Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/rpor

Original research article

Tracking, gating, free-breathing, which technique to use for lung stereotactic treatments? A dosimetric comparison

Jessica Prunaretty, Pierre Boisselier, Norbert Aillères, Olivier Riou, Sebastien Simeon, Ludovic Bedos, David Azria, Pascal Fenoglietto*

Institut du Cancer de Montpellier (ICM), Montpellier, France

ARTICLE INFO

Article history:
Received 6 April 2018
Received in revised form
4 September 2018
Accepted 10 November 2018
Available online 24 November 2018

Keywords:
Tracking
Gating
Free-breathing
Lung SBRT
Dosimetric comparison

ABSTRACT

Background: The management of breath-induced tumor motion is a major challenge for lung stereotactic body radiation therapy (SBRT). Three techniques are currently available for these treatments: tracking (T), gating (G) and free-breathing (FB).

Aim: To evaluate the dosimetric differences between these three treatment techniques for lung SBRT.

Materials and methods: Pretreatment 4DCT data were acquired for 10 patients and sorted into 10 phases of a breathing cycle, such as 0% and 50% phases defined respectively as the inhalation and exhalation maximum. GTV_{ph}, PTV_{ph} (=GTV_{ph} + 3 mm) and the ipsilateral lung were contoured on each phase.

For the tracking technique, 9 fixed fields were adjusted to each PTV_{ph} for the 10 phases. The gating technique was studied with 3 exhalation phases (40%, 50% and 60%). For the free-breathing technique, ITV_{FB} was created from a sum of all GTV_{ph} and a 3 mm margin was added to define a PTV_{FB}. Fields were adjusted to PTV_{FB} and dose distributions were calculated on the average intensity projection (AIP) CT. Then, the beam arrangement with the same monitor units was planned on each CT phase.

The 3 modalities were evaluated using DVHs of each GTV_{ph}, the homogeneity index and the volume of the ipsilateral lung receiving 20 Gy (V_{20Gy}).

Results: The FB system improved the target coverage by increasing D_{mean} ($75.87_{(T)}$–$76.08_{(G)}$–$77.49_{(FB)}$ Gy). Target coverage was slightly more homogeneous, too (HI: $0.17_{(T\text{ and }G)}$–$0.15_{(FB)}$). But the lung was better protected with the tracking system (V_{20Gy}: $3.82_{(T)}$–$4.96_{(G)}$–$6.34_{(FB)}$ %).

Conclusions: Every technique provides plans with a good target coverage and lung protection. While irradiation with free-breathing increases doses to GTV, irradiation with the tracking technique spares better the lung but can dramatically increase the treatment complexity.

* *Corresponding author at*: Institut du Cancer de Montpellier (ICM), Val d'Aurelle, Service Radiothérapie, 208 avenue des apothicaires, 34298 Montpellier, France. Tel.: +33 467613047.
E-mail address: jessica.prunaretty@icm.unicancer.fr (J. Prunaretty).

https://doi.org/10.1016/j.rpor.2018.11.003

1. Background

Radiation therapy is a reference treatment for non-operable lung cancers. Several studies showed encouraging results with low toxicity rates and a good local control for stereotactic body radiation therapy (SBRT).[1–4] With an ablative dose delivered in a few fractions, the major challenge of SBRT now is the management of breath-induced tumor motion. The average tumor motion in the superoinferior direction was shown to be up to 1 cm, especially for the lesions localized in the lower lobe.[5–8] Seppenwoolde et al.[5] studied the lesion trajectory using dual real-time fluoroscopic imaging and a fiducial marker implanted in or near the tumor in 20 patients. In 50% of cases, they reported a hysteresis trajectory from 1 to 5 mm during the inhalation and exhalation phases. From these observations, the report of the American Association of Physicists in Medicine (AAPM) Task group 76[9] recommended the management of respiratory techniques when tumor motion was greater than 5 mm in any direction or when normal tissue sparing was significant. With the improvements of the delivery and imaging techniques, several approaches are now available such as the free-breathing, the gating and the tracking techniques.

The free-breathing technique consists in the irradiation of the tumor for every possible position during the respiratory cycle. A solution to provide accurate information about the movement of the target and of the organs at risk is the use of 4D-computed tomography (4D-CT) developed by Saito et al. in the early 2000s.[10–12] Synchronizing the breathing signal and image datasets, a 3D-CT volume containing a moving structure is imaged over a period of time, creating a dynamic volume dataset.[13,14] An individualized internal target volume (ITV) can be delineated,[15–18] thus minimizing the target margins.

With the gating technique, the irradiation is limited to a specific respiratory phase (called a gate) during which the target motions are reduced. A mask is used to check ventilation and airbags to measure the thoracoabdominal pressure, Ohara et al.[19] were the first team to develop a respiratory gating technique in 1990. In the early 2000s, the technique was improved in particular with the development of real time monitoring free-breathing system.[20–23] For example, Varian Medical System (Palo Alto, USA) developed the Real-time Position management (RPM) system. With a reflective external marker placed on the patient and an infrared tracking camera, the tumor position can be correlated with the patient's respiratory cycle.[24–27]

The last innovative strategy is real time tracking during which the irradiation continuously follows the tumor motion. Murphy et al.[28] described three options to perform this technique in the case of a photon beam. The first is to shift the patient during treatment using a remotely-controlled couch as developed by Bel et al.[29] They demonstrated that the method was technically feasible but the continuous motion of the couch was uncomfortable for the patient. The second option is to compensate for the tumor motion with a dynamic multileaf collimator (DMLC) as proposed by Keall et al.[30] in 2001. Several studies investigated this strategy[31–36] and Poulsen et al.[37] were the first to perform an in-vivo DMLC tracking in a porcine model on a linear accelerator. This technique is not used clinically for lung lesions yet. Tumor motion can be compensated with a third option using a robotically-mounted lightweight linear accelerator as investigated by Schweikard et al.[38] With the development of the Synchrony Respiratory Tracking System, the Cyberknife (Accuray Incorporated, Sunnyvale, CA) is the first of these robotic linear accelerators to be coupled with an imaging system through a real-time control loop to monitor the tumor position following the external surrogate.[39] It can be used either with implanted markers[40–42] or with the fiducial-free Xsight Lung Tracking System.[43,44]

The purpose of the present work was to compare these three techniques and their dosimetric advantages.

2. Materials and methods

The study was conducted in ten patients previously treated with a linac-based SBRT. They were selected if they presented an amplitude of target motion larger than 5 mm (AAPM recommendations [9]). All patients had one lesion distant from the organs at risk.

Patient's positioning was performed with a personalized foam in a supine position with both arms raised. 4D-CT datasets (CT-General Electric) were acquired for each patient with a 2.5 mm spacing and using a respiratory positioning management device (RPM, Varian Medical Systems, Palo Alto, CA). The images were split into 10 phases during the breathing cycle such that the 0% and 50% phases defined the maximum inhalation and exhalation, respectively. Datasets were then imported into the Eclipse Treatment Planning System (Varian Medical Systems, Palo Alto, CA). For each treatment plan, a 3D conformal SBRT with 9 coplanar fields was used. The dose distributions were calculated using an anisotropic analytical algorithm (AAA, v10.0.28, Varian Medical Systems, Helsinki, Finland) on a Novalis TrueBeam STx linear accelerator equipped with a Varian High Definition 120 multileaf-collimator (MLC). The prescribed dose was 60 Gy in 4 fractions. Treatment plans were normalized such that 99% of the prescribed dose covered at least 99% of the planning target volume (PTV), as clinically used in the department, and such that it respected dose constraints of the ROSEL study (dose and quality indexes).[45]

For each patient, the free-breathing technique (FB), which is the standard in our institution, was compared with the gating (G) and tracking (T) techniques (Fig. 1).

For the free-breathing technique, a GTV_{ph} was delineated on each breathing phase CT. An internal target volume (ITV_{FB}) was created from the sum of the 10 GTV_{ph} delineated. Three millimeter margin was added to the ITV_{FB} to define a PTV_{FB}. The 3D conformal SBRT with 9 fields was adjusted to the PTV_{FB} and the dose distribution was calculated on the average intensity projection (AIP) CT images as recommended by Tian et al.[46] When the treatment plan was considered satisfactory (*i.e.* when all constraints of the ROSEL study[45] were respected), the beam arrangement with the same MLC shape was transferred to all respiratory phases. The monitor units were divided by the number of the phases for each plan.

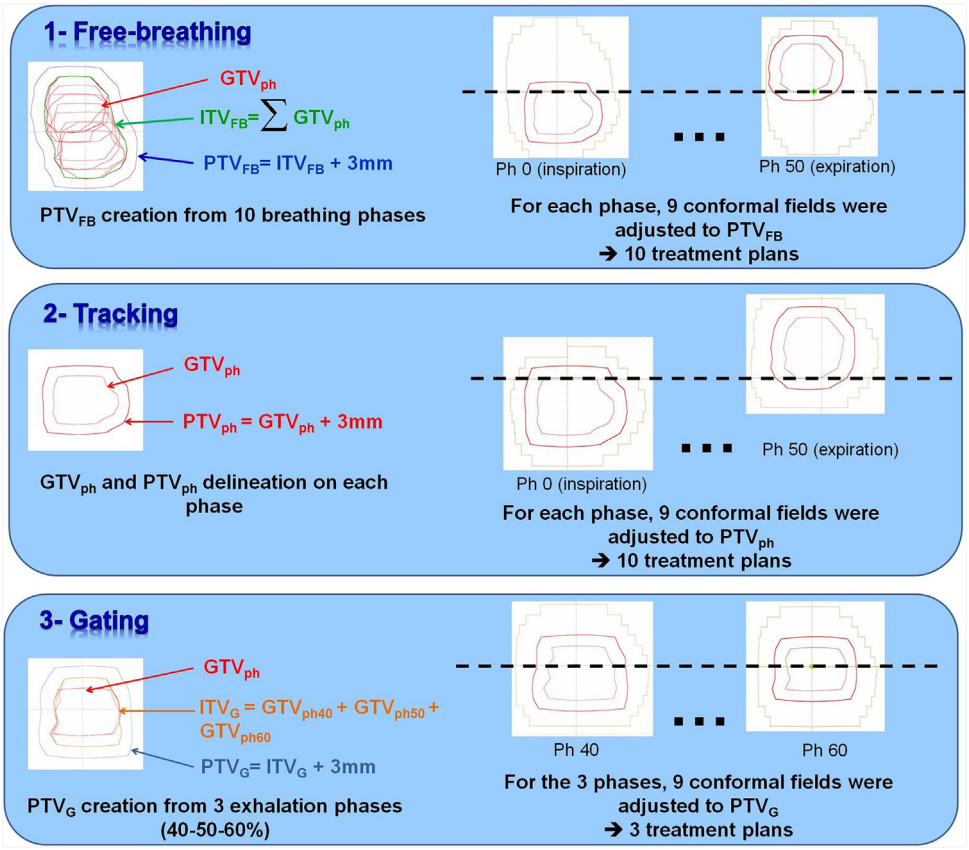

Fig. 1 – Description of the analysis process for the comparison of the free-breathing, tracking and gating techniques.

The gating technique was analyzed during 3 exhalation phases (40%, 50% and 60% phases) because of a smaller residual motion and a higher duty cycle. An ITV_G was created from the sum of the GTV_{ph40}, GTV_{ph50} and GTV_{ph60}. A 3 mm-margin was added to the ITV_G to generate the PTV_G. The 9 fields were adjusted to the PTV_G and the dose distribution was calculated on the AIP CT images of the 40%, 50% and 60% phases. The same planning parameters with the divided monitor units were reported on the 3 individual respiratory phases.

For the tracking technique, a treatment plan with 9 static fields was adjusted to each PTV_{ph} corresponding to the studied breathing phase. Consequently, 10 treatment plans were created and analyzed.

The nonrigid registration between the respiratory phases was not used because 3D doses to the GTV are a good approximation of the 4D dose calculations according to the Guckenberger et al.[47] Moreover, they showed minor differences for the doses to the GTV and the lung throughout the respiratory phases. Thus, for each technique, the dose volume histograms (DVH) of each GTV_{ph} and the ipsilateral lung were averaged and evaluated. Dosimetric parameter, such as the mean dose D_{mean} for GTV_{ph}, was identified. The volume of the ipsilateral lung receiving 20 Gy (V_{20Gy}) was investigated, too. Furthermore, the dose homogeneity within the GTV_{ph} was analyzed using the homogeneity index (HI). The HI was defined as the ratio of the difference between the maximum and minimum doses to the mean dose for the target volume:

$$HI = \frac{D_{max} - D_{min}}{D_{mean}} \quad (A)$$

For a homogeneous treatment plan, HI approached 0.

3. Results

Three tumors were located in the left lung and 7 in the right one. The mean gross tumor volume (GTV) was 2.71 cm^3 [range 0.19–8.53 cm^3]. The mean motion in the superoinferior direction was 0.93 cm [range 0.51–1.56 cm]. Patients were divided in two groups according to the target motion with a cut off value of 1 cm. Patient characteristics are summarized in Table 1.

The PTV volume was evaluated for each technique (PTV_{FB}, PTV_G and PTV_T) and for each patient (Table 2). The PTV_{FB} was the highest one with a mean of $12.43 \pm 9.35\ cm^3$ compared with a PTV_G and a PTV_T of $8.11 \pm 6.9\ cm^3$ and $6.85 \pm 6.0\ cm^3$, respectively.

The global DVHs for the GTV_{ph} and the ipsilateral lung are shown in Fig. 2.

Mean doses (D_{mean}) received by the target volume, and the HI are summarized in Table 3. The target motion had no significant impact on the GTV coverage. More precisely, the FB technique increased the D_{mean} of the GTV by 1.65 Gy (1.52 Gy

Table 1 – Patient characteristics.

Patient number	Tumor position	Volume GTV_{ph} (cm^3)		Motion SI (cm)
		Mean	SD	
1	LML	0.19	0.06	0.51
2	RLL	0.57	0.14	0.54
3	RLL	0.37	0.16	0.58
4	RLL	1.60	0.14	0.62
5	RML	8.53	1.06	0.86
6	RLL	8.05	1.20	1.00
7	LLL	1.22	0.27	1.08
8	RML	3.70	0.82	1.17
9	RLL	2.18	0.37	1.42
10	LLL	0.72	0.11	1.56

GTV: gross tumor volume; SD: standard deviation; SI: superoinferior direction; RML: right middle lobe; LLL: left lower lobe; RLL: right lower lobe; LML: left middle lobe.

Table 2 – Planning target volumes (PTV_{FB}, PTV_G and PTV_T) for the three techniques for each patient.

Patient number	PTV volume (cm^3)		
	FB	T	G
1	2.66	1.38	1.8
2	4.41	2.57	2.58
3	4.47	2.14	3.03
4	7.83	5	5.11
5	27.79	17.3	20.44
6	27.61	17.19	19.4
7	9.14	4.33	4.95
8	19.2	9.91	12.49
9	13.12	6.01	6.61
10	8.08	2.64	4.65
Mean ± SD	**12.43 ± 9.35**	**6.85 ± 6.0**	**8.11 ± 6.90**

PTV: planning target volume; FB: free-breathing technique; T: tracking technique; G: gating technique.

for motion <1 cm, 1.77 Gy otherwise) compared with the T technique. The gating technique provided similar D_{mean} as the tracking one. Also, the dose to GTV was slightly more homogeneous with the FB technique (0.15 ± 0.04).

The dose to the ipsilateral lung is shown in Table 4. The volume of the lung receiving 20 Gy (V_{20Gy}) was always lower than 10% and, consequently, respected the ROSEL constraints. Nevertheless, the lung was more protected with the tracking technique. Considering the FB to be the reference technique, the decrease with the T technique was 34% when the target motion was inferior to 1 cm and 44% when the motion was larger. Concerning the G technique, V_{20Gy} was lower by 17.5% (motion ≤ 1 cm) and 33% than the FB technique.

4. Discussion

In this study, all treatment plans respected the ROSEL study constraints and were clinically viable whatever the technique used.

Our study shows that the free-breathing technique increased the target coverage with a higher reported D_{mean} whatever the target motion. This difference may be due to a bigger PTV_{FB} compared with the PTV_G and PTV_T. Indeed, the PTV volume was increased by 45% and 35% compared with the PTV_T and PTV_G, respectively. This ratio was consistent with the one published by Underberg et al.[48] In their study, they evaluated the reduction between the gating volume (derived from the ITV generated from three consecutive expiration phases with a 3-mm margin) and a volume with a standard margin (derived from the addition of a 10-mm margin to the most central GTVs in the three phases selected for the gating technique) and found it to be 33.3%. Yet, the more important the PTV_{FB} volumes were, the larger the beam apertures, and if the build-up was reached easily, the dose profiles were flattened. The doses within the GTV were thus higher and more homogeneous. As regards the distribution homogeneity, a slightly stronger homogeneity was observed

Table 3 – Mean doses received by the GTV. and HI of the GTV.

Patient number	D_{mean} (Gy)			HI		
	FB	T	G	FB	T	G
1	81.54	78.01	78.24	0.11	0.13	0.17
2	77.82	76.49	77.89	0.16	0.19	0.18
3	79.67	77.66	75.9	0.11	0.14	0.17
4	77.64	76.23	76.71	0.2	0.2	0.19
5	76.8	77.73	77.33	0.16	0.18	0.2
6	77.96	76.8	76.97	0.2	0.23	0.21
7	73.97	71.82	73.57	0.08	0.11	0.11
8	74.85	73.54	73.61	0.13	0.15	0.14
9	79.02	76.47	74.84	0.16	0.18	0.13
10	75.64	73.97	75.76	0.15	0.17	0.16
M < 1 cm						
Mean ± SD	**78.70 ± 1.90**	**77.22 ± 0.80**	**77.21 ± 0.94**	**0.15 ± 0.04**	**0.17 ± 0.03**	**0.18 ± 0.01**
M ≥ 1 cm						
Mean ± SD	**76.29 ± 2.13**	**74.52 ± 2.09**	**74.95 ± 1.45**	**0.14 ± 0.04**	**0.17 ± 0.04**	**0.15 ± 0.04**

M: motion.

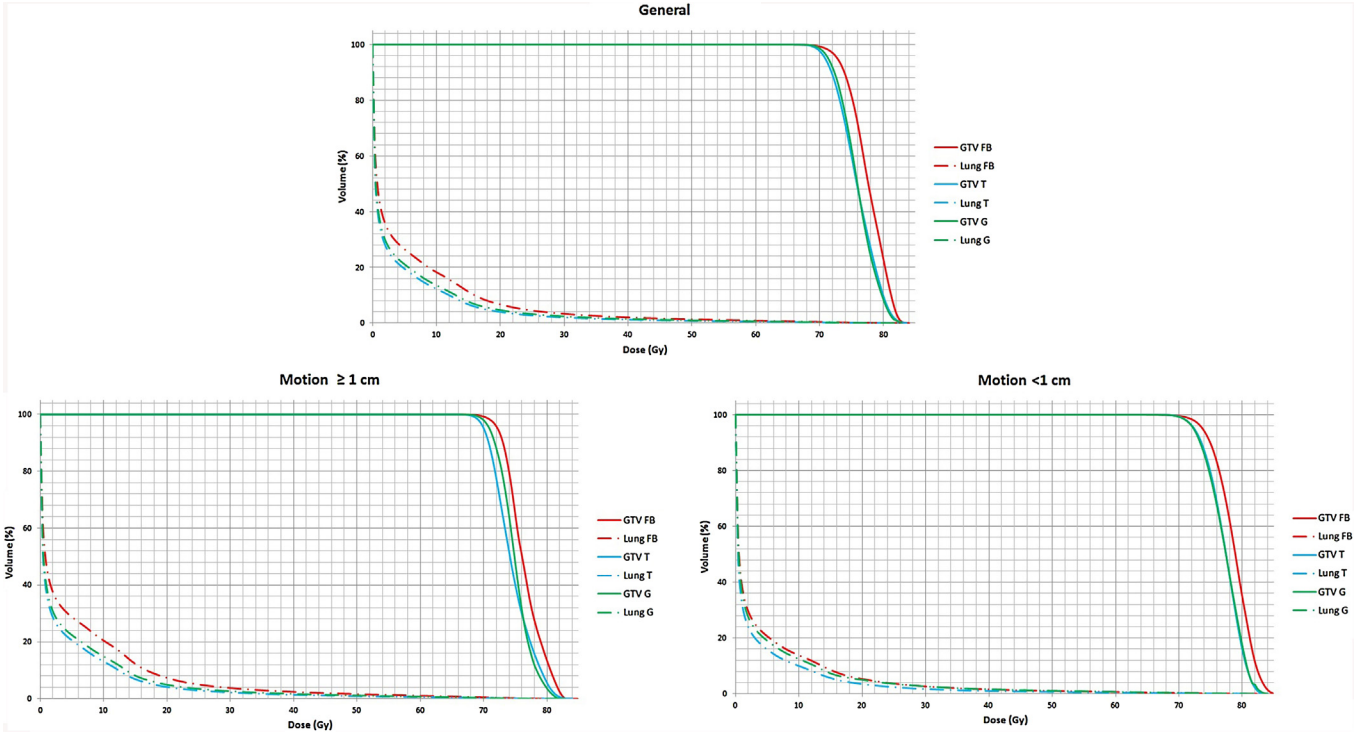

Fig. 2 – Dose volume histograms comparing the gross tumor volume (GTV), the planning tumor volume (PTV) and the normal lung volume for the free-breathing (FB), tracking (T) and gating (G) techniques.

Table 4 – V_{20Gy} received by the ipsilateral lung.

Patient number	V_{20Gy} (%)		
	FB	T	G
1	3.58	1.95	2.72
2	3.15	1.96	1.54
3	2.86	1.63	3.24
4	8.67	6.32	7.09
5	8.31	5.63	7.35
6	8.97	6.35	6.83
7	4.82	2.86	4.10
8	7.59	4.21	5.04
9	8.79	4.61	6.18
10	6.64	2.66	2.51
M < 1 cm			
Mean ± SD	**5.32 ± 2.91**	**3.50 ± 2.28**	**4.39 ± 2.66**
M ≥ 1 cm			
Mean ± SD	**7.36 ± 1.70**	**4.14 ± 1.50**	**4.93 ± 1.71**

M: motion.

for the free-breathing technique. Ding et al.[49] reached the same conclusion comparing the dosimetric characteristics of the Cyberknife and of the conventional linac-based SBRT with a 4D dose calculation methodology. Moreover, this homogeneity gap was increased by the use of unflattened beams with the Cyberknife technique.

The tracking and gating techniques provided a better protection of the lung with a correlation with the target motion. Our V_{20Gy} results were of the same order of magnitude as those of the Ding et al. study.[49] Thus, they had no statistically significant difference between free-breathing and tracking. This similarity may be due to the use of an abdominal compression which limited target motion. Several teams reported these results with more modest benefits according to the target motion and location.[48–52] Radiation pneumonitis is the main risk of complication in lung SBRT. Most studies found a correlation between the pulmonary toxicities and the dosimetric parameters, especially with V_{20Gy}.[53–55] However, there was no clear conclusion when V_{20Gy} was below 10%. For example, in the Mahowald et al. study,[56] the rate of grade 2/3 radiation pneumonitis was 4.5% when the ROSEL constraints were respected *versus* 21% in the contrary cases. But no conclusion was drawn regarding the V_{20Gy} reported much lower than 10%.

Treatment time is another parameter which should be taken into account for lung SBRT. Indeed, Fox et al.[57] showed the time required for a gated 3D treatment was 5.5 times longer than without gating. Yet, an increase of the treatment duration may lead to intra-fraction motions[58] and shifts in the patient's position.[59] As regards the tracking system, Chan et al.[60] compared the Cyberknife (with real-time tracking) and the VMAT (with 4D cone beam computed tomography) with 4D dose calculations. Among other dosimetric parameters, they showed that the beam-on time for Cyberknife was 22.3 min compared with 10.8 min for VMAT.

Our study showed the advantages and disadvantages of each of the three, free-breathing, tracking, and gating, techniques regarding the dosimetric parameters. However, the complexity of each technique should be taken into account, too. Indeed, the gating and tracking techniques are more complex than the free-breathing technique and could result in additional potential errors. Muirhead et al.[61] compared the potential clinical benefit of respiratory gated radiotherapy from continuous irradiation. With some disadvantages, such as the low correlation between internal and external motion, the treatment time, or the choice of the gate (end-inspiration or end-expiration), they concluded that gating should be used when a likely clinical benefit was confirmed. Concerning the tracking technique, all patients are not eligible. Indeed, the tracking modality currently needs fiducials implanted during a transthoracic intervention. The transthoracic needle biopsy is not without a risk and leads to a 20% average of pneumothorax.[62] Without these markers, the tumor can be tracked statically using spine for alignment. But, in this case, Descovich et al.[63] demonstrated that a uniform margin of 4.5 mm around the ITV was necessary to ensure a 95% target coverage for 95% of the fractions included in the analysis. For James et al.,[64] the set-up margin should be 10 mm. Consequently, for these patients, the tracking interest could be put into question.

5. Conclusions

The free-breathing, tracking and gating techniques all provided acceptable treatment plans with good target coverage and healthy lung protection. While an irradiation with the free-breathing technique increases doses to GTV, an irradiation with the tracking system better spares the lung but can dramatically increase the treatment complexity.

Author's contributions

JP is a lead author, who designed the study and performed treatment planning, collected and analyzed data, interpreted data, revised literature and drafted the manuscript. PF participated in the study design, discussion and interpretation of data and revised the manuscript critically. All authors read and approved the final manuscript.

Conflict of interest

None declared.

Financial disclosure

None declared.

REFERENCES

1. Timmerman R, Papiez L, McGarry R, et al. Extracranial stereotactic radioablation: results of a phase I study in medically inoperable stage I non-small cell lung cancer patients. *Chest* 2003;**124**(5):1946–55.
2. Nagata Y, Negoro Y, Aoki T, et al. Clinical outcomes of 3D conformal hypofractionated single high-dose radiotherapy for one or two lung tumors using a stereotactic body frame. *Int J Radiat Oncol Biol Phys* 2002;**52**:1041–6.

3. Hof H, Herfath K, Münter M, et al. Stereotactic single-dose radiotherapy of stage i non-small-cell lung cancer (Nsclc). *Int J Radiat Oncol Biol Phys* 2003;**56**:335–41.
4. Wulf J, Haedinger U, Oppitz U, Thiele W, Mueller G, Flentje M. Stereotactic radiotherapy for primary lung cancer and pulmonary metastases: a noninvasive treatment approach in medcally inoperable patients. *Int J Radiat Oncol Biol Phys* 2004;**60**(1):186–96.
5. Seppenwoolde Y, Shirato H, Kitamura K, et al. Precise and real-time measurement of 3D tumor motion due to breathing and heartbeat, measured during radiotherapy. *Int J Radiat Oncol Biol Phys* 2002;**53**:822–34.
6. Stevens CW, Munden RF, Forster KM, et al. Respiratory-driven lung tumor motion is independent of tumor size, tumor location, and pulmonary function. *Int J Radiat Oncol Biol Phys* 2001;**51**:62–8.
7. Liu HH, Balter P, Tutt T, et al. Assessing respiration-induced tumor motion and internal target volume using four-dimensional computed tomography for radiotherapy lung cancer. *Int J Radiat Oncol Biol Phys* 2007;**68**(2):531–40.
8. Barnes E, Murray B, Robinson D, Underwood L, Hanson J, Roa W. Dosimetric evaluation of lung tumor immobilization using breath hold at deep inspiration. *Int J Radiat Oncol Biol Phys* 2001;**50**(4):1091–8.
9. *AAPM report 91. The management of respiratory motion in radiation oncology*; 2006.
10. Saito Y, Aradate H, Miyazaki H, Igarashi K, Ide H. Development of a large area 2-dimensional detector for real-time 3-dimensional CT (4D-CT). *Radiology* 2000; **217**:405.
11. Saito Y, Aradate H, Miyazaki H, Igarashi K, Ide H. Large area two-dimensional detector system for real-time three-dimensional CT (4D CT). *Proc SPIE Med Imag Conf* 2001;**4320**:775–82.
12. Saito Y, Aradate H, Miyazaki H, et al. Development and evaluations of a real-time three-dimensional CT (4D-CT) scanner. *Proc SPIE Med Imag Conf* 2002;**4682**:801–8.
13. Keall PJ, Starkschall G, Shukla H, et al. Acquiring 4D thoracic CT scans using a multislice helical method. *Phys Med Biol* 2004;**49**:2053–67.
14. Vedam SS, Keall PJ, Kini VR, Mostafavi H, Shukla H, Mohan R. Acquiring a four-dimensional computed tomography dataset using an external respiratory signal. *Phys Med Biol* 2003;**48**(1):45–62.
15. Rietzel E, Chen GT, Doppke KP, Pan T, Choi NC, Willett CG. 4D computed tomography for treatment planning. *Int J Radiat Oncol Biol Phys* 2003;**57**(Suppl 2):S232–3.
16. Rietzel E, Liu AK, Doppke KP, et al. Design of 4D treatment planning target volumes. *Int J Radiat Oncol Biol Phys* 2006;**66**:287–95.
17. Underberg R, Lagerwaard F, Cuijpers J, Slotman B, van Sörnsen de Koste J, Senan S. Four-dimensional CT scans for treatment planning in stereotactic radiotherapy for stage I lung cancer. *Int J Radiat Oncol Biol Phys* 2004;**60**:1283–90.
18. Underberg R, Lagerwaard F, Slotman B, Cuijpers J, Senan S. Use of maximum intensity projections (MIP) for target volume generation in 4DCT scans for lung cancer. *Int J Radiat Oncol Biol Phys* 2005;**63**(1):253–60.
19. Ohara K, Okumura T, Akisada M, et al. Irradiation synchronized with respiration gate. *Int J Radiat Oncol Biol Phys* 1989;**17**:853–7.
20. Kubo HD, Hill BC. Respiration gated radiotherapy treatment: a technical study. *Phys Med Biol* 1996;**41**(1):83–91.
21. Keall PJ, Kini VR, Vedam SS, Moham R. Potential radiotherapy improvements with respiratory gating. *Australas Phys Eng Sci Med* 2002;**25**:1–6.
22. Minohara S, Kanai T, Endo M, Noda K, Kanazawa M. Respiratory gated irradiation system for heavy-ion radiotherapy. *Int J Radiat Oncol Biol Phys* 2000;**47**:1097–103.
23. Vedam SS, Keall PJ, Kini VR, Mohan R. Determining parameters for respiration-gated radiotherapy. *Med Phys* 2001;**28**:2139–46.
24. Ford EC, Mageras GS, Yorke E, Rosenzweig KE, Wagman R, Ling CC. Evaluation of respiratory movement during gated radiotherapy using film and electronic portal imaging. *Int J Radiat Oncol Biol Phys* 2002;**52**(2):522–31.
25. Vedam SS, Kini VR, Keall PJ, Ramakrishnan V, Mostafavi H, Mohan R. Quantifying the predictability of diaphragm motion during respiration with a noninvasive external marker. *Med Phys* 2003;**30**:505–13.
26. Hu W, Xu A, Li G, Zhang Z. A real time respiration position based passive breath gating equipment for gated radiotherapy: a preclinical evaluation. *Med Phys* 2012;**39**(3):1345–50.
27. Ramsey CR, Scaperoth D, Arwood D. Clinical experience with a commercial respiratory gating system. *Int J Radiat Oncol Biol Phys* 2000;**48**:164–5.
28. Murphy MJ. Tracking moving organs in real time. *Semin Radiat Oncol* 2004;**14**(1):91–100.
29. Bel A, Petrascu O, Van de Vondel I, et al. A computerized remote table control for fast on-line patient repositioning: implementation and clinical feasibility. *Med Phys* 2000;**27**:354–8.
30. Keall PJ, Kini VR, Vedam SS, Moham R. Motion adaptive X-ray therapy: a feasibility study. *Phys Med Biol* 2001;**46**(1):1–10.
31. Jiang S. Synchronized moving aperture radiation therapy (SMART): treatment planning using 4D CT data. In: *Proceedings of the 14th International Conference on the Use of Computers in Radiation Therapy*. 2004.
32. Neicu T, Shirato H, Seppenwoolde Y, Jiang SB. Synchronized moving aperture radiation therapy (SMART): average tumour trajectory for lung patients. *Phys Med Biol* 2003;**48**(5):587–98.
33. Sawant A, Venkat R, Srivastava V, et al. Management of three-dimensional intra-fraction motion through real-time DMLC tracking. *Med Phys* 2008;**35**:2050–61.
34. Tacke M, Nill S, Krauss A, Oelfke U. Real-time tumor tracking: automatic compensation of target motion the Siemens MLC. *Med Phys* 2010;**160**(37):753–61.
35. Davies GA, Clowes P, Bedford JL, Evans PM, Webb S, Poludniowski G. An experimental evaluation of the agility MLC for motion-compensated VMAT delivery. *Phys Med Biol* 2013;**58**:4643–50.
36. Ge Y, O'Brien RT, Shieh CC, Booth JT, Keall PJ. Toward the development of intrafraction deformation tracking using a dynamic multi-leaf collimator. *Med Phys* 2014;**41.**(6).
37. Poulsen PR, Carl J, Nielsen J, et al. Megavoltage image-based dynamic multileaf collimator tracking of a niti stent in porcine lungs on a linear accelerator. *Int J Radiat Oncol Biol Phys* 2012;**82**(2):321–7.
38. Schweikard A, Bodduluri M, Adler JR. Planning for camera-guided robotic radiosurgery. *IEEE Trans Robot Autom* 1998;**14**:951–62.
39. Schweikard A, Glosser G, Bodduluri M, Murphy MJ, Adler JR. Robotic motion compensation for respiratory movement during radiosurgery. *Comput Aided Surg* 2000;**5**:263–77.
40. Collins B, Erickson K, Reichner CA, et al. Radical stereotactic radiosurgery with real-time tumor motion tracking in the treatment of small peripheral lung tumors. *Radiat Oncol* 2007;**2**:39.
41. Sayeh S, Wang J, Main WT, Kilby W, Maurer Jr CR. Respiratory motion tracking for robotic radiosurgery. *Robot Radiosurg* 2007:15–29.

42. Karaman K, Dokdok AM, Karadeniz O, Ceylan C, Engin K. Intravascular placement of metallic coils as lung tumor markers for cyberknife stereotactic radiation therapy. *Korean J Radiol* 2015;**16**(3):626–31.
43. Bibault JE, Prevost B, Dansin E, Mirabal X, Larcornerie T, Lartigau E. Image-guided robotic stereotactic radiation theraoy with fiducial-free tumor tracking for lung cancer. *Radiat Oncol* 2012;**7**:102.
44. Fu D, Kahn R, Wang B, et al. Fiducial-free lung tumor tracking for CyberKnife radiosurgery. *Int J Radiat Oncol Biol Phys* 2008;**72**(1):S608–9.
45. Hurkmans CW, Cuijpers JP, Lagerwaard FJ, et al. Recommendations for implementing stereotactic radiotherapy in peripheral stage IA non-small cell lung cancer: report from the Quality Assurance Working Party of the randomized phase III ROSEL study. *Radiat Oncol* 2009;**4**:1.
46. Tian Y, Wang Z, Ge H, et al. Dosimetric comparison of treatment plans based on free breathing, maximum, and average intensity projection CTs for lung cancer SBRT. *Med Phys* 2012;**39**(5).
47. Guckenberger M, Wilbert J, Krieger T, et al. Four-dimensional treatment planning for stereotactic body radiotherapy. *Int J Radiat Oncol Biol Phys* 2007;**69**(1):276–85.
48. Underberg RW, Lagerwaard FJ, Slotman BJ, Cuijpers JP, Senan S. Benefit of respiration-gated stereotactic radiotherapy for stage I lung cancer: an analysis of 4DCT datasets. *Int J Radiat Oncol Biol Phys* 2005;**62**(2):554–60.
49. Ding C, Chang CH, Haslam J, Timmermann R, Solberg T. A dosimetric comparison of stereotactic body radiation therapy techniques for lung cancer: robotic versus conventional linac-based systems. *J Appl Clin Med Phys* 2010;**11**(3): 212–24.
50. Ehrbar S, Jöhl A, Tartas A, et al. ITV, mid-ventilation, gating or couch tracking – a comparsion of respiratory motion management techniques based on 4D dose calculations. *Radiother Oncol* 2017;**124**(1):80–8.
51. Jang SS, Huh GJ, Park SY, Yang PS, Cho EY. The impact of respiratory gating on lung dosimetry in stereotactic body radiotherapy for lung cancer. *Phys Med* 2014;**30**(6):682–9.
52. Kim J, Wu Q, Zhao B, et al. To gate or not to gate – dosimetric evaluation comparing Gated vs ITV-based methodologies in stereotactic ablative body radiotherapy (SABR) treatment of lung cancer. *Radiat Oncol* 2016;**11**:125.
53. Owen D, Olivier KR, Mayo CS, et al. Outcomes of stereotactic body radiotherapy (SBRT) treatment of multiple synchronous and recurrent lung nodules. *Radiat Oncol* 2015;**10**:43.
54. Baker R, Han G, Sarangkasiri S, et al. Clinical and dosimetric predictors of radiation pneumonitis in a large series of patients treated with stereotactic body radiation therapy to the lung. *Int J Radiat Oncol Biol Phys* 2013;**85**(1):190–5.
55. Zhang XJ, Sun JG, Sun J, et al. Prediction of radiation pneumonitis in lung cancer patients: a systematic review. *J Cancer Res Clin Oncol* 2012;**138**:2103–16.
56. Mahowald GK, DeWeese T, Olsen J, et al. Clinical and dosimetric factors predicting for radiation pneumonitis following Lung SBRT. *Int J Radiat Oncol Biol Phys* 2011;**81**(2):S167.
57. Fox T, Simon EL, Elder E, Riffenburgh RH, Johnstone PA. Free breathing gated delivery (FBGD) of lung radiation therapy: analysis of factors affecting patient throughput. *Lung Cancer* 2007;**56**(1):69–75.
58. Korreman S, Juhler-Nottrup T, Boyer AL. Respiratory gated beam delivery cannot facilitate margin reduction, unless combined with respiratory correlated image guidance. *Radiother Oncol* 2008;**86**:61–8.
59. Purdie TG, Bissonnette JP, Franks K, et al. Cone-beam computed tomography for on-line image guidance of lung stereotactic radiotherapy: localization, verification, and intrafraction tumor motion. *Int J Radiat Oncol Biol Phys* 2007;**68**:243–52.
60. Chan M, Kwong DL, Law GM, et al. Dosimetric evaluation of four-dimensional dose distributions of Cyberknife and volumetric-modulated arc radiotherapy in stereotactic body lung radiotherapy. *J Appl Clin Med Phys* 2013;**14**(4):136–49.
61. Muirhead R, Featherstone C, Duffton A, Moore K, McNee S. The potential clinical benefit of respiratory gated radiotherapy (RGRT) in non-small cell lung cancer (NSCLC). *Radiat Oncol* 2010;**95**:172–7.
62. Boskovic T, Stanic J, Pena-Karan S, et al. Pneumothorax after transthoracic needle biopsy of lung lesions under CT guidance. *J Thorac Dis* 2014;**6**(1):S99–107.
63. Descovich M, McGuinness C, Kannarunimit D, et al. Comparison between target margins derived from 4DCT scans and real-time tumor motion tracking: insights from lung tumor patients treated with robotic radiosurgery. *Med Phys* 2015;**42**(3):1280–7.
64. James J, Swanson C, Lynch B, Wang B, Dunlap NE. Quantification of planning target volume margin when using a robotic radiosurgery system to treat lung tumors with spine tracking. *Pract Radiat Oncol* 2015;**5**:e337–43.