Improving Immune Preservation for Lung Cancer Patients with Ultra-Fast Proton Therapy Using Pin Ridge Filters

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INTRODUCTION

Radiation-induced lymphopenia (RIL) is caused by the death of **circulating lymphocytes (CL)** within the blood

Lung patients are particularly vulnerable to RIL because large volumes of blood are irradiated during treatment

A substantial portion of IMPT delivery time is spent switching energies between spot layers, increasing irradiated blood volume. **Pin Ridge Filter (pRF)** plans use a single proton energy, eliminating energy switching to achieve **ultra-fast delivery**

This work evaluated whether pRF's ultra-fast delivery could improve **immune preservation** in lung patients by calculating **blood dose-volume histograms (bDVHs)** and CL **survival fractions (SFs)**

METHODS

Clinically deliverable pRF plans were created for 10 lung patients previously treated with IMPT (5x10 Gy RBE)

Blood circulation was simulated with **Hematological Dose (HEDOS)** [1], which models blood as stochastically circulating blood particles (BPs) Circulation simulations were coupled with a **temporal model of pencil beam scanning (PBS)** that calculates spot delivery, scanning, and energy switching times

PBS delivery was divided into 50ms HEDOS timesteps. The partial dose at each timestep was accumulated to BPs within the lung. **BPs followed random walks within the lungs** to approximate intra pulmonary circulation

A **saturation radiosensitivity model** ($\mathbf{SF_s}$) [2] was used to estimate SFs for stimulated and unstimulated CD4/CD8 CL subpopulations ($\mathbf{SF_{tot}}$)

$$\mathbf{SF_s(D_i)} = \exp\left(\ln(\mathbf{SF_{sat}})(1-\exp(-\mu \mathbf{D_i}))\right) \Rightarrow \mathbf{SF_{tot}} = \sum_i \mathbf{V_i}\,\mathbf{SF_s(D_i)}$$

SF_{sat} : Where $\mathbf{SF_s}$ saturates
μ : Rate of increase of DNA damage
V_i : bDVH relative volume
$\mathbf{D_i}$: Corresponding dose

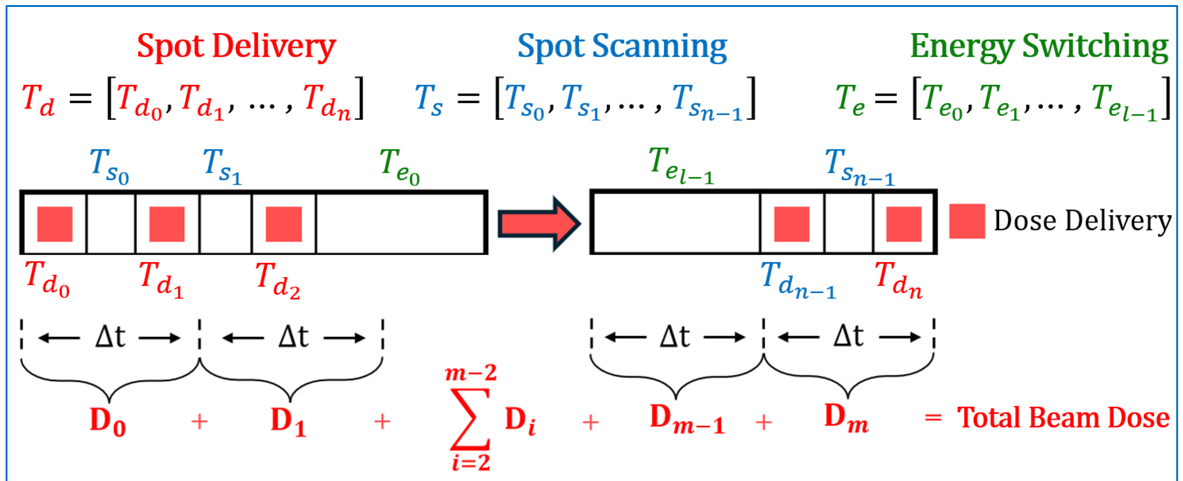

Figure 1: Blood dose accumulation workflow. PBS delivery has *n* spot delivery times (T_d), *n*-1 scanning times between spots (T_s), and energy switching between *l* energy layers (T_e). HEDOS provides the positions of blood particles (BPs) for *m* time steps of duration Δt = 50ms. Total beam dose is divided into partial doses and accumulated to lung BPs

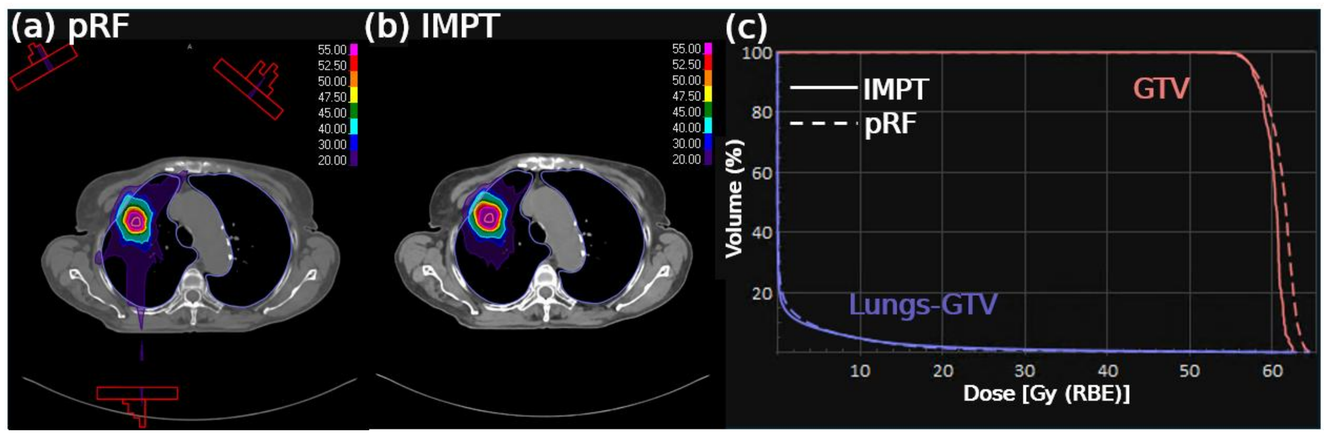

Figure 2: (a) Example pRF isodose with ridge filters contoured in red. **(b)** IMPT isodose on the same patient. **(c)** DVH comparison. pRF plans achieved the same GTV D95% as IMPT while slightly increasing GTV max dose and lungs-GTV dose

RESULTS

On average, pRF plans **reduced delivery time** by 85.3% and **irradiated blood per fraction** by 52.9%

pRFs **greatly reduced blood volumes receiving low doses** and slightly increased the volume at higher doses

pRFs **improved CL survival across all subpopulations**. Stimulated CL survival differences were modest, while unstimulated CL differences were much larger

Table 1: CL Survival Results

	IMPT SF_{tot} (%) (Mean, Range)	pRF SF_{tot} (%) (Mean, Range)
Stimulated CD4	(98.08, 1.18)	(98.35, 2.78)
Unstimulated CD4	(85.42, 11.96)	(93.32, 10.24)
Stimulated CD8	(97.25, 2.02)	(98.39, 2.54)
Unstimulated CD8	(84.84 12.87)	(93.46, 9.94)

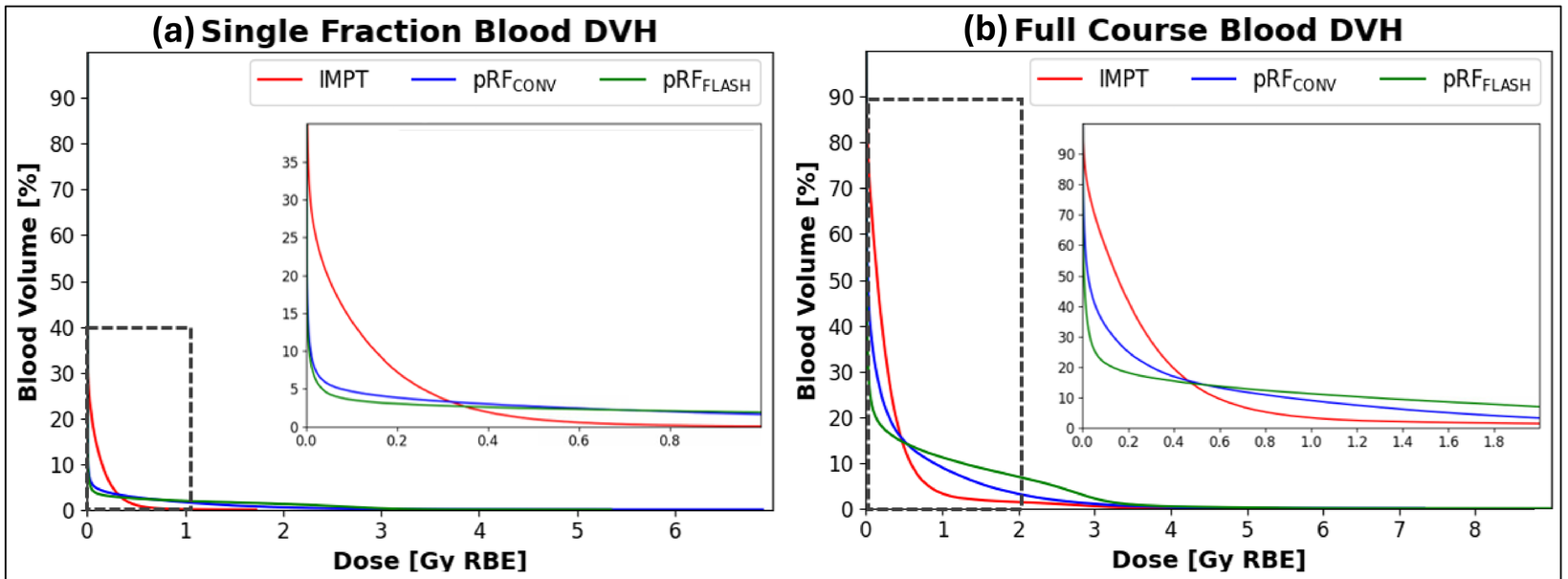

Figure 3: bDVH comparison for **(a)** single fraction and **(b)** the full treatment course

CONCLUSIONS

Compared to IMPT, pRF's ultra-fast delivery reduced the volume of irradiated blood and improved CL survival, particularly for the more radiosensitive unstimulated lymphocytes

This study demonstrated that **pRFs are a promising immune preservation technique** to mitigate RIL

REFERENCES

[1] Beekman C, et al. A stochastic model of blood flow to calculate blood dose during radiotherapy. Phys Med Biol. 2023 Nov 8;68(22):10.1088/1361-6560/ad02d6.

[2] Pham TN, et al. Lymphocyte radiosensitivity: An extension to the linear-quadratic model? Radiother Oncol. 2024 Sep;198:110406. doi: 10.1016/j.radonc.2024.110406. Epub 2024 Jun 24. PMID: 38925262.

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