Purpose: To investigate the feasibility of linear energy transfer (LET)-guided biological dose optimization in intensity modulated proton therapy (IMPT).

Methods: Multi-criteria optimization (MCO) module was utilized to generate Pareto-optimal IMPT plans, each one corresponding to defined objectives (base plans), for a pediatric chordoma case. A Monte Carlo (MC) platform was used to calculate the corresponding LET distributions for each base plan, as well as for a linear combination of the initial base plans (resulting in clinically acceptable plans). Comparison among calculated LET distributions was performed in terms of dose and LET volume histograms (DVH and LVH) for the target and organs at risk (OARs).

For verification purposes, the LET distribution of the clinically acceptable plan was also calculated as the dose weighted average of the LET distributions of the contributing base plans. It was then compared to the corresponding MC LET calculation.

Results: Significant differences were observed among the LET distributions for different Pareto-optimal base plans. Target LVHs demonstrated up to 10% differences in LET values within the range of 30% to 95% of the target volume. Plotted LVHs for the OARs showed more significant differences, more than 50% in the range of 10% to 90% of the structure volume.

Comparison between the MC calculated and dose weighted averaged LET distributions for the clinically acceptable IMPT plan showed no significant differences. This verifies the accurate calculation of the LET distribution as a dose weighted average of pre-calculated LET distributions.

Conclusions: By demonstrating the variability of LET distributions among Pareto-optimal IMPT plans in MCO and verifying the accuracy of the LET calculation method, our study suggests the feasibility of MCO-based planning optimization system, where the user will have access to both the LET and dose distributions while navigating on the Pareto-surface, towards effect-driven treatment planning.

Funding Support, Disclosures, and Conflict of Interest:

Federal Share of program income earned by Massachusetts General Hospital on C06 CA059267