Photon vs proton therapy for reduction of cardiac toxicity in locally advanced lung cancer using the model-based approach

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Objective
Identify a sub-group of patients with locally advanced lung cancer who would benefit most from proton therapy compared to photon therapy for reduction of cardiac toxicities using the model-based approach.

Materials/methods
Dual-arc volumetric modulated arc photon therapy (VMAT) and robust-optimised intensity modulated proton therapy (IMPT) plans were created in twenty proxy patients with locally advanced lung cancer to a physical dose of 70Gy in 35 fractions. Proxy patients were selected to represent varying anatomical locations of the primary tumour and nodal involvements (15/20 had nodal involvement). Contouring, treatment planning and organs-at-risk constraints followed RTOG 1308 trial. The following cardiac sub-structures were delineated-right and left: atriums, ventricles and coronary arteries, and sino-atrial node. Dose calculations and optimisation of IMPT plans were done using Monte-Carlo dose engine. Dose to the heart and sub-structures were compared. Risk estimates of grade 3+ cardiac toxicities were calculated based on normal tissue complication probability models which incorporated dose metrics and patients’ risk-factor - pre-existing cardiac disease (CD) (Dess et al, JCO 2018). Wilcoxon signed-rank test was used to assess statistical significance of the difference.

Results
There was no statistically significant difference in target coverage between VMAT and IMPT. Overall IMPT delivered lower doses to the heart (mean heart dose (MHD), V5 and V30). In VMAT plans, there were statistically significant positive correlations between heart dose and thoracic vertebral level (MHD, V5 and V30; Pearson correlation co-efficient, r: 0.67, 0.79, 0.48, P < 0.05). Between VMAT vs IMPT, there was no statistically significant difference in the mean cardiac dose or its sub-structures when the tumour (primary and nodes) extended above T7 vertebrae (n = 4). When tumour extended to and below T7 vertebrae (n = 16) IMPT delivered lower cardiac doses (MHD, V5 and V30), mean dose to all sub-structures, P < 0.001. Risk of G3+ cardiac toxicities when tumour extended to and below T7 vertebrae are presented in Table 1.

Conclusions
Our analysis suggests that IMPT could benefit patients with locally advanced NSCLC whose primary tumour and nodal spread overlapped with or is inferior to T7 vertebrae compared to VMAT. The greatest benefit was seen in patients with pre-existing heart disease followed by those at high-risk of heart disease. In the highest risk group, the RRR of grade 3+ cardiac complications was between 40 and 60%.

In an unselected patient group, not all patients would benefit from IMPT. Although the validity of photon NTCP models in proton is unclear, appropriate models could be used to aid randomised control trial design.

References