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Objectives

This study evaluates the implementation and outcomes of adaptive proton therapy for locally advanced non-small cell lung cancer (NSCLC) receiving concurrent chemoradiotherapy.

Methods

Between 2023 and 2025, 14 patients with unresectable stage III NSCLC received intensity-modulated proton therapy (IMPT) at the National Cancer Centre, Singapore. CT simulation was performed using either a customized Alpha Cradle or AIO with Thoracic Shell for immobilization, and 4DCT-based motion assessment guided strategies to limit tumour motion to <1cm. Prescription dose was 66 GyE in 33 fractions. IMPT was delivered with the first 2 cycles of chemotherapy in 12 patients, and 2 patients initiated IMPT with 4th cycle of chemotherapy. All plans employed robust optimization, accounting for 5 mm setup uncertainties and 3.5% range uncertainties. For tumors with motion exceeding 5 mm, 4D robust optimization was implemented, integrating average, maximum inhale, and maximum exhale CT phases. Weekly CT evaluations assessed both target coverage and organ-at-risk (OAR) doses, with replanning triggered when clinical objectives were compromised.

Results

The cohort (median age 65 years, 57% female) presented with adenocarcinoma (43%), squamous cell carcinoma (43%), and lymphoepithelioma-like carcinoma (14%), with tumors predominantly in the right lower lobe (36%). The median clinical target volume was 218 cc (range: 55-1013 cc). 5 patients (36%) required adaptive replanning, with 1 patient needing 2 replans. Median replanning week was at 3rd week. Tumor shrinkage was the primary reason for adaptation (80%), followed by OAR (esophagus) dose concerns (20%). Various 4D robust optimization techniques were employed, with "Ave+T0+T50" being the most common approach (57%). Adaptive interventions successfully restored target coverage while maintaining OAR sparing. 1 patient developed G2 pneumonitis and 1 patients had G3 dermatitis during the treatment, G3-4 lymphocytopenia was seen in 10/14patients.

Conclusions

This single-institution experience demonstrates that adaptive planning is frequently necessary in proton therapy for locally advanced NSCLC. The 4D robust optimization provides a foundation for treatment precision, but regular imaging assessment remains essential for adaptation. Future research should focus on developing predictive models to identify patients most likely to benefit from adaptive interventions and establishing standardized guidelines for implementation.
