PAUL SCHERRER INSTITUT

SpotOn+

Center for Proton Therapy :: Paul Scherrer Institut :: #2_3/2014

Dear Colleagues

Welcome again to this second edition of this newsletter. It is a pleasure to inform you that our first patient was treated with our new treatment unit, Gantry 2 in November 2013. Gantry 2 is an iso-centric compact gantry with a diameter of only 7.5 m, much smaller than any other gantries, which have diameters of approximately 10–12 m. More importantly however, Gantry 2 uses the same magnetic spot-scanning technique as Gantry 1, but is designed for the implementation of advanced fast parallel-beam scanning. This fast scanning (change of energies in less than 100 ms) enables the system to perform fast volumetric repainting, an important strategy for delivering a more robust dose distribution to moving organs. In addition, the new gantry is optimized to have a small spot size down to the lowest energies, and as the scanning magnets are installed before the last bending magnet, the beam is free from divergence over the whole scanning area. The clinical operation of this treatment unit is a major milestone for the Center for Proton Therapy and puts PSI once more at the forefront of proton therapy innovation.

In this edition of the newsletter, the clinical results obtained with pencil-beam scanning (PBS) proton therapy for parameningeal PMS will be detailed. For these high-risk patients, the outcome after PBS is remarkably good, with a 5-year tumor control of › 70% with univariate analysis indicating that the only significant factor was the timing of radiation therapy, stressing the importance of this treatment modality. In a second contribution, Dr Albertini reports on studies into the effects of range uncertainties introduced by titanium rods on PBS treatments. Interestingly, the artefacts, provided that they are managed appropriately during the planning process, induces no major dose degradations for PBS plans, which will come as good news for many chordoma or chondrosarcoma patients with implants. Finally, Dr Hrbacek details his current project, the clinical implementation of an automated treatment planning system for the treatment of uveal melanomas. Should this project prove to be successful, the manual aspect of the overall planning procedure would be minimized, potentially improving the overall treatment quality for these challenging eye tumors.

Please share any information in this newsletter with your colleagues, as the content is intended to be shared as much as possible, and please do not hesitate to contact me or one of my team on any clinical questions or other PBS-related matters.

Sincerely,

Prof. Damien Charles Weber, Head of CPT

Radio-Oncology News

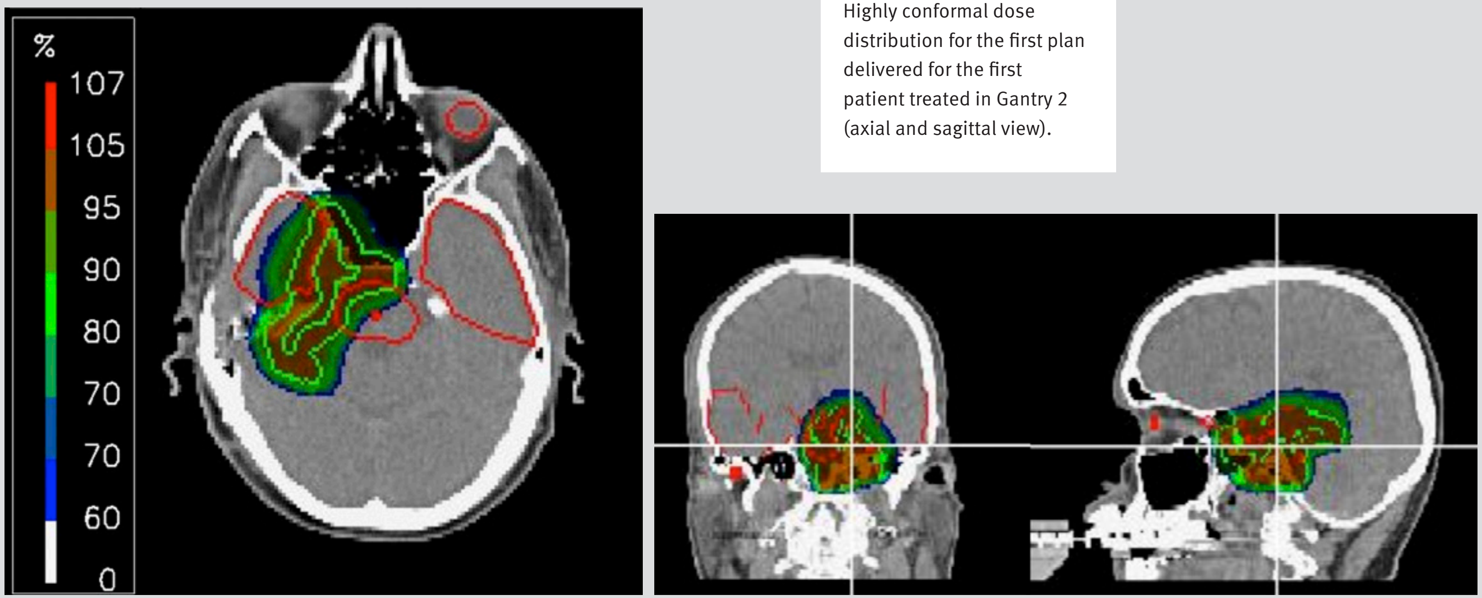
Gantry 2 came into operation – First clinical experience

The next generation of scanning gantry at PSI, Gantry 2, was ready for clinical use in November 2013. After the clinical commissioning, setting-up of the quality assurance program and obtaining the permission for clinical use from the authorities, the first patient started his treatment on the 25th of November. He is a 49 year old, male Swiss patient presenting with a Meningioma, who was treated, as usual in ambulatory setting, up to 54 Gy(RBE) in 30 fractions (see figure for dose distribution). Meanwhile the treatment was finished without any interruption beginning of January 2014 and was well tolerated by the patient.

The next patient, a 14 year old boy with an ependymoma has started proton radiation with Gantry 2 in January, as well as a 58 year old men diagnosed with a clivus chordoma. Both patients are in good conditions and the treatment will finish these days.

Patients in Gantry 1 are treated with remote positioning, as the daily images (topograms) are acquired on the CT used also for planning, which is located outside of the bunker. The patient is positioned on the couch with all the fixating devices in the preparation area, then he or she is transported to the CT for daily images and afterwards in the Gantry 1 room for treatment. For Gantry 2 we have a different approach as the positioning is taking place in the Gantry 2 bunker, where also a sliding CT is present and it is used to acquire planning CTs and daily images. Additionally a beam's-eye-view X-ray system is installed for positioning control at the gantry. Patients can now be optimally accessed in every treatment configuration due to the iso-centric layout of Gantry 2. Combining the rotation of the Gantry 2 and the movement of the table, the patient can be treated from all the directions. Due to the spot size the dose distributions for Gantry 2 present with steeper gradients as compared with Gantry 1's distributions. The treatment delivery time is also significantly shorter (15 minutes including gantry and couch movements).

Plan is to constantly increase the number of patients. Later this year we will start the treatment of very young children under anesthesia at Gantry 2. Thanks to parallel operation of Gantry 1 and Gantry 2 for the treatment of deep-seated tumours, more patients can benefit from proton therapy at PSI.



Highly conformal dose distribution for the first plan delivered for the first patient treated in Gantry 2 (axial and sagittal view).

Radio-Oncology News

Spot-scanning Proton Therapy for Pediatric Parameningeal Rhabdomyosarcomas: Clinical Outcome of 39 Patients Treated at PSI

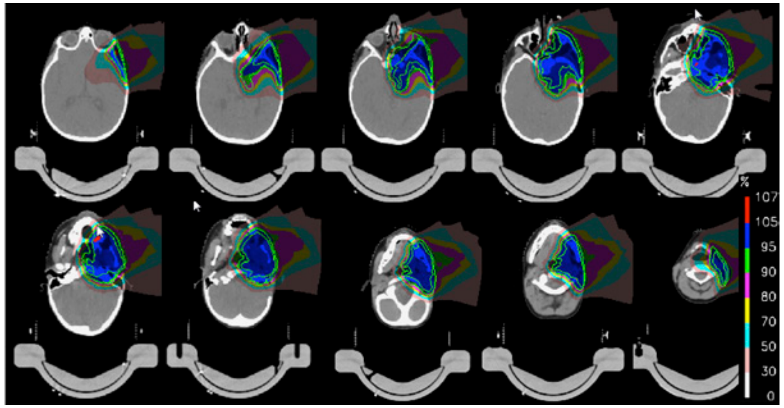
Rhabdomyosarcoma (RMS) is the most frequent soft tissue sarcoma of childhood, accounting for 4 % of solid tumors in children. Around 25 % of the RMS are found in parameningeal locations rarely amenable to surgical resection. The definitive treatment of these tumors consists on the combination of systemic chemotherapy and local or loco-regional irradiation. We evaluated the clinical outcome and late side effect profile of spot-scanning proton therapy (PT) in the treatment of pediatric patients with parameningeal embryonal rhabdomyosarcoma (PM-RMS). Between September 2000 and July 2012, 39 consecutive children with PM-RMS received neoadjuvant chemotherapy according to international protocols, followed by PT at Paul Scherrer Institute with concomitant chemotherapy. The median age was 5.8 years (range, 1.2 – 16.1 years). Twenty five patients (64 %) required general anesthesia for the irradiation procedure due to young age.

Patient immobilization.

This cohort of patients presented with significant percentage of patients with high risk features as follows: 29 patients (74 %) presented with intracranial extension, 7 (18 %) with positive regional lymph nodes and 7 (18 %) with distant metastasis at diagnosis.

The median time from the start of chemotherapy to PT was 13 weeks (range, 3 – 23 weeks). The median prescription dose was 54 Gy(RBE) (range, 50.0 – 55.8 Gy(RBE)) in 1.8 – 2 Gy(RBE) fractions to the primary tumor and involved lymph nodes.

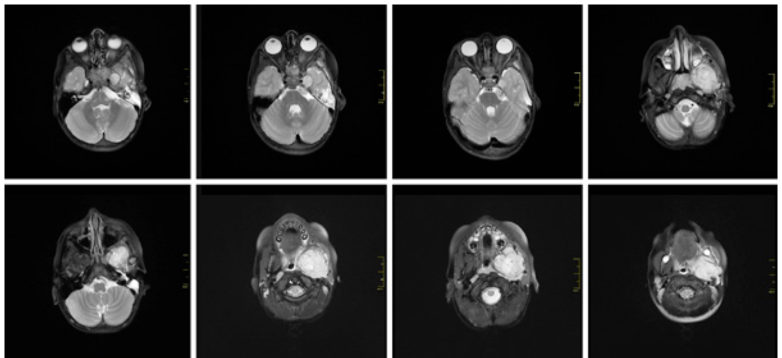
Dose distribution of full treatment to 54 Gy (RBE).



With a mean follow-up of 41 months (range, 9 – 105 months) 10 patients failed: 8 patients experienced in-field local recurrence only, 1 patient developed local relapse and distant lung metastasis and 1 patient developed a meningeal carcinomatosis. The actuarial 5 year local and loco-regional control were 73 % respectively and the 5 year overall survival was 77 %. In a univariate analysis the time from the begin of chemotherapy to the start of proton therapy with a cut-off point at 13 weeks was the only prognostic factor for local control. Four patients presented with high grade (≥ grade 3) late side effects related to proton therapy: three patients developed unilateral cataract requiring surgery and one patient required a hearing aid. Repeated general anesthesia was delivered safely and without complications.

Our data indicate the safety and the efficacy of spot-scanning based PT for pediatric patients with PM-RMS. The rates of tumor control and survival are comparable to that in historical controls with similar poor prognostic factors. Furthermore, rates of late effects from PT compare favorably to published reports of proton-treated cohorts.

Axial MRI slices at diagnosis.



Medical-Physics News

Experimental measurement with an anthropomorphic phantom of the proton dose distribution in the presence of metal implants

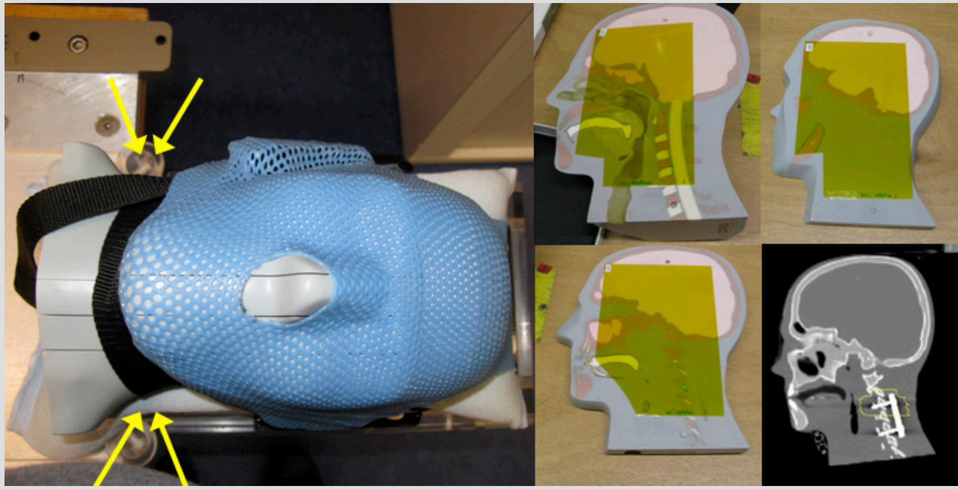


Figure 1: The anthropomorphic phantom is shown with the used immobilization device and the 4fields used for the plans. Additionally the three segments are shown with the inserted GafChromic® films. Finally, the sagittal view of the CT scan is presented at the level of the second segment. The metal rod and the artifacts are visible in the neck area. The PTV is indicated in yellow.

Background and Methods

Many patients referred to the Paul Scherrer Institute (PSI) for proton therapy are evaluated for post-operative radiotherapy. In the case of chordomas and chondrosarcomas along the spinal axis, surgery often means the partial or complete removal of one or more vertebral bodies, and afterwards the insertion of metal stabilizing rods. These rods, although essential for supporting the remaining vertebrae, potentially cause great problems for subsequent radiotherapy, particularly for proton therapy. Indeed, even if the titanium stopping power is known with an accuracy to better than 1%, the presence of metal itself cause an extremly sharp interface that could degrade the target dose coverage. Besides, the reconstruction artifacts, that occur in the planning CT, can introduce significant uncertainties in the range calculation.

To investigate how the presence of such metal implants affects the proton dose distribution we have designed an anthropomorphic phantom to emulate in-vivo measurements as accurately as possible. The phantom corresponds to an adult human head in size and in its anatomic structures. Additionally, it contains a titanium rod fixed with two screws implanted in a cervical vertebra (Figure 1). The phantom is sliced into four segments along the cranio-caudal direction such that GafChromic® films can be placed in three different planes, one being adjacent to the titanium rod.

The phantom was immobilized with an individualized thermoplastic mask to reproduce its positioning during both the CT planning process and the irradiation. Metal artifacts were manually outlined and all Hounsfield Unit (HU) values within these regions are set to the average HU for soft tissue. A planning target volume (PTV), simulating a cervical spine chordoma, was defined embedding the implant. Three different clinically relevant 4-fields plans were calculated, delivered and measured: a Single-Field-Uniform-Dose (SFUD) plan both with and without artifact correction implemented, and an Intensity-Modulated-Proton-Therapy (IMPT) plan with artifact correction.

The accuracy of the dose calculation was investigated by comparing the measured dose distributions for all plans to the corresponding distributions calculated by the treatment planning system.

Results

Results show a surprisingly good agreement between prescribed and delivered dose distribution for the composite plans when artifacts are corrected: >97% and 98% of points fulfill the gamma criterion of 3%/3 mm for the SFUD and the IMPT plans, respectively. Without artifact correction however, only 82% of measured points for the SFUD composite plan pass the same gamma criterion.

These results indicate that correcting manually for the metal artifacts improves substantially the accuracy of the calculated dose distribution, although this is also related to the use of multiple field directions which are differently affected by the residual rage uncertainties. Therefore, this implies that from a dosimetric point of view, when beam directions are carefully selected (i.e. by avoiding, if possible, passage through the metal) and reconstruction artifacts are corrected, patients with metal implants can be clinically treated with good accuracy using both multiple fields SFUD and IMPT plans.

For any further information, please refer to CPT,

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Medical-Physics News

Novel approach to treatment planning of uveal melanoma with proton therapy

Background and Methods

Uveal melanoma is treated at Paul Scherrer Institute since 1984. Over the 30 years, more than 6000 patients were already treated.
Most centers providing ocular proton therapy use a model-based treatment planning system (EyePlan) that simulates the eye model and position and shape of the tumor. Despite some simplifying assumptions, this established method results in good clinical outcomes (eye retention rate of 99.7 % for small and medium size tumors [1]). However, it remains relatively time-consuming.

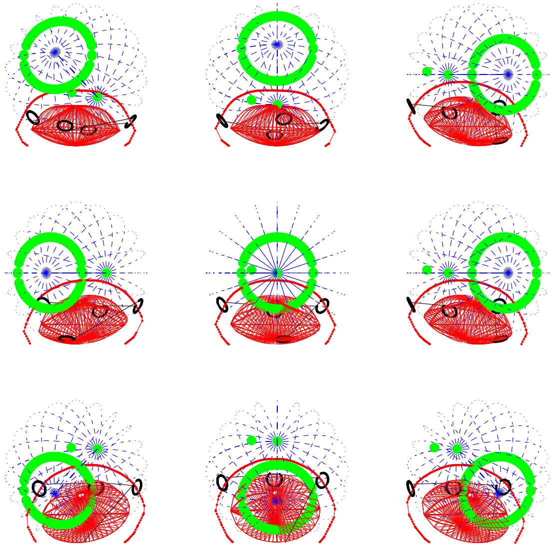


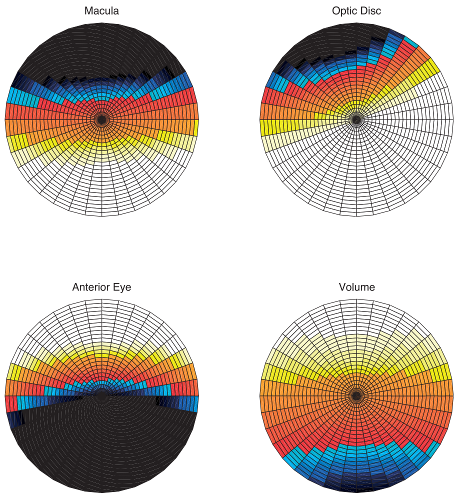
Figure 1: A patient example – eye and tumor model for 9 gazing angles selected from the patient's phase space (blue – sclera, red – tumor, red line – collimator aperture, black – clips, green circle – limbus, green points – optic disc and macula)

We currently develop and test an automated treatment planning (ATP) system with the aim of minimizing the manual part of the planning procedure and increasing efficiency to allow merging of image acquisition, treatment planning and treatment simulation into one session. The ATP constructs eye and tumor models identical to those of EyePlan, from which a phase space of all gazing angles is calculated. For each gazing angle, an organ penalty function (PFi) is constructed to grade the potential sparing of each organ at risk. A global penalty function (PF) is then obtained by weighting the PFi such as to mimic clinical decision-making. The ATP then generates a map of PF as a function of gazing angles and identifies the minimum as the optimal treatment position.
This approach was tested in a preliminary study on a group of 50 patients. The solutions found by ATP were then qualitatively compared with the clinically used angles for these cases.

Results

Analysis showed that, for 88 % of cases, differences between the ATP and clinical solutions were negligible. The remaining 12 % of cases showed that the dose sparing of the different organs at risk was superior in the ATP plans, however, other aspects, such as eye lid or orbital involvement were not taken into consideration and therefore the preference was given to the original clinical solution.
The fact that ATP successfully mimicked 88% of the analyzed cases demonstrates encouraging merit for its use in the treatment planning process. The reduced time for plan generation would allow for an "on-the-fly" approach to treatment planning. PF maps have also been found to be an intuitive visualization of treatment planning trade-offs and have proved to be a valuable tool for the treatment planner.

Figure 2: Corresponding organ penalty maps. A patient's eye is situated in front of the disc and each point on the map defines one gazing angle. Color represents the penalty value for the given gazing angle (white = favorable, black = unsuitable).



For any further information, please refer to CPT, **Jan Hrbacek**, Tel. +41 56 310 3736, jan.hrbacek@psi.ch

[1] Egger E., Zografos L., Schalenbourg A.,Beati D., Böhringer T., Chamot L., & Goitein G. (2003). *Eye retention after proton beam radiotherapy for uveal melanoma.* International Journal of Radiation Oncology* Biology* Physics, 55(4), 867-880.

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