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FULL PAPER

Potential for adaptive dose escalation in radiotherapy for patients with locally advanced non-small-cell lung cancer in a low mid income setting

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This work has been presented in parts as a poster presentation at the World Conference on Lung Cancer 2011, Amsterdam; ASTRO 2012, Miami, FL; and ESTRO 2012, Barcelona.

Objective: To evaluate the effect of tumour volume regression on adaptive treatment planning, reduction in doses to organs at risk (OARs) and dose escalation.

Methods: 20 patients undergoing radical chemoradiotherapy were imaged in the fifth week of radiotherapy (CT₄₅) to evaluate differences in tumour volume regression between concurrent and sequential chemoradiotherapy. Replanning was carried out in the CT₄₅ in those with >20% regression ($n = 10$) and evaluated for change in target coverage indices (the coverage index and external volume index) and doses to the OAR [mean lung dose, V_{20} and V_5 of whole and ipsilateral lung (MLD_{WL}, V_{20WL} , V_{5WL} , MLD_{IL}, V_{20IL} , V_{5IL}); mean oesophagus dose, $V_{50\text{oesophagus}}$; and maximum spinal cord doses]. The feasibility of maximum dose escalation was explored keeping the limit of the OAR below their tolerance limits.

Results: Tumour regression was higher with concurrent chemoradiotherapy as compared with sequential chemoradiotherapy ($p = 0.02$). With the adaptive plan, the

mean coverage index improved from $0.96 (\pm 0.14)$ to $1.29 (\pm 0.36)$, the mean external volume index changed from $1.39 (\pm 0.60)$ to $1.41 (\pm 0.56)$ and the reduction in doses to the OARs were MLD_{WL} 10.6%, V_{20WL} 1.3%, V_{5WL} 1.2%, MLD_{IL} 6.6%, V_{20IL} 1.5%, V_{5IL} 2.3%, mean oesophagus dose 7%, $V_{50\text{oesophagus}}$ 31% and maximum cord dose 0.35%. Dose escalation was possible in four patients in CT₄₅.

Conclusion: There is 35% reduction in tumour volume with chemoradiotherapy at 45 Gy which allows improvement in conformality, reduction in doses to the OARs and dose escalation in 40% of patients.

Advances in knowledge: This article emphasizes that adaptive planning with a single diagnostic scan at 45 Gy has the potential for improvement of radiotherapy planning indices, dose escalation while respecting the dose to the OAR. This simple strategy can be helpful in radiotherapy planning upto 60 Gy in 40% of the patients of locally advanced non-small-cell lung cancer in countries with limited resources.

INTRODUCTION

Chemoradiotherapy is the standard treatment of locally advanced lung cancer which is associated with significant toxicity.^{1,2} Toxicity of chemoradiotherapy can be reduced by smaller radiation fields which is possible by approaches that avoid elective mediastinal radiation and technologies such as four-dimensional (4D) CT and those using image-guided delivery techniques.^{3–7} Smaller fields, however, might be more susceptible to “target miss” during a course of chemoradiotherapy.⁵ The basic assumption of any radiotherapy (RT) plan is that both the planning target volume (PTV) and the dosimetric profile visualized at simulation are representative throughout the entire

treatment course. However, any undetected change during the treatment course could lead to either underdosage of the target or overdosage of critical structures. Variables that can affect the PTV over time include changes related to the tumour, such as progression or regression, shifts from the baseline position, changes in the motion pattern; changes in the tissues around the tumour, such as resolution or progression of atelectasis; and patient-related factors, such as weight loss. Such anatomical changes will inevitably alter the shape and location of the isodose volumes, potentially to a clinically significant degree.⁸ The dosimetric consequences of changes over time appeared to be minimal in patients with Stage I lung cancer treated with fractionated

stereotactic RT, but this is not true for a cohort of patients with locally advanced lung cancer receiving systemic doses of chemotherapy.⁹ Such changes can be dealt by adaptive RT, whereby frequent three-dimensional (3D) imaging of lung tumour during the course of RT to detect meaningful tumour regression and applying replanning strategies to the regressed tumour volume for dose escalation and effective tumour control.¹⁰ The optimal dose fractionation scheme for combined modality therapy in the context of Stage III non-small-cell lung cancer (NSCLC) is uncertain despite the results from the Radiation Therapy Oncology Group 0617 randomized controlled trial.¹¹ This trial has been criticized for reasons such as fewer patients on the high-dose arm completed consolidation chemotherapy, high-dose radiation given during 7.5 weeks allowed tumour repopulation to occur, treatment toxicity in the high-dose setting may have prompted inappropriately tight radiation fields, high-dose radiation was associated with a higher heart dose and that attributions of cause of death were inaccurate. Additionally, a comparative effectiveness investigation compared survival of a large database of patients treated with standard dose radiation therapy vs dose-escalated (intermediate doses between the Radiation Therapy Oncology Group 0617 treatment arms of 60 and 74 Gy) radiation therapy. Although no significant overall survival benefits were found with intermediate dose escalation, the survival curves seemed to separate after 15 months, and therefore, the authors were of the opinion that a small overall survival improvement associated with intermediate dose escalation could not be excluded.¹²

In developing countries, lung cancers usually present in advanced or metastatic stage.¹³ RT departments in such countries may not have the luxury of state-of-art facilities for adaptive RT.¹⁴ Can such centres adopt simple strategies for effective dose escalation beyond 45 Gy? We, therefore, designed a prospective planning study to assess the impact of tumour regression in the fifth week of chemoradiotherapy with an aim to adapt RT plan after 45 Gy for effective dose escalation without organ motion management and image guidance.

METHODS AND MATERIALS

Patient selection

20 patients of locally advanced NSCLC suitable for radical RT with conventional fractionation were selected for this planning study. All patients had inoperable disease and had identifiable pre-treatment gross tumour volume (GTV) on CT; could undergo systemic doses of either sequential chemotherapy followed by RT (SEQ, $n = 10$) or concomitant chemoradiotherapy (CONC, $n = 10$) as definitive treatment; and were scheduled to receive a radical dose of 60 Gy using standard fractionation. This study involved evaluation of tumour regression at 45 Gy by a repeat CT scan for feasibility of adaptive RT and dose escalation in patients who showed at least 20% regression of tumour volume.

Imaging, image segmentation and treatment planning

For radiation treatment planning purpose, a spiral CT scan was performed (CT_{sim}). The patients were scanned in the supine position on a 40-slice CT scanner (Somatom® Sensation Open;

Siemens, Erlangen, Germany). Immobilization was performed using an adjustable wing board with T-bar for hand support. Intravenous contrast was administered. The scans were acquired with 3-mm slice thickness and pitch 1. Image segmentation and treatment planning were performed on a computerized treatment planning system (Eclipse™ v. 8.6.17; Varian Medical Systems, Palo Alto, CA). Primary GTV (GTV_P) and gross nodal volume (GTV_N) were delineated separately and then combined by a Boolean operation to form a combined GTV. A 5-mm margin expansion to this target volume was given to form the clinical target volume and a further 1-cm expansion to this in all directions to account for setup errors and motion formed the PTV (PTV_{sim}) (except in middle and lower lobe tumours where craniocaudal expansion was 1.5 cm). The spinal cord (3 mm around spinal cord) and whole lung (obtained by Boolean operation for the right and left lung from which PTV was subtracted) were delineated as per the standard guidelines. The outer wall of the oesophagus was delineated from the thoracic inlet to the gastro-oesophageal junction. A second spiral CT scan (CT_{45Gy}) was performed in the fifth week of RT at completion of 45 Gy. Similar target volumes were drawn on the spiral CT_{45Gy} to derive GTV_P45, GTV_N45 and PTV_45.

For those who achieved >20% regression of GTV_P in CT_{45Gy} ($n = 10$), the effect of tumour regression on target coverage indices and the dose to organs at risk (OARs) were evaluated by a second treatment plan. The RT treatment plan consisted of 3–4 fields of 6-MV photons to deliver 60 Gy using 3D conformal RT (3D-CRT) techniques. No intensity-modulated RT plans were used because of lack of facility for addressing organ motion. All initial treatment plans (Plan 1: single-phase plan) aimed to achieve the International Commission on Radiation Units and Measurements (ICRU) objectives by having the 95% isodose volume (at a minimum) conform as tightly as possible to the PTV while respecting the dose constraints to the OARs.¹⁵ Dose constraints for the lung were percentage of lung volume outside the PTV scheduled to receive 20 Gy was limited to <37% ($V_{20} < 37\%$), mean lung dose <21 Gy (because in large tumours, quite often it is not possible to keep the mean lung dose <20 Gy), the maximum spinal cord dose was limited to 50 Gy, oesophagus V_{50} was limited to <40% and mean oesophagus dose was limited to <34 Gy. A second plan (Plan 2: double-phase plan) was derived for each patient which was the sum of two plans (Plan 2a with PTV_{sim} upto 45 Gy and Plan 2b with an additional dose of 15 Gy to PTV_45).

Comparative analysis

Tumour regression

Both the image sets were spatially co-registered by rigid registration (CT_{sim} data with the CT_{45Gy}) for evaluation of tumour regression. The mean volume of GTV_P and GTV_N in both CONC and SEQ arms before RT and at 45 Gy were tabulated and evaluated for statistical significance using *t*-test.

Adaptive planning

The effect of Plan 2 on target coverage indices such as the coverage index (CI), which is the ratio of 95% isodose volume covering PTV to PTV volume; external volume index (EI),

which is the ratio of difference of 95% isodose volume received by the body and PTV to the volume of PTV; and doses to the OARs (lung, oesophagus and spinal cord) were computed for 10 patients who showed marked regression ($>20\%$). It was intended to keep the CI close to but >1 and EI not >2 . For both the plans, lung dose parameters such as mean lung dose (MLD), V_{20} and V_5 to the whole lung and ipsilateral lung (MLD_{WL}, V_{20WL} and V_{5WL} ; MLD_{IL}, V_{20IL} and V_{5IL}); mean dose to the oesophagus and $V_{50\text{oesophagus}}$; and the maximum spinal cord doses were computed and evaluated.

Dose escalation

Both the plans in the above 10 patients were evaluated for feasibility of dose escalation upto a maximum of 90 Gy, keeping the limit of OARs tolerance <50 Gy (maximum spinal cord dose), <21 Gy (mean lung dose) and $<37\%$ (V_{20WL}).

RESULTS

Volumetric analysis

Patient characteristics are listed in Table 1. The mean ($\pm$ standard deviation) volume of GTV_P, GTV_N and PTV_{sim} in the CONC arm before the start of RT was 112.63 cm³ (± 64.3), 13.1 cm³ (± 9.4) and 567 cm³ (± 219) and that of the SEQ arm was 67.85 cm³ (± 49.4), 43.2 cm³ (± 31.2) and 446.2 cm³ (± 293), respectively. At 45 Gy, the mean GTV_P45, GTV_N45 and PTV_45 in the CONC arm was 39.5 cm³ (± 18.7), 11.0 cm³ (± 9.3) and 319.66 (± 166.4) cm³ and that of the SEQ arm was 39.5 (± 47.9) cm³, 15.3 (± 7.9) cm³ and 320.4 (± 187.2) cm³, respectively. The mean GTV_P, GTV_N and PTV reduction in the CONC arm was 73.05 (64.8%) cm³, 2.07 (15.7%) cm³ and 248 (43.7%) cm³ and that of the SEQ arm was 28.31 (41.7%) cm³, 27.9 (64.58%) cm³ and 125.8 (28.2%) cm³, respectively. The difference in GTV_P in the CONC arm as compared with the SEQ arm was significant ($p = 0.02$), resulting in a significant PTV difference between the two arms ($p = 0.04$) (Figure 1). There was no statistically significant difference ($p = 0.28$) in the regression of GTV_N between the two arms (Table 2).

Anatomical changes

At 45 Gy, the mean increase in the lung volume was 4% (range 13.2–25.4%). There was the appearance of cavitation within the mass in 2/10 patients, decrease in cavitation in 2/10 patients, the appearance of paraseptal bullae in 3/10 patients, regression of infiltrative lesions beyond GTV_P in 1 patient and no appreciable anatomical changes in 2 patients. No patient had atelectasis prior to treatment or developed pleural effusion on treatment.

Adaptive planning

With the adaptive plan, the mean CI improved from 0.96 (± 0.14) to 1.29 (± 0.36), but the mean EI changed from 1.39 (± 0.60) to 1.41 (± 0.56) only. The reduction in MLD_{WL} was 10.6% [17.1 Gy (± 8.06) to 14.3 Gy (± 3.4)], V_{20WL} 1.2% [27.8 (± 9.9) to 27.25 (± 9.6)], V_{5WL} 1.3% [46.1 (± 17.5) to 45.7 (± 17.8)], MLD_{IL} 6.6% [28.1 (± 7.4) to 25.8 (± 5.6)], V_{20IL} 1.5% [53.08 (± 15.6) to 51.4 (± 13.6)] and V_{5IL} 2.3% [64.8 (± 16.8) to 63.03 (± 15.9)]; the mean oesophagus dose was 7% [25.7 (± 5.4) to 24.07 (± 6.2)], $V_{50\text{oesophagus}}$ 31% [26.6 (± 14.4) to 19.0 (± 15.8)] and maximum cord dose 0.35% [42.3 (± 9.6) to 41.9 (± 9.3)] (Table 3, Figure 2a–e). Reduction in MLD and $V_{50\text{oesophagus}}$ was observed in 7/10 (70%) and 8/10 patients (80%), respectively.

Dose escalation

With CT_{sim}, dose escalation beyond 60 Gy was possible in only 3/10 patients (upto 73.8, 75.6 and 90 Gy) (Table 4). No organ was dose limiting for these three patients, and all had tumour in the upper lobe, had GTV_P ranging from 15.86 to 107 cm³ and PTV reduction ranging from 20.7% to 36.5%. In further 4 patients [where dose limiting organs on CT_{sim} were the lung ($n = 1$) and spinal cord ($n = 4$)], dose escalation was possible with CT_{45Gy}. Among these, three patients had upper lobe tumour (GTV_P ranging from 58.9 to 86.7 cm³, PTV reduction ranging from 23.7% to 55%) and one had lower lobe tumour (GTV_P 44.9 cm³, PTV reduction 68.9%). The mean dose escalation that could be achieved beyond 60 Gy was 22.44 Gy (range 1.8–30.6 Gy) (Figure 2). In the remaining 3/10 patients, dose

Table 1. Patient characteristics

Patient no.	TNM stage	Lobe	Treatment	GTV_sim	GTV_45 Gy	PTV_sim	PTV_45 Gy
1	T3N1M0	UL	SEQ-RT	73.88	32.14	282.90	215.73
2	T3N2M0	LL	SEQ-RT	37.80	23.14	707.55	520.76
3	T3N3M0	UL	SEQ-RT	15.86	13.15	263.09	263.00
4	T4N1M0	UL	SEQ-RT	86.75	61.47	420.00	437.00
5	T4N2M0	UL	CONC_RT	58.92	17.56	597.62	268.61
6	T3N1M0	LL	CONC-RT	97.13	44.60	642.38	335.57
7	T4N0M0	UL	CONC-RT	98.56	47.86	532.00	337.00
8	T2N1M0	LL	CONC-RT	44.90	4.69	289.18	81.69
9	T4N1M0	UL	CONC-RT	107.95	64.73	515.44	377.77
10	T3N3M0	UL	CONC-RT	116.20	51.00	550.81	406.20

CONC_RT, concurrent chemoradiotherapy; GTV_45 Gy, gross target volume in cubic centimetres at 45 Gy; GTV_sim, gross target volume in cubic centimetres at simulation; LL, lower lobe; PTV_45 Gy, planning target volume in cubic centimetres at 45 Gy; PTV_sim, planning target volume in cubic centimetres at simulation; SEQ-RT, neoadjuvant chemoradiotherapy; UL, upper lobe.

Figure 1. Representation of tumour volume before radiotherapy (RT) and at the fifth week of RT in the concurrent arm, with primary gross tumour volume (GTV_P) of 216.65 (a) and 57.0 cm³ (b), and in the sequential arm, with GTV_P of 130.05 (c) and 57.4 cm³ (d).

escalation was not possible beyond 55 Gy even with CT_{45Gy}. The dose limiting organs in these three patients were the lung ($n = 1$) and spinal cord ($n = 3$), and the site of the tumour was upper lobe in one and lower lobe in two. Meaningful dose escalation was not possible with CT_{sim} in all lower lobe tumours ($n = 3$) but with CT_{45Gy}, it was possible in one.

DISCUSSION

In this study, we demonstrated that all primary lung tumours regress significantly during the course of radical RT. >30% regression was detected in 75% of the patients and >60%

tumour regression in 35% of patients. The mean tumour shrinkage of 35% measured by CT is in agreement with the findings from other groups.^{16,17} Kupelian *et al*¹⁶ reported 0.6–2.6% regression rate per day on serial megavoltage images of patients treated by 3D-CRT in 10 patients with NSCLC with a median tumour volume of 20 cm³ and overall tumour volume <100 cm³ in majority. Siker *et al*¹⁷ evaluated tumour regression with megavoltage scans in a heterogeneous group of early and advanced NSCLC and observed 25% regression in 40% of patients treated with intensity-modulated RT. In both the above studies, patients did not receive chemotherapy.

Table 2. Summary of tumour regression

Parameter	Concurrent chemoradiotherapy, cm ³ (%)	Sequential chemoradiotherapy, cm ³ (%)	<i>p</i> -value
GTV_P	73.05 (64.8)	28.31 (41)	0.02
GTV_N	2.07 (15.7)	27.9 (64.5)	0.28
PTV	248 (43.7)	125 (28.2)	0.04
T size, cm	8.2	7	0.07

GTV_N, gross target volume of nodes; GTV_P, gross target volume of primary; PTV, planning target volume; T size, tumour length in centimetres in the craniocaudal axis.

Table 3. Change in conformity index and dosimetric parameters with adaptive plan

Parameter	Single-phase plan	Adaptive plan
Mean CI	0.96	1.29
Mean EI	1.39	1.41
MLD _{WL}	17.5	14.3
V _{20WL}	27.8	27.25
V _{5WL}	46.1	45.7
MLD _{20IL}	28.1	25.8
V _{20IL}	53.08	51.4
V _{5IL}	64.8	63.03
Mean oesophagus dose	25.7	24.07
V _{50oesophagus}	26.6	19
Maximum spinal cord dose	42.3	41.9

CI, coverage index; EI, external volume index; MLD_{IL}, mean lung dose ipsilateral lung; MLD_{WL}, mean lung dose whole lung; V_{5IL}, volume of ipsilateral lung receiving 5 Gy; V_{5WL}, volume of whole lung receiving 5 Gy; V_{20IL}, volume of ipsilateral lung receiving 20 Gy; V_{20WL}, volume of whole lung receiving 20 Gy; V_{50oesophagus}, volume of oesophagus receiving 50 Gy.

We found significant differences in tumour regression between CONC and SEQ which was also observed by Bral.¹⁸ Guckenberger¹⁹ reported 49% regression with concurrent chemoradiotherapy.

To minimize variations in setup, all scans were co-registered to the planning CT in our study. Interobserver variability was minimized by the use of a single observer. However, it is acknowledged that intraobserver variation may still occur. We could not account for respiratory motion due to the non-availability of facilities for addressing organ motion in our centre at the time of this study. Breath-hold techniques were not evaluated due to logistic reasons. The image quality of cone beam CT is inferior to diagnostic scans. Hence, we used diagnostic CT scans in our study. We performed a repeat CT scan in the fifth week because studies evaluating tumour regression at the third week have found insignificant tumour regression (<30%), and performing it later will have no impact on adaptive plans.^{20,21}

With an adaptive 3D-CRT plan without organ motion management and image guidance, better conformality could be achieved resulting in a significant decrease in dose to the OARs, *i.e.* mean lung dose decreased by 10.6% and V_{50oesophagus} by 31%. Incorporation of image guidance and organ motion management with 4D off-line adaptive plan and 4D online adaptive plan techniques, respectively, resulted in reduced mean lung doses of 26% and 31%.^{21,22} Guckenberger¹⁹ reported 5.0%, 5.6% and 7.9% reduction in the mean lung dose with single-plan adaptation at the third and fifth weeks, and double-plan adaptation at the third and fifth weeks, respectively. Woodford et al²⁰ observed 38% mean GTV changes over 30 fractions (range 12 to -87%) and a potential for plan adaptation was found for only 3/17 patients (17%) undergoing RT after neoadjuvant chemotherapy.

In our study, we aimed to test the hypothesis that an additional CT scan in the fifth week of RT would facilitate adaptive dose escalation due to tumour shrinkage. The tested shrinking field strategy in our study was simulated by the concern that treatment volume reduction at an early point of time may result in geographic miss.¹⁶ We therefore aimed to deliver a dose of 45 Gy to the initial target volume (which can take care of microscopic disease), and a reduction in treatment volume was tested thereafter. Our data on 10 patients with locoregionally advanced NSCLC indicate that appropriate doses (60 Gy) can be delivered with planning CT scan in only 30% of patients. With a repeat CT scan at 45 Gy, there is mean reduction in PTV of 39%, which allows meaningful dose escalation in 40% of patients, predominantly in those with upper lobe tumours. Studies which evaluated adaptation of treatment plan at the third and fifth weeks to the residual macroscopic tumour reported an escalation of the irradiation dose from 67 to 74 Gy with large interpatient variability.²³

The role of fluorine-18 fludeoxyglucose positron emission tomography (PET) scan has been reported to have superior sensitivity and specificity (64% and 74%) as compared with CT scan in tumour detection and alteration of tumour staging.^{24,25} The incorporation of PET alters the treatment volumes in 58% of patients due to either upstaging (identification of additional regional or parenchymal disease and preventing geographic miss) or downstaging (in cases of atelectasis which decreases the unnecessary inclusion of normal lung tissue in the GTV).²⁶ Studies evaluating tumour regression with PET found 20% regression in target volume with SEQ followed by RT to a dose of 66 Gy. Adaptation of RT plans to the residual metabolic volume resulted in an 8% increase in tumour control probability.¹⁸ Feng et al²⁷ applied single-plan adaptation to the residual fluorine-18 fludeoxyglucose PET positive volume and found a 10% decrease in the lung normal

Figure 2. (a) Dose colour wash showing 95% planning target volume (PTV) coverage of single-phase plan; prescribed dose of 59.4 Gy [primary gross tumour volume (GTV_P) volume 58 cm³]. (b) Dose colour wash showing 95% PTV coverage of double-phase plan (composite plan), after 45 Gy tumour regression (GTV_45 volume 17.5 cm³), dose escalation possible up to 90 Gy. (c) The dose-volume histogram (DVH) of single-phase plan; prescribed dose 59.4 Gy, PTV_{sim} is the PTV at simulation; whole lung V₂₀ is the volume of whole lung receiving dose of 20 Gy or more; the mean lung dose was 16 Gy; and maximum dose to the spinal cord (D_{max}) was 45.3 Gy. (d) The DVH of composite plan of double-phase plan; prescribed dose was 45 + 45 Gy = 90 Gy; PTV₄₅ is the PTV after tumour regression at 45 Gy, the mean lung dose was 21.7 Gy and D_{max} was 47.9 Gy.

tissue complication probability, and dose escalation to >80 Gy was achieved in five out of six patients. Adaptation of RT to a repeat CT scan had the potential to increase tumour control probability by >40% compared with RT planning without adaptive RT.

Current treatment guidelines advocate a dose of 60 Gy for optimal local control in locally advanced NSCLC.²⁸ This is possible in 80% of patients with the use of a single repeat planning scan at 45 Gy without the need of image guidance. This simple technique can be easily implemented in a resource-constrained setup. Only 20% of patients and perhaps those with lower lobe tumours would require image-guided adaptive RT for delivering 60 Gy. A prospective study with this strategy in a large number

of patients is needed to validate these results with local control rates.

CONCLUSIONS

The results of this study have demonstrated 35% mean reduction in tumour volume at 45 Gy with chemoradiation. Tumour regression is higher with CONC than with SEQ. A repeat scan at 45 Gy seems to be adequate for delivering 60 Gy in 80% of patients. Adaptive planning leads to an improvement in conformality, reduction in doses to OARs and dose escalation in 50% of patients. This simple strategy can be widely adapted in resource-constrained RT setups for delivering adequate doses for effective local control.

Table 4. Summary of dose escalation

Patient no.	Lobe	Plan	Maximum spinal cord dose	Mean lung dose	V_{20} whole lung	Dose escalation to PTV_sim	Dose limiting organ (Plan I)	Dose escalation to PTV_45 Gy	Dose limiting organ (Plan II)	PTV reduction (%)
1	LL	I	55.8	20.7	37.2	No	Lung, spinal cord	No	Lung	47
		II	45 + 10.8	17.9	36.2					
2	UL	I	90	18.48	20.74	Yes	–	Yes	–	36.5
		II	45 + 45	17.26	21.02					
3	UL	I	66	20.6	36.2	No	Lung	Yes	–	23.7
		II	45 + 45	19.42	27.91					
4	LL	I	59.4	13.8	22.7	No	Spinal cord	Yes	–	68.9
		II	45 + 45	19.42	27.91					
5	UL	I	75.6	19.9	28.25	Yes	–	Yes	–	26.7
		II	45 + 32.4	20.36	28.92					
6	LL	I	50.4	27.5	36	No	Spinal cord	No	Spinal cord	26.39
		II	45 + 5.4	28.3	37.6					
7	UL	I	73.8	20.7	34.8	Yes	–	No	Spinal cord	20.7
		II	45 + 28.8	19.7	33.4					
8	UL	I	50.4	11.99	23.66	No	Spinal cord	Yes	–	27
		II	45 + 45	18.44	23.87					
9	UL	I	64.8	18.11	28.75	No	Spinal cord	Yes	–	55.05
		II	45 + 45	21	32.22					
10	UL	I	59.4	7.1	10.2	No	Spinal cord	No	Spinal cord	26.25
		II	45 + 14.4	7.1	23.6					

LL, lower lobe; PTV_sim, planning target volume in cubic centimetres at simulation; PTV_45 Gy, planning target volume in cubic centimetres at 45 Gy; plan I, plan with CT_sim; plan II, plan with CT_45; UL, upper lobe.

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