5-1-2022

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PO-1505 Feasibility of acute hematologic toxicity model-based patient selection for proton beam therapy

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Purpose or Objective

To investigate the potential clinical benefit of utilizing IMPT to reduce acute hematologic toxicity for locally advanced non-small cell lung cancer (NSCLC) patients and explore the feasibility of a model-based patient selection approach via the normal tissue complication probability (NTCP).

Materials and Methods

Twenty patients with locally advanced NSCLC were enrolled.[ld1] Volumetric modulated arc photon therapy (VMAT) and intensity-modulated proton therapy (IMPT) plans were generated with a prescription dose of 60 Gy in 30 fractions. A wide range of cases with varied tumor size, location, stations of metastatic lymph nodes were selected to represent the general cancer group. Contouring and treatment planning followed RTOG-1308 protocol. Doses to bone marrow (BM) and other organ-at-risks were compared. Risk of grade ≥ 3 acute hematologic toxicity (HT3+) were calculated based on NTCP model and patients with reduction on NTCP of HT3+ (△NTCP_HT3+) ≥ 10% were considered to 'significantly benefit from proton therapy.'

Results

Dose to the BM, the lung, the heart, the esophagus and the spinal cord was significantly reduced via IMPT compared to VMAT. Tumor distance to thoracic vertebrae bodies (TVB) was significantly associated with > 10% △NTCP_HT3+ from IMPT to VMAT. For the patients with tumor distance ≤ 0.7 cm to TVB, the absolute reduction of dose (mean, V30 and V40) to BM was significantly lower than that in patients with tumor distance > 0.7 cm.

Figure.1 Possibility of HT3+ in 20 patients

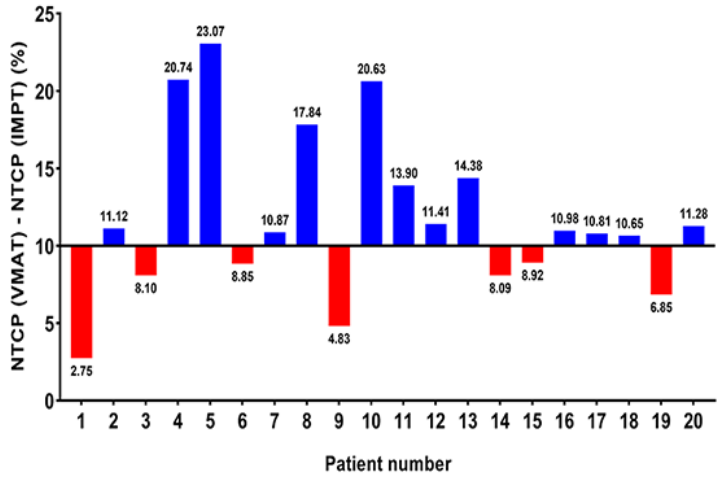

Table 1. Comparison of absolute reduction on dosimetric parameters of OARs

Parameters	Absolute Reduction		P value
	Distance >0.7cm	Distance ≤ 0.7cm	
BM			
V5(%)	32.32±11.01	22.47±12.09	0.073
V10(%)*	30.06.6±11.38	22.85±11.25	0.095
V15(%)*	26.99±13.47	24.84±12.11	0.370
V20(%)*	24.18±13.40	26.77±11.84	0.766
V30(%)*	16.40±14.89	28.01±10.02	0.006**
V40(%)*	8.18±9.35	24.31±9.24	0.002**
Dmean(GyE)*	9.75±4.38	12.77±4.38	0.020**
Lung			
V5(%)	21.43±5.88	22.91±12.78	0.735
V20(%)	7.16±3.65	11.77±4.72	0.024**
Heart			
V30(%)*	6.92±7.32	9.51±11.38	0.656
V50(%)*	5.43±12.93	2.21±3.54	0.710
Dmean(GyE)*	5.49±4.31	7.54±5.86	0.503
Esophagus			
Dmean(GyE)	7.65±5.22	8.61±5.20	0.688
Spinal cord			
Dmax(GyE)*	19.88±8.78	17.89±10.59	0.656

Abbreviations. BM, bone marrow; Dmean, mean dose; Dmax, maximal dose.
*Non-normal distribution parameters were analyzed with nonparametric tests (Mann-Whitney test); Otherwise, normal distribution parameters were analyzed with independent-sample t test.
** $p < 0.05$; otherwise $p \geq 0.05$.

Conclusion
IMPT reduced HT3+ compared to VMAT by reducing dose to the thoracic BM in NSCLC patients. Patients with tumor distance ≤ 0.7 cm to TVB are likely to benefit most from proton over photon therapy

PO-1506 Healthy tissue sparing in proton therapy of lung tumors using statistically sound robust planning

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Purpose or Objective
Robust planning is essential in proton therapy for ensuring adequate treatment delivery in the presence of uncertainties. For both robust optimization and evaluation, commonly-used techniques can be overly conservative by generating error scenarios from combinations of only maximum error values of each uncertainty source and they lack in providing quantified confidence levels. In this study, we explore whether a clinical benefit can be expected using scenario selection tools with improved statistical foundations, both at the level of robust optimization and evaluation.

Materials and Methods
Thirteen lung cancer patients were planned. Two robust optimization methods were used: scenario selection from marginal probabilities (SSMP) based on using maximum setup and range error values and scenario selection from joint probabilities (SSJP) that selects errors on a predefined 90% hypersurface. Two robust evaluation methods were used: conventional evaluation (CE) based on generating error scenarios from combinations of maximum errors of each uncertainty source and statistical evaluation (SE) via the Monte Carlo dose engine MCsquare which considers scenario probabilities. During evaluation we report for the target coverage the D_{98} (Gy) nominal and worst-case values as well as D_{mean} (Gy) and V_{30} (%) for heart and lungs-GTV and D_2 (Gy) for spinal cord and esophagus.

Results
Plans optimized using SSJP had, on average, 0.5 Gy lower dose in CTV $D_{98(worst\text{-}case)}$ than SSMP-optimized plans. This was expected as the SSJP tool aims at securing robustness at a predefined 90% confidence level with the aim of achieving a level of target robustness situated at the limit of clinical acceptability (i.e., adequate coverage for at least 90% of patients). When evaluated using CE only 76.9% of SSMP patients and 46.2% of SSJP patients passed our clinical threshold. Evaluating with SE, 92.3% of patients passed our clinical threshold in both optimization methods highlighting the impact of evaluating in a statistically consistent manner. Average gains in OAR sparing were recorded when transitioning from SSMP to SSJP in all metrics: esophagus (0.6 Gy $D_{2(nominal)}$, 0.9 Gy $D_{2(worst\text{-}case)}$), spinal cord (3.9 Gy $D_{2(nominal)}$, 4.1 Gy $D_{2(worst\text{-}case)}$) heart (1.1 Gy D_{mean}, 1.9% V_{30}), lungs-GTV (1.0 Gy D_{mean} , 1.9% V_{30}). The reduction of the target margin to the bare minimum is the main drive that enables substantial and consistent OAR sparing.