Dear Reader

Welcome to this last 2023 edition of our SpotOn+ Newsletter. I hope you are enjoying the modified version of our Newsletter. Do not hesitate to give some feed-back if you think some improvement is required. In this edition, Pica et al. are reporting the outcome of AYA patients with uveal melanoma (UM) treated with proton therapy. Considering that PSI has treated the largest cohort of UM patients in the world (approximately 21% of all UM patients treated with protons), this large group of 270 AYAs and 270 matched adults provide some interesting outcome information to the onco-ophthalmological community. Overall, ocular outcomes and local tumor control were similar in both AYA and adult groups. Five-years-cumulative metastasis incidence for both groups was 13% and 7.9%, respectively but this difference was not significant.
The second article summarises the analysis of 200 meningioma WHO grade 1-3 patients treated with pencil-beam scanned protons. Local tumor control was excellent for benign disease. On univariate analysis, factors which were significantly associated with worse local control were non-benign histology, male gender, and timing of treatment at progression or relapse among other factors. The latter factor is important when considering adjuvant therapy for WHO grade>1 meningiomas. The results of the ROAM-EORTC 1803 trial will not be available before 2026.
Lastly, an important step has been made by fast dose calculation and optimisation algorithm for proton therapy that will enable us to optimize treatment plans in real time.

I take the opportunity to wish you all happy holidays. Yes, it’s been said, many times, many ways, but we still mean it just as much! Happy New Year!

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

Radio-Oncology News

Clinical Outcomes in AYAs (Adolescents and Young Adults) Treated with Proton Therapy for Uveal Melanoma: A Comparative Matching Study with Elder Adults

Background

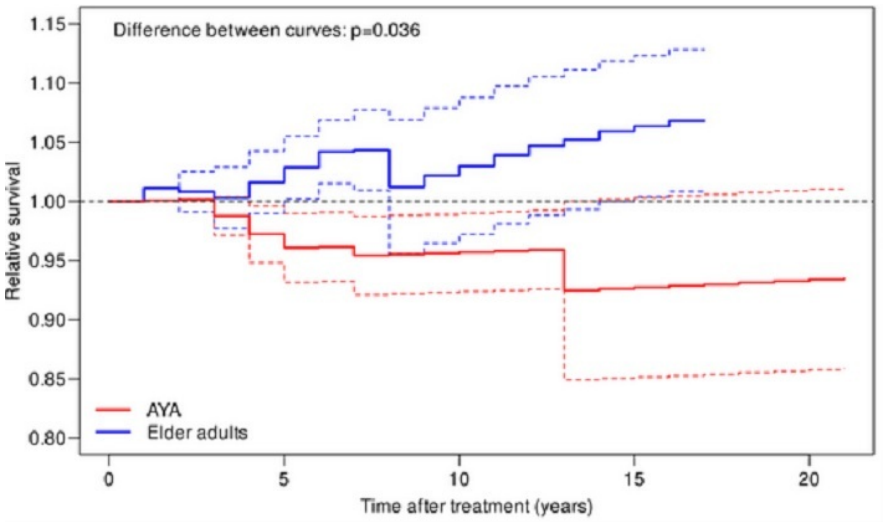
Uveal melanoma (UM) is the most common primary ocular malignancy in adults. Radiation therapy (RT) represents the standard care for this type of cancer. Proton therapy (PT) is associated with high local tumor control rates and has been used for several decades in our center to treat UM. The aim of this study was to compare the clinical outcomes of adolescents and young adults (AYAs) with those of elder adult patients treated with PT for UM.

Material and Methods

A retrospective, comparative study was conducted in UM patients who underwent treatment preparation and PT at the Ocular Oncology Unit of the Jules-Gonin Eye Hospital (University of Lausanne, Lausanne, Switzerland) and the Paul Scherrer Institute (PSI) (Villigen, Switzerland) between January 1997 and December 2007. Propensity score matching (PSM) was used to select for each AYA (between 15–39 years old) an elder adult patient (≥40 years) with similar characteristics. We assessed ocular follow-up, local tumor control, metastasis incidence, and overall and relative survival (OS and RS). Non-terminal outcomes were then compared between the two groups using competing risk survival analysis.

Results

Out of a total of 2261 consecutive UM patients, after excluding 4 children (<15 years) and 6 patients who were metastatic at presentation, we identified 272 AYA patients and matched 270 of them with 270 elder adult patients. Before PSM, the AYA patients had a higher incidence of primary iris melanoma (4.0% vs. 1.4%; $p = 0.005$), while the elder patients were more likely to have other neoplastic diseases at presentation (9% vs. 3.7%; $p = 0.004$). Ocular outcomes and local tumor control were similar in both groups. Cumulative metastasis incidence for the AYA and elder adult groups was 13% and 7.9% at 5 years and 19.7% and 12.7% at 10 years, respectively, which was not significantly different between the groups ($p = 0.214$). The median follow-up time for the whole cohort and for the surviving patients was 4.5 years and 4.8 years, respectively. Ten deaths were observed in both the AYA and elder adult groups. The OS was similar in the two groups ($p = 0.602$), with estimates in the AYA and elder adult groups of 95.5% and 96.6% at 5 years and 94.6% and 91.4% at 10 years, respectively. However, the relative survival (RS) estimation was worse in the AYA group than the elder group ($p = 0.036$).



Relative survival of the AYA and elder adult UM patients with respect to the general population of the same age. Dashed lines delimit a 95% confidence interval for the relative survival. The difference between the two relative survival curves was tested using a permutation test. The dashed black line indicates the survival in the general population.

Conclusion

While AYAs treated with PT for UM have similar ocular outcomes and present the same metastasis incidence and OS as elder adults, their RS is worse than that in elder adults, when compared with the population in general.

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

Radio-Oncology News

Long Term Outcome and Quality of Life of Intracranial Meningioma Patients Treated with Pencil Beam Scanning Proton Therapy

Background

Meningiomas are one of the most common primary brain tumors. The current standard therapy for symptomatic or growing lesions includes surgery and/or radiotherapy. In this retrospective study, we assess the long-term clinical outcome and prospectively assess the Quality of Life (QoL) of patients with intracranial meningiomas WHO grade 1,2, and 3 treated with Pencil Beam Scanning Proton Therapy (PBS PT) at the Center for Proton Therapy at PSI.

Material and Methods

The study population was comprised of patients with meningiomas WHO grade 1-3 treated with PBS PT between July 1997 and April 2022. Local failure was defined as clear radiologically observed tumor progression of any size after subtotal resection or local tumor recurrence after gross total resection of the treated meningioma. Acute and late side effects were classified with CTCAE v.5. Quality of life (QoL) was collected from the patient by the validated EORTC-QLQ-C30 and BN20 questionnaires.

Results

In total, 200 meningioma patients were included in the analysis (median age: 50.4 years; 72.5% female). Most tumors (n = 140; 70%) were WHO grade 1 and most patients (n = 162, 81%) underwent at least partial surgical resection before PT. The median delivered dose was 54 Gy (RBE) to grade 1 and 60 Gy (RBE) to grade 2/3 tumors, respectively.
In total, 20 (10%) local failures were observed during the follow-up period (Figure 1). On univariate analysis, factors which were significantly associated with worse local control were WHO grade 2 or 3 meningiomas, male gender, multiple meningiomas, timing of treatment at progression or relapse, and non-skull base location (all $p \leq 0.03$). The vast majority of patients did not suffer from any high grade late toxicity (n=176, 88%); however, a higher age (≥50 years) was associated with high grade toxicity (p=0.026).

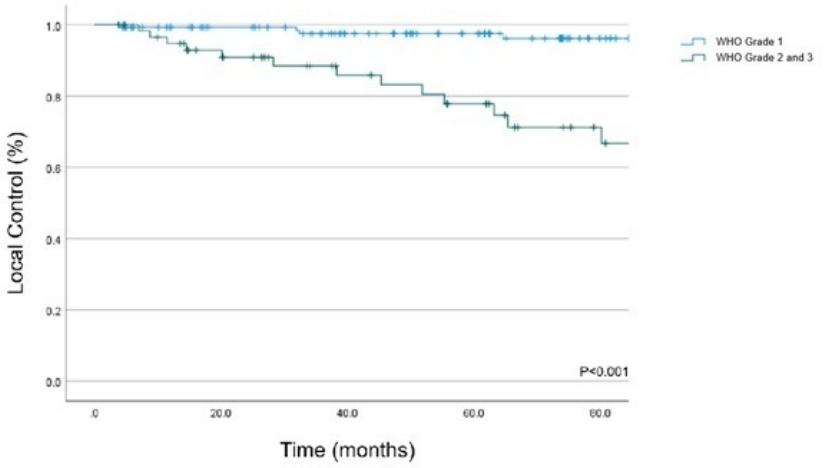


Figure 1: Local control in 200 intracranial meningioma patients treated with PBS PT.

On long-term follow-up, there was a slight trend to more patients having reported headaches. However, while there was a slight drop in the patient-reported global health value as well as an increase of fatigue and drowsiness during PBS PT, all these parameters recovered in the follow-up to baseline. The global health value was all the time in the range of the European norm value (Figure 2).

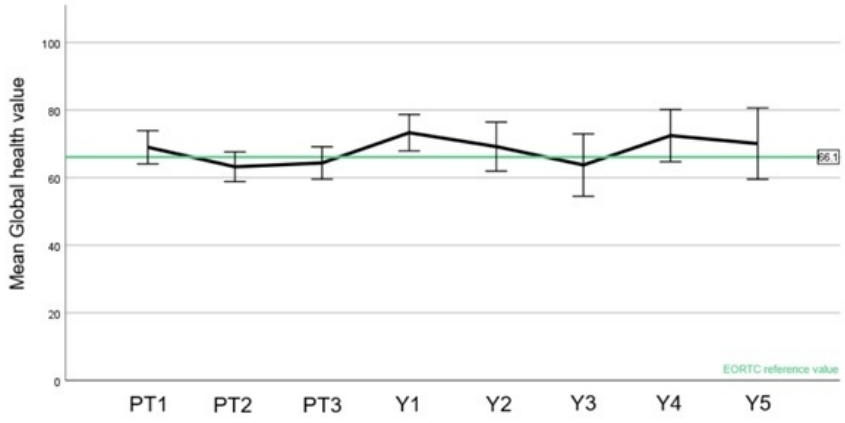


Figure 2: Mean values of the EORTC C30 global health value. European norm value (66.1) is highlighted in green. Error bars represent the 95% confidence interval. (PT1-PT3: Before, during and at the end of PT, Y1-Y5: Year 1-5 of follow-up).

Conclusions

We observed that PBS PT is a highly effective and safe treatment for intracranial meningiomas which preserves QoL. Older patients,

patients with high-grade histology, and patients not treated initially at diagnosis had a worse outcome in terms of local control and/or toxicity, which highlights the need for careful patient selection and up-front treatment.

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

Medical-Physics News

Innovative Advances for onboard MR guided Proton Therapy: Fast Dose Calculation and Optimization

Onboard MR for Proton Therapy and Dose Calculation Challenge

Online Magnetic Resonance (MR) guidance stands at the forefront of advances in radiotherapy, significantly enhancing the traditional image guidance during treatments. However, when it comes to proton therapy, a major hurdle presents itself in the form of dose calculation – a crucial step for efficient and effective treatment planning and implementation. The ability to quickly and accurately calculate doses in the presence of magnetic fields is essential, particularly when making real-time adjustments to treatment plans under online MR guidance. Traditionally, Monte Carlo (MC) simulations have been the benchmark for such calculation, but at the cost of significant time consumption.

A Leap forward with GPU-based Algorithm

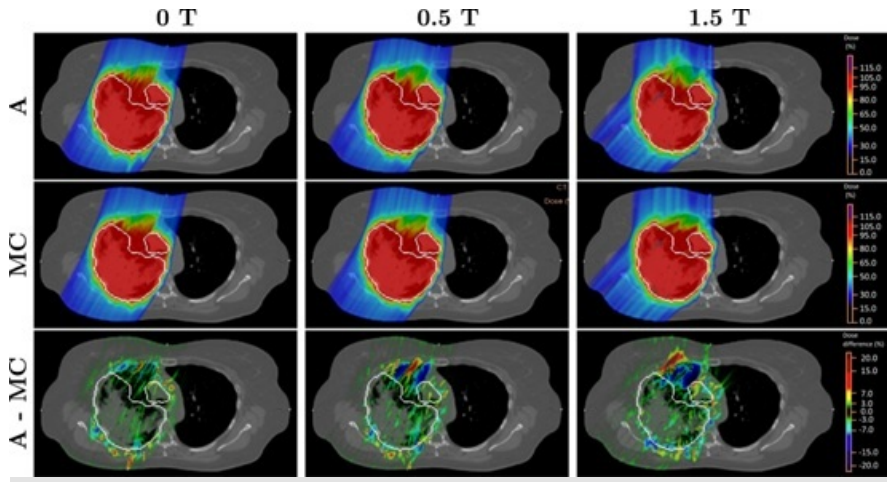
To overcome the limitations posed by MC simulations, a groundbreaking GPU-based modification of an analytical proton dose calculation algorithm has been developed. This new approach is specifically tailored for MRI-guided proton therapy, integrating the complexities of beam deflections due to magnetic fields into its calculations.

Methodology and Approach

The novel method involves simulating proton beams within a range of 70–229 MeV in magnetic fields of 0.5/1.5 Tesla using the TOPAS-MC framework. The core of the approach lies in the generation of look-up tables (LUTs) that detail incremental rotation angles as a function of water-equivalent depth. These LUTs are instrumental in reconstructing beam trajectories for the modified ray casting dose calculation algorithm.

Validation and Results

The new algorithm underwent extensive validation against traditional MC simulations across various scenarios: in water, different materials, and four patient cases. The results were promising, showing excellent alignment with MC dose distributions. The discrepancies noted were minimal, with sub-millimetre range deviations and lateral shifts under 2 mm, even in high-density scenarios. Remarkably, gamma pass rates with 2%/2 mm criteria were above 94.5% for most cases, proving the algorithm's efficacy. Moreover, the dose calculation times were significantly reduced to less than 30 seconds per field compared to MC, which is the gold standard, as well as time-consuming (hours/days).



Treatment plan for lung patients optimised for 0 T (left), 0.5 T (centre) and 1.5 T (right). Dose distributions calculated analytically (top), with TOPAS-MC (middle) and their difference (bottom) are shown.

Impact and Significance

This innovative method marks a significant milestone in proton therapy. It facilitates accurate and rapid proton dose calculations in magnetic fields, a capability essential for optimizing treatment plans in real time. The integration of this algorithm into treatment plan optimization regimes signifies a leap forward in MR-guided proton therapy, potentially enhancing patient outcomes through more precise and efficient therapeutic interventions.

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

Imprint

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