PAUL SCHERRER INSTITUT

PSI

SpotOn+

Center for Proton Therapy :: Paul Scherrer Institut :: #4_11/2014

Dear Colleagues

This is an anniversary issue of our SpotOn+, this edition being sent to you one year after the first edition in 2013. In the clinical section, the Study and Research Office presents the results of the atypical teratoid/rhabdoid tumor (ATRT) of the CNS of young patients treated at PSI with PBSS. Although the series is small, it builds to the body of recent studies published by the MDACC/Houston and MGH/Boston that suggest that PT is an effective treatment for young children with ATRT. Of note, 66 % of the patient in our series survived more than 2 years. Importantly, the (proxy-rated) quality of life was unaffected in these very young patients. In the physics' section, Ms. Bernatowicz reports quantitative analyses of the effect of motion on (water equivalent) proton range, calculated based on 4D CT data for lung and liver tumors. Range maps were calculated by converting the CT's Hounsfield Unit to proton stopping power. Interestingly, the mean range (normalized to end-exhale) decreased by 8 % and 15 % in liver and lung patients respectively. Unfortunately, large variations were observed and the impact of motion was indeed case-specific. The second part of the physics section pertains to a certain type of motion mitigation strategy, namely tumor tracking in 3 liver cases. More specifically, two beam tracking strategies have been assessed and inter-compared, using 4D dose calculations. The main difference between the two tracking methodologies is that 2D tracking adapts Bragg peaks to the fiducials, while full 3D tracking uses the 3D deformable motion extracted from the model based, motion reconstruction algorithm. Interestingly, dose corruption (i.e. D5-D95) induced by motion could be substantially decreased when 2D or 3D tracking was simulated but could not guarantee an appropriate tumor coverage. As such, re-tracking was simulated and the target coverage was improved, nearly achieving the no motion (i.e. static) dose metrics. These data are of paramount importance so as to quantify the impact of motion on the proton's range for moving targets and the way to mitigate the effect of motion on target coverage. PSI is committed to perform these analyses and optimize its R&D program, with the aim to treat moving targets in a not too distant future. More information can be found on our website: http://www.psi.ch/protontherapy/center-for-proton-therapy-cpt.

I take the opportunity to wish you all a relaxing winter time and a happy new year. Happy holidays!

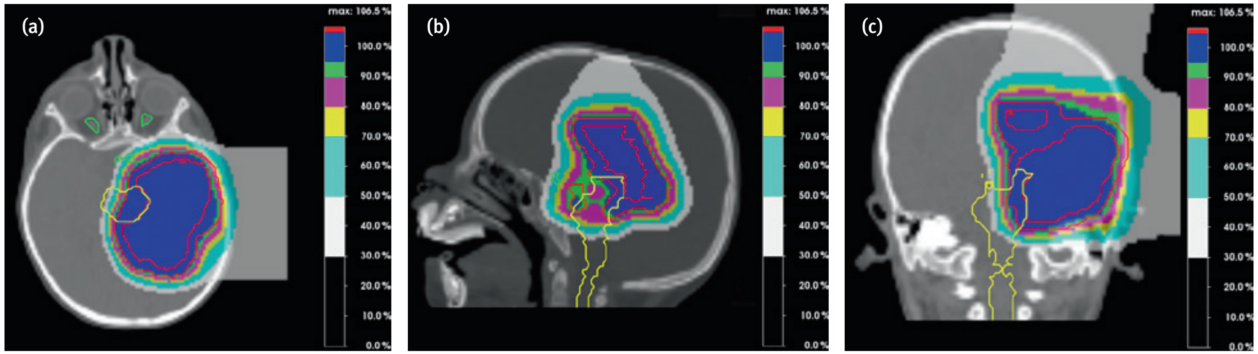
Sincerely,

Prof. Damien Charles Weber, Head of CPT

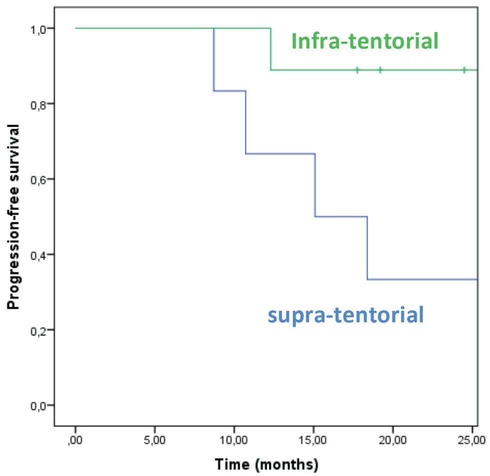
Radio-Oncology News

Spot-scanning Proton Therapy for pediatric atypical teratoid/rhabdoid tumors (ATRT): Clinical outcome of 15 patients treated at PSI

Dose distribution of a treatment plan superimposed on CT images of a patient with an supra-tentorial ATRT (**a** axial, **b** sagital and **c** coronal views). Note the rapid dose decline between the target and non-target volumes and the optional sparing of contro-lateral brain (coronal and axial slices). The isodose contours are represented by the color-wash (corresponding values are displayed on the right border of each photo).



Atypical teratoid/rhabdoid tumor (ATRT) of the CNS is a rare, highly malignant and extremely aggressive embryonal neoplasm of early childhood. This tumor accounts for 1 – 2% of CNS pediatric tumors but up to 20% of malignant CNS neoplasms in patients younger than 3 years of age. Administered treatments are not ATRT specific and are highly variable but typically includes multi-modality treatment, namely surgery, chemotherapy and radiation therapy (RT). Technical improvements in radiation therapy may improve the therapeutic ratio for these challenging patients. Unlike conventional radiotherapy, proton therapy (PT) allows for optimal dose distributions, with the added benefit of no exit dose. This absence of exit dose has triggered the rational of using protons for children with various cancer types.



We assessed the clinical results, not limited but including the recurrence pattern, toxicity and QoL, of pencil beam scanning (PBS) PT in the treatment of non-metastatic ATRT patients treated at the Paul Scherrer Institute (PSI). QoL was analyzed by the QoL working group at University of Münster, Germany. The results have been published online (Weber et al 2014).

Between May 2008 and January 2013, 15 consecutive children with non- metastatic ATRT aged from 4.6 to 27.4 (median, 18.9) months were treated with PBS PT at PSI. Eighty seven % of these patients were ‹ 24 months old and 20% ‹ 12 months of age. There were 7 girls and 8 boys. The majority (n = 12; 80%) of tumors were ‹ 5 cm. Mean age at diagnosis was 17.4 ± 7.0 months. The localization was infratentorial in 9 (60%) patients. Gross total resection of the primary tumors was achieved in 7 (47%) patients. The dose administered focally under sedation was 54 Gy (RBE). After a median follow-up of 33.4 months (range, 9.7 – 69.2), 3 (20%), 4 (27%) and 2 (13%) patients presented with local failure (LF), distant brain failure (DBF) and spinal failure (SF), respectively. Six patients died, all of tumor progression. The 2-year overall- and progression-free survival was 64.6% and 66.0%. Tumor location (supratentorial; Fig.) and the extent of surgical resection (non-gross total resection) were negative prognostic factors for both OS and PFS.

Our data suggests that PBS PT is an effective treatment for young children with ATRT. After PT, with or without concomitant chemotherapy, two third of the patients survived › 2 years. Importantly, focal only PT, as opposed to WBI with or without CSI did not result in an access of distant intracranial failures, the former accounting for 20% of all treatment failures. The acute toxicity was limited and our prospective parental-proxy reporting data do not suggest a decrease of QoL of these very young patients. Late toxicity was unusual. As such, we continue to treat these challenging young patients with focal only PT.

Reference:

Weber et al 2014 *Tumor control and QoL outcomes of very young children with atypical teratoid/rhabdoid Tumor treated with focal only chemo-radiation therapy using pencil beam scanning proton therapy.* Journal of Neuro-Oncology. Published online 02 Nov 2014

Medical-Physics News

Characterizing the effect of density variation on proton range in liver and lung as a result of respiratory motion

Background and Methods

Calculated proton ranges depend on density information extracted from the CT images. Density changes appearing due to respiratory deformation are local and temporal variations along the geometrical penetration path need to be quantified for accurate 4D dose calculations. Here, we report a quantitative analysis of the effects of motion on water equivalent range (WER) in proton therapy, calculated based on the 4D-CT images. Additionally, we evaluate density effects in simulated images (4D-CT(Sim)). 4D-CT(Sim) is interesting for advanced 4D planning, as it generates dose-free images and can represent the variability of respiratory motion over multiple breathing cycles.

Firstly, 4D-CTs of three liver and three lung patients were evaluated. Changes in tumor and organ volume were calculated and the tumor motion was estimated based on the image data. Single Field, Uniform Dose treatment plans were calculated using the PSI 3D-TPS. Three single-field plans: P1 – from the right lateral, P2 – posterior oblique, and P3 – posterior were created. Realistic WER maps were then calculated by converting the Hounsfield Unit Values to proton stopping power through the whole patient and then evaluated in the CTV region. Secondly, the corresponding simulated 4D-CT images were created using a static reference CT of liver patients and motion data extracted from the 4D-CT deformable registration. Density information from 4D-CT(Sim) and original 4D-CT images was then compared in terms of WER to evaluate the effect of using a warped CT image to generate a 4D data set. Similar method is applied to lung patients (data in preparation).

Results

As WERs vary over the respiratory cycle, mean WERs were normalized to end-exhale (WER_EE), and were extracted from 4D-CT images of all patients (covering three different field directions each). In general, mean WER_EE decreased by up to 8 % with inhale in liver patients and about 15 % in lung patients (Fig. 1). Locations exhibiting largest positive/negative differences were identified and analyzed with the WER map. The density information of 4D-CT(Sim) is compared with that of the 4D-CT: an excellent agreement was observed, with mean WER differences ‹3 mm in the liver region (Fig. 2).

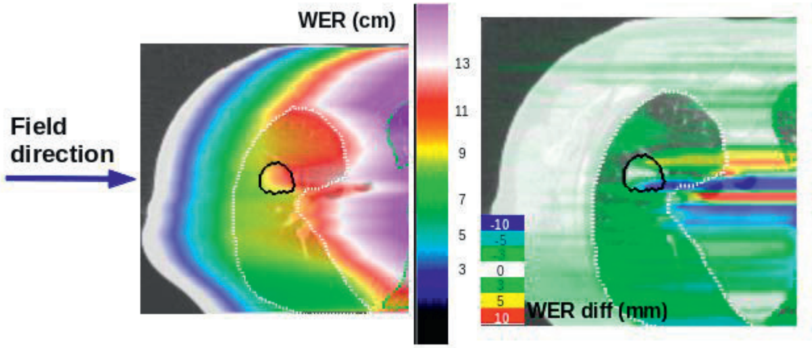
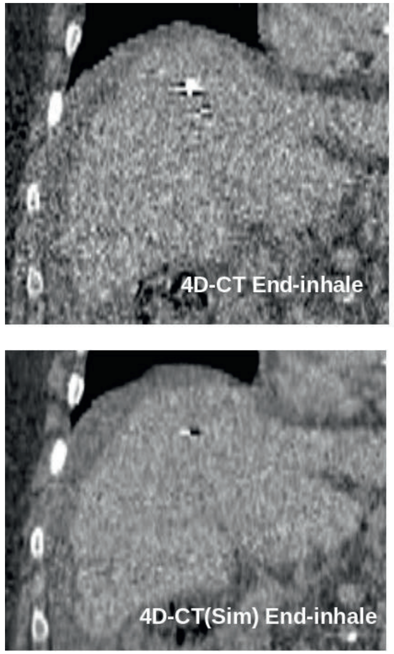


Figure 1 Water equivalent range (WER) calculated for the lung patient at end-inhale (left). The corresponding WER difference (=inhale - exhale) of the same patient. Note largest differences in the CTV occur at the distal edge of the target. Maximum differences (›1cm) were observed around the heart.



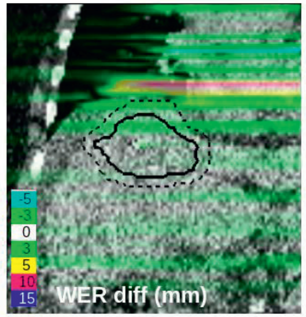


Figure 2 End-inhale liver image from 4D-CT (upper left) and simulated 4D-CT (lower left). The corresponding WER difference (= 4D-CT – 4D-CT(Sim)) of the same patient. Note largest differences occur outside of liver region.

Conclusion

In summary, intrafractional motion affects the beam range in proton therapy. WER variations are case-specific; depend on tumor motion, size and its position. This work will be presented on 28–29th of November at the 4D Treatment Planning Workshop organized by ICR and UCL in London.

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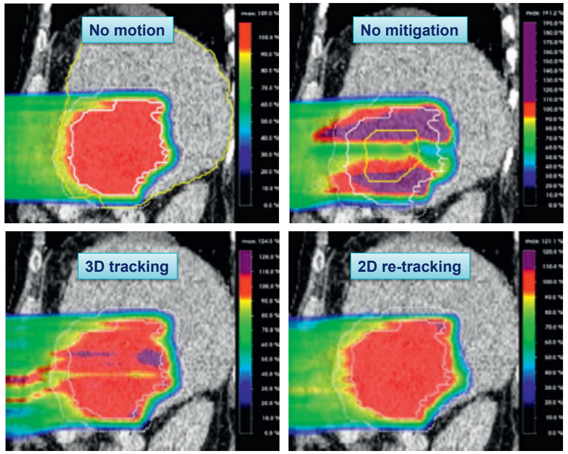
Medical-Physics News

Online Image-guided Scanned Beam re-Tracking: necessity and extra benefits

Figure 1 The 4D dose distribution with and without motion mitigation.



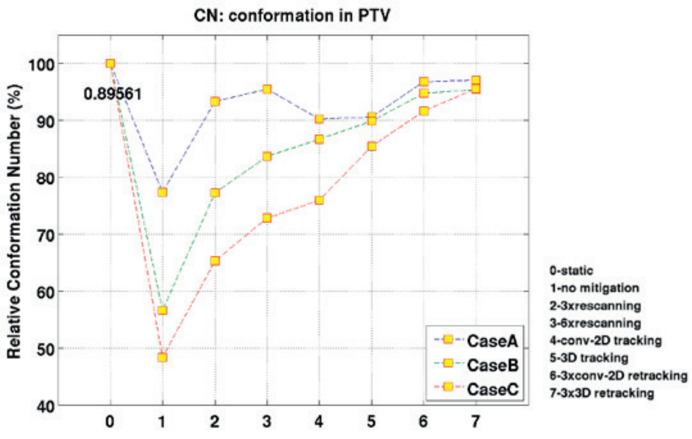


Figure 2 The relative conformity number in PTV of the 4D plan with different motion mitigation approaches.

Among all possible motion mitigation approaches, beam tracking has been considered as the optimal technique, since it should not lead to excessive treatment prolongation or target volume expansions. Due to sequential dose delivery and high sensitivity of proton beams to both small motion and range changes, knowledge on 3D motion in real-time, together with the resultant density variations, is a pre-requisite for clinically implementing such a technique. We have developed an efficient model-based motion reconstruction method (Zhang et al 2013) previously, which allows for online prediction of deformable motion from sparse surrogate motions tracked via an on-board, Beams' Eye View (BEV) X-ray imaging system. Further investigating the feasibility and effectiveness of tumour tracking using pencil beam scanning based on such an image-guided motion compensation approach is the objective of this study (Zhang et al 2014). Two beam tracking strategies have been simulated using 4D dose calculations (4DDC). Conventional 2D tracking laterally adapts Bragg peak positions directly according to fiducial marker motions tracked from time-resolved BEV images, while 3D tracking utilizes the full, 3D deformable motion extracted from the model based, motion reconstruction algorithm. To reduce the sensitivity of beam tracking to the inevitable uncertainties from both motion tracking and prediction, this study also investigated the potential for 're-tracking' (a combination of re-scanning and tracking), whereby all delivered pencil beams are delivered multiple times while also tracking the tumour.

Due to the relatively large motions considered, considerable over- and under-dosage can be observed for all cases when no motion compensation is applied. However, the D5-D95 can be substantially reduced to 17, 19 and 29 % or to 15, 18 and 23 % when 2D or 3D beam tracking is employed, compared to the D5-D95 value of 9 % that was achieved for the reference (static) plan. Thus, tracking alone (either 2D or 3D) cannot fully recover target dose coverage and homogeneity. By moving to 3x re-scanning (re-tracking), the robustness has been significantly improved, with even 2D re-tracking providing dose homogeneities in the PTV of almost comparable quality as the static plan, together with significant reductions of the 'inverse interplay effect' in the proximal regions.

This study has demonstrated the feasibility and potential advantages of clinically applying online image-guided scanned beam tracking for mobile tumours treatment. The dosimetric comparison has revealed only a small benefit for deformable 3D beam tracking with respect to 2D tracking, and these gains are mainly evident only for the larger motions. Our results have also shown that beam tracking alone cannot fully mitigate all motion effects, but that combining tracking with rescanning (re-tracking) could provide an approach which combines the best aspects of tracking (better dose conformation) and re-scanning (washout of interplay effects).

Reference:

- Zhang et al 2013 *Deformable motion reconstruction for scanned proton beam therapy using on-line x-ray imaging*. Physics in Medicine and Biology, Vol. 58(24), pp. 8621-8645
- Zhang et al 2014 *Online image guided tumour tracking with scanned proton beams: A comprehensive simulation study*. Physics in Medicine and Biology. accepted Oct 2014

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