EP-1415
Craniaw irradiation and sleep disorders in children with brain tumour: a case-control study
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Purpose or Objective: Brain tumours as many other neurological diseases may cause sleep problems interfering with the delicate mechanisms of sleep regulation. The presence of a disturbed sleep may have material daily performance effects. In growing subjects this aspect may determine emotional and behavioral problems. The prevalence of sleep disorders (SD) in children with brain tumours is unknown. The main aim of this study is to compare the prevalence of SD in children affected by brain tumours and treated with radiotherapy to the prevalence of SD in children treated only surgically.

Material and Methods: A retrospective case-control study was performed from October 2014 to April 2015 in a Pediatric Department and in a Pediatric Radiotherapy Centre. “Cases” included patients 2 to 16 years old with a diagnosis of CNS tumour at least 3 months after treatment conclusion (surgery and radiotherapy and/or chemotherapy). “Controls” were children 2 to 16 years old with CNS tumours treated only surgically. Children’s sleep quality was assessed with a questionnaire administered to parents (Child’s Sleep Habits Questionnaire, CSHQ). The sleep was considered disturbed if at least one of the following events was present: sleep delay, sleep duration, sleep-related anxiety, night waking, parasomnias and respiratory disorders. The risk of SD was estimated by the Odds Ratio (OR) and their 95% confidence intervals (95% CI) through logistic regression models.

Results: We enrolled 14 cases and 14 controls, for a total of 28 subjects. 9 out of 14 children in “case” group were treated with surgery, radiotherapy and chemotherapy. Our results highlighted a prevalence of SD of 57.4% among cases and 42.9% in controls. A statistically significant difference between the two groups (OR= 1.78 CI: 0.40-7.94) was not reached.

Conclusion: Cranial irradiation is required to treat many brain tumours in children. Some studies involving only children with midline tumours show that high-dose cranial irradiation in midline site in childhood is associated to objective and subjective changes in the sleep-wake rhythm in adulthood. Our study failed to show a statistically significant difference in SD between the two groups, but there is evidence of a greater prevalence among children treated with radiotherapy. Limitations of the study include the small number of patients involved and the lack of irradiation details, age and dose site. We expect that a relationship between cranial irradiation and SD will be statistically confirmed increasing the number of involved patients. We hope to better define the relationship with irradiation dose and site, as brain tumour position and consequent irradiation may have a role on SD development.

EP-1416
Analysis of childhood brain tumours treated with radiosurgery/stereotactic fractionated radiotherapy
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Purpose or Objective: The aim of the study is to evaluated data from radiosurgery (RS) and fractionated stereotactic radiotherapy (FSRT) performed in patients from 0 to 14 years of age in the Hospital Araújo Jorge, Goiânia, Goiás, Brazil, treated between 2000 to 2013.

Material and Methods: The authors retrospectively assessed medical reports of 65 patients from 0 to 14 years of age with diagnosis of brain tumors and who underwent RS/FSRT from 2000 to 2013. The analysis concerns age at diagnosis, primary location of the tumor, size of the tumor, risk assessment, and employment of either RS or FSRT.

Results: From the 65 records, 42 were included in the analysis for having all the information desired. Of those patients, 46.3% were male and 69.0% were diagnosed with malignant tumors. 29.3% of the patients were between 0 to 6 years, 31.7% between 7 to 10 years, and 39.0% between 11 to 14 years of age. The most frequent histopathological diagnoses were medulloblastoma (19.0%), arteriovenous malformation (14.3%), and glioma (11.9%). As for the treatment, 78.5% underwent to FSRT and 21.5% underwent to RS. The median total radiation dose prescribed dose was 54 Gy for the FSRT and 18 Gy for the RS. The most frequent prescription dose curves were 90% and 95%, respectively, whilst the conformity index for the RS varied from 1.23 to 2.04. It resulted in 42.9% of the patients having partial response to the performed treatment and 78.6% not having distant disease progression. The overall survival was 58.1 months for patients from 0 to 6 years, 69.3 months for those from 7 to 10 years, and 90.2 months for those in the 11 to 15 years range (p<0.037).

Conclusion: The results show a 13 years experience on treating pediatric tumors with RS/FSRT of that single institution. High precision conformal stereotactic techniques with RS/FSRT employing conservative margins than conventional radiotherapy in childhood tumors appears to be safe based on our experience. Long term prospective trials are required to test their real potential in sustaining local control and minimising treatment related acute and late morbidity.

EP-1417
ANDANTE: second cancers from neutrons following proton therapy: preliminary epidemiological results
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Purpose or Objective: Survivors of childhood cancer generally have an increased risk of developing secondary cancers associated with the treatment for the first primary cancer. Proton therapy represents a highly effective treatment technique for some types of childhood cancers but scattered radiation from secondary neutrons is an unwanted by-product.

Material and Methods: The ANDANTE project investigates the relative risk of neutrons compared to photons for tumorigenesis, as a function of dose and energy. The approach is multidisciplinary, including physical measurements and modeling, molecular biology, radiobiology and epidemiology. Based on stem cells irradiated in vitro with either photons or neutrons, a corresponding predicted model of the relative risk of cancer induction from photons or neutrons following pediatric radiotherapy is developed and tested on clinical data, leading to a proposal for a prospective epidemiological study to validate the relative risk of neutrons on the tumorigenesis in humans. The progress on the epidemiological aspects of this current work is reported here.

Results: In order to validate the dose-risk model developed earlier in the project, a feasibility study with clinical data from the Loma Linda University Medical Center was performed. A cohort of 242 patients was constituted in August 2013. Those patients were treated between 1991 and 2013, diagnosed with arteriovenous malformation (AVM) (n=108) or low grade astrocytoma (n=134) before the ages of 30 years, and were followed up later. All variables for statistical analyses were available but data extraction has not been finished yet. Results of this feasibility study will provide a basis for the development of the prospective.
epidemiological study, and will be used to test the validity of
a predictive risk model based on values of neutron RBE which
will be derived from the physics task in the ANDANTE project.
Based on the experience from the feasibility study at LUMC,
a proposal for a prospective epidemiological study using
pediatric proton therapy data collected from multiple proton
centers worldwide is prepared. For this purpose, published
results of epidemiological studies on second malignancy
neoplasms (SMN) after radiotherapy in childhood are reviewed.
Up to now, 57 papers were identified from 2001
until present with the objective to estimate the magnitude of
the effect of radiation exposure on the occurrence of SMN.
Furthermore, European proton therapy centers were
contacted in order to assess the feasibility of creating a
prospective database on pediatric patients. Five out of
thirteen proton therapy centers already replied, showing
great interest in preliminary participation in discussion on
forming a future prospective study.

Conclusion: This will be essential for investigating the far
reaching goal to enhance our understanding of the link
between radiation exposure to proton therapy and the risk of
SMNs.

EP-1418
Proton therapy in paediatric oncology - An Irish
perspective
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Purpose or Objective: To: (1) produce a descriptive study of
Irish children referred abroad for proton therapy (PT), and
(2) to discuss the case for PT in general.

Material and Methods: A retrospective review of all children
referred for PT before October 2015 was performed.
Information was gathered regarding general demographics,
diagnosis, tumour grade, other treatments, the PT referral
timeline, relapse where relevant, side effects attributable to
PT, current status and cost of treatment to the Irish state.
Additionally, a review of the relevant literature was performed.

Results: Sixteen children treated in Ireland have been
referred abroad for PT to date, with numbers increasing yearly.
The largest number referred was in the 0-4 year old
group. At initial diagnosis the median age was 5.0 years. Four
patients were referred for treatment of rhabdomyosarcoma,
3 for craniopharyngioma, 6 for intracranial ependymoma and
1 each for treatment of meningioma, germinoma and ATRT.
The average cost per child has been approximately €52,000.
Two patients suffered relapse of their disease - 1 has proven
fatal and the other is alive with disease. Four patients have
encountered PT-related adverse effects. The time from
referral to treatment has improved from 11 to 6 weeks
approx.

Conclusion: Despite the fact that >100,000 patients
worldwide have been treated with PT, the current level of
published evidence to support superiority over conventional
treatment remains low. Planning studies have clearly
demonstrated superior conformity and reduced risk to
normal tissues. It is debated that randomised control trials in
this area would be inconsistent with the principle of clinical
equipoise. In contrast, there is a call for level 1 evidence to
justify such drastic changes in patient care, particularly in
the light of recent reports of unexpected toxicities. If PT
were more widely available, the question remains in which
clinical situations would it be likely to show substantial
clinical and cost benefit? As no firm conclusions can be
derived from the literature, the answer is somewhat
speculative. In time, careful evaluation, follow-up and
clinical trials will likely support the argument for the
preferential use of proton therapy in children. Our challenge
remains: how best to use it in the meantime?

EP-1419
Proton irradiation in childhood and adolescence at
RINECKER Proton Therapy Center (RPTC)
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Purpose or Objective: In the multimodal treatment concept
for pediatric tumors the implementation of radiotherapy with
protons gains more and more importance due to their
outstanding radiobiological, physical and technical
characteristics. In particular the fact, that about 60% of the
irradiated volume of conventional radiotherapy are not
burdened by proton therapy, results in a considerable
reduced incidence of side effects with lowering the negative
impact on growth and development and a lower rate of
secondary malignancies. The German Society for Radiation
Oncology (DEGRO) clearly recommends preferably proton
therapy in the treatment of pediatric patients.

Material and Methods: Analysis of children and adolescents
undergoing proton radiation therapy since start of the RPTC
2009 (time period from Jun 2009 to Sep 2015). A highly
complex three-dimensional electromagnetic proton beam
control system (spot scanning) can applies the tumor dose
only to the planned target volume and spares surrounding
healthy tissue without significant neutron exposure to the
whole body. There is a wide range of free variety of dose
intensity to each spot.

Results: From 06/2009 to 07/2015 a total of 82 patients were
previously treated at the RPTC in 88 cases. The mean age at
start of irradiation was arithmetically 7.9 years (min. 11mo.;
max. 17y. 7mo.). These were mostly rhabdomyosarcomas
(RMS; n = 26 [29.5%]), of which 10 were alveolar and 16 were
embryonal RMS. In the field of central nervous system, 14
patients with low grade gliomas [16%], 11 high grade gliomas
[12.5%], 10 ependymomas [11%] and 2 medulloblastomas
were treated. From 12 cases with rare tumor types, 8 were
also localized in the CNS. 6 patients had chordoma and
chondrosarcoma, 5 Ewing tumors and 2 rare types of soft
tissue sarcomas.

Conclusion: At the field of pediatric oncology radiotherapy
with protons using spot scanning technology is certainly
feasible and a highly effective treatment method with
significantly lower toxicity of normal tissue. There is a close
coeoperation with the Children's Hospital of the Municipal
Hospital Munich/ Hospital of Munich Technical University for
the integration of multimodal therapy studies or to treat in
analogy with rule-based case discussions in interdisciplinary
tumor conferences.

EP-1420
Cyberknife® radiotherapy for recurrent or oligometastatic
tumours in children and adolescents
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Purpose or Objective: Despite the increasing availability of
sterotactic ablative body radiotherapy (SABR) and
sterotactic radiosurgery (SRS) there remains a lack of
evidence regarding their indications and role in the
treatment of recurrent & oligo-metastatic tumours in
children, teenagers & young adults (TYA).

Material and Methods: A retrospective review of paediatric
and TYA patients (age ≤24 years) treated with SRS or SABR
at The Royal Marsden Hospital from 2010 to 2015 was