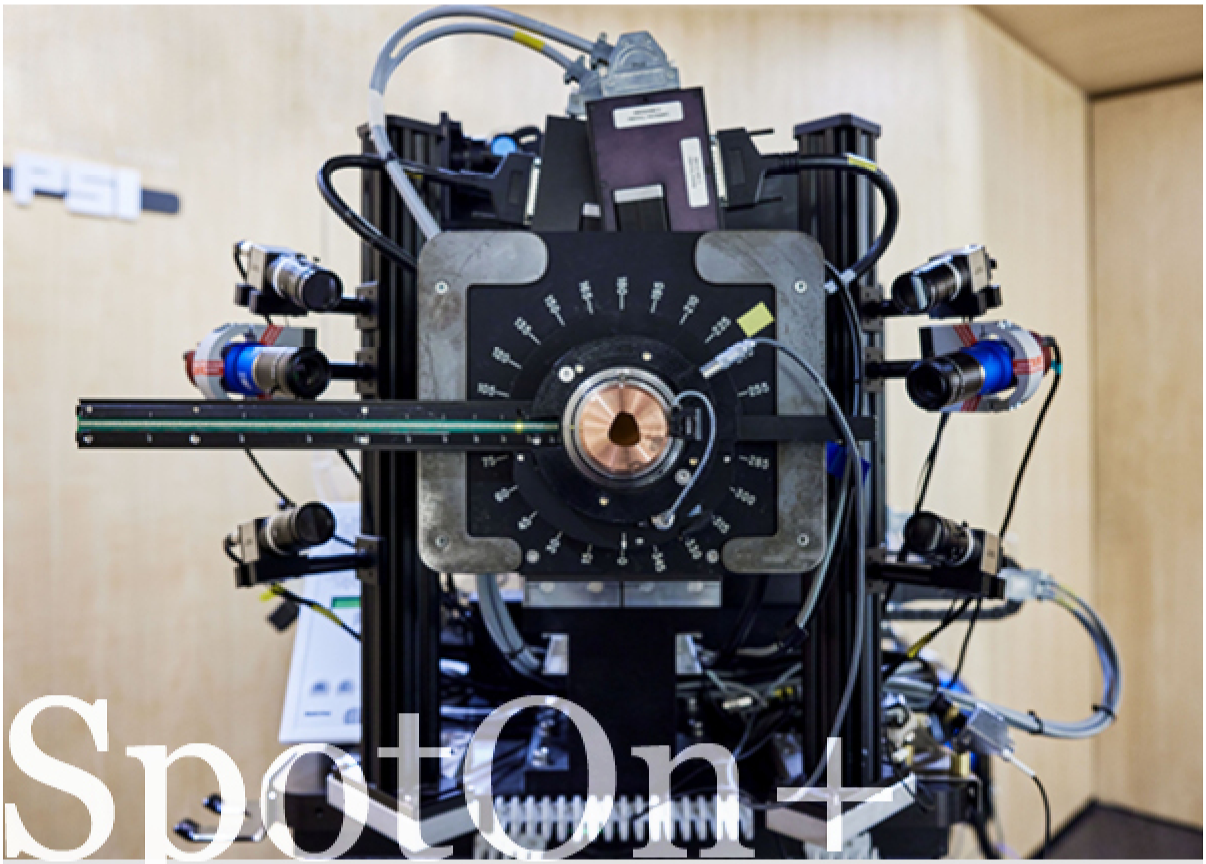
Paul Scherrer Institut
Center for Proton Therapy
Newsletter #31_03/2024



SpotOn+

Dear Reader

Welcome to this first 2024 edition of our SpotON+ Newsletter. The picture of this edition is one of our successful eye treatment program (or 'OPTIS') that was initiated exactly 40 years ago, the first in Europe. PSI has treated the largest number of eye tumor (mostly uveal melanoma) patients in the world, with a remarkable local tumor control rate. This endeavor would not have been possible without the critical collaboration of our colleagues from Lausanne (Hôpital Jules Gonin) and Zurich (Ophthalmology Department USZ).

Shifting to non-ocular tumor treatment with protons, one important current topic is adaptive proton therapy. Adaptive treatments are needed to counter morphologic changes of anatomical structure, being organs at risks or tumor volume, by creating new radiation plans during the course of treatment. In order to monitor the dosimetric impact of anatomical changes, imaging is key, be it with proton radiography or photon modalities. In this edition, Lundberg et al. summarises his work of comparing synthetic CT quality with the residual proton range from simulations based on the sCT utilising proton radiography. Anotherr clinical paper from Willmann et al. provides the outcome of low-grade glioma patients treated with protons. Overall, the QoL (Global health) was comparable to the reference values during and after proton therapy. The 4-year survival rate was excellent. Finally, treating mobile tumors, such as lung cancer, with pencil beams can lead to a corruption of dose deposition. As such, respiratory suppression techniques are key in order to mitigate the interplay effect, as shown previously by our group (Emert et al.). In this edition, Missimer et al. from the same group applied successfully an in-house automatic MRI lung contouring algorithm to assess lung volumes.

That being said, I hope this newsletter is of interest to you and I stay tuned for the next edition in about 4 month's time.

Sincerely,
Prof. Damien C. Weber,
Chairman Center for Proton Therapy,
Paul Scherrer Institute

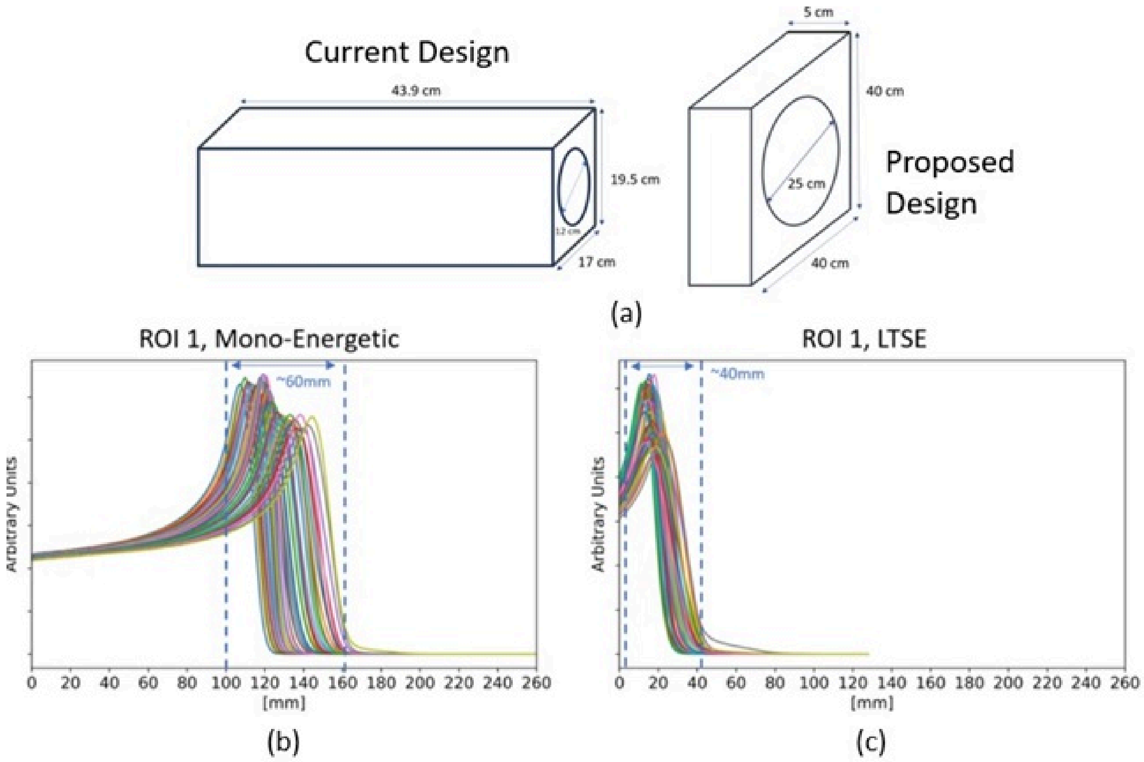
Medical-Physics News

Development of a simulation framework, enabling the investigation of locally tuned single energy proton radiography

Adaptive Proton Therapy (APT) is a fast-growing field with the possibility of improving patient outcomes. It aims to monitor the patient's anatomy to assess the dosimetric impact of changes and subsequently make treatment adjustments. Consequently, frequent imaging is required, with diagnostic computed tomography (CT) not being ideal due to the relatively high imaging dose. In current practice, a Cone-Beam CT (CBCT) is acquired for patient positioning prior to a treatment fraction. The CBCT delivers less imaging dose but suffers from artifacts and scattering effects, and, therefore, cannot directly be used to calculate proton dose distributions. Synthetic-CT (sCT) aims to combine the information of CBCT and diagnostic CT to create an image with updated anatomy and diagnostic image quality. To use sCTs in clinical workflows Quality Control (QC) tools and procedures need to be incorporated.

Proton Radiography (PR) has shown to be a promising QC tool verifying the sCT quality by comparing the residual proton range from simulations based on the sCT and measurements distal to the patient. Previous research has been performed with a mono-energetic PR acquisition, where the resdiual proton range can greatly vary depending on the transversed medium. To account for the variability, a Multi-Layer Ionisation Chamber (MLIC) was used, which has a large longitudinal axis of about 44cm and a Field of View (FOV) of 12cm in diameter, as seen in the figure. The size and dimension of the MLIC complicate its implementation into a clinical workflow where time and flexibility are important. Reducing the longitudinal axis would make it more manageable, and increasing the FOV would enable more available PR locations without any uncertainty-prone patient/couch repositioning.

We have developed a framework to predict proton energies that allow for PR acquisition with a more compact PR detector. By taking the thickness and material of the transverse path into account, each proton beam energy can be planned in such a way as to minimize the residual range after the patient, termed locally-tuned single energy (LTSE) PR acquisition. We validated this approach by comparing simulations with measurements performed at the Paul Scherrer Institute (PSI). We tested two PR acquisition approaches, mono-energetic and LTSE, in two regions of interest (ROI) within a head phantom. Our findings indicate that the LTSE acquisition approach is able to reduce the residual range of protons by up to 40% compared to the mono-energetic acquisition approach, as illustrated in the figure. More details on our work can be found in the recently published technical note (Lundberg et al. 2024).



Showing (a) the current and our proposed design of a Multi-Layer Ionisation Chamber, (b,c) the difference in residual Range and Bragg peak spread of using a 210 MeV mono-energetic approach and the predicted Locally-Tuned Single Energy (LTSE) approach for one of the ROIs.

This work is carried out in close collaboration between PSI, the Institute of Medical Engineering and Medical Informatics at the FHNW, and Ion Beam Applications (IBA) and works towards a compact PR detector design for sCT QC in an adaptive proton therapy treatment workflow.

Oncological Outcomes, Long-Term Toxicities, Quality of Life and Sexual Health after Pencil-Beam Scanning Proton Therapy in Patients with Low-Grade Glioma

Background

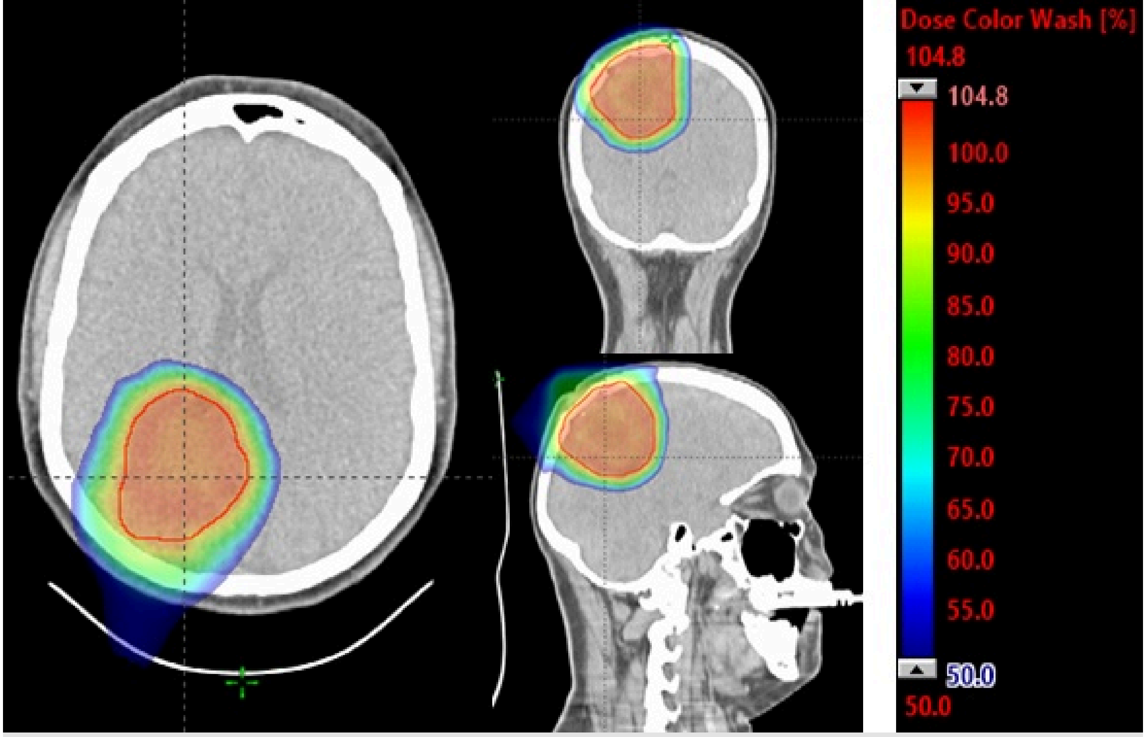
Gliomas are primary brain tumors that are graded from CNS WHO grade 1 to 4, with grade 1 and 2 representing low-grade glioma (LGG). LGGs have a more favorable prognosis as compared to high-grade glioma and are treated with surgery, radiotherapy and chemotherapy. Proton therapy (PT) is an alternative to conventional photon radiotherapy as it reduces the brain integral dose and essentially eliminates the exit dose behind the target volume. To date, there are only a limited number of studies on patients with LGG treated with PT. Besides side effects, which are physician-scored in most instances, patient-reported outcomes have gained clinical significance in recent years. To guide treatment decisions for patients with LGG, we analyzed oncological outcomes, toxicities, self-reported quality of life (QoL) and sexual health (SH) of LGG patients treated with pencil-beam scanning proton therapy (PBS-PT) at the Paul Scherrer Institute Center for Proton Therapy.

Material and Methods

We retrospectively analyzed 89 patients with LGG treated with PBS-PT (median dose 54 Gy (RBE)) from 1999 to 2022 at our institution. QoL was prospectively assessed during treatment and yearly during follow-up from 2015 to 2023, while a cross-sectional exploration of SH was conducted in 2023.

Results

The patients' median age was 25.4 years and most LGGs (n = 58; 65.2%) were WHO grade 2 and approximately half (n = 43; 48.3%) were located in the vicinity of the visual apparatus or thalamus. After a median follow-up of 50.2 months, 24 (27%) patients presented with treatment failures and most of these (n = 17/24; 70.8%) were salvaged. The 4-year overall survival was 89.1%. Only 2 (2.2%) and 1 (1.1%) patients presented with CTCAE grade 4 and 3 late radiation-induced toxicity, respectively. No grade 5 late adverse event was observed.



Proton plan of a 30-year old female patient with a high parietal low-grade glioma. The prescribed dose is 54 Gy(RBE). 95% of the dose surrounds the planned target volume (red line), and the lower dose limit has been scaled to 50%.

The global health as a domain of QoL remained stable and comparable to the reference values during PBS-PT and for six years thereafter. Fatigue levels rose above the normative reference values during PBS-PT and appeared comparable thereafter. Cognitive function was only slightly below the normative reference values, potentially decreasing slightly over the years of follow-up.

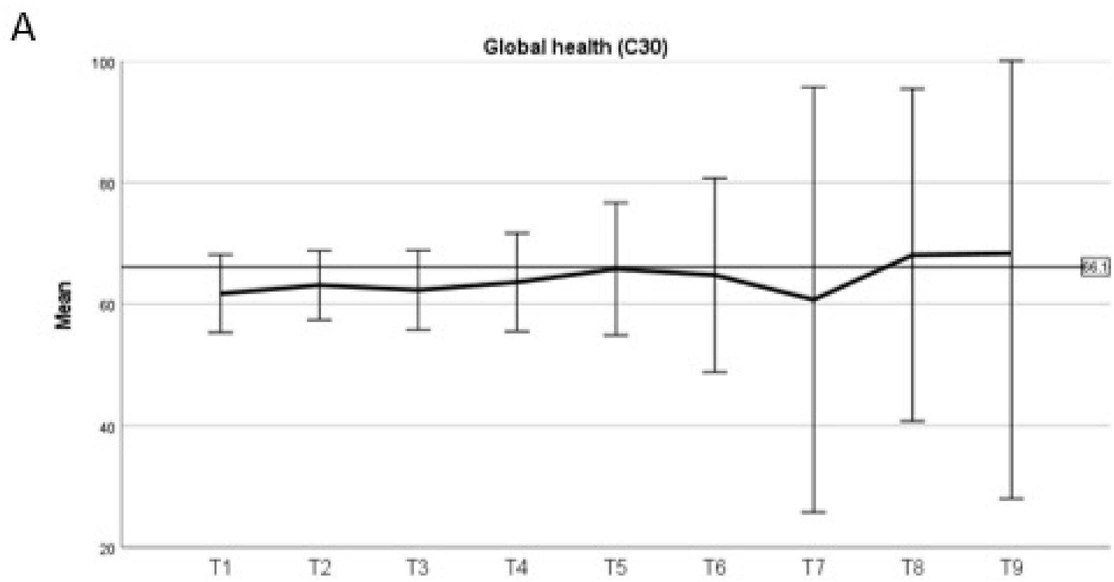


Figure 1: Global health before (T1), during (T2) and the end (T3) of proton therapy and yearly thereafter (T4-9). Error bars denote 95% confidence interval. Black line indicated normative reference value for the general population (value: 66.1).

Of 66 eligible patients for the cross-sectional analysis of SH, 14 patients returned the completed questionnaire. Our findings suggest comparable sexual satisfaction to the normative population.

Conclusions

LGG patients treated with PBS-PT achieved excellent long-term survival and tumor control, with exceptionally low rates of high-grade late toxicity, and favorable QoL and SH.

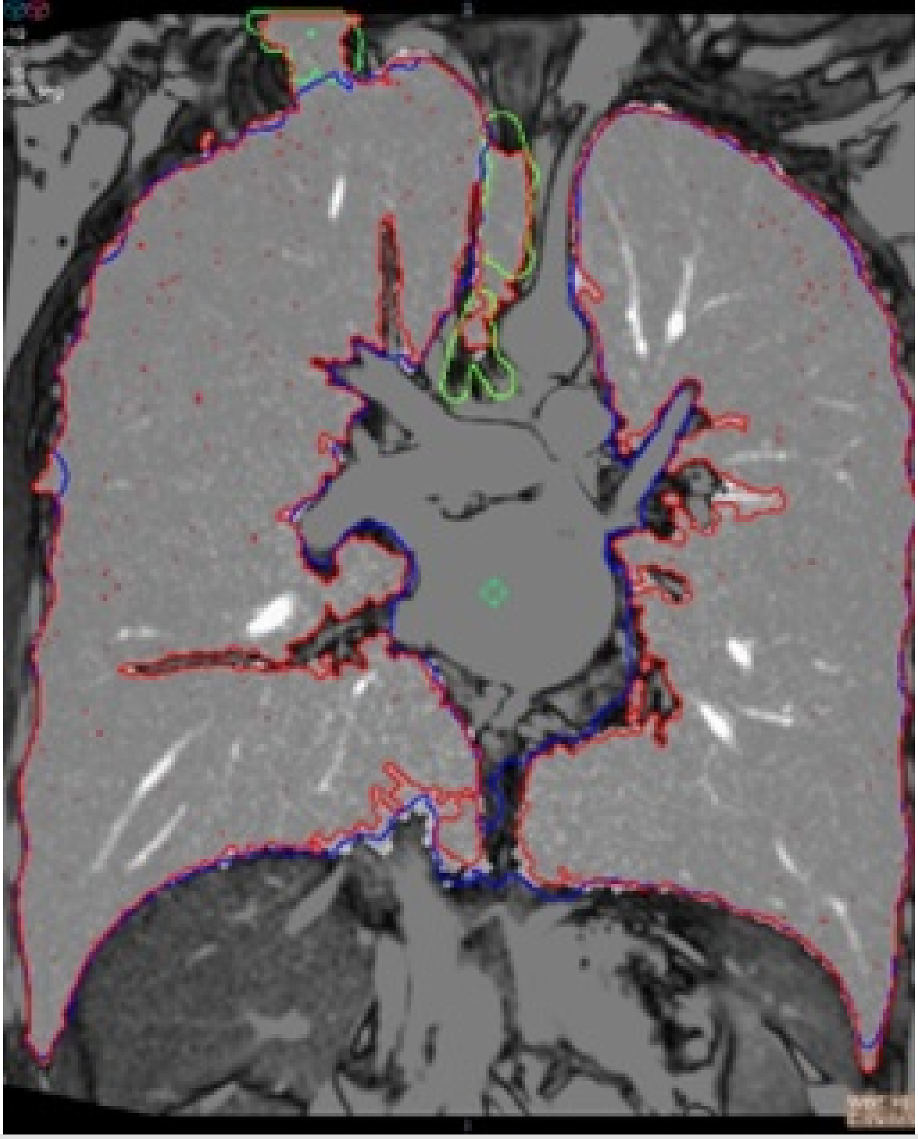
This work has recently been published (Willmann et al. 2023)

Medical-Physics News

Automatic lung segmentation of magnetic resonance images: A new approach applied to healthy volunteers undergoing enhanced Deep-Inspiration-Breath-Hold for motion-mitigated 4D proton therapy of lung tumors

Respiratory suppression techniques represent a very effective strategy for motion mitigation in 4D-irradiation of lung tumors with protons. Hereby, in a former in-house MRI-guided clinical study the feasibility of enhanced Deep-Inspiration-Breath-Hold (eDIBH) was successfully demonstrated by simulating and recording quasi-static lung irradiation fractions in an MR scanner with healthy volunteers. It was shown that (i) 3D-treatment conditions should also be possible for suitable lung patients, (ii) eDIBH is best achieved in presence of total lung capacity (TLC), which results in maximum sparing of healthy lung tissue and minimization of key dosimetric lung irradiation parameters (D_{mean}, $V_{20\%}$), and (iii) TLC conditions under eDIBH lead to excellent reproducibility of lung topology, including potential lung tumor localizations and adjacent organs, significantly minimizing intra- and interfractional positional deviations compared to similar methods.

In this context, accurate determination of lung volumes (LVs) through effective, precise and reliable contouring of the acquired lung MRIs is of crucial importance. Based on the analysis of 168 MRIs under eDIBH conditions, an automatic MRI lung contouring algorithm was developed in-house. A typical result is visualized in the picture below. The algorithm consists of 4 analytical steps: (i) image preprocessing, (ii) MRI histogram analysis with thresholding, (iii) automatic segmentation, (iv) 3D-clustering. To validate the algorithm, 46 eDIBH MRIs were manually contoured. Sørensen-Dice similarity coefficients (DSCs) and relative LV deviations were determined as similarity measures. Assessment of intrasessional and intersessional LV variations and their differences provided estimates of statistical and systematic errors.



Comparison of segmentation methods and illustration of artifacts: in this displayed acquisition of one subject red delineates automatic segmentation, blue manual segmentation. Green delineates artifacts, generated in the trachea and on the superior lobe of the right lung.

Lung segmentation time for 100 2D-MRI planes was ~10 s. Compared to manual lung contouring, the median DSC was 0.94 with a lower 95 % confidence level (CL) of 0.92. The relative volume deviations yielded a median value of 0.059 and 95 % CLs of -0.013 and 0.13. Artifact-based volume errors, mainly of the trachea, were estimated. Estimated statistical and systematic errors ranged between 6 and 8%. The presented analytical algorithm is fast, precise, and readily available. The results are comparable to time-consuming, manual segmentations and other automatic, mainly AI-based segmentation approaches. Post-processing to remove image artifacts is under development. The algorithm was developed and implemented in the widely used scientific software platform Matlab™ and is available upon reasonable request.

This work has recently been published (Missimer et al. 2024).

Imprint

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Villigen PSI, March 2024

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