in the number of aberrations was seen only starting with the second mitosis. A high number of complete chromosomes was lost in the second and third mitosis after neutron or X-ray-exposure. The lost chromosomes contributed, besides acentric fragments and polycentric chromosomes, to the micronucleus frequency of the cells.

The mouse strain used in the experiments responded to radiation exposure of the one cell stage not only with lethal events, but also with malformed fetuses (mainly gastroschisis). The number of malformed fetuses increased with the square of radiation dose and without an indication of a threshold dose. Further experiments confirming and expanding these results will be made.

Determination of DNA damage in germ cells (TNO Rijswijk)

Exposure of cells to ionizing radiation results in damage to the DNA. This damage comprises strand breaks and base modifications. These damages might lead to mutagenesis and carcinogenesis or, when induced in germ cells, to genetic abnormalities and other hereditary effects in the offspring. It is important, therefore, to inventorize and quantify the various damages to get information about their relative contribution and persistence. To this purpose we are developing sensitive immunochemical an biochemical methods to quantify single-strand breaks, alkali-labile sites and base damage. The immunochemical method is based on the binding of a monoclonal antibody to single-stranded DNA.

The technique is based upon the determination of the percentage single-strandedness resulting from the partial unwinding of cellular DNA under strictly controlled alkaline conditions. Strand breaks and alkali-labile sites form initiation points for the unwinding.

The extent of unwinding is a measure of the number of such sites. The results are compared with those obtained with "alkaline elution". Base damage can be quantified in a similar way when alkaline unwinding is preceded by treatment of the DNA with damage-oriented endonuclease (i.c. a Micrococcus luteus-extract).

The usefulness of these approaches to detect single-strand breaks and base-damage was demonstrated by detection of damage and its repair in unlabelled DNA-containing cells of human blood after in vitro and in vivo exposure to ionizing radiation. Single-strand breaks could be assayed down to doses as low as 0.5 Gy. Base-damage could be detected after in vitro irradiation in the dose range of 1.5 to 25 Gy. After 5 Gy, measurable base damage was still present at 1.5 h after exposure.

Also leukemia patients undergoing chemo- and radiotherapy were investigated. These patients were exposed to Endoxan and total body irradiation. Base damage induced by doses of 4.5 to 8.6 Gy could be detected, even at 90 min after irradiation.

We are now trying to apply these techniques to germ cells of the Syrian golden hamster. Preliminary results showed that, after a dose of 4 GY, base damage could be detected in the round spermatids 30 min after exposure.

This is in contrast to the single-strand breaks that were repaired almost completely within this period. Furthermore, it was found that in all stadia of the spermatogenesis there is a fast repair of single-strand breaks except in the latest stage, the so-called "elongated spermatids", before the differentiation to spermatozoa. Both after in vitro and in vivo irradiation, up to 90 min after exposure no removal of single-strand breaks was observed in the elongated spermatids.

So far it was not possible to study the induction and repair of single-strand breaks in the spermatozoa. To this aim modifications of the immunochemical method have to be made to make these cells accessible for investigation of DNA-damage induction and repair.

Relation between cell killing and genetic damage in spermatogonia (Univ. Utrecht)

Although contrasting reports exist, most authors agree that there is a correlation between cell killing and induction of mutations or reciprocal translocations in spermatogonial stem cells. In 1981, Leenhouts and Chadwick published a theoretical model which fitted most of the data on the induction of translocations by ionizing radiation in mouse spermatogonial stem cells. In this model it was assumed that there are radiosensitive and radioresistant spermatogonial stem cells, for both cell killing and the induction of translocations, although no D_0 values for the different types of stem cells were known at that time.

In recent years it has become clear that both the radiosensitivity for cell killing and the proliferative activity of the spermatogonial stem cells, varies during the cycle of the seminiferous epithelium. In CBA mice it was found that when the stem cells are actively proliferating (epithelial stages I-III), they have a D_0 value for X-rays of approximately 1.7 Gy. When these cells are quiescent (stages VI-VII) the D_0 is about 1.0 Gy, and when the quiescent stem cells gradually start to proliferate again, their D_0 is about 2.3 Gy (stages IX-XII).

This relation between proliferative activity and cell killing is closely similar to that found earlier in Cpb-N mice after fission neutron irradiation. Hence, quiescent spermatogonial stem cells are highly sensitive to the cell killing effect of irradiation, they have an intermediate radiosensitivity when actively proliferating and they pass through a very radioresistant phase when they are triggered out of quiescence.

Unfortunately, only few data on the induction of genetic damage in the above mentioned strains of mice are available. Therefore, we now want to study C3H/101 (3H1) hybrid mice, which are the most widely used type of mice in radiation genetic studies. Answers to the following questions will be sought:

1. What are the D_0 values for killing of proliferating, quiescent and "triggered" stem cells by X-irradiation in 3H1 mice?

2. How many stem cells are present per 3H1 testis and what is the density of these cells during the epithelial cycle?

3. What are the approximate numbers of proliferating, quiescent and "triggered" stem cells in a 3H1 mouse testis?

These data will then be used for a first evaluation of the model of Leenhouts and Chadwick. Most likely, also in 3H1 mice stem cells with an intermediate sensitivity will be found which will make it necessary to adapt the model. This project will be carried out in cooperation with Dr. B.M. Cattanach (Harwell) and Dr. P.P.W. van Buul (Leiden).

Experiments:

1. A dose-response experiment will be done in which 3H1 mice receive graded doses of X-rays ranging from 0.5 to 10 Gy. In sections of the testes of these mice taken at day 10 after irradiation, the number of undifferentiated spermatogonia will be counted in each epithelial stage as a measure of the number of surviving stem cells. From the dose effect relationships the D_0 value for stem cell killing in each stage can be calculated.

2. In tubular whole mounts the numbers of A_s spermatogonia, being the spermatogonial stem cells, relative to the number of Sertoli cells will be counted throughout the epithelial cycle. Using image analysis equipment and testis sections the absolute number of stem cells per testis will be determined.

3. A dose-response experiment will be performed in which 3H1 mice receive graded doses of fission neutron irradiation ranging from 0.25 to 3 Gy. D_0 values for stem cell killing and the size of the repopulating colonies will be determined as described earlier. As the dose effect relationship after fission neutron irradiation gives no shoulder these data will enable the calculation of the approximate numbers of radioresistant, radiosensitive and intermediate stem cells per testis.

B14 Assessment of genetic risks in man

Contract Bi6-226 Studies on spontaneously-arising genetic and partially genetic disorders in man within the framework of the evaluation of genetic radiation hazards.

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Description of research work:

Introduction

The overall goals of this research project are:

(1) to make a detailed analysis of the prevalence of, and detriment associated with spontaneously-arising diseases of complex aetiology (congenital abnormalities and common chronic diseases in adults) and of Mendelian (autosomal dominant, X-linked and autosomal recessive) diseases to examine the validity of the currently used prevalence estimates
(2) to develop methods to estimate the risk of multifactorial diseases in populations exposed to ionizing radiation and
(3) to re-assess the conceptual basis and assumptions used in genetic risk estimation in the light of advances in molecular and radiation genetics.

Project description

The epidemiological aspects of this work are carried out in collaboration with Dr. A. Czeizel (Dept of Human Genetics and Teratology, National Institute of Hygiene, Budapest, Hungary); current focus is on blindness, deaf-mutism and cancers. Mathematical modelling for multifactorial diseases is being carried out in collaboration with Dr. G. Tusnady (Mathematical Institute of the Hungarian Academy of Sciences, Budapest) and Dr. N. Yasuda (National Institute of Radiological Sciences, Chiba, Japan). The reassessment of the conceptual basis of genetic risk estimation has been, in part, necessitated by the recent findings in genetic studies of the A-bomb survivors in Japan which suggest lower genetic risks than those arrived at in the 1988 report of the United Nations Scientific Committee on the Effects of Atomic Radiation and in the 1990 report of the U. S. National Academy of Sciences.

B14 Assessment of genetic risks in man

Contract BiProp. 327 Molecular biology of paternal oncogenesis

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Description of research work:

The possible oncogenic effect through the germline of the father should follow molecular genetic mechanisms according to the Knudson two-hit hypothesis.

We intend to establish a model system using the mouse strains of the "specific locus test" (in cooperation with the GSF-Institute for mammalian genetics, Prof. U.H. Ehling). In this system ethylnitrosurea will be used as a paternal mutagen. ^{227}Th will be applied in F1-mice as a second hit agent. The germline transmitted somatic genetic events and the later changes in the tumour will be studied with a range of oncogene/tumour suppressor gene probes (Prof. H. Höfler, Dr.M. Atkinson). These molecular biological studies should allow an early monitoring of paternal oncogenic risk.

B15 Action of radionuclides on target cells in relation to radionuclide metabolism and studies on biological models for radionuclide-induced cancer

Contracts Bi7-002/6-089/6-064 Osteosarcoma and tumours of the haemopoietic system by low-dose irradiation.

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Description of research work:

The human radium-induced tumours, resulting from former industrial occupation as dial painters with ^{226}Ra and medical treatment with ^{224}Ra, continue to provide basic information on the effects of internal irradiation and radio-carcinogenesis in man. Animal experimentation and in vitro systems help to elucidate the problems of radiation hazards, and in addition increase our understanding of the mechanisms of radiation carcinogenesis. Bone tumours and tumours of the haematopoietic system have been induced experimentally by internal administration of many bone-seeking radioactive isotopes. For several short-lived radionuclides we have the basic knowledge of dose dependence and protraction effects in radiation-induced osteosarcomogenesis and leukaemogenesis. The additional induction of leukaemia, particularly at lower dose levels, raises the question of the target cell in alpha-radiation-oncogenesis. This is a further indication of the importance of extending studies of early events in haematopoietic and stromal bone-marrow cells and osteogenic cells. Data from the epidemiological study on ^{224}Ra patients also indicate the need for systematic investigations of the leukaemia risk after the incorporation of bone-seeking radionuclides. In addition experimental studies using ^{224}Ra offer the possibility of estimating the plutonium risk in humans. In studies of different age periods the role of possible sensitive periods during the whole life-span should be explored. In this proposal considerable emphasis is placed on molecular biological approaches to radiation carcinogenesis, both in appropriate animal models, in vitro systems and human tumours.

Studies with oncogenic retroviruses have revealed new aspects of the molecular basis of carcinogenesis. Several groups of genes have been detected which are involved in the development of tumours. These genes are normal constituents of the genetic make-up of the cell, but in carcinogenesis they seem to be over-expressed, mutated or combined with other genes. A more detailed molecular analysis of target genes for radiation carcinogenesis is envisaged. The research projects in this proposal are concerned with the general problem of radiation risk, especially with respect to radiation-induced cancer. The quantitative analysis of dose-effect relationships with special emphasis on time and quality factors, and the development and analysis of appropriate animal experiments and in vitro systems with the possibility of studying mechanisms of oncogenesis, will have immediate implications for improving the establishment of dose-limits. Inclusion of the whole life-span in the study of risk takes the age-pattern of a real population into account. The determination of the genes and gene products responsible for radiation carcinogenesis would offer the possibility of defining the critical radiation doses which induce or activate events in the cellular genome subsequently leading to cell transformation. This would contribute to the detection of individuals at risk of developing cancer, and to the establishment of new strategies of radiation protection. This would include abolishing those early effects of radiation on cells which are the first steps in tumour development, or interacting with the mechanisms involved in promotion and progression of radiation-induced malignancy. The work will be of great relevance to various groups within the CEC concerned with assessing the risk to human health following incorporation of bone-seeking radionuclides. The data will also be useful to the ICRP and various national bodies concerned with radionuclide toxicity. Coordination within EULEP is planned.

The participants and their particular contributions to the project are detailed below:

The induction of osteosarcoma by low-dose irradiation with different radionuclides: Dose dependence and early cellular and molecular events. Institute for Pathology, GSF-München, West Germany - Investigator Prof. H. Höfler.

In vitro investigation of radiation induced osteosarcomagenesis: Effects of low-dose alpha irradiation and radiation-activation of cellular retroviruses on the differentiation pathways of the cells of bone forming tissues. Department of Molecular Cell Pathology, GSF-München, West Germany - Investigator Prof. V. Erfle

The cellular target of the radiation-induced ostesarcomagenesis will be studied by the Department of Radioprotection, SCK-CEN, Mol, Belgium - Investigator dr. G. Schoeters, whilst the genetic targets of the radio-induced malignancies will be investigated by the Department of Molecular

Biology and Plant Physiology, University of Aarhus, Denmark - Investigator Dr. F. Pedersen and by the Department of Virology, Radiobiological Institute, TNO Rijswijk, Netherlands- Investigator Dr. Bentvelzen.

A comparison of anti-oncogene (tumour-suppressing genes) loss in human and radiation-induced murine osteosarcoma will be undertaken by the Institute of Pathology, Klinikum, Rechts der Isar, Technical University, Munich, West Germany - Investigator Prof. H. Höfler.

The effect of age upon the radiation-induced myeloid leukemia will be studied by the Radiobiological Unit, MRC, Chilton, UK - Investigator Dr. E. Humphreys

The dosimetry of radionuclides upon the tumour induction in the mouse skeleton will be examined by the Biomedical Effects Department, NRPB, Chilton, UK - Investigator Dr R. Saunders.

B15 Action of radionuclides on target cells in relation to radionuclide metabolism and studies on biological models for radionuclide-induced cancer

Contract Bi7-050 Assessment of Radon WL-values, lung tumour induction by radiation of different LET and on characteristics of in vivo and in vitro transformation of bronchial cells.

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Total Contribution by the Commission: 60 kECU
24 months under negotiation

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Description of research work:

1. Assessment of WL-values and their correlation with the resulting dose-rates to lung tissue.

The radioactive noble-gas Radon and its decay products ("daughters") are known to be inducers of lung cancer among uranium miners. Also, there is strong evidence from epidemiological studies and experiments on rats that there is a synergistic effect between Radon and tobacco smoke (by active or passive smoking) as well as to Radon (being present in indoor air in practically every building), the Radon problem has been recognized as being a potential health risk to all members of the general population. In LPP, Razès, as well as in TNO, animal experiments are carried out on the synergism between Radon exposure and tobacco smoke or Radon exposure and certain components of tobacco smoke, e.g. acetaldehyde (TNO). The exposure to Radon and its daughters, however, presents two major difficulties. Comparative measurements in TNO and in LPP, Razès, recently have revealed a great uncertainty in the assessment of the activity concentration in air, expressed in the unit "Working Level" (WL). Depending on the methods used, measurements of the same activity concentration might differ by a factor 2 or more. Second, these experiments also showed that the WL-level of inhaled air might be a rather poor measure of the actual dose-rate to the lungs. Direct measurements of the activity in the lungs of exposed rats indicated that dose-rates in rats, exposed in our inhalation facility, were approx. 5 times as high as in rats, exposed in the facillity in LPP, Razès, at the same WL-level. In radiation protection a direct relationship between WL-level and dose-rate to the lung is usually assumed, as is the validity of WL-measurements regardless of the methods by which they have been carried out. As our results show, these assumptions are at least questionable. We therefore propose to carry out a research project dealing with the following two subjects :

a) What is the usefulness of the WL-level of inhaled air in estimating the dose-rate to the lung, and which other physical or biological parameters might possibly be of importance? We wish to carry out Radon inhalation experiments on rats in which the dose-rate to the lungs is determined by killing rats immediately after Radon exposure and measuring the resulting activity in the lungs and other tissues. This should be done for different exposure conditions in TNO and in LPP, Razès, respectively, by varying parameters like the composition of inhaled activity (i.e. different ratios of daughter concentrations), aerosol conditions, breathing-rate of the animals.

b) By which measuring procedure can WL-levels best be determined? This should involve careful examination of some methods used in laboratory and mining practice, like the Thomas-method, the Rolle-method and the Lucas-method. Their reliability should be tested under different conditions of which the way of airsampling seems to be very important.

This may lead to recommendations on WL-measurements in the future, and to a re-evaluation of WL-values available at present.

2. Evaluation of dose-response relationships for lung tumour induction.

Researchs on the "Relative biological effectiveness for the induction of malignant characteristics in cells by fast neutrons and of lung cancer by radon" exposures of groups of rats to various Radon concentrations have been realized as well as exposures to acetaldehyde and combined exposure to both agents. The results on lung tumour development obtained with these experiments will be applied to determine dose-effect relationships on lung tumour induction in rats. The tumour incidence and pathology will be evaluated and compared with those published by LPP, Razès.

3. Lung tumour induction by radiations with low LET-values.

In previous experiments aimed at developing a lung tumour model in the rat, radioactive sources were implanted in a lobe of the lung of 3-4 week-old WAJ/Rij rats. The frequency of bronchus carcinomas induced in a group of 40 rats implanted with ^{192}Ir sources was 13 (32.5%). In a group of 20 rats, that received implants of ^{125}I seeds in the lung, only one animal developed a squamous cell carcinoma (5%). In the non-implanted lungs no tumours were found. These induction experiments were initiated to obtain bronchial tumours only and no attempt was made to study the influence of dose or dose rate. However, it is clear from these experiments that the induction rate is larger for the ^{192}Ir isotope than for the ^{125}I isotope. In view of the discussion on the quality factor for high LET-radiation and the choice of the reference low-LET-radiation (200-300 keV X-rays or gamma rays of Cs or Co), we propose the following studies :

a) lung tumour induction in two strains of inbred rats, i.e. WAG/Rij and BN rats, as a function of :

   a. radiation quality involving comparison of exposure to ^{192}Ir with gamma rays of 0.3-0.6 MeV versus ^{125}I X-rays of 27.4-35.5 keV;

   b. dose-rate; sources of different activities will be employed;

b) lung tumour induction as a result of the interaction of a single acute low dose of 6 MeV X-rays or 1.5 MeV neutrons on the thorax of animals implanted with a ^{125}I source as a function of time relative to the implantation date. Since chronic and acute exposures are associated with different risk factors for tumour induction because of differences in repair rates, it is of interest to study the combined effect of chronic and acute exposure.

B2 NON-STOCHASTIC EFFECTS OF RADIATION

B21 Radiation syndromes and their treatment after exposure of large parts of the body

Contracts Bi6-061/6-065/6-079/6-059 European network of experimental and clinical research of radiation accident casualities

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Total Contribution by the Commission: 833 kECU
24 months from 1/01/90 to 31/12/91

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Contract Bi6-059

Description of research work:

The contracts represent a joint effort of four Community laboratories to improve the scientific basis and the practice for the diagnosis and treatment of radiation accident victims. The participating laboratories have a long-standing expertise in this area and, for many years, have co-operated closely in research and treatment. They now aim to develop a European network for radiation accident mangement to serve as a center of expertise for the development of strategies to manage radiation accidents should they ever occur in the Community. Moreover, such a network will have an important role in the training of doctors and nurses in the particular handling of accident victims and thereby transmit the unique personnal experience of the participating groups to other institutions.

The management of radiation accidents is typically hampered by the lack of information available on the extent of damage inflicted to the organism and on the amount of tissue spared from radiation which might bring about the recovery of the organism. It should now be possible to develop an **expert system** based on the experience of past accidents and also using a spectrum of **biological indicators** to determine the extent of damage, the likelihood of recovery and the risk of permanent damage with emphasis on effects on the haemopoietic and immune systems.

Detailed information on 300 individual accident victims has been collected and some 200-300 other cases from recent accidents including Chernobyl will be added. Moreover, the recovery pattern of haemopoiesis in patients receiving total body irradiation and bone transplantation will also be included. This data base will be the backbone of an advisory system for the medical management of radiation accidents. (Ulm. Univ.).

The data will also be evaluated by means of bio-mathematical models to estimate damage to the stem cell pool that cannot be measured directly. In addition to the better known granulocytic system, the behaviour of the erythropoietic, lymphopoietic and, especially, the megakaryocytic-platelet system will be modelled. (Ulm. Univ.).

New **treatment modalities** have recently become feasible thanks to the development of bio-engineered **haemopoietic growth factors.** It can be envisaged that a judicious treatment with these factors could allow an optimal stimulation to promote a more speedy and complete recovery of the haemopoietic-immune system.

- In addition to clinical studies in irradiated patients, methods to enhance production of growth factors in vivo by pharmacological means and to influence the regulation of haemopoietic and immunological recovery will be investigated experimentally and in patients. (Ulm. Univ.).
- the effects of administration of different haemopoietic growth factors after therapeutic total body exposure will be studied in cases of bone marrow aplasia either idiopathic, or after failure of bone marrow graft (GM-CSF, IL3, 6...) (ICR).
- Experiments will be carried out on mice to compare the effects of immunoregulatory molecules such as recombinant cytokines (IL-3, IL-4, IL-5, IL-6, IL-7) and Synthetic Thymic Hormones after different radiation doses, and with different modalities of administration in order to define the conditions of optimal effectiveness to accelerate recovery immune system and to prevent radiation death (ENEA).
- The response of the haemopoetic system to the administration to rhesus monkeys of HGF will also be used to develop a prognostic indicator of haemopoietic damage. Such studies with Interleukine-3(IL-3) have now become possible since recombinant rhesus IL-3 has been obtained after it had been recognized that human IL-3 is not fully active in rhesus monkeys. It is of interest that earlier studies on the radiosensitivity of rhesus stem cells have demonstrated that, under conditions of optimal supportive care, doses can be tolerated by the haemopoietic system which hitherto were considered lethal so that the gastro-intestinal syndrome would determine survival. (TNO).
- Murine stem cells can be expanded in vitro 3-5 times by treatment with IL-3. This will be extended to preclinical studies with short incubation periods to IL-3 or GM GSF in rhesus monkeys and later in man. Identification of non-CFU-S populations in mice responsible for haemopoietic reconstitution of irradiated recipients will be attempt in rhesus monkeys and later in man. (TNO).

The development of new techniques for **the isolation of haemopoietic stem cells** has enabled bone marrow transplantation to become a more reliable and safer procedure in cases of very severe radiation accidents. Moreover, new methods of supportive care have become available.

- Concentration of haemopoietic stem cells and removal of T cells which are responsible for graft vs host disease would be of considerable benefit for imperfectly matched bone marrow transplantations. Considerable stem cell enrichment (40-140) with less than 1% contamination by T cells has already been achieved using a combined method of sedimentation and binding of T cells to a protein-A ICH3 complex covalently bound to immunomagnetic beads. This method will be improved and used for allogenic transplantation in MHC- matched, sex-mismatched rhesus monkeys using sustained chimerism (recognized from the presence of the Y chromosome) as an endpoint. This will be studied as a function of the radiation dose and the number of T cells present, and will be adapted to human treatment modalities; (TNO).

- Non-toxic conditioning treatment by immunosuppression could be decisive after a major accident when optimal transplants are not available and allogenic transplants would be considered which, although resulting ultimately in partial chimeras or rejection, could be of temporary benefit to ensure survival. Such treatment could also help grafting when immunosuppression after an accident is only partial because the exposure had been inhomogeneous. Earlier work in mice showed that treatment with monoclonal antibodies against T lymphocytes may be useful. A large spectrum of different antibodies will therefore be tested in mice ultimately selecting such antibodies for which equivalents in man are available and which could be tested in preclinical studies in rhesus monkeys. (TNO).
- Immature haemopoietic stem cells will be obtained by enrichment from umbilical cord blood. Different methods for the purification of stem cells from the umbilical cord blood will be investigated and the creation of a cell bank will be considered.

Finally, it may now be possible to reduce the risks of persons who have to participate in recovery operations by **prophylactic measures.** Haemopoietic injury could be mitigated after a planned radiation exposure during a rescue operation by reinfusing autologous stem cells taken previously from the patient. Such cells could be obtained most readily from blood. Factors,such as dextrane sulphate, which mobilize stem cells from bone marrow into human blood so that greater numbers of stem cells can be collected, will be investigated. The logistics needed for the establishment of such banks will also be studied. (Ulm. Univ.).

Diagnosis and treatment of radiation accident victims must be based on a sound understanding of the underlying **patho-physiological mechanisms** of damage and recovery after total and partial body irradiation, including the definition of the conditions which might lead permanent damage.

- Emphasis is placed on the study of the replication, differentiation and regulation of haemopoietic stem cells in man and large animals based on the most recent advances in stem cell test systems and haemopoietic growth factors. Normal growth and traffic between different areas of the bone marrow will be investigated in normal subjects and in patients subject to large field radiotherapy, as well as in large animals. The results should improve the understanding of the response of persons subject to inhomogeneous or partial body exposure. (Ulm. Univ.).
- Furthermore, circulating lymphocytes will be investigated with respect to chromosomal abnormalities in total body and bone marrow transplanted leukaemia patients as a function of time after exposure and of the exposure situation. Modern methods to characterize qualitative and quantitative changes in lymphocytes and their populations will help to understand the underlying patho-physiological mechanisms. (Ulm. Univ.).
- In order to develop early preventive treatment more understanding of the pathophysiology of late complications as fibrosis is required.Fibrosis, can lead to substantial functional impairment in many tissues including the bone marrow. Research will concentrate on the role of the fibroblast and will determine its cell cycle parameters and the influence of different newly characterized growth factors in fibroblasts cultured from controls and radiotherapy patients, or after irradiation in vitro. Fibroblasts isolated from irradiated skin or irradiated in vitro will be studied with respect to chromosome aberrations, changes in chromatin structure (using a newly developed high-sensitive fluorescence microscope) and for changes in gene activation using measurement of mRNA. Endothelial cells whose damage affects not only vascular alterations but also early oedema will be studied with respect to microscopic and macroscopic alterations and the correlation of serum concentrations of pro-aggregating and anti-aggregating factors. These studies will also contribute to the understanding of the pathogenesis of haemopoietic damage. (ICR).

In order to prepare a European Network for the Management of Radiation Accident Cassualities (ENMRAC), it is planned to jointly

- review the strategies and operational procedures developed in different countries (France and Germany) for the management of radiation accident victims,

prepare a draft for a specific protocol for doctors and nurses on the diagnosis and treatment of whole body exposure, radiological burns and internal radio-contaminations.

define the criteria for the selection of hospitals suitable for the treatment of radiation accident victims,

develop courses to train doctors and nurses in the treatment and handling of radiation accident victims.

B21 Radiation syndromes and their treatment after exposure of large parts of the body

Contract Bi7-058 Biological consequences of partial body irradiation in a monkey model

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Total Contribution by the Commission: 33 kECU
18 months from to 31/08/01

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Description of research work:

Chromosomal aberrations have been enumerated in human lymphocytes after irradiation in vitro. Apart from confirmation of a dose-effect relationship, interesting observations have been made on mixtures of irradiated and non-irradiated lymphocytes. The admixture of a small proportion of non-irradiated lymphocytes could be detected from a disproportionate increase in karyotypes without abnormalities. The latter are magnified , especially when the dose delivered by the irradiated population is relatively high, apparently because many of the irradiated lymphocytes are lost. In these experiments a 3% admixture of non-irradiated cells could be easily detected. Accidental exposures of humans are characterised by an inhomogeneous dose distribution over the body. Under many conditions of exposure smaller or larger parts of the body may be shielded. If those shielded parts contain bone marrow, enough hemopoietic stem cells in the shielded bone marrow may survive, to prevent hemopoietic failure of the victim. From data obtained in experimental animals, among these dogs and monkeys, it has been established that less than 1% of the bone marrow is sufficient to fully protect whole body irradiated subjects from hemopoietic death. In the case of accidental exposures with high doses, it is of great practical importance to determine the haematological prognosis of the victims, in order to decide whether bone marrow transplantation is required or not. Therefore it is essential to investigate whether the results described above for in vitro production of dicentrics can be confirmed in vivo. The bone marrow of humans contains up to 5% of T-lymphocytes, so that a protection of a part of the bone marrow might become expressed in the subsequent chromosome aberration scores of peripheral blood lymphocytes. It cannot be predicted whether a dependable relation between the amount of bone marrow shielded and chromosome aberration scores of peripheral blood lymphocytes will be obtained, because the contribution of the various lymphocyte depots in the body to the peripheral blood during post whole body irradiation conditions is not well known.

However, it is feasible to design experiments with larger animals like monkeys, to establish whether the shielding of 3% or less of the bone marrow results in a detectable preponderance of non-damaged karyotypes of lymphocytes from the peripheral blood at various times after the irradiation.

The experiments will be performed with a limited number of Rhesus monkeys, some exposed to homogeneous total body irradiation, others exposed to the same regimen but with about 3% of the bone marrow shielded. The latter will be accomplished by shielding the hands and wrists, which contain 2.74% of the total marrow space in standard man (ICRP 23, 1974, 90). The experiments can be completed in one year.

B22 Irradiation and committed exposure from incorporated radionuclides

Contract Bi6-347e The reduction of the risks of late effects from incorporated radionuclides (NRPB Association)

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Total Contribution by the Commission: 195 kECU
30 months from 1/01/90 to 30/06/92

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Description of research work:

Aims and Objectives

The aims of the studies described in this contract are to provide practical guidance to those responsible for the treatment of accidental overexposure to plutonium and other actinides.

Description of Project

The chelating agents identified in the proposal have been shown, by others, to be potentially superior to DTPA, the current agent of choice for enhancing the elimination of actinides from the body. Moreover, some of them appear to the active when administered orally, and hence have a high clinical potential for the treatment of severe human disease eg, thalassaemia (iron overload). Studies to be undertaken at the NRPB and CEA will involve the testing of these chelates in rodents after the inhalation of actinides in different chemical forms and in amounts which mimic

a wide range of intakes by humans. Any agents which show particular promise will also be tested in primates. Experiments at KfK with rats will involve the intravenous injection of the actinides and treatment by injection or oral administration. These latter studies will also be supported by in-vitro experiments designed to examine the ability of the chelating agents to remove plutonium from its iron transport protein transferrin. The KfK will also assess the effects of DTPA administration on the induction of bone tumours by ^{239}Pu and the micro distribution of the radiation dose.

Accidental exposure to industrial uranium and thorium compounds is becoming of increasing concern yet there is a paucity of data on optimal treatment regimes. Organo-phosphorus complex ones form strong complexes with these and other metals and the Contract will help support the cost of their syntheses at the Pierre and Marie Curie University Paris. In-vitro experiments designed to elucidate the most promising compounds will be undertaken by the CEA and these will be subsequently tested in-vivo at the CEA and NRPB.

The treatment of pregnant women with complexing agents is an important consideration in radiological protection since these agents also enhance the elimination of other trace metals from the body. The effect of such treatment on the fetus, fetal development and the reduction of the long term risk after incorporation of actinide and alkaline earth metals will be undertaken by the University of Antwerp. Promising new chelators identified in the above studies will also be examined. Other work will determine if haemopoietic-aggressive drugs or pollutants can induce radiation hypersensitivity.

Collectively, the European laboratories participating in this contract are uniquely placed, due to the diversity of the facilities and expertise available, to meet the objectives of the contract in the most cost effective manner. Generous technical support for the above work is being provided by the Chemistry Department, University of California, Berkeley, Lawrence Livermore Laboratory, Albright and Wilson plc, UK, and CEA-IPSN, Pierrelatte, France.

B23 Radiation syndromes and their treatment after local exposure to skin and subcutaneous tissues

Contracts Bi6-063-6-058/7-041/7-056 Radiation effects on skin and subcutaneous tissues: implications for radiation protection criteria and the treatment of localized accidental over-exposure

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Total Contribution by the Commission: 273 kECU
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BI6-063

Description of research work:

Introduction

A broadly based programme of clinical and experimental research is proposed. This will address many of the problems related to the improvement of radiation protection criteria for the skin and the search for improved treatment modalities for the skin and subcutaneous tissues following local, accidental, over-exposure.

The increased use of radio-isotopes in medicine/scientific research and problems inherent in the safe operation of nuclear power plants has increased concern about the present ICRP guidelines for the skin. This concern stems from the paucity of biological data on which the present guidelines are based and the potential over restrictive nature of present criteria, as for example in the nuclear industry with respect to unique exposures to small radioactive particulates. These factors have important economic and technical consequences for the CEC. Although the results of recent experiments have provided valuable information, some important questions still need to be answered. It is proposed to carry out studies to determine the anatomical site of the target cells

responsible for the different types of effect observed; this will indicate the depth in skin at which relevant dose measurements should be made. Although the results obtained from pig skin will provide the most relevant data for non-stochastic risks, a comparison of the results obtained with those for mice will help in the identification of target cells. Studies in mice will help in the understanding of the stochastic risk. Both species will be used to evaluate the effects of irradiation with very low energy ß-rays, α-particles, and small radioactive particulates with emissions of varying energy.

In cases of accidental over-exposure, information is required on the regional distribution of dose. Various aspects of hair, as a biological dosemeter, will be investigated in pig and man. The IAEA Advisory Group on Advances in Biological Dosimetry (Leningrad, November 1987) specifically identified work on hair as being most promising for localised skin exposure.

Cases of accidental over-exposure of the skin and subcutaneous tissues occur in both medicine and industry, but, as indicated by the Chernobyl experience, significant numbers of persons would be affected in a major accident situation. The skin doses in the Chernobyl victims were 20 times greater than the average bone-marrow dose. The pathogenesis of different syndromes observed after local exposure of skin and subcutaneous tissues will be assessed in the pig. After very high-doses, radionecrotic lesions develop within a few weeks. For this lesion the uptake of thallium-201 in muscle will be studied. For late dermal and subcutaneous necrosis vascular permeability and lymphatic clearance will be investigated. These methods may also be of diagnostic value in suggesting the need for subsequent therapy. The value of pharmacological agents in the treatment of both early and late radionecrotic lesions will be evaluated. Screening studies in rabbits might prove useful prior to more definitive work on pigs.

The possible synergistic effects of acute skin damage as a co-determinant of survival, when combined with total body irradiation, will be investigated in mice and the effect of radiation on wound healing will be studied in pigs.

The full evaluation of the research proposed would require support for a five year period. However, in the 2 years (1990 - 1991) for which funding is available specific aspects of the proposal will be completed.

I. CRC Normal Tissue Radiobiology Research Group (Oxford)

The contribution of this laboratory can be described under two broad headings:

(a) research related towards the improvement of radiological protection criteria and
(b) a better understanding of the pathophysiology of late radiation damage to the skin leading to potential improvements in treatment.

(a) Radiological protection criteria

The early and late non-stochastic effects of radiation will be studied in an experimental model system, namely the pig, whose skin structure and anatomical dimensions closely match those of man. Dose-effect relationships will be evaluated after exposure of the skin to different radiation energies with the specific intention of establishing threshold doses for different effects. There will be an evaluation of the anatomical site(s) and the target cell population(s), damage to which results in the various effects observed. Specific studies will involve:

(i) The early reactions seen following irradiation with α particles from curium-244 will be compared with those after exposure to low energy ß-rays (e.g. promethium-147; cobalt-60). In these studies only the epidermis is irradiated, with significantly higher doses being received by the upper layers of the viable epidermis than the basal layer.

(ii) An evaluation of the relative role played by the migration of epithelial cells from the edges of the irradiated area and from the hair follicle canal following exposure to sources, of different sizes, from strontium-90 (to irradiate the full skin thickness) and thulium-170 (to irradiate the epidermis and the upper dermis). This will involve serial morphological studies

from biopsies, coupled with the in vivo labelling of cells and auto-radiography. These studies will help in the understanding of the response of the skin to irradiation with area and radiation quality.

(iii) The determination of the effects of dose-rate on the early and late response of the skin to strontium-90 irradiation. A fixed source of 22.5mm diameter will be used, dose-rates will vary between 1 and 10cGy/min. The incidence of moist desquamation and the presence of dermal atrophy, at 39 weeks and 78 weeks, will be used as endpoints.

(iv) The establishment of the time course of the development of dermal atrophy following irradiation from thulium-170. This will be established from serial non-invasive measurements of dermal thickness using ultrasound (A scan). Two phases of development of dermal thinning have been reported after strontium-90 irradiation. It is hoped that a comparison with thulium-170 will provide an insight into the likely anatomical site of target cells.

(b) Pathogenesis of late radiation-induced damage, a guide to improved treatment modalities

Following the accidental over-exposure of the skin to radiation a late wave of erythema may develop after the main erythema reaction has faded. This late phase of injury represents vascular insufficiency in the dermal and subcutaneous tissues and is associated with oedema: This may in itself contribute further to any primary vascular changes. Severe vascular impairment will result in the development of necrosis to the dermis and deeper tissues when over-exposure is to high-energy radiations. It is proposed to study further these adverse reactions in pig skin by examining radiation-induced changes in vascular permeability. Radiation dose- and energy-related changes in lymphatic clearance will be evaluated using a recently developed, ^{99m}Tc-Rhenium sulphide colloid, clearance technique.

The prophylactic treatment of these late radiation-induced changes will be by the systemic or topical application pharmacological agents. Treatment will be directed either towards the reduction of inflammation and oedema or to methods of improving the vascular supply. The effectiveness of agents with a specific or a broad spectrum of action will be compared.

A further aspect of accidental over-exposure that needs to be addressed is the problem of wound-healing in irradiated skin. Trauma may be associated with accidental over-exposure or surgery may have to be carried out in an irradiated area to repair a necrotic lesion. This will be evaluated in pig skin using a standard surgical wound after irradiation with sources of varying energy. Healing will be evaluated from measurements of the mechanical strength of wounds and from histological observations. The 'in vitro' behaviour of fibroblasts from wounds, irradiated and unirradiated skin will be compared.

II. Laboratoire de Radiobiologie Appliquée (Gif sur Yvette)

The contribution of this laboratory can be described under two headings:

(a) The pathogenesis of severe acute radiation induced lesions and

(b) the treatment of radiation induced lesions.

Pathogenesis

Acute irradiation, with highly localised doses to pig skin, is the main experimental model used: it involves studies of induced radiolesions of the skin and in the underlying tissues (specially muscle). Studies on muscle radiolesions involve:

(1) aspects of cellular metabolism and principally the determination of the cells responsible for the uptake of thallium-201 (e.g. fibroblasts or macrophages).

(2) functional aspects with regards to muscle sensitivity and fatigability as measured by electromyographic methods and

(3) histological investigation of the role of ischemia in the development of fibrosis.

Treatment

Screening of pharmacological treatment agents is performed on rabbits locally irradiated with iridium-192-rays. The results of this screening are to be applied to locally irradiated pigs either by general or topical application.

III. Department of Radiobiology (London)

The contribution of this participant laboratory will be to concentrate on the effects of different energy radiations on mouse skin, the objective being to:

(a) Define, the anatomical site(s) of the target cell(s) for acute epidermal reactions for different absorbed doses and depth dose distributions. The studies will use curium-244 α-rays (to irradiate the epidermis only), promethium-147 ß-rays (to irradiate the epidermis and upper dermis); and thulium-170 ß-rays (to irradiate the full thickness of the skin). The relative roles of epidermal basal cells and hair follicle epithelial cells in the re-epithelialisation process will be investigated. A critical experiment to determine this will use promethium-147 on skin with hair follicles either in anagen (growing) when the follicle epithelial cells are ≥1mm deep in the dermis and out of range of the ß-rays or in telogen (resting) when the follicle epithelial cells are ≈0.25mm depth and within range of the promethium-147 ß-rays. These experiments will entail serial killing after irradiation and histological morphometry coupled with autoradiography.

(b) To clarify any such synergism, mice will receive either desquamative or ulcerative doses of ß-radiation to the skin coupled with sublethal whole body Cobalt-60-doses (2.8Gy) to simulate the conditions of a peacetime reactor accident. The effect of haemopoietic hypoplasia on the severity and duration of the skin lesions will be monitored.

(c) Develop appropriate models for radiation-induced skin cancer in several mouse strains with different anatomical skin types. This will be the major study of this contributory laboratory and it arises from a collaborative project partially funded by the CEC RTD Programme (Contract No. B16-057-UK) which involved irradiation of mice with a wide range of ß-doses (2-1000 Gy surface dose) using plane uniform 8cm^2 sources of thulium-170 or non-uniform arrays of 8 or 32 (2mm diameter) sources distributed over a same 8cm^2 area. These experiments have refuted the 'hot particle theory' since the tumour incidences were always highest following the uniform exposures. The increasing appreciation of the importance of radiation risks of skin cancer incidence and mortality come from both published clinical and epidemiological data and unpublished Hiroshima and Nagasaki data as well as our own experimental work. There is also epidemiological evidence for racial variations in radiogenic skin cancer susceptibility in man and this needs to be investigated. We propose to model and quantitate this phenomenon of skin cancer proneness in four strains of mice; two albino (SAS/4, CD-1), one brown (CBA/Ca) and one black (C57BL/6) strain. Each strain will receive a range of thulium-170 doses from 2-1000 Gy to study the spectrum of tumour pathologies, the dose-latency of the different tumour types and the shapes of the different dose response relationships. These endpoints will be related to the micro-anatomy of the skin. Furthermore, valuable RBE comparisons for high LET curium-244 α-radiations will be possible for one mouse strain (SAS/4) for skin cancer induction. These strain studies may also settle the inconsistencies between human and animal data over the relative roles of the epidermal and dermal origin of skin cancers.

IV. Radiological Protection Branch (Berkeley)

The value of plucked hair as a regional biological dosemeter will be assessed by an evaluation of radiation induced mitoses, pyknotic cells, micronuclei and other aspects of cellular damage to the hair follicle.

Fluorescence backlight staining is a technique whereby stained cells on the surface of a solid tissue sample can be observed by induced epifluorescence in the underlying cells. Human and pig hair (to be supplied by the Oxford group) will be assessed using this technique to detect any dose related

changes in cells of the hair bulb (specifically the differentiating cells of the cuticle, and cells of the inner and outer root sheaths). Direct intra-cellular damage, observable on plucking, will be investigated at various times after in vivo irradiation as will damage following culture in vitro (e.g. cytokinesis blocked cell and micronuclei).

In addition a preliminary study will be carried out to check the feasibility of using the distribution of micronuclei in cytokinesis-blocked peripheral lymphocytes as an indicator of highly non-uniform radiation exposure.

B23 Radiation syndromes and their treatment after local exposure to skin and subcutaneous tissues

Contract Bi7-049 European clinical research on practical protocols for the diagnostics and treatment of localized overexposure

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Total Contribution by the Commission: 175 kECU
24 months from 1/07/90 to 30/06/92

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BI7-049

Description of research work:

Local exposure of the skin and underlying tissue resulting in radiological burns are the most frequent type of accidents of irradiation. They have specific clinical characteristics because of their particular physiopathological mechanisms. The gravity of a radiological burn depends mainly on the energy deposited in the tissues. The dose and its spread have to be determined as accurately as possible in order to evaluate the prognosis and to manage the treatment. Three teams (Institut Curie (F), ENEA (I) and General Hospital of Madrid (S)) are collaborating on a European Level to set up practical protocols for physical dosimetry assessment, diagnosis and treatment of radiological burns.

Physical dosimetry.

The elaboration of personalised phantoms taking into account individual anatomical variations and the development of computer programmes to simulate reconstitution of accidents and to analyse dosimetric data will be carried out by all participants.

Diagnosis.

Available paraclinical methods using the modifications of the micro-circulation, such as infra-red thermography, capillaroscopy and isotopic investigations will be improved. For instance, dynamic

thermographic studies following cryostimulation and computered image analysis will be performed and the knowledge of the normal pattern of the hand and its physiological variations will be improved (F, I).

The development of an image-processing system for capillaroscopy will allow dynamic studies and quantification of images (F, I).
Isotopic investigations focus on vascular modifications and the reaction of bone. Early hyperfixation of bone-seeking tracers can be observed after irradiation to moderate doses. But after high doses, fixation in bone because of metabolic functions sideration can be observed. A systematic study of these parameters will be carried out (F, S).

New methodologies (micro-wave thermography) will improve our understanding of the underlying physiological mechanisms. (F, S, I) Biological dosimetry will be performed on fibroblast cultures to evaluate the dose/effect relation (F) and by quantification of chromosomal abnormality in skin and annex tissues (S).

Treatment.

Protocols for treatment will be developed by a joint effort of participants with emphasis on :

- optimisation of treatment with (superoxide dismutase alone or combined with other enzymes) during the acute and late phase as a way to reduce free radical production.

- Optimisation of pain treatment and study of ultrastructural modification of irradiated nerves (F,I).

- Effect of aloa-vera extracts on cicatrisation (S).

- Indications and optimal time of surgical interventions, improvement of different methods to cover the defect such as graft, skin scrape and artificial skin.

B24 Radiation damage to lens, thyroid and other tissues of relevance in radiation protection

Contract Bi7-005 Irradiation and thyroid disease.

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Total Contribution by the Commission: 120 kECU
24 months from 1/08/90 to 31/07/92

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Description of research work:

INTRODUCTION

Exposure of the thyroid to radioactive iodine represents a potential hazard of ionizing radiation and may lead to thyroid cancer or thyroid dysfunction. The project aims to define the risks of low doses to the thyroid, the biological effects of radioiodine and the potentials risks of preventive administration of stable iodine. To this end

- A human thyroid line will be developed to study the radiobiology of human thyroid cells.
- The relative carcinogenic risks of radioiodine and external radiation will be compared and set in relation with thyroid morphology.
- Uptake of stable iodine will be studied in several regions of the Community to obtain information on relative risks of stable iodine applications after an accident liberating radioiodine.

University of Brussels. J.E. Dumont

The project aims at developing tools for investigating the problems of the action of low radiation doses to the thyroid. To this end, attempts will be made to develop and characterize a human thyroid cell line. Various approaches will be tried, such as transformation by transfection of genes of human

papilloma virus, serial cultures of human tumour cells, X-ray and chemical transformation. The cell line obtained, and similar cell lines that may be developed in other laboratories, will be characterized with respect to the differentiation characteristics (particularly iodine metabolism), growth characteristics and growth factor requirements. The transformation of the cell line by oncogenes (such as SV40) will be assessed on the basis of formation of foci, subculturing, characterization of the transformed cell to evaluate the possibility to use the cell line for X-ray transformation studies. The investigation will concentrate on developing and quantifying parameters for malignant transformation of such cells. The paramaters will be compared to those of normal human thyroid cells in primary culture. This system will later be used to determine the risks of radiation-induced cell transformation and for investigating the role of oncogenes and protooncogenes in this process. The laboratory has already considerable experience in culturing and studying human thyroid cells obtained from biopsy material.

Federated Dublin Voluntary Hospitals. J. Malone

This part of the "Irradiation and Thyroid Disease" contract is concerned with a critical examination of two assumptions that underlay all the dose and level of exposure limits for thyroid irradiation; intervention levels; and counter measures used by governments and international organisations. First much of thyroid irradiation is due to ^{131}I and no firm basis in the scientific literature exists for the values for its biological effectiveness (for cell transformation) viz à viz high dose X or gamma Rays. In fact any value from 0 to 1 can be justified based on at least one reference from a well established group. (Values for ^{131}I biological effectiveness in cell survival studies are now much better established). Experimental methods based on cell culture techniques will be evaluated and established where worthwhile, to help clarify this area of uncertainty. Second there are serious reasons to doubt the validity of using absorbed dose only as a predictor of detriment in a gland whose mass may vary from 10g to 100 g in adults. The case for this statement is clearly made in the State of the Art Review with the original proposal. It is proposed to examine both the validity of the case and the most acceptable alternatives to absorbed dose.

University College, Dublin. P. Smyth

The dietary iodine intake of populations of both adults and schoolchildren residing in different parts of Ireland and in Wales is currently under evaluation. Dietary iodine is being assessed by measuring its excretion in random urine samples. As milk intake has been reported to form the major source of dietary iodine in Northern European Countries, the contribution of seasonal variations in milk iodine content to the daily dietary supply is also being evaluated. A relationship between seasonal variations in urinary iodine excretion and dietary milk iodine content is beginning to emerge. In view of the relative importance of milk in the diet of the young particular attention is being paid to such studies in schoolchildren.

The kinetics of oral iodine administration are being studied by giving known doses to adult volunteers and doing sequential urine and serum iodine estimations. The relative importance of iodine dosage and duration of therapy in achieving a desired plateau of circulating iodine is being investigated.

Finally, high resolution ultrasound scanning is being applied to the accurate measurement of thyroid volume and the frequency of occurrence of thyroid nodules in the study population. Findings are being compared to published results from other European countries.

B3 RADIATION EFFECTS ON THE DEVELOPING ORGANISM

B31 Damage to the central nervous system and hematopoiesis

Contract Bi7-003 Effects of radiation on the development of the central nervous system

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Total Contribution by the Commission: 238 kECU
24 months from 1/08/90 to 31/07/92

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Description of research work:

INTRODUCTION.

The deleterious effects of low doses (10 to 1000 mGy) of ionizing radiation on the development of the central nervous system represent a much debated issue. In contrast with recent work from us and others, some authors claim that doses as high as 500 mGy are largely innocuous to the developing organisms. The aims of the present project are to compare and analyze the effects of protracted versus short low-dose radiation exposures (<500 mGy) using a number of approaches. These range from ultrastructural observations to nerve cell cultures. The experiments and analyses will be performed in Mol, Barcelona and Bruyères-le-Châtel. Frequent contacts between contractors and other workers in the field will occur within the frame of EULEP and during the congresses of the European Society of Radiobiology. In addition, 1-day working sessions including the 3 contractors and EEC representatives have been planned.

DESCRIPTION OF THE INDIVIDUAL SCIENTIFIC TOPICS

Two protocols of irradiation are used by the 3 different contractors: chronical and acute exposure. In chronical experiments, pregnant rats are exposed from 0 to 1000 mGy during the whole or only the last week of pregnancy. Acute irradiations are attempts not only to detect the most sensitive phases of brain development but mainly to find the reasons for such radiosensitivity. Collection of material (autopsies) will take place from a few days before birth to 3 months later.

Morphology (CEN/SCK)

Six different endpoints will be considered:

1. An ultrastructural analysis of the development of synapses in the cingular cerebral cortex of the young adult rat.

   Main Question: are they quantitatively and qualitatively modified after prenatal irradiation? This is in coping with morphometric studies (Konermann, Norton, d'Amato, Ferrer) claiming that after very small doses (100 mGy), changes can still be found in the dendritic arborization of the large neurons.

2. Electron microscopic analysis of the development of the lamellar bodies and Nissl blocks in the neurons from cortical layers II to V.

   Main question: idem as in 1.: are they quantitatively and qualitatively modified after prenatal irradiation ? The lamellar bodies are characteristic organelles unique to neurons. Their function is unclear although we claimed, as early as 1976, they play a role in the origin and formation of the endoplasmic reticulum (Nissl blocks). However, a majority of authors think they intervene in synaptic transmission. In coping with our hypothesis, we suppose they will be depleted in prenatally irradiated neurons.

3. Semi-automatic image analysis of myelination in the white matter (cingulum bundle and corpus callosum).

   Main question: is the atrophy of the prenatally irradiated cingulum caused by myelin depletion (oligodendrocyte damage)? We showed recently the cingulum bundle, a subsidiary of the corpus callosum to be depleted significantly after as low as 25 mGy 600 KeV neutrons. We suspected this depletion to be caused by lack of emergence of axons coming from the nearby cortical neurons. However, this view is actually challenged by Ferrer's group in Barcelona who noted recently that the normal phenomenon of postnatal neuronal cell death is reduced in the cerebral cortex after prenatal irradiation (Ferrer, in press).

4. Assessment of the density of the glial progenitors (residual embryonic cells) after irradiation at day 15 post conception in 2 different rat strains: Wistar versus Sprague- Dawley.

   Main question: is the stem cell stock in irradiated animals lower than in controls?

   Also included in this topic is an assessment of the possible difference in radiosensitivity between 2 rat strains using brain weight and cingulum volume as simple but very sensitive criterions. Main question: is the large difference in radiosensitivity (30%) which is found in the adult brains of these 2 strains, already noticeable in the prenatal Central Nervous System?

5. Measurements of the cytokines interleukin 1 (IL-1) and IL-6 in normal versus irradiated rats. Treatment with indomethacin to prevent IL formation. (in collaboration with R. Hooghe).

   Main question: do IL-1 and IL-6 increase after prenatal irradiation as a consequence of injury? IL concentrations are measured in a dialysate obtained through microperfusion of the brain. The expression of genes coding for IL-1, IL-6 and the receptor of IL-6 is monitored by in situ hybridization with cDNA probes. The receptor for IL-1 is detected by immunocytochemistry.

6. Analysis of the development of radial glia in prenatal brains.

   Main question: are low doses of radiation able to modify the radial glia arborization? Radial glia is detected by histochemistry.

Physiological cell death in early postnatal neurons (Barcelona Univ.)

They will consider 4 different parameters. Part of the material to be studied was irradiated and perfusion fixed in Mol in January 1990.

1. Comparison of the "physiological" neuronal cell death in normal versus irradiated early postnatal brains.

   Main question: does it increase after prenatal irradiation? Very recent data, already acquired under this contract, revealed that contrarily to expectations, the physiological neuron death is actually reduced after prenatal irradiation in the 7 day old cerebral cortex (Ferrer, in press)!

2. Changes in the adult GABAergic neuronal cell populations after prenatal irradiation.

   Main question: do they decrease after treatment? This **in situ** evaluation is parallel to the **in vitro** experiments realized by Coffigny at Bruyeres and focus to the problem of the possible differential radiosensitivity among neuroblasts of various classes. This problem is also dealt with using an immunocytochemical approach in topic 4.

3. Changes in dendritic arborization and spines in 1 month old pyramidal nerve cells.

   Main question: do they decrease after treatment? There is a normal overproduction of dendritic spines during early brain development. Will treatment influence this phenomenon?

4. Immunocytochemical study of transitory populations of parvalbumin containing neurons in the future corpus callosum (cortical embryonic subplate).

   Main question: Is the fate of this particular class of neurons different from the non-parvalbumin ones. In other words:

   a) is physiological cell death restricted to certain classes of nerve cells, or general?

   b) is there a differential radiosensitivity for this class of cells.

Behaviour of irradiated neuroblasts in tissue culture. (CEA-Bruyères-le-Châtel)

1. Influence of prenatal irradiation on the **in vitro** lethality of the nerve cells.

   Main question: Does prenatal irradiation fragilize neuroblasts?

2. **In vitro** assessment of neurotransmitter uptake.

   Main question (in correlation with Barcelona 2d point): Do the GABA (and dopamine) neuronal uptake decrease after prenatal irradiation?

3. A quantitative appraisal of the dendritic arborization of the dopaminergic and gabaergic neurons (identified by autoradiography).

   Main question (in correlation with Barcelona 3d point and with Mol 1st point): is it reduced by the treatment?

4. In situ immunocytochemical analysis of the distribution of the dopamine and GABA neurotransmitters (in collaboration with Y. Vernois).
   Main question: (see Barcelona 2d point): do they decrease after treatment?

5. A study of 2.5 MeV (non monochromatic) neutrons using brain weight as an endpoint (after prenatal irradiation at day 15).

   Main question: What is the RBE of these neutrons?

B32 Carcinogenesis after exposure in utero

Contract Bi7-001 Dysfunction and neoplasias of haemopoietic and osteogenic tissue following external irradiation or bone-seeking radionuclide contamination in utero or during neonatal development

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Total Contribution by the Commission: 376 kECU
24 months from 1/09/90 to 31/08/92

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Description of research work:

Introduction

The potentially greater sensitivity of tissues in the developing than in the adult animal to the effects of α-particle irradiation is of crucial current importance. In mice, it has recently been shown that small amounts of ^{239}Pu administered in utero and giving a total dose to haemopoietic tissue in foetal liver of 10 - 14 mGy, cause a significant depression of haemopoiesis in the neonate offspring. Long-term bone marrow cultures prepared from the offspring of mice contaminated in utero and via lactation with ^{241}Am have been shown to have a reduced capacity to maintain CFU-

GM proliferation. There was evidence also that the quality of the haemopoietic stem cells is diminished but that the nature of effects on the stromal elements is currently somewhat equivocal; they appear to support better the production of in vitro CFC but perhaps at the expense of the more pluripotent progenitor. The effects of α-irradiation measured by these methods is greater for a given amount of ^{241}Am administered in utero than to adult animals. Similarly, the late effects of external irradiations are characterized by reduced stem cell quality and a lowered ability of the stromal elements to maintain the stem cell population. This latter effect is dose-rate-dependent.

All this evidence suggests that the incidence of myeloid leukaemia caused by irradiation in utero could be considerably greater than that induced by the irradiation of adult animals as demonstrated by the CBA/H mouse model.

The aims of the contract therefore are to determine:

1. The most radiosensitive period during pre- and post-natal development for both the response of stromal and haemopoietic marrow cells and for the dysfunction or induction of neoplastic change in bone and bone marrow following contamination with α-particle emitting radionuclides or comparable doses of external low LET irradiation.
2. The functional quality of mature cells generated from haemopoietic tissue damaged by such radiations.
3. The identity and location of the sensitive cell populations.
4. The role of haemopoietic growth factors in the regulation and recovery of irradiation damaged tissue.
5. The features of the stromal populations identified by cellular and molecular techniques.

MRC Radiobiology Unit, Chilton.

Recent experiments have shown that haemopoiesis is affected in the foetal and neonatal stages of development by the injection of ^{239}Pu into pregnant BDF1 mice. ^{239}Pu (30 Bq g^{-1}) injected on day 4 of pregnancy caused a 30% depression of CFU-S numbers in foetal liver measured at 17 days and a 30% depression in femur and spleen CFU-S numbers measured at eight weeks after birth. The injection of 30 Bq g^{-1} on day 13 of gestation did not cause a reduction in foetal liver CFU-S measured on day 17 but there was a 40% reduction in numbers of femur and spleen CFU-S eight weeks after birth. Since such a small fraction of the administered ^{239}Pu crosses the placenta into the foetuses (1% - 2%), it is unlikely that the damage caused to neonatal haemopoiesis would have resulted from the presence of ^{239}Pu in the neonatal tissues. Rather it is the result of the primary damage caused by the ^{239}Pu in the foetus. Whatever the initial insult, however, sufficient damage was caused to suggest that leukaemogenic changes might ensue over a long period. The amounts of ^{239}Pu given to these pregnant mice therefore, have been used as a guide to putative leukaemogenic amounts.

The initial aims of the project are to observe the late effects of 32, 64 and 128 Bq g^{-1} ^{239}Pu injected into pregnant CBA/H mice on days 4 and 13 of gestation. Only the male offspring will be kept and a total of 200 mice will be entered into each group. Subsequently, following investigations carried out on the diaplacental transfer and effects of ^{224}Ra on haemopoiesis in CBA/H mice, a similar experiment is planned for the late effects of ^{224}Ra also in CBA/H mice.

SCK/CEN, Mol.

A. Identification of the radiosensitive developmental period after ^{241}Am contamination of Balb/c mice. After in utero contamination of Balb/c mice on the 14th day of gestation with ^{241}Am, damage to the femoral bone marrow was observed as exhibited via in vitro long term bone marrow cultures (LTBMC's) which persisted at least 71 weeks after contamination. The associated α-particle radiation dose was far below the radiation dose at which similar damage was observed after contamination at adult age.

After various regimes of dose administration (single injection before and during gestation, continuous contamination via lactation, repeated injections or X-irradiation), the long-term marrow culture model will be used to evaluate which developmental age is more or less sensitive, compared with our previous experiment in which contamination occurred at 14 days gestation.

Complementary LTBMC's will be set up after external X-irradiation to verify the radiosensitive developmental stages.
A survival study will be carried out using the same contamination protocol as for the mice which displayed persistent radiation damage in their bone marrow. The efficiency of induction of long-term effects will be evaluated with emphasis on haemopoietic and osteogenic neoplasias and disorders.

Retention of ^{241}Am in the offspring will be measured radiochemically to calculate the radiation dose in relation to the observed effects.

B.Cellular and molecular origin of residual radiation damage in marrow after low doses with emphasis on stromal cells.
The stromal system is a heterogeneous cell population and will be studied at the cellular and molecular level using whole marrow or purified cell populations (prepared by flow cytometry at The Radiobiological Institute, Rijswijk). These cell populations will be examined for the quantity and quality of stromal stem cells characterized with respect to:

1. Their proliferative capacity and their spatial organization using the CFU-F technique.
2. Their haemopoietic function in long-term cultures recharged with purified haemopoietic stem cells.
3. Their osteogenic function using an in vitro model for osteogenesis.
4. Their cellular and molecular features (e.g. synthesis of cellular and molecular components, in situ hybridization, etc.). Cultures of sorted stromal cells will be used originating from haemopoietic organs from mice at different developmental ages. Classic LTC of these organs have different haemopoietic capacities and therefore is a very useful tool to study the components in the stromal system essential for the maintenance of haemopoiesis.

When we have more information on the origin of the mechanisms causing deregulation in haemopoiesis we shall look for repair mechanisms to promote recovery in cell populations responsible for residual marrow injury.

Paterson Institute, Manchester.

a) The placental transfer of radionuclides and their distribution in foetal and neonatal tissues following acute or chronic administration at various phases of pregnancy and infancy (in close collaboration with MRC Radiobiology Unit, Chilton).

b) Assessment of long-term damage to the haemopoietic progenitor cells in terms of total number, proliferative activity and self-renewal capacity after radionuclide contamination or after homogeneous low LET irradiation given at different dose-rates.

c) Resulting long-term disturbances in the spatial distributions of haemopoietic progenitor and stromal cells in the marrow spaces.

d) Assessment, (using marrow culture techniques), of long-term damage to the haemopoietic microenvironment and its capacity to generate a bone capsule supporting haemopoiesis under the renal capsule. Manipulation of cell production using growth factors.

The non-random distribution of haemopoietic and stromal cell populations in marrow together with heterogeneities in their self-renewal, proliferative and differentiative capacities complicate

interpretation of their response to short range α-particles emitted from bone-seeking radionuclides. Evaluation procedures (b) and (c) will be used for haemopoietic stem cell responses and (d) for the microenvironment.

Dose-response relationships for long-term injury after gamma- or X-irradiation, compensating mechanisms and stromal sparing using low dose rates, have been documented. Manipulation of low-LET radiation injury using growth factors and other bioregulators in long-term cultures produced from irradiated marrow will be used as a baseline for the more complex situation following radionuclide contamination.

The proposed work will complement the studies on long-term induction of neoplasia following similar contamination protocols at MRC, Chilton and also information obtained for other radionuclides studied at SCK/CEN, Mol. It will provide material for an assessment of any functional damage arising in the mature cell populations being studied by Universidad Complutense, Madrid.

Radiobiological Institute, TNO, Rijswijk.

Stem cells, purified from mouse bone marrow (young and adult) and from mouse fetal liver will be cultured on stromal layers (mostly in collaboration with SCK/CEN, Mol) where the interaction between the purified stem cells and the stromal cells will be analyzed by the techniques of molecular biology.

Using similar methods to those used to purify stem cells, attempts will be made to identify and isolate the precursors of the cultured stromal cell layer. In collaboration with SCK/CEN, Mol, the growth kinetics and clonogenicity of these precursors will be characterized in order to evaluate the replacement of stromal cells after radiation damage.

Fluorescent in situ hybridisation methods will be developed to detect which cells in the stromal layers are producing haemopoietic growth factors and to what extent that production can directly or indirectly be damaged by radiation. Several methods have been developed in our group recently to facilitate the detection of genes and of mRNA by nonradioactive methods; application of such techniques to stromal and haemopoietic cells in situ in long term cultures are expected to require only slight adaptations.
Growth factors labelled with biotin (without impairing their function) will be prepared and added to the long term cultures, subsequently to be traced in the extracellular matrix by avidin-based detection methods. At present, IL-2 and IL-3 could be labelled to study their receptors on lymphocytes and other haemopoietic cell-lines respectively. The biotinylation of other haemopoietic growth factors is in progress.

Universidad Complutense de Madrid, Madrid.

After irradiation, long-term bone marrow damage may be latent for a prolonged period and coexist with near normal numbers of mature functional cells in the blood. This may be followed by a delayed syndrome of haemopoietic failure. This suboptimal stage may be sensitive to further neoplasias. In this context, stroma seems to have an important role in the damage which may be manifested at different levels.

Whereas radiation effects are usually related to the structure and function of DNA, other cellular effects can be expressed as a dysfunction of mature cells and such injury has been found in granulocytes in preliminary studies. Therefore, our contribution in this project will be focused on the biochemical characterization of functional deficiencies induced by radiation. Residual damage will be assessed by:

1. Functional damage of mature granulocytes (phagocytosis dysfunction).
2. Metabolic and energetic "status" of the stromal cells and their ability to synthesize matrix molecules.

The studies will be carried out on mice of different ages, including newborn, young and adults irradiated with single and repeated doses of external low LET irradiation or contaminated with α-

particle emitting radionuclides in collaboration with Paterson Institute, Manchester, MRC Radiobiology Unit, Chilton and CIEMAT, Madrid. We will establish LTBMC's at different post-irradiation times.

In mature granulocytes obtained from the supernatant of LTBMC's, we will evaluate the phagocytic activity by means of oxygen consumption, formation of superoxide anion and oxidation of glucose via hexose monophosphate shunt. Cellularity, protein concentration and GM-CFC will be followed in these supernatants during the period studied. In vivo studies will be carried out in granulocytes obtained from peripheral blood.

Intracellular levels of the principal metabolites in stromal cells will be measured and their main glycolytic enzyme activities quantified. The ability of the marrow to synthesize the matrix molecules will be defined by their electrophoretic mobilities and chromatographic behaviour. Particular attention will be paid to the collagenous molecules secreted by these cells. The proliferative capacity of the stromal cells will be quantified by the clonogenic assay of CFU-F.

CIEMAT, Madrid.

Residual haemopoietic damage induced by irradiation of newborn and adult mice will be analyzed in terms of stem cell proliferation and differentiation. Total number, proliferative activity and self-renewal capacity of the haemopoietic stem and progenitor cells will be evaluated.

Differentiation will be assessed by following the fate of stem cells genetically marked with the retrovirus pXT1 after transplantation in animals or in LTBMC's. This retrovirus contains the prokaryote gene of neomycin resistance which can be used as a specific marker of stem cell clones since it is randomly integrated and has no homologous sequences in the cell genome. The excision with restriction enzymes and Southern blot analyses of DNA obtained from the progeny of the infected stem cells allows the identification of those stem cells that undergo proliferation and differentiation.

Those irradiation protocols (sublethal low LET external irradiation or contamination with radionuclides) that induce residual damage in the progenitor populations will be used to determine also the effects on stem cell differentiation.

Three types of analysis will be performed:

1. Engraftment and expansion of haemopoietic stem cells in previously irradiated animals or LTBMC's.
2. Longevity and clonal succession of transplanted haemopoietic stem cells, by examining serial blood samples. The succession or eventual disappearance of certain stem cell clones will be correlated with the damage induced by the irradiation of the haemopoietic stem cells or of the stroma.
3. Multipotency of the haemopoietic stem cell. Southern blots will be performed with DNA obtained from purified populations taken at long times after the irradiation and reconstitution of mice with the infected haemopoietic cells.

B33 Transfer of radionuclides in utero

Contract Bi6-347d The dosimetry and effects of fetal irradiation from incorporated radionuclides (NRPB Association)

Coordinator NRPB
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Tel: 235-831600/2227

Total Contribution by the Commission: 160 kECU
30 months from 1/01/90 to 30/06/92

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Description of research work:

Aims and Objectives

An important aspect of the assessment of risks from incorporated radionuclides is the possibility of intakes by pregnant women and in utero exposure of the developing fetus. For the development of dosimetric models and adequate assessment of risk, more information is needed on the uptake of radionuclides by the fetus, the location of activity relative to sensitive cells and changes in sensitivity at different stages of gestation. The project brings together work on biokinetics, dosimetry and effects and considers natural alpha emitters as well as fuel-cycle radionuclides.

Description of Project

Human fetal tissue concentrations of ^{210}Po (and ^{226}Ra) are being determined using TASTRAK (CR-39) plastic track detector at the University of Bristol and by radiochemical methods at NRPB. Fallout $^{239/240}$Pu is being measured by mass spectrometry in collaboration with AWE, Aldermaston. The ^{210}Po content and distribution in term human placentae will be determined using TASTRAK.

Animal studies at NRPB are initially concentrating on comparing the uptake and distribution of ^{210}Po, ^{238}Pu and ^{241}Am in rats and guinea pigs for different exposure conditions. The data obtained in these studies is being used, together with the human data, to develop dosimetric models.

Studies of the effects of in utero irradiation are being carried out at CEA using mice. External irradiation at different times during gestation is providing information on changes in the radiosensitivity of particular tissues. Dose-effect relationships are being determined for short-term (lethality, body weight loss) and long-term effects (changes in brain and gonadal tissue) after neutron irradiation during the whole of part of the gestation period and compared with results obtained after gamma irradiation. The effect of dose rate is also being studied.

C RISKS AND MANAGEMENT OF RADIATION PROTECTION

C1 ASSESSMENT OF HUMAN EXPOSURE AND RISKS

C11 Evaluation and statistics of the different types of human exposure

Contracts Bi6-213/7-053/6-229/6-111/6-116 Statistics of human exposure and analysis of registry data

Coordinator NRPB
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Tel: 235-831600/2227

Total Contribution by the Commission: 274 kECU
24 months from 1/01/90 to 31/12/91

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Contract Bi6-116

Description of research work:

BI6-213

Aims of Project

It is intended to analyse data from the UK's National Registry for Radiation Workers with the following aims.

(1) To determine whether there is any evidence of differences in the cause of and the age at death of workers exposed to different levels of radiation, and if any differences are found whether it seems likely that they can be attributed to radiation.

(2) If any differences are found which seem likely to be attributed to radiation, to estimate the magnitude of the risk.

(3) To estimate bounds to the possible risk for particular types of malignancy, such as leukaemia.

(4) To compare the mortality experience of radiation workers with national mortality data, and also that of other industrial groups for whom data exist.

Description of Project

Current estimates of radiation risk are based mainly on epidemiological studies of populations exposed to high doses and high dose rates. Consequently their use in the protection of those occupationally exposed to low radiation doses involves considerable extrapolation. Studies of radiation workers themselves, however, can provide a direct, if imprecise measure of any health effects associated with their radiation exposure.

The National Registry for Radiation Workers (NRRW) was instituted by the NRPB in 1976. There are at present over 95,000 workers within the UK for whom registration has been completed, and agreement in principle exists in respect of some 10,000 more. The median life-time recorded dose of workers registered is about 10mSv.

Data collection has been the dominating need in the early years of this study but work on the first analysis is now underway. The analysis will cover a number of areas, proposals for which were described in 1989.

External Analysis:

Standardised Mortality Ratios for relevant causes of death will be calculated for the radiation workers by using UK national population mortality data to calculate expected number of deaths, taking age, sex and calendar year of death into account. It will be necessary to explore whether any correction for regional variation and/or social class can be made, both factors being known to have a substantial effect upon mortality.

Internal Analysis:

It will be possible to carry out an examination of the evidence for a significant dose-response relationship within the set of radiation workers. If such a relationship is assumed to be linear, it may be shown that a good test for trend of mortality with radiation dose is provided by calculating the test statistic used in the analysis of the mortality of radiation workers at the Hanford plant.

The method depends upon stratifying the deaths and the person-years at risk according to factors known to influence mortality, so that in essence comparisons are drawn between groups of workers similar in respect to such factors but who have different cumulative radiation exposures. NRPB has developed, tested and supplied to other research workers the software necessary to do this, and has carried out trial analysis on the Hanford data-set.

Other work in 1990/91:

There are a number of other specific studies that are also envisaged for this period. These are:

a) the integration of further personal and dose information into the NRRW database;
b) improvement of follow up by cross checks between the National Health Service Central Registers and the Department of Social Security;
c) improvements in data quality by cross checks with integrated employment and radiation dose histories compiled by employers' central records;
d) consideration of doses from internal emitters. Development of as many as practicable of the following:

   (i) a criterion to distinguish those almost certainly not exposed from those possibly exposed;

   (ii) division of those possibly exposed into low and high dose bands;

(iii) reasonable estimates of dose on an individual basis.

e) An examination of the likely effect of dose record keeping practices on the analysis of data from epidemiological studies.

BI7-053

Statistical Results of the Personal Dosimetry Service at GSF

Since 1952 a large scale Personal Dosimetry Service operates at GSF. This service is the biggest of the 4 official Personal Dosimetry Services in the Federal Republic of Germany. Statistical data are reported in a regular and uniform way since 1980 and in retrospective the findings before 1980 are intended to be explored in the same way. Actually approximately 120,000 occupationally exposed persons are monitored monthly by this service.

The first aim of the project is to indicate the trends in personal and collective doses on the available data base and to correlate it eventually to

- the administrative infrastructure of radiation protection in the different states (Bayern, Hessen, Baden-Württemberg, Schleswig-Holstein),
- the dosimetric techniques by comparing the measurements of their service with measurements by the users (and the utilities),
- other influencing factors (e.g. public discussion of occupational exposure).

The second aim is to assess individual life time doses in view of the already implemented 400 mSv lifetime effective dose limit in the Federal Republic of Germany.

The third aim is to detect specific workplaces where a need for workplace-specific conversion factors between the measured personal doses and the effective dose equivalent is evident.

In particular, "partial body" doses are considered and related to the "whole body" dosemeter readings.

BI6-229

Description

Objectives

- To compare the mortality of JEN workers with the national rates
- If there were any evidence suggesting that the mortality at JEN is greater than that in Spain, to establish wether this difference is related to radiation exposure.

Methods

The study design corresponds to a retrospective cohort study on 5303 JEN workers from 1954 to 1986. This cohort constitutes the 85% of the JEN labor force. Data collection for each worker comprises:

administrative and clinical data,

exposure information (dosimetry) and

cause specific mortality data.

The statistical analysis has been carried out in two steps:

a) External comparison of the JEN mortality with the mortality of the spanish population, through standardized mortality ratios.

b) Internal comparison of the cohort mortality by radiation exposure, through log-linear models.

Results

So far the results suggested that the mortality among JEN workers is generally lower than the national rates ("healthy worker effect"). However, it has been observed a significant increase in the cancer mortality among the study cohort. This increase has not shown a radiation dose-effect relationship.

BI6-111

Quantification of radiation risks, optimization procedures and analysis of occupational exposure

The quantification of somatic radiation risks (i.e. the probabilities for the induction of cancer or leukaemia by radiation) of low doses of ionizing radiation remains an important problem of scientific and practical interest. This is particularly true after the publication of the new results from the Radiation Effects Research Foundation in Japan indicating significantly higher somatic radiation risks than hitherto assumed. The quantification problems are mainly due to various uncertainties regarding the extrapolation of radio-epidemiological data presently available to

- future times (until all members of the collective have died),
- lower doses than 1 Gy,
- lower dose rates than acute irradiation,
- other populations than those from which risk factors were derived, and,
- for other types of radiation fields (e.g. neutrons and alpha particles).

In this project the data of the most important radio-epidemiological study, i.e. the Japanese "Life Span Stuffy" of the atomic bomb survivors of Hiroshima and Nagasaki will be used in close co-operation with the Departments of Epidemiology and Statistics of RERF to establish estimates of the confidence regions for the somatic risk factors

- at low doses and low dose rates (by analysis of the shape of the dose-response curves),
- at future times (by employing different time extrapolation models), and
- for the contribution from neutrons (by comparing the responses in both cities).

This will be done by application of the stochastic simulation program for epidemiological data SIRIS, which has been developed by the GSF recently in the framework of the present CEC-Research Programme, in combination with the advanced statistical evaluation program AMFIT developed recently by Preston and Pierce at RERF, which is employed in the RERF-Analysis work and in the preparation of the BEIR-V Report of the U.S. Academy of Science.

The original, individual data of the Life Span Study Data Base (differential in age at exposure, sex, city, organ doses due to photons and neutrons, and the local base line risk of mortality) will be used together with various dose-time response models to calculate with the Monte Carlo simulation-program SIRIS sets of late effects for the same population with the same radiation exposure. These "artificial" epidemiological data will be used to evaluate with AMFIT the statistical significant conclusions based on the original data, and to attempt own estimates of the regions of various somatic risk factors and their sensitivity on the underlying model assumptions.
To technically achieve this goal,

- the voluminous RERF-data have to be brought into appropriate form,
- the AMFIT-program has to be transported onto the computer on which the SIRIS-program is executed to allow a direct analysis after each (of thousands) of the simulations.

Further on, several plausible parameter-sets of dose-time-effect models for late effects (relative, absolute, linear-quadratic models, etc.) have to be developed in close co-operation with the partners of RERF.

BI6-116

Description

Project 1 : Plate-out of Radon Daughter Aerosols in Domestic and Mine Environments

The risk of lung cancer following the exposure to radon daughters is determined by the dose absorbed by bronchial tissue. This depends on two factors : intake of potential alpha-energy and the distribution of potential alpha-energy with aerosol particle size. The objective of this project is to assess radon gas concentrations measured in large-scale surveys of dwellings in terms of effective dose equivalent. This requires an understanding of the physical parameters determining aerosol characteristics in room air in order to model the range of dose conversion coefficients applicable to domestic environments.

Conversion from radon gas concentration to exposure to potential alpha-energy requires knowledge of the daughter equilibrium factor (F) and the unattached fraction of potential alpha energy (f_p). These parameters are affected by ventilation rates, aerosol concentration and size distribution, and other factors.

In order to study the radioactive aerosols in dwelling and mines, it was first necessary to develop appropriate instruments. Under this contract, a five-channel parallel diffusion battery was developed to allow the size distributions of the radioactive aerosols to be studied. An aerosol generator capable of producing monodisperse aerosols of 10-125 nm diameter was constructed and used to calibrate the parallel diffusion battery.

The performance of the diffusion battery was compared with instruments used at EML in the USA, at Göttingen University in the FRG and at Gent University in Belgium. Satisfactory agreement was obtained. The equipment was used to measure the radioactive aerosols conditions in various homes and mines. These and other results indicated that previous models used to estimate lung doses had assumed unattached fractions of the radon daughter aerosol which were lower than those found in typical homes. A new model relating radon gas levels in homes to doses in lungs was developed and published. Work is continuing to establish the range of radioactive aerosol conditions found in homes and mines.

Project 2 : Deposition of aerosols in the upper respiratory tract

In order to calculate lung doses from inhalation of radioactive aerosols, it is necessary to know the proportion of the aerosols removed by the nasal and oral cavities as a function of size. This is particularly important for radon daughter aerosols, where a large fraction of unattached daughters may be removed.

In this study, the penetration of a wide range of aerosol sizes through nasal casts is being examined. Three nasal casts are being used : two obtained from cadavers and one made by carrying out nuclear magnetic resonance imaging of a live subject. Sheets of polymethyl methacrylate were cut according to the slice images from NMR and assembled to make an airway model which included an oral cavity.

It has been found that 50% of the unattached fraction of radon daughter activity is trapped in the nasal casts, whereas very little of the aerosol greater than 10 nm diameter is deposited. A gamma camera study of one cast showed that 65% of the activity was deposited in the anterior part of the cast. The penetration of aerosols through the oral cavity of the sectioned cast was similar to that through the nasal casts, implying that the lung dose from attached radon daughters is not strongly dependent on the manner of breathing - by nose or mouth. The data collected will be analyzed to provide input for a model for calculating lung doses from radon daughters.

Project 3 : The application of CR-39 Etched-Track Detectors to Low Background Counting and Particle Sizing of Air Samples

Personal Air Samples (PAS) are currently used for routine individual monitoring for workers who are at risk of exceeding 30% of the annual limit on intake (ALI) of long-lived alpha-emitters. In monitoring chronic exposures to plutonium, however, the sensitivity of the PAS is unsatisfactorily low, owing to uncertainty in correcting the observed alpha-counts for counter background, i.e., it is

equivalent to about O.1 ALI. The objective of this project is to develop the technique of alpha-track registration on CR-39 plastic to the stage where it is suitable for routine assay of long-lived alpha-activity collected on PAS filters. This technique has the potential for measuring significantly lower levels of activity than the counting methods used at present.

Initially, the effects of clumping of activity in discrete particles on the efficiency of track registration using CR-39 was investigated. This potential problem was solved by determining the optimum spacing between the active filter and the CR-39 detector to avoid overlap of tracks and yet preserve information on particle aggregation. Autoradiographs of PAS filters have been analyzed using a Cytoscan image analyzer. Software was written to allow the Cytoscan to recognise the tracks, to discriminate between genuine tracks and background, and to plot the track density across the autoradiograph. The position on the filter paper at which aerosols are collected depends to some extent on their aerodynamic diameter, so positional information on track density allows some size discrimination. Information on activity per particle can also be derived from the clumping tracks. The ability of the Cytoscan to identify tracks and plot their locations has been demonstrated and the potential of the technique for use in routine monitoring will be evaluated.

C12 Exposure to natural radioactivity and evaluation of parameters influencing these risks,

Contract Bi6-344 Design and realisation of a calibration device for Rn-222 and its short-lived daughter products in air (study contract)

Coordinator CEA - FAR
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Total Contribution by the Commission: 35 kECU
9 months from 1/01/90 to 30/09/90

Participating Scientists

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Description of research work:

The aim of the project is to adapt an existing radioactive aerosol calibration installation "ICARE" at the Saclay Nuclear Research Centre (CEA), in order to provide precise activity concentrations of ^{222}Rn and its short-life decay products that may be used to calibrate measuring instruments.

ICARE is currently being used for the certification of instruments employed in measurement of artificial radioactive particulate airborne contamination. ICARE is essentially a wind tunnel in which aerosols calibrated in size and labelled with ^{137}Cs or ^{239}Pu are injected upstream of the test section.

To extend ICARE's field of application to the case of instruments employed in measurement of natural radioactivity, a new line of injection has been designed during 1989 including three standard sources of ^{222}Rn and a reference device for the activity concentration measurements of this gas. These new processes and devices are covered in two patent applications.
The supplementary test bench equipment used to produce and measure ^{222}Rn decay products, and the instrument test chamber, are subject to a second CCE contract in 1990.

The new system will be designed for:

- producing aerosols, size and number concentration calibrated, to carry a fraction of radon daughters; the AMAD of this fraction being representative of environmental conditions (0.2 - 0.3 μm), and the attached fraction adjustable from a few percent to 100%,
- measuring the three daughters activity concentrations and potential alpha energies, using a computing system and a new software based on a mathematical deconvolution of the scintillation counting of alpha particles deposited on two sampling filters located downstream the ageing volume,
- allowing the calibration tests of instruments either inside a chamber for the smallest ones or outside for the biggest ones, the velocity of the chamber air flow being adjustable up to 5 cm/s and the activity concentration of ^{222}Rn from 4 to 4,000 Bq/m^2.

C12 Exposure to natural radioactivity and evaluation of parameters influencing these risks,

Contracts Bi6-347f/6-114/6-314/6-208 Radon sources and models (NRPB Association)

Coordinator NRPB
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Total Contribution by the Commission: 568 kECU
30 months from 1/01/90 to 30/06/92

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Contract Bi6-208

Description of research work:

Aims and Objectives

(1) To carry out surveys of radon concentrations in homes in those countries where insufficient data is available.

(2) To develop and test techniques for identifying areas with a potential for high radon concentrations in homes, both on a large scale and for individual building sites.

(3) To improve the understanding of, and develop mathematical models of, the movement of radon from the ground to sub-floor spaces and into buildings.

(4) To develop and test countermeasures against radon in homes using laboratory and field studies.

Description of Project

LNETI (P), University of Cantabria (E), University of Athens (GR) and NSCR Demokritos (GR) will carry out surveys of the exposure of the population to radon in Portugal, Spain and Greece. These will be carried out using passive etched track detectors and active measurement techniques. Additional data will be collected on the radon decay product equilibrium factors and on the origins and characteristics of the radon sources. The average radon concentrations in homes will be calculated, and the variations in concentrations mapped.

BGS (UK) and NRPB (UK) will identify appropriate geological and radiological parameters for radon potential mapping. Existing data will be evaluated, and programmes of collection of relevant data including radionuclide contents of rocks and soils will be started in defined areas. This information will be used to construct maps of radon potential, which will be compared with data on radon concentrations in homes, both from earlier surveys and from new surveys designed to test the validity of the maps.

KVI (NL), CSTC (BE), TNO (NL) Risø (DK) and SSI (S) have under development mathematical models of radon movement and availability in the soil, movement into buildings through sub-floor spaces where present, and subsequent dilution and dispersion. Different models emphasise different parts of this process. These laboratories will meet to exchange information on their models and to draw up a programme of model comparison. The results from the models will also be compared as closely as possible with measurements and will be used to identify the most important parameters for measurement in assessing radon problems in homes.

KVI (NL), the Technical University of Denmark and Risø (DK) will study soil factors influencing radon availability to buildings using laboratory and field studies. These will include the radon exhalation rate of materials, the influence of porosity, permeability and groundwater on radon movement, and the development of improved instrumentation for characterising soils on site. The results of this work will be used as input for the mathematical models described above.

WTCB (BE) and TNO (NL) will carry out laboratory and site studies of constructional factors influencing the entry of radon into buildings from the ground. The insight gained will be used in the development and testing of remedial and preventive measures to avoid high levels. This will include the testing of the effectiveness and durability of barrier and diversion techniques for preventing the entry of soil gas.

In the UK, some existing buildings have had remedial measures installed and thousands of new buildings have been constructed using anti-radon designs. NRPB will survey the radon levels in a representative sample of these buildings to determine the effectiveness and durability of different countermeasures in practice.

In view of the wide scope of these contracts, it has been found necessary to set up small working groups to coordinate the work on particular topics where there might otherwise be duplication of effort. These groups will exchange information and will meet as required. NRPB will attend the meetings of the groups. The Technical University of Denmark, KVI and the University of Cantabria will collaborate on the subject of soil permeability measurements. KVI, Risø, CSTC and the Technical University of Denmark will collaborate on models of radon movement in soils and into homes. SSI, CSTC and TNO will collaborate on compartmental models of airborne radon movements within homes, also using data from earlier KVI studies. Within each group the first named laboratory will take the lead in arranging the collaboration, with assistance from NRPB as required.

Apart from cooperation on the specific topics mentioned, all the laboratories will maintain communication with each other and with laboratories in Europe and North America on topics of mutual interest.

C12 Exposure to natural radioactivity and evaluation of parameters influencing these risks,

Contract Bi7-013 Retrospective assessment of radon exposure from long-lived decay products.

Coordinator Univ. Lund
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Total Contribution by the Commission: 164 kECU
24 months from 1/09/90 to 31/08/92

Participating Scientists

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Description of research work:

It has recently been shown that a dwelling "remembers" past radon (Rn-222) levels via long-lived decay products which are permanently embedded by alpha particle recoil in glass or other hard surfaces. This radon memory effect implies that there are radon detectors with the potential of being retrospective in all dwellings. There is an urgent need to investigate this new technique in order to clarify its potentials and limitations.

The investigation of long-lived radon decay products in the indoor environment comprises a new area in radon research. Suitable detection methods are lacking and our knowledge of the plate out and alpha recoil deposition phenomena in a realistic indoor situation is poor.

The objectives of the project are to study the chain of processes which in the indoor environment leads from airborne radon to embedded long-lived daughters and to reveal those exposure conditions in which the surface activity concentration of the long-lived radon decay products is a useful estimate of lung cancer risk.

The study of the embedded long-lived decay products of radon-222 is the only presently known method for "measuring" accumulated radon concentration levels from the past. The results from this investigation will be therefore of importance when assessing past and future indoor exposures to radon and its decay products and will also improve our understanding of the fate and behaviour of radon daughters in the indoor environment. The major potential application area of the long-lived radon daughter method is radon epidemiology and as a number of these studies are now underway the development of this technique is very timely and appropriate.

Generally the work will be devoted to

A) the development of detection methods for short-and long-lived radon decay products deposited on large surfaces

B) studies of the long-term variability in the deposition rate of short-lived decay products on macroscopic surfaces and the resulting removable/unremovable surface activity.

Area A comprises developments mainly along three different lines.

A1) An instrument based on the track-etching technique for real-time plate-out measurements of short-lived radon daughters will be developed by UCD and modified versions suitable to field work will be used by the other participants.

A2) The feasibility of auto radiographic track-etch methods for measuring Po-210 embedded in surfaces will be investigated. The image analysis facilities at SSI and UCD for analyzing alpha track densities, track shape and track size distributions over areas up to 15x15 cm will be used. The alpha energy discrimination ability of these facilities will also be investigated.

A3) Alpha spectrometry using pulse ionization chambers will be a reference method for the Po-210 analysis of large area samples. An open-flow transportable ionization chamber will be developed by LU with support from DTH. In this new type of chamber samples can be measured in a non-destructive fashion.

The execution of part B will initially rely on the existing facilities of the participating laboratories. During the programme period the equipment developed under A will add to this existing battery of instruments. The work during will be focused on plate-out exposures under well controlled laboratory conditions, comparisons of the experimental results with model calculations and the development of the non-destructive technique for the measurement of embedded Po-210. Cleaning studies in order to differentiate between adsorbed and absorbed surface activity will be performed by the RUG group with support from the CEN group.

Field studies in dwellings are also in the programme. The room to room variation of the surface Po-210 activity will be recorded in a few houses and the feasibility of the track-etch auto radiographic technique will be tested in small scale studies.

The two-year goal of the project is to reveal the usefulness of the polonium-in-glass method, or any other similar technique involving long-lived decay products, and to identify areas in which further studies are warranted.

C12 Exposure to natural radioactivity and evaluation of parameters influencing these risks,

Contract Bi7-047 Characteristics of radon- and thoron daughters aerosols.

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Total Contribution by the Commission: 257 kECU
24 months from 1/05/90 to 30/04/92

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Description of research work:

In all dosimetric models the particle size of the aerosol-attached and "unattached" activities of short-lived radon and thoron daughters are important parameters for the estimation of the radiation exposure.

Experiments will be continued to determine aerosol size characteristics of radon and thoron decay products in real living indoor and outdoor atmospheres. The results will be compared with model calculations.

The physical and chemical interaction (particle growth, cluster formation, plate-out rates, etc.) of the unattached radon and thoron daughters with trace gases (SO_2, NO_x, humidity) and other aerosol particles will be studied in chambers under controlled conditions.

For these investigations the sensitivity and efficiency of different experimental techniques for measurements of the size distributions have to be improved and modified techniques will be developed (e.g. diffusion batteries, low-pressure impactors, multi-jet impactors, electrostatic classifier). These techniques have to be calibrated with monodisperse aerosol particles. The different methods including various data evaluation methods have to be compared during joint exercises.

I) Isotopenlabor, University of Göttingen, DE:

1) With different calibrated experimental techniques (high-volume screen diffusion batteries, low pressure cascade impactors) the measurement of size characteristics (size distribution, f_p, F) of the short-lived radon daughters will be continued in the ambient air and first measurements of properties of thoron gas and decay products will be performed. Studies are planned in low and moderate ventilated rooms to estimate the influence of typical aerosol sources and air cleaners on the size distributions and on the air activity concentrations.

Detailed studies will be performed to determine the correct shape of the size distribution of the ultrafine cluster mode (unattached activity). For these investigations the screen diffusion battery technique has to be improved as well as the data evaluation method.

2) In a radon chamber the growth and cluster formation processes, the influence of trace gases (SO_2, NO_x), humidity, and ambient air and the interaction with monodisperse aerosol particles will be investigated. These studies require the development, modification and calibration of different experimental techniques (e.g. electrostatic classifier in connection with the alpha spectroscopy, condensation nuclei counters) for measuring in the diameter size range smaller than 20 nm.

3) Different data evaluation methods concerning the size distribution measurements (Twomey-, expectation-maximization-, Simplex-, and Monte Carlo methods) will be compared.

II) Nuclear Research Centre (SCK/CEN) Mol, BE and
III) State University of Ghent, BE:

The complex interactions between the radon decay products and the indoor aerosol determine the unattached fraction which is responsible for about half of the lung dose. The factors influencing the concentrations of attached and unattached decay products will be studied in laboratory and in building environments. For instance, it will be investigated if there is a difference in deposition rate and as a consequence in diffusion coefficient between the three unattached decay products.
A significant difference in diffusion coefficient would explain some of the difficulties we found in fitting the mathematical model for predicting the dynamics of radon decay products in the indoor atmosphere to the data collected during our case studies.

A close collaboration will be established between the partners. For instance, the techniques and methodologies to determine the active and inactive size distribution of the decay products, the unattached fraction and the equilibrium factor will be compared during a joint exercise in a normal living environment.

According to Hopke et al. (Health Physics; 1990, 58, 291) it is possible to simulate the deposition of the radon decay products in the nose and in the bronchi with a simple measurement system consisting of three sampling heads. An open-faced filter giving the total airborne activity, a screen covering the filter yielding the nasal deposition and five screens covering the filter yielding nasal and bronchial deposition.The measurement system will be designed and constructed during the first year. The design will allow to test other sets of screens and to be operated at different face velocities. During the second year the system will be calibrated and a representative number of measurements will be performed in a normal living environment.

IV) University of Lund, SV:

In a research programme funded by the Swedish Natural Research Council new techniques for characterization of radon daughters are being developed and tested. As part of the project a radon room (volume about 20 m^3) has been calibrated. In this room it is possible to vary the radon concentration, the air exchange rate and the concentration and size distribution of the aerosol.

One objective of the programme is to develop alpha spectrometry using detection over larger areas. This will increase the sensitivity and be of great value to future plate-out and diffusion battery measurements.

A second objective is to determine the activity distributions of the attached radon daughters by using two new techniques; a multi-jet impactor, which combines a low cut-off and a high flow rate and a combination of a differential mobility analyzer (TSI 3071) and track-etch plastic film.

We intend to work with the following problems:

1) The new techniques will be used for studies of processes of attachment under well-controlled conditions in the laboratory.
2) Development of new techniques to acquire new knowledge about the ultra-fine part of the activity distribution (the "unattached" fraction). We plan to use pulse ionization chambers to detect the radon daughters on large areas (wire screens or filters) and will thus be able to detect low levels of radon daughters. One approach is to use a differential mobility analyzer which allows collection of ultra-fine particles (2-100 nm). The radon daughters may, in this case, also detected on a plastic film.
3) Measurements of the total activity distribution both under well-controlled conditions in the laboratory and in a limited number of realistic environments. These measurements could be used to improve the models describing the total radon budget in a room, the deposition in the respiratory tract and the attachment process of the radon daughters onto the particles.

V) National Institute of Radiation Protection (SSI), Stockholm, SV:

In earlier work performed at SSI the respiratory tract deposition of radon progeny in humans has experimentally been studied in dwellings, mining atmospheres and under laboratory conditions.

SSI will improve the earlier technique and contribute with deposition studies including measurements of the "unattached" fraction. The inhalation studies will also include deposition studies on the inactive aerosols.

SSI will also contribute in the work to improve the technique to calibrate and measure the "unattached" fraction collected on fine mesh wire screens.

VI) Laboratoire de Physique des Aerosols et de Radioactivite Atmospherique, University of Brest, FR:

1) Improvement of alpha-activity data treatment given by SDI 2000 (inertial and diffusional sampling device) to obtain size distributions of each short-lived radon daughters in houses.
2) Elaboration of a technique for measuring size distributions of the unattached activities of the radon progeny.
3) Measurements in houses of the Bretagne having radon gas levels above 400 Bqm^{-3}:
   - research of radon sources.
   - general studies of indoor environments (fp, F) and size distributions of radon daughters.

VII) Institut de Tecniques Energetiques, Universitat Politécnica de Catalunya, INTE(UPC), Barcelona, ES:

The INTE(UPC) will participate as a sub-contractor of the Isotopenlabor, University Göttingen, DE. The INTE(UPC) has been doing its research activities on radiation protection for the last ten years. The radiation protection section is devoted to the fields of gamma dosimetry and is dedicated to the field of low level radioactivity measurements.
In this project different experimental set-ups will be built up, in close collaboration with the Isotopenlabor of Göttingen, for measuring air activity concentrations of radon and thoron gas and of short-lived decay products and for measuring activity size distributions.
Measurements of aerosol size characteristics (size distributions, f_p, F) will be performed in a limited number of houses under real living conditions.

C12 Exposure to natural radioactivity and evaluation of parameters influencing these risks,

Contract Bi7-0059 Assessment of the geological factors influencing the occurrence of radon hazard areas in a karstic region

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Total Contribution by the Commission: 130 kECU
18 months from to (Under negotiation)

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Description of research work:

Research objectives

The primary objectives of the project will be to carry out an integrated multidisciplinary investigation of certain high radon exhalation sites in Ireland in order to (i) refine field sampling methodology in radon detection and (ii) determine the geological controls of radon production and migration in karstic limestone terrain.

Such information may (i) assist in the formulation of more efficient and effective field sampling strategies in radoniferous areas throughout the EC (ii) assist the EC in the formulation of policies aimed at limiting or reducing exposure to indoor radon in the population at large.

Methodology and Work Programme

A multidisciplinary team of researchers from agencies in Ireland and Germany will combine knowledge from the fields of geology, hydrogeology, geochemistry and radiation physics.

An integrated field sampling campaign will be planned and carried out by the team at two selected radoniferous sites in karstic terrain in the west of Ireland (Moycullen and Belclare areas of Co. Galway) where significant clusters of dwellings with elevated indoor radon levels have been delineated.

At each radoniferous site a co-ordinated series of detailed ground surveys and sampling will be carried out as follows:

(a) The bedrock geology, rock structures, overburden characteristics and hydrogeological features of each site will be mapped in detail. Systematic soil profiling and bedrock recovery will be undertaken where appropriate.

(b) Ground geophysical surveys (electrical and VLF methods) will be employed to determine the depth to bedrock and the depth to the water table locally.

These surveys will also delineate buried structures (planar discontinuities and fractures) in both bedrock and overburden near radoniferous dwellings. Such structures are likely to constrain groundwater and radon migration locally.

(c) Helium gas filled surveys will be used to confirm radon migration pathways delineated by geophysical means both regionally and in the immediate vicinity of radoniferous dwellings. The helium survey techniques developed by workers at BGR is specially suited to this task.

(d) In each study area, passive alpha track radon detectors will be deployed in each participating household. Measurement of track densities on these detectors will be effected by a computerised image analysis system at U.C.D. The data will be integrated with the results of the other surveys to aid in the better definition of the local radon anomaly pattern.

(e) At specific radoniferous dwelling, specially fabricated soil probes will be deployed in the immediate vicinity of the dwelling to determine the local concentration of radon in soil gas, the exhalation rate of radon from soil and soil permeability. The surface exhalation rate of radon from soil at each dwelling will also be determined.

(f) Soil, water and, wherever possible, bedrock samples will be recovered at high radon sites. Radium and uranium contents of samples will be determined by high resolution gamma espectrometry.

Mineralogical investigation of uraniferous samples will be carried out by autoradiography, electron microprobe analysis and fission track registration to determine the precise nature of uranium-bearing mineral phases likely to be responsible for radon build-up.

Schedule of work

The project should commence on 1 October, 1990 and run until December 31, 1991.

Activity	Year 1	Year 2
Delineation of areas and methods		
Existing database compilation		
Fabrication of soil probes		
Field sampling/mapping campaigns		
Sample analysis		
Data processing and integration		
Data interpretation		
Review/Progress Reports		
Final Reports		

Anticipated benefits to EC

1. The database produced in the case study may assist in the identification of the ultimate sources of radon, an environmentally important chemical species, and in tracing its migratory routes in the natural environment and ultimate accumulation in human dwellings.

2. The results of the study are likely to be of use in future epidemiological studies involving radon and its daughters.

3. The results should help in more accurate prediction of where radon-hazard areas are most likely to occur in the various EC Member States where similar geological conditions may prevail.

4. The results will be of use in assessing the effectiveness of certain field-based sampling techniques in radon potential mapping.

C13 Comparative assessment of exposure and risks

Contract Bi6-122 Consequences of irradiation of population and workers. (CEA Association)

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Total Contribution by the Commission: 295 kECU
24 months from 1/01/90 to 31/12/91

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Description of research work:

Project 1

EVALUATION OF INDUSTRIAL IRRADIATION / EUROPEAN DATA BASE

1 - European Data Base: EUROGRID

EUROGRID provides data that are needed for the assessment of health consequences and economic impacts of large releases, either radioactive or chemical, within the European Community. Data are estimated for all the meshes of an European grid. The development of two software packages has been undertaken in 1990. The first software allows to formulate queries to select parts of the data base (subfiles). It has been developed using the PARADOX data base management system, and now it is available free of charge (as a run-time version). The second software, under development, uses a graphical representation of the meshes on a map of Europe. The results of a query (formulated as above), for the large meshes (10 000 km^2), appear graphically or numerically. This consultation is also available for little meshes (100 km^2).

For 1991, it is expected to complete the data of the little meshes (for the moment available only for Great Britain), to add other parameters and informations relative to the distribution of food products between meshes.

2 - Decision Aiding System in Case of Contaminated Foodstuffs: DACFOOD

The objective of DACFOOD is to provide a conversational tool which evaluates preferences into the set of possible actions about contaminated foodstuffs. This tool could be used profitably for the search of a more complete knowledge about the management of such a crisis situation. Different points of view are analyzed in countermeasure evaluation: effectiveness, feasibility, direct and indirect cost, international reglamentation. In its present form, the system provides a classification of possible countermeasures, according to cost-benefit analysis, taken into account doses received by different groups of population. Other aspects (public reactions, local considerations) are more difficult to deal with. The emphasis is on the representation of these aspects, using an expert system.

The DACFOOD prototype will become operational on January 1991. A technical document will then be available; it will be used as a users' guide and it will lay the basis of future developments.

For 1991, a more extensive collaboration with other laboratories (namely TNO) is to be developed, with the objective of integrating the viewpoints of different potential decision makers, and also of using it with diverse scenarios.

Project 2

EVALUATION OF OBJECTIVE DETRIMENT IN RELATION TO ECONOMICAL CONSIDERATIONS

1 - Research on humans beings

Within a comparative approach, methods of evaluation of radiological and chemical detriments are analyzed for the highlighting of criteria presently used in regulatory policies. On one hand, directly acting chemicals for which carcinogenicity is highly suspected in humans, are considered ; for these, procedures for making extrapolation of risk from animal carcinogenesis data base to human are discussed, using a case by case approach focusing on speciation and relevance of administration routes. For the radiological detriment experimental results on plutonium compounds will be critically reviewed in 1990, toxicological profile being established for the various physicochemical compounds from updated literature ; the standardized animal data base on chemical and radiological agents will be gathered for testing various alternative assumptions relative to the carcinogenic risk management in humans

2 - Research on vegetal species

Comparative genotoxicity for environmental factors

Studies with the genetic system a1+/a1 a2+/a2 of the tobacco xanthi variety (nicotiana tabacum L.), allowed to assess the mutagenic potential of various environments. The heterozygote structure of this system determines for the chlorophyll a partial deficiency which gives the green-yellow colour to the young leaves. Certain genetic changes in the above formula may increase or cancel the chlorophyll deficiency. The last situation, i.e. cancellation, is connected to system reversions and is the more frequently observed. Then, tobacco leaves present dark green spots, the number and surface of which allow to calculate the average rate of reversion p by cell generation. This p value is used to assess the mutagenic potential associated with tobacco growing conditions.

Tobacco has already been used, in situ or in the laboratory, to demonstrate genetic effects at low doses of natural and artificial radioactivity : existence of a plateau for the natural background that corresponds to a dose of 4 cGy per year ; a linear response from this dose rate up to the maximum dose rate experienced of 87,6 Gy per year.

Genetic effects that are statistically significant appear in urban or industrial environments (Toulouse, Marseille, Fos, Gardanne, Lacq, Pau) in some places and on some periods of time in relation to the importance of pollution. However in certain cases (Camargue), equally important genetic effects have been noticed outside those urban or industrial environments. This shows either the possibility for pollutants to intervene at large distances or the existence of natural mutagenic factors.

These in situ studies have been completed by laboratory experiments for testing new methods and techniques in order to assess the genetic effects of particular contaminants of the atmospheric environment. It has been demonstrated that SO_2 is lethal when its atmospheric concentration is around one ppm. For SO_2 concentrations between 0 and 110 ppb, there is a significant linear increase of the reversion rate. For radon in inhalation chambers it has been shown that 1) there is no lethal effect for a concentration that is 1000 times higher than the maximum admissible concentration ; 2) mutagenic potential appears for this same concentration and also for lower concentrations.

Currently, it can be assumed that the environment has mutagenic impacts on this tobacco variety that are characterized by a large heterogeneity in space and time.

Project 3

SUBJECTIVE DIMENSIONS OF THE RADIOLOGICAL DETRIMENT

Within a comparative approach, the subjective dimensions of risk perception are analyzed by considering various hazardous activities and different groups of people. The final goal is to propose methods or at least recommendations for integrating this subjectivity in risk management and more precisely in risk communication.

In 1990, the risk perception of various groups of risk specialists is under study. Specialists were interviewed in 1989 and results will be reported in 1990. A workshop will be dedicated to a comparative analysis of public opinion on risks and nuclear activities in the EC countries.
In 1991, due to the seriousness of the radioactive waste problem in people's minds, an in depth study of radioactive waste perception in the EC is planned.

SUB-CONTRACTS:

SC-001-F University Paul Sabatier, Toulouse; M. Delpoux.
Comparative genotoxicity of the principal environmental agents.

SC-002-F Study Centre for the Evaluation of Protection in the Nuclear Field (CEPN), Fontenay aux Roses; J. Lochard.
Analysis of the adopted countermeasures in the different countries of the EEC following the Chernobyl accident.

SC-003-F University Paul Sabatier, Toulouse; M. Delpoux.
Comparative genotoxicity of the principal environmental agents (continuation).

SC-004-NL Dutch Central Organization for Applied Physical Research (TNO), Den Haag; G. Wagenaar.
Decision aiding expert system: application to the early phase of the accident and consideration of psycho-sociological parameters; validation by decision makers.

SC-005-B State University of Gembloux; O. Burton.
Soil-plant and plant-animal transfer of radionuclides released during accidents at nuclear installations.

SC-006-I University of Piacenza; S. Silva.
Soil-plant and plant-animal transfer of radionuclides released during accidents at nuclear installations; fermentation of vegetal products.

C13 Comparative assessment of exposure and risks

Contract Bi7-004 Comparative assessment and management of the health and environmental impact of energy systems and studies related to the expression of the detriment associated with radiation exposure.

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24 months from 1/05/90 to 30/04/92

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Description of research work:

State of the art:

During the last decade, there has been a relative stagnation of energy demand. At the same time, protection of the environment has become a growing matter of concern (acid rain, deforestation, global warming, nuclear accidents). Today, the energy demand has started to rise again and new programmes must be discussed. So there is a new focus on the link between energy policies and environmental and health effects. Moreover, the re-evaluation of the Hiroshima-Nagasaki data has now induced much international discussion about the revisions of the system of dose limitation, which has highlighted inadequacies in the current health detriment indicator, ie number of cancer deaths and serious hereditary effects in the first two generations. In addition, the use of health detriment indicators is not limited to dose limitation problems ; liability and tolerability questions are other fields of application.

In such a context, it seems necessary to develop a methodological framework to put into perspective radiological and non radiological risks related to different energy systems, taking into account social costs of different energy programmes.

Objectives:

The basic aim of the project is to provide a coherent methodological framework for incorporating environmental and health impacts of energy systems into decision making processes related to risk control. It will involve an analysis that will put radiological risk and protection efforts related to nuclear energy into perspective with other energy systems and that will permit a comprehensive assessment approach: it will encompass guidelines for the choice of detriment indicators, and tools for their computation. The work will progress simultaneously in two parts:

1) Development of new detriment indicators. Investigation of the potential use in radiation protection of the concepts of 'years of lost life', 'Quality adjusted life years' (QALYs) and other expressions of health detriment from radiation exposure. Such expressions will incorporate measures of both fatal and non-fatal cancers as well as genetic effects. The work will additionally consider various schemes for costing the man Sievert in the light of these ideas.

2) Comparative study of radiological and non radiological risk. Testing of the proposed methodological framework will be based on evaluations carried out on a regional level in Germany (Baden-Würtenberg Region) and in the South East of France. This second part will be structured according to the following steps:

A - Overview of past experience with comparative studies on energy systems.
This phase should lead to identifying any remaining problems in the assessment and management of different kinds of risks related to the various installations or technical systems part of the fuel cycles. Both aspects of electricity production and end use of energy (substitution of electricity to other sources of energy) will be addressed.

B - Assessment of impacts.
This step will be devoted to the up-dating of health and environmental impacts of the various installations within the fuel cycles, and, at the level of end use within houses, taking into account the basic dimensions such as: occupational and public risks, normal operation and accidental situations, observed and estimated impacts. This work will be based on the most recent information available in the various institutions and also integrating, when still valid, results of the comparative studies performed in the past (Baden-Wurtenberg, South East of France.).

C - Economical valuation of detriment.
Health and environmental impacts will be evaluated in physical terms using the exposure-risk relationship. An economic valuation of these impacts and other social costs will be performed, bearing in mind local situations and an objective of pricing externalities. This phase should provide new elements (with regard to the first generation of comparative studies) on the economic dimension of external effects of energy systems.

D - Risk-management on a regional level.
This final step will aim at defining regional scenarii for electricity supply and end use, and also evaluating their differential impacts in terms of health and environmental risks, taking into account the cost and effectiveness of possible protection measures at the various steps of the fuel cycles or at the end use point.

Economic/technical benefits to CEC:

This work will improve the reliability of such studies in permitting the choice of pertinent parameters as well as avoiding unwarranted sophistication. Secondly, the area has a high political profile, and disagreement between scientists leads to a poor public image of the radiation protection community. Finally, it is expected that these elements will be of great help, should global environment policies be implemented, either through pricing policies or direct regulatory constraints.

Work programme:

Within the two year period of the contract a first synthesis will be made on items 1. Concerning item 2, a synthesis will be made on past comparative studies (point A) as well as the up-dating of impacts (point B). Point C and D will be covered on a methodological level with the objective of designing what could be an integrated decision support system (computer assisted) to manage health and environmental impacts related to energy systems on a regional level.

Specific tasks allocation:

The project will be performed by five institutions on an integrated basis. In particular, all participants will be involved in the development of the methodological framework and the analysis of the suitability of detriment indicators and environmental impacts with respect to the various decisional problems.
Specific developments will be made in the field of radiological detriment and decision analysis problems relating to the evaluation and comparison of the various risks associated with energy systems. The evaluations will be carried out on a regional level either in West Germany (Baden-Würtenberg Region) or in the South East of France. The specific tasks of each participant will be as follow :

- NRPB will look at the suitability of health detriment indicators with respect to classical radiation protection questions: dose limitation and optimisation.
- University of East Anglia will research into the values to be attached to the QALY measure and the scaling factors appropriate for different sources and effects of radiation exposure.
- University of Stuttgart will be in charge of reviewing available information on the risk-assessment analysis, developing externalities (especially related to environmental impacts), and testing the methods on the basis of generic installations located in Baden-Wurtenberg.
- IPSN will be in charge of reviewing available information on the identification and evaluation of health impacts of energy systems. This work will be mainly performed on the basis of past analyses relating to installations located in the South East of France.
- CEPN will co-ordinate the project, and work on the definition of new formulations for the expression of detriment, with a special regard to the treatment of population specific life tables. It will also be responsible for the synthesis on past experience, and will look at the development of the methodological framework, taking into account the decision analysis problem, and identifying which health or economic detriments are the most critical according to the decision situation.

Beyond the general methodological objectives, the project should help in the comparison of radiological and non radiological impacts of energy systems. It will also be helpful in the delineation of a harmonized framework for environmental and health risk-assessment, and management practices in European countries, thanks to the systematic comparison of both evaluation models, and differential regional impacts.

C14 Epidemiological studies in human populations

Contract Bi6-126 Statistical methods for the analysis of geographical correlations, application to the analysis of the correlation between population radiation exposure and cancer mortality

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Total Contribution by the Commission: 37 kECU
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Description of research work:

The research project has a double purpose: first to investigate statistical methods suited to the analysis of associations between the spatial variations of health indicators and risk factors, then to apply these methods to study the link between some indicators of low dose radiation exposure, industrial pollution and the mortality for cancer of specific sites by using aggregated data collected at a regional level.

Correlation and regression are the statistical methods that are commonly used for testing association between a set of variables. The standard framework for these methods assumes that the sample consists of variables measured at different geographical locations since typically these variables will exhibit some spatial dependence (autocorrelation). Hence modifications of the classical tests of the correlation or regression coefficients are necessary.

In the statistical part of this project, several ways of modifying or adapting the standard tests of association to take into account spatial autocorrelation are considered and compared. Firstly modified tests of simple or partial correlation coefficients are developed and their statistical performance is assessed. These tests are based on an estimation of an effective sample size which is typically less than the number of geographical locations in the case of positive autocorrelation. Secondly multiple regressions with different types of spatial structure for the errors are studied. This allows a sensitivity analysis of regression results to the choice of errors structure to be performed. Finally the different methods will be compared on an example.

The epidemiological part of this project consists in the analysis of a data file which contains mortality rates for some cancer sites (lung, breast, thyroid, leukaemia) for three time periods (per department), estimation of radiodiagnostic examinations exposure (per region), measures of radon and background irradiation exposures (some departments), cigarette consumption per inhabitant (per departments), percent of employed male population in specific industrial branches (per department). This analysis will be carried out using the different methods developed.

C14 Epidemiological studies in human populations

Contract Bi6-221 Epidemiological studies of radiation carcinogenesis and its biophysical basis.

Coordinator GSF
Gesellschaft für Strahlen und Umweltforschung mbH
Ingolstädter Landstraße 1
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Tel: 89-3187-0

Total Contribution by the Commission: 211 kECU
24 months from 1/01/90 to 31/12/91

Participating Scientists

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211 kECU

Description of research work:

The lens of the human eye has long been recognized to be particularly sensitive to ionizing radiation. There have been a variety of studies on humans, and various animal experiments. However, there is mainly one study on man, namely the follow-up on the survivors of the atomic bomb explosions, that has provided quantitative dose-effect relationships. It indicates a threshold or a near threshold at approximately 2 Gy of gamma-rays.

For densely ionizing radiation there has been little information from human studies. The observations on the US dial painters suggest, that incorporated ^{226}Ra induces cataracts, but the data are not sufficient to establish a dose dependence to a reasonable degree of precision or a numerical value of the RBE of alpha-rays.

Spiess et al. have conducted a follow-up on 836 patients, who have been injected with ^{224}Ra in Germany shortly after World War II. This follow-up is the objective of project 2 in the cooperative research programme BI6-083-D (B) of the GSF, and the university of Munich. The mathematical analysis of the data is part of project 3 (Univ. München). The cooperation has earlier resulted in a detailed analysis of the osteosarcoma incidence among the ^{224}Ra patients and in revised risk estimates for osteosarcomas.

Recent work within the two projects has predominantly been concerned with the analysis of ^{224}Ra induced cataracts in the same group of patients. The result of this study is a dose dependence, which is largely equivalent to the one found in the atomic bomb survivors, provided an injected activity of 10μCi per kg. body weight is equated to 2 Gy of gamma-rays. An essential conclusion is the presence of a threshold, or quasi-threshold, for alpha-rays, as it has been inferred for gamma-rays. From ongoing work on the transfer of radium in the human body, and especially from the studies of Thorne, one may within the foreseeable future expect conversion factors between injected activity and the absorbed dose of alpha-rays to the lens or its sensitive equatorial zone.

In view of the singular nature of the collective of patients and the improbability that a comparable study will be possible again at any future time, it appears imperative to utilize the remaining information full and to conduct examinations on the younger group of the surviving patients for incipient lens opacifications, and to follow the eventual progression of such lesions. In this way more definite statements on the dose dependence, the latent periods, and the presence of a threshold should become possible questions of central importance to radiation protection, and issues relevant to the current controversies concerning the distinction between so-called stochastic and non-stochastic radiation effects.

There are, at present, 133 surviving patients in the study, who were treated with ^{224}Ra at ages up to 20 years, and who are now in the age group up to about 55 years. These patients shall be called in for careful ophthalmological examinations to be performed at the University of Munich. The patients will be contacted by Prof. H. Spiess who will take responsibility for the organization of this extended project. The mathematical evaluation will be performed within project 3 (Prof. Kellerer) of the current research programme.

Within the next two years the majority of the 133 patients can be motivated to participate in the project.

Project 1: Late effects in ^{224}Ra treated ankylosing spondylitis patients
GSF - Prof. Gössner

Project 2: Late effects in ^{224}Ra treated juvenile and adult patients
Universität München - Prof. Spiess

Project 3: Emidemiology of radiation carcinogenesis
Universität München - Prof. Kellerer

The three projects of this research programme are aimed at the epidemiological study of radiation effects in patients injected with ^{224}Ra.

Project 1 is concerned with more than 1500 ankylosing spondylitis patients treated with intravenous injections of ^{224}Ra. The alpha-ray doses to the skeleton of the patients are considerably lower than the doses in the earlier patients who are being studied in project 2. The analysis of the causes of death and of lesions related to the disease in the group of Ra-224 patients with a low mean skeletal dose of .67 Gy is paralleled by the study of a control group of ankylosing spondylitis patients not treated with radioactive drugs or X-rays.

Project 2 continues the study of patients who were treated in a German clinic shortly after the war as juveniles for bone tuberculosis and as adults for ankylosing spondylitis. The data, particularly for osteosarcomas, are largely complete, but additional recent observations on various other mostly non-stochastic, radiation effects are still being collected. Furthermore dose assignments and modifications of additional parameters will be updated.

Closely related are the epidemiological studies to be carried out in project 3. This project is concerned with the statistical evaluation of the data in projects 1 and 2. Past epidemiological work in the related earlier project BIO-D-461-81-D(B) has been performed for other data, and these studies will continue. However, the work has recently been focused on the analysis of the osteosarcoma data of project 2. The preliminary results have led to unexpected conclusions that will require further analysis by modern statistical techniques, such as the maximum likelihood analysis in terms of the proportional hazards model or related approaches. The essential problems are the presence or absence of differences of the sensitivity of juveniles and adults, and also the confirmation or rejection of a dose-rate effect.

C14 Epidemiological studies in human populations

Contracts Bi6-298/6-333/7-055 Thorotrast-investigations to evaluate the long term effects caused by artificial radiation in man (thorotrast patients follow-up study in Germany and Denmark)

Coordinator Deutsches Krebsforschungszentrum
Im Neuenheimer Feld 280
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Total Contribution by the Commission: 226 kECU
24 months from 1/01/90 to 31/12/91

Participating Scientists

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Contract Bi7-055

Description of research work:

Introduction

In 1929 Radt (Berlin) and Oka (Tokyo) introduced a stabilized 25% colloidal solution of thoriumdioxide as a radiodiagnostic contrast medium which was sold under the trade name "Thorotrast". The predominant form of application was an intravascular injection, especially for cerebral angiography. After intravascular injection the ThO_2 aggregates accumulate in the reticuloendothelial system (RES) and are stored for life.

Biophysical data

232-Thorium has a natural radioactivity; the half life is more than 10^{10} years and 95% of the radiation is alpha-particles. About 97% of the intravascularly injected colloidal thoriumdioxide (ThO_2) is retained by the organs of the RES: liver 59%; spleen 29%; bone marrow 9%; skeleton (except marrow) 2%; lungs 0.7%; kidneys 0.1%. The concentration of the ThO_2 is high in regional lymph nodes of the liver and spleen but very low in other lymph nodes of the body. With regard to individual organs there may be differences in thoriumdioxide content by up to a factor of 100.

From the data of the ^{232}Thorium distribution in the tissue and the activity ratios combined with information about the various types of radiation, the average energy per decay of each radionuclide and the cell absorption of alpha-particles in ThO_2 aggregates KAUL and NOFFZ (1978) calculated the mean values of the annual radiation dose of the organs of the RES. A mean intravascular injection of 25 ml Thorotrast in a 70 kg person causes the following absorbed dose rates: liver 25 cGy/year; spleen 70 cGy/year; bone marrow 9 cGy/year; endothelial layer in bone 16 cGy/year; kidneys 0.4 cGy/year. The radiation dose in the lung tissue is mainly caused by the daughter product ^{220}Rn which is exhaled by the breath.

Aim of the study

The objective of the German Thorotrast study was

- to trace the largest possible number of Thorotrast-patients who had been given intravascular injection of Thorotrast
- to determine the thorioumdioxide quantities incorporated
- to compare the health and the fate of Thorotrast patients with those of a control group
- to relate long term effects of Throtrast found to the radiation dose in the depository organs

Apart from answering these scientific questions, it was intended to provide a comprehensive treatment for these patients and to advise the physicians as well as the patients themselves.

Patients and methods of examination

Most of our patients were injected intravascularly with Thorotrast in the period between 1937 and 1947. The names and addresses of more than 5000 patients who had cerebral arteriography (70%) or arteriography of the upper and lower limbs (30%) with Thorotrast were obtained from the records of different hospitals in West Germany (van Kaick et al., 1984). In none of our patients Thorotrast was injected for the actual detection of liver diseases.

A pseudo-randomized "Non Thorotrast control group" was set up. It was made up of persons who had been in-patients at the same hospital and in the same year as the Thorotrast patients. To set up the roster, only patients with a surname starting with the letter "B" were used. The conditions for which either the Thorotrast patients or the controls were admitted to hospital was not considered in the selection. The control group and the group of Thorotrast patients were only matched for age and sex of the patients. In 1968 when the study was started a large number of the Thorotrast patients had already died. The causes of the death of those patients were clarified by hospital records, post mortem examinations, etc.. Patients who died in the first three years after Thorotrast injection were excluded from the evaluation to minimize the influence of the underlying diseases. Excluding the patients who died within the first three years, patients who were not traceable and those not responding, the German Thorotrast study comprises 2326 Thorotrast patients and 1890 control patients of which 2151 Thorotrast patients and 1493 controls have died up to 1990 (Table I).

Table I

German Thorotrast Study - Patients evaluated

Patients' Status	Throtrast	Control
Examined	899	662
Still living	175	397
Deceased	724	265
Not examined	1427	1228
Total	2326	1890

The groups of examined patients are followed up every two years by out-patient examination including biophysical measurements, radiological and clinical examination. Currently we are following up the remained 175 Thorotrast and 397 control patients.

Results

The final fate of the Thorotrast patients is the most important parameter for the calculation of Thorotrast late effects. A significant excess rate was observed in malignant liver tumours, liver cirrhosis, myeloid leukaemias and bone marrow failure (Table II). The statistical analysis of this data are published (van Kaick et al., 1989).

Table II

German Thorotrast Study - Diseases with High Excess Rate

Status '90 Cause of death	Thorotrast n=2,326		Control n=1,890	
Liver cancer	405	(17.40%)	2	(0.11%)
Liver cirrhosis	186 [+171]	(15.35%)	47 [+3]	(2.65%)
Myeloid leukaemia	36 [+3]	(1.68%)	4	(0.21%)
Bone marrow failure	29	(1.25%)	4	(0.21%)

[ ] Additional cases with another disease leading to death.

Open questions

Recently several other diseases displayed a possible excess rate (Table III). However we have to keep in mind that twice the number of control patients are still alive so these figures may change in the following years.

Table III

German Thorotrast Study - Diseases with possible excess

Status '90 Cause of death	Thorotrast n=2,326		Control n=1,890	
Ca. ext. bill. ducts	27 [+3]	(1.16%)	6	(0.32%)
Ca. pancreas	18	(0.77%)	5	(0.26%)
Ca. esophagus	7 [+1]	(0.34%)	1	(0.05%)
Ca. larynx	6 [+1]	(0.30%)	1 [+1]	(0.11%)
Non Hodgkin lymphoma	14 [+1]	(0.64%)	4	(0.21%)
Bone sarcoma	4	(0.17%)	1	(0.05%)
Plasmacytoma	7 [+2]	(0.39%)	1	(0.05%)
Mal. Mesothelioma				
Pleural	4	(0.17%)	0	
Peritoneal	2	(0.09%)	0	

[] Additional cases with another disease leading to death.

Also those diseases without an apparent excess rate are of interest (Table IV). An important result of the study is the similar number of lung cancers in both groups though the bronchi are exposed to chronic alpha-radiation by the exhaled thoron.

The kidneys are exposed to a mean dose of 50 mGy/year but increase in renal cancer could not be observed.

Table IV

German Thorotrast Study - Diseases without Apparent Excess

Status '90 Cause of death	Thorotrast n=2,326		Control n=1,890	
Chron. lymph. leukaemia	3	(0.13%)	3	(0.16%)
M. Hodgkin	3	(0.13%)	2	(0.11%)
Lung cancer	49 [+2]	(2.19%)	48	(2.54%)
Kidney cancer	6 [+2]	(0.34%)	5	(0.26%)
Urin. bladder Ca.	5 [+3]	(0.34%)	4 [+1]	(0.27%)
Adrenal cancer	2	(0.09%)	1	(0.05%)
Stomach cancer	30 [+3]	(1.42%)	44	(2.33%)
Colon cancer	10 [+3]	(0.56%)	17	(0.90%)
Rectal cancer	8 [+3]	(0.47%)	13 [+1]	(0.60%)
Prostate cancer	18	(0.77%)	13	(0.60%)
Breast cancer	8	(0.34%)	17	(0.90%)
Ovary cancer	5	(0.22%)	4	(0.21%)
Brain cancer	18	(0.77%)	11	(0.58%)

[ ] Additional cases with another disease leading to death

Organs with extremely low doses from the locally incorporated Thorotrast are reached however by the daughter product radon which is distributed over the blood stream. It is of high interest to calculate the cumulative dose for those organs which show no cancer excess rate.

During the past years there has been a constant trend for Thorotrast patients to die earlier compared to controls. This phenomenon depends on the amount of Thorotrast injected. Excluding from the analysis those patients who died from Thorotrast specific diseases (liver cancer, cirrhosis or leukaemias) we see similar results in dose-rate-dependent life-shortening. So it is most probable that there is a Thorotrast dependent influence on age at death.

Objectives for 1990/91

The working program will be continued according to the recommendations of the coordinating committee.

- Regular correspondence with about 600 patients of the Thorotrast and control group as well with the respective family physicians
- Out-patient reexaminations of Thorotrast carriers and patients of the control group at two years intervals
- Computer suitable registration of examination data and medical reports of the family doctors as well as the treating hospitals
- Controlling of the stored data and preparation of final statistical evaluation

References

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The German Thorotrast Study - report on 20 years follow-up.
BIR Report 21:98-104

C14 Epidemiological studies in human populations

Contract Bi6-319 Survey on childhood leukaemia.

Coordinator International Agency Research Cancer
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Total Contribution by the Commission: 45 kECU
0 months from 1/01/90 to 31/12/91

Participating Scientists

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Description of research work:

A summary of scientific background to the study and of progress to date is contained in the attached Abstract, presented at the 9th Conference of the American Statistical Association on Radiation and Health, in Colorado, USA (8-12 July 1990). Since the previous progress report, dated 9th November 1989, the following changes should be noted:

(1) Data collection for the period 1980 - 1987 is almost complete.

(2) Incidence rates for the period 1980-85 have been calculated, also those for 1986 and 1987, for national populations.

(3) The definition of the sub-national areas for which UNSCEAR has calculated dose estimates are now available. Incidence rates for these subdivisions have yet to be calculated.

(4) the participation of Bulgaria in the ECLIS study has been agreed. The quality of available data, and the requirements related to verifying registrations against clinical records remain to be defined.

(5) Data have been promised from those parts of the USSR most affected by the accident. However, there remain unquantified problems in the validation of any routine statistical data from areas without a comprehensive population-based cancer registry. A separate contract may be required for any comprehensive study within the USSR.

THE EUROPEAN CHILDHOOD LEUKAEMIA/LYMPHOMA INCIDENCE STUDY

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(on behalf of the ECLIS study Group)*

Following the accident at the Chernobyl nuclear power plant on 26 April,1986, radioactive materials were deposited over large areas of Europe. There were three successive "plumes" of material affecting (1) the Eastern USSR, Poland and Sweden (2), Central Europe - especially Austria, Bavaria, North Italy and part of Switzerland, and finally (3) Romania and Bulgaria.

Most exposure was to ^{131}I, ^{134}Cs, ^{137}Cs, and was generally of rather low magnitude. Exposure to humans was both external (mainly from ground deposition) and internal (from ingestion of contaminated food). Estimated average exposures require rather complex models, and differ according to the methods used. UNSCEAR has produced estimates for all national populations in Europe (and by sub-region within some countries). Nationally, the highest average exposures outside the USSR were in Bulgaria (760 uSv) and the lowest in Portugal (2 uSv). These figures can be compared with the average (worldwide) exposure from natural sources of 2400 uSv per person - although there is considerable geographic variation.

Outside the immediate vicinity of the accident, the predicted health effects due to radiation are rather small. Nevertheless, these health effects should be monitored for several reasons. Firstly, its a matter of great public concern, and already there are reports of clusters of Leukaemia, excess infant mortality and excess premature births among malformed children in sub national areas with higher than average exposures. Investigation of apparent clusters is greatly facilitated by a large scale systematic study. Secondly, it is possible that either dose estimates or the models used in predicting cancer risk are in error, and the excess will be higher than expected.

Childhood leukaemia is the most logical choice of adverse health effect for monitoring. Radiation-induced leukaemias appear early (2-10 years) after exposure, and provide the largest excess incidence of any cancer. Background incidence of leukaemia is relatively constant in Europe. Finally, a fairly comprehensive monitoring scheme is already in place in the form of registers of cancer and childhood cancer, so that a study of geographical and temporal trends in incidence requires no special data collection systems in most countries. It should be noted that the relatively good prognostic of childhood leukaemia in many countries, and likely improvements in therapy and survival in others, means that mortality data are virtually useless for monitoring risk.

The European Childhood Leukaemia/Lymphoma Incidence Study (ECLIS) was set up in 1987. It involves cancer registries in 17 European countries (Some million children live in the areas covered, and approximately 2400 cases of leukaemia are expected every year. BEIR provides a formula for calculating relative risk. Assuming (a) a latent period of 2 years, and (b) that risk at 2-4 years is the same as that at 5-10 5TO WHICH THE BEIR data apply).

The approximation RR = 1 + (0.243d) xexp (4.885) can be obtained, where d = dose in Sv. For an average exposure of 500 uSv, the relative risk is thus 1.016. The estimated excess cases in each country using this formula yields on average increase of 0.8%, with a maximum in Byelorussia (around 6%).

The study involves the collection of data on all recorded cases of childhood leukaemia and lymphoma occurring in the populations covered by the registries. Collation of data from the different centres and its analysis is coordinated by IARC. Registries send an update file of every case registered, with details of age, date of birth, date of diagnostic, place of residence, and histological diagnosis, at annual intervals. Data collection to the end of 1987 is now almost complete.

The period 1980-85 will serve as a baseline to investigate differences in the incidence between regions, and to provide information on underlying trends in incidence in the 6 years preceding the accident. Changes in 1986 and subsequent years will be studied to see if they bear any relationship to the estimated exposure levels in different regions. Since the place of residence of all cancer cases is recorded, it is possible to study almost any geographic units. The basic analyses will, however, comprise either national populations or broad subregions within certain countries, for which exposure estimates have been prepared by UNSCEAR.

Preliminary results confirm the rather constant background incidence of leukaemia, around 40 per million children per year. There is a slight male preponderance in almost all countries.Time trends in 1980-85 are rather variable in different countries, but several show small increases in incidence, against which future changes (post accident) will have to be evaluated.

A first complete analysis of background incidence, and age-specific incidence rates in 1986-87 will be completed during 1990. However, it is too early to relate any of the incidence data to the exposure estimates. Future analyses will also examine birth-cohort specific incidence, with particular interest focused on children born in may 1986 - January 1987 (prenatal exposure).

* ECLIS Study Group (July 1990), Dr D.M. Parkin, Dr J.M.Kaldor (Dr D.R. English) Mr E.Masuyer (IARC), Dr H. Hansluwka (Austria), Dr J. Augustin (Czechoslovakia-Bohemia/Moravia), Dr I.Plesko (Czechoslovakia-Slovakia), Dr H. Storm (Denmark), Dr S.Karjalainen (Finland), Dr J-M. Lutz (France), Dr W.Staneczek (GDR), Dr J. Michaelis (FRG), Dr M. Vargha (Hungary), Dr B. Terracini (Italy), Dr J.W. Coebergh (Netherlands), Dr. F. Langmark (Norway), Dr W.Zatonski (Poland), Dr L. Barlow (Sweden), Dr L. Raymond (Switzerland), Mr C.A. Stiller (UK., England & Wales), Dr R. Black (U.K., Scotland), Dr M. Rahu (USSR,Estonia), Dr R. Kriauciumas (USSR, Lithuania), Dr V. Merabishvili (USSR Statistics), Dr V. Pompe-Kirn (Yugoslavia).

C14 Epidemiological studies in human populations

Contract Bi6-347h Statistical studies of radiation risks (NRPB Association)

Coordinator NRPB
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Total Contribution by the Commission: 370 kECU
30 months from 1/01/90 to 30/06/92

Participating Scientists

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Description of research work:

Aims and Objectives

This project addresses a number of topics in the epidemiology of radiation-induced cancer. Several groups exposed for medical reasons are being studied, namely patients with medical exposures to I-131 in the Saarland (Germany), Swedish patients given radiotherapy for skin haemangioma in childhood, and Italian cancer patients given radiotherapy. Statistical models are being fitted to data on populations exposed to high doses, such as the Japanese atomic bomb survivors and groups of uranium miners. Methods and software for examining data on populations exposed to low doses are being developed. Preparatory work is being performed on the compilation of 'probability of causation' tables that are specific to EC countries.

Description of Project

(i) Modelling Radiation Risk in Populations Exposed to High Doses (NRPB, UK/GSF, Germany)

Results from the follow-up of the Japanese survivors of the atomic bombings of Hiroshima and Nagasaki, based on the new DS86 dosimetry system, have recently been published by the Radiation Effects Research Foundation. These results were used by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) in deriving cancer risk estimates for their 1988 report.

Health effects models have been developed at NRPB on the basis of the 1988 UNSCEAR report (Stather et al, 1988, NRPB-R226). Under this contract it is intended to analyze the full data set on cancer risks among the Japanese atomic bomb survivors based on the DS86 dosimetry. In particular, the influence of dose, time since exposure, age at exposure and sex on the cancer risk will be studied in depth. It is also intended, in cooperation with the Radiation Effects Research Foundation in Japan, to create synoptic diagrams of essential features of the A-bomb data. These will include scatter-plots of the locations at time of bombing of the cancer cases in relation to those of the other survivors. There will also be plots of cumulative hazard functions for cancer mortality for both sexes, for both Hiroshima and Nagasaki, and for different age cohorts.

Comparisons will be made with other data sets on populations exposed to high doses, such as UK ankylosing spondylitis patients given x-ray therapy (in conjunction with the Imperial Cancer Research Fund, Oxford) and uranium miners in the US (Colorado Plateau) and Czechoslovakia (in conjunction with the Institute of Epidemiology, Prague). Of particular interest is the comparison of the pattern of risk with time since exposure. Implications of different time-projection models, such as those published in the BEIR IV and BEIR V reports, will be examined. Information relevant to transferring risks of radiation-induced cancer between populations will be reviewed. The relationship between radiation exposure and smoking on the risk of lung cancer will also be studied using the Colorado uranium miner data.

(ii) Assessment of Data from Populations Exposed to Low Radiation Doses (NRPB)

Risk estimates for use in radiological protection have been derived mainly from epidemiological studies of populations exposed to high doses of radiation at high dose rates. Thus their use in the protection of radiation workers or the general public involves an extrapolation to low doses and low dose rates, which introduces a degree of uncertainty.

Data from epidemiological studies of populations exposed to low doses of radiation, such as radiation workers, can be used to check that current risk estimates are not too low by at least an order of magnitude. The NRPB is analyzing data from the UK's National Registry for Radiation Workers (NRRW) under CEC contract BI6-F-213-UK. Some statistical software for analyzing such data - in particular, the program ARFAR (At Risk For Any Reason) - have been developed under the previous CEC contract BI6-F-116-UK. It is intended that the development, refinement and validation of software for the NRRW analysis continue during 1990-91. These software may be compared with programs written elsewhere.

In recent years there have been reports of raised incidences of childhood cancer -in particular, leukaemia- near several UK nuclear installations. However, these have not been explained on the basis of assessments of the radiation exposure of the relevant populations. There is currently a paucity of information on the underlying geographical distribution of childhood cancer which would allow the results around nuclear installations to be viewed in context. Also, further development of statistical methods for analyzing such data is required, since current methods have been criticised for their lack of power at detecting 'clustering' effects. It is intended to study both these topics during 1990-91. A database on the distribution of childhood cancer throughout Great Britain is being constructed by the Childhood Cancer Research Group (University of Oxford). It is hoped to be able to assist in the analysis of these data, and to examine the power of various statistical techniques.

There is increasing concern with the potential consequences of irradiation of the embryo and fetus. Studies of the effects of prenatal x-rays have indicated excesses of childhood cancer, unlike that of

the Japanese atomic bomb survivors. The latter study, however, has recently shown possible excesses of adult cancers following irradiation in utero. It is intended to examine published results from these studies.

(iii) Radioepidemiological Tables of the Probability of Causation for Use in the Countries of the EC and their Extension to Radon Daughter Exposures (GSF)

In 1985, the American National Institutes of Health, NIH, published its "Radioepidemiological Tables". These tables summarise values of the so-called "probability of causation" (PC), which provides an objective scale in arbitration and compensation cases for cancers that might have been caused by exposures to ionising radiation. Similar needs in the countries of the EC suggest the adaption of these data. Further, due to substantially revised risk estimates these tables and their underlying methods need to be carefully revised and actualized. It will be the aim of this project to prepare the compilation of PC-values for EC-countries.

This calculation requires the knowledge of spontaneous cancer incidence rates, specific for age and secular period in various countries. There are considerable differences in the availability and reliability of these data in the various EC-countries. For some countries this information is rather poor and incidences will have to be estimated on the basis of mortality rates. The objectives of the work will be:

1. a review of the present American NIH-tables, of the concepts, models and data used for their computation;
2. the definition and compilation of data needed, ie, national and regional cancer incidences;
3. the development of algorithms and computer codes for the final computations;
4. the preparation of future cooperations with institutions in other EC-countries in view of the necessary exchange of incidence data and codes.

An important issue, until now not treated by NIH, concerns exposures to radon daughters. The extension of the available models and data bases to this problem will be a second major objective of this project.

The project will be performed in close cooperation with the NIH committee. The final calculations of PC-tables will await the availability of the most recent data from RERF after the revision of the atomic bomb dosimetry.

(iv) Epidemiological Research with the Aim to Determine the Morbidity and Mortality Risks of Thyroid Gland Carcinoma (University of Saarland, Germany)

In the event of a nuclear power plant accident radioactive isotopes of the element iodine may be released, the most important of which is ^{131}I. Iodine is of particular importance since a high percentage accumulates in the thyroid gland in a very short time. It is therefore desirable to obtain further information on the risks of morbidity and mortality from thyroid gland carcinoma caused by uptake of ^{131}I.

In the Department of Nuclear Medicine at Homburg/Saar a data bank exists in which about 24000 patients, treated with ^{131}I, are registered. From this data bank - two cohorts are being created: first, all the in-patients of the department and second, all the patients who lived at the time of examination date in the Saarland.

The first cohort includes about 3700 patients. It will be updated to 1990. The activity of ^{131}I applied is in the range of GBq. The second cohort consists of about 12500 patients. About 1500 patients of these are in-patients. For the out-patients the activity of ^{131}I applied is in the range of MBq.

As a first step it is planned to consider all the patients who lived at the time of examination date in the Saarland, because the Saarland has a good functioning "Krebsregister" (about 94% of all the incident carcinoma in the Saarland are registered).

A first comparison between the persons registered in the "Saarländisches Krebsregister" and the cohort of Saarland patients is being carried out. The complete evaluation of that first comparison is not yet finished. At the same time the former patients and - if known - the family doctors of these patients will be written to. Beyond that it is hoped to get information on death or change of domicile from the registry offices. The information on morbidity and mortality risks will be analyzed in relation to estimates of doses to the thyroid.

(v) Cancer Incidence and Mortality Following Radiotherapy for Skin Haemangioma in Childhood (Karolinska Institute, Sweden)

During the period 1920-1959, a total of 18,460 patients under the age of 20 years were admitted to Radiumhemmet, Karolinska Hospital, Stockholm for skin haemangioma. Radiotherapy with ^{226}Ra or orthovoltage x-rays (≥100kV peak) was given to approximately 70% of the patients, 14% received contact x-rays and the remaining 16% received no radiotherapy. For patients given radiotherapy the total risk of cancer incidence relative to the general population was 1.18 (95% confidence internal (CI) 1.03-1.35). Mortality from all cancers was also increased (Standardised Mortality Ratio=134, 95% CI=111-160). The mean dose from all different parts of the body to radiosensitive organs, from the brain to the gonads, was calculated to be in the range 0.03-0.2 Gy. A case-control study has shown dose-response relationships for thyroid cancer and for bone and soft tissue tumours.

The work planned for 1990-91 is as follows.

Cancer risks - New and updated record-linkages with the Swedish Cancer Register for the period 1958-1986 and the Swedish Cause-of-Death Register for the period 1951-1988 will be performed. This will add several years at risk to the earlier analyses.

Total individual dosimetry - Dosimetry will be performed for patients younger than 18 months at the time of treatment, and treated with ^{226}Ra (n=14, 647). The absorbed dose to the thyroid, breast, lungs, stomach, colon, gonads, and bone marrow will be calculated for each individual patient using radium needles, radium tubes, and glass containers from the original treatments. Reconstruction of treatments will be made on a tissue equivalent phantom representing a 6-month old child.

Dose-response relationship - Cancer incidence and cancer mortality in the cohort will be related to the absorbed dose, and dose-response patterns will be analyzed.

(vi) Epidemiology of Second Tumours in Radiotherapy Patients (University of Florence and Other Italian Centres)

Clinical records of the radiotherapy patients carefully documented dose, irradiated volume, and treatment schedules as well as clinical data. The dose to the irradiated volume was accurately measured and the dose absorbed by other parts of the body was calculated with reasonable accuracy since the conditions relating to the radiation source and the patients were recorded.

Most patients (about 2500 per year) were followed for many years (some for 30 years) for periodic evaluation of the disease and of possible late radiation damage. About 1800 new patients underwent radiotherapy each year. Different radiation sources (2 telecobalt units, 2 linear accelerators, after-loading sources) were used for external and endocavitary radiotherapy. Moreover, radiometabolic treatments with ^{131}I for thyroid carcinoma, hyperthyroidism and toxic adenoma were performed. Conventional fractionation (2 Gy/day, 5 days/week) was used for external radiotherapy with x-rays and accelerated electron beams from linear accelerators. More recently, different fractionation schedules (1 Gy x 3/day, 2 Gy x 3/day and 2 Gy x 2/day) have been introduced. The use of these different radiation sources and treatment schedules allow evaluation of the different acute and late effects of ionising radiations.

The aim of the research was to follow up the patients in order to evaluate the incidence of a second primary tumour, either in the irradiated area or outside of it. Patients come to follow up every year. Most subjects were affected by breast cancer, gynecologic tumour, lymphoma, head and neck tumour or thyroid carcinoma.

During the treatment and during the follow up, besides clinical and radiological examinations, the concentrations of some molecules considered to be important tumour markers or biochemical indicators of radiation injury were assessed.

The analysis will examine the correlation between treatment with ionising radiation and secondary tumour incidence. In addition to the rate of incidence of secondary tumours, the time since the initial tumour, the dose to the tissue from which the secondary tumour arises as well some biochemical parameters and tumour-markers in these patients will be studied. Retrospective dosimetry will be carried out using Monte Carlo methods. The histopathology of the second tumours will be verified.

Several Institutes will collaborate in the study by providing information on patients. In addition to the University of Florence where about 2500 patients per year are being treated, the University of Modena can contribute about 27000 patients treated from 1972-1989 as well as, with smaller numbers of patients, the Universities of Pisa, Brescia, Siena, Bologna and the General Hospital Varese.

C14 Epidemiological studies in human populations

Contracts Bi7-007/6-295 Radon and Lung Cancer in the Ardennes and Eifel Region

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Total Contribution by the Commission: 577 kECU
24 months from 1/05/90 to 30/04/92

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Description of research work:

The Ardennes - Eifel Project consists of three major studies on the role of radon in the etiology of lung cancer :

- Radon and Lung Cancer in the Ardennes - Eifel Region;
- Radon dans les Habitations de Bretagne et du Massif Central et Risque de Cancer du Poumon;
- Improved Estimates of the Risk of Radon-Daughter Inhalations.

The Ardennes - Eifel study is a hospital based case-control study, situated in a geologically distinct area covering parts of Belgium, France, Germany and Luxembourg. Out of national and regional surveys it became clear that in this region the range of indoor radon exposures is quite large and that an important fraction of the population is living in high radon houses.

The study is aimed to arrive at complete data of some 1200 cases and 3600 controls over a period of 5 years. Based upon local population distribution patterns and geological extent of the region a total amount of 1800 subjects will be identified in Belgian and German hospitals, while some 600 will be delivered by French and Luxembourg clinics. Only subjects who are currently living within the defined study area and who lived there for at least 25 out of the last 35 years will be included.

The radon history will be reconstructed through 6 months measurements in the living and bedroom of the different dwellings. The comparability of the detectors and associated procedures used in the different centres will be investigated through yearly quality control exercises.

The cases will be selected in the departments of pneumonology, bronchoscopy and thoraxsurgery. Only histologically confirmed cases will be included in the analysis. Study subjects will be interviewed with a standard questionnaire covering risk factors related to lung cancer as active and passive smoking, occupational exposure and other factors of interest as residential history, house characteristics and health history. Patients aged 75 years or over on their first visit to hospital will be excluded. As controls only persons suffering from diseases not strongly related to tobacco and that are not likely to render them incapable of participating in the study will be included. In each country a local reference pathologist will review the pathological material.

The radon intercomparisons will be organised by the Belgian participant (Univ. Gent), who acts as coordinator for this project. He will also collect all data from the different contractants in an appropriate form and transmit them to the German participant (Univ. Wuppertal) for statistical analysis. The treatment of the data will be done in close collaboration with the epidemiological research team from Oxford. This unit is also taking part in the setting-up of the study protocol, in order to develop the study along common lines with the U.K. project. Finally, through contacts with research groups e.a. in Sweden and the USA, we aim to arrive at comparable data registration within all studies on this topic.

In close collaboration between the C.E.A., the Univ. of Brest and INSERM, a case-control study about the risk of indoor radon is also organised in Bretagne and the Massif Central region. In this study the same protocol will be applied as in the Ardennes - Eifel study. It is aimed to arrive at complete data for some 600 cases and 1200 controls over a period of 5 years.

A review of the report ICRP-50 and BEIR IV will be prepared by the Institüt für Strahlenschutz (GSF). Particular attention will be given to the assumptions and models underlying the analysis of the BEIR IV committee. Improved models will be set up to separate the influence of the major co-factors as age at exposure, smoking habits and duration of exposure. In addition improved algorithms will be developed for use on the Czech miner data. The C.E.A. will apply these algorithms to the follow-up data of the French uranium miner study.

C2 OPTIMIZATION AND MANAGEMENT OF RADIATION PROTECTION

C21 Optimisation of radiological protection

Contract Bi6-324 Development of fundamental data for radiation protection

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Total Contribution by the Commission: 77 kECU
24 months from 1/01/90 to 31/12/91

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Description of research work:

1. Introduction

The radiation protection standards recommended by the International Commission on Radiological Protection (ICRP, hereafter called the "Commission") have formed the basis for most radiation protection guidelines and regulations which have been issued by international and national institutions or authorities, respectively. They have been also applied in the past by the Commission of the European Community and its member states. Thus the work of ICRP has contributed effectively to an international harmonisation of protection standards on this field.

2. New basic recommendations in radiological protection

A major event in this period is to be the publication of a new set of basic recommendations in radiological protection and the relevant supporting material. A task group of the main Commission has been established to undertake the preparation of this report and several task groups of the Committees have been established to provide input data for use in the revision.

Experience has shown since the publication of the last basic recommendations in 1977 that there was a need to produce further advice to supplement the recommendations as their implications became apparent in practice. This advice has been presented in a number of statements and amendements and in about 30 more detailed technical reports (see Annals of the ICRP).

Development in the last few years have now made it necessary to issue a completely new set of recommendations. In doing so, the Commission has had three aims in mind:

(a) to take account of the new biological information and of trends in the setting of safety standards,
(b) to improve the presentation of the recommendations,
(c) to maintain as much stability in the recommendations as is consistent with the new information.

The Commission has extended its basic principles to a system of radiation protection, namely that activities involving exposures should be justified, the protection arrangements should be optimised and stochastic effects should be limited by the application of individual dose or risk limits.

Recent epidemiological studies indicate an increase in the radiation induced risks of fatal cancer by a factor of about four compared to what was estimated in 1977.

This has called for some quantitative changes in the Commission's recommendations. One such change to be recommended by the Commission is a reduction of the dose limit for occupational exposure. The previous figure for 50 millisievert in a year is reduced to 20 millisievert per year, with some allowance for flexibility.

The current principal limit for the public (1 millisievert per year) is retained, but increased protection is provided by limiting the averaging period to five years and recommending the use of additional source-related constraints. The Commission will differentiate in its new recommendations between practices giving rise to radiation exposures, and intervention where existing radiation exposures require decisions on remedial actions to reduce exposure.

The anticipated date of publication of the new recommendations is 1991.

3. Task group activities

Several task groups, through the Committees, are aiding the ICRP Main Commission. They include task groups providing:

- risk estimates for cancer and genetic effects at doses appropriate to radiation protection. The data will quantify risks for site-specific cancers related to age and sex and will allow the ICRP to derive tissue weighting factors reflecting the sensitivity of different organs to developing radiation-induced cancers.
- information on the effects of radiation on skin and how this is related to the type of radiation, its penetrative properties, the area of skin involved and the cells at risk. This is relevant to the problem of skin contamination and the recommendation of dose limits in the nuclear industry.
- dosimetry of incorporated radionuclides as a function of age at exposure, thus allowing a prediction of the doses to tissues resulting from accidental exposure of members of the public following a major radionuclide release into the environment. A report on isotopes of hydrogen, carbon, strontium, zirconium, niobium, ruthenium, iodine, caesium, cerium, plutonium, americium and neptunium has already been published. An impending second report will include age-dependent biokinetic data for the elements sulphur, cobalt, nickel, zinc, silver and tellurium.
- a critical examination of particle deposition in the human respiratory tract and the doses associated with the subsequent mechanical clearance of particulates and the translocation of radioactive materials to blood and to eventual sites of deposition. This study will update the current ICRP lung model used for dosimetry.
- new information on the mass, dimensions and elemental composition of tissues and organs paying particular attention to normal variations at different ages and in different races. This information is necessary for dosimetric modelling of incorporated radionuclides.
- a set of logical principles on protecting the public in the event of a major radiation accident, considering the consequences at long times as well as immediately after the accident, and in the far field as well as the near field.
- the application of principles of radiation protection and safety in considering exposures not intended to occur (potential exposure).
- measures for protection against radon, considering the establishment of intervention levels in houses, and workplaces, and the various remedial measures available with their cost and effectiveness.

Reports on cancer and genetic risks, the biological basis for dose limitation in the skin, new respiratory tract models are anticipated in 1991.

C21 Optimisation of radiological protection

Contract Bi6-347i Application of ALARA in complex decision-making situations (NRPB Association)

Coordinator NRPB
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Total Contribution by the Commission: 175 kECU
30 months from 1/01/90 to 30/06/92

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Description of research work:

Aims and Objectives

The objectives of this project are:

a) to develop appropriate software and tools for undertaking optimisation of protection;

b) to develop appropriate databases on incidence of failure;

c) to investigate the application of ALARA to decision-making in complex situations and to propose a general methodology to aid decision-making in such situations.

Description of Project

One of the fundamental principles underpinning radiation protection is that all exposures shall be kept as low as reasonably achievable, economic and social factors being taken into account. This principle was expressed in that form during the 1970s and since that time considerable effort has applied to understanding how it should be implemented at the practical level. A guide to the practical implementation of the principle has been developed jointly by NRPB and CEPN under a previous CEC contract (BI6-F-110-UK) and the work being undertaken under the Association Agreement is a sequel to this developmental work.

Software and Tools for Practical Implementation of Optimisation of Protection

The work undertaken under the previous joint NRPB/CEPN project clearly showed that the protection of workers would be greatly assisted by the development of appropriate software, tools and databases.

A software package for performing simple and extended cost-benefit analysis in the optimisation of radiation protection will be developed. This package will present the results from such analyses in graphical and tabular forms and will facilitate sensitivity analyses.

Implementation of the optimisation principle into certain operations, particularly those involving high dose rates, can be facilitated by task-specific dosimetric systems, databases of past experience and software for planning and managing a job. The intention is to develop such systems that would link into electronic dosemeter systems.

This part of the work is being carried out by CEPN and NRPB with CEPN taking the lead.

Databases on Failure Incidences

To enable the principle to be fully implemented into the design of safety systems of industrial facilities, there is a need to collate data on the incidence of failures of various safety systems, eg: interlocks, fail-safe mechanisms. In this part of the project, the intention is to set up a database of information on such failures. Such a database would then be available for subsequent analysis providing information on where problems might exist in the design of particular facilities.

This part of the project is initially being undertaken by NRPB.

Complex Decision Making

While the principle of optimisation is relatively well-established in radiation protection in normal operations, there are more complex situations involving such things as low probability events, long term effects, different forms of detriment, and equity questions. For such, there is no straightforward way of applying the optimisation principle. This part of the project is therefore aimed at developing appropriate methodologies to assist in these more complex situations. Several stages are envisaged:

a) The first will involve a critical review of the approaches currently proposed for managing risk in complex situations. It will address decision-making methodology, criteria used, the justification of weighting factors and any special features of the decision-making process.

b) The next stage will involve the definition of the various categories of complex situations, the identification of the parameters pertinent to these situations, the development of numerical values for the various weighting factors and the proposition of a general methodology and decision-aiding tools applicable to these problems.

c) The final stage will involve carrying out several case studies that will demonstrate the ideas that will be developed in this project.

This part of the project is being undertaken principally by SRD and CEPN.

C22 Reduction of patient exposure in medical diagnostic radiology

Contract Bi6-342 Establishment of a common protocol for the use of a whole body counter

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Total Contribution by the Commission: 27 kECU
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Description of research work:

1. Elaboration of a "Common protocol for the use of whole body counters"

   This requires:

   - the establishment of a working procedure as well as
   - a meeting of experts from various Member States for discussion and for setting up the necessary documentation as specified by the working procedure.

2. Implementation of the "Common protocol for the use of whole body counters" in the Hippokration Hospital of the University of Athens.

   This requires:

   - a four week training of 2 Greek physicists in the Federal Republic of Germany (FRG).
   - a two week assistance in Athens of 2 experts from the FRG in implementing the common protocol.

C22 Reduction of patient exposure in medical diagnostic radiology

Contract Bi6-347g Reduction of patient exposure in medical diagnostic radiology. Dosimetry and risk

Coordinator National Radiological Protection Board (NRPB)
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Total Contribution by the Commission: 250 kECU
24 months from 1/01/90 to 31/12/91

Participating Scientists

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Description of research work:

Aims and objectives

The overall objectives of the projects included in this contract are to study various aspects of the measurement and calculation of doses received by patients during medical X-ray examinations, the influence of different components of X-ray imaging equipment on patient dose and the risks associated with these doses.

Description of Project:

Dosimetry

Part of this contract is concerned with the further development of numerical methods of patient organ dosimetry based on Monte Carlo codes and mathematical phantoms (NRPB/GSF). Calculations based on geometrical phantoms (MIRD type) will be extended to cover conventional X-ray examinations on paediatric patients of different ages and sizes and to model new types of computed tomography (CT) scanner. Comparisons will be made with similar calculations based on more realistic "voxel" phantoms that will be derived from CT images.

This contract also includes projects designed to improve understanding of the impact of the performance of important components in medical imaging systems on the dose received by the patient. Components to be studied include film-screen combinations used in general radiology where unambiguous methods will be developed for measuring the speed of commercially available systems (GSF).

The response of automatic exposure control devices and film-screen combinations to the radiation qualities experienced in mammography will be studied, to improve the reliability of automatic exposure control in producing satisfactory mammograms (PTB). Accurate dosimetric methods for mammography will be developed with measurements carried out in phantoms and on patients with a view to optimising all the technical exposure conditions so as to achieve maximum image quality with minimum dose to the radiosensitive areas of the breast (TNO).

Participation will continue in the CEC Study group developing 'Quality criteria for diagnostic radiographic images' including the provision of a postal TLD service for European trials of the Criteria (NRPB).

Risks

The harm to be attributed to patient organ doses will be studied by applying the latest radiation health effects models in a manner that takes into account the special demographic statistics of patient populations. The usefulness of Quality Adjusted Life Years (QALYs) lost as a measure of harm in the health care context will be investigated (NRPB).

Part 1: Patient Dosimetry and Risk analysis

Head of project: B.F. Wall

1. Practical assistance in patient dosimetry will be provided in support of international trials of the "Quality Criteria for diagnostic radiographic images" for both adult and paediatric patients that are being developed by CEC study groups. The patient dose guidelines will be revised in the light of the results of these trials and in response to comments received from professional institutions in diagnostic radiology throughout Europe.

2. Further Monte Carlo programs for calculating organ doses in a standard patient will be developed, both in conventional radiography and in computed tomography (CT). The effects of changes in patient size on organ doses will be studied including calculations for infants and children. Calculations will be necessary to model the scanning parameters of new types of CT scanner as they come on the market.

3. NRPB are developing new radiation health effects models based on the latest analyses of the Japanese atomic bomb survivor data. Methods will be developed for applying these models to medical exposures in a manner that takes into account the special demographic statistics of patient populations. Quality Adjusted Life Years (QALYs) lost will be studied as a measure of harm from medical exposures.

Part 2: Film-screen speed, organ doses and photon spectra

Head of project: G. Drexler

A standardised method for the determination of the speed of numerous, commercially available film-screen combinations will be developed. There are serious doubts whether the existing standard methods (ANSI, DIN) lead to the same results and whether the manufacturers' specifications are in compliance with the real values.

Further realistic mathematical phantoms for children and adults using tomographic data (voxel phantoms) will be used with a Monte Carlo code simulating the transport of photons and secondary electrons, for organ dose calculations for typical X-ray examinations, specially for the examination parameters recommended in the CEC Quality Criteria for diagnostic radiographic images. The results will be compared to the doses obtained using MIRD-5-type phantoms and will be applied in radiological practice on patients of similar size to the phantoms. "Scale factors" will then be established which will allow the estimation of organ doses for patients of any size.

Photon spectra inside a water or tissue equivalent phantom will be calculated. The knowledge of these spectra is essential for absorbed dose measurements in phantoms, calibration of dosemeters and to calculate dose equivalents assuming an energy dependent quality factor.

Part 3: Investigation of automatic exposure control systems in mammography

Head of project: H.M. Kramer

As analysis of the performance of automatic exposure control systems in mammography is vital as the overall success of a screening program depends crucially on the magnitude of the exposure, which implies that even minor deficiencies in an automatic exposure control system must be eliminated.

The essential steps in the project:

1. Investigation of the properties of the radiation fields behind phantoms of various thicknesses for a range of tube voltages and field sizes. Monte Carlo code will be used to determine the relative dose contributions due to direct and scattered radiation. These results will be backed up by some experimental studies under selected conditions.
2. Investigation of the radiological properties of automatic exposure control systems produced by various manufacturers mainly with respect to the influence quantities tube voltage, phantom thickness and field size (see point 1) and beyond that in view of their dynamic range.
3. Investigation of the response of a selection of films and film screen combinations as a function of tube voltage, patient or phantom thickness and field diameter (see point 1 above).
4. Evaluation of recommendations for improving the automatic exposure control systems examined with the objective to reduce the number of non-acceptable radiographs and to extend the range of the applicability of the automatic exposure control systems examined.

Part 4: Dosimetric and technical aspects of mammography: Optimisation and quality control

Head of project: J.J. Broerse

The dosimetric aspects of the project include investigations of absolute dosimetry, studies on monitoring of dose to the breast in actual mammography and dose specification. The technical aspects concern studies on determination of physical image quality as well as optimisation of technical conditions (eg. film/screen combinations, film processing, use of antiscatter grids, tube voltage and automatic exposure control units) to achieve maximum physical image quality at minimum absorbed dose. Quality control is essential to maintain optimum conditions.

Concerning absolute dosimetry, a comparison will be made between dose measurements with ionisation chambers in phantoms of various materials and calculation of dose distributions in-phantom. Displacement correction factors of ionisation chambers in-phantom will be investigated for various materials at a radiation quality relevant for mammography. In collaboration with the Breast Screening Centre (BOC) associated with the Comprehensive Cancer Centre Rotterdam, studies will be performed on monitoring of patient dose during actual mammography. For various film/screen combinations and several film processing techniques, physical image quality and absorbed dose required to obtain a photographic density of D = 1.0 will be determined. The protocol for quality control of mammography formulated previously and in use at the BOC, Rotterdam, will be evaluated.

C22 Reduction of patient exposure in medical diagnostic radiology

Contracts Bi7-014/6-343 Quality criteria, tolerances, limiting values, dosimetry and optimization in a number of fluoroscopic, digital fluoroscopic, DSA and digital radiological systems.

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Total Contribution by the Commission: 140 kECU
24 months from 1/07/90 to 30/06/92 **Bi7-014**
24 months from 1/01/90 to 31/12/91 **Bi6-343**

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Tel. 911-3982303
30 kECU
Contract Bi6-343

Description of research work:

BI7-0014

This contract initiates work on bridging a gap which has opened up between major advances in radiological equipment and techniques, and the lack of developments in Quality Assurance, Patient/Staff Dosimetry, Comparative Dosimetry, and Optimisation of Automatic Exposure Control and Automatic Brightness Control in a number of systems.

Task 1 :

Characterisation, Evaluation, Comparison and Optimisation of Automatic Exposure Control and Automatic Brightness Control in a number of systems.

Task 2 :

Identification of Important Variables, and where possible Tolerances/Limiting Values, in the Fluoroscopic/TV/Cine/100mm/Multiformat Cameras, and Digital Imaging Systems. The variables are to include those suitable for Constancy Testing at one level and for Acceptance/Write-off of Equipment at another.

Task 3 :

Dosimetry and Optimisation Studies of Conventional and Corresponding Digital Techniques for Cardiac, G.I., Chest, Peripheral Vascular and Paediatric Studies.

Task 4 :

Patient and Staff Dosimetry in Selected Clinical Studies.

In addition to the above, the work of the contract is being coordinated with that of Dr. Th. Schmidt BI6-343 so that the work programme in Tasks 3 and 4 will be integrated and the progress/final reports will be grouped.

Project J. F. Malone:

Task 1 :

Characterisation and description of the performance and control systems used in a range of automatic exposure and brightness control (AEC and ABC) systems in medical fluoroscopic and digital imaging. The inputs to the control systems are being identified and assessed. The resultant images are being evaluated for quality in terms of a number of quantitative and qualitative endpoints.

An assessment of the extent to which these systems contribute to the optimisation of the dose/image quality relationship is being made.

Task 2 :

Important variables in assessing the performance and specifying system optimisation are being sought and identified throughout the imaging chain in medical fluoroscopy and digital imaging systems. The system components examined include the X-Ray Generator/Tube, the Image Intensifier, the TV System, 100mm and Cine Cameras, Multiformat Cameras, and Digital Systems.

Quantitative or objective measures are being used where possible. However, in the first instance a carryover of existing qualitative approaches is also required for a number of reasons. Later extensions of this work will ensure the identification, justification and establishment of tolerances, limiting values and protocols for the variables selected. The present study concentrates on the identification and description of the variables for a selected range of equipment with a view to defining how they should be used for optimisation purposes in the acceptance/commissioning of equipment and in its eventual write off.

Task 3 :

Dosimetry studies are being performed in association with the other partners and in a range of clinical investigations which is complimentary to those being undertaken by the partners and elsewhere in the Radiation Protection Programme. In particular special emphasis is being placed on cardiac studies. The relationship between doses using digital and traditional techniques is, where possible, being assessed and characterised. In addition studies of a number of other new special/interventional procedures e.g. ERCP (Endoscopic Retrograde Collangio Pancreatography), other interventional techniques not being evaluated elsewhere in the programme is being undertaken. All of the above require participation in the dosimetry standardisation process referred to in the Project K. Boddy/K. Faulkner.

Task 4 :

Dosimetric investigations for staff is being performed in the areas in which patient studies are being undertaken. In addition participation in the staff dosimetry being carried out by the other partners will also be undertaken where necessary, to provide additional numbers in inter-institutional comparisons.

Project K. Boddy/K. Faulkner:

Studies into Quality Assurance, patient dosimetry and optimisation in fluoroscopy and digital imaging has been started. The main emphasis is on the development of quantitative techniques for image quality assessment and patient dosimetry. In addition, preliminary investigations are underway into the optimisation of common fluoroscopic procedures (such as barium meals and enemas) as well as recently introduced diagnostic and therapeutic procedures based on fluoroscopy and digital imaging systems. The group of K. Boddy/K. Faulkner is contributing to all the tasks outlined above. Details of the proposed studies are described below:

Task 1 :

The use of automatic exposure control (AEC) and automatic brightness control (ABC) systems used on fluoroscopy and digital imaging units is being investigated. This includes evaluation of the AEC/ABC requirements for specific examinations, together with an assessment of the patient dosimetry implications. A theoretical model is being developed to predict the energy absorption in the image intensifier input surface, relative to the exposure monitored by an ionisation chamber, for a range of x-ray beam qualities and phosphor materials/thicknesses. The accuracy of the theoretic model is initiated to determine the most appropriate methods of assessment of AEC/ABC systems.

Task 2 :

The identification of appropriate image quality parameters for fluoroscopy and digital imaging units is underway. Particular emphasis is being placed on the development of quantitative techniques to assess image quality. This includes the development of protocols for constancy tests of fluoroscopy and digital imaging units as well as protocols for acceptance/write off of fluoroscopic equipment. Once these preliminary studies have been completed, an investigation into methods of automatically monitoring image quality parameters on digital imaging units is planned.

Task 3 :

Dosimetric and optimisation studies on fluoroscopy and digital imaging units are underway. A wide range of clinical examinations are under review for assessment. Particular emphasis is being placed on peripheral vascular and paediatric studies. It is essential in a comparative dosimetric study of this nature that suitably calibrated dosemeters and standardised measurement protocols are used. Hence all dosimetry instruments are being referred to the approved laboratory in the Regional Medical Physics Department. Patient dosimetry protocols are related to specific clinical examinations and treatments.

Task 4 :

Dose levels associated with the use of digital imaging units are being monitored. A detailed investigation into staff dosimetry in digital imaging and specialised interventional procedures is underway. A series of experiments is being planned to assess the protection afforded to staff by various protective devices.

Project H. P. Busch:

The areas in which work in the Institute of Radiology in Mannheim is being undertaken include :

Quality Assurance

At present there is no standard way of evaluating parameters for quality control of digital radiography systems. In this study constancy tests for digital image intensifier radiography and storage phosphor radiography are being developed. Constancy tests which include the whole imaging chain and the film processing system are undertaken weekly.

Dosimetry and optimization studies of conventional and corresponding digital techniques for G.I., Chest, Peripheral Vascular and Paediatric studies

Optimization studies are being performed for digital image intensifier radiography and storage phosphor radiography. For digital imaging the dose is a preselectable parameter. The dose value is adapted to the imaging quality necessary to answer the diagnostic question. For many indications (paediatric studies, control of tubes and catheters etc.) it is possible to decrease the dose by a significant fraction of that involved with a conventional film/screen combination. The determination of the limits of dose reduction is being reviewed.
Image quality is being compared to conventional film/screen technique using performance parameters (spatial resolution, contrast detectability etc.).

Using dosimetry (dose area product, thermoluminescent dosimetry) digital radiography is being compared to conventional techniques for chest examinations, barium studies and peripheral vascular studies (DSA).

Patient and staff dosimetry in selected clinical studies

Patient and staff dosimetry are being evaluated for barium studies and peripheral vascular studies using thermoluminescent dosimetry.

Project Th. Schmidt BI6-343:

The aim of this work is to assess the relationship between the radiation exposure of Interventional Radiology and the risk of alternative methods and to investigate the storage phosphor mammography considering to reduce the exposure.

A central documentation of Interventional Radiology was started. More than 100 hospitals and medical surgical interventions are included. All kinds of interventional techniques were taken into account with this questionnaire. Additionally to the questions of radiation exposure parameters, like time of fluoroscopy and number and kind of images, exemplary dose measurements have to be done. The standard data of the angiographic unit will be gathered, too. The mean values of the measured and calculated organ and effective dose equivalents and total absorbed energy enable to compare the risk of cancer induced by radiation to the risk of operation and narcosis. A great collective is necessary to get representative results, considering the strong variation of dose values.

A further clinical study of Angiography and Interventional Radiology is started to determine the exposure of the staff. At both conventional and digital over and undertable x-ray tube units the dose at the fingers will be measured by official ring-dosemeters. Additional TLDs will be used to determine the dose to head and neck.

The third part is to investigate the suitability of storage phosphor radiography for mammography. Objective physical parameters like spatial resolution, signal-to-noise ratio or Wiener Spectrum will be correlated with the dose at the imaging system. Additionally a ROC-Analysis (Receiver Operating Characteristic Curve) compares digital and conventional mammograms.

C22 Reduction of patient exposure in medical diagnostic radiology

Contract Bi7-019/6-132/6-211/6-214/6-136 Quality assurance and reduction of patient exposure.

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Total Contribution by the Commission: 449 kECU
24 months from 1/04/90 to 31/03/92 **Bi7-019**
24 months from 1/01/90 to 31/12/91 **Bi6-132/6-211/6-214/6-136**

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Contract Bi6-136

Description of research work:

BI7-019

QUALITY ASSURANCE AND REDUCTION OF PATIENT EXPOSURE

C. Maccia, CAATS-INSERM (F)

This co-ordinated project is a natural follow-on from the previous research projects in the Radiation Protection Programme particularly on "Establishment of quality criteria for diagnostic radiographic images". The CEC workshops held in Brussels and in Oxford in 1988 have highlighted a need for further Radiation Protection guidelines and for practical Quality Control tools to be developed. Almost all laboratories involved in this project have considerable experience in this field and have already contributed to the practical implementation of Quality Assurance Programmes in diagnostic radiology.

The project deals with two important areas of Radiation Protection in medicine, namely 1) Improvement of Quality Assurance (QA) in diagnostic radiology, 2) Expert systems (ES).

1) **Improvement of QA in diagnostic radiology** : this directly follows the Community wide trial carried out in 1988, checking the impact of the Quality Criteria in the routine practice, developing new test procedures and more updated calculation codes which are better able to fulfil the proposed guidelines and extending the quality criteria to further examinations, pediatric and digital radiology, etc.

2) **Expert systems** (ES) as a guide for reducing patient dose and optimising image quality; there are three parts in this area :

   a) Identification and definition of the "applicable clinical domains": (mammography, pediatric radiology, digital radiology). The ES will be conceived in a way that subsequent extension without any major revision will be possible.

   b) Development of a package software for the assessment of the patient dose according to current radiological techniques. Implementation of a system for automatic data acquisition.

   c) Selection of an adequate knowledge-acquisition tool, implementation and revision of a prototype.

The work programme is perceived as extending over two periods. The first period lasting two years is focused on the achievement of objectives 1 and 2a with some progress on objectives 2b and 2c. The second period lasting a further three years would complete the project.

The work of the project is based on the collaboration of all coordinated partners together with those of some prolonged.

- CAATS-INSERM (prolonged contract n° BI6-132-F) together with USL n°7 (prolonged contract n° BI6-136-I) and the IRS Ltd are being involved in the expert system approach for Q. A. in mammography, computed tomography and digital radiology;
- The University of Madrid (prolonged contract n° BI6-214-E) is contributing to the analysis of a series of relevant parameters influencing both patient dose and image quality;

- The University of Linköping together with the Royal Marsden Hospital in London are mainly concerned with Monte Carlo calculations with a view to evaluating the optimal choice of the grid under various scatter conditions. Theoretical considerations in this area might be used as a part of the Expert System;
- The University of Ferrara is designing a "real time" instrument which will be useful for quality control in mammography. This could be checked either within the work programme of the CAATS - INSERM project or the common Greek one of the University of Patras and Anti-cancer Hospital;

Each partner will be involved in the development of a framework which will serve as a guideline for the optimisation of medical radiation protection either in adult radiology or in pediatric radiology: already established links with the group of the University of Munich (prolonged contract n° BI6-211-D) will be particularly reinforced.

BI6-132

QUALITY ASSURANCE AND REDUCTION OF PATIENT EXPOSURE

F. Fagnani, C. Maccia, CAATS - INSERM, Cachan (F)

Part 1 : Image Quality Optimisation in Mammography.

Diagnostic performances of mammography is dependent on the "optimal" compromise between dose and image quality and it requires an "effective" Quality Assurance (QA) protocol to be set on. This part of the contract will at evaluate the importance of given physical parameters (limiting values of detectability, contrast, film-processing etc.) that interact with both image quality and radiologist's interpretation of the film. The relevance of all these parameters are being assessed in close cooperation with the IRS Ltd which is already engaged in mammographic quality control. Within the specific context of a breast screening programme (Bas-Rhin region), QA protocol is being set up using a specific mammographic "kit" designed by the Ferrara group. All the above mentioned parameters are being checked in order to produce key-components of an expert system, the aim of which will be the optimisation of the mammographic procedure and the possibilities to carry out risk estimates in mammography. Collaboration with other contractors dealing with the various aspects of mammography will be established.

Part 2 : Risk analysis for medical exposure.

The computation of the somatic and genetic detriment associated with low doses of ionizing radiation integrates a number of parameters and assumptions which serve as inputs for the extrapolation model. Usually, the indices of harm are imposed by the published results of cohort studies, and are restricted to mortality or morbidity by cause. The extrapolation models produce then life-long risk estimates in terms of extra-mortality or extra incidence of cancer of different tissues. This kind of indicators presents, nevertheless, a number of limitations, namely : the specific tissues exposed in diagnostic procedures are usually aggregated in the so called "other organ" coefficients, the age and sex of exposed population are different from those of the general population etc. A simple way to deal with some among those dimensions is to take loss of life expectancy as an index of harm. A more sophisticated way might be to adjust the survival by the corresponding quality of life between diagnosis and death. In this perspective, a number of recent approaches are being developed at international level. One recent study is related to the QALYs methodology, which is precisely intended to qualify the perceived benefit associated with different health status integrating, for instance, functional as well as distress dimensions. This concept is developed by another coordinated group and in this project the approach will be validated for specific uses in radiation protection in medical diagnostic radiology.

Part 3 : Expert system for quality assurance in diagnostic radiology.

Implementing QA indicates on the status of the radiological equipment and the consistency of the operating procedures used in performing x-ray examinations. The considerable experience gathered in the past CEC Radiation Protection Programmes allows to pursue toward an Expert System (ES) approach by which the collected data can be made available at a larger scale. CAATS-INSERM is being involved in each step of the ES design, identification of the problem, definition of key-concepts,

selecting data, dose assessment modelling, implementing prototype, testing etc. The specific contribution of CAATS-INSERM, in collaboration with a medical imaging film maker, deals with the film processing. Initially, different types of film-screen combinations processed on different developing machines are compared to provide a data base which will be used as basic parameters for the ES. In a second phase, an "intelligent" processing system will be developed and evaluated to be used as a training aid for demonstrating and facilitating discrimination of various factors influencing the image quality.

Part 4 : Quality criteria in digital radiology : the Computed Tomography technique.

The CEC Working Document on "Quality Criteria for diagnostic radiographic images " concentrates on image quality, radiographic techniques and patient dose for some conventional radiological examinations. There is a need for establishing the same kind of guidelines for digital radiology. CT examinations, for instance, are being routinely practised and may represent 10% of the total effective collective dose equivalent due to diagnostic radiology. As a first attempt, statistical data obtained within the context of the previous CEC Radiation Protection Programme are used to find the "optimum" examination technique to be performed. On the other hand, physical parameters (noise, spatial resolution etc.) which may influence both image quality and patient received dose are taken into consideration to define the minimum acceptable level of image quality compatible with the visualisation of the anatomical and structural details. This will form a baseline data for both clinical evaluation and the extension of the CEC Quality Criteria Document.

QUALITY ASSURANCE AND REDUCTION OF PATIENT EXPOSURE

B. M. Moores , IRS Ltd, Liverpool (UK)

The project is investigating more fully the relationship in mammography between image quality, radiographic factors and patient dose.

Part A : Image Quality Criteria - Further Development.

The image quality criteria employed in the CEC Document concentrates solely upon the clinical image. At present nearly all quality control programmes for mammography which are in existence employ test phantoms as part of the evaluation programme. This approach provides an objective visual measure of performance which can act as a bridge between the scientific and technical performance criteria, inherent in the guidelines on patient dose and radiographic factors, and the technical performance criteria inherent in the image quality criteria.

In this part of the project a framework is being developed for linking objective image quality criteria inherent in phantom measurements to the radiographic factors employed in an examination. Test phantoms demonstrating a variety of radiographic conditions including kV, filtration, mAs, focal spot, focus to object distance etc. The link and importance of these radiographic factors to objective image quality criteria are evaluated. This involves the development of an expert system approach analogous to that already applied to the analysis of the data generated by the trials of the CEC Document. In this way the relationship between objective image quality and individual radiographic factors will be quantified. Some attempt will be made to relate the objective measures of image quality to the clinical image criteria already contained in the CEC Document for breast images. The first year of the project deals with the collection of the image quality data for a wide range of radiographic conditions. The second year will be spent developing the expert system methodology and analyzing the objective image quality data which will be used to further refine the expert system in order to produce a predictive capability to assess image quality from a given set of radiographic factors.

Part B : Risk evaluation in mammography.

In this part of the project (first year) a comprehensive review is being undertaken of all relevant published work in this area and the preparation of a discussion document for consideration by the CEC Radiation Protection Group.

The framework for risk assessment is then applied to study the effects of different radiographic factors on overall risk in mammography which together with work undertaken in part A will form the basis of a risk-benefit analysis, when benefit is measured in terms of image quality (second year).

This data will form the basis of an expert system approach to evaluating risks arising from a given combination of radiographic factors when employed with breasts of differing composition.

DOSIMETRICAL AND TECHNICAL ASPECTS OF MAMMOGRAPHY: OPTIMIZATION AND QUALITY CONTROL

O. Rimondi, Università degli Studi di Ferrara, Ferrara (I)

A dedicated kit for QA in mammography designed in the laboratory is being used within the context of Italian and French Breast screening programmes.
An electronic instrument will be designed for measuring, in real time and in a single shot, waveform, kVp, ripple, HVL, exposure time and exposure of a mammographic unit.
Such a device consists of four solid state detector probes, an acquisition electronics and a portable computer.

Additionally such a device allows :

- a common basis for dosimetry in mammography to be achieved,
- relevant information on absorbed dose during actual mammography to be obtained,
- quality control procedures to be improved.

DOSE AND PICTURE QUALITY EVALUATION IN MAMMOGRAPHY - A NATIONWIDE PROJECT

A. Flioni-Vyza, Anti-Cancer Institute, Athens (GR), B. Proimos, Univ. of Patras, Patras (GR)
Part 1:

The project concerns the optimisation of mammographic x-ray units installed in all Greek hospitals. The necessary measurements will be carried out by previous appointment with each radiological department equipped with a mammographic equipment.

For comparable and useful results, the two teams will jointly establish a protocol which will specify the following :

a) Parameters to be measured and their exact definition

b) Methods and techniques to be used for the measurement of each parameter

c) Instruments to be used and their calibration in order to perform meaningful, reliable and comparable measurements.

The project will include dose and image quality evaluation.

In particular the following parameters will be measured :

- KVp
- HVL and total filtration
- focal spot size
- patient absorbed dose
- reproducibility and linearity of exposures
- automatic exposure control system
- image resolution
- bucky and cassettes
- dark room and film processor.

Part 2 :

Professor Proimos' team will perform the required quality control measurements and check for the area of Peloponnesus and Western Greece.

The analysis and evaluation of results as well as the preparation of reports will be made jointly.

THE CHOICE OF ANTI-SCATTER GRIDS FOR RADIOLOGY : THE OPTIMIZATION OF IMAGE QUALITY AND THE REDUCTION OF ABSORBED DOSE.

G.A. Carlsson, Univ. of Linköping, (S), D.R. Dance, The Royal Marsden Hosp., London (UK)

Part 1 :

The project will evaluate the optimal choice of grid under various scatter conditions, i.e. for different types of examination (e.g. children, lungs, abdomen, skeleton). This is important because it is known that the angular distribution of scattered photons is dependent of patient thickness and tissue composition. It is expected that the optimal grid parameters and X-ray spectrum will vary accordingly. The optimal grid will yield the required image quality at the lowest absorbed dose in the patient.

The angular and energy distribution of the scattered radiation behind the patient will be simulated by means of Monte Carlo calculations and simplified phantoms, the size, shape and tissue composition of which will be varied, possibly including in homogeneities. Both conventional and cross grids will be evaluated for a range of test contrasting details (iodine contrast agent, bone, fat, air). For film-screen radiography, image contrast will be used as a measure of image quality. Grid performance will be evaluated in terms of the associated contrast improvement and dose increase. For digital radiography, there is no dose constraint, for a properly exposed image and grid performance will be evaluated in terms of the signal-to-noise ratio. Radiation risk will be evaluated by means of absorbed dose in simple phantoms and by the effective dose equivalent in man-like phantoms.

Experiments are planned to verify the calculational results using similar (idealized) phantoms. The results should also be tested using more realistic, man-like (inhomogeneous) phantoms.

The project is carried out jointly with the Royal Marsden Hospital, London UK.

Part 2 :

The contribution of the Royal Marsden Hospital will be :

1) to share jointly in the design and management of the experimental and theoretical aspects of the project and the supervision of the PhD student
2) to advise and participate in the design and development of the Monte Carlo code, particularly with reference to the incorporation of the grid and the choice of scattering cross sections
3) to participate in the critical analysis of the results of both the calculations and experiments.

BI6-211

OPTIMIZATION OF PAEDIATRIC RADIOLOGY : THE PRINCIPLES AND THE PRACTICABILITY OF QUALITY CONTROL AND QUALITY ASSURANCE IN PAEDIATRIC RADIOLOGY.

H. Fendel, Kinderspital der Universität, München (D)

The project concerns screening and assessing problems related to radiation protection in paediatric radiology. Optimisation, quality control, and quality assurance of radiological imaging studies of newborns, infants, and children are different from those in adults. They are, however, mandatory in terms of radiation protection of the public because they concern the most sensitive part of the general population. It will be surveyed how individual optimisation measures can be effective in daily routine and to what extent they are practicable with the final goal of establishing standards for quality control and quality assurance in paediatric radiology.

Phantom measurements have been made for some typical examinations of children in selected clinics and departments which regularly x-ray children as well as in private practices of radiologists, orthopaedists and paediatricians.

Similar surveys and dosimetry measurements on patients, i.e. for a defined age group up to 2 years, will be continued in a number of paediatric radiology departments headed by a full-time paediatric radiologist in nearly all Member-States and the quality of the examination and image criteria in comparison to the established quality criteria will be evaluated.

Comparisons will be made between the measured patient entrance surface dose and both the respective technique and the evaluated quality of the x-ray film.
Simultaneously, the usefulness and applicability of these quality criteria are being evaluated.

Phantom measurements in 149 clinics/private practices and dosimetry measurements in 90 departments have been completed. A document "Quality Criteria for Medical Diagnostic Radiographs in Paediatrics" is being compiled by this team which parallels the CEC Working Document for adults "Quality Criteria for Diagnostic Radiographic Images" (June 1990). The first analysis of the phantom measurements indicate that examination centres which are not headed by an full-time paediatric radiologist generally have higher patient exposures and the technique used is less optimised for the paediatric specialties. Dose variation for these departments and practices is much higher than the known and expected variations for respective adult examinations.

A correlation between higher dose and image quality does not seem to exist. Consequently, quality criteria will be more specifically developed and dose ranges established. This project is made with the help of experienced paediatric radiologists acting as representatives of the European Society of Paediatric Radiology and in cooperation with medical physicists from the NRPB in Chilton (UK), the USL n°7 Udine (Italy) and the GSF in Neuherberg (FRG), using their experience with comparable research studies for adults as a model.

BI6-214

QUALITY ASSURANCE AND REDUCTION OF PATIENT EXPOSURE

E. Vaño, Universidad Complutense de Madrid, Madrid (E)

The project will contribute :

- to establish an operational Quality Control protocol in diagnostic radiology which enables causes leading to anomalies of both image quality and dose to be identified.
- to settle simple and useful procedures which allow corrective actions to be undertaken. Such a protocol concerns X-ray generator, X-ray tube, films, screens and cassettes, storing and processing film conditions, viewing boxes, TV monitors, image intensifiers and also operating procedures.
- to create a comprehensive data base which contribute to the design of a future dedicated expert system for Quality Assurance in Diagnostic Radiology.
- to contribute to the practical implementation of such an expert system.

BI6-136

QUALITY ASSURANCE AND REDUCTION OF PATIENT EXPOSURE

R. Padovani, Ospedale S. M. della Misericordia, USL n°7 Udine (I)

A. Expert system for Quality Assurance in medical radiological imaging.

Quality Assurance (QA) programmes assess the performance of radiological equipment by verifying that all parameters believed to influence either the Image Quality (IQ) or Patient Doses (PD) lie inside the tolerance levels. The use of methods using Artificial Intelligence may help to introduce expertise and efficient QA and therefore achieving widespread patient dose reduction. The knowledge on the relationships between equipment performance, IQ and PD includes empirical associations and heuristic methods and seems well suited to an Expert System (ES) devoted to the complex task of finding out causes of, and possibly remedies to, insufficient performance of radiological imaging system. The ES may infer situation descriptions and system malfunctions from observables which can be directly obtained by monitoring instruments and/or by automatic or interactive image analysis of radiographs of suitable test-objects (ex: sensitometric film strips for assessing film processor performance) and/or simply by interacting with the user at the keyboard.

The project of building ES includes the following steps:

1) Identifying problem to avoid tasks too large or unwieldy for the resources available.
2) Defining key concepts and relations.

3) Specifying data (inventory of the type of the available data), and choosing instruments and methods for measuring observables.
4) Developing a simplified dose assessment model for interactive determination of patient dose and risk.
5) Choosing appropriate knowledge-acquisition tools.
6) Implementing a prototype.
7) Testing
8) Prototype revision.

B. Image quality and patient dose in CT: the optimisation process.

This part of the project will at define the minimum acceptable levels of image quality in CT. which may be specified in terms of anatomical and structural details, which should be visible in the image, and/or physical parameters, such as noise, low-contrast detectability, spatial resolution.

C. Patient Dosimetry.

The dosimetry laboratory is continuing to develop and improve the dosimetry system to measure patient doses in diagnostic radiology. Support is being provided to international trials of the CEC study group on the development of quality criteria for diagnostic radiographic images (adult and paediatric patients).

C22 Reduction of patient exposure in medical diagnostic radiology

Contract Bi7-054 Diagnosis related doses: a comparative investigation in some European hospitals

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Total Contribution by the Commission: 80 kECU
18 months from 1/09/90 to 29/02/92

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Description of research work:

The main sources of low dose radiation to the population of Europe are the medical diagnostic examinations in radiology and nuclear medicine. The amount of radiation given before a certain diagnosis is made, depends on factors of medical, technical and/or organizing character:

- In the medical sector, the justification of an examination and the protocol leading to a diagnosis identified;
- In the technical sector a series of variables is identified and the effects of quality assurance are being evaluated with a view to establishing guidelines for the improvement of image quality and the reduction of patient dose;
- In the organizing sector, several extrinsic and logistic factors - e.g., factors that are linked to the differences in the organization of the health services - can compete with an optimal cost/benefit relation.

The dose assessment and the establishment of a correct diagnosis in different European hospitals can be related to these three factors. The concept of diagnostic groups (DGs) can contribute to a better understanding of this relationship : a DG is the set of steps and examinations that leads to one and the same diagnosis. A method for evaluating the DG- related doses will be developed and tested. The tool developed in this pilot study may be used for evaluating the DG-related doses in European hospitals on a large scale.

The project will be carried out jointly by a Belgian and a Dutch research team. One part of the study will be devoted to the inventory of existing useful methods of dose assessment in diagnostic radiology; the actual entrance dose under standard conditions of different hospitals will be compared by thermoluminescent dosimetry and ionization chamber measurements. This dosimetry will be based on the work done by the co-operative group "Dose Assessment and Evaluation of Risk" coordinated by B.F. Wall (NRPB, UK). A few DGs will be selected for the pilot study : the medical teams will evaluate the existing work done in the field, define relevant DGs and test them in the participating hospitals. Once the procedure is established, a number of relevant patient files will be analyzed; an inventory will be made of the different radiological examinations performed before the diagnosis; the corresponding dose per examination will be calculated.

The physical/technical details and the medical parameters will together allow the received dose per DG for each participating hospital to be assessed. Finally, the applicability and validity of the total procedure will be tested by analyzing the different data sets per DG. The first question to be answered will be : is it possible to collect the relevant medical and technical data with this procedure for a sufficient number of patients? Secondly, which other elements are detectable within diagnostic procedures that are related to the doses per diagnosis, such as organization of health services and other? This study can contribute to elaborating recommendations or guidelines for the optimization of diagnostic radiology procedure to reduce the exposure of the European population to ionizing radiation and lead to a better use of national health resources.

Two contractors are involved in this project, and will share the tasks, as well those in physics as those of the radiological team.

The group of the Vrije Universiteit Brussels will be responsible for the coordination and the preparation of the progress reports, and the coordination of the work on DGs. A medical doctor of Akademische Ziekenhuis - VUB will contribute to the definition of relevant DGs. The work in Brussels will be performed with external consultancy of Dr. Lemort (Radiology) and Dr. Piron (Medical Physics) of the "Bordet Institute" and Dr. Perlmutter of "Reine Fabiola" Hospital's Radiology Department in Brussels.

The group of the Akademische Ziekenhuis Nijmegen will coordinate the assessment of dose per examination by thermoluminescent dosemeters. This team will use of its equipment and calculation programmes for the technical analysis. Seven physicists of the Department of Radiology, Nijmegen, will collaborate. The NRPB protocol will be analysed on applicability in this project, in cooperation with the NRPB.

C22 Reduction of patient exposure in medical diagnostic radiology

Contract Bi7-057 Patient dose from radio-pharmaceuticals

Coordinator Univ. Lund
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Total Contribution by the Commission: 90 kECU
18 months from 1/09/90 to 29/02/92

Participating Scientists

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Description of research work:

Patient dose from radiopharmaceuticals

The accuracy of the current data on absorbed dose from radiopharmaceuticals to patients, specifically to children of various ages, will be improved. This will be done by:

1. Improving the biokinetic data for selected radiopharmaceuticals by repeated uptake and retention measurements on patients. Special attention will be given to
   a) new radiopharmaceuticals recently taken into clinical use and
   b) biokinetics for children.
2. Improving the physical basis for the dose calculations by:
   using detailed voxel-phantoms based on CT/MR data for Monte Carlo calculations of new S-values, especially for children.

The results will be used to quantify organ doses as well as effective dose equivalents. The results will help to compare different radionuclides for labelling in view of balancing diagnostic benefit and radiation dose and to determine the appropriate activity to be administered in order to avoid unnecessary radiation exposure of the patient.

Project S. MATTSSON

In a group of 10-20 patients for each radiopharmaceutical, short and long term biokinetics will be studied in patients undergoing investigations with new radiopharmaceuticals (monoclonal antibodies labelled with Tc-99m, In-111 or Se-75, Tc-99m-isonitril, -HMPAO and - MAG3). For these studies gamma cameras as well as whole-body counters will be used together with measurements on samples of blood, urine etc.

Biokinetic data will be collected for newborn and children up to 18 years old who are subject to nuclear medicine investigations using Tc-99m-HMPAO, Tc-99m-MDP and Tc-99m-DTPA. Experimental measurements will be carried out of the excretion through breast milk of radiopharmaceuticals for which there is still lack of data, e.g. Tc-99m-pertechnetate, Tc-99m MAG_3 and Tc-99m-HMPAO.

Biokinetic models will be formulated along the lines of ICRP 53.

Project T. SMITH

Internal dosimetry studies will be carried out on patients undergoing clinical investigation with radiopharmaceuticals and on volunteers administered radiopharmaceuticals specifically for dosimetry. In addition, every effort will be made to obtain biodistribution and biokinetic data for making dose assessments on newborn and children of different age groups undergoing diagnostic investigations with radiopharmaceuticals, whenever such opportunities arise. These studies will be supported, when appropriate, by experiments with phantoms. The participant has an honourary contract with Northwick Park Hospital which shares a site with the Clinical Research Centre. Work involving human subjects will be carried out in collaboration with the medical staff of Northwick Park Hospital. Such studies will involve the derivation of biokinetic data using the following equipment: hybrid scanner (profile distribution and high-level whole-body counting); scanning LFOV gamma-camera (organ uptake and retention by conjugate counting); high sensitivity whole-body counter (long-term retention); bulk-sample counter (excreted radioactivity) and automatic gamma counters (blood sample analysis). These data will be used to formulate biokinetic models along the lines of ICRP 53, and estimates of organ radiation doses and effective dose equivalents will be obtained using a computer programme which incorporates physical data ('S' values) for radionuclides, obtained from the Oak Ridge National Laboratory.

Project K. HENDRICHS

Voxel-phantoms developed by G. Drexler et al. and based on CT-scans of real persons will be used for internal dosimetry of internally deposited radioactive emitters. The factors Specific Absorbed Fractions and Specific Effective Energies, which describe the radiation transport within the human body will be calculated for at least one child (of 7 years or 4 weeks) on the basis of voxel-phantoms derived from CT-scans. The results of this method will be compared to those using mathematical anthropomorphic phantoms describing the anatomy of the body and will demonstrate whether the improvements, which may be expected especially for children, are sufficiently substantial to continue with the development of other voxel-phantoms (other ages) for internal dosimetry. These results will be of special importance for nuclear medicine procedures, because patients usually show considerable differences in comparison to the ICRP reference phantoms.

C22 Reduction of patient exposure in medical diagnostic radiology

Contract Bi Prop.328 Quality criteria and dose reduction in computed tomography

Coordinator Univ. Aarhus - Hospital
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Total Contribution by the Commission: 20 kECU
12 months under negotiation

Participating Scientists

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Description of research work:

Quality Criteria for computed tomography (CT) will be defined based on the assessment of the influence of the practical implementation of quality assurance programmes on patient doses during the various CT examinations. There is indication that for some CT examinations the doses are considerable higher than can be justified by the demand for an acceptable image quality and which may be caused by the extended use of non optimized standard procedures. The relevance of quality assurance for optimization in paediatric CT examinations will be demonstrated.

CT based on TLD and ionisation chamber dosimetry will be developed. Dosimetric intercalibration for actual CT geometries and radiation beams will be performed between the contractors.

Both contractors have performed nationwide surveys of the clinical use of CT examinations in their respective countries Portugal and Denmark and performed dose measurements free-in-air in the isocenter of the CT scanners for scanning parameters used in routine examinations. These data bases will be used for calculation of organ doses, taking into account the updated conversion factors available from other contractors and for calculation of collective effective dose equivalent from CT. Results from such calculations will be compared with existing results in order to make an assessment of the influence on doses from pre-patient filtration and other parameters.

The work of the contract will be coordinated with that of the contractors B. Wall (NRPB, UK), C. Maccia (CAATS-INSERM, F), W. Panzer (GSF, FRG), and R. Padovani (USL n°7,I)

Part 1

Work will be undertaken towards an agreement upon objective measurements of image quality parameters (dose, noise, spatial and contrast resolutions etc.) and the assessment of the limits for such measurements in order to establish acceptable quality criteria for CT images.

A further evaluation of the methods for dosimetric measurements of CT scanners will be performed. Dose profiles free-in-air obtained with TLD dosimeters producing computed tomography dose index (CTDI) values have to be related to other methods such as ionisation chamber measurements in/on phantoms of different sizes. For a better assessment of the beam quality, measurements with/without filtration will be carried out for a selected group of CT systems. Dosimetric intercalibration in actual CT geometries will be initiated between contractors.

New calculations of organ doses will be performed based on the latest organ doses conversion factors produced by NRPB. Data in the existing database from the survey on CT examinations and the measured dose values collected under the previous contract (BI6-0317-DK) will be utilised. The results will permit a comparison with the calculations already performed using the GSF tables which do not take the shape of the pre-patient filter into account. Such a comparison is important for evaluating the influence, filter shapes may have on organ doses. Details about the beam filtration are often difficult to get from the manufacturer and the possibility to establish simple correction methods has therefore to be investigated.

The dose distribution in the patient, undergoing a CT examination, caused by the steep dose gradients, may result in large variations of organ doses depending on the details of the diagnostic procedures. An assessment of dose ranges will be performed for different procedures and compared with Rando Alderson phantom measurements and if possible with results from other contractors.

Besides the technical contribution outlined above, the work necessary to coordinate the project as a whole will be undertaken.

Part 2

The work will be developed in order to optimize some CT paediatric examinations and to investigate the role of quality assurance on patient doses and images quality.

Research will be carried out in radiology and neuroradiology departments of Lisbon hospitals with the aim of defining the minimum acceptable level of image. Relationships between image visibility of anatomical structures and details, technical factors and doses will be studied as well as their contribution for the improvement of those examinations.

Using the data base obtained in a previous CT survey in Portugal the evaluation of adult patient organ doses for the more frequent examinations will be performed. Organ doses will be calculated through conversation factors produced by NRPB in close cooperation with the Aarhus University Hospital.

The development of methodology for radiation dose assessment, the harmonization of methods and dosimetric intercalibration for TLD and ionization chambers will be carried out with the other contractors.

C24 Probabilistic risk assessment and real-time models for assessing the consequences of accidental releases and for evaluating the effectiveness and feasibility of countermeasures

Contract Bi6-128/6-127/6-125/6-227 Methodology for evaluating the radiological consequences of radioactive materials released in accidents including uncertainty analysis and economic impact.

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Total Contribution by the Commission: 616 kECU
24 months from 1/01/90 to 31/12/91

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Description of research work:

Introduction

The project MARIA (Methods for Assessing the Radiological Impact of Accidents) was initiated in 1983 as part of the CEC Radiation Protection Research Programme. The aim of the project was, firstly, to review and then to develop further methods and models for accident consequence assessment (ACA) within the EC. A European ACA code, COSYMA (COde SYstem from MAria), is now available as a result of the many investigations performed within the MARIA project.

There remain a number of areas within the field of ACA modelling where further development and refinements are required, in addition, the COSYMA code and its databases also require maintenance and some further development. These are the aims of the current extension of the MARIA project under the 1990-1991 Radiation Protection Programme.

Topics to be studied under the 1990-1991 MARIA project

This summary describes the work being undertaken as a part of the MARIA project by the Nuclear Research Centre Karlsruhe (KfK), FRG, and the National Radiological Protection Board (NRPB), UK.

(i) COSYMA development and maintenance

The COSYMA system is an important tool for research and application, and as such requires continuous up-dating, testing and improvement. The COSYMA code will be maintained by KfK and NRPB throughout the period covered by the contract, and there will be further development of its databases by both organisations.

The increasing availability of small computers, and the need of inexperienced ACA code users for the COSYMA code as a tool, necessitate the development of a reduced and simpler version of the code. This version will be more limited in its flexibility, but will be consistent in its basic assumptions and data with the full COSYMA code, and will produce compatible results. This work will be undertaken largely at NRPB, in co-operation with KfK.

Under the MARIA contract, NRPB and KfK will participate jointly, with the COSYMA code, in the international ACA code intercomparison exercise being organised by the CEC and NEA. It is anticipated that the participation of the code in this exercise will indicate any weak aspects in coding and in data which will be improved in future releases of COSYMA.

(ii) Uncertainty analysis techniques

Continuing research will be undertaken into the application of available uncertainty analysis techniques to ACA code systems. An important task is research into techniques for the reliable and defensible quantification of the variation in model parameters, including the use of expert judgement. Both NRPB and KfK will be involved in these studies, together with other CEC contractors.

(iii) Model and code development

A number of areas have been identified where further modelling development is needed; these will be considered during the period of this contract. These include:

- at NRPB, there will be investigations with COSYMA to examine the effects of using models of different complexity in the area of atmospheric dispersion
- at KfK, wet deposition processes will be included in the foodchain module of COSYMA
- at NRPB, there will be further development of the urban contamination model EXPURT. Consideration will be given to incorporating EXPURT results in a COSYMA database
- at KfK, the economics module will be extended to incorporate specific data on the economic productivity of the region near to the release point
- at KfK, there will be further development of the health effects models used in COSYMA. In particular, the method of calculating loss of life expectancy will be improved, and the dependence on dose and dose rate of both the dose/risk relationships for non-stochastic health effects and of the cancer risk factors will be included.

BI6-125

Description of research work:

A probabilistic uncertainty and sensitivity analysis provides:

a) quantitative statements about the combined influence of parameter, modelling and phenomenological uncertainties on the computational assessment

b) a ranking of the uncertainties with respect to their contribution to the combined influence.

The analysis results are, therefore, indispensable for the application of computational assessments in decisions under uncertainty.

It is only through a) that comparisons between

- assessments and safety goals

- assessments to alternative designs, strategies or sites
- assessments performed by different teams

become meaningful. The sensitivity information b) is essential for the decision on where to improve the state of knowledge through additional data collection, experiments and research in order to reduce assessment uncertainty efficiently.

Within the 1985 - 1989 Radiation Protection Programme a package for uncertainty and sensitivity analysis on mainframe computers was developed. It supports the following analysis steps:

Programme	Analysis step
DIVIS	Probabilistic modelling of parameter uncertainties and state of knowledge dependence
MEDUSA	Generation of Experimental Designs
EQUUS	Derivation of quantitative uncertainty statements
SAMOS	Derivation of sensitivity measures
TUSSIS	Derivation of time-dependent uncertainty statements and sensitivity measures.

Applications of the package have suggested several extensions which are subsequently summarized. They are the subject of the work being carried out under the present contract which the work consists of three parts:

1) A so-called Driver programme is being developed for the package.
Its tasks are to:

   - guide the user through the steps of a probabilistic uncertainty and sensitivity analysis
   - support selection of a suitable combination of options from those offered by the programmes in the package
   - perform the data transfer between the programmes as well as, where possible, between the programmes and the assessment model
   - support design extensions for parameters where the quantitative expressions of the state of knowledge (or where the expressions of state of knowledge dependence) cannot be readily handled by MEDUSA.

   The aim is a largely continuous flow of the analysis requiring as little user interference as possible.

2) After completion of the Driver programme the package is available for use in mainframe computers. It would greatly promote the performance of uncertainty and sensitivity analysis and encourage the use of the package within the Community if a Personal Computer version were available supplemented by sample analysis to illustrate its application. This PC version of the complete package, including the Driver programme, will be produced in the second part of the project.

3) The value of an uncertainty and sensitivity analysis depends largely on the quality of the subjective probability distributions needed for propagation of the state of knowledge through the model. A major source for the required quantitative expressions of the state of knowledge (as well as state of knowledge dependence) is expert judgement which needs to be elicited. In the third part of this project guidance will be provided for this important aspect of the analysis to support the user of the package.

   The guidance will specifically cover the subjects:

   - Compilation of uncertainties
   - Typification of uncertainties
   - Elicitation of expert judgements to obtain quantitative expressions of the state of knowledge
   - State of knowledge dependence
   - Processing of expert judgements.

BI6-227

Description of research work:

Two are the main objectives for the research in the period 1990-1991:

(1) Intercomparison of models for assessing the off-site economic consequences of nuclear accidents.
(2) Development of a new model for cost-effectiveness analysis of long-term countermeasures.

(1) An intercomparison of the model MECA (Model for Economic Consequence Assessment, developed in the previous period of the contract) is being carried out against the model COCO-1, developed by NRPB and KfK, and presently included in the European ACA code, COSYMA. The intercomparison will consist of three phases, essentially: (1) theoretical analysis and discussion of the different concepts and assumptions used by each model; (2) comparison of results for deterministic scenarios; and (3) comparison of results for probabilistic scenarios using MECA with the US MACCS code and COCO-1 with COSYMA.

The intercomparison will be a good way to verify the functioning of models and codes, as a part of the quality assurance process. It will give a better knowledge of both models, since modelling differences and their impact on the results will be clearly shown.

(2) The second objective is the development of a model of the impact of different countermeasures against chronic exposure, following a large accidental release of radionuclides. The model could be a useful decision-aiding tool, as it will facilitate the cost-effectiveness analyses of different alternative actions and criteria. It will enable comparisons of the effectiveness, in terms of dose reduction, against the resulting economic costs and social disturbance, based on measured land contamination and radiation levels and on a detailed site-specific description of population and land-use distributions, as well as on the available protective actions.

For dose calculations, the model will consider both external and internal exposure pathways. Direct exposure from gamma emitters deposited onto various locations and surfaces will be assessed using a dynamic linear compartmental model to calculate the retention and migration of radionuclides. Three different environmental areas (urban, rural and other) will be considered, with different contributors to the external dose and to the internal dose by inhalation of resuspended material. Different countermeasures (decontamination and interdiction mainly) will be evaluated for each area. Indirect exposure resulting from the ingestion of contaminated foodstuffs and water will be estimated using a dynamic model to simulate the transport of fallout radionuclides through food chains to man. The impact of countermeasures, like food disposal or temporary interdiction of agricultural areas for food production, will be also evaluated.

The model will use, for the assessment of the economic impact of countermeasures, the previously developed economic model MECA and its associated socio-economic data base, which includes detailed distributions of population, livestock and agriculture for all the municipalities of Spain.

Uncertain parameters affecting countermeasures and dose calculation will be treated probabilistically.

C24 Probabilistic risk assessment and real-time models for assessing the consequences of accidental releases and for evaluating the effectiveness and feasibility of countermeasures

Contract Bi7-010 Deposition of radionuclides and their subsequent relocation in the environment following an accidental release to the atmosphere.

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Total Contribution by the Commission: 190 kECU
24 months from 1/06/90 to 31/05/92

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Description of research work:

Objectives

To improve, where necessary, the models and parameterizations used in estimating the intensity and spatial distribution of deposited activity and the total health/economic impact of such deposits in assessments of the consequences of accidental releases of radioactivity, and to this end to attain a better understanding of:

- the influence of various weather conditions on deposition, particularly weather conditions which can lead to high deposition fluxes such as fog, snow or intense rain;
- resuspension of deposited ^{137}Cs activity;
- the weathering of deposits in urban and rural environments and its impact on long-term external exposure;
- the ultimate fate and dosimetric impact of radionuclides carried by urban run-off water;
- the impact that a change in the method of representing the atmosphere's dispersion capabilities would have on the end-points of consequence assessment.

Work programme

Below, the work programme is given separately where possible for the first and second years. Not all aspects mentioned below could be fully explored in the two years, and the work could be carried forward into subsequent years if the Programme continues.

A) The influence of weather condition on the intensity and pattern of deposition

In the first year, SRD will investigate the factors influencing the incorporation of radionuclides into fog. The first stage would be an appraisal of recent developments in reactor-accident source-term research, particularly regarding the solubility characteristics of released particles, in order to address the question of the competition with the natural aerosol for the available fog water. It will also assess the feasibility of utilizing routinely-recorded meteorological data to provide information on the presence of fog and an indication of its intensity and type.

SRD would also commence the assessment of the impact of changing the representation of the dispersive capability of atmospheric states. The vehicle for carrying out this investigation would be an uncertainty/sensitivity analysis of the atmospheric dispersion module of the CONDOR code (a state-of-the-art probabilistic consequence assessment code). In contrast to the more usual parametric uncertainty analyses, this study would examine the impact of changes in some aspects of the modelling implemented in the atmospheric dispersion module.

GSF will apply a tracer method to the measurement of washout of particles by rain and snow. A modified La Mer generator will be used to produce a monodisperse aerosol tagged with a tracer. The adjustable size of the aerosol (0.3-5 mm) covers the range relevant to the wash-out of particles from the atmosphere. Deposition parameters for each specific particle size will be determined from the measured tracer concentration in the precipitation.

In the second year - and beyond if appropriate - SRD will consider the design of algorithms for including foggy conditions in consequence-assessment codes. It would also continue the model uncertainty/sensitivity analysis commenced in the first year.

GSF will focus on the direct measurement of the wet deposition of atmospheric aerosol. Here, the trace element content of the atmospheric aerosol will be used to quantify aerosol deposition parameters. Trace elements on aerosols transported over long range may be scavenged predominantly by processes in clouds, ie by rain-out, whereas wash-out determines the deposition of trace elements with dominant local sources. The use of a set of trace elements which encompass both these deposition routes will allow wet deposition to be studied in detail under various meteorological conditions. Analysis of the samples of particles collected by cascade impactors will be done by proton-induced X-ray emission (PIXE) at the accelerator at GSF. The collected precipitation will then be analyzed for the same trace elements by ICP (inductively coupled plasma) spectrometry. The use of generated aerosol in the first year and trace elements in the second will provide a complete picture of wet deposition: wash-out both on its own and together with rain-out can be studied. The methods will be applied to precipitation in the forms of rain and of snow.

B) Weathering and run-off of ^{137}Cs in urban and rural environments

In the first year, GSF will carry out in-situ gamma-ray spectrometry at about 55 locations in urban, suburban and rural environments in Bavaria which have been continuously investigated since the reactor accident at Chernobyl. The spectra will be evaluated with respect to the reduction of the gamma-dose due to weathering. Risø will investigate run-off and weathering for impervious urban surfaces, as follows.

(a) The time behaviour of deposits arising from the Chernobyl accident will be followed in heavily contaminated areas, for example in the town of Gavle in Sweden. The surfaces considered will include busy roads, pavements and roofs; three test roofs at Risø will be used, supplemented by a test roof from Gavle rebuilt at Risø.
(b) Run-off experiments using short-lived isotopes will be conducted on a test road constructed at the Risø laboratory. The results will be compared against the simple 'Ritchie' model, to test whether this gives an adequate representation of run- off or a more sophisticated model is required.

In the second year - and beyond if appropriate-

GSF will continue to record and evaluate gamma-spectra for the sites mentioned above. The time behaviour of the reduction of the gamma-dose rate in the first five years after deposition will be approximated by analytical functions. For the lawns located at the original 55 measuring places in Bavaria, the caesium concentration in the soil will be measured and compared with the results obtained in the first few months after deposition. From this the effect of possible depletion processes can be detected and information also obtained pertinent to the question of radionuclides entering the freshwater cycle.

Risø will continue the investigation of weathering for those surfaces dealt with in the first year and will move on to consider surface coverings such as grass, trees and soil. The weathering of the Gavle red-tile roof will be compared to that of the roofs at Risø. In addition, more run-off experiments will be performed, if necessary, with a view to developing a model for run-off from impervious surfaces such as red-tile roofs, silicon-treated roofs, asphalt roads and concrete roads.

C) Resuspension of deposited ^{137}Cs activity

In the first year, Risø will collect data on the content of resuspended ^{137}Cs in rainwater and also on deposition levels of ^{137}Cs with a view to correlating the two sets of data. Where possible, the corresponding air concentration will also be measured. In addition, rain will be collected at an elevated location in order to test whether the surprisingly high concentrations of resuspended ^{137}Cs found in rainwater collected at ground level may be caused by splash from the ground. In the second year, the data collected in the first year will be processed.

GSF will measure the resuspension of Cs in urban environments and subsequent deposition on construction surfaces, vegetation, etc., in Goiania (in cooperation with the Inst. Radioprotecçao e Dosimetria, Rio de Janeiro), where an accident with a medical caesium source led to highly localized contamination in a city of 1.3 million inhabitants. The procedure will be to take size- differentiated air samples in weather episodes and to make measurements on environmental and construction surfaces (roofs, walls etc.). This will lead to the development of a resuspension model which will enable an estimate to be made of the distribution of initial contamination and, thus, the usefulness of decontamination measures in urban environments after major radioactive contaminations.

D) Ultimate fate of deposited radionuclides

In the first year, SRD will identify the dominant mechanisms determining the patterns of retention and redistribution of radionuclides throughout the system of urban drainage, storm run-off and water-treatment plants. This work would commence with a review of pertinent information, including that available from non-nuclear contexts.

In the second year, and beyond if appropriate, SRD will seek to quantify the radiological impact of run-off into the urban drainage system in terms of its contribution to the endpoints of consequence assessment.

C24 Probabilistic risk assessment and real-time models for assessing the consequences of accidental releases and for evaluating the effectiveness and feasibility of countermeasures

Contract Bi7-012 RADE-AID, the development of a Radiological Accident DEcision AIDing system.

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Total Contribution by the Commission: 110 kECU
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Description of research work:

Introduction

The RADE-AID project was set up by the Commission of the European Communities (CEC) as a post-Chernobyl project. The project was to be jointly executed by three contractors, TNO (NL), KfK (D) and NRPB (UK) and it was to run initially for two years from January 1988. The purpose of the contract was to develop a computer system which could aid decisions on countermeasures following a radiological emergency. As a result of the contract a prototype computer program has been written which helps a decision-maker structure the problem and investigate the consequences of and possible bases for, different countermeasure strategies. In order to demonstrate the potential of this decision tool, some illustrative applications were developed, which explored its use for decisions on the countermeasures of relocation and food interdiction. The prototype and a copy of the final report are available for organisations actively involved in research related to the RADE-AID project. The present contract is a continuation of the first RADE-AID contract. The computer system will be further developed with particular reference to the user-interface, the decision logic, the database of model predictions supplied for use with the system and in consultation with decision-makers. In addition to providing assistance to a decision-maker following an accident, it is intended that this system could be used in the development of emergency plans and as a tool for assisting in the training of those with responsibility for managing the response of accidents.

Detailed project description and role of contractors

The basis of the computer system is the decision logic which enables the decision-maker to evaluate the consequences of a range of decision options. This decision logic uses multi-attribute value theory to compare decision options in terms of the preferences of a decision-maker for the outcomes of each option, quantified against a number of relevant factors or attributes. Such attributes are likely to include the doses averted, the social upheaval incurred and the level of monetary expenditure required. The degree of preference felt for each outcome may be expressed directly by a decision-maker or obtained from a value function which maps each outcome ('score' for an attribute) onto a level of preference (or 'value'). Preferences for different attributes are compared by weighting each attribute according to its perceived importance. By combining the preferences for each option, a relative ranking of the options is achieved.

The prototype provides facilities for the user to specify the decision options, the attributes relevant to the problem, the relative weight factors and the value functions for these attributes. It also provides limited facilities for investigating the sensitivity of the ranking of the options to the assumed weight factors and value functions.

During the present contract, three areas have been identified for attention: the improvement of the decision logic software, the expansion of the database of model predictions for use with the system and the consultation of decision-makers. All of the contractors will be involved in each of these aspects of the work, but the degree of involvement will vary as indicated below.

Improvement of decision logic software

This work involves two main activities: the investigation of the applicability of other procedures for the obtaining of weight factors and value functions and the improvement of the user-interface. New procedures for the elicitation of weight factors and value functions will be considered. The facilities for specifying attributes, weight factors and value functions will be improved. In addition, the facilities for undertaking sensitivity studies will be extended, particularly so that sensitivity of the ranking to the value functions can be explored. TNO will have prime responsibility for this activity in consultation with the other contractors and with reference to the feedback from decision-makers.

Expansion of database of model predictions

The illustrative applications carried out for the demonstration of the prototype required the provision of a limited database of model predictions, including predictions of environmental contamination following specified accidents, numbers of people receiving different levels of dose, the dose reduction likely to be achieved by the implementation of selected countermeasures and the monetary costs involved. In order for the system to be used more widely, the database needs to be expanded to cover a wider range of accident and countermeasure options. Within the present contact it is planned to expand the database in this way, particularly to include more food countermeasures and for the interaction of decontamination with relocation to be more fully explored. In addition, data appropriate for the Netherlands will be included with those for the UK and Germany. NRPB will have the prime responsibility for this activity, but support will be provided by TNO and KfK, particularly for the provision of country-specific data.

Interaction with decision-makers

Feedback from decision-makers (and other relevant sources) has to be obtained so that better guidance on the choice of attributes, weight factors and value functions may be provided,

All three contractors will be involved in this activity, with, in particular, NRPB placing their main emphasis on this work.

C24 Probabilistic risk assessment and real-time models for assessing the consequences of accidental releases and for evaluating the effectiveness and feasibility of countermeasures

Contract Bi7-015 Indoor deposition and relationship between indoor and outdoor air concentration

Coordinator Risø National Laboratory
P.O. Box 49
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Tel: 3-71212/4226

Total Contribution by the Commission: 100 kECU
24 months from 1/07/90 to 30/06/92

Participating Scientists

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Description of research work:

Background

In order to assess the effect of staying indoors during an air pollution episode, including that caused by a nuclear accident, it is essential to find as well the reduction in inhalation dose as the deposition on indoor surfaces.

Some estimations of the reduction in inhalation dose by staying indoors and the dosimetric consequences of indoor deposits have been made by the group proposing this work and elsewhere. These indicate that within the range of the variation in data, the dose commitment arising from indoor deposits may be of the same magnitude as that arising from outdoor deposits. However, no model of aerosol transport processes into and within dwellings has yet gained sufficient confidence to be accepted in generic studies of the indoor environment or in major risk assessment models. This is due to the lack of knowledge of the role of the filtering effect relative to that of internal deposition in causing the reduction factor, for different air exchange rates and particle sizes.

Protective measures that may be undertaken by the householder are relevant to seeking optimal strategies in protecting the individual. In relation to aerosols, one decontamination method during cloud passage is the use of a vacuum cleaner as a tool for cleaning indoor air. Some investigations have been carried out by this method, but these have been sparse and more investigations have to be done in order to demonstrate its efficiency.

Full-scale investigations of house filtration and indoor deposition which have been carried out at Risø (with some collaboration from Imperial College) have so far used polluted air from natural air-pollution episodes, including the Chernobyl case. However, the technique developed by Imperial College, using stable tracer labelled monodisperse silica particles, may be further developed to full-scale measurements of indoor deposition. This would be made with particular particle sizes in the range of interest for accidental releases and so give improved understanding and sound data for modelling purposes.

Objectives

The objectives of the work proposed will be:

- to examine - and improve if necessary - the techniques for estimating the reduction of inhalation dose by staying indoors and the deposition on indoor surfaces.
- to examine the influence of the surface type, for instance the importance of furniture on the deposition process.
- to consider the range of measures that may be taken to alleviate indoor exposure and in particular to examine a vacuum cleaner as a tool for reduction of the indoor air pollution.
- to improve models for generic and risk assessment purposes in radiation protection.

Work programme

In the first year, Risø would carry out the following:

a) Indoor/outdoor air concentration

In a test house using cosmogenic ^{7}Be-particulate as tracer to find the indoor/outdoor air concentration and by varying the air exchange rate to find the filtering factor and the deposition constant.

b) Indoor deposition

To implement the method, in collaboration with Imperial College, using monodisperse silica-particulate in the test house (until now it has only been used in a small scale experiment).

c) Vacuum cleaner as a tool for countermeasures

Begin to investigate the efficiency of different vacuum cleaners as air filters.

In the first year Imperial College would:

a) obtain, from its standard supplies, samples of monodisperse silica particles in the size range 1-10 microns, and check the size characteristics using the Imperial College APS analyzer.

b) make use of Imperial College's PALAS particle dispersion generator and associated ^{85}Kr de-ionising source in experiments in cross checking airborne particle count against air filter measurements using stable tracers. The stable tracer techniques have been developed under contract from UK industry. These comparative experiments would be conducted in the aerosol test chamber.

c) to confirm stable tracer labelling techniques (which have been shown to have a detection limit of 10-100 ng particles), using the Reactor Centre facilities.

d) the assistant would travel to Risø for a 3 month work period to participate in indoor deposition measurement using cosmogenic aerosol and to carry out the first experiment with labelled monodisperse aerosols (probably 3 micron aerosol) using air filter techniques. Imperial College would transport labelled particle supplies, dispersion generator and related equipment to Risø.

e) make use of models to assist experiment design.

At the end of the first year the participants would meet to review progress. In particular they would consider the implications of the results of the first year work-programme for the continuing direction of the work in the second year. In view of this the second year programme cannot be as closely defined as the first, but the following gives some indications of potential directions. Not all aspects mentioned below could be fully explored in the second year. This research could be continued subsequently if the Programme continues.

In the second year - and beyond if appropriate - Risø would address some or all of the following aspects:

a) Indoor/outdoor air-concentration

Reactive (depositing) gases would be used as tracers. More houses would be investigated using ^{7}Be as tracer.

Houses from different places in the EC would be investigated.

b) Indoor deposition

Full scale experiments using monodisperse silica-particulate would be performed, in collaboration with Imperial College, in real houses.

c) Vacuum-cleaner as a tool for countermeasures

Experiments in real houses will be performed and the normal vacuum cleaners used in the EC would be investigated.

In the second year Imperial College would:

a) participate in a wider range of full-scale experiments using monodisperse aerosols covering size ranges down to 1 micron and up to 10 micron. This will involve about 3 months spent at Risø and the transport and provision of the appropriate College equipment.

b) to develop data and models, in collaboration with Risø, that can take account of the differences in behaviour expected to be found between particles in the 1-10 micron range, and to disseminate the results of model studies.

Looking ahead to following years, the vital question of separating the effects of infiltration from deposition needs to be answered, as a function of particle size. Also the mean residence time of deposited material, and its resuspension and cleaning needs to be addressed; preliminary work on this has been done already using Imperial College's UV scanning system DIADEM, developed under the current CEC Programme.

C24 Probabilistic risk assessment and real-time models for assessing the consequences of accidental releases and for evaluating the effectiveness and feasibility of countermeasures

Contract Bi7-017 Validation- training- and uncertainty-study experiments for real-time atmospheric dispersion models.

Coordinator Risø National Laboratory
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Total Contribution by the Commission: 70 kECU
24 months from 1/08/90 to 31/07/92

Participating Scientists

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Description of research work:

The objective of this project is to quantify and assess inherent uncertainties likely to arise during nuclear accidents involving near-site atmospheric dispersion scenarios. Our task is to perform and document full-scale aerosol-plume dispersion experiments over various terrain types, and for a variety of different atmospheric conditions - including non-idealistic but indeed realistic dispersion events occurring during non-stationary and time-changing meteorology. The end-product will consist of "reference and validation data sets" applicable as references for real-time dispersion models and will include training and evaluation experiments suitable for real-time uncertainty handling and on-line emergency training relevant for nuclear accidental releases.

Assisted by our German cooperators at DLR, we are conducting a series of full scale aerosol-plume dispersion experiments at various sites, where, by use of LIDAR's, we obtain fast and high-resolution plume tracking capabilities. Real-time sequential data of plume dispersion, in the form of "movies" of instantaneous concentration profiles, provide the raw-data for building a realistic diffusion data base. From this we establish plume-profile statistics of such statistical quantities as mean- and mean-square concentration profiles of the horizontal and vertical plume spread, in addition to the entire concentration probability function for each experiment. Extensive meteorological mean and turbulence measurements are simultaneously taken during each experiment in order to provide extensive input-data for the dispersion models to be evaluated and used for simulations. The contribution from our collaborators at DLR (Institute of Opto-electronics) is to provide scientific and technological support to this project regarding processing and interpretation of the Lidar measurements of the plume concentrations.

C24 Probabilistic risk assessment and real-time models for assessing the consequences of accidental releases and for evaluating the effectiveness and feasibility of countermeasures

Contracts Bi7-045/Bi6-106/Bi7-062 Development of a comprehensive decision--aiding system for the off-site emergency management.

Coordinator KfK
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Total Contribution by the Commission: 650 kECU
24 months from 1/11/90 to 31/10/92

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Contract Bi6-106

10 Dr. S.P. Ratti
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Contract Bi7-062

Description of research work:

1. Context of the proposed project

After a nuclear accident, quick and well-founded decisions are needed in order to mitigate the potential radiological impact on the exposed population. A pre-requisite for such decisions is information on

(1) the current and future radiological situation at both near and far distances,

(2) the main features and effects of implementing selected countermeasures, for example in terms of areas and numbers of persons affected, time required, doses and/or health effects averted, monetary costs, etc.,

(3) the feasibility of different countermeasures in the context of existing constraints, e.g. time, weather, transport conditions, available resources and equipment, etc.,

(4) the ranking or relative merits of alternative countermeasures and the levels at which they might be implemented which will require a balancing of relevant quantities such as those evaluated under point (2), with due consideration of more subjective factors such as risk perception and socio-political aspects.

For these purposes, estimates have to be performed with models describing the transfer and behaviour of radionuclides in the environment (atmosphere, soil, plants and animals), emergency actions, including their effectiveness and economic impact, the exposure of the population and the resulting health effects. These models have to be fed with data and information, whose quantity, quality and significance may change with time and distance from the release, especially when radioactive material is transported across national boundaries.

It is obvious that the task of decision-makers in this area will be facilitated by access to good quality information in a timely manner. Computer based systems can satisfy these needs and provide information in a manageable and effective form for evaluating countermeasures strategies in the early, intermediate and late phases of the accident.

There are several potential users of such computer based systems (e.g. utilities, local authorities, national governments, international agencies) each of whom will have different detailed needs and uses. Therefore, any generically based system will have to be structured to reflect and accommodate these different requirements.

2. Task description

The purpose of the research is to develop the essential ingredients of a decision supporting system which has the potential for wide scale application in Europe. The structure of the system will be modular in form with separate components corresponding to data input facilities, data banks, atmospheric transport, environmental and economic models, logic routines, output facilities, etc.. The modular structure of the system and the detailed parameterization of calculational procedures will provide great operational flexibility which will enable the system to cope with differing

- amounts and quality of measured and radiological data,
- site and source term characteristics,
- national regulations, emergency plans, responsibility structures, and
- needs of the user.

In addition to its role in providing decision support in the case of a real emergency, the structure and design of the system will be such that it can be used as a powerful tool in training of decision makers, in exercising emergency plans and as a means for gaining experience with emergency plans and recommendations for long-term countermeasures and recovery actions.

The work of the various institutes will be closely integrated and directed towards the major objective of developing a comprehensive decision support system. Each partner will be involved in structuring the overall system and providing well-defined parts corresponding to its special expertise and research priorities. The activities in the first project period 1990-1991 will be concentrated on the following areas:

Project 1 (KfK):

Development of a real-time system for aiding decisions about emergency actions in the early phase of an accident, such as evacuation and sheltering. Besides the estimation of radiological quantities, the modelling of emergency actions, and the evaluation and ranking of alternative actions by an expert system, emphasis is given to the installation of an operational system as framework for a comprehensive decision support system.

Project 2 (GSF):

In the framework of a preceding research programme a real-time emergency dose prediction system including countermeasures has been developed. This computer code has been designed for adaption to the different living habits, climatic and agricultural conditions in the different regions of the European Community.

It is intended to continue this work with the aim to integrate the existing code into the framework of the decision support system under development. In addition, the prediction models for some foodstuffs and certain climatic regions will be improved and the data base will be extended to further radionuclides. Further, the computer programs will be optimized in order to improve their user friendliness, to facilitate the adaption to different computers and to reduce the required computing times.

Project 3 (CEA and NCSR Demokritos):

A code system calculating the atmospheric dispersion of pollutants will be developed, based on the MC31 code which solves the diffusion-advection equation by Monte-Carlo techniques, and the ADREA code, which is a 3-D time-dependent transport code, suitable for complex terrain.

The common precise description of the orography will be achieved by a triangularisation of the topographical disturbances. A graphic package will be created for better representation of the wind velocity and the pollutant concentration fields. Improvements on the modelling of the wet and dry deposition will be proposed, including a new simple approach of the run-off effect for the rain water. A verification programme will be initiated.

Project 4 (ENEA):

The phase of the evaluation of input parameters for meteo-diffusive codes plays a very important role during a run of an emergency system, so it is essential to develop a software package to provide in real-time those input parameters which are neither directly measured nor available on the data base, and to format the data as required by the specific input files of the models. In particular, this package should include several routines to estimate input model parameters like:

- atmospheric stability category;
- mixing layer depth;
- scaling parameters (friction velocity, Monin-Obukhov length, etc.).

A recommended feature of the pre-processing package is that it should be as flexible as possible, in the sense that for a given input parameter more than one method of estimate will be foreseen. The choice of one method will be suggested to the user on the basis of the availability of different kinds of data, depending on the location of the accident and on site instrumentation.

In the present research project, the feasibility of using stochastic methods (grey box models) for the local prediction of some of the above mentioned parameters will be studied.

Project 5 (Risø):

A portable atmospheric dispersion module will be created, based on the combination of our mesoscale puff-model RIMPUFF and an updated version of the diagnostic, non-hydrostatic flow model LINCOM. During 1990-1991, we plan to emphasize the following:

- Interfacing with other modules in the decision support system,
- Creation of a flexible user interface allowing easy interactive communication between user and computer,
- Mapping techniques and methods to produce fast and clear graphics, including menu-driven set-up's,
- Correction-facilities for one-line data-acquisition, feed-back and quality assurance.

A functional demo-system will be established.

Project 6 (ICSTM):

Under the post-Chernobyl programme a computer model, 3-DRAW, has been developed in a preliminary form as a tool to simulate atmospheric dispersal and deposition out to continental scale distances, in the context of real-time assessment (following a nuclear accident). This project will concentrate on validation and improvement by addressing:

i) the performance and accuracy of the model in critical meteorological situations such as frontal systems
ii) improved parameterization, particularly with respect to conditions in the boundary layer, and their assessment from available meteorological data (collaboration with ENEA here)
iii) the practical use of the model in an emergency situation including its combined use with measurements to optimise and update predictions
iv) investigation of potential benefits of advances in computer technology, specifically through parallel processing techniques.

Project 7 (SMHI):

An extension of a 3-dimensional Eulerian meso-scale dispersion model to the European scale will be performed, for the use as an operational real-time model. The resolution of the model will be 55x55 km^2 in the horizontal and with three vertical levels, where the vertical structure of the model is variable in time and space depending on the state of the boundary layer. An operator split time integration scheme is used. The horizontal flux is calculated by means of a finite element method (the Weighted Residual, Bubnow-Galerkin, Method). The vertical flux is obtained from variations of the boundary layer height, the vertical wind and the turbulent vertical flux (K-theory). Meteorological fields needed will be provided by a high resolution, state-of-the-art numerical weather prediction system developed within the HIRLAM project, which is a joint Nordic, Dutch and Irish research project. The HIRLAM system, at SMHI, will be based on an operational access to ECMWF analyzed and forecasted meteorological fields.

3. Cooperation with other research projects:

A close connection to those CEC-supported research projects, which can provide direct input to the overall decision support system will be established, such as the contributions of JRC-Ispra and SCK/CEN, Mol. A brief description of their projects is given:

JRC-Ispra Environment Institute, Italy

In the past, JRC has been looking at the possibility of interaction between radiological monitoring data from nation wide monitoring networks and long range transport models (M/M interaction), in order to update 1-2 days predictions on where the cloud is going. In that exercise a trajectory model and a comprehensive transport and diffusion model have been used. It was illustrated that M/M interaction improves the predictions in a significant way. Having information on the time and space resolution of real time monitoring networks in the EC and on the procedures that will be adopted in international rapid information systems (CEC, IAEA), JRC will develop an interface module between the latter information systems and a long range transport model, in order to allow for an on-line M/M interaction. The model should preferably be one that will be selected within the overall framework but using ECMWF meteo data.

SCK/CEN, Mol, Belgium

A feasibility study concerning the possibility of feed-back of environmental measurements into a model, to reduce gross uncertainties, has been undertaken for the short range. Conditions under which this seems possible have been pointed out. During the prolongation of this contract, a further analysis concerning the interaction of monitoring data (all kind: concentrations, external radiation, deposition...) versus model assessment will be performed.

A demonstration software package will be built to accept (simulations of) environmental data in order to resolve the main model parameter uncertainties. The model will be either a simple bi-gaussian plume model (SCK/CEN) or a tri-gaussian puff model (SCK/CEN, ENEA, Risø). The opportunity, firstly, to perform a preliminary feed-back cycle with the aid of a simple model, then afterwards, to feed a more complex model will also be examined.

ANNEXES

ANNEX I: LIST OF RESEARCH CONTRACTS

A HUMAN EXPOSURE TO RADIATION AND RADIOACTIVITY

A1 MEASUREMENT OF RADIATION DOSE AND ITS INTERPRETATION

Bi6-026-A1 1/1/90 -31/12/91 24 Months 77 kECU EURADOS-CENDOS ..... *1*[1]
Collaboration on research and development concerned with the methodology and data in radiation dosimetry.

1 Dennis	EURADOS-CENDOS	77 kECU

Bi6-322-A1 1/1/90 -31/12/91 24 Months 75 kECU ICRU *5*
Quantities, units and measurement techniques for ionizing radiation.

1 Allisy	ICRU	75 kECU

A11 Development and implementation of standards and procedures linked to the concept of dose equivalent quantities

Bi6-347a-A11 1/4/90 - 31/3/92 24 Months 240 kECU NRPB *7*
The implementation of the operational dose quantities into radiation protection dosimetry (NRPB Association).

1 O'Riordan	NRPB	50 kECU
2 Marshall	AEA Technology	50 kECU
3 Lembo	ENEA	80 kECU
4 Chartier	CEA - FAR	60 kECU

A12 Radiation measurement and instrumentation for individual and area dosimetry

Bi7-020-A12 1/11/90- 31/10/92 24 Months 246 kECU Univ. Limoges *10*
Study and development of an individual electronic neutron dosemeter.

1 Decossas	Univ. Limoges	80 kECU
2 Tommasino	ENEA	47 kECU
3 Zamani-Valasiadou	Univ. Thessaloniki	31 kECU
4 Barthe	CEA - FAR	70 kECU
5 Fernández Moreno	Univ. Barcelona Autónoma	18 kECU

Bi7-025-A12 1/8/90 - 31/7/92 24 Months 135 kECU Univ. München *13*
Use of the variance-covariance method in radiation protection.

1 Kellerer	Univ. München	80 kECU
2 Lindborg	Nat.Inst.Radiation Protection	15 kECU
3 Jessen	Univ. Aarhus	40 kECU

[1] Numbers in italics refer to page numbers

Bi7-027-A12 1/6/90 - 31/5/92 24 Months 183 kECU Risø National Laboratory *15*
The measurement of environmental gamma doses

1 Bøtter-Jensen	Risø National Laboratory	54 kECU
2 Lauterbach	PTB	29 kECU
3 Delgado Martínez	CIEMAT	100 kECU

Bi7-028-A12 1/8/90 -31/7/92 24 Months 154 kECU Risø National Laboratory *18*
Dosimetry of beta and low-energy photon radiation using extrapolation chambers and thin solid state dosimeters.

1 Christensen	Risø National Laboratory	41 kECU
2 Chartier	CEA - FAR	40 kECU
3 Herbaut	CEA - Grenoble	38 kECU
4 O'Riordan	NRPB	10 kECU
6 Gasiot	Univ. Montpellier	15 kECU
5 Fernández Moreno	Univ. Barcelona Autónoma	0 kECU
7 Scharmann	Univ. Giessen	10 kECU

Bi7-030-A12 1/5/90 - 30/4/92 24 Months 436 kECU Univ. Saarlandes *22*
The use of microdosimetric methods for the determination of dose equivalent quantities and of basic data for dosimetry.

1 Grillmaier	Univ. Saarlandes	85 kECU
2 Brede	PTB	100 kECU
3 Zoetelief	TNO - Rijswijk	70 kECU
4 Schmitz	KFA	100 kECU
5 Segur	ADPA	81 kECU

Bi7-031-A12 1/7/90 - 30/6/92 24 Months 327 kECU PTB *26*
Determination and realisation of calibration fields for neutron protection dosimetry as derived from spectra encountered in routine surveillance.

1 Klein	PTB	100 kECU
2 Thomas	NPL	50 kECU
3 Chartier	CEA - FAR	80 kECU
4 Schraube	GSF	97 kECU

Bi7-051-A12 1/6/90 - 31/5/91 12 Months (study contract) 20 kEC U CEA - FAR .. *29*
Dosimetry and spectrometry measurements of the leakage radiation fields from the SILENE reactor with various shields

1 Medioni	CEA - FAR	20 kECU
2 Delafield	AEA Environmental and Energy	0 kECU

A13 **Derivation of organ doses and effective dose equivalents**

Bi7-021-A13 1/9/90 - 31/8/92 24 Months 100 kECU Nuclear Electric 31
Calculation and measurement of doses from particulate radioactive source.

1 Charles	Nuclear Electric	60 kECU
2 Herbaut	CEA - Grenoble	29 kECU
3 Patau	Univ. Toulouse III	11 kECU

A14 Assessment of internal exposure

Bi6-341-A14 1/10/89 - 31/3/91 18 Months (study contract) 30 kECU Istituto Superiore di Sanità *34*

Radionuclide transfer factor for human milk

1 Campos-Venuti	Istituto Superiore di Sanità	30 kECU

Bi6-347b-A14 1/4/90 - 31/3/92 24 Months 384 kECU NRPB *36*

The calculation of doses from intakes of radionuclides by inhalation or ingestion implementation of the operational dose quantities into radiation protection dosimetry (NRPB Association).

1 Bailey	NRPB	50 kECU
2 Kendall	NRPB	40 kECU
3 Stahlhofen	GSF	100 kECU
4 Roy	CEA - FAR	65 kECU
5 Patrick	MRC	30 kECU
6 Kaul	Bundesamt für Strahlensch.	80 kECU
7 Taylor	KfK	17 kECU

Bi7-024-A14 30/4/90 -31/10/91 18 Months (study contract) 40 kECU AEA Technol. ... *40*

The assessment of internal dose: the establishment of registries of dose assessment, autopsy data and models

1 Gibson	AEA Technology	40 kECU

Bi7-029-A14 1/5/90 - 30/4/92 24 Months 337 kECU GSF *44*

Assessment of internal dose from radionuclides using stable isotope tracer techniques in man.

1 Roth	GSF	95 kECU
2 Molho	Univ. Milano	57 kECU
3 Hislop	AEA Technology	75 kECU
4 Taylor	KfK	72 kECU
5 Henrichs	GSF	38 kECU

A2 Transfer and Behaviour of Radionuclides in the Environment

Bi6-052-A2 1/1/90 -31/12/91 24 Months 65 kECU UIR *47*

Promotion of formation and exchange of information in radioecology (International Union of Radioecologists).

1 Myttenaere	IUR	65 kECU

A21 **Environmental behaviour of radionuclides in situations meriting particular attention for long-term behaviour or post-accident conditions**

Bi7-008-A21 1/5/90-30/4/92 24 Months 482 kECU NERC *50*
Modelling the transport of radionuclides through the freshwater environment

1 Hilton	Nat.Center for Marine Research	100 kECU
2 Galvão	LNETI	50 kECU
3 Cremers	Univ. Leuven (KUL)	80 kECU
4 Foulquier	CEA - Cadarache	20 kECU
5 Pieri	Univ. Nantes	50 kECU
6 Belli	ENEA	60 kECU
7 Vanderborght	Rijksunivers. Centrum Antwerpen	40 kECU
8 Serrano	Univ. Malaga	12 kECU
9 Hambuckers - Berhin	Univ. Liège	40 kECU
10 Comans	Netherlands Energy Research	30 kECU

Bi7-042-A21 1/11/90 -31/10/92 24 Months 314 kECU Univ. College Dublin *52*
Radioecology of transuranics in the marine environment.

1 Mitchell	Univ. College Dublin	80 kECU
2 Iranzo	CIEMAT	100 kECU
3 Guegueniat	CEA - Cherbourg	34 kECU
4 Damiani	ENEA	100 kECU

A22 **Natural radioactivity in the environment and its pathways to man**

Bi7-006-A22 1/6/90 - 31/5/92 24 Months 158 kECU RIVM *55*
Behaviour of Polonium-210 and Lead-210 in European marine environments. Application of bioindicators.

1 Köster	RIVM	50 kECU
2 Guegueniat	CEA - Cherbourg	36 kECU
3 Duursma	NIOZ	36 kECU
4 Galvào	LNETI	36 kECU

A23 **Influence of speciation, chemical modification, changes in physico-chemical properties and biological conversion**

Bi6-339-A23 1/1/89 - 31/12/91 36 Months (study contract) 30 kECU SCOPE-RADPATH *57*
Biogeochemical pathways of artificial radionuclides

1 Plocq	SCOPE	30 kECU

Bi6-345-A23 1/1/90 -31/12/91 24 Months 55 kECU Inst.Radioökol.Niedersachsen ... *59*
Transfer and conversion mechanisms of H-3 and C-14 compounds in the local environment.

1 Bunnenberg	Inst. Radioökologie Niedersachsen	55 kECU

Bi7-011-A23 1/7/90 - 30/6/92 24 Months 190 kECU RIVM *61*
The bio-availability of long-lived radionuclides in relation to their physico-chemical form in soils

1 Lembrechts	RIVM	60 kECU

2 Wilkins	NRPB	50 kECU
3 Sandalls	AEA Technology	50 kECU
4 Cremers	Univ. Leuven (KUL)	30 kECU

A24 The behaviour of accidentally released radionuclides, evaluation of the reliability of transfer parameters and experimental studies

Bi7-018-A24 1/4/90 - 31/3/92 24 Months 557 kECU Inst. Terrestrial Ecology *63*
Factors affecting radiocaesium transfer to ruminants.

1 Howard	Inst. Terrestrial Ecology	100 kECU
2 Vandecasteele	CEN/SCK Mol	100 kECU
3 Mayes	McAulay Land Use Research Inst.	62 kECU
4 Belli	ENEA	80 kECU
5 Stakelum	Agricult. Food Development Auth.	50 kECU
6 Colgan	NEB	50 kECU
7 Assimakopoulos	Univ. Ioannina	50 kECU
8 Unsworth	Univ. Nottingham	50 kECU
9 Jones	Univ. Agricultural Sci. of Sweden	15 kECU

A25 The role of retention and release of radionuclides in natural ecosystems and in marginal agricultural areas

Bi7-009-A25 1/4/90 - 31/3/92 24 Months 280 kECU Imp.Coll.Science,Techn.,Med. . . . *67*
Deposition of radionuclides on tree canopies and their subsequent fate.

1 Minski	Imperial College Science, Techn.,Med.	80 kECU
2 Belot	CEA - FAR	40 kECU
3 Rauret	Univ. Catalunya - Politécnica	80 kECU
4 Ronneau	Univ. Catholique Louvain - LLN	80 kECU

Bi7-016-A25 1/4/90 - 31/3/92 24 Months 340 kECU Bundesamt für Strahlenschutz . . *71*
Behaviour of Cs and Sr in natural ecosystems and the potential radiation exposure of their extensive use.

1 Wirth	Bundesamt für Strahlenschutz	90 kECU
2 Fraiture	Univ. Liège	40 kECU
3 Palo	Univ. Agricultural Sci. of Sweden	50 kECU
4 Nimis	Univ. Trieste	60 kECU
5 Bergman	Swedish Defense Research Establish.	50 kECU
6 Wickman	Univ. Umeå	15 kECU
7 Melin	Nat.Instit. of Radiation Protection	35 kECU

Bi7-044-A25 1/7/90 - 30/6/92 24 Months 265 kECU NEB *73*
Radioecology of seminatural ecosystems.

1 Colgan	NEB	75 kECU
2 Horrill	NERC	50 kECU
3 Aarkrog	Risø National Laboratory	50 kECU
4 Johanson	Univ. Agricultural Sci. of Sweden	50 kECU
5 Veresoglou	Univ. Thessaloniki	40 kECU
6 Spyropoulos	Inst. Soil Science	0 kECU

A26 **Development of countermeasures to reduce the contamination in the environment and to impede its transfer to man**

Bi6-325-A26 and Bi6-122 — 36 Months 882 kECU CEA - Cadarache 77
(1/1/89 - 31/12/90 — 24 Months 500 kECU)
(1/1/91 - 31/12/91 — 12 Months 202 kECU + 1 Commission staff)
(Associated research — 180 kECU)

Rehabilitation of soil and surface after an accident (RESSAC) (CEA Association)

1 Grauby 1/1/89 - 31/12/90	CEA - Cadarache	500 kECU
2 Maubert 1/1/91 - 31/12/91	CEA - Cadarache	202 kECU

Associated Research:

Bi6-326-A26 1/5/89 - 30/4/91 — 24 Months 65 kECU Risø National Laboratory
Design and development of a skim and burial plough for reclamation of contaminated land

Roed	Risø National Laboratory	65 kECU

Bi6-327-A26 1/7/89 - 31/12/90 — 18 Months 50 kECU Fac.Sciences Agronom. Gembloux
Study of the transfer of accidentally released radionuclides in agricultural products with the aim of developing appropriate countermeasures

Kirchmann	Faculté Sciences Agronom. Gembloux	50 kECU

Bi6-329-A26 1/1/89 - 31/12/90 — 24 Months 65 kECU Univ. Milano-Sacro Cuore (Gemelli)
Chemical treatments to reduce the transfer of caesium radioisotopes to the human foodchain after a serious nuclear accident

Silva	Univ. Milano - Sacro Cuore (Gemelli)	65 kECU

Bi7-046-A26 1/6/90 - 31/5/92 — 24 Months 432 kECU CIEMAT *83*
Transfer of accidentally released radionuclides in agricultural systems (TARRAS)

1 Cancio	CIEMAT	100 kECU
2 Maubert	CEA - Cadarache	20 kECU
3 Rauret	Univ. Barcelona, Fac. Química	80 kECU
4 Colle	CEA - Cadarache	70 kECU
5 Derwent	AEA Technology	60 kECU
6 Grandison	Univ. Reading	60 kECU
7 Gutierrez	CIEMAT	42 kECU

B CONSEQUENCES OF RADIATION EXPOSURE TO MAN; THEIR ASSESSMENT, PREVENTION AND TREATMENT.

Bi6-099-B 1/1/90 -31/12/91 — 24 Months 444 kECU EULEP *93*
Late somatic effects of ionizing radiation on the mammalian organism.

1 Maisin	EULEP	444 kECU

B1 STOCHASTIC EFFECTS OF RADIATION

B11 Interpretation of low doses and low dose rate effects with the help of microdosimetry

Bi7-032-B11 1/5/90 - 30/4/92 24 Months 319 kECU GSF *87*
Biophysical models for the effectiveness of different radiations.

1 Paretzke	GSF	100 kECU
2 Goodhead	MRC	99 kECU
3 Terrissol	ADPA	55 kECU
4 Leenhouts	RIVM	65 kECU

Bi7-040-B11 1/5/90 - 30/4/92 24 Months 176 kECU INFN - Frascati *91*
Specification of radiation quality at the nanometer level.

1 Colautti	INFN - Frascati	40 kECU
2 Watt	Univ. St.Andrews	48 kECU
3 Harder	Univ. Göttingen	38 kECU
4 Leuthold	GSF	32 kECU
5 Izzo	Univ.di Studi Roma	18 kECU

B12 Repair and modification of genetic damage and individual radiosensitivity

Bi7-022-B12 1/8/90 - 31/7/92 24 Months 190 kECU Inst. Curie *96*
Individual radiosensitivity and its relation to colo-rectal cancer

1 Dutrillaux.	Inst. Curie	80 kECU
2 Léonard	Univ. Catholique Louvain	60 kECU
3 Rueff	New Univ. of Lisbon UNL	50 kECU

Bi7-026-B12 1/9/90 - 31/8/92 24 Months 380 kECU Univ. Leiden *98*
The genetic and biochemical basis of human DNA repair and radiosensitivity

1 Lohman	Univ. Leiden	80 kECU
2 Bridges	MRC	80 kECU
3 Bootsma	Univ. Rotterdam - Erasmus	80 kECU
4 Moustacchi	Inst. Curie	70 kECU
5 Thacker	MRC	50 kECU
6 Backendorf	Univ. Leiden	20 kECU

B13 Cellular, molecular and animal studies to determine the risk of stochastic somatic effects of radiation with respect to low dose, low dose rate and radiation quality

Bi6-225-B13/Bi6-166/Bi6-223/Bi6-146/Bi6-171 1/1/90 -31/12/91 24 Months 135 kECU NRPB . *102*
Evaluation of the frequencies of chromosomal aberrations induced in human blood lymphocytes by low doses of neutrons.

1 Lloyd	NRPB	35 kECU (Bi6-225)
2 Natarajan	Univ. Leiden	35 kECU (Bi6-166)
3 Obe	Univ. Essen	20 kECU (Bi6-223)
4 Verschaeve	CEN/SCK Mol	25 kECU (Bi6-146)
5 Palitti	Consiglio Nazionale delle Ricerche	20 kECU (Bi6-171)

Bi6-338-B13 1/3/89 - 28/2/91 24 Months (study contract) 35 kECU Univ. Leiden . . *104*
Cytological follow-up of individuals exposed in the Goiania (Brazil) accident

1 Natarajan	Univ. Leiden	35 kECU

Bi7-023-B13 1/1/90 -31/12/91 24 Months 158 kECU NEB *105*
Evaluation of existing and development of new human epithelial cell transformation systems and determination of their potential in radiation protection studies.

1 Seymour	NEB	100 kECU
2 Riches	Univ. St.Andrews	40 kECU
3 Pertusa	Univ. Valencia	18 kECU

Bi7-033-B13 1/6/90 - 31/5/92 24 Months 190 kECU GSI *109*
Cellular and molecular studies on radiation quality: a comparison between genetically relevant damage and cell inactivation.

1 Kraft	GSI	80 kECU
2 Sideris	NCRS "Demokritos"	50 kECU
3 Lloyd	NRPB	20 kECU
4 Natarajan	Univ. Leiden	40 kECU

Bi7-034-B13 6/ 1/90 - 5/31/92 24 Months 327 kECU Univ. Leiden *113*
Radiation induced processes in mammalian cells: principles of response modification and involvement in carcinogenesis.

1 Van der Eb	Univ. Leiden	49 kECU
2 Sarasin	CNRS	80 kECU
3 Devoret	CNRS	80 kECU
4 Rommelaere	ULB Rhode St.Genèse	60 kECU
5 Bertazzoni	Consiglio Nazionale delle Ricerche	40 kECU
6 Thomou-Politi	NCRS "Demokritos"	18 kECU

Bi7-035-B13/Bi6-004/Bi6-075 1/7/90 - 30/6/92 24 Months 420 kECU Hosp. Acad.Leiden *119*
Methodology for the analysis of radiation carcinogenesis studies and application to ongoing experiments.

1 Broerse	Hosp. Academic Leiden	40 kECU	
2 Chmelevsky	GSF	40 kECU	
3 Masse	CEA - FAR	22 kECU	
4 Morin	CEA - FAR	50 kECU	
5 Zurcher	TNO - Rijswijk	30 kECU	
6 van Bekkum	TNO - Rijswijk	30 kECU	
7 Coppola	ENEA	168 kECU	(Bi6-004)
8 Broerse	TNO - Rijswijk	40 kECU	(Bi6-075)

Bi7-036-B13 1/9/90 - 31/8/92 24 Months 169 kECU INFN - Frascati *124*
Molecular and cellular effects of protons, deuterons and alpha-particles.

1 Moschini	INFN - Frascati	50 kECU
2 Goodhead	MRC	19 kECU
3 Belli	Istituto Superiore di Sanità	60 kECU
4 Michael	Hosp. Mount Vernon	40 kECU

Bi7-037-B13 1/10/90 -30/9/92 24 Months 200 kECU CEN/SCK Mol *127*

Cellular and molecular mechanisms of radiation-induced myeloid leukaemia in the mouse.

1 Janowski	CEN/SCK Mol	100 kECU
2 Cox	NRPB	100 kECU

Bi7-038-B13 1/8/90 - 31/7/92 24 Months 230 kECU Univ. Amsterdam *129*

Automated detection of radiation induced chromosome aberrations by slit-scan flow cytometry.

1 Barendsen	Univ. Amsterdam	80 kECU
2 Green	MRC Human Genetics Unit	75 kECU
3 Nüsse	GSF	25 kECU
4 Bauchinger	GSF	25 kECU
5 Aubele	GSF	25 kECU

Bi7-0039-B13 1/9/90 - 31/8/92 24 Months 531 kECU Univ. Leiden *132*

Studies on basic and applied aspects of radiation-induced chromosomal aberrations in human cells

1 Natarajan	Univ. Leiden	80 kECU
2 Savage	MRC	30 kECU
3 Olivieri	Univ. Roma "La Sapienza"	30 kECU
4 Cortés-Benavides	Univ. Sevilla	51 kECU
5 Bryant	Univ. St.Andrews	40 kECU
6 Ahnström	Univ. Stockholm	50 kECU
7 Baverstam	Natl.Instit. of Rad.Protection	35 kECU
8 Feinendegen	KFA	20 kECU
9 Johanson	Univ. Agricult.Sci.Sweden	10 kECU
10 Ehrenberg	Univ. Stockholm	50 kECU
11 Palitti	Univ. Tuscia	25 kECU
12 Laurent	Univ. Liège	40 kECU
12 Pantelias	NCRS "Demokritos"	40 kECU
14 Jorge	Inst.Francisco Gentil	20 kECU
15 Pereira-Luis	LNETI	10 kECU

Bi7-043-B13 1/6/90 - 31/5/92 24 Months 458 kECU AEA Technology *137*

Measurement of transformation of C3H 10T 1/2 cells by low doses of ionizing radiation.

1 Morgan	AEA Technology	100 kECU
2 Mill	Nuclear Electric	100 kECU
3 Kellerer	Univ. München	78 kECU
4 Frankenberg	GSF	100 kECU
5 Tallone Lombardi	Univ. Milano	80 kECU

B14 Assessment of genetic risks in man

Bi6-156-B14/Bi6-143/Bi6-166/Bi6-069/Bi6-077/Bi7048/Bi7-052 1/1/90 -31/12/91 24 Months 458 kECU *139*

Radiation-induced genetic effects in germ cells of mammals

1 Ehling	GSF	120 kECU (Bi6-156)
2 Cattanach	MRC	85 kECU (Bi6-143)
3 Van Buul	Univ. Leiden	55 kECU (Bi6-166)
4 Jacquet	CEN/SCK Mol	55 kECU (Bi6-069)
5 Streffer	Univ. Essen	50 kECU (Bi6-077)
6 Van der Schans	TNO - Rijswijk	43 kECU (Bi7-048)
7 De Rooij	Univ. Utrecht	50 kECU (Bi7-052)

Bi6-226-B14 1/1/90 -31/12/91 24 Months 30 kECU Univ. Leiden *146*

Studies on spontaneously-arising genetic and partially genetic disorders in man within the framework of the evaluation of genetic radiation hazards.

1 Lohman	Univ. Leiden	30 kECU

Bi7-Proposal 327-B14 under negotiation 12 Months 40 kECU GSF *147*

Molecular biology of paternal oncogenesis

1 Höfler	GSF	40 kECU

B15 Action of radionuclides on target cells in relation to radionuclide metabolism and studies on biological models for radionuclide-induced cancer

Bi7-002-B15/Bi6-089/Bi6-/064 1/7/90 - 30/6/92 24 Months 674 kECU GSF *148*

Osteosarcoma and tumours of the haemopoietic systemm by low-dose irradiation.

1 Höfler	GSF	100 kECU
2 Höfler.	Univ. München - Technische	40 kECU
3 Erfle	GSF	100 kECU
4 Skou Pedersen	Univ. Aarhus	80 kECU
5 Schoeters	CEN/SCK Mol	100 kECU
6 Bentvelzen	TNO - Rijswijk	50 kECU
7 Saunders	NRPB	99 kECU (Bi6-089)
8 Humphreys	MRC	105 kECU (Bi6-064)

Bi7-050-B15 under negotiation 24 Months 60 kECU TNO - Rijswijk *151*

Assessment of Radon WL-values, lung tumour induction by radiation of different LET and on characteristics of in vivo and in vitro transformation of bronchial cells.

1 van Bekkum	TNO - Rijswijk	30 kECU
2 Bredon	CEA/COGEMA LPP	30 kECU

B2 NON-STOCHASTIC EFFECTS OF RADIATION

B21 Radiation syndromes and their treatment after exposure of large parts of the body

Bi6-061-B21/Bi6-065/Bi6-079/Bi6-059 1/1/90 -31/12/91 24 Months 833 kECU Univ. Ulm *153*
European network of experimental and clinical research of radiation accident casualties

1 Fliedner	Univ. Ulm	290 kECU (Bi6-061)
2 Jammet	CIR	290 kECU (Bi6-065)
3 van Bekkum	TNO - Riswijk	175 kECU (Bi6-079)
4 Doria	ENEA	78 kECU (Bi6-059)

Bi7-058-B21 under negotiation 18 Months 33 kECU TNO - Den Haag *157*
Biological consequences of partial body irradiation in a monkey model

1 Broerse	TNO - Rijswijk	19 kECU
2 Natarajan	Univ. Leiden	14 kECU

B22 Irradiation and committed exposure from incorporated radionuclides

Bi6-347e-B22 1/1/90 - 30/6/92 30 Months 195 kECU NRPB *159*
The reduction of the risks of late effects from incorporated radionuclides (NRPB Association)

1 Stradling	NRPB	30 kECU
2 Volf	KfK	50 kECU
3 Métivier	CEA - Bruyères-le-Châtel	15 kECU
4 Burgada	ADFAC	40 kECU
5 Peetermans	Univ. Antwerpen	40 kECU
6 Archimbaud	CEA - Pierrelatte	20 kECU

B23 Radiation syndromes and their treatment after local exposure to skin and subcutaneous tissue

Bi6-063-B23/bi6-058/Bi7-041/Bi7-056 1/1/90 -31/12/91 24 Months 273 kECU Univ. Oxford .. *161*
Radiation effects on skin and subcutaneous tissues: implications for radiation protection criteria and the treatment of localized accidental over-exposure

1 Hopewell	Univ. Oxford	75 kECU (Bi6-063)
2 Daburon	CEA - FAR	50 kECU (Bi6-058)
3 Wells	Nuclear Electric	88 kECU (Bi7-041)
4 Coggle	Hosp. St. Bartholomew	60 kECU (Bi7-056)

Bi7-049-B23 1/7/90 - 30/6/92 24 Months 175 kECU Inst. Curie *166*
European clinical research on practical protocols for the diagnostics and treatment of localized overexposure

1 Gongora	Inst. Curie	75 kECU
2 Strambi	ENEA	50 kECU
3 Herranz-Crespo	Hosp. General Marañón	50 kECU

B24 **Radiation damage to lens, thyroid and other tissues of relevance in radiation protection**

Bi7-005-B24 1/8/90 - 31/7/92 24 Months 120 kECU Univ. Bruxelles (ULB) *168*
Irradiation and thyroid disease.

1 Dumont	Univ. Bruxelles (ULB)	20 kECU
2 Malone	Federated Dublin Vol. Hosp.	50 kECU
3 Smyth	Univ. Dublin - College	50 kECU

B3 RADIATION EFFECTS ON THE DEVELOPING ORGANISM

B31 **Damage to the central nervous system and haematopoiesis**

Bi7-003-B31 1/8/90 - 31/7/92 24 Months 238 kECU CEN/SCK Mol *170*
Effects of radiation on the development of the central nervous system

1 Reyners	CEN/SCK Mol	100 kECU
2 Ferrer	Hosp. Principes de España	69 kECU
3 Coffigny	CEA - Bruyères-le-Châtel	69 kECU

B32 Carcinogenesis after exposure in utero

Bi7-001-B32 1/9/90 - 31/8/92 24 Months 376 kECU MRC *173*
Dysfunction and neoplasias of haemopoietic and osteogenic tissue following external irradiation or bone-seeking radionuclide contamination in utero or during neonatal development

1 Humphreys	MRC	20 kECU
2 Vandenheuvel	CEN/SCK Mol	60 kECU
3 Lord	South Manchester Health Auth.	80 kECU
4 van Bekkum	TNO - Rijswijk	56 kECU
5 Tejero	Univ. Madrid - Complutense	80 kECU
6 Bueren	CIEMAT	80 kECU

B33 **Transfer of radionuclides in utero**

Bi6-347d-B33 1/1/90 - 30/6/92 30 Months 160 kECU NRPB *178*
The dosimetry and effects of fetal irradiation from incorporated radionuclides (NRPB Association)

1 Harrison	NRPB	50 kECU
2 Henshaw	Univ. Bristol	80 kECU
3 Coffigny	CEA - FAR	30 kECU

C RISKS AND MANAGEMENT OF RADIATION PROTECTION

C1 Assessment of Human Exposure and Risks

C11 Evaluation and statistics of different types of human exposure

Bi6-213-C11/Bi7-053/Bi6-229/Bi6-111/Bi6-116 1/1/90 -31/12/91 24 Months 274 kECU *180*
Statistics of human exposure and analysis of registry data

1 Stather	NRPB	113 kECU	(Bi6-213)
2 Regulla	GSF	25 kECU	(Bi7-053)
3 Artalejo	CIEMAT	26 kECU	(Bi6-229)
4 Jacobi	GSF	55 kECU	(Bi6-111)
5 Stather	NRPB	55 kECU	(Bi6-116)

C12 Exposure to natural radioactivity and evaluation of parameters influencing these risks

Bi6-344-C12 1/1/90 - 30/9/90 9 Months (study contract) 35 kECU CEA - FAR *186*
Design and realisation of a calibration device for Rn-222 and its short-lived daughter products in air

1 Charuau	CEA - FAR	35 kECU

Bi6-347f-C12/Bi6-114/Bi6-314/Bi6-208 1/1/90 - 30/6/92 30 Months 568 kECU NRPB *187*
Radon sources and models (NRPB Association)

1 O'Riordan	NRPB	100 kECU	
2 De Meijer	Univ. Groningen	80 kECU	
3 Damkjaer	Univ. Denmark - Tech.	32 kECU	
4 Majborn	Risø National Laboratory	37 kECU	
5 De Mets	CSTC	37 kECU	
6 De Jong	TNO	37 kECU	
7 Ball	NERC	40 kECU	
8 Proukakis	Univ. Athens	40 kECU	
9 Enflo	Nat.Instit.Rad.Protection	35 kECU	
10 Kollas	NCRS "Demokritos"	30 kECU	(Bi6-114)
11 Quindós Poncela	Univ. Santander	50 kECU	(Bi6-314)
12 Galvào	LNETI	50 kECU	(Bi6-208)

Bi7-013-C12 1/09/90 - 31/08/92 24 Months 164 kECU Univ. Lund *190*
Retrospective assessment of radon exposure from long-lived decay products.

1 Samuelsson	Univ. Lund	50 kECU
2 Jonassen	Univ. Denmark Tech.	28 kECU
3 Falk	Nat.Instit.Rad.Protection	15 kECU
4 Poffijn	Univ. Gent	20 kECU
5 Vanmarcke	CEN/SCK Mol	20 kECU
6 McLaughlin	Univ. Dublin	31 kECU

Bi7-047-C12 1/5/90 - 30/4/92 24 Months 257 kECU Univ. Göttingen *192*
Characteristics of radon- and thoron daughters aerosols.

1 Porstendörfer	Univ. Göttingen	80 kECU
2 Poffijn	Univ. Gent	25 kECU
3 Vanmarcke	CEN/SCK Mol	25 kECU
4 Akselsson	Univ. Lund	50 kECU
5 Tymen	Univ. Brest	30 kECU
6 Falk	Nat.Instit.Radiation Protection	5 kECU
7 Ortega	Univ. Catalunya - Politécnica	42 kECU

Bi7-059-C12 under negotiation 18 Months 130 kECU Irish Geological Survey *196*
Assessment of the geological factors influencing the occurrence of radon hazard areas in a karstic region

1 O'Connor	Geological Survey (Irish)	40 kECU
2 Madden	NEB	30 kECU
3 McLaughlin	Univ. Dublin - College	15 kECU
4 McAulay	Univ. Dublin	15 kECU
5 Brock	Univ. Galway - College	0 kECU
6 Van den Boom	BGR	30 kECU

C13 Comparative assessment of exposure and risks

Bi6-122-C13 1/1/90 -31/12/91 24 Months 295 kECU CEA - FAR *199*
Consequences of irradiation of population and workers. (CEA Association)

1 Uzzan	CEA - FAR	295 kECU

Bi7-004-C13 1/5/90 - 30/4/92 24 Months 385 kECU CEPN *202*
Comparative assessment and management of the health and environmental impact of energy systems and studies related to the expression of the detriment associated with radiation exposure.

1 Lochard	CEPN	130 kECU
2 Wrixon	NRPB	25 kECU
3 Kemp	Univ. East Anglia	50 kECU
4 Friedrich	Univ. Stuttgart	80 kECU
5 Anguenot	CEA - FAR	100 kECU

C14 Epidemiological studies in human populations

Bi6-126-C14 1/1/90 -31/12/91 24 Months 37 kECU INSERM U.12 ..... *205*
Statistical methods for the analysis of geographical correlations, application to the analysis of the correlation between population radiation exposure and cancer mortality

1 Hémon	INSERM U.12	37 kECU

Bi6-221-C14 1/1/90 -31/12/91 24 Months 211 kECU GSF *206*
Epidemiological studies of radiation carcinogenesis and its biophysical basis (German Ra-224 study)

1 Gössner	GSF	211 kECU

Bi6-298-C14/Bi6-333/Bi6-055 1/1/90 -31/12/91 24 Months 226 kECU DKFZ *208*
Thorotrast: investigations to evaluate the long-term effects caused by artificial radiation in man (thorotrast patients follow-up study in Germany and Denmark)

1 Van Kaick	Deutsches Krebsforschungsz.	145 kECU
2 Jensen	Danish Cancer Society	60 kECU (Bi6-333)
3 Storm	Danish Cancer Society	21 kECU (Bi7-055)

Bi6-319-C14 1/1/90 -31/12/91 24 Months 45 kECU IARC *213*
Survey on childhood leukaemia.

1 Kaldor	IARC	45 kECU

Bi6-347h-C14 1/1/90 - 30/6/92 30 Months 370 kECU NRPB *216*
Statistical studies of radiation risks (NRPB Association)

1 Muirhead	NRPB	50 kECU
2 Kellerer	Univ. München	80 kECU
3 Chmelevsky	GSF	70 kECU
4 Oberhausen	Univ. Saarlandes	80 kECU
5 Holm	Inst. Karolinska	30 kECU
6 Becciolini	Univ. Firenze	60 kECU

Bi7-007-C14/Bi6-295 1/5/90 - 30/4/92 24 Months 577 kECU Univ. Gent *221*
Radon and Lung Cancer in the Ardennes and Eifel Region

1 Poffijn	Univ. Gent	80 kECU	
2 Tirmarche	CEA - FAR	120 kECU	
3 Wichmann	Univ. Wuppertal	80 kECU	
4 Kayser	Dir.de la Santé Div. Radioprot.	80 kECU	
5 Darby	Imperial Cancer Research Fund.	12 kECU	
6 Jacobi	GSF	90 kECU	
7 Clarke	NRPB	55 kECU	(Bi6-295)
8 Tirmarche	CEA - FAR	60 kECU	
9 Tymen	Univ. Brest	0 kECU	

C2 Optimization and Management of Radiation Protection

Bi6-324-C2 1/1/90 -31/12/91 24 Months 77 kECU ICRP *223*
Development of fundamental data for radiation protection

1 Smith	ICRP	77 kECU

C21 Optimisation of radiological protection

Bi6-347i-C21 1/1/90 - 30/6/92 30 Months 175 kECU NRPB *225*
Application of ALARA in complex decision-making situations (NRPB Association)

1 Wrixon	NRPB	50 kECU
2 Lochard	CEPN	75 kECU
3 Meggitt	SRD	50 kECU

C22 Reduction of patient exposure in medical diagnostic radiology

Bi6-342-C22 1/10/90 - 31/1/91 4 Months (study contract) 27 kECU Bundesamt f.Strahlensch. *227*
Establishment of a common protocol for the use of a whole body counter

1 Schmitt-Hannig	Bundesamt für Strahlenschutz	27 kECU
2 Proukakis	Univ. Athens	0 kECU
3 Barbina	Centro di Recerca e Document.	0 kECU
4 Cunningham	NEB	0 kECU

Bi6-347g-C22 1/1/90 - 31/12/91 24 Months 250 kECU NRPB *228*

Reduction of patient exposure in medical diagnostic radiology. Dosimetry and risk

1 Wall	NRPB	50 kECU
2 Drexler	GSF	100 kECU
3 Kramer	PTB	50 kECU
4 Broerse.	TNO - Rijswijk	50 kECU

Bi7-014-C22/Bi6-343 1/7/90 - 30/6/92 24 Months Bi7-014 ..... *231*

Bi6-3431 1/1/90 - 31/12/91 24 Months 40 kECU Feder. Dublin Voluntary Hosp.

Quality criteria, tolerances, limiting values, dosimetry and optimization in a number of fluoroscopic, digital fluoroscopic, DSA and digital radiological systems.

1 Malone	Hosp. Federated Dublin Volunt.	60 kECU
2 Boddy/Faulkner	Regional Radiation Physics Newcastle	40 kECU
3 Busch	Univ. Heidelberg	40 kECU
4 Schmidt	Univ. Erlangen- Nürnberg	30 kECU (Bi6-343)

Bi7-019+ Bi6-132-22/Bi6-136/Bi6-211 ..... *235*

1/4/90 - 31/3/92 24 Months Bi7-019

1/1/90 - 31/12/91 24 Months Bi6-132/Bi6-211/Bi6-214/Bi6-136
449 kECU CAATS-INSERM

Quality assurance and reduction of patient exposure.

1 Fagnani	CAATS-INSERM	95 kECU (Bi6-132)
2 Moores	Integrated Radiological Serv. Liverpool	50 kECU
3 Alm Carlsson	Univ. Linköping	40 kECU
4 Dance	Hosp. Royal Marsden	11 kECU
5 Proimos	Univ. Patras	13 kECU
6 Flioni-Vyza	Greek Anticancer Institute	20 kECU
7 Rimondi	Univ. Ferrara	40 kECU
8 Fendel	Univ. München - Kinderklinik	60 kECU (Bi6-211)
9 Vano Carruana	Univ. Madrid - Complutense	70 kECU (Bi6-214)
10 Padovani	Serv. Fisica Sanit. Udine	50 kECU (Bi6-136)

Bi7-054-C22 1/9/90 - 29/2/92 18 Months 80 kECU Univ. Bruxelles (VUB) *243*

Diagnosis related doses: a comparative investigation in some European hospitals

1 Van Loon	Univ. Bruxelles (VUB)	45 kECU
2 Thijssen	Univ. Nijmegen	35 kECU

Bi7-057-C22 1/9/90 - 29/2/92 18 Months 90 kECU Univ. Lund *245*

Patient dose from radiopharmaceuticals

1 Mattsson	Univ. Lund	30 kECU
2 Smith.	MRC	30 kECU
3 Henrichs	GSF	30 kECU

Bi7-Proposal 328-C22 under negotiation 12 Months 20 kECU

Univ. Aarhus - Hospital *247*

Quality criteria and dose reduction in diagnostic radiology with emphasis on computed tomography

1 Jessen	Univ. Aarhus - Hospital	20 kECU
2 Galvão	LNETI	20 kECU

C24 Probabilistic risk assessment and real-time models for assessing the consequences of accidental releases and for evaluating the effectiveness and feasibility of countermeasures

Bi6-128-C24/Bi6/127/Bi6-125/Bi6-227 1/1/90 -31/12/91 24 Months 616 kECU KfK *249*

Methodology for evaluating the radiological consequences of radioactive materials released in accidents including uncertainty analysis and economic impact.

1 Kessler	KfK	235 kECU (Bi6-128)
2 Cooper	NRPB	186 kECU (Bi6-127)
3 Hofer	GRS	130 kECU (Bi6-125)
4 Alonso	Univ.Politéchn. Madrid	65 kECU (Bi6-227)

Bi7-010-C24 1/6/90 - 31/5/92 24 Months 190 kECU AEA Technology *253*

Deposition of radionuclides and their subsequent relocation in the environment following an accidental release to the atmosphere.

1 Underwood	AEA Technology	80 kECU
2 Roed	Risø National Laboratory	50 kECU
3 Paretzke	GSF	50 kECU
4 Nixon	AEA Technology	10 kECU

Bi7-012-C24 1/9/90 - 31/8/92 24 Months 110 kECU TNO - Apeldoorn *256*

RADE-AID, the development of a Radiological Accident DEcision AIDing system.

1 Wagenaar	TNO - Apeldoorn	60 kECU
2 Ehrhardt	KfK	10 kECU
3 Morrey	NRPB	40 kECU

Bi7-015-C24 1/7/90 - 30/6/92 24 Months 100 kECU Risø National Laboratory *258*

Indoor deposition and relationship between indoor and outdoor air concentration

1 Roed	Risø National Laboratory	50 kECU
2 Goddard	ICSTM	50 kECU

Bi7-017-C24 1/8/90 - 31/7/92 24 Months 70 kECU Risø National Laboratory *261*

Validation- training- and uncertainty-study experiments for real-time atmospheric dispersion models.

1 Mikkelsen	Risø National Laboratory	60 kECU
2 Werner	DLR Deutsche Forschungsanst.	10 kECU

Bi7-045-C24/Bi6-106/Bi7-062 1/11/90 - 31/10/92 24 Months 650 kECU KfK *262*

Development of a comprehensive decision-aiding system for the off-site emergency management.

1 Ehrhardt	KfK	70 kECU
2 Robeau	CEA - Fontenay-aux-Roses	80 kECU
3 Bartzis	NCRS "Demokritos"	100 kECU
4 Caracciolo	ENEA	60 kECU
5 ApSimon	ICSTM	80 kECU
6 Thykier-Nielsen	Risø National Laboratory	50 kECU
7 Paretzke	GSF	50 kECU
8 Persson	Swedish Meteorol.Hydrol.Inst.	30 kECU
9 Goevarts	SCK/CEN	90 kECU (Bi6-106)
10 Ratti	Univ. Pavia	40 kECU (Bi7-062)

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ANNEX III: GEOGRAPHICAL DISTRIBUTION OF CONTRACTS

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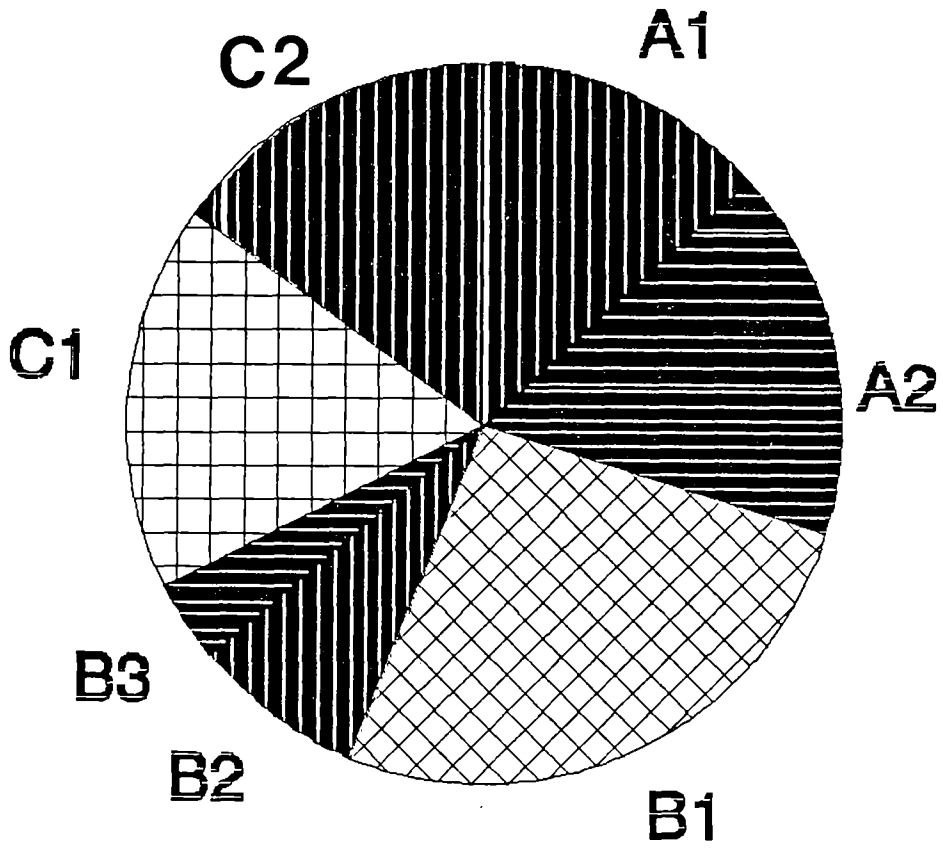

1 Distribution of funds among the sectors of the Programme

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