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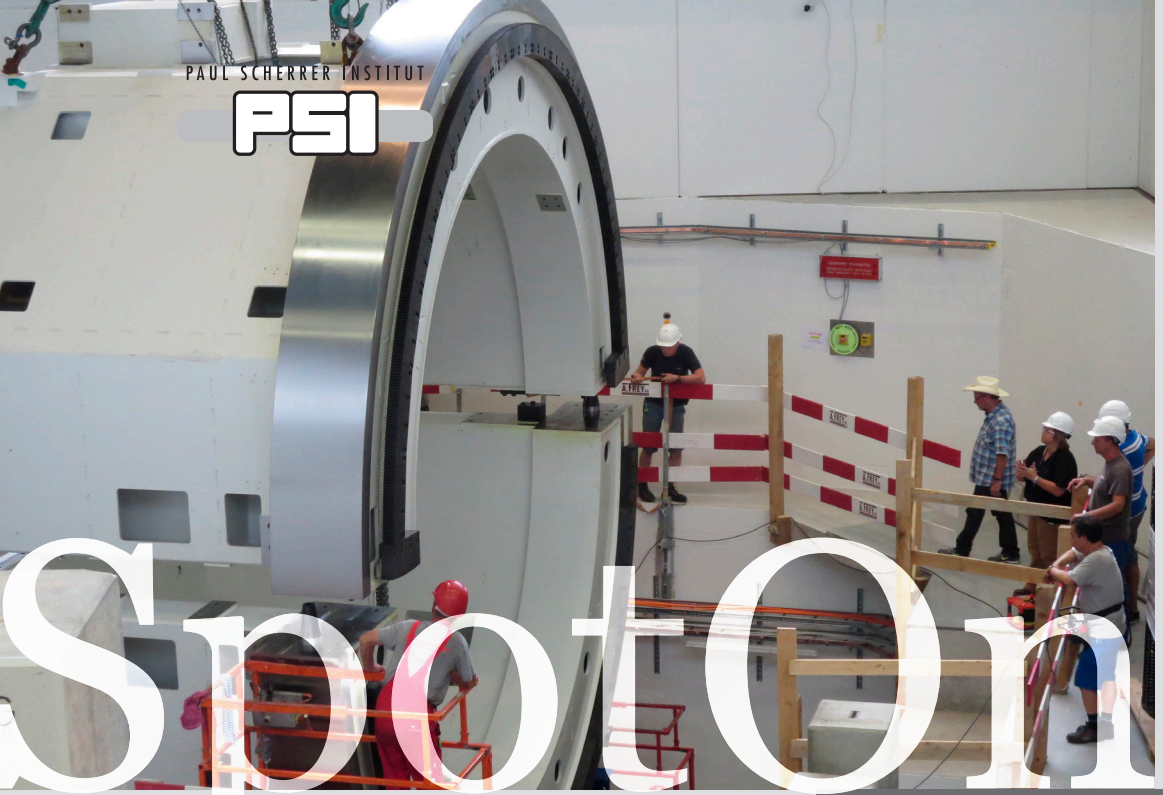

SpotOn

Center for Proton Therapy :: Paul Scherrer Institut :: #6_8/2015

Dear Colleagues

The bulk of the Gantry 3 hardware has arrived at PSI and is currently installed in the dedicated area – see photos above (kindly provided by Dr. Jürgen Duppich). The technical commission of this treatment unit should start this fall and the first patient is scheduled to be treated Q3 2016. A joint clinical program will be established with the University Hospital of Zurich and both teams on either side of the Aare are very excited in this endeavor. This Gantry will deliver Pencil Beam Scanning (PBS) only protons to cancer patients, as do all of our Gantries at PSI. We have treated over a 1000 patients with PBS protons, which is the largest treated PBS-cohort in the world. In this Newsletter the results of our study on optic nerve toxicity after PBS proton therapy are detailed. Importantly, 29% of skull base tumor patients had to be excluded from the analysis because the optic apparatus received less than 45 GyRBE, showing how conformal protons delivered to administer a mean dose of 70.7 Gy RBE can be. With a median follow-up of more than 5 years, the rate of radiation-induced optic neuropathy was 8.3%. Interestingly, the mean dose delivered to the chiasma and optic nerve was low, highlighting that visual toxicity is always an adverse event after high-dose radiation therapy that has to be discussed during the inform consent process, especially so with elderly patients with or without hypertension. The second article analyses the effect of anatomical changes and its dosimetric impact in 951 patients treated at PSI. As a result of these anatomical changes a substantial number of patients were re-planned during the course of the treatment, highlighting how important imaging is in the concept of image-guided radiotherapy for extremely conformal treatment plans. Finally, proton therapy has been lacking behind the concept of image-guided radiation treatments but the proton community is definitively bridging the gap. In the last article Mr. Hammi describes the concept of range probe to monitor intra- and inter-fractional misalignments of patients. His work follows the seminal studies performed some years ago at PSI with proton radiography and PSI has been acknowledged to have developed this innovative field. One of the main advantages is that patients are imaged in the same geometrical treatment conditions and that the dose delivered to the patients is decreased compared to photon based on-board imaging. Stayed tuned for some more exciting news from SpotOn. Happy holidays!

Sincerely,
Prof. Damien Charles Weber,
Chairman of CPT

Radio-Oncology News

Optic nerve toxicity after high dose proton beam therapy with spot scanning at the base of skull: a retrospective study in 156 patients

Background and Methods

Chordomas, chondrosarcomas and other tumors at the base of skull require high-dose radiation therapy. Constraints to the optic nerve (ON) and to the chiasma restrict dose delivery to the target. Usually 56 Gy(RBE), in exceptional cases a maximum dose of 60 Gy(RBE) is the accepted constraint for ON and chiasma at PSI when performing proton beam radiation in these challenging cases. In this retrospective study we evaluated the occurrence of radiation induced optic neuropathy (RION) in patients with skull base tumors. Doses and volumes of optic nerves and chiasma were extracted from the planning system. Contours were reviewed by two physicians. In selected cases, contours of the optic nerves and chiasma were re-delineated and re-calculated. Toxicities were defined according to CTCAE V4.0.

Results

220 patients with skull base tumors underwent irradiation with proton beam at PSI between 1999 and 2011. 64 patients had to be excluded because they received less than 45 GyRBE to the ON and chiasma, received combined photon-proton treatments, previous or concomitant chemotherapy, previous radiotherapy or were younger than 18 years old. 156 patients (thereof 82 females) with mean age of 47.3 years and mean follow-up time of 60.7 months were included in the statistical analyses. The mean total dose to the planning target volume (PTV) was 70.27 (range: 54 – 77.4) GyRBE. RION developed in 13 patients (8.3%), 10 unilaterally (8 patients with grade 4, 2 patients with grade 3 toxicity) and 3 with bilateral involvement (1 patient with bilateral grade 4 toxicity, 2 patients with grade 4 toxicity in one eye and grade 2 in the other eye). The mean and maximum dose delivered to the chiasma of these 13 patients were 52.3 and 58.1 GyRBE. The respective doses to the ON with toxicities were 35.1 and 57.9 GyRBE. With the help of Chi-square statistical testing, the factors age ≥70 years, hypertension, tumor abutment/compression of the ON and histology (meningioma and adenoid cystic carcinoma vs. others) could be identified as significant risk factors for developing RION. Number of surgeries (≤1 vs. >1), initial vs. recurrence treatment, diabetes, bite block vs. mask as fixation device and dose per fraction (>1.9 vs. ≥1.9 GyRBE) show no significant impact in our univariate analyses.

Conclusions

The outcome of our study is comparable to published data after high dose photon therapy. Grade 3 and 4 toxicities after spot scanning proton beam therapy correlate well with the delivered high doses. Based on our analyses, hypertensive patients, older than 70 years, with a diagnosis of meningioma or adenoid cystic carcinoma and a tumor which compresses the optic nerve tend to develop more likely RION after radiation therapy.

These results were presented at the PTCOG meeting this year in San Diego, USA.

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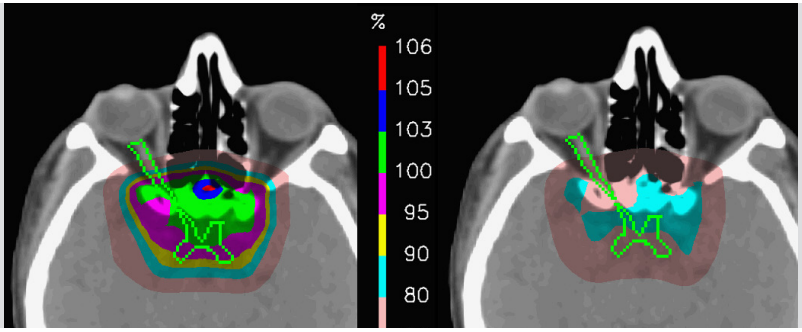
Case Report
Female patient with diabetes and hypertension, 73 years old, with a skull base chordoma, which compresses the chiasma, was irradiated with a total dose of 74 GyRBE with 2 GyRBE per fraction. She developed 18 months after end of proton therapy a grade 4 neurotoxicity at the right optic nerve. The two pictures show the dose distribution at the chiasma and optic nerves for the first serie as well as for the whole treatment

First serie: 50 GyRBE
Chiasma:
Dmax: 51.40
Dmean: 49.65
Right-ON:
Dmax: 51.40
Dmean: 29.55
Left-ON:
Dmax: 50.60
Dmean: 27.70



Treatment: 74GyRBE
Chiasma:
Dmax: 60.16
Dmean: 57.42
Right-ON:
Dmax: 57.87
Dmean: 29.58
Left-ON:
Dmax: 56.83
Dmean: 30.46

Medical-Physics News

The effect of anatomical changes on PBS proton dose distributions: a retrospective review of 951 patients treated at PSI

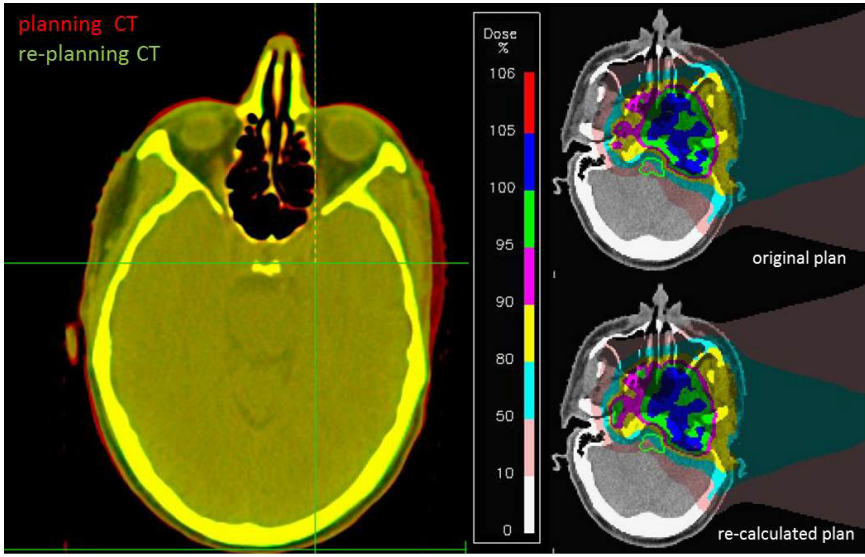
In proton therapy, due to the presence of the steep dose gradient in the depth direction, any shift of the Bragg peak in depth could potentially increase the dose to the organs at risk (OARs) or under coverage the target. Therefore, the evaluation of the exact range in the patient is particularly important when treating with proton. Unfortunately, several sources of uncertainties affect the accuracy of range calculation in the patient even if most of them are carefully monitored. The most unpredictable are the anatomical changes in patient.

In this work we wanted to quantify the dosimetric impact of the anatomical changes on the dose distribution and estimate how often an anatomical change translates into the necessity of performing a new plan on a re-planning CT (rePCT). To estimate the dosimetric effect in case the treatment would have been continued ignoring the anatomical difference and based on the original CT, the original plan has been recalculated on the rePCT, without any optimization. To assess the effect of changes, a number of dosimetric parameters (e.g. DVHs, max and min dose, D2%, mean dose, V95%, D98%) for both planning target volumes (PTVs) and all OARs have been used.

951 patients treated at PSI between 2000 and 2014 with PBS proton therapy (PT) were included in this retrospective study. Patients were divided according to the anatomical area of their treatment: skull base, head and neck (H&N), extra cranial and pelvic. The presence of a control CT (CCT) and of a rePCT has been analyzed.

For 244 patients (25.6%), more than one CCT have been acquired during the course of the proton treatment. However, for only 47 patients (4.9%) (22 skull-base, 12 H&N, 7 extra-cranial and 6 pelvic) the rePCT was acquired due to anatomical changes occurring during the therapy. The most affected group by the anatomical changes is the skull-base treatment area, due to the variation in the nasal sinus cavity filling (86%). Brainstem, optic nerve and spinal cord are the OARs mostly affected by the anatomical variation. Except for one patient that shows a difference in the max dose difference of 21.6% in the spinal cord, there are not variations › 10% difference (considering D2%, mean and max dose) between the re-calculated and the original plan. Regarding the H&N group, the brainstem, chiasma, optic nerves, spinal cord, parotid glands and temporal lobes are the most frequent OARs affected due to tissue variation, weight loss/gain and, in some cases, due to nasopharynx cavity filling. Only three cases show a difference › 10% in the max dose differences and only in one case a difference › 10% was detected with respect to the mean dose. A slight target under coverage (‹ 5%) was detected for both previously mentioned groups. The Extra cranial and Pelvic group show substantial target under coverage in terms of the V95%, but always ‹10%.

Despite substantial anatomical variations, clinically delivered plans have been found to be robust to anatomical variations with re-planning being deemed necessary in 19% (anatomical rePCT/ CCT) of cases. However, as the dosimetric effect of the changes can be quite large, they have to be monitored and (if detected) evaluated on an individual basis. As such, predictive factors, in combination with plan robustness optimization, would be desirable to minimize the number of control CTs and to focus the attention on those cases that will be more affected by anatomical changes.



On the left side: the tissue difference (reduction) is shown matching the planning CT (red) and the re-planning CT (green). On the right side: comparison between the original plan (top) and the re-calculated plan (bottom), obtained by recalculating the original plan on the re-planning CT. The tissue reduction leads to an over dosage of the brainstem, such as an increase of the maximum dose of 5.8%.

These data were presented at the PTCOG meeting this year in San Diego, USA.

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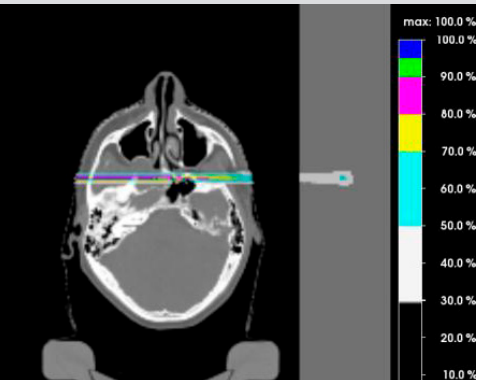
Medical-Physics News

Range Probe: An innovative technique to detect on-line patient misalignments

The main physical advantage of proton therapy is the presence of a sharp distal dose fall-off that can be used to deliver higher doses to the tumor volume, and to spare normal tissues beyond the end of the delivered field. On the other hand, and in contrast to photon therapy, the superiority of this technique is based on the accuracy with which the intended dose is delivered in the target volume during the fractionated treatment. Recently, modern image-guided radiation therapy (IGRT) technology has become a standard. Positioning accuracy to below 2 mm has been reported for patient setup [1]. In the face of the advantages of using such techniques, all these methods suffer, however, from some important drawbacks, e.g. treatment verification being done under different geometrical conditions compared to those used during treatment and the excessive patient expansion. In addition incorrect patient orientation, weight gain or anatomical site cannot be directly measured since these methods are based on planar images of the patient.

We developed what we call 'range probe finger-printing' (RP) [2] [fig.1], an innovative and easy-to-perform method to determine online intra- and inter-fraction positioning misalignment of the patient with sufficient accuracy. The superiority of this tool include reduced imaging dose to the patient compared with X-ray radiation imaging systems and the short beam time demand. Furthermore, this technique uses the same treatment geometrical condition (proton beam's eye view). A RP is a narrow, low-dose proton pencil beam of sufficient energy such that the proton beam traverses completely through the patient, and can be detected on the exit side. The residual integral depth dose curve can be measured using a wide area range telescope or multi-layer-ionisation-chamber (MLIC).

Figure 1 Model of the range probe setup.



To conduct this study, a retrospective study has been performed based on head and neck patients treated at PSI. From the nominal planning CT of each selected patient new CT's were generated, assuming all possible daily misalignment scenarios for a given set-up error in all geometrical axes, resulting in 2197 scenarios. Three RPs have been carefully selected which are unique characteristics found within the anatomical density pattern (range probe finger prints'). This holds true as the range of proton beam with a given energy is determined by the integral stopping power crossed in the beam path and the 'Bragg Peak' is degraded due to the lateral scattering of protons caused by Multiple Coulomb Scattering between adjacent regions differing in density [fig. 2]. The RPs have been calculated using Monte Carlo techniques for each beam with the range of possible daily positioning errors, to generate a patient-specific RP database. The same RPs were then recalculated through re-planning CTs. Using the pre-calculated database and the pattern matching technique, the actual 'daily' shift error could be determined. The results are compared to the actual translational corrections determined from daily orthogonal planar x-ray images, corresponding to the CT data sets. The results show that millimeter accuracy can be achieved.

With this study we have demonstrated the potential of a small number of low dose proton range probes for detecting on-line, residual misalignments of patients with a high level of accuracy (1 mm). The technique is fast, and can effectively reconstruct either translational or rotational positioning errors from a single proton incident angle.

This work was presented at the ESTRO meeting this year in Barcelona, Spain.

[1] Bolsi A. et al., 2008 Experiences at the Paul Scherrer Institute with a remote patient positioning procedure for high-throughput proton radiation therapy. Phys. Med. Biol, Vol. 71.

[2] Mumot M. et al., 2010 Proton range verification using a range probe: definition of concept and initial analysis. Phys. Med. Biol, Vol. 55.

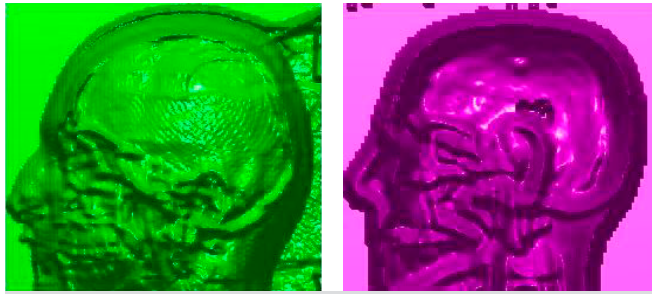


Figure 2 (left) Proton range mapping. Range dilution mapping (right).

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