6-2023

# A Comprehensive Investigation of Linear Energy Transfer Optimization Effectiveness in Intensity-Modulated Proton Therapy Via Alternating Direction Method of Multipliers (IMPT Let-ADMM)

Q Fan

G Liu

Lili Zhao

Xiaoqiang Li

Xuanfeng Ding

*See next page for additional authors*

Authors
Q Fan, G Liu, Lili Zhao, Xiaoqiang Li, Xuanfeng Ding, and S Dai

tailored to LET modeling and optimization in order to solve the problem effectively and efficiently. Specifically, nonlinear dose-averaged LET term is iteratively linearized and becomes convex during ICR, and nonconvex dose-volume constraint and minimum-monitor-unit constraint are also handled by ICR, then the solution for LET optimization is obtained by solving a sequence of convex and linearized convex subproblems. A 1cm normal-tissue expansion of CTV (excluding CTV), i.e., CTV1cm, is defined as an auxiliary structure to minimize the LET during treatment planning, since the high LET occurring mostly near the target. **Results:** ICR was validated in comparison with QN for all cases. ICR was effective for LET optimization, which reduced the LET and biological dose in CTV1cm, with preserved dose conformality to CTV. Compared to QN, ICR had smaller LET, physical and biological dose in CTV1cm, higher conformity index values, and higher computationally efficiency, which was about 3 times faster than QN. **Conclusion:** We have developed a LET-specific optimization method based on ICR for solving proton LET optimization, which generates better plan quality in terms of LET, biological and physical dose conformality, and is more computationally efficient than generic nonlinear optimizer via QN.

**MO-930-IePD-F4-3**, A Comprehensive Investigation of Linear Energy Transfer Optimization Effectiveness in Intensity-Modulated Proton Therapy Via Alternating Direction Method of Multipliers ($IMPT_{LET\text{-}ADMM}$): Q. Fan[1], G. Liu[*2], L. Zhao Ph.D[3], X. Li[3], X. Ding[3] and S. Dai[4], (1)School of Mathematics and Statistics, Wuhan University, Wuhan, China, (2)Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, (3)Department of Radiation Oncology, Corewell Health William Beaumont University Hospital, Royal Oak, MI, (4)School of Mathematics and Statistics, and Hubei Key Laboratory of Computational Science, Wuhan University, Wuhan, China

**Purpose:** Linear energy transfer (LET)-guided optimization in intensity-modulated proton therapy (IMPT) via alternating direction method of multipliers (ADMM) has the potential to improve its biological effectiveness ($IMPT_{LET\text{-}ADMM}$), in which the LET distribution in target can be escalated, while the LET distribution in the organs at risk can be mitigated. This study aims to quantitatively investigate the effectiveness of LET optimization in IMPT via ADMM with different solvers in its iteration loop. **Methods:** The clinical dose-volume-histogram (DVH) constraint noted dose sub-problem and clinical LET-volume-histogram (LVH) constraint noted LET sub-problem are combined to generate a composite objective function, which is available to LET incorporated IMPT optimization. Such optimization problem can be solved through ADMM. In the iteration loop of ADMM, the dose sub-problem is a linear least-square problem, which can be effectively solved by conjugate gradient method. At the same time, the LET sub-problem is a nonlinear least-square problem, which can be solved using gradient descent methods. In this study, the BB, LMF, and L-BFGS methods are adopted to solve the LET sub-problem, respectively. Three representative cases (brain, prostate and liver cancer) were used for testing purposes. The dose and LET distribution were assessed. **Results:** With a similar physical dose distribution compared to the clinical IMPT plan, LVH comparison indicated $IMPT_{LET\text{-}ADMM}$ with L-BFGS solver (LETOpt[L-BFGS]) has the best LET distribution. More specifically, for the brain case, the mean LET of CTV was improved by 0%, 3%, 10% by LETOpt[BB], LETOpt[LMF], LETOpt[L-BFGS]; the max LET of the brainstem was reduced by 21%, 39%, 48% compared to the clinical IMPT. The other two cases show similar results. **Conclusion:** $IMPT_{LET\text{-}ADMM}$ is able to modulate the LET distribution while maintaining dose distribution. L-BGFS solver is more effective in LET distribution modulation than BB and LMF solver.

**MO-930-IePD-F4-4**, Noisy Non-Modulated Dose Map Augmented Accurate and Efficient Deep Learning-Based Dose Prediction for Pencil Beam Scanning Proton Therapy to Treat Prostate Cancer: L. Zhang[*1], J. M. Holmes[1], C. E. Vargas[1], N. Y. Yu[1], S. R. Keole[1], J. C. M. Rwigema[1], S. E. Schild[1], S. A. Vora[1], W. W. Wong[1], M. Bues[2], J. Shen[2] and W. Liu[1], (1)Department of Radiation Oncology, Mayo Clinic, Phoenix, AZ, (2)Mayo Clinic Arizona, Phoenix

**Purpose:** Deep learning (DL) has shown promising dose prediction results in photon therapy. However, more DL improvement is needed to handle challenging dose prediction in pencil beam scanning proton therapy (PBSPT). Inspired by the traditional way to calculate the influence matrix during PBSPT treatment planning, we propose to use a noisy non-modulated dose map to augment the deep learning-based dose prediction for PBSPT in prostate cancer. **Methods:** PBSPT plans of 103 previously treated prostate cancer patients (97 for training and 6 independent patients for testing) were included in the study, each with CT scans, structure sets, plan dose calculated by the in-house developed Monte-Carlo dose engine. To improve the accuracy of the DL model for proton dose prediction, we used a novel noisy non-modulated dose map calculated by the in-house developed Monte-Carlo dose engine with unit spot weights and 500 times fewer initial primary protons compared to the ones used in regular plan dose calculation (thus much faster). Fully connected 3D-Unet was adopted as the DL backbone. Dose volume histogram indices and 3D Gamma passing rates with a threshold of 3%/3mm/10% were used as evaluation metrices. **Results:** The proposed model achieved dosimetric performance comparable to the manually derived clinical plans with the differences of clinical-target-volume D95 <0.3 Gy and most organs-at-risk (OARs) Dmean <0.4 Gy. The 3D Gamma passing rates between the model-predicted doses and the clinical plan doses within targets, OARs and BODY are 99.99%±0.02%, 97.03%±1.59% and 96.23%±1.38%, respectively. The average dose prediction time is 189± 25ms. **Conclusion:** An accurate and efficient DL-based proton dose prediction framework has been developed for PBSPT, which can predict accurate dose distributions not only inside but also outside targets and OARs. The framework can potentially reduce the planning and adaptive replanning workload for prostate cancer patients treated with PBSPT.