PAUL SCHERRER INSTITUT

SpotOn+

Center for Proton Therapy :: Paul Scherrer Institut :: #14_3/2018

Dear Reader,

it is my distinct pleasure to present you with our first 2018 edition of SpotOn+.

In a couple of weeks, the operational start of our new Gantry 3 will manage our first patients on campus. This treatment unit is the result of the collaboration between USZ-UZH and a joint partnership with industry. Our next edition will detail the milestones of Gantry 3's implementation in the center and will elaborate on the foreseen collaboration between USZ and our industrial partner. In the meantime, I would like to bring your attention to our planning comparative study performed with the Radiation Oncology Department of Inselspital, Bern. We decided to change the hypothesis paradigm and tried in this study to disprove that protons delivered for intracranial germ-cell tumors (GCTs) would be potentially beneficial to children and adolescents and young adults. Eleven patients presenting with GCT were treated with PBS proton therapy with whole ventricular irradiation and a boost, if needed, to the primary tumors. All patients were re-planned in Bern with IMRT with the same dose-constraints and the dosimetry on brain structures was analyzed. Not surprisingly, the integral dose to the brain was significantly decreased but other structures, such as Willis circle and the temporal lobe were optimally spared with protons. This dose-reduction could lead to less vascular or cognitive long-term toxicity. On the medical physicist side, I am happy to report the work of Dr Fattori who assessed the impact of alternating intra-field scan direction during re-scanning for motion mitigation during PBS delivery. Tumor or OARs motion during the delivery of dynamic pencil beams induces dose corruptions (i.e. interplay effect) that have to be optimally mitigated. We have shown previously that dose-corruption mitigation can be obtained with 5–8 re-scanning providing that the motion is reasonable. Mitigation needs however to be improved in a substantial number of clinical cases and could be achieved by modifying the lateral meander direction within the field during the rescanning process. By changing scanning direction between rescans (and not energy layers), his team proved that fewer rescans were necessary (with a gamma-index endpoint) to experimentally mitigate a 6 mm motion for a liver treatment simulation in a phantom. Finally, modifying the beam current intensity for spot deposition within iso-energy layers has been assessed by Christian Bula et al. To achieve this, the control system of our treatment unit Gantry 2 was modified with an optical connection to one part of the cyclotron (vertical deflector is key in the regulation of beam intensity). As a result, this modification enables a substantial shortening of the time needed for a beam current change from several milliseconds (ms) to ca. 0.1 ms. The idea is that some low-weighted spots cannot be delivered (approximately 0.5 % of the total dose for clinical plans) as a result of the inherent latency of the beam switch-off mechanism between spots and the beam-intensity threshold. In our simulations, the low-dose spots around 50 monitor units were deliverable when reducing the beam current, thus increasing the dose conformality of the overall plan as shown in the Figure. Importantly, no detrimental effect on treatment time was observed. These two studies performed by my two colleagues and respective teams show undisputedly that substantial R&D input is needed for PT to increase the overall 'quality' of the radiation. To achieve this, proton centers need to have knowledgeable teams that can not only plan and deliver proton therapy but also push the limit of this delivery technology for the benefit of cancer patients.

That said, stay tuned for our next edition for some additional info on Gantry 3.

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

Radio-Oncology News

Whole ventricular irradiation for intracranial germ cell tumors: dosimetric comparison of pencil beam scanned protons vs. IMRT

Intracranial germ-cell tumors (GCT) represent a rare primary central nervous system (CNS) and histologically heterogeneous group of predominantly midline, mainly pineal (56 %) and/or suprasellar (28 %) neoplasms.

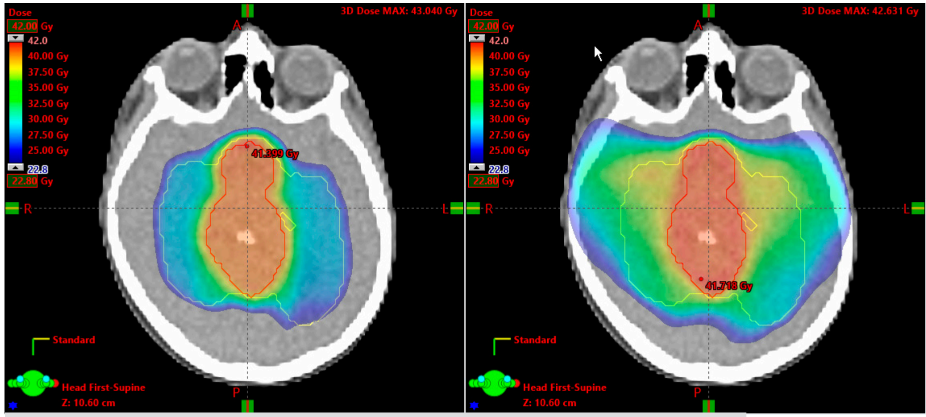
Incidence varies substantially across the continents, accounting for 2–4 %, approximately 3 %, and ‹5 % of all brain tumors in individuals aged 0–19 years in Europe, other western countries and in the USA, respectively; whereas in Asia they constitute between 8 % and 18 % of all pediatric CNS tumors, indicating that both genetic and environmental factors play vital roles in the development of this disease. In general, they comprise about 1% of all primary brain tumors in adults, and 2–18 % in children. They are most common in the second decade of life, with a peak incidence between 10 and 14 years of age, with a reported male-to-female ratio of 3–5 to 1. The World Health Organization has classified intracranial GCT into germinomas (50–70 %) and non-germinomatous germ cell tumors, the latest comprising a heterogeneous subset of tumors.

Germinomas are one of the most radiosensitive tumors known and are curable by radiotherapy alone, with an overall survival exceeding 90 % at 10 years, where secondary malignancies and stroke might affect an even better long-term survival. This excellent prognosis makes it imperative that the risk of long-term treatment-related side effects be kept at an absolute minimum by better sparing of normal tissue, specially taking into account that pediatric patients seem to be more sensitive to radiation than adults.

As surrogate for neurotoxicity (vascular abnormalities, demyelination, white matter necrosis, damage to the neuron stem cell compartment, limbic circuit and hippocampus), dosimetric sparing of eloquent structures may reduce the incidence and severity of neurocognitive and vascular late adverse events. Proton therapy provides a radiation technique that has the potential to further reduce the genesis of radiogenic impairment.

Whole ventricular irradiation (WV-RT) followed by a boost to the tumor bed (WV-RT/TB) is recommended for localized intracranial GCT. As the eloquent brain areas are mainly in direct vicinity of the target volume, it is unknown if proton therapy indeed substantially spares these organs at risk (OAR). Therefore, a dosimetric comparison study of WV-RT/TB was conducted to assess whether protons or modern photon radiotherapy achieve better critical organ sparing.

Eleven children with GCT received 24 Gy(RBE) WV-RT and a boost up to 40 Gy(RBE) in 25 fractions of 1.6 Gy(RBE) with pencil beam scanning proton therapy (PBS-PT). Additional critical structures for neurocognition have been delineated (brain, supra-/ infratentorial regions, subventricular zone, hippocampus, amygdala, hypothalamus, thalamus, Willi's circle, besides the brainstem, pituitary, chiasm, optic nerves, cochleae and temporal lobes). Respective intensity-modulated radiation therapy (IMRT) plans were generated for these patients, and plans were compared for target volume coverage (homogeneity index (HI) and inhomogeneity coefficient (IC)), critical neurocognition structures and OAR sparing.



Treatment plan of a child treated for an intracranial GCT to a total dose of 40 GyRBE. Left: PBS-PT plan (PSI); right: IMRT plan (Inselspital Bern).

Target volume coverage was similar for both modalities. Compared to IMRT, PBS-PT showed statistically significant dose reduction ($p<0.05$) in: maximum (Dmax), mean (Dmean) and integral dose (ID) of the normal brain (2.6 %, 35.4 %, 35.7 %); Dmean of the Willis' circle (6.7%), and brainstem (7.4 %). Likewise, the volume receiving ≥20 Gy (V20Gy) of the right (24.2 %) and left (20.9 %) temporal lobes was significantly decreased. No significant difference was observed for the dose-metrics/hippocampus.

Dosimetric comparison of WV-RT/TB in GCT demonstrates PBS-PT's advantage over IMRT in critical organ sparing, while keeping target volume coverage the same. PBS-PT may decrease the likelihood of vascular/neurological sequelae, as well as the risk of radio-induced secondary malignancies.

This evaluation was done in cooperation between Inselspital Bern and PSI by a resident staying one year at PSI. The results will be presented at the International Symposium on Pediatric Oncology (ISPNO) end of June in Denver and will be published soon (Correia et al. *Whole ventricle irradiation for intracranial germ cell tumors: pencil beam scanned protons vs. photons).*

Medical Physics News

Alternating intra-field scan direction in rescanning for improved motion mitigation

Pencil beam scanning (PBS) is an advanced technique for dose delivery used in particle therapy for high precision treatments. Target coverage is progressively built up patching together the contributions from thousands of narrow dose spots delivered while meandering through the target laterally and in depth, using energy modulation. Being inherently sequential, PBS is particularly vulnerable to intra-fractional organ motion, due to distortions of spots range and geometric misalignment during the progression of the treatment. Patients' breathing is therefore critically detrimental for dose homogeneity, as the beam delivery interplays with deforming anatomy and soft tissues, generating hot- and cold-spots in the clinical target volume.

Moderate organ motion can be mitigated by repeating the dose painting multiple times, so-called rescanning, to average dose distortions due to interplay. However, unsought positional and temporal correlations between patient breathing and the dynamics of rescanning may arise, undermining its efficacy. This effect is possibly emphasised by the fixed meandering scheme that sets lateral beam deflection in one direction at a time, to cover each energy layer with consecutive segments of dose spots line by line. Here we investigate the effectiveness of systematically changing the lateral meander direction within the field to increase interplay mitigation due to rescanning. Alternation of the meander path can be performed by either switching the primary direction of scanning between each energy layer or between each rescan.

This concept, shown in Figure 1 for the exemplary case of two times volumetric rescanning, is generally applicable to layered rescanning as well, as it does not require specific modification in the treatment unit, but rather a resorting of the spots' delivery order.

The motion mitigation capability of alternating intra-field scan directions has been experimentally investigated using a platform-mounted ionisation chamber array. The detector was moved to replicate a cranio-caudal target displacement (ca. 6 mm) of a liver carcinoma patient (PTV 76.59 cm^3), and the conventionally generated machine control files modified to scan either along or crosswise to the motion, or to alternate between energy layers (EE) or between each rescan (ER). In addition, the reference breathing signal has been processed to include random fluctuations in amplitude and period, simulating the effect of irregular patient breathing patterns.

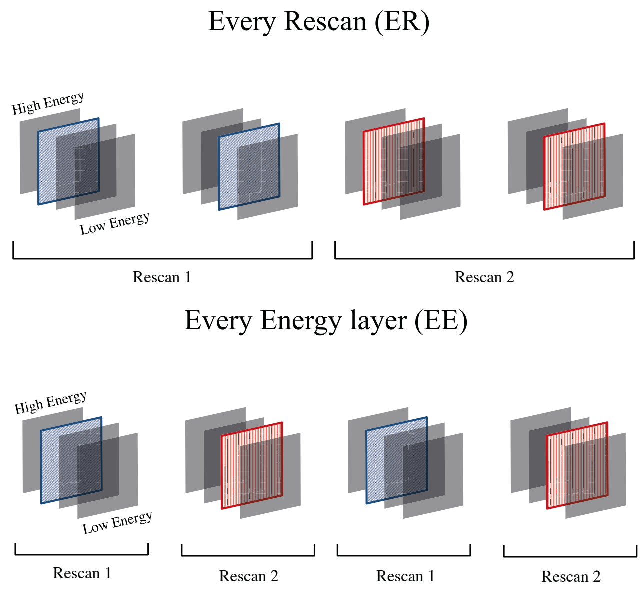


Figure 1: The concept of alternate field scan directions at a glance. Row-wise we follow the treatment progression, from highest to lower energy, according to volumetric rescanning regime.

Results from central plane measurements are shown in Table 1 and demonstrate that, to achieve a high gamma pass rate (~90% at 1%/1mm), a substantially smaller number of rescans was required when using ER (4x) compared to best-case conventional (non-alternating) rescanning (8x), and that ER was marginally more effective than EE. When introducing additional random amplitude and breathing fluctuations however, agreement was compromised for all scenarios, but was still consistently higher for the EE and ER scenarios (87.2%/95.7% pass rates for 8x) than conventional rescanning (best case 71.7% for parallel re-scanning). In conclusion, alternating scanning directions during re-scanning can further help mitigate interplay effect.

This study will be presented at the 57th annual conference of the particle therapy co-operative group (PTCOG) taking place on May 21st in Cincinnati, United States.

Table 1: Gamma score 1%/1mm for a liver cancer patient. The beam scanning direction is referred to the target motion as along (//), crosswise (⊥) and alternate Every Energy layer (EE) or Every Rescans (ER).

	Rescanning none				4x rescan				8x rescan			
	//	⊥	EE	ER	//	⊥	EE	ER	//	⊥	EE	ER
Patient breathing motion	33.3	33.3	45.5	--	53.2	48.9	89.4	93.5	82.6	76.1	89.4	93.6
Amplitude and period fluctuations	31.8	33.3	36.4	--	43.5	48.9	71.7	63.8	71.7	26.5	87.2	95.7

For any further information, please refer to CPT

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Physics News

Dynamic beam current control for improved dose accuracy in PBS proton therapy

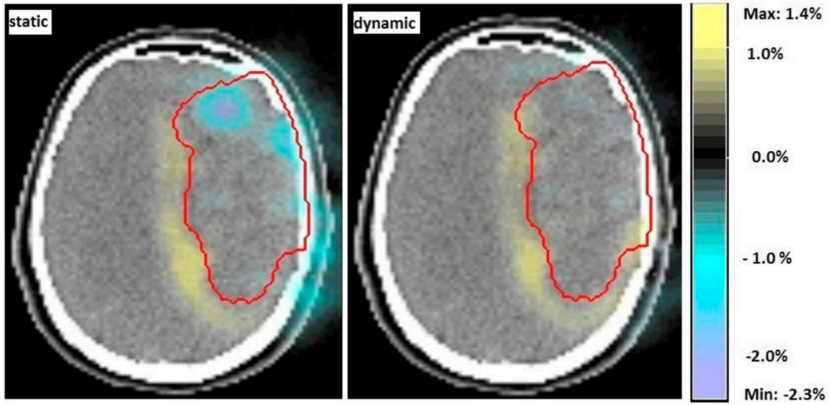
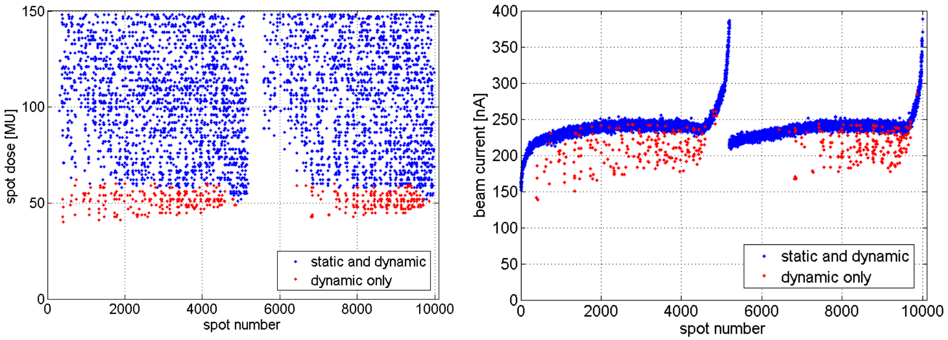


Figure 2: Relative difference of delivered and nominal dose per voxel for a head patient's field. On the left, the beam current is constant within an iso-energy layer (static mode), while on the right the current is reduced for low-dose spots (dynamic mode).

The step-and-shoot method of pencil beam scanning applies the dose on a three-dimensional grid in the target volume, with one dimension defined by the proton energy. While the spot dose may vary substantially within an iso-energy layer, the beam current typically remains constant. In this static operation mode, the inherent latency of the beam switch-off mechanism results in a lower limit for the deliverable spot dose, which may conflict with part of the low-weighted spots prescribed by the treatment planning system.

To overcome this limitation, we enhanced the control system of our PSI Gantry 2 by an optical communication link to the vertical deflector, a system located at the center of the cyclotron allowing fast regulations of the beam current. This direct connection shortens the time needed for a beam current change from several milliseconds (ms) to ~ 0.1 ms and hence opens the possibility to adjust the current for individual low-dose spots dynamically. Figure 1 shows the effect of this advanced operation mode on the delivery of a clinical field. The low-dose spots around 50 monitor units (Figure-1a, left side) become only deliverable when reducing the beam current accordingly (Figure-1b, right side). In a detailed analysis of 9 clinical fields, we found that on average 5% of spots (0.5% of dose) were skipped in the static operation mode, while the dynamic mode allowed delivering all spots. No adverse effect on the treatment time was observed. The accuracy of the delivered dose compared to the planned distribution was generally improved, as illustrated in figure 2 for one of the clinical fields analyzed. In this example, the maximum missing dose per voxel could be lowered from 2.3% to 1.3%. The method was successfully commissioned and is in clinical operation since fall 2017.

Figure 1: Dose per spot (left) and corresponding beam current (right) for a clinical field consisting of two patches. The blue dots represent spots delivered in both modes (static and dynamic), while the red dots show the low dose spots only deliverable in the dynamic mode with an associated beam current adjustment as shown in (b).



We consider dynamic beam current control to be a valuable contribution to cyclotron-based spot scanning technology, especially in the context of new modalities such as rescanning and high-intensity deliveries, where the number of low-weighted spots is even more pronounced.

This work will be presented at the 57th annual conference of the particle therapy co-operative group (PTCOG) mid of May in Cincinnati, USA.

For any further information, please refer to CPT

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