PAUL SCHERRER INSTITUT

SpotOn+

Center for Proton Therapy :: Paul Scherrer Institut :: #11_3/2017

Dear Reader

It is my distinct pleasure to present you with our latest issue of SpotOn+. I would like to take the opportunity of this newsletter to inform you that PSI will perform some repairs on our ion source in May and June. After 10 years of diligent & assiduous service, our COMET cyclotron will undergo a major revision, starting on May 5th. The clinical program will resume beginning of July. I have taken the decision that the virtual tumor board will be maintained during the shut-down period, so if you have a patient you feel should benefit from protons do not hesitate to present her/his case during our WebEx meeting. Referral to another proton center can be easily arranged by PSI as we have a number of European connections that will allow us to do so. Having said that, let us go back to the newsletter. In this edition, Dr Murray details the unpublished results of our large cohort of meningioma patients treated with pencil beam scanned protons. The 5-year local control rates were above 85% which is substantial and in line with other studies. The high-grade radiation-induced toxicity-free rate was excellent. Interestingly, patients treated with upfront radiation therapy had a substantial better outcome than those treated for tumor progression or tumor recurrence. The timing of radiotherapy for this disease is an important issue after the failed attempt to perform a PRT for grade I meningioma (EORTC 22021–26021). Hopefully, the newly open ROAM intergroup trial (EORTC 1308) will be able to answer this critical question for grade II tumors that were completely resected (Simpson 1–3). The PhD student Carla Winterhalter assesses the lateral fall of PBS proton therapy in the Med. Physics section of this newsletter. One part of her thesis is to evaluate how to improve the lateral dose fall-off that can be problematic at certain energies. Three delivery techniques were assessed (edge enhancement, collimation and a mixture of these two techniques) using a water tank. Collimation was indeed interesting reducing penumbra substantially for depths of 4 cm to 10 cm which could be clinically relevant for head and neck superficial tumors and children. Finally, Dr Fattori, working as a Postdoc at PSI, assessed the scanning direction so as to mitigate the interplay effects that are relevant when treating moving targets with PBS. As mentioned in his abstract, the dose-degradation scanning direction was found in a majority of analyses performed between 2001 and 2015. The added value of this analysis is that this assessment is made not only on simple simulations using non-clinical tumor geometries. Rather, the delivered fields are assessed using either geometries with gating experiments or clinical radiation plans for the treatment of lung cancer. Interestingly, although the primary parallel scanning achieved good motion mitigation results for single energy 2D measurements, these results were not confirmed in a clinical setting using 3D energy levels, emphasizing that motion mitigation is a complex issue in a clinical setting outside the realm of 2D simulations.

That said, I would like to thank you for reading this Newsletter and wish you a happy spring and SASRO meeting.

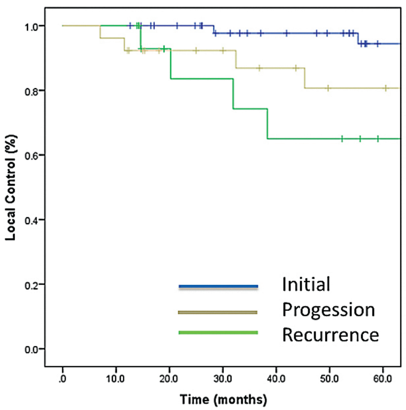
Yours sincerely,
Prof. Damien Charles Weber,
Chairman of CPT, Paul Scherrer Institute

Radio-Oncology News

Local control of benign and non-benign intracranial meningiomas treated with pencil beam scanning proton therapy at PSI

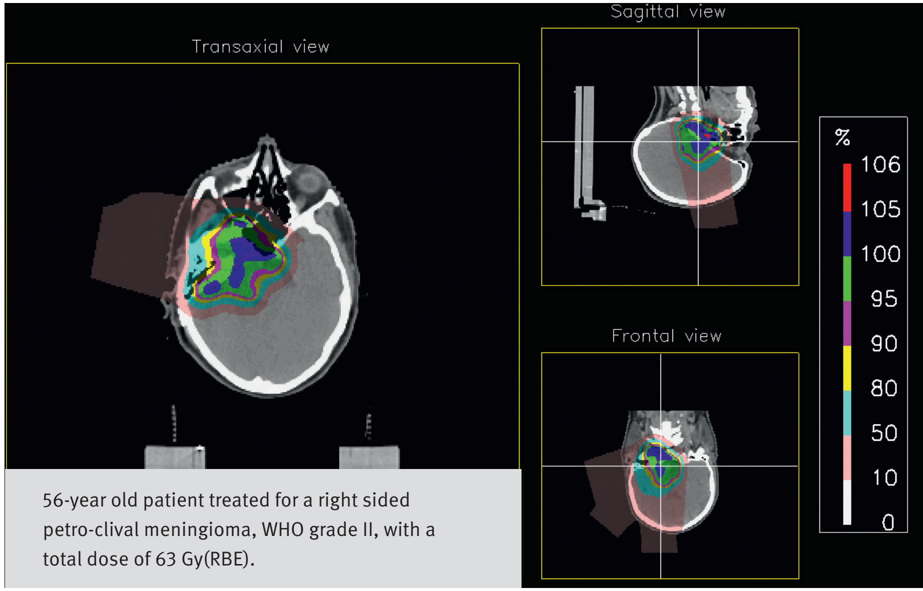
Accounting for approximately one-third of all primary brain tumors, meningiomas are the most common intracranial tumors in adults. Depending on the histologic characteristics, the World Health Organization (WHO) distinguishes benign (WHO I), atypical (WHO II) and malignant (WHO III) grades of meningiomas. This grading represents an important prognostic factor for disease recurrence and treatment response. Five year progression free survival (PFS) of Grade I meningiomas was shown to be approximately 90 %, Grade II ~50 %, and Grade III ~13 %. Surgery, with the goal of gross total resection (GTR), remains the initial treatment of choice for clinically symptomatic or enlarging meningiomas.

Kaplan-Meier estimates of local control stratified by timing of PT (initial vs recurrence or progressive disease).



Radiation therapy (RT) is the most commonly employed postoperative, adjuvant, or salvage therapy and has shown the capacity to reduce recurrence rates in all grades of disease. Escalated RT doses have achieved better local control in atypical and malignant meningiomas. Improvements in delivery (e.g. Intensity modulated RT [IMRT]) have led to improved therapeutic ratios, yet these tumors often arise in close proximity to organs at risk (OARs; e.g. optical nerve, chiasm, cochlea, pituitary, hippocampus, etc.). Proton therapy (PT) is characterized by its unique dose-deposition pattern (i.e. Bragg peak) with low entrance and virtually no exit dose. Active spot scanning was pioneered at the PSI and has been employed clinically since 1996. Spot scanning, also known as pencil beam scanning (PBS) PT, is achieved utilizing a magnetic beam scanning technology by which mono-energetic proton pencil beams ("spots") can be individually modulated to target a volume in three dimensions. This improves OARs sparing through highly conformal dose distributions. In regards to this and even though intracranial meningiomas are successfully being treated with regular photon irradiation all over the world, indications for proton therapy are especially tumors with complex geometries and those which are in close proximity or abutting to OARs, due to the highly conformal and OARs sparing effect of PT.

The Center for Proton Therapy at the Paul Scherrer Institute (PSI) has been treating meningioma patients for more than 20 years since 1996. In total, 96 patients (male/female, 29/67; median age 52.8 years) of all histology subtypes (~ two-third WHO Grade 1) were considered for this analysis. Fitting to the indications for PBS PT mentioned above, all meningiomas treated at PSI were complex and considered high risk tumors. In addition, compared to other studies, the average tumor volume was rather large with a median gross tumor volume (GTV) of 21.4 cm^3 (max. 546.5) and a median planning target volume (PTV) of 123.4 cm^3 (max. 1142.0). All patients were followed for at least 1 year, in average 5 years. Local failure was defined as radiologically observed tumor progression after subtotal resection or tumor recurrence after gross total resection.



56-year old patient treated for a right sided petro-clival meningioma, WHO grade II, with a total dose of 63 Gy(RBE).

Thirteen (14 %) failures were observed over the entire follow up period (median: 32.4 months). This corresponds to a 5-year actuarial local control (LC) of 86.4 % and is comparable to other studies. Nine of the encountered failures (69 %) were detected after treating non-benign tumors. Female gender had a favorable impact on tumor control. In addition, patients treated at initial diagnosis had a significantly better local control than those treated for recurrence or disease progression after having undergone initial treatment followed by a watch and wait period. Five-year high-grade toxicity-free survival almost reached 90 %.

The results demonstrate that PBSPT is an effective and safe treatment modality for highly complex intracranial meningiomas. Up-front radiation likely results in improved outcomes and should be considered especially for patients with non-benign tumors and/or for those with incomplete resections.

Results have been presented as a poster at the annual meeting of the American Society for Radiation Oncology (ASTRO) last year in Boston, USA.

For any further information,
please refer to CPT
Dr. Fritz Murray
Tel. +41 56 310 3499
Fritz.murray@psi.ch

Medical-Physics News

A comprehensive study of lateral fall-off for proton pencil beam scanning (PBS).

Purpose

The aim of radiation therapy is to deliver as much dose as possible to the tumour while minimising the dose to the surrounding, healthy tissue. In proton pencil beam scanning, this is achieved using magnets to direct small proton beams into the target. A sharp lateral fall-off (penumbra) of the resulting dose distribution is of high importance to spare organs at risk located adjacent to the target. Three different techniques to improve the lateral fall-off are investigated, i.e., edge-enhancement, collimation and edge-enhanced collimation.

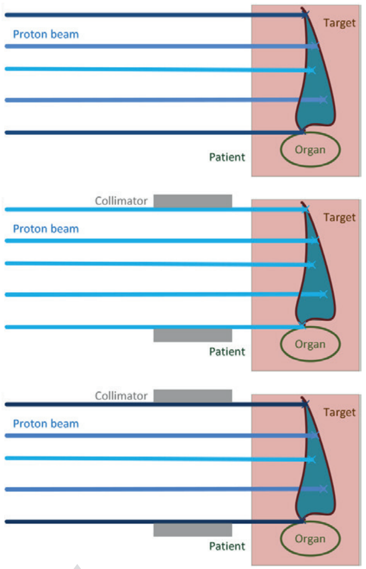


Figure 1: To achieve a sharp lateral falloff, (a) the weights of the uncollimated pencil beams are optimized, darker lines represent spots with more protons (edgeenhancement), (b) uniform weighted pencil beams are collimated (collimation) or (c) the weights of the collimated pencil beams are optimized (edgeenhanced collimation).

Methods

Optimization approaches: Mono-energetic, square fields have been simulated in a water phantom using the TOPAS 3.0.p1 Monte Carlo tool. For edge-enhancement, the weights of the beams are optimized to achieve a sharp lateral fall-off, no additional hardware is needed (figure 1a). In contrast, for collimation, a physical aperture is inserted to cut the field-edge pencil beams (figure 1b). Edge-enhanced collimation is the combination of the two techniques explained above; a collimator is inserted into the beam and the weights of the collimated pencil beams are optimized (figure 1c).

Pre-absorber strategies: At Gantry 2, the lowest deliverable energy is 70 MeV, corresponding to a 4 cm proton range in water. To deliver Bragg peaks closer to the surface of the target, a 2.5 cm graphite block (pre-absorber) is inserted into the beam to lower the range of the incoming particles. Currently, if one spot with a range below 4 cm is included in the field, the pre-absorber is used for all spots in this field. The effect on the lateral fall-off of replacing this fixed pre-absorber with an automatic one, which is inserted for the low energy Bragg peaks only, has been evaluated. Additionally, instead of inserting a piece of material with a fixed thickness, using a variable pre-absorber consisting of eight mini range shifter plates and inserting only the necessary amount of material has been investigated. These three pre-absorption techniques have been combined with collimation, edge enhancement and edge-enhanced collimation.

Results

Optimization approaches: For a 10 cm airgap between the collimator/pre-absorber and the water tank, collimation alone improves the penumbra compared to edge-enhancement only for ranges between 4 cm and 10 cm (figure 2a). Edge-enhanced collimation minimizes the penumbra, reducing it by up to 2.6 mm compared to edge-enhancement alone. However, even with this advanced collimation technique, no substantial improvement of penumbra is gained from using the aperture for ranges above 15 cm.

Pre-absorber strategies: For a 10 cm airgap and for ranges above 4 cm, the penumbra is reduced by up to 2.7 mm for the automatic compared to the fixed pre-absorber approach (figure 2a). For ranges below 4 cm, it could be reduced by up to 2.0 mm assuming a variable pre-absorber (figure 2b). For all strategies, it is best to place the pre-absorber downstream of the collimator and to keep the airgap as small as technically possible.

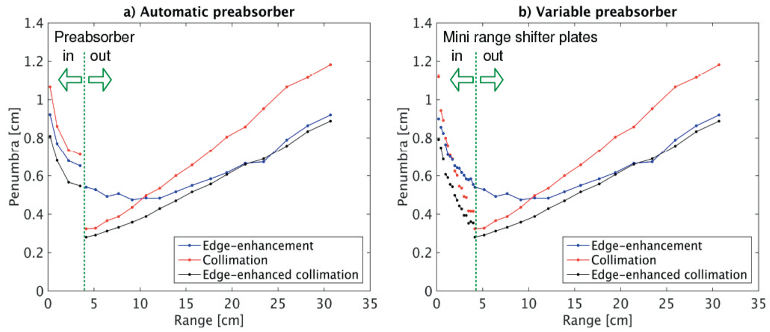


Figure 2: Penumbra at the Bragg peak for edge-enhancement (blue), collimation (red) and edge-enhanced collimation (black). The initial beam energy is reduced using (a) a pre-absorber, which is inserted for the delivery of low energy Bragg peaks only (automatic pre-absorber) or (b) a combination of up to eight mini range shifter plates (variable pre-absorber).

Conclusion

Multiple optimization and pre-absorption techniques to improve the lateral fall-off for proton pencil beam scanning have been analysed. For the clinically relevant airgap of 10 cm, collimation alone reduces the penumbra only for depths of 4 cm to 10 cm. Sharpest penumbras are achieved with a combination of collimation, edge-enhancement and a variable pre-absorber, which is positioned downstream of the collimator.

This work was supported by the research grant from Varian Medical Systems – Particle Therapy, Germany. The results will be presented at the 56th annual conference of the particle therapy co-operative group (PTCOG) mid of May in Yokohama, Japan.

For any further information, please refer to CPT,

Carla Winterhalter
Tel. +41 56 310 54 24
carla.winterhalter@psi.ch

Medical-Physics News

Optimized beam scanning direction: a technique to mitigate for interplay effects?

Proton therapy based on pencil beam scanning (PBS) exploits the favourable spatial dose distribution of proton beams for the delivery of conformal radiotherapy treatments even in most challenging situations. However, the physiological deformation of patient's anatomy, due to respiratory organ motion, can interplay with the dynamics of dose painting and hence detrimentally affect the quality of treatments for tumours located in the thorax or abdomen. Motion mitigation techniques are therefore applied in such cases to dilute dose distortions by gating, rescanning or tracking the radiation beam. The extremely flexible control of beam steering that is enabled by PBS, however, opens up to further options to manage the motion interference by, for instance, optimizing the scanning path and direction.

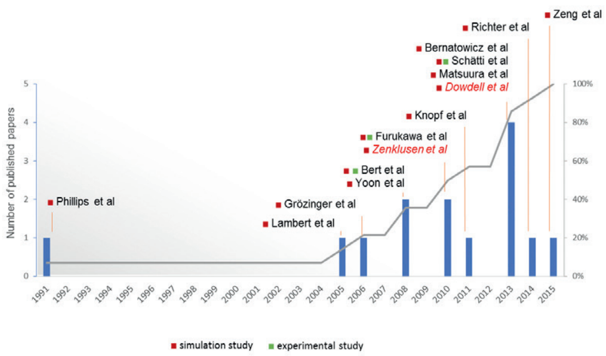


Figure 1: literature discussing the scanning direction in the context of motion mitigation. Items in red italic question the direction-dependence of organ motion mitigation capabilities.

The role of scanning direction for the mitigation of interplay effects in PBS proton therapy is indeed well reported in the literature, with 12 out of 14 papers published between 2001 and 2015, mentioning a direction-dependence (Figure 1). In published material, this scanning effect is however mostly supported by simulations, or by experiments using simple geometries which may not represent a realistic clinical scenario. To clarify this controversy, we have analysed multiple 4D measurements collected at PSI, to seek experimental evidence for the mitigating effect of scanning direction in more clinical situations.

All experimental data were acquired from multiple currently running 4D projects, using a sliding-platform mounted dosimeter. The sequence of spot positions defined by the treatment plans was edited to verify the dosimetry for the two most extreme cases of having the fastest scanning direction either parallel or orthogonal to the dosimeter's motion. Dose distributions were measured at mid spread out Bragg peak position with a CCD system and ionization chamber array, and compared to the static reference irradiations using the gamma criterion (3%/3mm). In our collection, the delivered fields range from geometrical targets such as 2D dose layers or spheres, to clinical plans for the treatment of lung cancer. Optical tracking was applied for motion-synchronized beam delivery, ensuring consistent measurement conditions for a variety of motion models, including patient-specific breathing curves and sinusoidal trajectories with amplitudes of up to 20 mm.

An exemplary excerpt of dose distributions measured for alternative primary scanning directions is reported in Figure 2. The transversal dose at iso-center for a circular field at 150MeV (0.2 Gy) shown in panel (a) was acquired during a gating experiment, with the dosimeter in sinusoidal motion and a gating window size of 4 mm. The result for a spherical target (2 Gy) in presence of 5 mm sin4 motion under similar experimental conditions is shown in Figure 2b, whereas the panel (c) is a clinical patient field (1 Gy) with 4 times volumetric rescanning and 5 mm motion.

Results from single energy (2D) measurements tended to confirm that if the primary scanning is parallel to the motion, a large mitigation of the interplay effect can be achieved (Figure 2a). This was however not confirmed for more realistic clinical settings using multiple energy levels (3D), where the interplay among energy layers (Figure-2b) and the use of highly modulated patient fields (Figure-2c) generally annihilate the scanning direction effect.

The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n.°290605 (PSI-FELLOW/COFUND). This work will be presented at the 56th annual conference of the particle therapy co-operative group (PTCOG) mid of May in Yokohama, Japan.

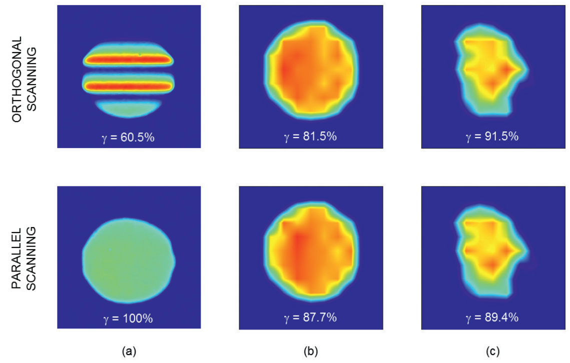


Figure 2: measured dose distributions scanning under similar experimental settings for single energy layer (a), spherical target (b) and patient field (c). γ-scores calculated at 3%/3mm for all pixels above 5% of prescribed dose.

For any further information, please refer to CPT,
Dr. Giovanni Fattori
Tel. +41 56 310 36 85
giovanni.fattori@psi.ch

Imprint

Editor
Dr. Ulrike Kliebsch

Chairman
Prof. Damien C. Weber

Chief Medical Physicist
Prof. Tony Lomax

Design and Layout
Monika Blétry

Contact

Center for Proton Therapy
CH-5232 Villigen PSI
protonentherapie@psi.ch
www.protonentherapie.ch
Tel. +41 56 310 35 24
Fax +41 56 310 35 15

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