Paul Scherrer Institut
Center for Proton Therapy
Newsletter #36_12/2025

Dear Reader

Welcome to this last 2025 edition of our *SpotOn+* Newsletter.
Proton therapy is entering a decisive phase in its evolution. While the clinical promise of protons — precise dose deposition with reduced exposure to healthy tissue — has long been recognized, the field must now reconcile its technological potential with the realities of daily clinical practice. The sensitivity of proton dose distributions to anatomical changes makes adaptive strategies indispensable, yet the community continues to grapple with imaging, verification, and workflow limitations that may somewhat impede routine clinical implementation.

Photon therapy has demonstrated that online adaptation is feasible, safe, and scalable when supported by fast imaging, automation, and efficient workflows. Proton therapy faces tighter image quality constraints and the added challenge of range uncertainty, reinforcing the urgency for solutions tailored to its unique needs. In this newsletter, we detail our early clinical experience, such as in-room CT–based online adaptation at our institute, show that robust adaptive workflows are achievable with acceptable treatment times and improved conformity.

Parallel innovation is occurring in other cutting-edge domains. The FEATHER FLASH trial has established a comprehensive quality assurance and reporting framework for ultra-high dose rate proton therapy, addressing a major barrier to

clinical translation. Our team reported on the inclusive QA and reporting protocol for a FLASH clinical trial at our institute.

Lastly, long-term outcomes in pediatric rhabdomyosarcoma reveal encouraging survival, tolerability, and quality-of-life results following pencil beam scanning proton therapy, highlighting the enduring value of technological progress for patients.

Together, these developments illustrate a field moving toward standardization, clinical maturity, and patient-centered innovation. The challenge now is not only to generate evidence, but to embed adaptive and advanced proton techniques into sustainable, routine practice.

That being said, I hope that this last newsletter of the year was of interest to you. I would like to finish by spreading seasonal cheer by wishing Merry Christmas & Happy New Year to all readers.

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

Medical-Physics News

Time to Adapt: Bringing Protons Up to Speed and Connecting with Photons

The promise of proton therapy is well known: a peaked depth–dose profile that can spare organs at risk and reduce integral dose. The same Bragg peak, however, makes proton plans highly sensitive to daily anatomy and set-up. To stay safe, we rely on generous margins and conservative set-up settings — diluting part of the advantage. Adaptive radiotherapy shifts the focus from "adapting the patient" to "adapting the plan". Offline adaptation is established; true online adaptation demands fast volumetric imaging in treatment position, reliable deformable image registration (DIR), automated contouring and plan generation, and online verification — within an appointment length teams can run every day.

Photon therapy has shown this is possible in routine care since 2017, driven by integrated MR-linacs and more recently by high-quality onboard cone-beam

CT (CBCT) with mature synthetic CT (sCT) methods and streamlined workflows. Proton therapy needs adaptation at least as much — arguably more — yet faces tighter constraints on image quality and possibly range verification.

Three recent journal initiatives highlight the momentum (PMB special issue on adaptive radiotherapy 2023, phiRO special issue on particle therapy 2024, RED Journal focus on adaptive radiotherapy 2025).

From the technical side, our PMB editorial [Albertini et al. 2025] and PHIRO editorial [Wagenaar et al. 2025] synthetize a treatment roadmap: CT-based imaging where available (e.g. in-room CT), robust pipeline to convert CBCT to sCT, automation with QA-by-design (auto-segmentation checks, DIR quality metrics), "time engineering" of the session (e.g. with fewer daily fields, fast/robust optimization, triggered adaptation when a full replan isn't needed), and independent online verification.

At the Paul Scherrer Institute, this approach has already translated to patient in 2023 using an in-room-CT–based daily online adaptive workflow [Albertini et al. 2024]. Our early experience with a small, carefully selected cohort shows positive patient feedback with only a minor increase in daily fraction time, while improving dose conformity by adapting to day-to-day anatomy.

To help proton centres adopt safely and consistently, an ESTRO/EPTN Adaptive Task Force was launched in 2023. Current outputs include a harmonized terminology for adaptive particle therapy (to standardize "what we mean" across rationale, timing and timescale, *see Figure*), a community SWOT analysis (manuscript under review) identifying real weaknesses — CBCT image quality, end-to-end tooling, resources and training — but no show-stopping threats, QA/commissioning recommendations progressing under ESTRO Guidelines governance, a role-based competence matrix to empower RTT-led tasks, and preparatory imaging guidance on when CBCT can be accepted for dose calculation in online adaptive proton therapy.

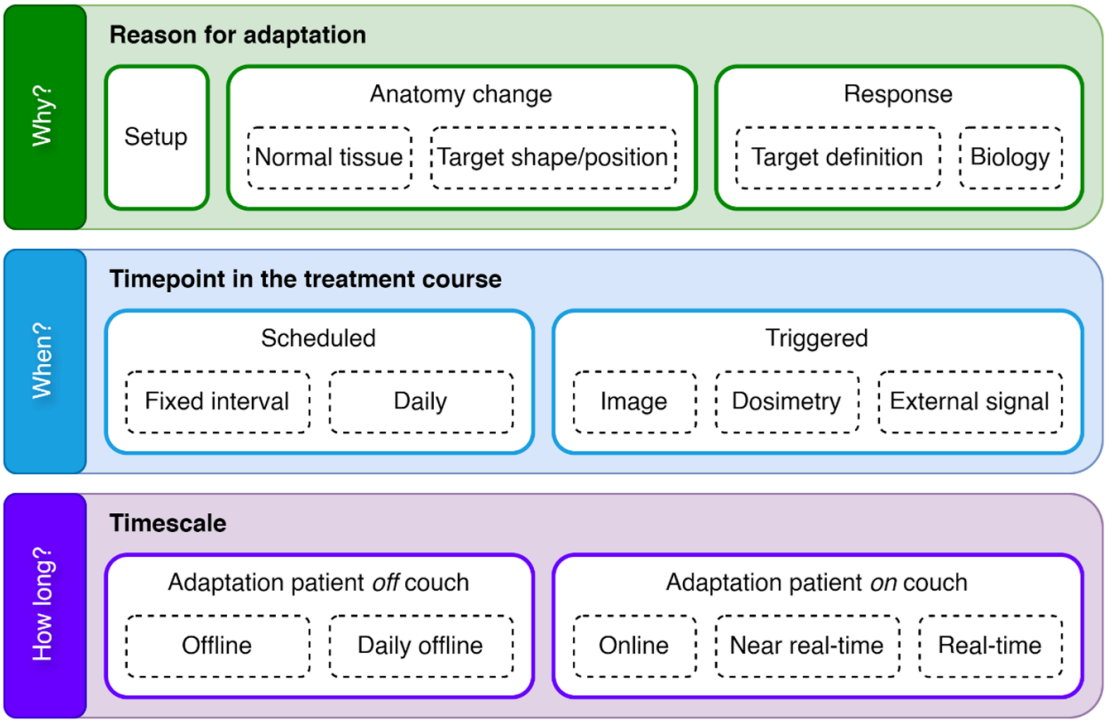


Figure: Terminology classification for adaptive particle therapy

Why this matters now

Adaptive therapy is central to personalization and is essential for safe, practical hypofractionation. Many building blocks are modality-agnostic, e.g. speeding up daily contour review and enabling RTT-only workflows for economic sustainability.

Those wishing to engage further may consider two independent upcoming events: the *SASRO Adaptive Workshop* (23 March 2026, Aarau), a Switzerland-forum to strengthen national collaboration with sessions on current practice, challenges, and pathways to clinical adoption, and the *ESTRO Pre-Meeting Course on Online Adaptive RT* (15 May 2026, Stockholm), a multidisciplinary, cross-modality course. Please see the SASRO and ESTRO websites for program and registration details.

Physics News

Quality assurance and reporting for FLASH clinical trials: the experience of the FEATHER trial

Background and Purpose

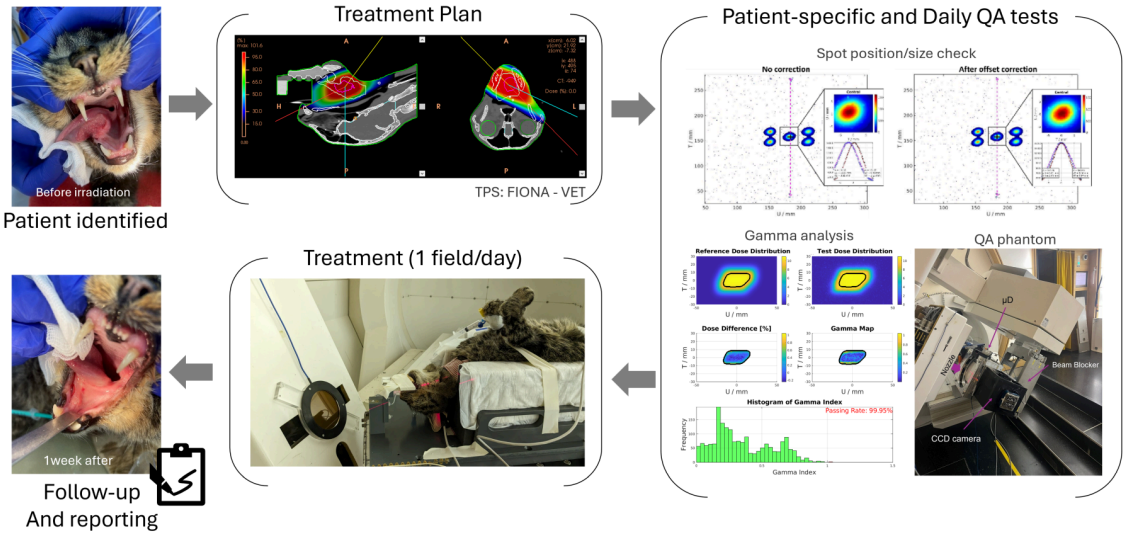
Research on ultra-high dose (UHDR) radiation therapy has indicated its potential to spare normal tissue while maintaining equivalent tumor control compared to conventional treatments. The FEATHER clinical trial (FEline orAl squamous cell carcinoma to model human Head&Neck tumors: A phase II/III randomized trial assessing early toxicity and anti-tumor efficacy of UHDR vs. conventional dose rate proton THERapy) at the Paul Scherrer Institute in collaboration with the University of Zurich Animal Hospital is one of the first curative domestic animal trials to be attempted, and it is designed to provide a good example for human trials. However, the lack of standardized quality assurance (QA) guidelines for FLASH clinical trials presents a significant challenge in trial design.
This work aims to demonstrate the development and testing of QA and reporting procedures implemented in the FEATHER clinical trial.

Methods

We have expanded the clinical QA program to include UHDR-specific QA and additional patient-specific QA. Furthermore, we have modified the monitor readout to enable time-resolved measurements, allowing delivery log files to be used for dose and dose rate recalculations. Finally, we developed a reporting strategy encompassing relevant parameters for retrospective studies.

Results

We evaluated our QA and reporting procedures with simulated treatments. This testing confirmed that our QA procedures effectively ensure the correct and safe delivery of the planned dose (3%/3mm gamma criteria, pass >90%). Additionally, we demonstrated that we could reconstruct the delivered dose and dose rate using the delivery log files.



Workflow set-up in the FEATHER clinical trial

Conclusions

We developed and used in practice a comprehensive QA and reporting protocol for a FLASH clinical trial at our institute. This work aims to establish guidelines and standardize reporting practices for future advancements in the FLASH-RT field.

This work has been recently published (Med Phys.2025;52:e18100)

Radio-Oncology News

Two Decades of Outcomes and Quality of Life Following Pencil Beam Scanning Proton Therapy in Children and Adolescents with Rhabdomyosarcoma

Background and Purpose

Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children. Pencil beam scanning proton therapy (PBS PT) enables highly conformal dose delivery with reduced exposure to surrounding healthy structures, making it particularly suited for RMS in critical anatomical regions. Long-term clinical outcome data for this new radiation technique are scarce. This study reports

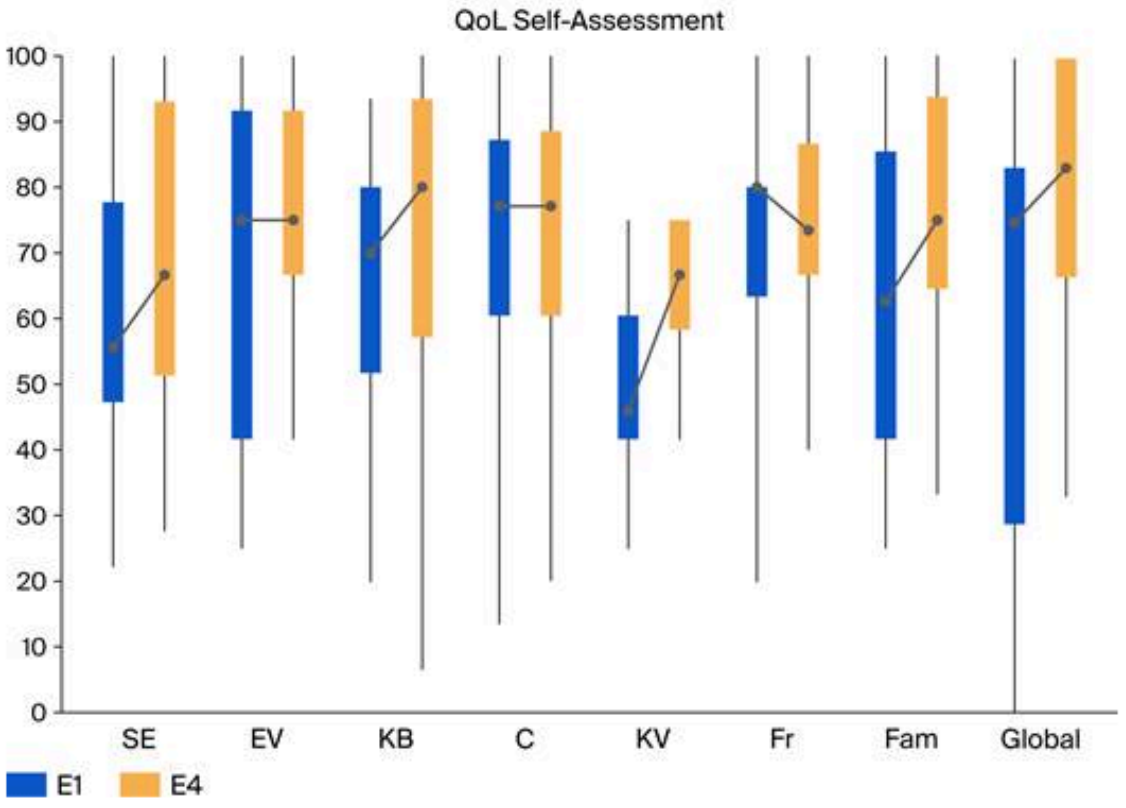
long-term outcomes and quality of life (QoL) after PBS PT in children and adolescents with RMS, providing a comprehensive view of both disease control and functional impact.

Material and Methods

We retrospectively reviewed 114 children and adolescents with RMS (mostly embryonal, n = 100; 87.7%) treated between 2000 and 2020. Their median age was 4.6 years (range, 0.3–18). Most common tumor site were parameningeal head&neck (50.9%) and orbital (21.9%). All received systemic chemotherapy according to prospective protocols. The median total PT dose of 51.9 Gy (RBE; range, 41.4–64.8) was delivered in a median of 28 (range, 23-36) fractions.

Results

After a median follow-up period of 7.1 years (range, 0.3 to 17 years), we observed 26 failures overall; 21 (80.8%) occurred in-field. The 5-year local control and overall survival were 81.2% and 81%, respectively. PBS PT was well tolerated. In total, only 19 patients (16.6%) experienced any type of grade 3 acute toxicity. The most common grade 3 late toxicity were visual complications (23.7%) followed by hearing impairment (4.4%). The composite endpoint (non-ocular grade ≥3 toxicity- and failure-free survival) counting the first occurrence of any failure (local or distant), death, or non-ocular CTCAE v5.0 grade ≥3 toxicity was 77.3% at 5 years. At the start of PT, parents and children reported a QoL significantly worse than that of a German normative group, but during the follow-up period, their scores improved to normal values in nearly all domains within two years.



Two years after the end of proton therapy (E4), the self-reported QoL ratings in all domains were better than or similar to those at the start of proton therapy (E1), except for the domain "social functioning with peers (Fr)", which worsened.

Conclusions

Our two decades of experience with PBS PT provide data that reflect good local control rates and minimal late non-ocular grade 3 toxicity. We also show that QoL returned to normal scores in nearly all domains within 2 years. Children and adolescents with RMS seem to benefit from PBS PT in terms of toxicity and quality of life, but further prospective, multi-institutional comparative trials are needed.

This work has been recently published (Leiser and Dantonello et al. 2025).

Last chance to register:

We offer a 4-day training course in proton therapy from **18 - 23 January 2026**. Lectures in basic science, clinical experience and new technologies are on the program, as well as the possibility to visit the proton radiation facilities. There are still available places. For further information and registration (deadline 18 December), kindly refer to the official PSI Winterschool Website.

Imprint

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