



# Comparison of Photon and Proton-based Lattice Radiation Therapy for the Treatment of Bulky Liver Cancer

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## Abstract

Spatially Fractionated Radiotherapy (SFRT) delivers radiation in a non-uniform pattern, creating alternating high- and low-dose regions within the tumor while sparing nearby organs. Lattice Radiation Therapy (LRT), a form of SFRT, arranges high-dose spheres (VTVH) and low-dose regions (VTVL) within the tumor to enhance tumor control while minimizing side effects. This study developed a proton-LRT planning approach and compared its dosimetric advantages to traditional photon-LRT in 22 retrospective patients with bulky liver tumors. Photon-based LRT (photon-LRT) was created using VMAT, while proton-based LRT (proton-LRT) used Intensity Modulated Proton Therapy (IMPT), with beam angles optimized for VTVH/VTVL structures. Results showed that proton-LRT maintained comparable target coverage while significantly reducing VTVL mean dose, improving plan quality and respecting organ-at-risk constraints. Additionally, proton-LRT demonstrated superior peak-to-valley dose ratios, suggesting potential for dose de-escalation and improved patient outcomes.

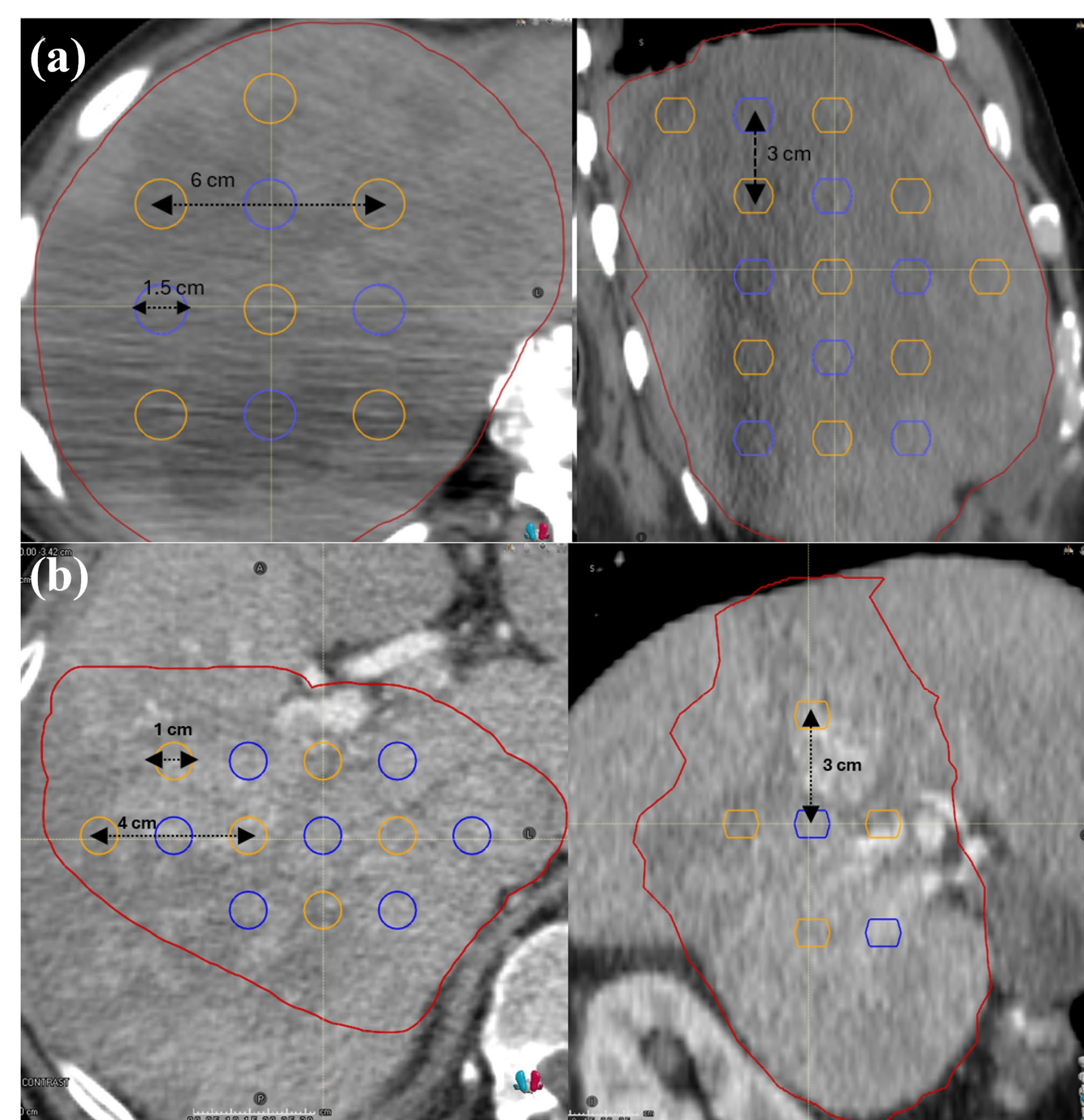
**Keywords:** Spatially Fractionated Therapy, Lattice Radiation Therapy, Volume Modulated Arc Therapy, Proton Therapy, Liver Cancer

## Introduction

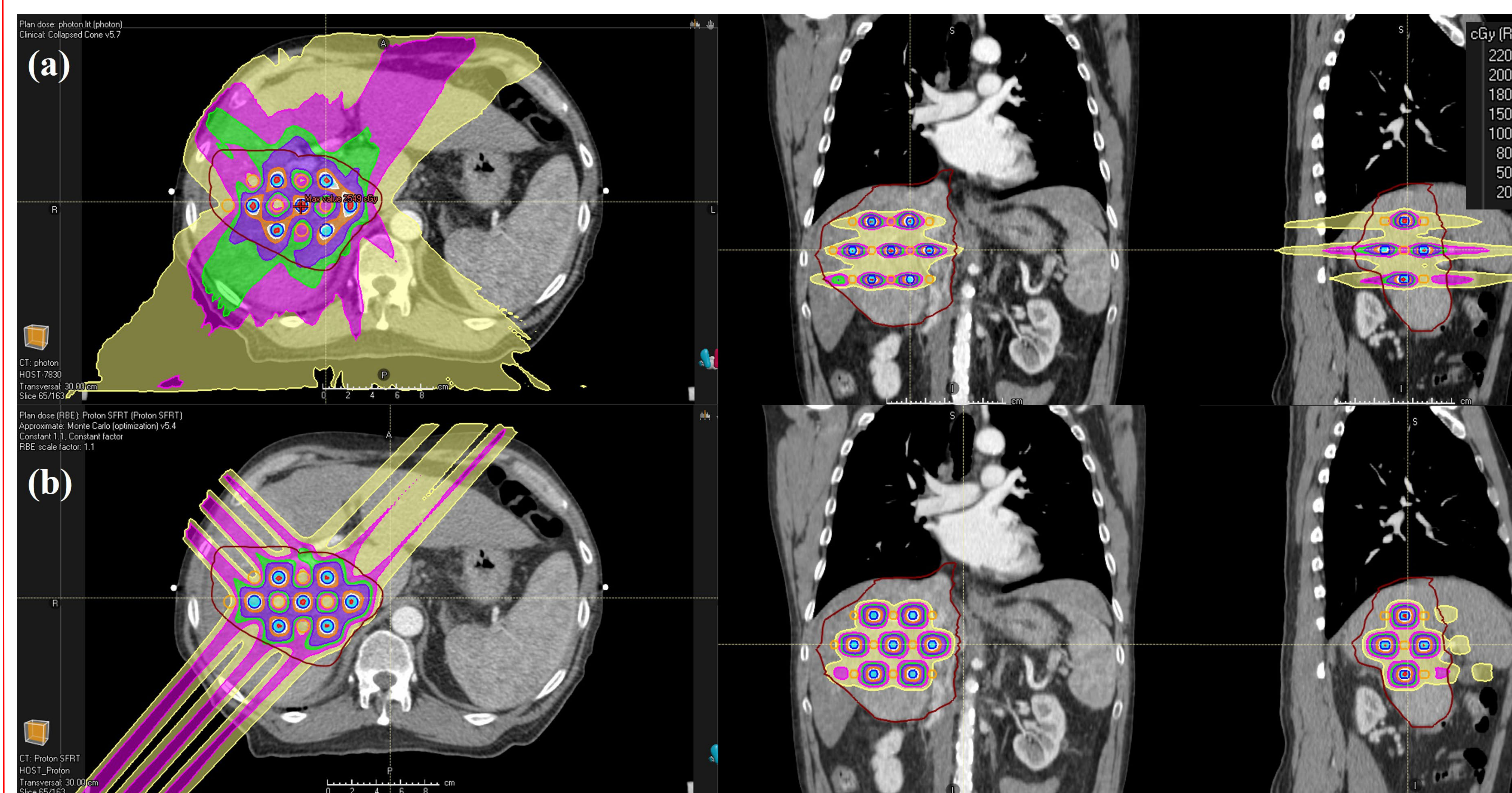
Bulky tumors are difficult to resect and often respond poorly to traditional radiation therapy. One of the earliest spatially fractionated radiotherapy (SFRT) techniques, GRID, used a physical collimated block with hexagonal beam apertures to create alternating high and low-dose regions within the tumor, reducing skin toxicity and sparing nearby organs-at-risk (OARs).<sup>1,2</sup> The development of modern linear accelerators enabled Lattice Radiation Therapy (LRT), a 3D radiotherapy technique that delivers high-dose spherical vertices within the tumor while minimizing radiation exposure to surrounding healthy tissue.<sup>1</sup> Proton-LRT follows a similar dose distribution as photon-LRT but offers enhanced biological effectiveness associated with proton therapy.<sup>3</sup> As LRT is a relatively new treatment, standardized clinical protocols are not yet established, and most hospitals are in the early stages of implementation.<sup>4</sup> This research compares photon-based and proton-LRT to evaluate their dosimetric performance and explore proton LRT as a potential alternative treatment for bulky liver tumors.

## Methods

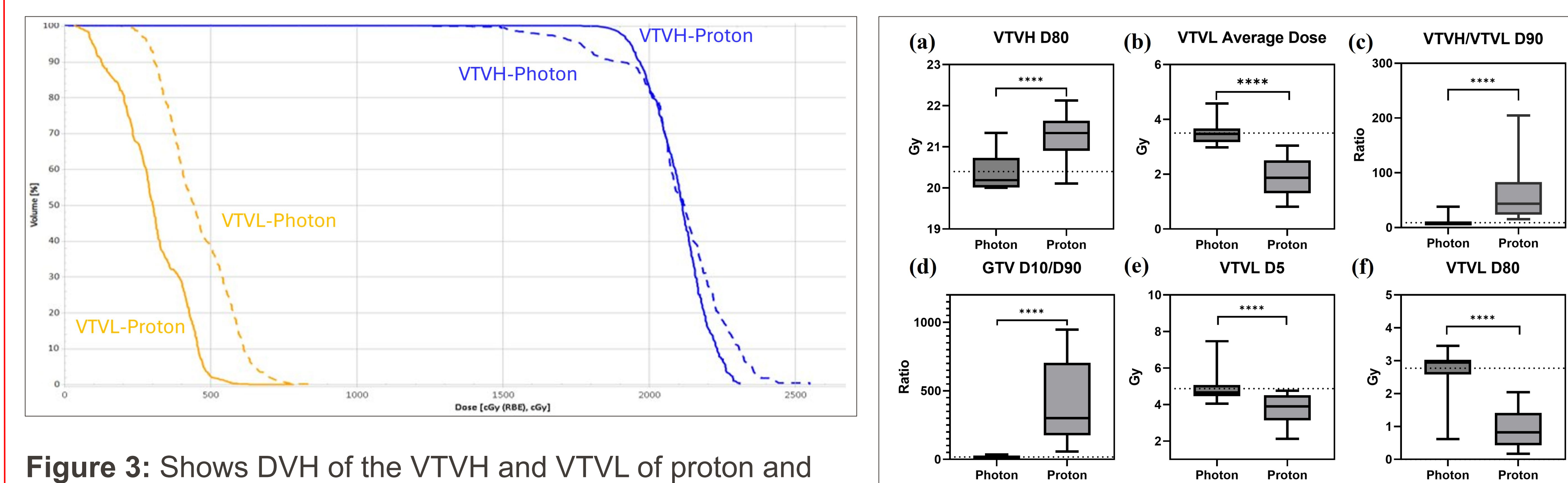
A custom script optimized the positioning of VTVH and VTVL spheres based on isocenter placement and specific parameters using RayStation delivered via VMAT using the TrueBeam system with a 6FFF beam. The aim was to cover 80% of VTVH with 20Gy while limiting the average VTVL dose to 4Gy. Proton LRT planning additionally accounted for proton-specific density variations and setup uncertainties by incorporating a specialized treatment couch and robust optimization safeguards. Using duplicated CT datasets, density uncertainty was set at 3.5%, and isocenter uncertainty at 3 mm, with three strategically placed beams ensuring optimal VTVH coverage while maintaining safe distances from VTVL. Both techniques were tested on 22 retrospective patients, with dosimetric comparisons evaluating target coverage and dose constraints to VTVH and VTVL.



**Figure 1:** (a) shows the sphere creation and layout for tumors with a volume greater than or equal to 1000 cm<sup>3</sup>. (b) shows the sphere creation and layout for tumors with a volume less than 1000 cm<sup>3</sup>.



**Figure 2 :** Shows the 3-view dose distribution of (a) photon and (b) proton plan for a patient.



**Figure 3:** Shows DVH of the VTVH and VTVL of proton and photon-LRT.

**Figure 4 :** Boxplot comparison of Photon and Proton LRT for 6 different dose metrics. Statistical significance between proton-based and photon-LRT is denoted by asterisks, with four asterisks (\*\*\*\*) indicating  $p < 0.0001$ .

## Results

**Figure 2** shows 3-view dose distribution: transversal (left), coronal (center), and sagittal (right). The isodose lines displayed on the right, indicate dose levels in cGy corresponding to their respective colors. The VTVH spheres are represented in blue, the VTVL spheres in orange, and the GTV is outlined in red. (a) presents the photon dose. Similarly, (b) depicts the proton dose distribution. A DVH plot comparison, **Figure 3**, was done between the VTVH (orange) and VTVL (blue) of proton and photon-LRT, with the solid line representing proton-LRT and dashed line representing photon-LRT. **Figure 4**, shows 6 key dose metrics to evaluate plan quality. The VTVH D80 box plot represents the dose (Gy) received by 80% of the VTVH spheres (a), while the VTVL average dose (b) indicates the mean dose (Gy) delivered to the VTVL spheres. The VTVH/VTVL D90 boxplot (c) compares the ratio of the dose received by 90% of the spheres. The GTV D10/D90 (d) compares the ratio of the dose received. The VTVL D5 (e) boxplot represents the dose received by 5% of the VTVL spheres. The VTVL D80 box plot (f) depicts the dose (Gy) received by 80% of the VTVL spheres.

## Conclusion

Proton-LRT and photon-LRT were compared to evaluate their dosimetric advantages and limitations. Our results suggest that proton-LRT achieves comparable target coverage while significantly reducing dose to normal tissue, highlighting its potential superiority over photon-LRT in treatment planning. This reduction in normal tissue exposure could lead to fewer treatment-related toxicities and improved patient quality of life. Further investigation is needed to validate these findings through clinical studies and assess short-term and long-term benefits of proton-LRT.

## References

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