The Influence of Lobe-based Radiotherapy Plan Optimization Method on Different Lymph Node Irradiation Schemes for Operable LA-NSCLC Patients

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Abstract

Purpose Various target volume delineation schemes differ greatly for stage IIIa NSCLC radiotherapy. Although tightened target volume may give patients the opportunity to receive radiotherapy, it is not absolutely safe to narrow the irradiation area. For IIIa NSCLC patients who will undergo lobectomy, a new neoadjuvant radiotherapy based on sparing preserved lung lobes may improve the dose distribution of the preserved lobe, and provide freedom for physicians in optimizing treatment strategies. Materials and methods Computed tomography imaging data of 20 IIIA- p N2 NSCLC patients were used to produce conventional IMRT(IMRT) and Preserved Lobe based IMRT(P-IMRT) plan respectively according to two different target volume delineation schemes(OPT1 and OPT2). Dose results of target coverage, Total lung, Ipsilateral lung, Preserved Total Lung, Preserved Ipsilateral Lung, Contralateral Lung, Resected Lobe and other OARs in the four groups were analyzed. Results All plans met dose limits. Lobe-based IMRT significantly reduce the irradiated dose of Lung lobes, especially Preserved Total Lung and Preserved Ipsilateral Lung, for both delineation schemes. Mean Dose of Preserved Total Lung decreased from 819.93 cGy to 690.98 cGy (OPT1) and 542.47 cGy to 469.62 cGy (OPT2), Mean Dose of Preserved Ipsilateral Lung decreased from 1282.95 cGy to 1068.55 cGy (OPT1) and 955.83 cGy to 795.97 cGy (OPT2), respectively. While the dose indices of Resected Lobe increased slightly for only about 1%. Comparing the four groups of plans, it's more effective in optimizing the dose of lung lobes by this method for the delineation scheme with a large target volume. The lung dose metrics in P-IMRTOPT1 can be reduced to a value very close to that in IMRTOPT2, and some values are even lower than that in IMRTOPT2. Conclusion For IIIA-N2 NSCLC patients who will undergo lobectomy, no matter which target delineation scheme is chosen, preoperative neoadjuvant radiotherapy using a lobe -based planning can significantly reduce the radiation dose that preserves the lobes. Especially for the large-scale lymph node irradiation scheme, this method can also reduce the dose of preserved lung lobe to a level that is comparable to or lower than that of the conventional IMRT small-area lymph node irradiation scheme, and reduce the obstacles for clinicians in selecting the optimal individualized scheme.

Introduction

Radiotherapy is one of the standard treatments for LA-NSCLC locally advanced non-small cell lung cancer, but the outcome is still unsatisfactory. Local recurrence and distant metastasis are the main causes of failure. For locally advanced NSCLC cases, the target area contains primary lesions and metastatic lymph nodes, and the irradiation range is too large, which will cause excessive irradiation of normal lung, heart, esophagus, spinal cord and other important tissues and organs. At the same time, the dose of normal tissues and organs is limited, and it is difficult to increase the dose of tumors.

At present, to balance target area control and reduction of normal tissue side effects, clinicians prefer Involved field irradiation when designing target area delineation scheme, which is more effective and safer than Elective Node Irradiation (ENI). RTOG9311 conducted a dose escalation study of 3D CRT for non-operable NSCLC. Without selective mediastinal lymph node irradiation, the dose of radiotherapy

could be safely raised to 77.4 Gy (25% < V20 < 36%) or 83.8 Gy (V20 < 25%). The 2-year local control rate was 50% − 78%.

ESTRO ACROP guidelines [1] provides two choices in defining the target area of locally advanced NSCLC: 1 lymph node stations: inclusion of the whole pathologically affected lymph node station (Fig. 2) including at least a 5–8 mm margin around the GTV to ensure that the recurrence rate of the mediastinum in the field is minimized; 2 geometric expansion, which ensures the target dose and reduces the normal tissue irradiation through such an IFI target delineation strategy.

Literatures [2,3] reported that nearly 20% patients diagnosed as clinical N0 and N1 were upgraded to N2 stage after mediastinal lymph node dissection,and 20.4% patients diagnosed as pathological of N0 stage were confirmed to occur micro-metastasis after immune-histochemical staining [4]. In previous studies[5] 3D-CRT technology was used, although some adjacent lymph nodes were not included in the target area, they still received a slightly lower radiation dose than the target area, thus ensuring a lower recurrence rate of lymph nodes in the field. But now IMRT and VMAT technology are widely developed, which can achieve more conformal dose distribution and more. A steep dose drop, although it allows sufficient dose coverage of the target area and reduces the dose of surrounding normal tissues, may result in a lower exposure dose to out-field lymph nodes than in the past. This requires more careful selection of CTV_{ln} in LA-NSCLC cases, so as to avoid increasing the recurrence rate in the field.

Previous studies based on lobe protection to reduce preoperative neoadjuvant radiotherapy dose for IIIA-N2 NSCLS showed that this method could reduce the dose of preserved lobes while ensuring target dose coverage, and increase only about 1% for V_5-V_{20} in lobe that will be resected.

In this paper, 20 cases of neoadjuvant radiotherapy of IIIA-N2 NSCLC were studied. The design method of radiotherapy planning based on preserving lung lobe protection was applied to two different target delineation schemes. The effect of the two schemes on target dose coverage and normal lung tissue irradiation dose was studied. Whether this method can be used to control lung irradiation dose while giving clinicians free of choice for appropriate target delineation strategy.

Materials And Methods

Case information

Twenty patients with lung cancer who underwent surgical lobectomy in our institution from February 2017 to November 2017 were retrospectively analyzed. All patients were pathologically proved to be stage IIIA N2 non-small cell lung cancer. The case information was shown in Table 1.

Table 1
Patient characteristics

	n	%
Patients	20	
Gender		
Male	12	60
Female	8	40
Tumor Location		
LUL	7	35
LLL	2	10
RUL	5	25
RML/RLL	6	30
PTV-OPT1 (cm3)		
Mean ± SD	444.25 ± 152.44	
Median (range)	420.07(236.7-862.2)	
PTV-OPT2 (cm3)		
Mean ± SD	252.56 ± 138.97	
Median (range)	240.50(68.3-627.05)	

Abbreviations: LUL = Left Upper Lobe; LLL = Left Lower Lobe; RUL = Right Upper Lobe; RML = Right Medial Lobe; RLL = Right Lower Lobe.

ROI Contour

Preoperative CT of 20 patients were transfered to Pinnacle^3 9.10 through PACS system. Left Lung, Right Lung, Heart, Spinal Cord were automatic contoured and can be adjusted manually if necessary. An experienced radiotherapist delineates the PTV, esophagus and lung lobe(LUL/LLL/RUL/RML/RLL) to be resected for surgery, which is then approved by the superior physician.

Target Volumes:

Two sets of target areas are delineated for each case according to two target delineation strategies. Figure 1 shows the PTV delineated in one case according to these two schemes. The specific defining rules are as follows:

Target Option 1:

GTV-OPT1: Contains gross tumor and metastatic lymph nodes; CTV-OPT1: GTV-OPT1 + preventive lymph node areas (right lung lesions preventive lymph nodes are 2R, 4R, 7, 10R, left lung lesions preventive lymph nodes are 2, 4, 5, 7, 10L; CTV-OPT1 expands 0.6 cm margin to form PTV-OPT1. This method originated from previous studies of our center [6]

Target Option 2:

GTV-OPT1: Contains gross tumor and metastatic lymph nodes; CTV-OPT2: GTV-OPT2 expands 5 mm margin to form CTV-OPT2; PTV-OPT2: CTV-OPT2 expands 6 mm margin to form PTV-OPT2.

For all plans, 95% of the volume of PTV is required to reach a prescription dose of 4000 cGy.

Treatment planning

For each case, two target delineation schemes were designed. And then two plans were optimized with 6 MV photon beams for a Elekta Synergy linear accelerator (Elekta Ltd, Crawley, UK) for each scheme. The prescription dose was 40 Gy in 20 fractions (daily dose = 2 Gy). Plans were normalized to deliver prescription dose to 95% of the PTV. IMRT plan based on conventional dose parameters and P-IMRT plan based on lobe protection optimization method. Re-optimized plan and conventional IMRT plan have the same beam directions, target and other normal tissue dose constraints. The P-IMRT plan is obtained by replacing the original total-lung and R/L lung parameters with the dose parameters of lung lobes that will be retained after operation.

Dose Comparison

Dose distribution of planning target volume (PTV) and organs at risk (OARs) was assessed by dose-volume histogram (DVH). Target area evaluation parameters included: Conformity Index(CI) [7] CI = $V_{T,ref}/V_T \times V_{T,ref}/V_{ref}$, $V_{T,ref}$ is the volume of PTV receiving prescription dose, V_T is the volume of PTV, V_{ref} is the volume of all regions receiving prescription dose. The ideal value is 1 and it decreases as the dose distribution becomes less conformal. Homogeneity index(HI) [8]: HI=$(D_2-D_{98})/D_p$*100%,where D_2 and D_{98} are the minimum dose in 2% and 98% of the target volume and D_p is the prescribed dose. The ideal value is Zero and increase as homogeneity decreases.

Dose metrics for lung lobes: V_5, V_{10}, V_{13}, V_{15}, V_{20} and Mean Dose of Ipsilateral Lung-GTV, Contralateral Lung, Total Lung-GTV, Resected Lobe-GTV, Preserved Ipsilateral Lung-GTV and Preserved Total Lung-GTV.

Other OARs: Spinal Cord D_{max}, Esophagus D_{max}, Heart D_{mean}, Heart V_{30} and Body D_{mean}.

Statistical analysis:

Summary statistics for variables were expressed as mean ± standard deviation (SD). Differences of two groups in means for continuous variables were compared using Student's t-test. Statistical significance was defined as $P < 0.05$ using a 2-tailed test. All analyses were performed using SPSS Statistics v22.0 (IBM Corp, Armonk, NY, USA).

Results

Figure 2 shows the volume change of PTV in each case based on two scenarios. The average volume of PTV-OPT1 is 444.25 ± 152.44 cm^3, while the average volume of PTV-OPT2 is only 252.56 ± 138.97 cm^3. This huge difference in PTV volume will greatly affect the difficulty of planning and the irradiated dose of OARs.

PTV

Table 2 showed the difference of dose in four groups of PTV. All four groups of plans met their prescription dose requirements. For PTV-OPT1, CI and HI of conventional IMRT plan were 0.67 ± 0.08 and 0.15 ± 0.01, respectively. CI and HI of P-IMRT plan which controls preserved lung lobes dose were 0.58 ± 0.09 and 0.2 ± 0.03, respectively, with statistical difference ($p < 0.001$); for PTV-OPT2, CI and HI of conventional IMRT plan and P-IMRT plan were 0.63 ± 0.12 vs 0.59 ± 0.13 ($p = 0.056$) and 0.14 ± 0.03 vs 0.15 ± 0.04 ($p = 0.15$), there was no statistical difference. For larger, more irregular target areas with more complex relationship with surrounding normal tissues, strengthening the control of preserved lung lobes dose will have a certain impact on the conformity and homogeneity of target.

Table 2
Dosimetric comparison of PTV

	OPT1			**OPT2**		
	IMRT	P-IMRT	*p*	IMRT	P-IMRT	*p*
D_2(cGy)	4489.6 ± 37.84	4641.8 ± 100.17	.000	4458.5 ± 86.29	4495.5 ± 117.35	.160
D_{50}(cGy)	4249.1 ± 30.44	4325.2 ± 100.17	.002	4237.35 ± 56.53	4252.85 ± 68.7	.359
D_{98}(cGy)	3907.5 ± 16.13	3838.2 ± 43.08	.000	3918.05 ± 41.47	3906.6 ± 40.58	.172
CI	0.67 ± 0.08	0.58 ± 0.09	.000	0.63 ± 0.12	0.59 ± 0.13	.056
HI	0.15 ± 0.01	0.2 ± 0.03	.000	0.14 ± 0.03	0.15 ± 0.04	.150

Lung

Table 3 shows a comparison of Total Lung and Lung lobes doses in conventional IMRT and P-IMRT plans for two target delineation schemes. For PTV-OPT1, V_5-V_{20} and Mean Dose of Total Lung, Preserved Total Lung, Ipsilateral Lung, Preserved Ipsilateral Lung and Contralateral Lung all decreased, except Total lung V5, Ipsilateral Lung V5, Mean dose and Contralal Lung V5, and the dose reduction of V_{10}-V_{20} was quite significant, especially for Preserved Total Lung and Preserved Ipsilateral Lung. Preserved Total Lung V_{10} (26.07–20.99%), V_{13} (22.58–16.65%), V_{15} (20.55–14.63%) V_{20} (16.01–10.93%), Mean Dose (819.93 cGy to 690.98 cGy); Preserved Ipsilateral Lung V_{10} (43.29–34.45%), V_{13} (39.03–28.56%) V_{15} (36.24%) V_{20} (29.5–20.01%), Mean Dose (1282.95 cGy to 1068.55 cGy). For Resected Lobe, V_5 increased from75.98–78.21%, the increase range of V_{10}-V_{20} was about 1%, only V_5 and V_{10} had statistical difference.

Table 3
Dosimetric comparison of lung

		OPT1			OPT2		
		IMRT	P-IMRT	*p*	IMRT	P-IMRT	*p*
Total Lung	V_5(%)	46.3 ± 7.58	45.51 ± 9.86	0.218	35.59 ± 9.51	34.42 ± 9.99	0.074
	V_{10}(%)	33.93 ± 4	30.28 ± 4.34	< 0.001	25.59 ± 7.21	22.55 ± 5.96	< 0.001
	V_{13}(%)	30.27 ± 3.6	25.76 ± 3.22	< 0.001	22.7 ± 6.63	19.52 ± 5.02	< 0.001
	V_{15}(%)	28.08 ± 3.44	23.53 ± 2.86	< 0.001	20.92 ± 6.34	17.92 ± 4.59	< 0.001
	V_{20}(%)	23.08 ± 3.24	19.17 ± 2.56	< 0.001	16.63 ± 5.27	14.67 ± 3.85	0.002
	D_{Mean}(cGy)	1077 ± 148.19	993.51 ± 152.36	< 0.001	813.99 ± 223.11	767.44 ± 194.09	0.001
Preserved Total Lung	V_5(%)	38.64 ± 10.98	36.98 ± 13.17	0.029	27.09 ± 11.08	25.25 ± 11.57	0.024
	V_{10}(%)	26.07 ± 6.24	20.99 ± 5.95	< 0.001	17.14 ± 7.8	13.25 ± 6.22	< 0.001
	V_{13}(%)	22.58 ± 5.37	16.65 ± 4.18	< 0.001	14.51 ± 6.9	10.53 ± 4.92	< 0.001
	V_{15}(%)	20.55 ± 4.82	14.63 ± 3.52	< 0.001	12.97 ± 6.38	9.2 ± 4.36	< 0.001
	V_{20}(%)	16.01 ± 3.81	10.93 ± 2.63	< 0.001	9.3 ± 4.82	6.71 ± 3.47	< 0.001
	D_{Mean}(cGy)	819.93 ± 191.44	690.98 ± 180.21	< 0.001	542.47 ± 225.21	469.62 ± 194.62	< 0.001
Ipsilateral Lung	V_5(%)	66.69 ± 12.26	65.99 ± 12.89	0.083	56.71 ± 14.49	55.14 ± 13.71	0.007
	V_{10}(%)	54.58 ± 9.31	50.3 ± 7.41	< 0.001	46.34 ± 12.44	41.61 ± 9.9	< 0.001
	V_{13}(%)	50.27 ± 8.41	44.66 ± 6.18	< 0.001	42.33 ± 11.61	37.26 ± 8.76	< 0.001
	V_{15}(%)	47.46 ± 7.9	41.65 ± 5.64	< 0.001	39.62 ± 11.13	34.85 ± 8.18	< 0.001
	V_{20}(%)	40.66 ± 7.22	35.47 ± 5.17	< 0.001	33.05 ± 9.77	29.85 ± 7.09	0.004

		OPT1			OPT2		
	D_{Mean}(cGy)	2230.42 ± 2274.63	1633.55 ± 262.79	0.252	1439.35 ± 375.89	1370.3 ± 312.55	0.006
Preserved Ipsilateral Lung	V_5(%)	55.87 ± 25.05	52.79 ± 25.29	< 0.001	44.03 ± 22.74	40.37 ± 21.38	< 0.001
	V_{10}(%)	43.29 ± 17.88	34.45 ± 13.91	< 0.001	33.38 ± 17.35	25.12 ± 12.76	< 0.001
	V_{13}(%)	39.03 ± 15.39	28.56 ± 10.73	< 0.001	29.33 ± 15.22	20.72 ± 10.47	< 0.001
	V_{15}(%)	36.24 ± 13.77	25.6 ± 9.4	< 0.001	26.61 ± 13.94	18.51 ± 9.54	< 0.001
	V_{20}(%)	29.5 ± 10.81	20.01 ± 7.37	< 0.001	20.15 ± 10.85	14.35 ± 8.01	< 0.001
	D_{Mean}(cGy)	1282.95 ± 453.44	1068.55 ± 396.26	< 0.001	955.83 ± 463.87	795.97 ± 382.52	< 0.001
Contralateral Lung	V_5(%)	28.14 ± 7.47	27.32 ± 9.39	0.408	17.08 ± 7.47	16.31 ± 7.18	0.507
	V_{10}(%)	15.94 ± 5.13	13.23 ± 4.29	< 0.001	7.86 ± 4.86	6.63 ± 3.93	0.009
	V_{13}(%)	13.08 ± 4.43	9.94 ± 3.29	< 0.001	6.11 ± 4.13	4.96 ± 3.16	0.005
	V_{15}(%)	11.58 ± 4.12	8.51 ± 3.02	< 0.001	5.27 ± 3.73	4.18 ± 2.79	0.005
	V_{20}(%)	8.48 ± 3.45	5.99 ± 2.58	< 0.001	3.33 ± 2.74	2.71 ± 2.17	0.018
	D_{Mean}(cGy)	542.14 ± 133.51	480.01 ± 127.61	< 0.001	312.25 ± 125.26	291.75 ± 112.93	0.050
Resected Lobe	V_5(%)	75.98 ± 13.13	78.21 ± 13.56	0.003	69.75 ± 18.21	71 ± 17.85	0.003
	V_{10}(%)	65.92 ± 13.53	67.83 ± 14.16	0.011	60.73 ± 18.18	61.12 ± 17.42	0.525
	V_{13}(%)	62.12 ± 13.61	63.23 ± 13.98	0.132	57.15 ± 17.98	57.34 ± 17.15	0.825
	V_{15}(%)	59.67 ± 13.66	60.53 ± 13.71	0.277	54.76 ± 17.79	54.9 ± 16.69	0.873
	V_{20}(%)	53.61 ± 13.92	54.37 ± 13.77	0.362	48.78 ± 17.02	49.33 ± 16.01	0.539

		OPT1			OPT2		
	D_{Mean}(cGy)	2093.73 ± 496.63	2299.85 ± 528.04	0.094	2011.29 ± 618.48	2072.32 ± 613.32	0.013

For PTV-OPT2, the situation is almost similar.

Table 4 shows the difference of dose reduction between IMRT plan and P-IMRT plan in two scenarios, and compares the dose parameters of $IMRT_{OPT1}$ and $P\text{-}IMRT_{OPT1}$ with that of $IMRT_{OPT2}$, respectively. For PTV-OPT1, V_{10}-V_{20} of preserved total lung in P-IMRT decreased by about 5%, Mean Dose decreased by 128.95 cGy, V_{10}-V_{20} of preserved ipsilateral lung decreased by 8–10%, Mean Dose decreased by 214.4 cGy; comparing to PTV-OPT2, V_{10}-V_{20} of preserved total lung in P-IMRT decreased by only 3%, Mean Dose decreased by 72.85 cGy, V_{10}-V_{20} of preserved ipsilateral lung decreased by 5%-8%, Mean Dose decreased by 159.86 cGy. Obviously, for larger and more complex target volume, it is more satisfactory to control the preserved lobes dose in order to reduce the lung dose.

Table 4
Grouped comparison of preserved total lung and preserved ipsilateral lung dose changes

		$IMRT_{OPT1}$ VS $P\text{-}IMRT_{OPT1}$)	$IMRT_{OPT2}$ VS $P\text{-}IMRT_{OPT2}$	$IMRT_{OPT1}$ VS $IMRT_{OPT2}$	$P\text{-}IMRT_{OPT1}$ VS $IMRT_{OPT2}$
Preserved Total Lung	V_5(%)	-1.66	-1.84	11.55	9.89
	V_{10}(%)	-5.08	-3.89	8.93	3.85
	V_{13}(%)	-5.93	-3.98	8.07	2.14
	V_{15}(%)	-5.92	-3.77	7.58	1.66
	V_{20}(%)	-5.08	-2.59	6.71	1.63
	D_{Mean}(cGy)	-128.95	-72.85	277.46	148.51
Preserved Ipsilateral Lung	V_5(%)	-3.08	-3.66	11.84	8.76
	V_{10}(%)	-8.84	-8.26	9.91	1.07
	V_{13}(%)	-10.47	-8.61	9.7	-0.77
	V_{15}(%)	-10.64	-8.1	9.63	-1.01
	V_{20}(%)	-9.49	-5.8	9.35	-0.14
	D_{Mean}(cGy)	-214.4	-159.86	327.12	112.72

Table 5
Dosimetric comparison of other OARs

OAR	OPT1			OPT2		
	IMRT	P-IMRT	*p*	IMRT	P-IMRT	*p*
Body D_{mean}(cGy)	676.8 ± 124.05	652.96 ± 122.85	.000	488.2 ± 145.66	480.03 ± 137.68	.072
Spinal Cord D_{max}(cGy)	3353.24 ± 112.87	3509.28 ± 135.73	.000	2901.98 ± 596.97	3045.33 ± 485.86	.026
Heart D_{mean}(cGy)	1644.11 ± 732.03	1643.77 ± 779.29	.993	1354.85 ± 855.19	1416.17 ± 918.54	.103
Heart V_{30}(%)	24.9 ± 13.83	23.78 ± 13.31	.299	17.4 ± 13.43	19.66 ± 16.27	.044
Esophagus D_{max}(cGy)	4473.54 ± 82.12	4614.77 ± 170.71	.000	4198.63 ± 583.68	4210.5 ± 598.08	.650

Comparing IMRT and P-IMRT plans of PTV-OPT1 with IMRT plans of PTV-OPT2, although the lung dose of $IMRT_{OPT1}$ is much higher than that of $IMRT_{OPT2}$, the lung dose metrics except V_5 of $P\text{-}IMRT_{OPT1}$ decreases by controlling the preserved lobes dose to comparable values in $IMRT_{OPT2}$, especially V_{13}, V_{15} and V_{20} of Preserved Ipsilateral Lung, they are even lower than those in $IMRT_{OPT2}$. Difference between those groups is shown in Fig. 3.

Other OARs

For the two scenarios, dose to some OARs in IMRT and P-IMRT plans will increase. For PTV-OPT2, there is no statistical difference except Spinal Cord D_{max} and Heart V_{30}. However, Heart V_{30} in $P\text{-}IMRT_{OPT1}$ decreased slightly, possibly because these OARs did not exceed the dose limit of OAR constraints in conventional IMRT plans, and P-IMRT plans only changed the lung dose limitations and did not further control the dose of OARs. However, the results also showed that the dose of Body D_{mean} in P-IMRT decreased for both PTV-OPT1 and PTV-OPT2. For PTV-OPT1, Body D_{mean} decreased from 676.8 ± 124.0 cGy to 652.96 ± 122.85 cGy($p < 0.001$), indicating that the overall dose of the patient outside the target volume was reduced.

Discussion

In this study, we evaluated the impact on target dose coverage and normal lung tissue by the application of lobe-preserving radiotherapy planning in two different target delineation schemes for neoadjuvant radiotherapy patients with IIIA-N2 NSCLS. The results show that this method can significantly reduce lung dose, especially the dose to preserved lung lobes after operation, without compromising target coverage.

The target volume of LA-NSCLC radiotherapy includes primary tumors and metastatic lymph nodes. When treating a large target volume, it can be challenging to deliver desired prescription dose to the target due to the need to spare organs at risk (OARs) [9]. In clinic, in order to improve loco-regional control and survival rates without increasing normal tissue toxicity, target delineation strategy was adjusted by optimizing the irradiation area of mediastinal lymph nodes and reducing the field size [10]. Although previous studies [11,12] showed that limited target volume of IFI did not increase the risk of local recurrence, randomized controlled studies showed that the prescribed dose of IFI could be escalated for a small field, with a 5-year LC rate (51%:36%, P = 0.032) and a 2-year OS rate (39.4%:25.6%, P = 0.048). The 5-year OS rate (25.1%:18.3%, P > 0.05) were better than ENI, but these studies were based on 3D-CRT technology.

With the development of technology, the performance of radiotherapy equipment has been improved continuously. The radiation delivery system has also progressed from conventional 2D-RT, 3D-CRT to IMRT. Image-guided IMRT can deliver radiation dose to target more accurately and protect normal tissue better. Dosimetric studies and clinical data of LA-NSCLC patients treated with IMRT radiotherapy have been reported [13–15]. An analysis of an RTOG 0617 study shows that IMRT was associated with lower rates of severe pneumonitis and cardiac doses, which proves the rationality of applying IMRT to LA-NSCLC, which improves target coverage while minimizing radiation to surrounding tissues [16]. However, at present, image-guided IMRT has become a conventional radiotherapy method, it remains to be seen whether highly conformal dose distribution and tightened margin may adversely affect the control of microscopic lesions of in-field lymph node stations. In addition, IMRT technology may lead to an increase in the incidence of severe and fatal RP. It is necessary to increase the dose-volume limits of low-dose lung to reduce the incidence of fatal pneumonia [17].

Our results show that, for any target delineation scheme, the doses of all lung lobes and total lung except resected lobe can be significantly reduced by changing the optimization parameters and ensuring that the target dose coverage meets the clinical requirements while keep the dose of Resected Lobe within acceptable range. However, for different target delineation schemes, the reduction range of the radiation dose of the lung lobes is different by controlling the radiation dose to the preserved lobes. For larger and more complex target volume, controlling the preserved lung lobes dose can significantly reduce the lung dose.

Moreover, by controlling the preserved lobes dose, the lung dose metrics in P-IMRT$_{OPT1}$ was reduced very close to the value in IMRT$_{OPT2}$ except V_5, especially V_{13}, V_{15} and V_{20} of Preserved Ipsilateral Lung were even lower than that in IMRT$_{OPT2}$, which made it possible for clinicians to select target delineation scheme for such beneficiary cases.

There are still some limitations in this study: the number of cases in this study is small, and no further in-depth study has been carried out. There were few studies on LA-NSCLC radiotherapy for lung lobe protection before, and there was not much experience to refer to. We are still in the exploratory stage.

Conclusion

Individualized precise radiotherapy is the future development direction. Our research results show that for IIIA-N2 NSCLC patients who are going to undergo lobectomy, no matter which target delineation scheme is selected, neoadjuvant radiotherapy based on lung lobe sparing can significantly reduce the radiation dose to the preserved lobes. Even if the scheme of large-scale lymph node irradiation is chosen, the radiation dose to the preserved lobes can be reduced to the same or even lower level as that of IMRT in small-scale lymph node irradiation, which can reduce the constraints for clinicians in selecting the optimal individualized scheme for patients.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and material

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

HG contributed to the conception of the study and performed the experiment, data analyses and wrote the manuscript.

HL performed the manually contouring of lung lobes , and was a major contributor in writing the manuscript.

XF and ZX contributed to the conception of the study and helped perform the analysis with constructive discussions.

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Figures

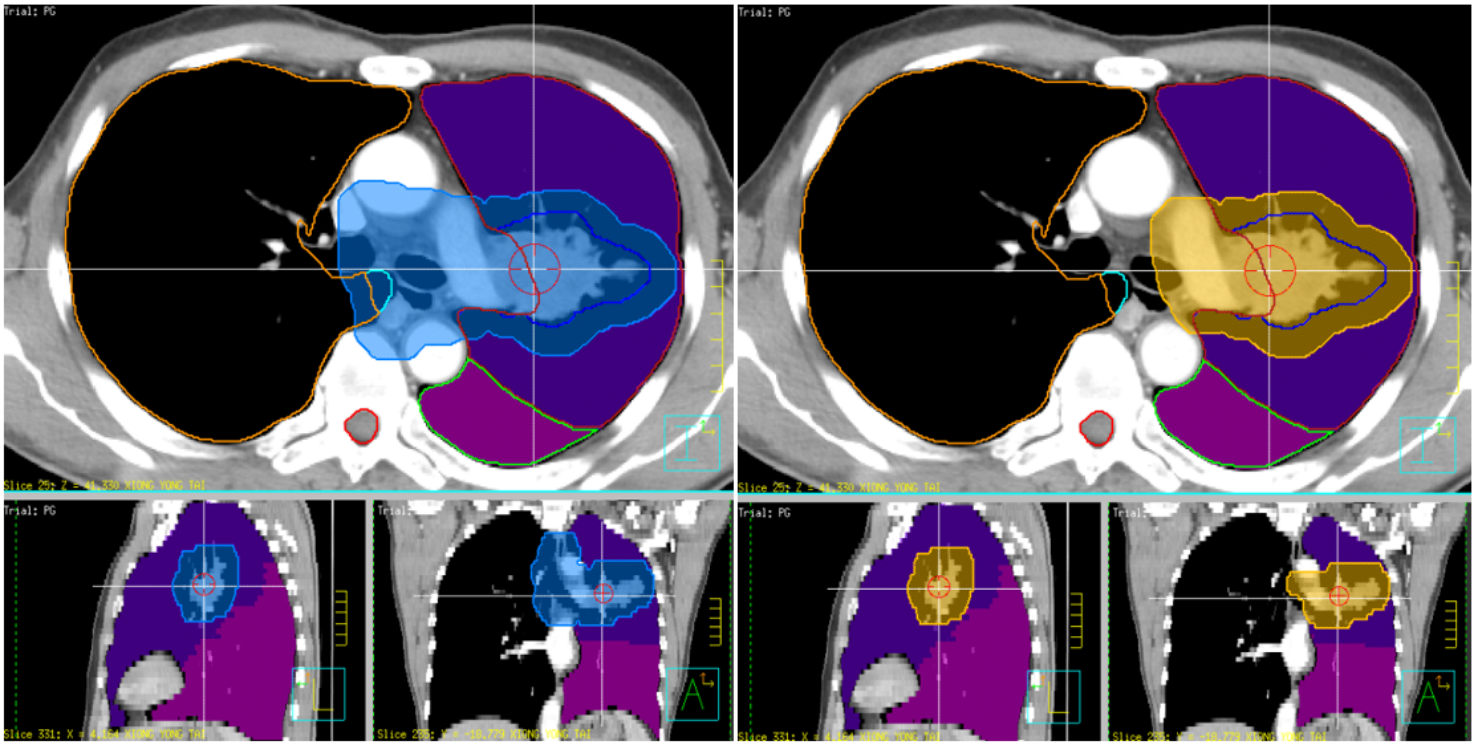

Figure 1

PTV delineated in one case according to these two schemes. Lightblue: PTV-OPT1; lightorange: PTV-OPT2; purple: Preserved ipsilateral lung; slateblue; Resected lobe

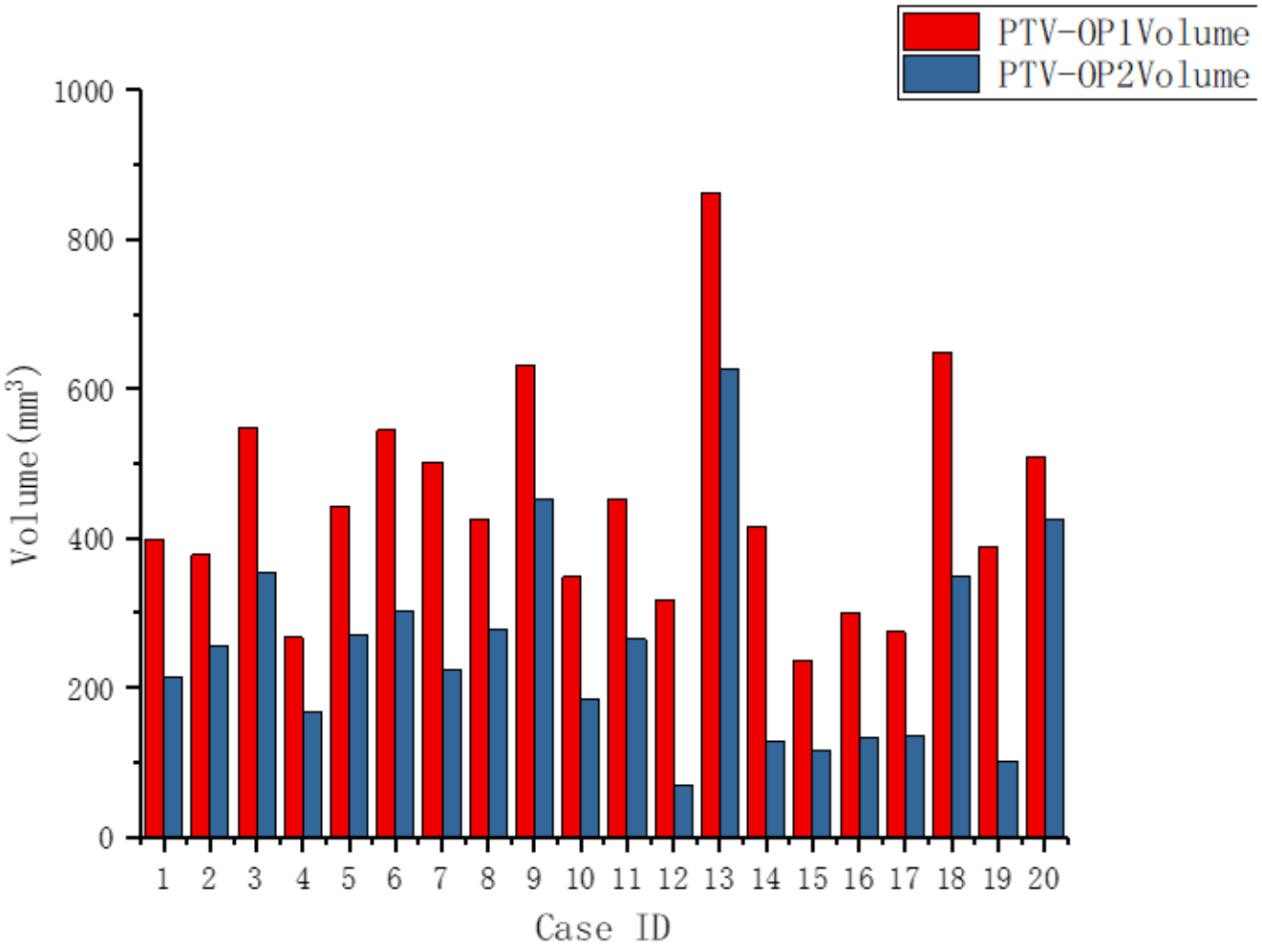

Figure 2

Target volumes comparison for 2 delineation schemes

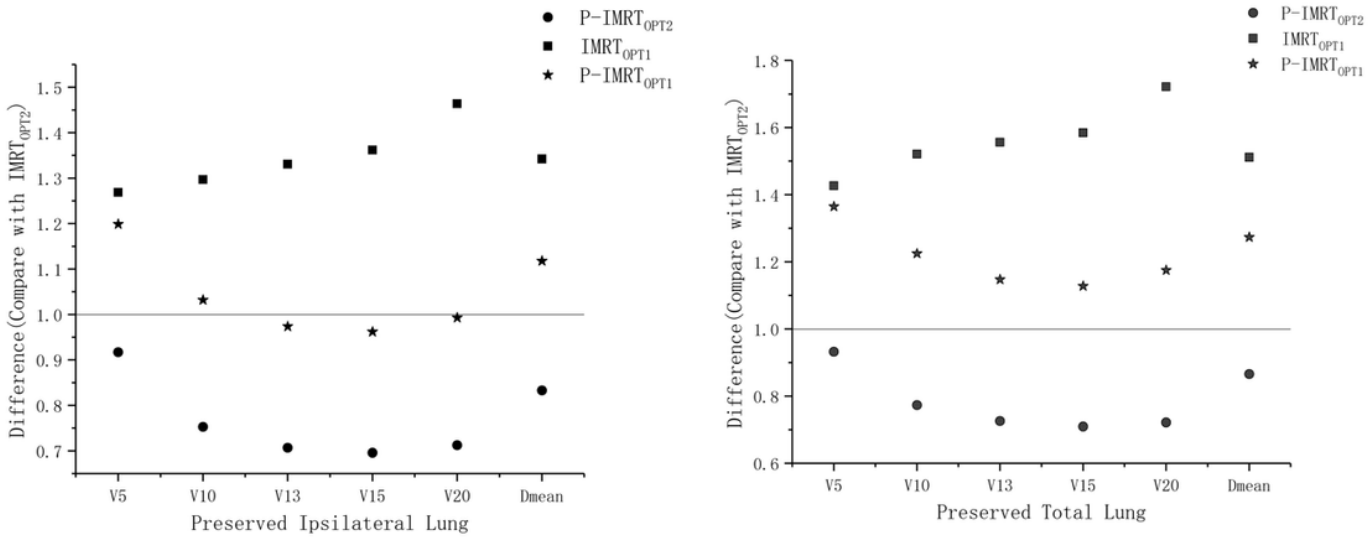

Figure 3

Difference of Preserved Total Lung and Preserved Ipsilateral Lung Dose