e-ISSN 2083–4640
ISSN 1507–1367

RESEARCH PAPER

Reports of Practical Oncology and Radiotherapy
2022, Volume 27, Number 5, pages: 897–904
DOI: 10.5603/RPOR.a2022.0106
Submitted: 16.07.2022
Accepted: 16.08.2022

Dynamic conformal arc radiotherapy for locally advanced lung cancer: a comparison with static-beam conformal radiotherapy

Masaki Goto[1], Naoko Sanuki[2, 3], Masaru Kasae[1], Ryo Terabayashi[1], Yurika Nishiwaki[1], Yuya Ogita[1], Junya Tone[1], Hidetoshi Seta[4]

[1]Department of Radiation Engineering, Mie General Medical Center, Mie General Medical Center, Hinaga, Yokkaichi-city, Mie, Japan
[2]Department of Radiation Oncology, Mie General Medical Center, Mie General Medical Center, Hinaga, Yokkaichi-city, Mie, Japan
[3]Department of Radiology, Yokkaichi Municipal Hospital, Yokkaichi Municipal Hospital, Shibata, Yokkaichi-city, Mie, Japan
[4]Department of Radiology, Mie General Medical Center, Mie General Medical Center, Hinaga, Yokkaichi-city, Mie, Japan

ABSTRACT

Background: This study investigated whether the dose distribution of lung cancer can be improved by dynamic arc conformal radiotherapy (dynamic CRT) compared with static multiple-beam radiotherapy (static CRT).

Materials and methods: A dummy study of static CRT and dynamic CRT was performed, designed to meet the predetermined dose constraints. A dose of 60 Gy in 30 fractions was administered using two dose prescription methods: dose prescribed to the isocenter (IC prescription), and dose prescribed to > 50% of the planning target volume (D50 prescription). Dose–volume parameters were compared between the plans.

Results: Among 20 patients with locally advanced lung cancer, dose conformity was significantly better with dynamic CRT than static CRT (median conformity index: 1.3 *vs.* 2.2; $p < 0.01$). As for the lung dose, compared with static CRT, dynamic CRT did not increase the percentage lung volume receiving ≥ 20 Gy (18.9% *vs.* 19.3%, $p = 0.09$). The maximum spinal cord dose was significantly reduced by dynamic CRT (static *vs.* dynamic CRT: 44.1 *vs.* 25.2 Gy, $p < 0.001$). With the change from IC to D50 prescription, the 95% isodose volume increased by 18.3 cc in static CRT and by 4.1 cc in dynamic CRT, while doses to the lung and spinal cord remained within the acceptable ranges.

Conclusion: The dynamic CRT technique showed better target coverage and lower doses to the spinal cord in exchange for increased low-dose lung area, compared with static CRT. Dynamic CRT with D50 prescription instead of prescription to the isocenter has excellent dose distribution profiles without compromising doses to organs at risk for lung cancer at favorable locations.

Key words: lung; lung neoplasms; organs at risk; radiation oncology; radiotherapy; conformal; radiotherapy planning; computer-assisted

Rep Pract Oncol Radiother 2022;27(5):897–904

Introduction

Radiation therapy is a key treatment for locally advanced non-small-cell lung cancer (NSCLC). The advantages of intensity-modulated radiotherapy (IMRT) or volumetric-modulated arc therapy (VMAT) compared with three-dimensional conformal radiation (3DCRT) have been reported

Address for correspondence: Naoko Sanuki, Department of Radiology, Yokkaichi Municipal Hospital, 2-2-37, Shibata, Yokkaichi-city, Mie 510-8567, Japan, tel: (81) 59-354-1111, fax: (81) 59-352-1565; e-mail: naokosanuki@icloud.com

for NSCLC1 [1]. Yet, these new treatment techniques have technical obstacles, and they are not available in many centers worldwide. In practice, IMRT/VMAT is restricted depending on the institution or the priority of the case, and the vast majority of patients still receive 3DCRT. It is challenging, however, to achieve a satisfactory dose distribution with 3DCRT which often utilizes multiple static beam arrangement. In this study, we investigated whether dynamic conformal arc radiation therapy (dynamic CRT) can improve dose distribution profiles compared with static multiple-beam radiation therapy (static CRT).

Materials and methods

Patient characteristics

The eligibility criteria for this study were patients with locally advanced NSCLC consecutively treated with curative chemoradiotherapy whose planning target volume (PTV) exceeded 100 cc. To include tumors from different locations, five tumors each of left, right, upper, and middle/lower leaflet origin were selected, for a total of 20 cases.

Simulation and target volume definitions

For treatment planning, all patients in the treatment position underwent slow-scan CT encompassing the entire thorax under shallow free breathing with 3 mm thickness. A board-certified radiation oncologist contoured the target on planning CT scans. The gross tumor volume (GTV) encompassed the primary tumor and involved regional lymph nodes, while the clinical target volume (CTV) comprised the GTV plus 5 mm margins. The CTV did not include prophylactic lymph nodes. The internal and set-up margins added to the CTV to create the PTV were determined arbitrarily and varied from 5 to 15 mm, depending on the tumor locations and cranio-caudal or lateral directions. Organs including the total lung, heart, esophagus, and spinal cord were delineated.

Treatment planning

The treatment plans were generated using the Eclipse® radiotherapy treatment planning system (version 13.6; Varian Medical Systems, Palo Alto, CA). Doses were calculated using the anisotropic analytical algorithm. Multi-leaf collimators were set 5 mm outside the PTV. All patients were treated with a dose of 60 Gy in 30 fractions with static CRT, via a 6-MV photon beam, using the Clinac EX linear accelerator (Varian Medical Systems).

Static CRT

For the static multiple-beam conformal plan, main static 4 conformal beams consisted of anterior-posterior opposing beams and off-cord oblique opposing beams which were set in 2:1 weight. Plans were manually optimized using a field-in-field technique, with two to four small fields of small weights to improve the dose distribution.

Dynamic CRT

The dynamic conformal arc plan consisted of a single dynamic conformal arc rotating from 0° to 180° and static conformal fields (Fig. 1). A dynamic

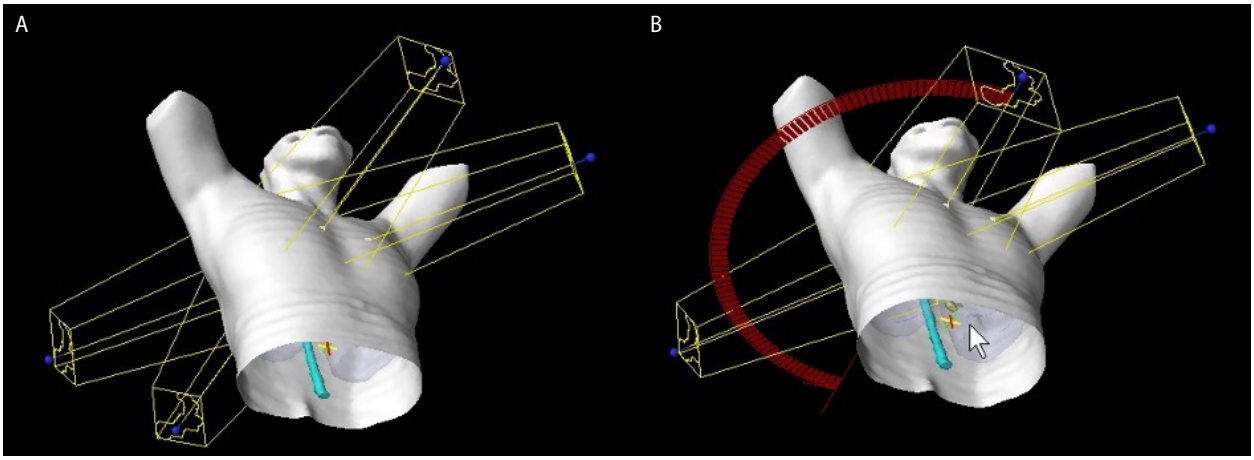

Figure 1. Typical beam arrangements for static conormal radiotherapy (CRT) (**A**) and dynamic CRT (**B**) plans

conformal beam was arranged using multileaf collimators for beam shaping during gantry rotation. An opposing pair of static conformal fields was set in the two directions at angles selected to minimize the dose to the spinal cord and lungs. Two to four field-in-field beams were added if needed to optimize the dose distribution. The weights of the dynamic arc and static conformal beams were adjusted to reduce the dose to organs at risk (OARs).

Dose specification and dose constraints

Two dose prescriptions were evaluated to determine how they improve the dose distribution. The first was delivery of the prescribed dose to the isocenter (IC prescription), and the second was delivery of the prescribed dose to > 50% of the PTV (D50 prescription). The maximum dose did not exceed 110% of the prescribed dose in either plan.

Normal organ parameters were obtained as follows. For the lung, we obtained the percentage of the lung volume receiving a dose of ≥ 5 or ≥ 20 Gy (V5 and V20, respectively) and the mean dose to the total lung, where the total lung was defined as the bilateral lung volume minus the GTV. Other OAR parameters included the doses to the heart, spinal cord, and esophagus. The dose constraints of these OARs were derived from the National Comprehensive Cancer Network guidelines, version 3.2020 [2], as shown in Supplementary File — Table S1. The dose constraints of the spinal cord were the highest priority.

Dose distribution and data analysis

For comparison of the target dose coverage between the static and dynamic CRT plans, and between the IC and D50 prescriptions for each plan, the conformity index (CI) and homogeneity index (HI) were calculated [3]. CI is defined as the ratio of the body volume receiving the prescribed dose to the volume of the PTV receiving the same dose. The closer the CI is to 1, the higher the dose convergence. The HI was defined as $D5_{PTV}/D95_{PTV}$, where $D5_{PTV}$ and $D95_{PTV}$ are the doses delivered to 5% and 95% of the PTV, respectively. The closer the HI is to 1, the higher the dose uniformity.

Parameters for the PTV and OARs were obtained from the dose–volume histograms of both plans. The parameters were analyzed using the Wilcoxon signed rank test. A p-value of < 0.05 was considered statistically significant. The doses delivered to the PTVs and OARs as well as the dose convergence were compared for each plan and prescription method, and the factors influencing the dose factors were analyzed. For statistical calculation, EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan): a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) was used [4]. This study, which used images of patients for radiation treatment re-planning only, was conducted on an opt-out basis approved by the institutional ethical review board.

Results

A total of 20 patients, five each with tumors in the right upper, right middle/lower, left upper, and left lower lobes, were selected. The median PTV was 225 cc (range, 112–699 cc), and the PTVs to the right upper, right middle/lower, left upper, and left lower lobes were 166, 193, 290, and 225 cc, respectively. The median normal lung volume was 4057 (range, 2310–5687 cc).

Comparison of static and dynamic CRT using the IC prescription

The target coverage parameters of static and dynamic CRT using the IC prescription are summarized in Table 1. The median $D95_{PTV}$ (52.6 and 53.9 Gy) and median 95% isodose volume (149.8 and 166.1 cc) were both increased between static and dynamic CRT. Dose conformity was significantly better with dynamic than static CRT (median CI: 1.3 *vs.* 2.2; $p < 0.01$), whereas dose uniformity, based on the HI, was identical between the plans. The PTV coverage was the lowest in the left upper lobe, but this was thought to be due to one case with a bulky tumor close to the spinal cord, and not due to the site. The dose distributions of one of the cases, as an example, after static and dynamic CRT are shown in Figure 2. The high-dose area such as 57 Gy or more outside the PTV was smaller in dynamic CRT than in static CRT.

OAR parameters

Table 2 shows the median dose-volume parameters of the OARs. Dynamic CRT did not increase lung V20 values (static *vs.* dynamic CRT: 18.9% *vs.*

Table 1. Median target coverage parameters of static conformal radiotherapy and dynamic conformal radiotherapy

		RUL	RMLL	LUL	LLL	All lobes				
		IC				IC	D50	p*1 (SCRT *vs.* DCRT with IC)	p*2 (SCRT *vs.* DCRT with D50)	p*3 (IC *vs.* D50)
$D95_{PTV}$ [Gy]	SCRT	52.3	52.7	52.7	52.5	52.6	54.2	0.004	0.014	0.002
	DCRT	55.7	54.0	52.8	55.3	53.9	55.0			0.040
95% isodose volume [cc]	SCRT	98.1	124.4	230.7	163.0	149.8	168.1	0.027	0.409	< 0.001
	DCRT	121.3	137.0	216.0	178.0	166.1	170.2			0.006
CI	SCRT	2.1	1.8	2.3	2.6	2.2	2.7	< 0.001		
	DCRT	1.4	1.2	1.3	1.4	1.3	1.4			
HI	SCRT	1.4	1.2	1.2	1.2	1.2	1.2	0.202		
	DCRT	1.1	1.1	1.2	1.1	1.1	1.2			

*1. Comparison between SCRT vs. DCRT for IC prescription; *2. Comparison between SCRT vs. DCRT for D50 prescription; *3. Comparison between IC vs. D50 for each radiotherapy method; RUL — right upper lobe; RMLL — right middle/lower lobe; LUL — left upper lobe; LLL — left lower lobe; $D95_{PTV}$ — dose delivered to 95% of the planning target volume (PTV); SCRT — static conformal radiotherapy; DCRT — dynamic conformal radiotherapy; IC prescription — delivery of the prescribed dose to the isocenter; D50 prescription — delivery of the prescribed dose to 50% of the PTV; CI — conformity index; HI — homogeneity index

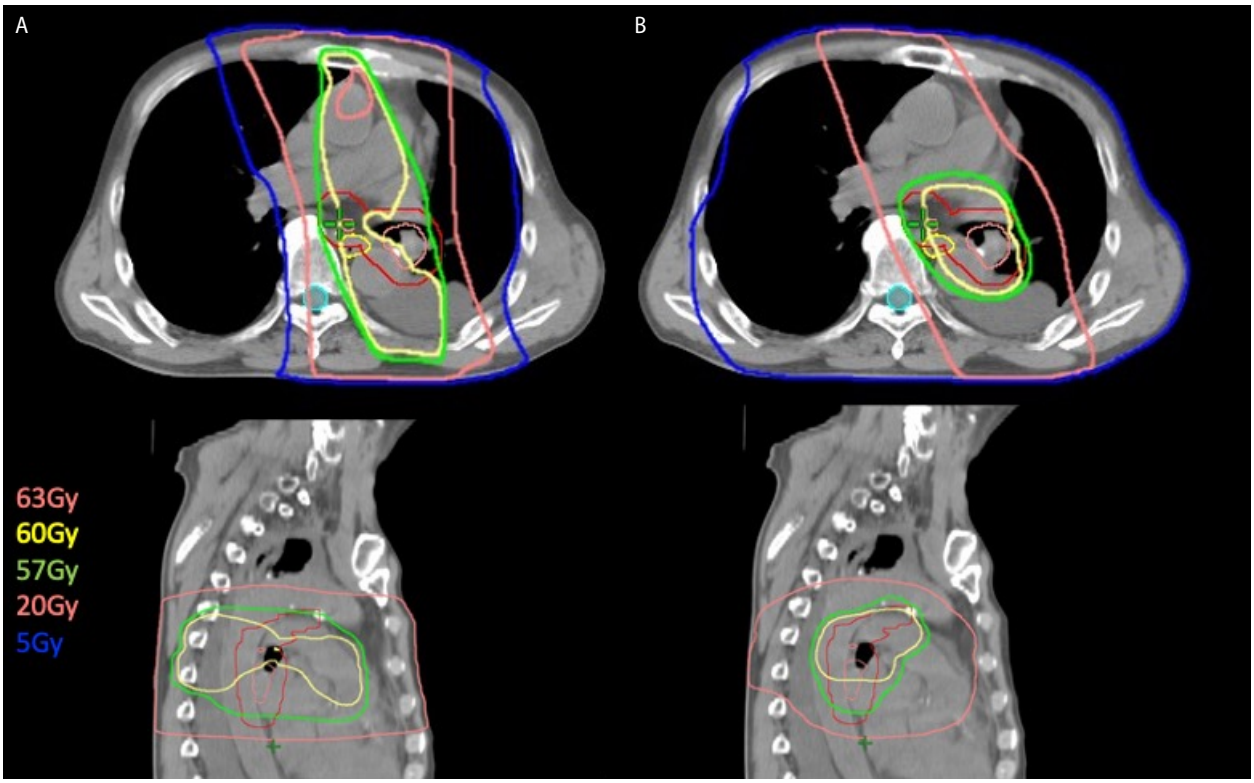

Figure 2. An example of differences in the dose distributions of static conformal radiotherapy (CRT) (**A**) and dynamic CRT (**B**). The planning target volume is depicted by the fine red line. The isodose lines are shown according to the colour scale. Changes in the lung volume encompassed by the 20 and 5 Gy isodose lines are shown

19.3%, p = 0.09). In contrast, it increased the lung V5 values (static *vs.* dynamic CRT: 31.6% *vs.* 48.6%, p < 0.001) as well as the mean lung dose (static *vs.* dynamic CRT: 9.7 Gy *vs.* 11.5 Gy, p < 0.001) compared with static CRT. In one patient whose PTV was 699 cc, the lung V20 after static CRT slightly exceeded the dose constraint (37%), while this value was 33% after dynamic CRT.

The mean heart dose and heart V50 were similar in both plans, while the heart dose parameters were greater in the left lower lobe than in other regions. The mean esophageal dose was increased slightly

Table 2. Median dose-volume parameters of the organ at risks

			RUL	RMLL	LUL	LLL	All lobes				
			IC				IC	D50	p*1 (SCRT *vs.* DCRT with IC)	p*2 (SCRT *vs.* DCRT with D50)	p*3 (IC *vs.* D50)
Spinal cord	Dmax [Gy]	SCRT	43.5	44.7	46.1	41.9	44.1	45.5	< 0.001	< 0.001	< 0.001
		DCRT	27.4	20.8	33.3	27.0	25.2	26.9			0.004
Lung	V20 (%)	SCRT	15.6	30.1	19.7	14.2	18.9	19.3	0.090	0.007	< 0.001
		DCRT	18.8	28.8	20.6	15.4	19.3	21.5			0.040
	V5 (%)	SCRT	25.7	43.8	34.2	27.6	31.6	31.9	< 0.001	< 0.001	< 0.001
		SCRT	42.8	57.4	49.1	54.9	48.6	50.4			0.013
	Mean [Gy]	SCRT	9.5	15.1	8.9	7.8	9.7	10.4	< 0.001	0.001	< 0.001
		DCRT	10.8	16.6	11.9	11.2	11.5	11.8			0.040
Esophagus	Dmax [Gy]	SCRT	58.0	56.4	60.3	60.5	59.4	60.6	0.294	0.475	< 0.001
		DCRT	58.9	56.6	61.9	61.8	60.1	59.7			0.522
	Mean [Gy]	SCRT	11.2	13.0	38.3	32.2	26.6	27.1	0.003	< 0.001	< 0.001
		DCRT	17.0	14.9	38.1	37.0	24.8	26.3			0.177
Heart	V50 (%)	SCRT	0.0	0.8	0.1	13.4	0.5	0.6	0.100	0.038	0.004
		DCRT	0.0	1.1	0.1	4.6	0.3	0.1			0.398
	Mean [Gy]	SCRT	0.6	3.8	2.5	20.7	4.3	4.4	0.294	0.701	< 0.001
		DCRT	0.8	7.1	3.3	13.6	6.7	6.5			0.189

*1. Comparison between SCRT vs. DCRT for IC prescription; *2. Comparison between SCRT vs. DCRT for D50 prescription; *3. Comparison between IC vs. D50 for each radiotherapy method; RUL — right upper lobe; RMLL — right middle/lower lobe; LUL — left upper lobe; LLL — left lower lobe; SCRT — static conformal radiotherapy; DCRT — dynamic conformal radiotherapy; IC prescription — delivery of the prescribed dose to the isocenter; D50 prescription — delivery of the prescribed dose to 50% of the PTV; V20 — the lung volume receiving 20 Gy or more; V5 — the lung volume receiving 5 Gy or more

(by 1.8 Gy) with static CRT compared with dynamic CRT. The maximum and mean doses were increased in the ranges of roughly 3–4 and 21–23 Gy in the left lung compared with the right lung with both plan methods. The median maximum spinal cord dose was lower with dynamic than static CRT (25.2 *vs.* 44.1 Gy, $p < 0.001$).

The effect of the D50 prescription on target coverage

The dose parameters were compared after changing the dose prescription method from IC to D50 prescription (Tab. 1, 2). The median $D95_{PTV}$ was slightly increased (1.6 and 1.1 Gy increase in static and dynamic CRT, respectively), while the 95% isodose volume increased by 18.3 cc with static CRT and 4.1 cc with dynamic CRT after changing to the D50 prescription from the IC prescription. With the D50 prescription, the spinal cord constraint was exceeded in two cases using static CRT but in none of the cases using dynamic CRT. Only one case (with a large PTV of 699 cc) had a lung V20 higher than the dose constraint with both plans and both prescription methods, but V5 did not exceed the dose constraint with either prescription method in any case. The mean esophagus dose with the D50 prescription was higher than the dose constraint in five cases (three tumors in the left upper lobe and two in the left lower lobe) with both plans. The dose constraint in the heart could not be met by static and/or dynamic CRT using the D50 prescription in four cases; three cases were in the left lower lobe and one in the right lower lobe.

Static CRT using the IC prescription, which is the standard method in clinical practice, was compared with dynamic CRT using the D50 prescription, which has more optimal dose distribution (Supplementary File — Fig. S1). The target dose was increased significantly with the latter plan compared with the former plan, with median $D95_{PTV}$ values of 52.6 and 54.2 Gy ($p = 0.006$) and 95% isodose volumes of 149.8 cc and 170.2 cc ($p = 0.23$) for static CRT and dynamic CRT, respectively. Regarding the lung doses, the median V20 remained similar (18.9% *vs.* 21.5%, $p = 0.402$) and V5 was increased (31.6% *vs.* 50.4%, $p < 0.001$) from static to dynamic CRT. Dynamic CRT significantly de-

creased the max spinal cord dose compared with static CRT (26.9 *vs.* 44.1 Gy, $p < 0.001$). The mean esophageal dose and the mean heart dose remained unchanged, after dynamic CRT.

Discussion

The results of this study revealed the advantages of dynamic CRT for locally advanced lung cancer. In thoracic radiation therapy, static multiple-beam plans are designed to irradiate the target from arbitrary directions while shielding the normal tissues such as the lung and spinal cord. However, depending on tumor size and site and body thickness, the surrounding lung tissue or areas near the chest wall outside of the target receive a higher dose than that received by the tumor. On the other hand, dynamic CRT can improve the dose constraint by combining static beams with rotational irradiation to achieve the highest dose concentration to the target.

Such an approach has been evaluated in small tumors. Kim reported the results of a planning study in 20 lung cancer cases with central tumors or tumors close to or invading the mediastinum treated with a maximum field size of 15 cm [5]. The dose-volume parameters of hybrid static and dynamic arc plans were compared with those of static multi-arc beam plans in terms of target volume coverage, dose conformity, and sparing of OARs. The hybrid static and dynamic arc plans showed better dose conformity and reduced the doses to the lung and spinal cord. Pokhrel et al. compared hybrid 3D conformal arc and VMAT plans using flattering filter-tree beams in a stereotactic body radiation therapy setting for small, early-stage NSCLC [6]. They found better target coverage, higher tumor dose parameters, and a shorter overall treatment planning time for the hybrid conformal arc plan. As described above, 3DCRT using arc beams is thought to have certain advantages in small tumors, but the performance of this method in large tumors is unknown. In the present study, we investigated the characteristics of dynamic CRT in locally advanced lung cancer. The results showed a better dose distribution with dynamic CRT than static multiple-beam plans even in large tumors.

In radiotherapy for locally advanced lung cancer, IMRT has attracted attention as a method to concentrate the dose as much as possible within the target volume while reducing the dose to normal organs. The clinical benefits of IMRT have been demonstrated [7]. However, for the treatment of tumors that move with respiration, there are concerns about dose delivery uncertainties associated with small-field dosimetry and motion interplay effects due to multiple beamlets in the delivery of highly modulated doses. Whereas the irradiation fields of IMRT plans block a certain region of the moving target volumes during certain moments, dynamic CRT plans are hardly affected by interplay effects, and the field always captures the entire moving target. In addition, dynamic CRT simplifies treatment planning and, therefore, can be promptly initiated before IMRT initiation.

In recent years, IMRT has been rapidly gaining popularity. In the United States, it was utilized in 11% of limited-stage small cell lung cancer cases in 2004, and this rate steadily rose to 57% by 2014 [8]. However, the likelihood of receiving IMRT is influenced by location (urban or rural area) and education status, and the IMRT prevalence varies greatly depending on the country and type of institution (e.g., high-volume center). There will continue to be lung cancer patients worldwide who cannot benefit from IMRT until it becomes the standard of care. Although there are many issues to be addressed before IMRT becomes widely used for lung tumors, dynamic CRT plans can be superior to static multiple-beam plans, and even simpler, depending on the site.

One possible disadvantage of dynamic CRT compared with static CRT is the increased low-dose area in the lungs. Studies have shown an increased risk of radiation pneumonitis with a lung V5 > 60%. Silva et al. compared hybrid VMAT, VMAT-only, and 3DCRT plans in patients with locally advanced lung cancer [9] and reported significant reductions in the dose to normal organs, including the lungs, using hybrid VMAT compared with the other plans. After a median follow-up time of 17 months, there was no symptomatic radiation pneumonitis in patients with a median V5 value of 57–58%. Other reports have evaluated the effect of V5 on radiation pneumonitis; Yom et al. reported that > grade 3 radiation pneumonitis occurred in 2% of cases with a V5 < 70% and 21% of cases with a V5 > 70% [10]. Dynamic CRT in the current study showed lower median V5 values (50.4% with D50 prescription) compared with those reported

in IMRT dosimetric studies. The significance of an increase in V5 with chemoradiotherapy has not been determined. IMRT has shown reduced rates of pneumonitis compared with 3DCRT. The Radiation Therapy Oncology Group 0617 trial showed significantly lower rates of severe pneumonitis in patients treated with IMRT compared with 3DCRT, and V20 may be more predictive of the risk of pneumonitis than V5 [11].

The compromised dosimetric profiles of 3DCRT compared with IMRT may be compensated by the prescription method. 3DCRT has often been performed using IC prescriptions; however, in thoracic radiation therapy with heterogeneous electron density due to the lungs and mediastinum, unnecessary irradiation outside of the PTV and insufficient irradiation of the target are often observed with static multiple-beam plans (Fig. 2). D50 prescriptions in dynamic CRT may provide a sufficient increase in the target dose in select patients. In fact, dynamic CRT was able to maintain an acceptable dose to the spinal cord while increasing the PTV dose by adopting the D50 prescription, whereas static CRT often exceeded the upper limit. In the left lower lobe, doses to the heart and esophagus more often exceeded the dose constraint in static CRT. On the other hand, in cases with tumors in close proximity to the spinal cord or with massive tumors, the dose constraint could not be met by either method although the number of cases was small. Since D50 prescription shifts the dose volume histogram only to the right, the good dose conformity of dynamic CRT itself enables increasing the target dose safely while satisfying the dose constraint.

A limitation of this study is the small number of cases, especially because five cases of each of the four target tumor locations may not reflect adequate diversity. In addition, we emphasized uniformity and consistency in the treatment planning in our study and, therefore, deliberately minimized optimization of individual plans. However, the present results suggest that it is feasible to increase the dose to the target while reducing the dose to normal tissues using 3DCRT with lower V5 values compared with those of IMRT. Dynamic CRT with D50 prescription may contribute to the treatment of lung cancer as part of an optimal 3DCRT plan, especially in facilities where IMRT is not widely available or where treatment is urgently needed until IMRT can be initiated. Therefore, dynamic CRT with D50 prescription may be an attractive alternative to IMRT for lung cancer if the tumor location is favorable.

Conclusion

The dynamic CRT technique using a single half-rotated conformal arc and static field-in-field beams showed better target coverage and lower doses to the spinal cord in exchange for increased low-dose lung area, compared with static CRT. Dynamic CRT with D50 prescription instead of prescription to the isocenter has excellent dose distribution profiles without compromising doses to OARs for lung cancer at favorable locations.

Conflict of interests

There are no conflicts of interest.

Funding

This publication was prepared without any external source of funding.

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