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FULL PAPER

Tumour volume changes assessed with high-quality KVCT in lung cancer patients undergoing concurrent chemoradiotherapy

¹Y H LEE, MD, ¹Y S KIM, MD, PhD, ¹H C LEE, MD, ¹S W LEE, MD, ¹Y N KANG, PhD, ²J H KANG, MD, PhD, ²S H HONG, MD, PhD, ³Y K KIM, MD, PhD, ³S J KIM, MD, PhD, ⁴M I AHN, MD, PhD, ⁴D H HAN, MD, PhD, ⁵I R YOO, MD, PhD, ⁶J G PARK, MD, PhD, ⁶S W SUNG, MD, PhD and ⁷K Y LEE, MD, PhD

¹Department of Radiation Oncology, Seoul St Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

²Department of Medical Oncology, Seoul St Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

³Department of Internal Medicine, Seoul St Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

⁴Department of Radiology, Seoul St Mary's Hospital, Seoul, College of Medicine, The Catholic University of Korea, Republic of Korea

⁵Department of Nuclear Medicine, Seoul St Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

⁶Department of Thoracic Surgery, Seoul St Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

⁷Department of Pathology, Seoul St Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Address correspondence to: Professor Yeon Sil Kim

E-mail: yeonkim7@catholic.ac.kr

Objective: We evaluated tumour volume changes in patients with lung cancer undergoing concurrent chemoradiotherapy using image-guided radiotherapy (RT).

Methods: The kilovoltage image was obtained using CT on rail at every five fractions. The gross tumour volumes (GTVs), including the primary tumour and lymph nodes (LNs), were contoured to analyse the time and degree of tumour regression.

Results: 46 patients [32, non-small-cell lung cancer (NSCLC), and 14, small-cell lung cancer (SCLC)] were included in this study. In total, 281 CT scans and 82 sites of GTVs were evaluated. Significant volume changes occurred in both the NSCLC and SCLC groups ($p < 0.001$ and 0.002), and the average GTV change compared with baseline was 49.85 ± 3.65 [standard error (SE)]% and 65.95 ± 4.60 (SE)% for the NSCLC and SCLC groups, respectively. A significant

difference in the degree of volume reduction between the primary tumour and LNs was observed in only the NSCLC group ($p < 0.0001$) but not in the SCLC group ($p = 0.735$). The greatest volume regression compared with the volume before the five fractions occurred between the 15 and 20 fractions in the NSCLC group and between the 5 and 10 fractions in the SCLC group.

Conclusion: Both primary tumour and LNs were well defined using CT on rail. Significant volume changes occurred during RT, and there was a difference in volume reduction between the NSCLC and SCLC groups, regarding the degree and timing of the tumour reduction in the primary tumour and LNs.

Advances in knowledge: NSCLC and SCLC groups showed differences in the degree and timing of volume reduction. The primary tumour and LNs in NSCLC regressed differently.

Lung cancer is the most common cause of cancer mortality in the Republic of Korea, accounting for 22.2% all cancer deaths. Although the survival rate continues to increase, the prognosis remains poor with a 5-year relative survival rate of 20.7% in patients diagnosed from 2007 to 2011.¹ Multimodality treatment, including radiotherapy (RT), is a mainstay in the treatment of locally advanced non-small-cell lung cancer (NSCLC) and limited-stage small-cell lung cancer (SCLC) because it improves local control and overall survival.^{2–5} Several recent studies have shown that an increasing radiation dose resulted in the improvement of local control and overall survival.^{6–9} Currently, Phase III randomized studies are under way to determine the

optimal dose and fractionation schedule. Radiation oesophagitis and pneumonitis are major complications that limit the potential for dose escalation. Changes in tumour volume, patients' weight, pulmonary atelectasis and pleural effusions were noted during RT and modification of the treatment plan may be required over the course of the treatment. Adaptive planning can reduce the radiation exposure of an organ at risk (such as normal lung and oesophagus) and may improve local control.

Several studies have reported that tumour shrinkage occurs during RT using the various image-guided RT modalities, such as electronic portal imaging, megavoltage (MV) and

Table 1. Patient characteristics

Characteristics	Non-small-cell lung cancer	SCLC
Age (years)		
Median	63	65
Range	45–79	59–75
Sex (<i>n</i>)		
Male	23	13
Female	9	1
Stage (<i>n</i>)		
IIA	1	
IIB	2	
IIIA	8	
IIIB	14	
IV ^a	3	
Recurrent	4	
Limited disease-SCLC		13
Extensive disease-SCLC		1
Histology (<i>n</i>)		
Squamous cell carcinoma	17	
Adenocarcinoma	13	
Large cell carcinoma	1	
Sarcomatoid carcinoma	1	
Treatment aim (<i>n</i>)		
Radical	22	13
Post-operative (residual lesion)	6	
Pre-operative	4	
Consolidative ^b		1
Concurrent chemotherapy (<i>n</i>)		
Docetaxel + cisplatin	28	
Carboplatin	2	
Paclitaxel	2	
Etoposide + cisplatin		14
Radiation dose (Gy)		
Median	66	54
Range	34–66	45–55.8

SCLC, small-cell lung cancer.

^aConcurrent chemoradiotherapy was performed in patients with limited distant metastasis; one patient had a single brain metastasis, which was grossly removed before radiation; one patient had a single rib metastasis, which regressed after primary chemotherapy; and one patient had neck lymph node metastasis, which was included in the radiation field.

^bOne patient with extensive disease received radiotherapy after primary etoposide + cisplatin chemotherapy with consolidative aim.

kilovoltage (KV) cone beam CT (CBCT) and MVCT at tomotherapy.^{10–14} However, there are few studies reporting the tumour regression timing of both the primary tumour and lymph nodes (LNs) owing to the limited image quality for LN evaluation. In this study, we analysed the degree of tumour regression in the primary tumour and LNs for patients with lung cancer undergoing concurrent chemoradiotherapy using CT on rail to determine the appropriate timing for adaptive planning.

METHODS AND MATERIALS

The data collection, storage and analysis were all performed in compliance with the institutional review board at St Mary's Hospital, Seoul, Republic of Korea. Patients who were treated with concurrent chemoradiotherapy for lung cancer were evaluated with image-guided radiation therapy (IGRT) for tumour volume change and target localization during their course of RT. They were treated at St Mary's Hospital between June 2009 and June 2011.

Planning CT scans were obtained with a SOMATOM® Sensation Open CT simulator (Siemens, Forchheim, Germany) with a slice thickness of 3 mm, under free-breathing conditions. A second CT scan, four-dimensional (4D) CT, was obtained using an Anzai respiratory monitoring system (AZ-733 V; Anzai Medical Co. Ltd, Tokyo, Japan) for tumour motion assessment and internal target volume generation. The clinical target volume (CTV) included the gross tumour volume (GTV) with an additional uniform 5 mm expansion and high-risk, uninvolved mediastinal LNs as well as the ipsilateral hilar LNs. Each tumour's motion was assessed with a Leonardo system (Siemens, Forchheim, Germany). The planning target volume was generated by adding 5- to 10-mm margins to the CTV according to the respiratory motion in the superiorinferior, anteroposterior and left–right directions. Patients were treated with the three-dimensional conformal technique using 6- or 10-MV photons. Patients were treated on a linear accelerator with CT on rail system (CTVision™; Siemens, Forchheim, Germany), providing a KV image. During the RT course, patients were scheduled to undergo KVCT every five fractions. For once-a-day treatment with 1.8–2.0 Gy per fraction, KVCT was obtained once a week, and for twice-a-day treatment with 1.5 Gy per fraction, KVCT was obtained twice a week.

The images were exported to the Pinnacle³ treatment planning system (Philips Healthcare, Milpitas, CA). Contours were drawn at the baseline of the free-breathing simulation CT and then on KVCT at fractions 5, 10, 15, 20, 25, 30 and 35. Primary tumour volumes and the abnormally enlarged LNs were separately contoured if they were well defined on each CT image set. The abnormally enlarged LNs having high 18-fluorodeoxyglucose (¹⁸F-FDG) uptake on positron emission tomography (PET) CT or confirmed pathologically were included in this evaluation. Contours were drawn by a single physician with the same mediastinal and lung window setting for each GTV.

We summarized the changes in the tumour volume using descriptive statistics. Absolute tumour volumes, as well as the percentage change from the initial volume and the previous volume, were recorded. Repeated-measures analysis of variance

Figure 1. Absolute volume regression of tumour of non-small-cell lung cancer (NSCLC) and small-cell lung cancer (SCLC). Tumour volume change over time was evaluated with repeated-measure analysis of variance. The mean gross tumour volume of the NSCLC (a) and SCLC (c) groups regressed over time with significance ($p < 0.0001$ and $p = 0.002$, respectively). The primary tumour and the lymph nodes (LNs) of NSCLC and SCLC are presented separately (b, d). fx, fractions.

was used to evaluate the change of tumour volume over time. p -values < 0.05 were considered to be significant. Statistical analyses were performed using SAS® v. 9.1 (SAS Institute, Cary, NC).

Figure 2. Volume change compared with baseline gross tumour volume (GTV) (%). This plot shows volume change as a percentage of baseline GTV (volume in simulation CT). The percentage volume reduction was significant after 10 fractions (fx) in the small-cell lung cancer (SCLC) group ($p = 0.018$) and after 15 fractions in the non-SCLC (NSCLC) group ($p < 0.0001$).

RESULTS

Patient characteristics

46 patients, including 32 with NSCLC and 14 with SCLC, were evaluated for GTV regression. All of the patients received concurrent chemoradiotherapy. Their age, sex, stage, histology, treatment aim, chemotherapy regimen and radiation dose are listed in Table 1. The histology of NSCLC was squamous cell carcinoma (53%), adenocarcinoma (40.6%), large cell carcinoma (3.1%) and sarcomatoid carcinoma (3.1%). Patients were treated with a radical aim (68.75%), post-operative aim (18.75%) and pre-operative aim (12.5%) for NSCLC and with a radical aim (92.9%) and consolidative aim (7.10%) for SCLC. Most patients with NSCLC were treated with 1.8–2.0 Gy daily fractions, while half of the patients with SCLC were treated with a twice-daily schedule of 1.5 Gy per fraction. A total of 281 CT scans including the simulation CTs were obtained and 82 sites of GTVs were evaluated. For each patient, a median number of six CT data sets (range, 4–8 datasets) were contoured. 20 primary tumours and 39 LN sites were evaluated for volume regression in the 32 patients with NSCLC, while 9 primary tumours and 14 LN sites were examined in the 14 patients with SCLC.

Volume regression

For NSCLC, the median initial total tumour volume was 10.79 cm^3 (range, 0.62 – 263.33 cm^3). When the initial primary tumour and LN groups were evaluated separately, they showed medians of 51.26 cm^3 (range, 4.09 – 263.33 cm^3) and 5.04 cm^3

Table 2. Tumour volumes (cm³) of primary tumour and lymph nodes (LNs) every five fractions (fx)

Radiotherapy	Primary tumour	LNs	Group time
	Mean $\pm$ SE	Mean $\pm$ SE	<i>p</i> -value
Non-small-cell lung cancer (<i>n</i> = 59)			
Baseline	70.60 $\pm$ 15.03	8.87 $\pm$ 1.53	<0.0001
5 fx	72.71 $\pm$ 18.87	8.57 $\pm$ 1.51	
10 fx	64.32 $\pm$ 16.81	7.57 $\pm$ 1.29	
15 fx	51.66 $\pm$ 13.42	6.54 $\pm$ 1.12	
20 fx	43.36 $\pm$ 11.62	5.22 $\pm$ 0.92	
25 fx	35.92 $\pm$ 10.77	4.76 $\pm$ 0.84	
30 fx	35.04 $\pm$ 10.71	4.44 $\pm$ 0.79	
35 fx	34.12 $\pm$ 10.74	4.02 $\pm$ 0.74	
Small-cell lung cancer (<i>n</i> = 23)			
Baseline	15.94 $\pm$ 6.33	11.36 $\pm$ 4.52	0.735
5 fx	11.84 $\pm$ 4.68	10.45 $\pm$ 4.58	
10 fx	9.14 $\pm$ 4.66	8.33 $\pm$ 4.00	
15 fx	8.59 $\pm$ 5.20	6.70 $\pm$ 3.99	
20 fx	5.82 $\pm$ 2.81	4.55 $\pm$ 2.23	
25 fx	5.37 $\pm$ 2.82	4.39 $\pm$ 2.24	
30 fx	5.20 $\pm$ 3.37	3.09 $\pm$ 1.15	

SE, standard error.

Repeated-measures analysis of variance was used to evaluate the tumour volume changes over time.

(range, 0.62–41.98 cm³), respectively. At the completion of treatment, the median volumes had decreased to 3.89 cm³ (range, 0.24–56.84 cm³), 12.76 cm³ (range, 2.70–56.84 cm³) and 2.87 cm³ (range, 0.24–11.57 cm³) for total gross tumour, primary tumour and LNs, respectively. Figure 1a shows the mean total GTVs measured at every five fractions. Significant volume changes occurred during RT ($p < 0.0001$). An average of the total GTV change compared with the baseline GTV (the volume of the initial total GTV contoured in simulation CT) was $49.85\% \pm 3.65\%$ [standard error (SE)], shown in Figure 2.

There was a difference in volume distribution between the primary tumour and the LN sites ($p < 0.0001$). Significant volume changes occurred during RT in both groups ($p < 0.0001$), but there was a difference in the pattern of decrease ($p < 0.0001$) between the two groups, as shown in Table 2 and Figure 1b.

For SCLC, the median initial tumour volumes were 6.12 cm³ (range, 0.65–65.76 cm³), 7.57 cm³ (range, 0.65–51.59 cm³) and 5.28 cm³ (range, 1.02–65.76 cm³) for total gross tumour, primary tumour and LNs, respectively. These volumes decreased to medians of 1.98 cm³ (range, 0.30–31.84 cm³), 2.33 cm³ (range, 0.37–31.84 cm³) and 1.76 cm³ (range, 0.30–16.52 cm³), respectively, at the end of RT. There were significant volume changes during RT ($p = 0.002$) as shown in Figure 1c, and the average of the total GTV changes at the completion of treatment compared with the initial volumes measured at baseline (simulation CT) was $65.95\% \pm 4.60\%$ (SE) (Figure 2). In contrast to the NSCLC group,

there was no difference in volume distribution between the primary tumour and the LNs ($p = 0.700$) in SCLC. Both the primary tumour and the LN sites showed significant volume changes with time ($p = 0.002$), but there was no significant difference in the pattern of decrease between the two groups ($p = 0.735$), as presented in Table 2 and Figure 1d.

The greatest tumour volume regression

To identify the time point at which the greatest tumour volume regression occurs, the mean volume changes relative to the previous GTV (volume before the five fractions) were also evaluated. The greatest volume regression appeared between 15 and 20 fractions for NSCLC, reaching approximately a mean of $16.29\% \pm 2.96\%$ (SE). The primary tumour showed the greatest tumour volume regression between 10 and 15 fractions with $20.07\% \pm 3.91\%$ (SE), and the LNs showed the greatest tumour volume regression between 15 and 20 fractions with $16.56\% \pm 3.73\%$ (SE). For SCLC, the greatest tumour volume regression occurred earlier than for NSCLC, between 5 and 10 fractions with an average of $23.18\% \pm 5.28\%$ (SE): primary tumour, 5 and 10 fractions, $24.53\% \pm 9.05\%$ (SE), and LN, 10 and 15 fractions, $26.5\% \pm 8.29\%$ (SE) (Figure 3).

Initial tumour volume effect

To evaluate the difference in the magnitude of volume changes between large and small tumours, we divided the initial volumes of tumours into two groups: small and large, depending on the median value. Both the primary tumour and the LN group of

Figure 3. The greatest tumour volume regression. This graph displays volume change as a percentage of the previous gross tumour volume (GTV) [volume before the five fractions (fx)]. The greatest volume reduction occurred between 15 and 20 fx in the non-small-cell lung cancer (NSCLC) group (a, b), and 5 and 10 fx in the small-cell lung cancer (SCLC) group (c, d). The primary tumour and lymph nodes (LNs) showed differences in the time of the greatest tumour volume regression compared to previous GTV.

NSCLC showed a significant difference in tumour volume between the initial large and small tumour volumes ($p = 0.004$ and $p < 0.0001$, respectively). They regressed with treatment over time in a significant manner ($p < 0.0001$ and $p < 0.0001$, respectively). Notably, initial large tumour volumes resulted in a greater rate of regression than those of the smaller initial tumours in both the primary tumour and the LN group ($p = 0.002$ and $p < 0.0001$, respectively). In the primary tumours in the SCLC group, there were no significant differences in the tumour volume ($p = 0.181$), and the pattern of their regression between the initial large and small group ($p = 0.078$). However, the tumour volume regressed with time in both initial large and small groups ($p = 0.036$). The LNs of the SCLC group showed a similar pattern to the primary tumours (Table 3).

DISCUSSION

In lung cancer, the regression of primary tumours and LNs is expected during the course of RT, but the degree of regression and appropriate timing of treatment plan modification have not been well established. Recently, several studies regarding tumour regression have been published with various IGRT modalities, but difficulties relating to the interpretation of the results exist owing to the small number of patients and heterogeneity in treatments.^{10–15}

In our study, the largest volume regression compared with the previous GTV (before the 5 fractions), occurred between 15 and 20 fractions (Figure 2), and the graph of volume regression showed a plateau after 20 fractions (Figure 1). Therefore, it may be

appropriate to consider adapting the plan within the first 20 fractions of NSCLC. Lim et al¹⁰ described the volumetric and positional changes of the primary tumour, using respiratory-correlated CBCT imaging during the course of radical RT to a dose ≥ 45 Gy with concurrent chemotherapy in NSCLC. There was a mean per cent decrease of 51.1% by the completion of treatment in 31 patients, which was comparable to our result of 49.85%. Furthermore, they found that greater rates of tumour volume regression occurred during the initial week, compared with those during the later phases of the treatment. A study by Woodford et al¹¹ evaluated GTV changes by using MVCT and concluded that adaptive planning is beneficial as long as the GTV decreases by $>30\%$ in 20 fractions.

It has been considered that SCLC is both chemosensitive and radiosensitive, but the tumour behaviour of SCLC during the radiation treatment is not well known. Recently, Yee et al¹² quantified tumour volume shrinkage in limited disease of SCLC cases undergoing concurrent chemoradiotherapy and conducted serial chest CT scans 3 times a week in 10 patients. Most of the tumour regression occurred during the first week of RT, and the tumours regressed up to 12.4%, relative to the pre-RT volume, by the completion of treatment. In our study, the greatest tumour volume regression of SCLC occurred between 5 and 10 fractions, and the mean GTV relative to the pre-RT volume was 34.05% at the end of treatment. Yee et al did not differentiate between the primary tumours and LNs, and included conglomerated tumour volumes. Their initial GTV was larger than ours, which may have influenced the degree of volume reduction.

Table 3. Tumour volumes (cm³) by an initial large and small volume every five fractions (fx)

Radiotherapy	Initial small	Initial large	Group time
	Mean ± SE	Mean ± SE	<i>p</i> -value
Non-small-cell lung cancer (<i>n</i> = 59)			
Baseline	23.51 ± 4.99	117.68 ± 20.88	0.002
5 fx	22.20 ± 4.53	123.21 ± 30.26	
10 fx	19.72 ± 4.26	108.91 ± 27.07	
15 fx	15.01 ± 2.84	88.30 ± 21.29	
20 fx	13.43 ± 3.25	73.30 ± 18.99	
25 fx	11.85 ± 3.04	59.98 ± 18.76	
30 fx	11.82 ± 3.05	58.25 ± 18.85	
35 fx	11.26 ± 2.60	56.99 ± 19.09	
LN			
Baseline	2.51 ± 0.30	14.90 ± 2.25	<0.0001
5 fx	2.48 ± 0.33	14.36 ± 2.28	
10 fx	2.33 ± 0.35	12.54 ± 1.93	
15 fx	2.28 ± 0.40	10.59 ± 1.72	
20 fx	1.86 ± 0.35	8.41 ± 1.44	
25 fx	1.68 ± 0.37	7.67 ± 1.32	
30 fx	1.63 ± 0.38	7.11 ± 1.23	
35 fx	1.50 ± 0.36	6.41 ± 1.18	
Small-cell lung cancer (<i>n</i> = 23)			
Baseline	3.10 ± 1.53	26.20 ± 9.13	0.078
5 fx	3.01 ± 1.57	18.91 ± 7.01	
10 fx	2.66 ± 1.64	14.33 ± .84	
15 fx	2.49 ± 1.45	13.46 ± 9.09	
20 fx	2.35 ± 1.49	8.60 ± 4.76	
25 fx	2.27 ± 1.52	7.84 ± 4.88	
30 fx	1.15 ± 0.43	8.44 ± 5.90	
LNs			
Baseline	3.11 ± 0.59	19.61 ± 8.09	0.090
5 fx	2.88 ± 0.61	18.02 ± 8.45	
10 fx	2.13 ± 0.32	14.53 ± 7.51	
15 fx	1.78 ± 0.39	11.62 ± 7.80	
20 fx	1.56 ± 0.49	7.53 ± 4.29	
25 fx	1.42 ± 0.50	7.36 ± 4.31	
30 fx	1.26 ± 0.48	4.92 ± 2.09	

LN, lymph node; SE, standard error.

Repeated-measures analysis of variance was used to evaluate the tumour volume changes over time.

Some studies did not find significant tumour volume regression during RT. A study by Siker *et al*¹³ suggested that a field reduction is not recommended during RT because a substantial volumetric decrease of the primary tumour did not occur in weekly MVCTs. However, some patients in that

study were treated with a palliative aim or stereotactic radioablation.

Volume changes of the primary tumour in lung cancer are frequently described, but little is known about the volume

changes of the LNs. Many studies expect that the LNs behave in a similar fashion to the primary tumour, but van Elmpt et al¹⁴ showed a different result. They investigated the relationship between the positional and volumetric changes in the primary tumour and LNs of NSCLC. An ¹⁸F-FDG PET CT scan was obtained before RT and in the second week of RT, and the volume and positional change of both the primary tumour and LNs were evaluated. They suggested that repeated mediastinal imaging may be necessary during RT, because LN behaviour differs from that of the primary tumour. However, Bosmans et al¹⁵ observed that changes in the nodal volume and motion tend to fall within the commonly applied margins and suggested that the repeated imaging of the nodes seems to be of limited value. There are difficulties in delineating the mediastinal LNs, using KV- and MV-CBCT or MVCT at tomotherapy. CT on rail uses the scatter-reducing fan beam geometry; thus, it has an outstanding image quality for soft-tissue contrast, such as mediastinal structures. We are able to delineate the central primary tumour and mediastinal LNs, as well as peripheral primary tumour, using CT on rail. Owing to the volume dynamics of the primary tumour being different from that of the LNs in NSCLC, as shown in the present study, we suggest that adaptive planning should be considered separately for the primary tumour and mediastinal LNs.

This study showed the results regarding the initial volume effect in NSCLC and SCLC. In NSCLC, both the primary tumour and LNs showed that initially large tumours regressed more markedly than small tumours. Lim et al¹⁰ found similar results that larger tumours had a greater rate of regression than did smaller tumours of the peripheral primary tumour in NSCLC. However, in the SCLC cases in our study, this difference did not occur between the initial large

and small tumour of the primary tumour and LNs. This observation may be explained by the rapid proliferation capacities of SCLC in the primary tumour and LNs, compared with NSCLC.

The limitation of this study is that respiratory motion was not accounted for, because it is difficult to acquire 4D respiratory motion information, owing to the fast image acquisition of CT on rail. The acquisition of a whole lung volume can be completed within approximately 10 s.

CONCLUSION

Both the primary tumour and LNs were well defined using CT on rail. Significant volume changes occurred during RT, and the largest volume regression compared with previous GTV occurred between 15 and 20 fractions in the NSCLC group and 5 and 10 fractions in the SCLC group, undergoing concurrent chemoradiotherapy. In the NSCLC group, the difference in the pattern of volume regression of the primary tumour and LNs was observed, and the initial large tumour regressed more rapidly. These results would be useful for reducing the probability of complications and to improve the therapeutic ratio of patients with lung cancer.

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REFERENCES

1. Jung KW, Won YJ, Kong HJ, Oh CM, Lee DH, Lee JS. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2011. *Cancer Res Treat* 2014; **46**: 109–23. doi: [10.4143/crt.2014.46.2.109](https://doi.org/10.4143/crt.2014.46.2.109)
2. Toschi L, Cappuzzo F, Jänne PA. Evolution and future perspectives in the treatment of locally advanced non-small cell lung cancer. *Ann Oncol* 2007; **18**(Suppl. 9): ix150–5. doi: [10.1093/annonc/mdm311](https://doi.org/10.1093/annonc/mdm311)
3. Pignon JP, Arriagada R, Ihde DC, Johnson DH, Perry MC, Souhami RL, et al. A meta-analysis of thoracic radiotherapy for small-cell lung cancer. *N Engl J Med* 1992; **327**: 1618–24. doi: [10.1056/NEJM199212033272302](https://doi.org/10.1056/NEJM199212033272302)
4. Warde P, Payne D. Does thoracic irradiation improve survival and local control in limited-stage small-cell carcinoma of the lung? A meta-analysis. *J Clin Oncol* 1992; **10**: 890–5.
5. De Ruysscher D, Pijls-Johannesma M, Vansteenkiste J, Kester A, Rutten I, Lambin P. Systematic review and meta-analysis of randomised, controlled trials of the timing of chest radiotherapy in patients with limited-stage, small-cell lung cancer. *Ann Oncol* 2006; **17**: 543–52. doi: [10.1093/annonc/mdj094](https://doi.org/10.1093/annonc/mdj094)
6. Kong FM, Ten Haken RK, Schipper MJ, Sullivan MA, Chen M, Lopez C, et al. High-dose radiation improved local tumor control and overall survival in patients with inoperable/unresectable non-small-cell lung cancer: long-term results of a radiation dose escalation study. *Int J Radiat Oncol Biol Phys* 2005; **63**: 324–33. doi: [10.1016/j.ijrobp.2005.02.010](https://doi.org/10.1016/j.ijrobp.2005.02.010)
7. Bradley J, Graham MV, Winter K, Purdy JA, Komaki R, Roa WH, et al. Toxicity and outcome results of RTOG 9311: a phase I-II dose-escalation study using three-dimensional conformal radiotherapy in patients with inoperable non-small-cell lung carcinoma. *Int J Radiat Oncol Biol Phys* 2005; **61**: 318–28. doi: [10.1016/j.ijrobp.2004.06.260](https://doi.org/10.1016/j.ijrobp.2004.06.260)
8. Belderbos JS, Heemsbergen WD, De Jaeger K, Baas P, Lebesque JV. Final results of a phase I/II dose escalation trial in non-small-cell lung cancer using three-dimensional conformal radiotherapy. *Int J Radiat Oncol Biol Phys* 2006; **66**: 126–34. doi: [10.1016/j.ijrobp.2006.04.034](https://doi.org/10.1016/j.ijrobp.2006.04.034)
9. Chi A, Liao Z, Nguyen NP, Xu J, Welsh JS, Jang SY, et al. Dosimetric selection for helical tomotherapy based stereotactic ablative radiotherapy for early-stage non-small cell lung cancer or lung metastases. *PLoS One* 2012; **7**: e35809. doi: [10.1371/journal.pone.0035809](https://doi.org/10.1371/journal.pone.0035809)
10. Lim G, Bezjak A, Higgins J, Moseley D, Hope AJ, Sun A, et al. Tumor regression and positional changes in non-small cell lung cancer during radical radiotherapy. *J Thorac Oncol* 2011; **6**: 531–6. doi: [10.1097/JTO.0b013e31820b8a52](https://doi.org/10.1097/JTO.0b013e31820b8a52)
11. Woodford C, Yartsev S, Dar AR, Bauman G, Van Dyk J. Adaptive radiotherapy planning on decreasing gross tumor volumes as seen on megavoltage computed tomography images. *Int J Radiat Oncol Biol Phys* 2007; **69**: 1316–22. doi: [10.1016/j.ijrobp.2007.07.2369](https://doi.org/10.1016/j.ijrobp.2007.07.2369)

12. Yee D, Rathee S, Robinson D, Murray B. Temporal lung tumor volume changes in small-cell lung cancer patients undergoing chemoradiotherapy. *Int J Radiat Oncol Biol Phys* 2011; **80**: 142–7. doi: [10.1016/j.ijrobp.2010.01.056](https://doi.org/10.1016/j.ijrobp.2010.01.056)
13. Siker ML, Tomé WA, Mehta MP. Tumor volume changes on serial imaging with megavoltage CT for non-small-cell lung cancer during intensity-modulated radiotherapy: how reliable, consistent, and meaningful is the effect? *Int J Radiat Oncol Biol Phys* 2006; **66**: 135–41. doi: [10.1016/j.ijrobp.2006.03.064](https://doi.org/10.1016/j.ijrobp.2006.03.064)
14. van Elmpt W, Ollers M, van Herwijnen H, den Holder L, Vercoulen L, Wouters M, et al. Volume or position changes of primary lung tumor during (chemo-)radiotherapy cannot be used as a surrogate for mediastinal lymph node changes: the case for optimal mediastinal lymph node imaging during radiotherapy. *Int J Radiat Oncol Biol Phys* 2011; **79**: 89–95. doi: [10.1016/j.ijrobp.2009.10.059](https://doi.org/10.1016/j.ijrobp.2009.10.059)
15. Bosmans G, van Baardwijk A, Dekker A, Ollers M, Wanders S, Boersma L, et al. Time trends in nodal volumes and motion during radiotherapy for patients with stage III non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2008; **71**: 139–44. doi: [10.1016/j.ijrobp.2007.08.071](https://doi.org/10.1016/j.ijrobp.2007.08.071)