Clinical Verification of *In Vivo* Range and 3D Dose Reconstruction Using a Multi-Slit Prompt-Gamma Camera in Spot-Scanning Proton Therapy

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ABSTRACT

Purpose: In proton therapy, precise beam range measurement and dose verification are critical to overcome range uncertainty and ensure patient safety. This study developed and evaluated a technique to reconstruct and visualize *in vivo* dose distribution from spot scanning proton therapy using the beam range information acquired by a multi-slit prompt-gamma camera (MSPGC).

Methods: The MSPGC measures the prompt gamma distribution to determine the *in vivo* proton beam range. Using the measured beam ranges, the 3D dose distribution is reconstructed and visualized via a superposition-based method using a precomputed dose dataset containing planned and range-shifted dose distributions. The MSPGC was applied to clinical cases of glioblastoma and skull-base tumor patients treated at the National Cancer Center, Korea. We evaluated range discrepancies, defined as the difference between the measured and planned ranges, and inter-fractional variations. The agreement between the visualized and the planned dose was also evaluated using gamma index analysis and dose-volume histogram (DVH).

Results: The developed technique reduced the range confidence interval by approximately 75% compared to the treatment safety margin. The analysis of inter-fractional variations confirmed that target coverage was consistently maintained across all fractions. The visualized dose distributions demonstrated high agreement with the treatment plans. Specifically, the 2%/2 mm gamma passing rates exceeded 95% in all cases (95.16%, 95.77% for glioblastoma, 95.43% for skull-base), and DVH analysis confirmed minimal deviation (<0.03 Gy for CTV D98% and brainstem D50%, D90%).

Conclusion: The proposed MSPGC-based technique demonstrated a significant reduction in range uncertainty and verified target coverage. Additionally, the visualized dose distributions showed high agreement with treatment plans. These results validate the developed technique as an effective tool for enhancing treatment precision and patient safety in proton therapy, paving the way for adaptive proton therapy.

REFERENCES

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Introduction

- In proton therapy, **beam range uncertainty (~4%)** causes deviations between the planned and delivered dose[1].
- To ensure **target coverage** and **organ-at-risk (OAR) sparing**, large margins (1.5σ distal to the target, 2σ for OARs) are applied along the beam direction — increasing normal-tissue dose and limiting the degree of freedom in beam direction selection.
- Direct *in vivo* range measurement is therefore highly desirable. We developed a **multi-slit prompt-gamma camera (MSPGC)** that measures the beam range from the prompt-gamma distribution[2], and a technique to **reconstruct and visualize the *in vivo* 3D dose distribution** from the measured ranges.
- In this study, the MSPGC-based technique was **applied clinically** in spot-scanning proton therapy to verify both the ***in vivo* beam range** and the **reconstructed 3D dose** against the treatment plan.

Materials and Methods

❖ Multi-slit prompt-gamma camera (MSPGC)

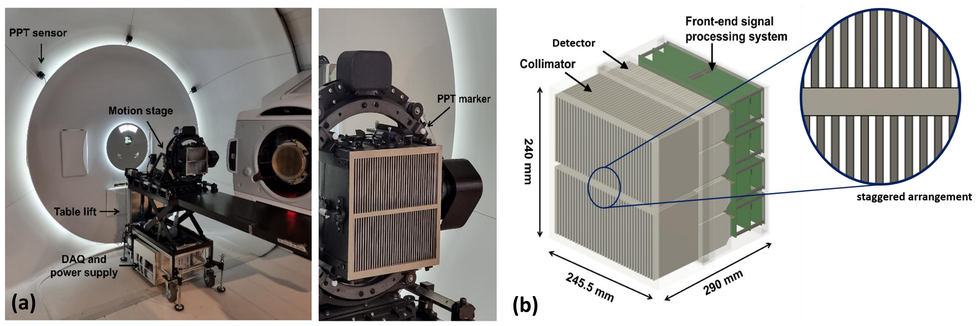

Figure 1. (a) Positioning system of MSPGC. (b) Schematic of camera head and collimator.

- The MSPGC measures the **prompt-gamma distribution** along the proton path to determine the *in vivo* beam range, using a parallel-slit tungsten collimator (FOV: 216 mm) and a CsI(Tl) scintillation detector array.
- For clinical use, a dedicated **positioning system** was developed — sub-millimeter Precision Position Tracking (PPT; WorldViz, CA) and a 6D high-precision servo trolley — which automatically aligns the camera to the beam direction.

❖ Dose reconstruction & evaluation

- Using the measured ranges, the **3D dose distribution** was reconstructed by a **superposition-based method** with a **precomputed dose dataset** (planned + range-shifted distributions, computed with the fast Monte-Carlo code **MCsquare**).
- We evaluated the **range discrepancy** (= measured − planned) and **inter-fractional variation**, and assessed the agreement between the reconstructed and planned dose using 2%/2 mm **gamma-index analysis and dose-volume histograms (DVH).**

❖ Clinical proton therapy cases

Female glioblastoma case **Male glioblastoma case** **Male skullbase case**

Figure 2. Clinical application images for performance evaluation of the developed technique at National Cancer Center.

- National Cancer Center, Korea: **female/male glioblastoma, male skullbase.**
- During the treatment, the MSPGC was aligned with the beam direction and measured beam range. The distance between the camera and the beam isocenter was 150 mm.

Results

❖ Range verification

- The **range discrepancy** (= measured − planned) was **small across all cases**. Average range errors were +0.8 mm for female glioblastoma, +0.6 mm for male glioblastoma, and +0.4 mm for the skull-base case — all well **within the treatment margin.**
- Accordingly, the technique **reduced the range confidence interval** by ~75% relative to the treatment safety margin, and analysis of inter-fractional variation confirmed that target coverage was **consistently maintained across all fractions.**

❖ Dose distribution visualization per case

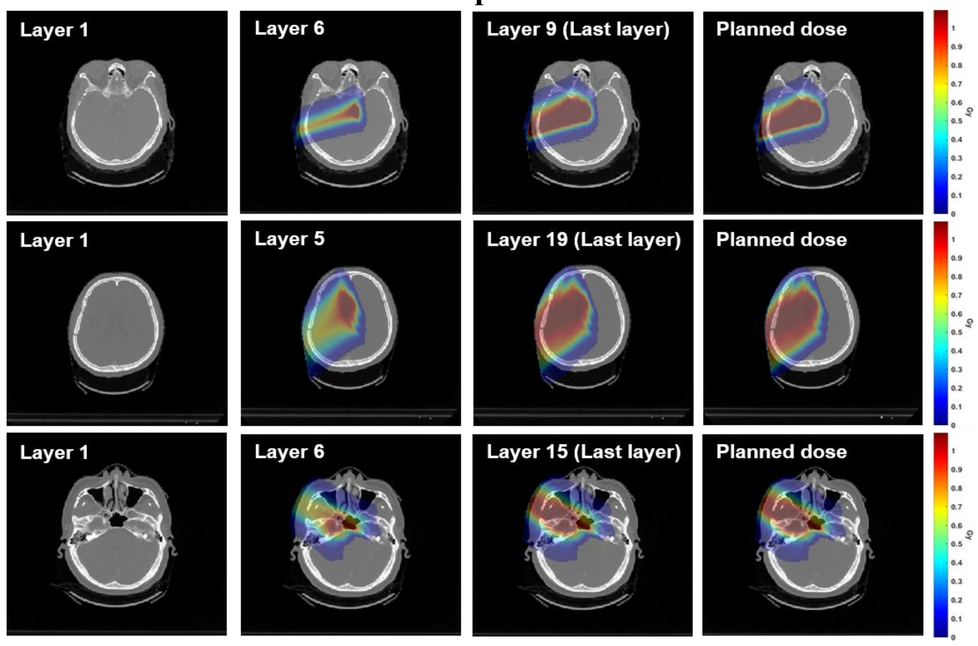

Figure 3. Visualized dose distributions compared with the planned dose for each clinical case.

- The **reconstructed 3D dose** was visualized on each patient's CT and compared with the treatment plan for every clinical case.
- The distributions showed **high agreement** with the plans: the 2%/2 mm gamma passing rate **exceeded 95%** in all cases (95.16%, 95.77% for glioblastoma, 95.43% for skull-base).

❖ DVH per case

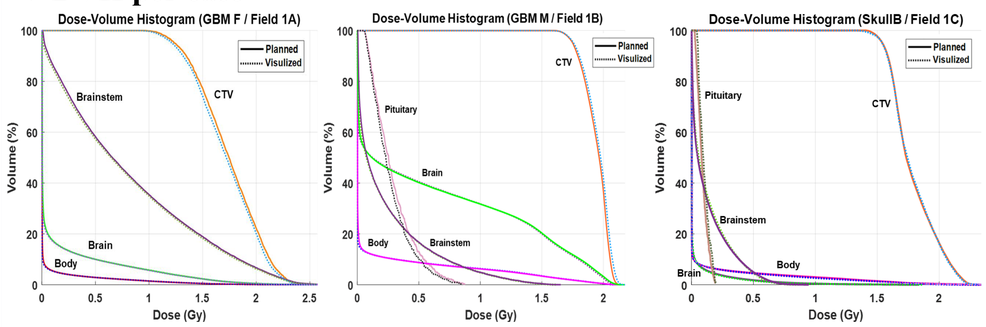

Figure 4. Dose-volume histogram analysis results for each clinical case.

- DVH analysis of the reconstructed vs. planned dose confirmed **minimal deviation** (< 0.03 Gy) for CTV $D_{98\%}$ and brainstem $D_{50\%}$, $D_{90\%}$.
- This demonstrates that **cumulative target and OAR doses** were accurately reproduced across all cases.

Conclusion

- The proposed **MSPGC-based technique** achieved a **significant reduction in range uncertainty** and **verified target coverage** across all fractions.
- The **reconstructed 3D dose distributions** agreed closely with the treatment plans (2%/2 mm gamma > 95%; DVH deviation < 0.03 Gy).
- These results validate the technique as an effective tool for enhancing treatment precision and patient safety in proton therapy, paving the way for **adaptive proton therapy.**