End-to-end verification of multi-field-optimization FLASH-IMPT using an example GBM case

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Introduction

FLASH is promising for radiotherapy to potentially reduce side effects. While scanned protons are a good candidate for FLASH due to the inherently high spot beam current, maintaining IMPT plan quality while achieving FLASH dose rates is challenging. The two main obstacles for conventional IMPT to achieve FLASH dose rates are:

- The **energy switching time** between the layers greatly reduces the average dose rate.
- For cyclotron-based systems, introducing an energy **degrader** at the accelerator exit substantially reduces the gantry beam current.

For this study, we thus applied **FLASH-IMPT**, which circumvents both limitations mentioned above.

FLASH-IMPT

IMPT-like plans can be created using a **single-energy** beam delivery and **patient-specific hardware**. Thanks to the lack of energy layer switching and high beam transmission at 250 MeV, FLASH dose rates are achievable.

In this study, we verified an **end-to-end workflow** for FLASH-IMPT modeling, optimization, delivery, and measurement.

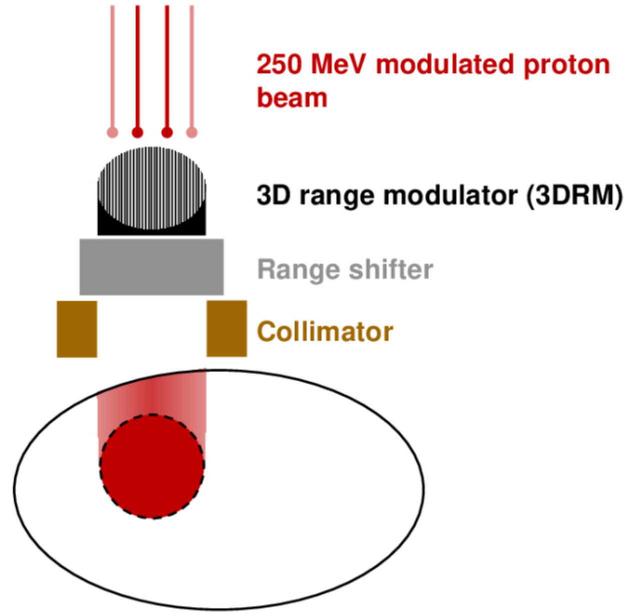

Figure 1: Components used for FLASH-IMPT.

Plan optimization

For a glioblastoma case, a **two-field** proton plan was created following the hypofractionated stereotactic radiotherapy protocol [1] to deliver **24 Gy** to the PTV with a simultaneous integrated boost (**SIB**) of **36 Gy** to the GTV in 6 fractions. The 250 MeV spot list and the 3DRM design were optimized for both fields simultaneously using **MFO**. To be able to increase the beam current, a minimum of **600 MU/spot** was enforced during the optimization. As our technique requires an extended range shifter, the scattering needs to be limited by fitting a collimator to the target shape.

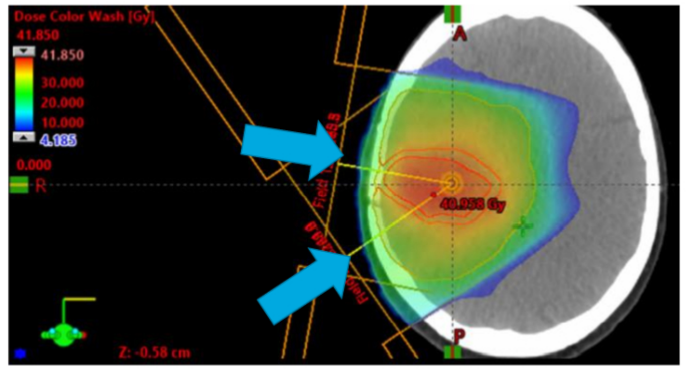

Figure 2: Optimized dose distribution for the two-field plan, the angles are indicated by the arrows. The SIB in the target center is clearly distinguishable.

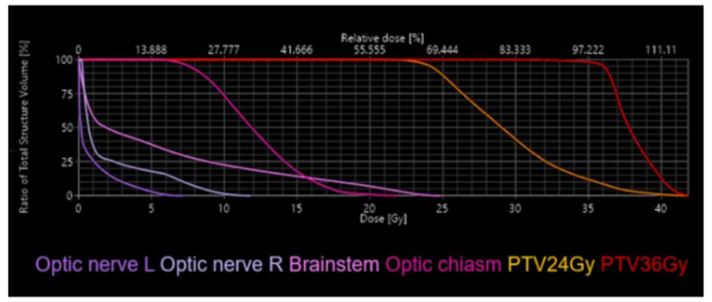

Figure 3: Dose volume histograms for the optimized plan.

The dose and the dose rate distributions were modeled using a research-only version of **Eclipse** (16.1 plus ESAPI). For better comparison with the measurements, both distributions were modeled in a **water phantom** in addition to the **patient CT**. Lastly, the dose in water was also modeled through **Monte Carlo** (MC) by incorporating all hardware components into FLUKA.

Measurements

Using a quality-assured 3D printer, the 3DRM was manufactured with a **precision of ≤ 20 µm** and a pin spacing of 3 mm. The collimator was milled out of a solid brass block.

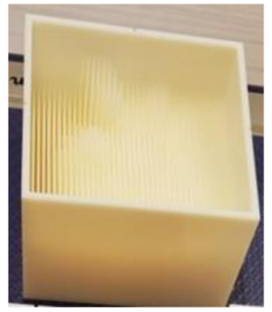

Figure 4: 3D printed 3D range modulator.

The measurements were performed using an **Octavius 1600XDR** ionization chamber array and a **customized water phantom** [2] that moves the array step-wise through the water. The 3D dose distribution of one of the modulated fields was measured with an extremely high resolution (> 100k dose points) on a **ProBeam** system in research mode.

Using the same setup, the **dose rate distribution** was measured based on the PBS dose rate definition [3] with a timing dose threshold of 2.5 % maximum slice dose.

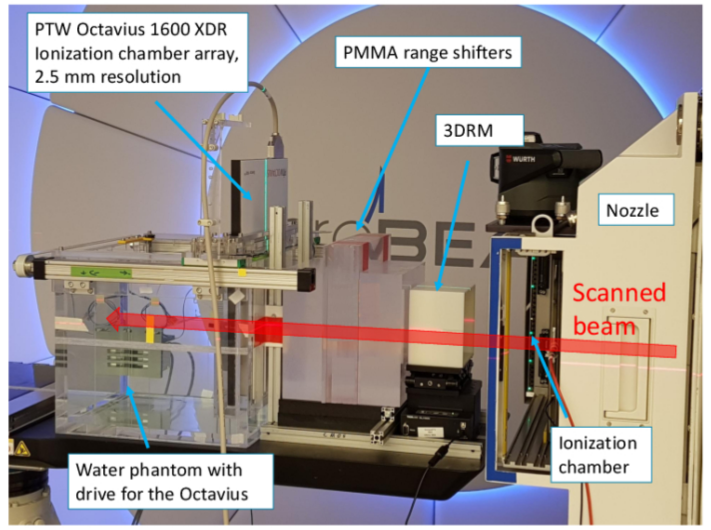

Figure 5: Measurement setup showing all hardware components.

Results

The FLASH-IMPT plan quality was **clinically acceptable** (see DVHs in Figure 3).

The measured dose in water agreed very well with the corresponding MC simulation and the dose modeled in Eclipse, and **reproduced the highly modulated dose** distribution of a multi-field-optimized SIB plan.

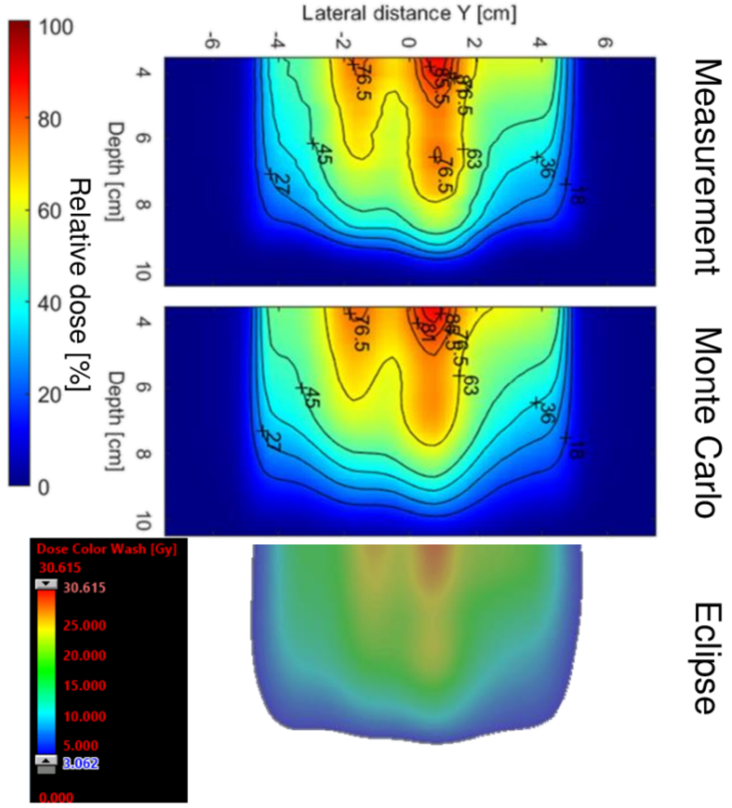

Figure 6: Comparison of the dose that was measured (top), simulated using Monte Carlo (middle), and modeled using Eclipse (bottom).

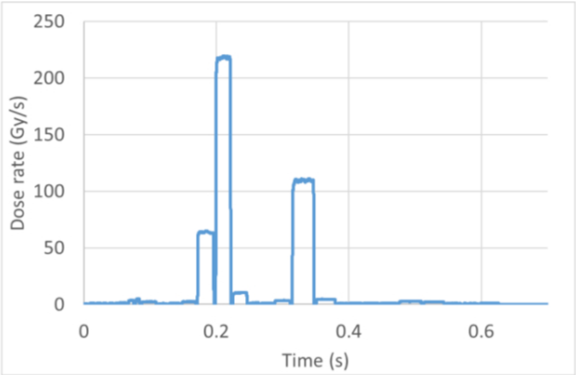

Figure 7: Instantaneous point dose rate measured in the entrance region of the dose.

Dose rates **>40 Gy/s** were measured in the relevant high dose regions of the target, despite the beam current being reduced to ensure detector compatibility.

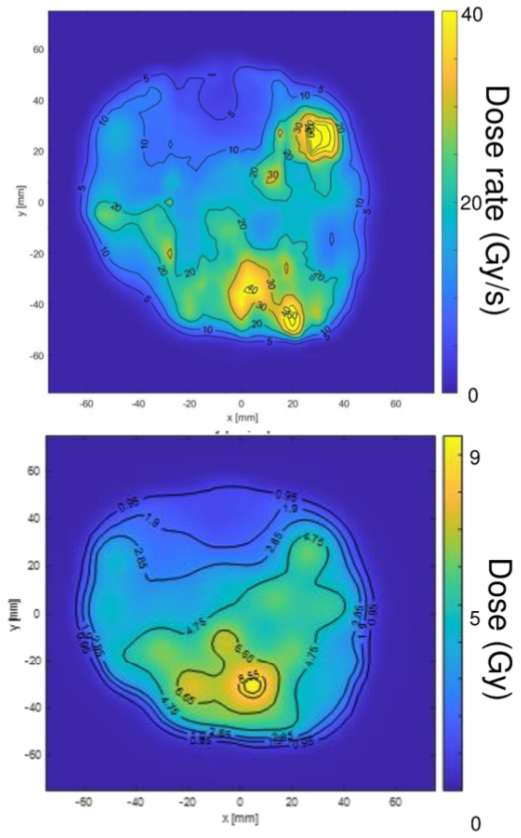

Figure 8: 2D dose rate distribution at target depth (top) and the corresponding dose distribution (bottom).

Conclusion

Complex, highly modulated proton plans using FLASH-IMPT can be modelled, optimized, delivered, and measured, with the measurements agreeing well with the models. Our work proves the **feasibility of an end-to-end workflow** for FLASH-IMPT using 3D range modulators for a complex patient case.

References

[1] https://doi.org/10.1158/1078-0432.CCR-14-0822

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[3] M. Folkerts et al. *Medical Physics* (2020).

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FLASH therapy is under development and not available for commercial sale.

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