increasing the quality of life. A prospective trial to test decision making with the model versus a controlled group with standard treatment is the next step towards implementation of a decision support system for rectal cancer.

**SYMPOSIUM: FUTURE RADIOTherAPY CLINICAL TRIALS: SALT, PAPRIKA AND MOLECULAR SIGNATURES AND RT**

**SP-0423**
The implications & challenges for clinical trial design involving radiotherapy

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Modern radiotherapy research is built on well validated biological and physical hypotheses which will be tested in the clinical trial. The trial design must enable the investigator to obtain a clear answer to the primary trial objective, through clear enunciation of the primary hypothesis, the endpoint to be measured and an appropriate statistical design to enable the hypothesis to be evaluated in a way which is reliable. The extreme heterogeneity of cancer is leading some investigators to think that conventional clinical trial methodology is outmoded and that fundamentally different approaches are required. Individualisation of therapy on the basis of tumour genotype, imaging or both is portrayed as the goal of modern cancer therapy. Individualisation of radiotherapy occurs in every case through the treatment planning process and within clinical trials this must be undertaken within the constraints of a prospectively optimised and agreed radiotherapy treatment protocol and commensurate RT quality assurance process to be delivered before and during the trial. Similarly biomarker or imaging based treatment allocation or randomisation requires the use of rigorous technical delivery of the assay or scan and an agreed method of interpretation of the outcome. In phase I drug radiation trials, delays while waiting for assessment of radiotherapy toxicity risk making such studies too slow and relatively early dose escalation and ‘flip-flop’ design evaluating two novel agents in alternating dose escalation cohorts is an efficient design. Multi-stage trial designs can speed up the phase II/III evaluation of novel therapies, while enabling early termination for futility. The SCOPE-1 trial of the addition of cetuximab to chemoradiotherapy for oesophageal cancer is an example. Prospective molecular stratification of patients for intervention trials relevant to the specific abnormalities in their tumour can be designed but require extensive collaboration and large numbers. Such designs are coming into stratified drug trials such as the FOCUS4 study in metastatic colorectal cancer and the applicability to radiotherapy studies will be discussed.

**SP-0424**
Fractionation protocols in the age of targeted therapies: how should we change and how?

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**SYMPOSIUM: METHODS FOR QUALITY MANAGEMENT**

**SP-0425**
Molecular imaging as biomarker in future clinical trials: The proof of the pudding is in the eating

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Integration of molecular imaging techniques into therapy selection strategies and radiation treatment planning can serve several purposes. First, pretreatment assessments can steer decisions about radiotherapy modifications or combinations with other modalities. Second, biology-based objective functions can be introduced to the radiation treatment planning process by co-registration of functional imaging with planning CT-scans. Thus, customized heterogeneous dose distributions can be generated with escalating doses to tumor areas where radiotherapy resistance mechanisms are most prevalent. Third, monitoring of temporal and spatial variations in these radiotherapy resistance mechanisms early during the treatment can discriminate responders from non-responders. With such information available shortly after the start of the treatment, modifications can be implemented or the radiation treatment plan can be adapted tailing the biological response pattern.

Currently, these strategies are in various phases of clinical testing, mostly in single-center studies but more and more also in multi-center set-up. Ultimately, this should result in availability for routine clinical practice requiring stable production and accessibility of tracers, reproducibility and standardization of imaging and analysis methods and general availability of knowledge and expertise. Small studies employing adaptive radiotherapy based on functional dynamics and early response mechanisms demonstrate promising results. This approach is closest to large scale clinical testing with good prospects for success.
The role of quality and safety in radiation therapy

1) The role of quality and safety in radiation therapy operations

2) Modern approaches to quality management which are adoptable to radiation therapy operations

3) The role of automation, decision support, and knowledge-based tools for management of safety and quality in radiation therapy

Monitoring of quality in radiotherapy using external audits

It has been estimated (UNSCEAR, 2000) that there are worldwide about 2000 million X-Ray studies, 32 million nuclear medicine studies and over 6 million radiation therapy treated annually, and the numbers are constantly increasing.

The process of radiotherapy (RT) is complex and involves understanding of the principles of medical physics, radiobiology, radiation safety, dosimetry, radiation treatment planning, simulation and interaction of radiation with other treatment modalities. Each step in the integrated process of RT needs quality control and quality assurance (QA) to prevent errors and to give high confidence that patients will receive the prescribed treatment correctly. Recent advances in RT, including intensity-modulated and image-guided RT, focus on the need for a systematic RTQA program that balances patient safety and quality with available resources. It is necessary to develop more formal error mitigation and process analysis methods, such as failure mode and effect analysis, to focus available QA resources optimally on process components. External audit programs for RT can serve to improve patient safety and quality of care, and thus are also effective; these can be found in some national or international regulatory authorities and professional societies.

In addition to an on-site audit, an off-site audit, such as a postal dosimetry audit program, is necessary to assure the dose from RT equipment. For more than three decades, some international authorities and national/continental professional societies have operated some independent dosimetry audits (post nasal thermoluminescent dosimetry (TLD) or radiochromic films dosime-tic-aiding programme) for more than 2000 RT institutions in 120 countries. A global and steady improvement in the performance of dosimetry audits has been occurring to such that 95% of the participating institutions are within the 5% acceptance limit for beam calibration.