The ULICE project started in 2009 to address two different complementary issues: the development of the appropriate instruments for hadrontherapy, with emphasis on carbon ion therapy, and the need for intensive collaboration among the existing and planned centres, as well as with the European hadrontherapy community at large. ULICE was funded by the European Commission and involved 20 European institutions coordinated by CNAO in Pavia. All the existing and planned European ion therapy facilities were involved in the project, together with two research centres (CERN and GSI) and industrial companies. The approach of ULICE to hadrontherapy dealt with all its aspects from medical physics to radiobiology, from accelerators to particle beams in clinics. The experience being built up in Heidelberg (HIT), with more than 2000 patients treated, and Pavia with more than 500 patients treated, helped the development of hadrontherapy in Europe and provided patients throughout Europe access to these centres with treatment according to standardized protocols. In addition, other centres planned in Europe (MedAustron) which are due to start, were benefit from this experience. One of the most relevant results of the ULICE project was the establishment of an international board - IONTREB International Ion Beam Therapy Research Board - focusing on clinical aspects of the hadrontherapy. The project consisted of 3 pillars, Joint Research Activities - focused on the development of instruments and protocols, Networking - to increase cooperation between facilities and research communities, and Transnational access - to allow access to hadrontherapy facilities to researchers wanting to perform radiobiological and physics experiments as well as clinical studies. The Joint Research Activities was coordinated by the Medical University of Vienna and focused on improving the performance of hadrontherapy facilities through the development of various instruments. The JRA pillar dealt with clinical issues such as developing novel adaptive treatment planning, including clinical protocols that combine different types of irradiations, and developing a computer assisted patient selection program accessible to the whole European community; this was not only enable an efficient patient referral to the existing facilities, but also allow to pursue the clinical research focused on tumours with specific biological characteristics and/or critical location. These tools provided a research infrastructure producing scientifically sound evidence on the efficacy of hadrontherapy. Among the technical issues that ULICE will address through JRA is the challenge of reducing the dimensions and cost of the gantries. The Networking Activities pillar was coordinated by CERN and focuses on communication, interaction and interdisciplinary discussion among the 20 partners and with the external world, and dissemination of the project results to the wider community involved in cancer care. Networking activities provided the external research community with a clear knowledge of what is possible and what is needed in terms of research to be carried out at the facilities (both through dissemination activities, residential training for researchers and through scientific events and publications). The Transnational Access was coordinated by the University Hospital of Heidelberg, and aims at providing access, at HIT and CNAO, for external researchers to the ion therapy facilities for preclinical research with the available beams of particles. Beam time was allocated to the external researchers through a review committee, that assessed the scientific impact of the proposed research project. The Transnational Access pillar also produced agreed protocols for multi centric clinical trials, and allowed external researchers to participate in these trials. These goals were facilitated making an extensive use of advanced e-science grid technology.

SP-0305
Role of proton therapy in the treatment of paediatric malignancies
B. Timmermann

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Radiation therapy represents an important part of multimodal cancer therapy in children. Due to increasing efficacy of cancer therapy overall treatment outcomes considerably improved. Over the last about 50 years the situation in childhood malignancies has changed from an inevitably fatal condition to one that is potentially curable, with overall 5-year survival rates approaching 80%. However, it is well understood that growing tissues are particularly sensitive to radiation injury. The burden of multimodal treatment consisting often of surgery, cytotoxic and radiation therapy jeopardizes the future life of the patients. Therefore, reduction of late sequelae and improvement of quality of life have become a major concern in paediatric cancer survivors.

Proton beam therapy (PT) has become of increasing interest in paediatric oncology. Several dosimetric studies clearly demonstrated that PT can better limit the irradiated volume as compared to photon technique. Therefore, PT is a promising method to reduce the risk for acute and late effects, especially with regard to paediatric tumors. Over the last decades clinical experience in PT in childhood cancer was restricted due to limited availability and very few facilities being hospital based. So far, prospective approaches were missing, cohorts were small and observation times short, especially with regard to very young children being treated with PT. However, the number of children being treated with protons for solid tumors is currently increasing due to a growing number of proton facilities being in operation worldwide. In Europe and US common indications for treatment with PT in the paediatric cohort are as well local tumors of central nervous system (CNS) (i.e. glioma, medulloblastoma, ependymoma, craniopharyngeoma, and intracranial germ cell tumors) as non-CNS tumors (i.e. chordoma/chondrosarcoma, and rhabdomyosarcoma).

Treatment results are promising with regard to local control rates. Recent data on neurocognitive functioning and quality of life seem to confirm favourable outcome after PT. Additional, first experiences suggest that secondary cancer induction can be reduced when using PT. Still, more clinical data will need to emerge and to quantify the clinical benefit of PT. Therefore, PT should be established in a prospective approach within multimodality cancer concepts to ensure optimal treatment and careful future evaluation.

SP-0306
New radiation techniques in paediatric cancers (proton excluded)
S. Bolle
University College London Hospitals NHS Foundation Trust, selectively decreased by the means of IMRT, low dose is usually defined as metastatic disease over the age of one M.N. Gaze IMRT provided local control equivalent to 3D CRT with irradiation of very sensitive organs at risk located at distance of secondary malignacies or unexpected toxicities related to raised in the rest of the body with theoretical increased risk decreased clinical and planning target volume margins. Integration of multimodal imaging in target delineation, use of CT for treatment planning (3D conformal radiation therapy) and immobilization devices have significantly decreased clinical and planning target volume margins. Intensity modulated radiation therapy could be particularly useful in cases of complex and large volume closed to critical structures. While high dose to neighboring structures can be selectively decreased by the means of IMRT, low dose is raised in the rest of the body with theoretical increased risk of secondary malignancies or unexpected toxicities related to irradiation of very sensitive organs at risk located at distance of target volume. Number of prospective studies comparing IMRT to 3D CRT is low. However available data suggest that IMRT provided local control equivalent to 3D CRT with favorable short term toxicity profile and reduction of some sequelae. No excess of second tumor is described but follow-up is still limited.

Concerning strategies for management of internal target movement due to respiratory motion, the more widespread modality in pediatric radiotherapy is 4-dimensional CT for radiation. Other techniques such as active breathing control or respiratory gating is not widely widespread because their use is conditioned by collaboration ability and patient age. Up to now stereotactic radiation therapy has been mainly used in childhood for intracranial benign disease by neurosurgeon. However development of non-invasive repositioning system and LINAC dedicated to stereotactic irradiation gives the opportunity of hypofractionated treatment of metastasis or recurrence in previously irradiated field with minimal impact of quality of live in palliative setting.

With high precision techniques, reproducibility in daily set-up becomes more critical to prevent geographic misses and image-guided RT (IGRT) has become a common practice of care for children as for the adults. One of the most applied IGRT technique is cone-beam computed tomography (CBCT). A limitation in use of CBCT among pediatric population is the extra dose deposit to critical structures which is higher in children than in adults. Because of potential of yielding a secondary cancer at long term, it is essential to adapt scanning protocol when CBCT is applied to pediatric cancer patients routinely.

SP-0307
131-Iodine meta-iodobenzylguanidine molecular radiotherapy for neuroblastoma
M.N. Gaze
Institut Gustave Roussy, Radiation Oncology, Villejuif, France

Despite late complications related to radiation therapy, RT remains a standard component of treatment among pediatric patients. The current aim of many pediatric clinical trials is to reduce dose and volume of irradiation to decrease side effects without affecting the rate of local control using multimodality treatment.

Recent advances in radiotherapy technology contribute also to improve therapeutic ratio thanks to better conformal dose distribution and avoidance of surrounding critical structures.

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M.N. Gaze
University College London Hospitals NHS Foundation Trust, Clinical Oncology, London, United Kingdom

Neuroblastoma, predominantly a cancer of young children, is derived from the sympathetic nervous system. Patients are risk-stratified by age, stage and molecular pathology to guide treatment and predict outcome. High-risk neuroblastoma, usually defined as metastatic disease over the age of one year, or the presence of MYCN amplification, is the most common risk group, and carries a high mortality. New and better treatments are necessary.

Neuroblastoma cells usually express the Noradrenaline Transporter (NAT) molecule which takes up meta-iodobenzylguanidine (mIBG), a noradrenaline analogue. Labelled with iodine-123 for imaging or iodine-131 for therapy, mIBG has been used clinically in neuroblastoma and other NAT expressing tumours for about 30 years. Semi-quantitative scoring of 123I-mIBG scintigraphy has become the gold standard imaging technique for staging, response assessment and follow-up of patients with neuroblastoma.

Molecular radiotherapy with 131I-mIBG is an attractive treatment option for children with high-risk metastatic neuroblastoma because (1) the disease is disseminated, making local therapies alone inadequate, (2) 123I-mIBG scintigraphy is a predictive imaging biomarker for avid accumulation of 131I-mIBG in the primary tumour and metastatic sites, and (3) neuroblastoma is often relatively radiosensitive meaning impressive responses to treatment can be seen.

Initially used in relapsed patients with only palliative intent, the use of 131I-mIBG therapy has in recent years been brought forward in the course of the illness as either a first- or second-line strategy with the aim of increasing the prospects for cure. Further research efforts, especially randomised trials, are however needed to demonstrate its true value.

The principal and therefore dose-limiting toxicity of 131I-mIBG therapy is haematological. The whole body absorbed radiation dose correlates with the haematological toxicity, and so whole body dosimetry can be used, in conjunction with peripheral blood stem cell support, to allow the use of higher administered activities than were previously considered safe. There is laboratory evidence to support the hypothesis that improvements in outcome may possibly be achieved by the simultaneous use of radiosensitising drugs such as topoisomerase I inhibitors. Initial clinical experience has been published, and clinical trials using irinotecan and topotecan in conjunction with 131I-mIBG are in progress or planned to evaluate this approach further.

There are practical challenges when young children need to receive high administered activities of 131I-mIBG. The use of comforters and carers, usually the child’s parents, is an essential addition to medical and nursing care. All individuals involved need to appreciate the risks, and be trained in sensible radiation protection precautions.

Other forms of molecular radiotherapy for neuroblastoma are being investigated, particularly peptide receptor radionuclide therapy targeting the somatostatin receptor, using radio labelled somatostatin analogues. Examples are 90Y-DOTATOC and 177Lu-DOTATATE. These are not necessarily alternatives to 131I-mIBG therapy. Both immunohistochemical studies of NAT and somatostatin receptor expression in neuroblastoma tissue, and imaging comparisons of 123I-mIBG scintigraphy and 68Ga-DOTATATE PET/CT demonstrate a heterogeneity of appearances suggesting that they may be complementary.

This presentation reviews the published evidence in relation to 131I-mIBG therapy for neuroblastoma, and describes the plans to further evaluate its place through clinical trials in the context of other systemic treatments for this hard-to-cure disease.

OC-0308
Identification of significant biological subvolumes from MRI in pediatric ependymoma related to treatment outcome

1Institut Gustave Roussy, Radiation Oncology, Villejuif, France
2University College London Hospitals NHS Foundation Trust, Clinical Oncology, London, United Kingdom

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