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Technical Report

A lung SBRT treatment planning technique to focus high dose on gross disease ☆

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ABSTRACT

This study investigated a straightforward treatment planning technique for definitive stereotactic body radiation therapy (SBRT) for patients with early-stage lung cancer aimed at increasing dose to gross disease by strategically penalizing the normal tissue objective (NTO) in the Eclipse™ treatment planning system. Twenty-five SBRT cases were replanned to 50 Gy in 5 fractions using static and dynamic NTO methods (50 plans total). The NTO had a start dose of 100% at the target border, end dose of 20%, fall-off rate of 0.4/mm, and a priority of 150. For the static NTO plans, a lower planning target volume (PTV) objective was placed at 52 Gy with a priority of 100. Maximum dose was not penalized. Optimization was performed without user interaction. In contrast, the planner incrementally increased the priority of the NTO on the dynamic NTO plans until 95% of the target volume was covered by the prescription dose. Further, the dynamic NTO plans used both PTV lower and upper objectives at 63-64 Gy with priorities of 50. Maximum dose was penalized to ensure that the hot spot was within ± 2% of the static NTO global maximum dose. Following optimization, all plans were normalized so that the prescription dose covered 95% of the PTV. Plans were scored based on RTOG 0813 criteria, and dose to the internal target volume (ITV) and PTV was evaluated. The Wilcoxon signed-rank test (threshold = 0.05) was used to evaluate differences between the static and dynamic NTO plans. All plans met RTOG 0813 planning guidelines. In comparison to the static NTO plans, the dynamic NTO plans exhibited statistically significant increases in PTV mean dose, ITV mean dose, and PTV-ITV mean dose. Notably, the dynamic NTO plans more effectively concentrated the high dose on gross disease at the center of the PTV. As compared to the static NTO plans, the mean dose was 4.6 Gy higher in the ITV while only 1.3 Gy higher in the PTV-ITV rind of the dynamic NTO plans. Global maximum doses were similar. There were some small yet statistically significant differences in dose conformity between plan types. Furthermore, the dynamic NTO plans demonstrated a significant reduction in total monitor units (MU). This study demonstrated an efficient optimization strategy for lung SBRT plans that concentrates the highest dose in the gross disease, which may improve local control.

Introduction

Stereotactic body radiation therapy (SBRT) is known for its precision in delivering high doses to well-defined, tumors across diverse anatomical locations.[1] SBRT is often used for definitive treatment of early-stage non-small cell lung cancers.[2] High-quality lung SBRT plans are characterized by highly conformal dose distributions with steep dose gradients. Lung SBRT plan quality may be evaluated based on the planning guidelines detailed in the Radiation Therapy Oncology Group (RTOG) 0813 trial protocol.[3] The guidelines have various metrics to benchmark plan quality, including conformity index (CI). The conformity index is a ratio of an isodose line's volume to the target volume, though CI typically refers to the prescription isodose line. There are many treatment planning techniques that may be used to steepen the dose gradient falling away from the target volume to spare healthy tissues. Optimization structures, i.e., concentric shells, have been shown to generate quality lung SBRT plans.[4] Another treatment planning tech-

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nique is the utilization of the Normal Tissue Objective (NTO) in the Eclipse™ treatment planning system. The NTO is a spatially-varying, one-dimensional dose gradient penalty in the optimization workspace that can help improve the compactness of the isodose distribution by penalizing progressively lower isodose lines as distance increases from the target.[5] The manipulation of the NTO allows the user to modify how the dose gradient is penalized outside of the target.[5] A study conducted by Bell et al explored the effects of various NTO settings on lung SBRT plan quality.[6] However, their study did not consider the spatial distribution of the dose within the planning target volume (PTV) or the internal target volume (ITV), which is a motion envelope of the gross disease. Since that publication, a meta-analysis has demonstrated the importance of increasing the dose to the gross disease, as this may enhance local control.[7]

The static NTO technique described by Bell et al.[6] used a lower PTV objective equal to the prescription dose in combination with an NTO that allowed the prescribed dose to extend 1 mm beyond the PTV surface before incurring a penalty. At greater distances outside the PTV, the dose gradient was penalized with varying NTO curves of different priorities. This combination of a lower-objective PTV and NTO does not penalize the dose gradient within a PTV. However, it is possible to reconfigure the optimization settings to penalize the dose gradient both within and beyond the PTV to concentrate the highest dose on the gross disease at the center of a PTV. We present here a dynamic NTO technique where the PTV lower objective is significantly higher than the prescribed dose. By dynamically increasing the NTO priority during optimization, the PTV surface dose is lowered to approximately the prescription dose, thereby creating a dose gradient within the PTV. We demonstrate that a dynamic NTO can escalate PTV dose, preferentially concentrating high dose on the ITV, while achieving similar normal tissue sparing as a static NTO plan.

Methods

Case selection

Twenty-five lung SBRT cases treated at our institution between 2016 and 2022 were used for this study. An ITV was created for all cases to account for respiratory motion using a 4 DCT, and a 5-mm expansion was placed on the ITV to create the PTV. All target volumes were generated and approved by a board-certified radiation oncologist. For each case, a PTV-ITV structure was created by cropping the ITV from the PTV to create a 5-mm outer rind. Target sizes varied across cases: PTV volumes ranged from 6 cc to 130 cc. The prescription dose was 50 Gy in 5 fractions. Cases where the PTV overlapped or bordered a dose limiting organ at risk (OAR) were excluded from the analysis. This retrospective study was conducted under Institutional Review Board-approved protocol #00006087.

Treatment planning

Volumetric modulated arc therapy (VMAT) plans with 2 lateral 180° arcs on the ipsilateral side were used for all cases. Arcs were separated by ±15° couch angles while collimator angles were set at 45° and 315°. The Varian Eclipse™ Arc Geometry Tool (Version 16.1.0; Varian Palo Alto, CA) was used to automatically conform the field size to the PTV. Plans were optimized for a Varian Edge linear accelerator equipped with a high-definition multileaf collimator, utilizing 6X-FFF at a 1400 MU/min dose rate. Clearance was verified by the Radformation CollisionCheck software. In cases where collision risks were identified by the software, the isocenter was adjusted to achieve at least 2 cm clearance between the gantry and the patient, any immobilization devices, and the treatment couch.[8] VMAT optimization was conducted using the Varian Eclipse™ treatment planning system (Version 16.1.0), employing Photon Optimizer (version 16.1.1) and Acuros (version 16.1.0) for dose calculations. Inhomogeneity and air cavity corrections were applied during optimization, and the convergence mode was turned off.

A static NTO plan was optimized with no user interaction to serve as the benchmark for the plan quality comparisons. The static NTO plan had 2 optimization objectives: one to achieve target coverage and another to steepen the dose gradient. More specifically, a lower dose objective of 52 Gy was set for the PTV with a priority of 100. The second objective was an NTO with a starting dose of 100% (50 Gy) at 0 cm from the PTV surface, a dose fall-off rate of 0.40/mm to the 20% isodose, and a priority of 150. Dynamic NTO plans were crafted using a similar workflow, but user interaction was allowed during optimization to adjust the NTO priority. Dynamic NTO plans had 3 optimization objectives: 2 on the target and one aimed at steepening the dose gradient. A lower PTV objective and an upper PTV objective were used to achieve coverage while ensuring that max dose was within ± 2% of the static plans; priorities were set at 50 for the PTV objectives.

In contrast to the static NTO plans, lower PTV dose objectives on dynamic NTO plans were substantially higher than the prescribed dose. For example, if the desired global hot spot was 130% (65 Gy), the lower objective would be placed around 126% (63 Gy) and the upper at 128% (64 Gy). The third objective was the NTO. The NTO settings were identical to the static NTO plans. After defining these objectives, the optimization process was started but was promptly paused at the first resolution level. During this pause, the priority of the NTO was iteratively increased until 95% of the PTV was at the prescribed dose of 50 Gy. Once target coverage was reduced to this level, the optimizer resumed, and the plan progressed without any further user intervention. Automatic optimization mode and intermediate dose calculation were used for all plans. All plans were normalized such that 100% of the prescription dose covered 95% of the PTV following the final dose calculation with Acuros.

Data analysis

Plan quality was evaluated by criteria as described in the RTOG 0813 protocol. Conformity index metrics such as CI100%, CI75%, CI50%, and CI25% were recorded for each plan. Further, dose was evaluated within the target volumes by considering the maximum and mean doses to the ITV, PTV and PTV-ITV rind. Biologically effective doses (BED) were calculated for targets using an $\alpha/\beta = 10$. All dosimetric endpoints were recorded in Gy. A Wilcoxon signed-rank test was used to assess for statistically significant differences between the static and dynamic NTO plans.

Results

Dose conformity metrics are summarized in Table 1. The CI100% is significantly lower for the dynamic NTO plans while the CI50% and CI25% are significantly higher for the static NTO plans, though absolute differences are within 3%. Table 2 lists additional dosimetric endpoints. There was a significant increase in PTV mean dose,

Table 1
CI metrics for static and dynamic NTO plans (n = 50).

	CI100%	CI75%	CI50%	CI25%
Static NTO	0.993	1.739	3.504	12.455
Dynamic NTO	0.986	1.727	3.552	12.846
p-value	0.028*	0.083	0.006*	<0.001*

All metrics are presented as the average across all cases.
*The differences were considered significant when $p < 0.05$.

Table 2
Dosimetric endpoints for static and dynamic NTO plans (n = 50).

	Total MUs	PTV Max Dose (Gy)	PTV Mean Dose (Gy)	ITV Max Dose (Gy)	ITV Mean Dose (Gy)	PTV-ITV Max Dose (Gy)	PTV-ITV Mean Dose (Gy)
Static NTO	4251.375	66.62	55.71	65.38	57.24	66.16	55.08
Dynamic NTO	3168.262	66.45	58.13	66.16	61.82	65.74	56.34
p-value	<0.001*	0.166	<0.001*	0.166	<0.001*	0.010*	<0.001*
BED Static NTO		133.24	111.42	130.76	114.49	132.32	110.16
BED Dynamic NTO		132.90	116.26	132.32	123.64	131.48	112.68

BED = Total Dose x (1 + (Fraction Dose/(α/β))); $\alpha/\beta = 10$.
All metrics are presented as the average across all cases.
*The differences were considered significant when $p < 0.05$.

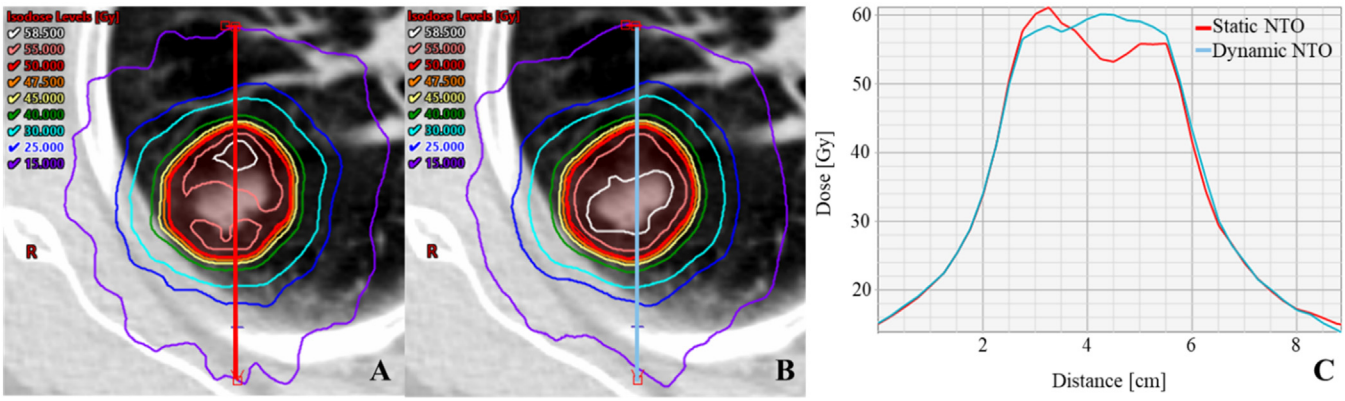

Fig. 1. Dose profile comparison for a representative case. (A) Static NTO isodose distribution (global max 122.3%), (B) Dynamic NTO isodose distribution (global max 121.5%), (C) Dose profile showing the distribution of the dose for the static NTO (red line) and the dynamic NTO (blue line).

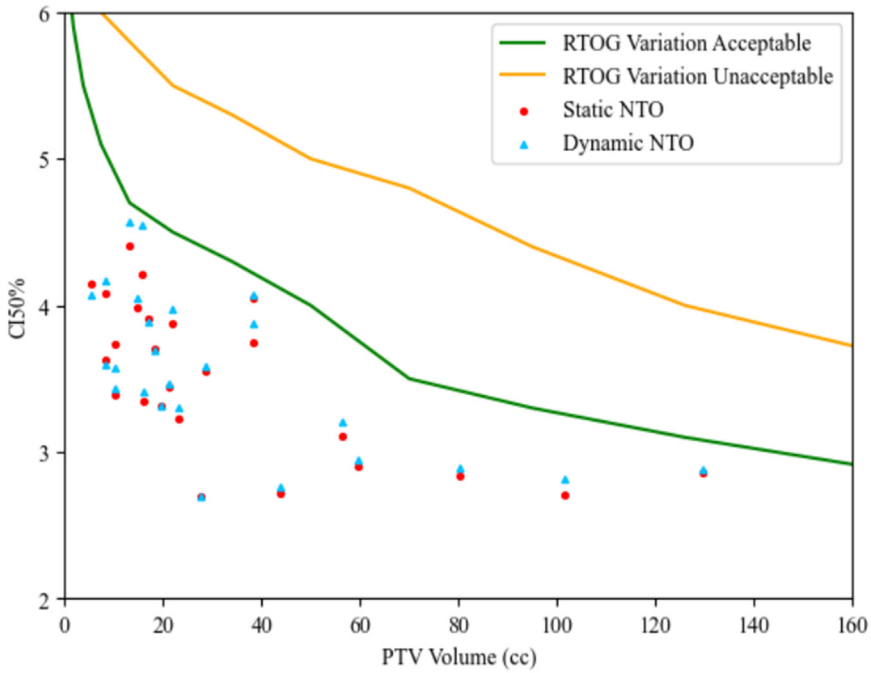

Fig. 2. The CI50% of the static (red circles, n = 25) and dynamic (blue triangles, n = 25) NTO plans and the RTOG 0813 limits for minor/variation acceptable (green line) and major/variation unacceptable (yellow line) deviations.

ITV mean dose, and PTV-ITV mean dose in the dynamic NTO plans as compared to the static NTO plans. The ITV mean dose increased by an average mean of 4.6 Gy for the dynamic NTO plans, compared to the static NTO plans which led to an ITV mean BED increase of 9.1 Gy. The difference between the PTV-ITV mean dose and the ITV mean dose is greater for the dynamic NTO plans, showing preferential dose escalation in the ITV where the gross disease resides throughout the respiratory cycle. There were no statistically significant differences in the global maximum doses between the 2 planning techniques. The total MUs per plan were significantly lower in the dynamic NTO plans as compared to the static NTO plans. Overall, OAR doses were similar (Table 3). The skin was the only OAR with a statistically significant difference; however, skin dose was well below the clinical goal in all cases.

Table 3
Average and standard deviation of RTOG 0813 dosimetric endpoints for the static and dynamic NTO plans (n = 25 each) with associated *p*-values.

	Static NTO	Dynamic NTO	*p*-value
Spinal Cord D0.25cc (Gy)	7.46 ± 5.93	7.23 ± 5.88	0.35
Spinal Cord D0.5cc (Gy)	7.01 ± 5.74	6.86 ± 5.73	0.49
Brachial Plexus D3cc (Gy)	0.27 ± 0.26	0.27 ± 0.27	0.10
Skin D10cc (Gy)	6.30 ± 2.14	6.59 ± 2.22	0.006*
Lungs D1500cc (Gy)	0.93 ± 0.83	0.91 ± 0.82	0.71
Lungs D1000cc (Gy)	1.72 ± 1.37	1.72 ± 1.40	0.08
Esophagus D5cc (Gy)	6.71 ± 8.20	6.71 ± 8.21	0.85
Heart D15cc (Gy)	5.83 ± 6.66	5.94 ± 6.82	0.24
Great Vessels D10cc (Gy)	9.20 ± 8.44	9.18 ± 7.96	0.36
Trachea D4cc (Gy)	4.26 ± 7.15	4.36 ± 7.17	0.51
Ipsilateral Bronchus D4cc (Gy)	8.90 ± 12.29	8.92 ± 12.36	0.90

An asterisk (*) denotes a significant result ($p < 0.05$).

Figure 1 shows a dose profile comparison of a representative case. The dose profile shows the concentration of the highest dose in the center of the target (Fig. 1C) without an increase in the PTV maximum dose. The concentration of the highest dose volume in the center of the target can also be visually seen in Fig. 1B compared to Fig. 1A. Figure 1A shows the highest dose of the target concentrated at the outside edge of the PTV while in Fig. 1B the highest dose is concentrated within the gross disease. Figure 2 is a plot of the CI50% for static and dynamic NTO plans and the RTOG 0813 variation acceptable and unacceptable criteria. For all 50 plans, CI100% and CI50% met the RTOG 0813 recommended values.

Discussion/Conclusion

Fine tuning the static NTO settings is important for achieving clinical goals. In this study, the dynamic NTO planning method proved to be an effective and straightforward optimization strategy for lung SBRT planning, successfully concentrating the highest dose regions within the gross disease. Prior studies[6,8] using the static NTO show wide variation in the high dose region and distribution. While it is unknown if a static NTO can position high dose in the gross disease, as with the dynamic NTO, this would be a more efficient planning technique and deserves more investigation. The flexibility and ease of clinical application of the dynamic NTO technique make it suitable for implementation across other disease sites. However, this study did not explore all available planning techniques. Bell et al.[6] showed a wide variation in plan MUs based on the various static NTO settings. Smaller MLC apertures are associated with higher MUs. In this study, the dynamic NTO had lower MUs than the static NTO plans, however, we did not use the same fall-off setting that Bell et al.[6] used to produce the fewest MUs. While this study focuses on peripheral lung cases, which tend not to be limited by OARs, knowledge-based planning and deep learning models can be explored in conjunction with the NTO for estimating OAR doses for centrally located cases.

Our research demonstrates that the NTO, in combination with PTV lower and upper objectives, can be used to escalate dose to gross disease in lung SBRT plans. The findings indicate significant escalation of central dose without any clinically meaningful difference in dose conformity and OARs while using fewer MUs. This simple optimization framework, with only 3 objectives, is designed for direct implementation into clinical practice.

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