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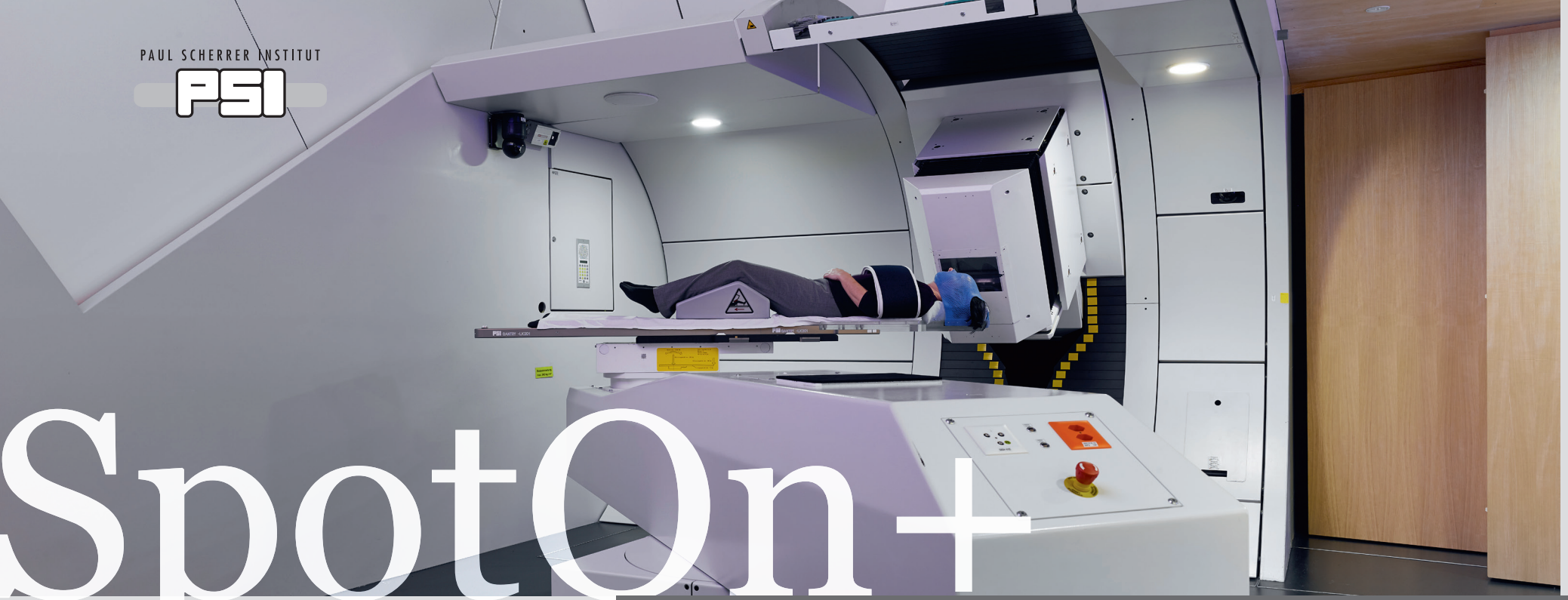

SpotOn+

Center for Proton Therapy :: Paul Scherrer Institut :: #5_3/2015

Dear Colleagues

On January 2015, the 1000th patient has been treated with a Gantry at PSI. Gantry 1 was built in the 1990s and clinically commissioned in 1996. Thanks to the creative input from Eros Pedroni who conceptualized this treatment Unit at that time, Gantry 1 has successfully treated cancer patients for nearly 20 years continuously. It had a non-isocentric design which makes it one of the most compact Gantry ever designed. The results of our series of low-grade gliomas treated with Gantry 1 are reported in this issue of SpotOn+. Dr Badyan reported a 3-year survival of 83.4 % for patients with this type of brain tumor occurring in young patients.

New technological innovations based on many years of experience gained in the development and operation of Gantry 1 was implemented in the Gantry 2 design which was also conceptualized by Eros Pedroni with the addition of David Meer. One of the design differences between the two treatment units is that Gantry 2 uses two fast magnets to scan the tumour, while Gantry 1 uses only one fast magnet to deviate the protons. Additionally, in the third dimension (i.e. the depth of penetration of the protons) the design of the beamline and gantry allows a change from one tumour layer to the next in about 100 msec (5 mm difference in proton range). Therefore a repainting strategy is possible (i.e. during the same treatment the same volume is scanned through several times), which is one of the cornerstone of the movement mitigation process that is currently implemented at PSI for moving targets. Dose-Repainting is described in this issue by Dr Perrin. Using the LuCa phantom, dose-degradation (i.e. cold and hot spots within the target volume) could be substantially decreased with dose homogeneities similar to those of the static case, with a rescan factor of 8. An example of advanced scanning technique, potentially delivered with our Gantry 2, is also described by Dr Meier in this issue. In a simulated example of a skull-base tumor, the brainstem dose could be decreased by 10 % to 20 % with contour scanning, with no substantial increase of the dose inhomogeneity within the target volume. These results are remarkable, as high-radiation dose must be delivered to skull base tumors and the dose-constraints of this OAR are of paramount importance to guarantee a safe delivery of radiation.

1000
Gantry Patients

For our next issue of SpotOn+ we have another 1000th anniversary, but it will be for a totally different type of tumor and beam line. Stay tuned for more!

Sincerely,
Prof. Damien Charles Weber,
Head of CPT

Radio-Oncology News

Clinical and radiological outcomes of adults and children with low-grade glioma treated with pencil beam scanning proton therapy at PSI

Background and Methods

Low-grade Gliomas (LGG) are an uncommon group of brain tumors accounting for approximately 20 % of pediatric brain tumors and 10 % of adult brain tumors. The treatment regimen includes a multidisciplinary strategy comprised of surgery, chemotherapy, and radiotherapy depending specifically on tumor grade, extent of surgery, age of the patient and symptoms. Due to the relatively long survival of LGG patients, the treatment strategy is individually adapted to optimize the likelihood of cure, while trying to minimize the risk of late treatment toxicity. Over the last few decades, advances in radiation therapy have improved the therapeutic ratio for these tumors. Amongst the modern radiation therapy options, proton therapy (PT) allows for the greatest dose conformality, and thus is a particularly attractive treatment option for children and young adults with LGG.

We assessed the clinical and radiological outcomes of adults and children with LGG of the brain treated with pencil beam scanning (PBS) PT at the Paul Scherrer Institute (PSI). The results have been submitted in abstract form to the 54th annual meeting of the Particle Therapy Co-Operative Group.

Results

Between 1997 and 2014, 28 patients (female, n = 14) were treated with PT, 20 (71 %) of whom were less than 18 years of age. Median age at start of proton therapy was 12.3 years (range 2.2 – 53.0). Twelve (43 %) patients received chemotherapy prior (n = 11) to, or concurrently (n = 1) with, PT. A median dose of 54 Gy (RBE) (range 46–64) was administered. Radiological response to PT was determined using the Response Evaluation Criteria in Solid Tumors (RECIST) criteria. After a median follow-up of 30.5 months (range, 4.2 – 193.6) ten (36 %) patients presented with a clinical local failure (LF). Three (11 %) patients died, all of tumor progression. Best radiographic tumor response by RECIST was evaluable in 11 (39 %) patients. Of these 11 patients, eight (72 %) patients had stable disease, one (9 %) had progressive disease, one (9 %) had a partial response, and one (9 %) a complete response to proton therapy.

The 3-year overall- and progression-free survival (PFS) was 83.4 % and 56.0 %, respectively. PT was well tolerated. No grade >2 acute toxicity was observed. Grade 3 late radiation necrosis developed in one (4 %) patient, and grade 2 in two patients (7 %). Eight patients (29 %) developed late grade 2 hypopituitarism. Two (7 %) patients developed late grade 2 memory or cognitive impairment. No radiation induced tumors were observed.

Conclusions

Our data suggests that PBS PT is a highly conformal and effective treatment for adults and children with LGG. After PT over 80 % of patients survived over 3 years. Importantly, treatment was tolerated very well with no instances of grade 3 or higher acute toxicity and very low rates of radiation necrosis, and long term pituitary dysfunction or cognitive dysfunction. We will continue to offer this excellent treatment to patients with LGG.

For any further information, please refer to CPT,

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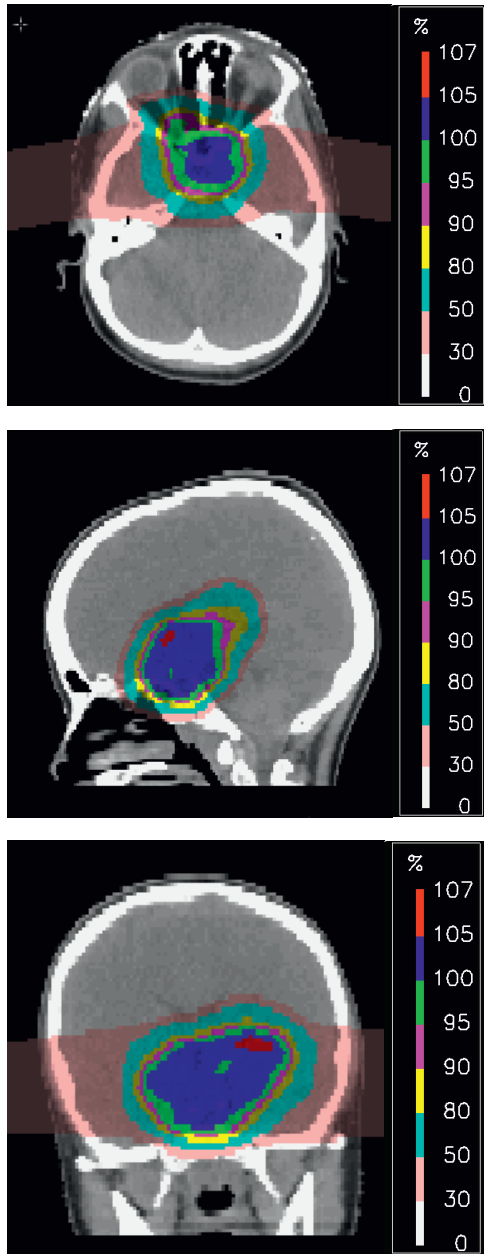

Dose distribution of a treatment plan superimposed on CT images of a patient with a low-grade glioma (axial, sagittal and coronal views). Note the tight conformality of the dose distribution. The isodose contours are represented by the color-wash (corresponding values are displayed on the right border of each photo).

Medical-Physics News

Contour scanning for pencil beam scanned proton therapy

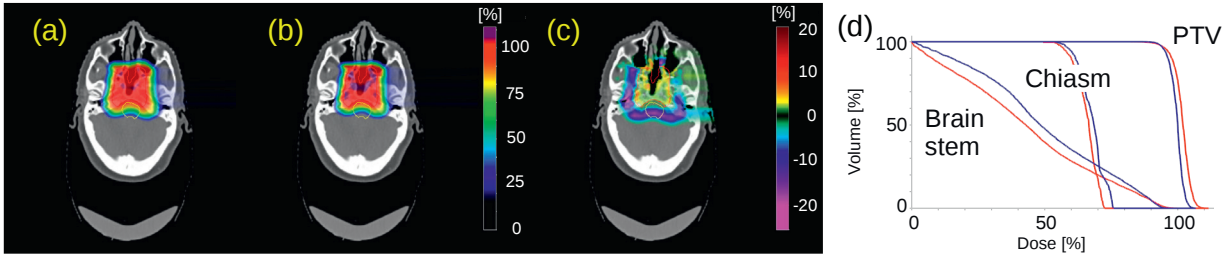

Figure 2 Dose distribution for grid scanning (a) and contour scanning (b) approach with dose difference distribution (c). DVHs (d) for grid scanning in blue and contour scanning in red. The doses were normalized to have the same D98.

In pencil beam scanned (PBS) proton therapy, the dose is deposited by many thousands of pencil beams of varying energy. By individually optimizing the number of protons delivered by each of these "spots", highly conformal dose distributions can be achieved both distal and lateral to the target volume. However, due to the finite width of the pencil beam in air, and subsequent broadening due to scattering in the patient, the lateral penumbra of PBS plans can be compromised. Therefore improvements of the lateral penumbra, as well as lateral dose conformation, are the subject of ongoing research in our group.

In our current practice, pencil beams are placed on a rectilinear grid such as to cover the target volume at each energy level and up to a distance of 5 mm outside its surface (figure 1a). While such a regular spot distribution is necessary for the 1D magnetic scanning of Gantry 1, the double scanning delivery provided by Gantry 2 allows for more advanced spot placements.

As an extension to an independent dose calculation tool developed for quality assurance dose reconstructions, a different approach called 'contour scanning' to spot placement has been implemented. From the initial contours as drawn by the clinician, a three dimensional wireframe model is constructed. This is then cut by planes perpendicular to the beam direction, with the resulting contours subsequently being shrunk to obtain a set of concentric closed paths along which the Bragg peaks are positioned (see figure 1b).

A number of clinical skull base cases have been re-planned using this new approach. These cases are characterized by the close proximity of several organs at risk (brain stem, optic nerves and chiasm) to the target volume and were thus expected to benefit most from the new spot placement method.

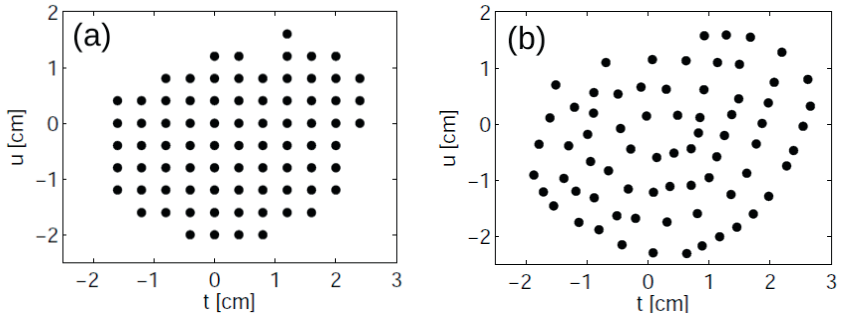

Figure 1 Single energy layer for standard grid (a) and contour spot placement (b).

The resulting dose distributions show a marked reduction of dose to the area surrounding the tumor (e.g. up to 20 % reduction of dose in the organs at risk). This corresponds to a 2 mm shift of the 50 % isodose as well as a 15 % reduction of the penumbra (P80-20). The cost of this improvement is a slight reduction of the dose homogeneity (D5/D95) in the PTV of 3.4 (± 0.2) %.

Proof of concept dosimetry measurements for simple geometries in water, as well as for realistically shaped targets in an anthropomorphic head phantom, have confirmed the expected lateral dose reductions, and have shown that the delivery of contour scanned plans is possible within the existing delivery infrastructure. Further improvements to the penumbra are expected to result from optimizing the lateral spacing of the concentric contours based on the beam size. Additionally, the potential of combining the two approaches by placing spots on the surface and using a rectilinear grid placement for the center of the target is being investigated with the aim of achieving better dose homogeneity while maintaining the improved dose conformation of the contour scanning approach.

This work has been submitted in abstract form to the 54th annual meeting of the Particle Therapy Co-Operative Group.

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Medical-Physics News

Rescanning measurements in a 4D anthropomorphic phantom

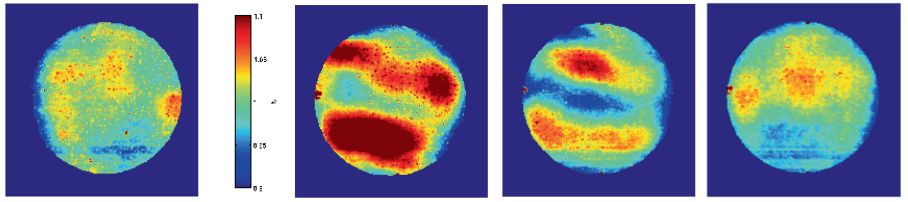
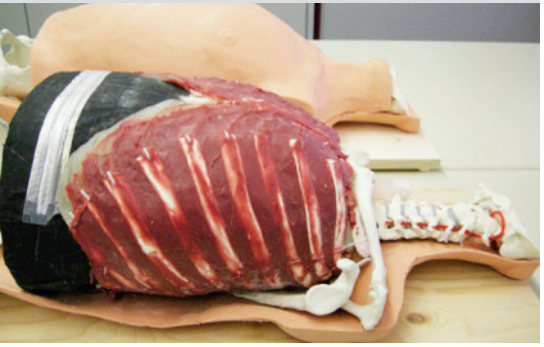


Figure 2 Central plane of target in static, moving with 10 mm sine motion, with variable rescanning. Colour scales shows %Dose normalized to the mean dose of the static control film, ranging from blue = 90 % to red = 110 %.

Pencil beam scanning (PBS) proton therapy using protons can deliver a precise treatment to a tumour while reducing the dose to surrounding tissue. However, in mobile organs such as the lung, precise targeting of the dose is difficult. Organ and tumour motion deteriorates the dose distribution because there may be a rift between the radiation delivery time-line and the time-line of the tumour motion; the "interplay" effect [1]. This led to the design of a new gantry and beam line components that can deliver an extremely fast scanning beam. This gantry is now at our disposal (PSI's Gantry 2) for pioneering measurements of rescanned PBS proton therapy. This fast scanning technology is beneficial for "motion mitigation" methods such as the "rescanning" technique, which involves scanning the beam through the tumour several times, and as a result averaging out the interplay effect.

Figure 1 LuCa, CPT's dynamic breathing thorax phantom.



In recent developments we have modelled a patient thorax in an anthropomorphic phantom (LuCa), incorporating a lung tumour model and typical thoracic anatomy, such as inflating lungs, moving ribs and a vertebral column (see Figure 1). Changes in position and density along the beam path during breathing are modelled in this phantom, which is inflated and deflated with custom breathing patterns. Film is placed in the model tumour to measure the dose distribution.

The phantom was utilized to perform end-to-end treatment verifications, investigating the ability for rescanned PBS proton therapy to recover the dose distributions in mobile lung tumours. Five planes of Gafchromic film in the coronal plane were used to measure the dose distributions resulting from PBS proton therapy for a range of rescan factors (ie. the number of times the beam scans through the tumour volume) and peak-to-peak motion amplitudes (4 –10 mm). A PBS treatment was planned to the phantom using our in-house planning system, and rescanning was applied while generating the beam steering files for the plan. The ITV was generated from the maximum excursion of the target as visualised on the mean projection CT calculated from a 4DCT scan. Two non-coplanar Single Field Uniform Dose (SFUD) fields (2 CGyE prescribed dose) were employed at the following angles (gantry, couch): (–25, 30), (45, 180). Prior to delivery, phantom and film positioning was checked and corrected using CT imaging. Table shifts were applied to match the ribs, and the tumour mid-ventilation position was aligned cranio-caudally by adjusting the position of the tumour in the lung. The phantom was programmed to move with a sinusoidal motion with maximum excursions of up to 4 and 10 mm for deliveries with rescan factors between 1 and 8. Reference films were acquired with the phantom and tumour stationary, and with a moving tumour with no rescanning.

Hot spots of up to 116 % of the prescribed dose, with a pattern typically expected with the interplay effect, were clearly observed on the film with 10 mm motions (see Figure 2), while with 4 mm motion, only a faint interplay pattern was observed. With application of rescanning, these hot spots largely were removed. With a rescan factor of 8, even in the case of 10 mm motion, dose homogeneities similar to those of the static case could be achieved (D5-D95 of static and 10 mm motion was 8.4% and 8.8 % respectively).

We have shown by our measurements in an anatomically-realistic case that rescanning PBS proton therapy can deliver clinically acceptable dose distributions, provided an appropriate rescan factor is used for dose averaging. This work was submitted to the ESTRO congress this year and was awarded with the Donal Hollywood prize.

[1] Phillips M H, Pedroni E, Blattmann H, Boehringer T, Coray A and Scheib S 1992 Effects of respiratory motion on dose uniformity with a charged particle scanning method Phys. Med. Biol. 37 223–33

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Villigen PSI, March 2015