Proton Linear Energy Transfer Depends on the Beam Delivery Method

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INTRODUCTION

Advanced radiation therapy techniques contribute to enabling 85% of children with cancer to survive 5 years or more, most of whom become long-term survivors. Proton therapy, delivered via pencil-beam–scanning (PBS) or passive-scattering (PS) methods, is the most widely available advanced particle therapy. The theoretical advantages of proton therapy stem from its superior pattern of physical dose deposition, which is largely insensitive to the delivery method. The biologic effectiveness of proton physical dose, however, purportedly rises with increasing ionization density, termed linear energy transfer. Nevertheless, the effect of proton delivery methods on linear energy transfer, and thereby its biologic effects, is poorly understood.

CONCLUSIONS

The major finding of this study is that the proton beam delivery method affects LET_D. These findings are important because early studies seeking to establish the relation between LET_D and biologic effects were performed largely with PS systems. Our findings suggest that such studies, as well as other dosimetric proton therapy studies, may not directly translate to modern PBS treatments. Given the rapid expansion of PBS availability and use, future studies are needed to confirm the applicability of PS-derived scaling factors to modern PBS treatments to ensure their safety and effectiveness for the growing population of patients who are treated with proton therapy.

AIM

The objective of this study was to determine the extent in which proton delivery methods affect the dose-weighted average linear energy transfer (LET_D). To achieve this goal, we characterized the similarities and differences in the LET_D for the PBS and PS methods.

METHOD

SINGLE FIELDS IN WATER

- Calculated LET_D for PBS and PS via Monte Carlo methods (TOPAS)
- Tested for differences in the distribution of LET_D magnitudes between PBS and PS in clinically relevant regions of interest (Figure 1)

CLINICAL TREATMENT PLANS

- Calculated LET_D for 2 cohorts of patients with craniopharyngioma brain tumors (Table 1) via Monte Carlo methods (TOPAS)
- Tested for differences in the distribution of LET_D metrics (Figure 2) computed in clinically relevant regions of interest (Figure 3) between PBS and PS

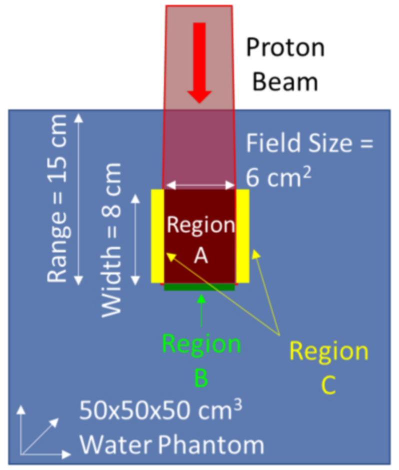

Figure 1. Treatment geometry and regions of interest for simulations in water.

Characteristics	Cohort 1	Cohort 2
Number of patients	94	77
Delivery method	PS	PBS
Prescribed dose (Gy)	54	54
Number of fractions	30	30

Table 1. Treatment details of patients considered in this study.

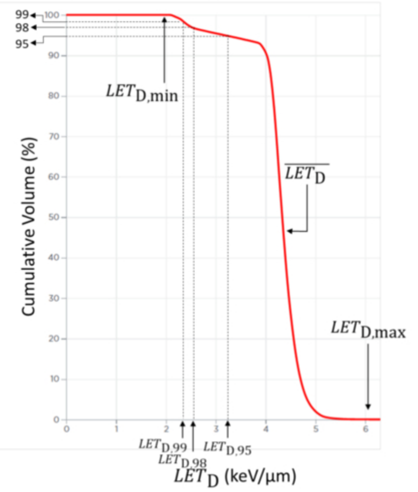

Figure 2. LET_D metrics computed from LET_D-volume histograms of clinically relevant regions of interest.

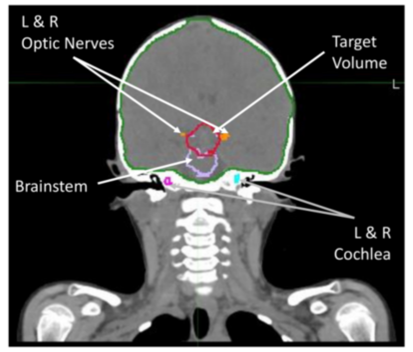

Figure 3. Clinically relevant regions of interest in which LET_D metrics were computed and compared.

RESULTS

SINGLE FIELDS IN WATER

- The absorbed dose from PBS and PS fields in water is comparable (Figure 4).
- PBS produced a significantly larger LET_D than did PS in all 3 regions of interest (Figures 4 & 5).

CLINICAL TREATMENT PLANS

- Most statistical comparisons were significant, indicating that PBS produced a significantly larger LET_D than did PS inside and outside the targeted volume (Figure 6).
- $LET_{D,min}$ exhibited the largest differences, averaging 1.98 keV/μm more in children who received PBS than in those who received PS.
- The largest LET_D differences were observed in the brainstem, in which LET_D computed metrics were an average of 4.08 keV/μm greater for PBS than for PS.

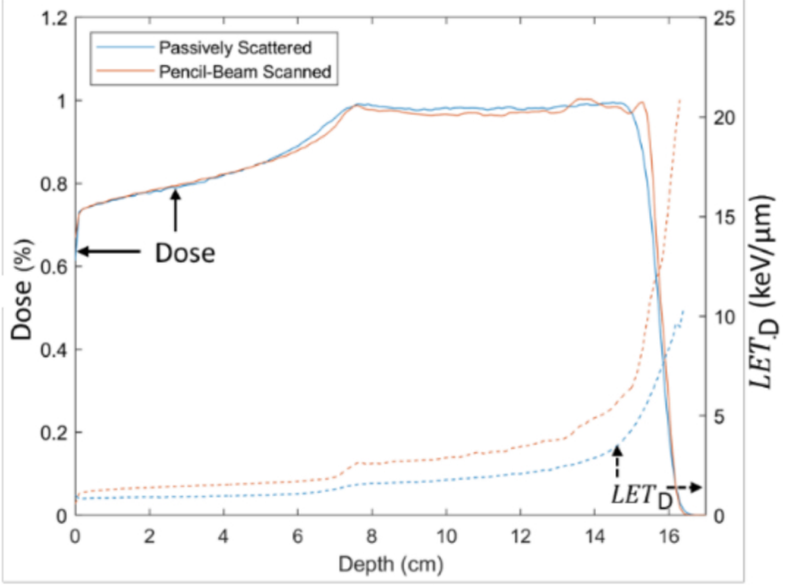

Figure 4. Monte Carlo–calculated dose and LET_D versus depth in a simulated water phantom for single passively scattered (PS) and pencil-beam scanned fields (PBS).

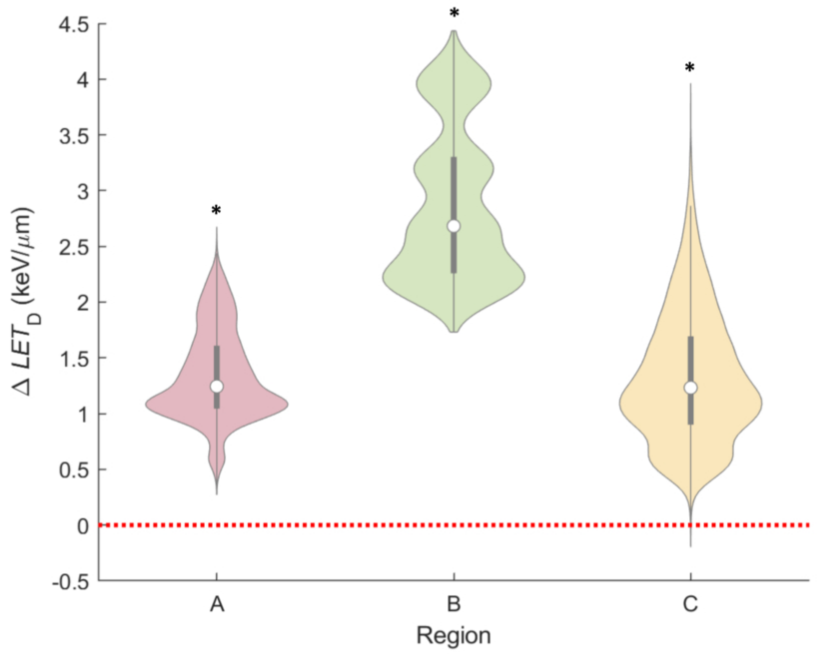

*Figure 5. Violin plots of the voxel-wise deviations of the dose-weighted average linear energy transfer (ΔLET_D) from PBS and PS fields in each of the 3 regions of interest in a simulated water phantom (see Figure 1). The width of each violin plot represents the probability density of each LET_D magnitude. White circles represent the median of each ΔLET_D distribution; thick vertical bars show the interquartile range (IQR); and thin bars represent 1.5 × IQR. The red dashed line indicates a deviation of null. *Statistical significance of α = 0.01*

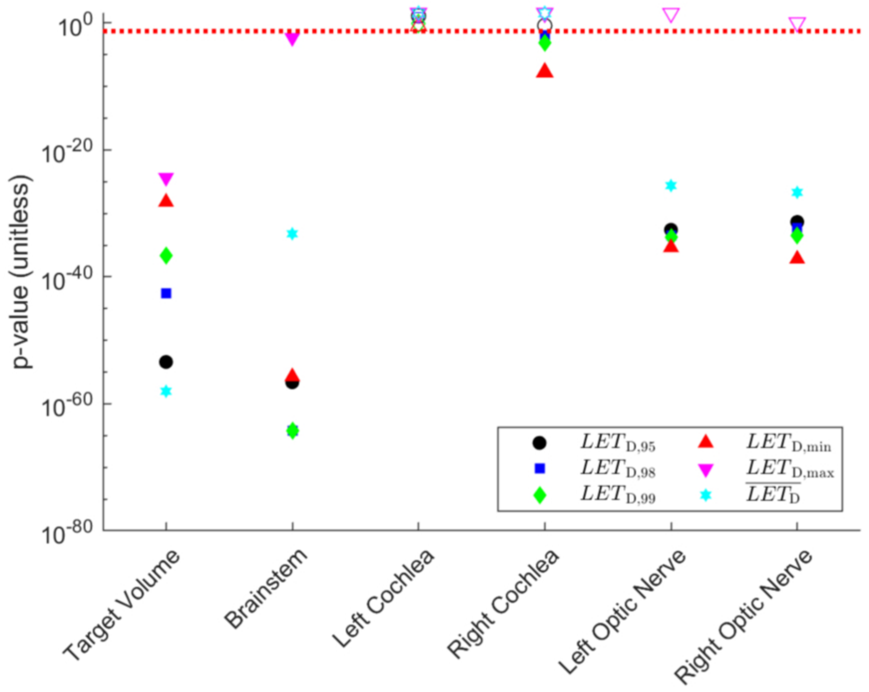

Figure 6. Results of Welch t-test statistical comparisons of LET_D computed metrics in the target and organs of risk of children who received PBS or PS proton therapy. Filled markers represent significantly different comparisons. The red dashed line indicates a significance level of α = 0.05.

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