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Original article

Chest wall pain following lung stereotactic body radiation therapy using 48 Gy in three fractions: A search for predictors

Douleur pariétale après radiothérapie stéréotaxique pulmonaire de 48 Gy en trois fractions : une recherche de prédicteurs

J. Albers[a,*], W. Parker[a,b], J. Kildea[a,b,c], C. Pembroke[d], S. Faria[e]

[a] *Medical Physics Unit, McGill University, 1001, boulevard Décarie, H4A 3J1 Montréal, Québec, Canada*
[b] *Gerald Bronfman Department of Oncology, McGill University, 5100 de Maisonneuve boulevard West, Suite 720, H4A 3T2 Montréal, Québec, Canada*
[c] *Cancer Research Program of the Research Institute of the McGill University Health Centre, 1001, boulevard Décarie, H4A 3J1 Montréal, Québec, Canada*
[d] *Velindre Cancer Centre, Velindre road, CF14 2TL Cardiff, United Kingdom*
[e] *Department of Radiation Oncology, McGill University Health Centre, 1001, boulevard Décarie, H4A 3J1 Montréal, Québec, Canada*

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ABSTRACT

Purpose. – Chest wall pain is an uncommon but bothersome late complication following lung stereotactic body radiation therapy. Despite numerous studies investigating predictors of chest wall pain, no clear consensus has been established for a chest wall constraint. The aim of our study was to investigate factors related to chest wall pain in a homogeneous group of patients treated at our institution.
Patients and methods. – All 122 patients were treated with the same stereotactic body radiation therapy regimen of 48 Gy in three fractions, seen for at least 6 months of follow-up, and planned with heterogeneity correction. Chest wall pain was scored according to the Common Terminology Criteria for Adverse Events classification v3.0. Patient (age, sex, diabetes, osteoporosis), tumour (planning target volume, volume of the overlapping region between planning target volume and chest wall) and chest wall dosimetric parameters (volumes receiving at least 30, 40, and 50 Gy, the minimal doses received by the highest irradiated 1, 2, and 5 cm^3, and maximum dose) were collected. The correlation between chest wall pain (grade 2 or higher) and the different parameters was evaluated using univariate and multivariate logistic regression.
Results. – Median follow-up was 18 months (range: 6–56 months). Twelve patients out of 122 developed chest wall pain of any grade (seven with grade 1, three with grade 2 and two with grade 3 pain). In univariate analysis, only the volume receiving 30 Gy or more ($P = 0.034$) and the volume of the overlapping region between the planning target volume and chest wall ($P = 0.038$) significantly predicted chest wall pain, but these variables were later proved non-significant in multivariate regression.
Conclusion. – Our analysis could not find any correlation between the studied parameters and chest wall pain. Considering our present study and the wide range of differing results from the literature, a reasonable conclusion is that a constraint for chest wall pain is yet to be defined.

Mots clés :
Radiothérapie en conditions stéréotaxiques
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Paroi thoracique
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RÉSUMÉ

Objectif de l'étude. – La douleur de la paroi thoracique est une complication tardive plutôt rare, mais problématique de la radiothérapie stéréotaxique pulmonaire. Malgré de nombreuses études sur les prédicteurs de la douleur pariétale, aucun consensus clair n'a été établi quant à une contrainte dosimétrique pour la paroi thoracique. L'objectif de notre étude était d'analyser les facteurs liés à la douleur pariétale dans un groupe homogène de patients pris en charge dans notre centre.
Patients et méthodes. – Cent-vingt-deux patients ont été pris en charge par une radiothérapie stéréotaxique de 48 Gy en trois fractions planifiée avec une correction d'hétérogénéité et ont été observés pendant

* Corresponding author.
E-mail address: julia.albers@mail.mcgill.ca (J. Albers).

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au moins 6 mois après le traitement. La douleur pariétale a été évaluée selon le Common Terminology Criteria for Adverse Events, version 3.0. Les différents paramètres relatifs aux patients (âge, sexe, diabète, ostéoporose), aux tumeurs (volume cible prévisionnel, volume commun entre le volume cible prévisionnel et la paroi thoracique) et à la dosimétrie de la paroi thoracique (volumes recevant au moins 30 Gy, 40 Gy, ou 50 Gy, et la dose minimale dans le volume de 1, 2 ou 5 cm^3 le plus irradié, et la dose maximale) ont été recueillis. La corrélation entre la douleur pariétale (de grade 2 ou plus) et les différents paramètres a été évaluée en utilisant une régression logistique unifactorielle et multifactorielle.

Résultats. – Le suivi après le traitement médian était de 18 mois (extrêmes : 6–56 mois). Douze des 122 patients ont souffert d'une douleur pariétale (sept de grade 1, trois de grade 2 et deux de grade 3). En analyse unifactorielle, seul le volume recevant 30 Gy ($p = 0{,}034$) et le volume de la région chevauchante entre le volume cible prévisionnel et la paroi thoracique ($p = 0{,}038$) prédisaient significativement la douleur pariétale, mais ces variables se sont révélées plus tard non significatives en régression multifactorielle.

Conclusion. – Notre analyse n'a pas trouvé de corrélation entre les paramètres étudiés et la douleur pariétale. Compte tenu de notre étude actuelle et du large éventail de résultats différents provenant de la littérature, une conclusion raisonnable est qu'une contrainte pour la paroi thoracique doit encore être définie.

1. Introduction

Stereotactic body radiation therapy has emerged as an appropriate alternative to surgical resection for patients with early stage non-small cell lung cancer or oligometastatic lesions to the lung [1]. In fact, local control with stereotactic body radiation therapy has been found to be similar to surgery but with less toxicity, mainly because of its non-invasive nature [2]. Furthermore, numerous single-institutional series and phase II studies investigating lung stereotactic body radiation therapy have demonstrated high local control rates of 70 to 90% with an acceptable risk of severe toxicity of less than 10% [1–5].

However, early reports of lung stereotactic body radiation therapy demonstrated unique toxicity events that have not been previously seen with conventionally fractionated thoracic radiotherapy. In particular, chest wall toxicity, for which symptoms may not be apparent until 6 months after stereotactic body radiation therapy, has been only more recently described with varying incidences [6]. Chest wall toxicity includes a spectrum of clinical findings including rib fracture (symptomatic or asymptomatic), skin changes (from erythema to ulceration) and chest wall pain believed to be neuropathic and unrelated to rib fracture. Despite these known complications, there are no clear dose constraints for the chest wall, particularly related to pain. Bothersome chest wall pain unrelated to rib fracture is an uncommon but important side effect that can occur after lung stereotactic body radiation therapy and that may significantly affect the patient's quality of life. The majority of publications to date on predictors of chest wall pain after stereotactic body radiation therapy have limitations including studies with analysis of a mix of patients treated with different dose and fractionation regimens [7–15], short follow-up times (less than 6 months) that do not account for the latency of toxicity [9,12,13,15–18], analysis of patients treated with stereotactic body irradiation planned without appropriate heterogeneity correction making it impossible to know the true dose received by the chest wall [11–13,16], or analysis of a small cohort of patients (less than 100 cases) [4,13–15,18,19].

In this article, we report on our institutional experience with chest wall pain and the search for dose constraints for the chest wall as an organ at risk in a group of patients treated with stereotactic body irradiation with the same dose and fractionation, with at least 6 months of follow-up, planned with appropriate heterogeneity correction and without any assigned dose constraint to the chest wall at the initial treatment planning.

2. Materials and methods

2.1. Inclusion criteria

Records from patients treated at our institution by stereotactic body irradiation to the thorax due to any peripheral lung tumour (primary or metastatic) between January 2007 and June 2016 were reviewed for this study. Peripheral lung tumours were defined as located beyond 2 cm of the central bronchial tree. Amongst these patients, only those with a clinical follow-up longer than 6 months were considered to account for the latency of chest wall pain onset, which typically is of a median greater than 6 months [6,19]. In addition, in order to ensure a homogenous cohort, only patients that received our institutional "standard" dose for peripheral lesions of 48 Gy in three fractions and planned with heterogeneity correction were included. With these criteria considered, 122 patients treated for 135 lesions were analysed. All patients were planned and treated without contouring the chest wall nor any specific chest wall avoidance criteria. This study was approved by the research ethics board of our institution.

2.2. Treatment planning and delivery

A four-dimensional computed tomography (CT) was acquired (3 mm slice separation) for each patient from which the internal target volume was contoured. The treatment planning was carried out using Eclipse™ (Varian Medical Systems, Palo Alto, CA) treatment planning system with the use of the superposition-convolution algorithm with heterogeneity correction. Patients were treated either with volumetric modulated arc therapy or conventional static fields for which five to seven static fields were used with the multileaf collimators positioned to shape the fields. A free breathing CT was used for dose calculation and contouring of non-target structures. The dose prescription to the planning target volume (defined as the internal target volume with an added 5 mm isotropic margin) and the constraints to the organs at risk were based on the Radiotherapy Oncology Group (RTOG) 0236 protocol [20]. A cone beam CT was acquired prior to each fractionation to verify patient positioning. The treatment planning and delivery characteristics are summarized in Table 1.

Table 1
Study on chest wall pain following lung stereotactic body radiation irradiation: treatment characteristics, constraints and standard procedure.

Planning and treatment parameters	
Dose prescription	48 Gy in three fractions 95% of planning target volume covered by the prescription isodose
Dose planning procedure/calculation algorithm	Eclipse™ (Varian Medical Systems, Palo Alto, CA)/superposition–convolution algorithm with heterogeneity correction
Beam type	6 MV photon
Target volume definition	Internal target volume: drawn from four-dimensional computed tomography using maximum intensity projection protocol Planning target volume: internal target volume with 5 mm isotropic margin
Image-guided radiotherapy	Cone beam computed tomography before each fraction
Dose constraints	
Planning target volume	V48Gy > 95%
Spinal cord	D_{max} < 18 Gy (6 Gy/fraction)
Oesophagus	D_{max} < 27 Gy (9 Gy/fraction)
Heart	D_{max} < 30 Gy (10 Gy/fraction)
Brachial lexus	D_{max} < 24 Gy (8 Gy/fraction)
Both lungs–gross tumour volume	V20Gy < 15%

V*x*Gy: volume receiving *x* Gy or more; Dmax: maximum point dose.

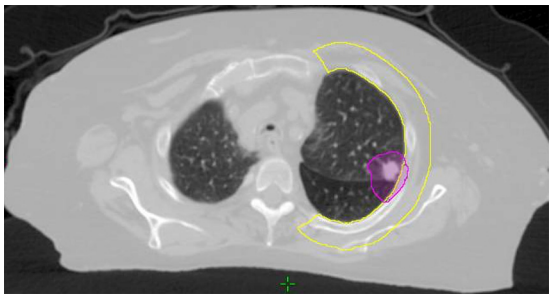

Fig. 1. Study on chest wall pain following lung stereotactic body radiation therapy: chest wall definition. The chest wall region is defined by the yellow C-shaped contour. The planning target volume is shown in magenta, involving the chest wall.

2.3. Follow-up and chest wall pain grading

All patients were seen for a follow-up at 1 to 2 months after completion of the stereotactic body radiation therapy, and every 4 to 6 months thereafter. The charts of all eligible patients were reviewed and chest wall pain was retrospectively graded by two physicians according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 for pain [21]. Accordingly, grade 1 is defined as mild pain that does not interfere with function, grade 2 is moderate pain where the pain or analgesics interfere with function without interfering with activities of daily life, grade 3 is severe pain with pain or analgesics severely interfering with activities of daily life, and grade 4 is described as disabling pain.

2.4. Chest wall definition

The chest wall was contoured retrospectively for each patient and defined as a 2 cm expansion from the visceral pleural surface as illustrated in Fig. 1; a similar definition to what was previously described by Dunlap et al., but with a 2 cm expansion instead of 3 cm [13]. The posterior limit of the chest wall contour finished at the border of the vertebral bodies and the anterior limit at the sternum or manubrium. The chest wall was contoured not more than 1 to 2 cm above and below the planning target volume.

Table 2
Study on chest wall pain following lung stereotactic body radiation therapy: patient and tumour characteristics of the study cohort.

Patient characteristics	
Patients	122 (100%)
Age median [range]	71 [44–90]
Female	61 (50%)
Osteoporosis	6 (5%)
Diabetic	18 (15%)
Tumour characteristics	
Total number of lesions	135 (100%)
Primary lung cancer	113 (84%)
Pulmonary metastasis	22 (16%)
Cases of pain	13 (10%)
Grade 1	8 (6%)
Grade 2	3 (2%)
Grade 3	2 (1%)
Cases of rib fracture	6 (4%)
Follow-up (mo)	Median: 19.9 Median: 18.0

2.5. Data collection

Using the electronic medical records and Eclipse™ (Varian Medical Systems, Palo Alto, CA) treatment planning system, various patient, tumour and dosimetric parameters were gathered. The patient parameters included the age, sex, and the presence of diabetes or osteoporosis at the time of consultation. The tumour parameters extracted were the planning target volume and the volume of the overlapping region between the planning target volume and the chest wall, both in cubic centimetres. The chest wall dosimetric parameters were the volumes receiving at least 30, 40, or 50 Gy ($V_{30\,Gy}$, $V_{40\,Gy}$, $V_{50\,Gy}$), the minimum dose to the most irradiated contiguous volume of 1, 2, or 5 cm^3 ($D_{1\,cm^3}$, $D_{2\,cm^3}$, $D_{5\,cm^3}$) and the maximum point dose (D_{max}) of the chest wall, all in absolute values.

2.6. Data analysis

Data analysis and data correlation were carried out using the SAS® 9.4 (SAS Institute Inc., Cary, NC) statistical software. To verify the correlation between the patient, tumour and dosimetric parameters and chest wall pain (grade 2 or higher), logistic regression analysis was performed using both univariate and multivariate models. A *P* value of 0.05 or less was considered for statistical significance. The univariate analysis was performed for each of the aforementioned parameters and the statistically significant factors from the univariate analysis were used as predictors in the multivariate regression.

3. Results

3.1. Patients and chest wall pain

Table 2 summarizes the patient and tumour characteristics of the study cohort. One-hundred and twenty-two patients treated for 135 lung lesions (113 primary lung cancer and 22 pulmonary metastases) met the inclusion criteria of the present analysis. The median age was 71 years with half of the patients being female. Six patients (5%) were previously diagnosed with osteoporosis and 18 (15%) with diabetes at the time of consultation. Median follow-up time was 18 months (range: 6–56 months), and 12 of the 122 patients (10%) expressed chest wall pain of any grade at a median of 6 months (range: 2–25 months) with seven patients (6%) reporting grade 1 chest wall pain, three patients (2%) grade 2 and two

Table 3
Study on chest wall pain following lung stereotactic body radiation therapy: chest wall dosimetry mean, median and standard deviation by toxicity.

	All tumours ($n = 135$)			Pain (grade ≥ 2) ($n = 5$)			No pain (grade ≤ 1) ($n = 130$)		
	Median	Mean	Standard deviation	Median	Mean	Standard deviation	Median	Mean	Standard deviation
D_{max} (Gy)	55.4	52.1	9.7	55.8	55.8	2.2	55.4	51.9	9.9
$D_{1\ cm3}$ (Gy)	51.7	47.6	10.7	53.8	53.9	1.9	51.7	47.3	10.8
$D_{2\ cm3}$ (Gy)	50.1	45.5	10.9	52.5	52.5	2.3	49.7	45.3	11.0
$D_{5\ cm3}$ (Gy)	43.7	41.1	10.7	49.2	48.5	54.5	43.3	40.8	10.8
$V_{30\ Gy}$ (cm^3)	18.7	23.1	21.4	39.4	45.1	31.6	18.2	22.3	20.4
$V_{40\ Gy}$ (cm^3)	7.0	9.8	12.1	15.7	21.2	19.4	6.9	9.4	11.5
$V_{50\ Gy}$ (cm^3)	2.0	3.9	6.8	3.6	9.9	12.8	1.8	3.7	6.3
Planning target volume (cm^3)	28.2	33.8	24.7	50.8	53.6	35.05	28.1	33.1	23.9
Overlapping volume between chest wall and planning target volume (cm^3)	1.2	2.6	4.2	3.1	7.2	9.2	1.1	2.5	3.7

D_{max}: maximum point dose; $D_{x\ cm3}$: minimum dose to the highest irradiated$x$ cm^3; $V_{x\ Gy}$: volume receiving x Gy or more.

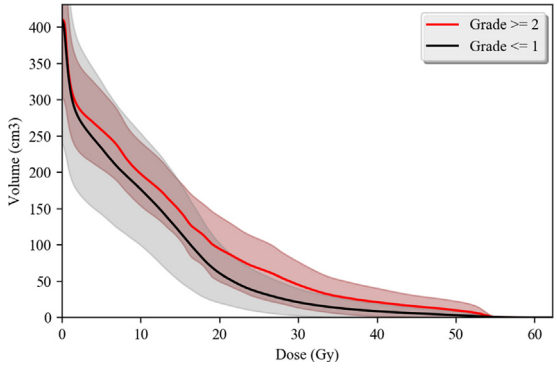

Fig. 2. Study on chest wall pain following lung stereotactic body radiation therapy: dosimetric parameters. Mean chest wall dose–volume histograms with shaded standard deviation envelopes for patients with (grade 2 or higher) and without (grade 1 or less) chest wall pain.

patients (2%) grade 3. Of the five patients with pain of grade 2 or higher, four reported chest wall pain on at least two consecutive visits, and the other was not seen in another follow-up after the first report of chest wall pain. Six patients presented rib fractures, half of whom also had chest wall pain that seemed unrelated to the rib fracture. Typically, the patients with chest wall pain complained of persistent burning-type pain radiating through the chest wall around the area where they received the treatment. The pain was generally controlled with opioid pain medication such as fentanyl patches and/or hydromorphone, and in some cases lasted for weeks.

3.2. Correlation of dosimetric/tumour/patient parameters with chest wall pain

Median, mean and the standard deviation of each of the analysed dosimetric parameters separated by toxicity are shown in Table 3. Mean values of the chest wall dose–volume histograms were computed for all patients who had chest wall pain of grade 2 or higher and for all those without reported chest wall pain or grade 1 chest wall pain as shown in Fig. 2. The shaded envelopes around each curve indicate the standard deviation of the respective data set. Logistic regression was performed to estimate odds ratios and evaluate the correlation between the characterizing parameters and chest wall pain (grade 2 or higher). The odds ratios and P values for both the univariate and multivariate analyses are shown in Table 4. The univariate analysis results demonstrate that only the volume receiving 30 Gy ($P = 0.0339$) and the overlapping volume between the chest wall and the planning target volume ($P = 0.0376$) are of statistical significance in terms of correlation with chest wall pain. Dosimetric variables such as the chest wall V_{40Gy}, $V_{50\ Gy}$, $D_{1\ cm3}$, $D_{2\ cm3}$, $D_{5\ cm3}$ and planning target volume as well as clinical parameters, such as age, osteoporosis and diabetes all failed to show any statistical significance. The overlapping volume between the chest wall and the planning target volume and the chest wall $V_{30\ Gy}$ were then used in a multivariate model for further analysis of correlation with chest wall pain. For this purpose, multivariate logistic regression including these two parameters as predictors was performed. Considering a P value of 0.05 or less for statistical significance, none of the parameters remained predictive for chest wall pain after multivariate analysis.

Table 4
Study on chest wall pain following lung stereotactic body radiation therapy: univariate logistic regression of all patient, tumour and dosimetric parameters considered and multivariate regression combining the volume of chest wall receiving 30 Gy ($V_{30\ Gy}$) and the overlapping volume between the chest wall and the planning target volume.

Factor	Odds ratio (95% confidence interval)	P value
Univariate analysis		
$V_{30\ Gy}$	1.030 (1.002–1.059)	0.0339
$V_{40\ Gy}$	1.042 (0.999–1.087)	0.0581
$V_{50\ Gy}$	1.064 (0.992–1.141)	0.0840
$D_{1\ cm3}$	1.139 (0.923–1.406)	0.2248
$D_{2\ cm3}$	1.131 (0.939–1.362)	0.1963
$D_{5\ cm3}$	1.106 (0.966–1.266)	0.1430
D_{max}	1.073 (0.904–1.274)	0.4189
Planning target volume	1.024 (0.997–1.052)	0.0862
Overlapping volume between chest wall and planning target volume	1.130(1.007–1.267)	0.0376
Age	1.064 (0.952–1.188)	0.2744
Multivariate analysis		
$V_{30\ Gy}$	1.022 (0.981–1.064)	0.2963
Overlapping volume	1.057 (0.894–1.249)	0.5146

D_{max}: maximum point dose; $D_{x\ cm3}$: minimum dose to highest irradiated x cm^3; $V_{x\ Gy}$: volume receiving x Gy or more.

4. Discussion

Chest wall pain is widely recognized as an important adverse effect of lung stereotactic body radiation therapy and has been the subject of multiple studies since 2010 [6–19,22–27]. Symptoms can range from mild and transient to severe and chronic. In some cases, pain may remain incompletely relieved despite aggressive medical management. The exact pathophysiology of chest wall pain is not well understood, however, it is thought to be caused by injury to the intercostal nerves resulting in neuropathic pain [6].

Interestingly, the reported incidences of chest wall pain after stereotactic body radiation therapy vary widely ranging from 8% to 46% [14,26]. Furthermore, the incidence for grade 3 chest wall pain

ranges from 0% to 28% [13,17,19]. These large ranges suggest that the assessment of chest wall pain needs to be improved and perhaps routinely done in a prospective way. Our findings are in the lower range of these brackets, with 10% of our cohort that developed chest wall pain of any grade and only 1% with grade 3 pain.

Dunlap et al. have the merit of being among the first to analyse predictors of chest wall toxicity including pain and rib fracture, and to suggest a chest wall constraint for lung stereotactic body radiation therapy [13]. In 2010, they reported a retrospective review of 60 patients treated by stereotactic body irradiation in two different institutions, with total doses varying from 21 Gy to 60 Gy given in three to five fractions and with constraints for organs at risk according to the RTOG 0236 protocol. They did not mention whether heterogeneity correction was used during treatment planning. The chest wall was not designated as a constrained structure for the original treatment plans. They were the first to suggest contouring the chest wall volume similarly as in our present study, an approach which has also been reproduced by different groups [8,10,13,19]. They reported a surprisingly high 28% rate of grade 3 chest wall pain. The authors suggested that, to reduce the risk of chest wall toxicity without compromising tumour coverage, the chest wall $V_{30\,Gy}$ should be limited to 30 cm^3. It is to be noted that this suggestion practically eliminates the use of stereotactic body radiation therapy with three to five fractions in any case where the planning target volume overlaps the chest wall and is ultimately unrealistic.

Mutter et al. performed a similar exercise reviewing 126 patients that received stereotactic body radiation therapy with doses varying between 40 Gy to 60 Gy also given in three to five fractions [9]. Again, the chest wall was not a constrained structure during the treatment planning. In spite of similar dose and fractionation compared to the study by Dunlap et al., they found "only" 15% of grade 3 chest wall pain, although still a much higher rate than in our study. In their analysis, rather than 30 cm^3, a chest wall volume over 70 cm^3 receiving more than 30 Gy was significantly correlated with chest wall pain of grade 2 or higher. The drawbacks of these two important studies are the mix of different number of fractions from three to five in the same analysis, the inclusion of patients with follow-up times less than 6 months and the possible lack of appropriate heterogeneity correction, which we believe are non-negligible factors.

A few other early studies also had the same limitation of mixing different dose/fractionation schemes in the same analysis. One of which is the study published in 2011 by Andolino et al. reviewing 347 cases treated with doses varying from 18 to 72 Gy in three fractions and with only some cases corrected for inhomogeneity [12]. They reported that the maximum point dose to the chest wall should be limited to 50 Gy and that the $V_{40\,Gy}$ should be kept below 5 cm^3. Also in 2011, Bongers et al. reported on a large cohort of 500 patients treated with 60 Gy in three, five and eight fractions where the risk factors found to be associated with chest wall toxicity were the tumour size, the planning target volume and the distance of the tumour from the chest wall, but dosimetric variables were not analysed [11]. Creach et al. reviewed 140 patients irradiated with either 54 Gy in three fractions or 50 Gy in five fractions, planned with heterogeneity correction and concluded that the relative volume of chest wall receiving over 30–40 Gy should be minimized [10].

With the same objective of studying chest wall pain after lung stereotactic body radiation therapy, Stephans et al. reported a retrospective review of 48 patients for which all received the same prescription of 60 Gy in three fractions as per the RTOG 0236 protocol, but also without heterogeneity correction at the time of treatment planning [19]. Median follow-up was 18.8 months (range: 5.6–30.7 months). Contrary to the previous studies mentioned above, albeit a more similar incidence as in our study, they did not find any grade 3 chest wall pain in their cohort in spite of giving 60 Gy in three fractions. Patient characteristics such as age, diabetes, hypertension, peripheral vascular disease, smoking or body mass index were not predictive for chest wall toxicity. However, tumour size and chest wall dosimetry were correlated to late chest wall toxicity (pain and rib fracture). In their review, they found that restricting the chest wall $V_{30\,Gy}$ below 30 cm^3 and the chest wall $V_{60\,Gy}$ below 3 cm^3 should result in a risk of late chest wall toxicity of less than 15%.

More recently, in 2016, Murray et al. reviewed 192 patients all receiving the fractionation scheme of 55 Gy in five fractions [16]. Similarly to our study, they focused on chest wall pain of grade 2 or higher and found an incidence of 10.9%, for which the tumour size and the $D_{1\,cm^3}$ were significant predictors. However, it is unclear whether heterogeneity correction was used during treatment planning, and the inclusion of patients in the study was not limited by a minimum follow-up time, which ranged from 0.3 to 45 months.

Also in 2016, Thibault et al. reported on their institutions' experience with rib fracture and chest wall pain following irradiation with 48 to 60 Gy in four to five fractions; they reviewed 289 lesions from 239 patients [8]. The median follow-up was 21.0 months and 16% of patients experienced chest wall pain. Dose calculation was performed with heterogeneity correction and, similarly to the previous studies, target coverage was not compromised to spare the chest wall. However, unlike all other publications mentioned above, they reported that in their cohort no clinical or dosimetric factors were found to be predictive of chest wall pain.

In our present study, we solely focused on patients receiving 48 Gy in three fractions with heterogeneity correction and with a minimum follow-up of 6 months, and we also could not find any correlation between chest wall pain and the studied dosimetric variables, particularly the volume receiving 30 Gy as suggested by many groups [9–11,13–15,17–19]. Despite the average dose–volume histograms differing between the cases with and without chest wall pain of grade 2 or higher as seen in Fig. 2, our statistical analysis showed that this difference is not significant, at least in the volume receiving at least 30 Gy to 50 Gy region. Although our study has the same limitation as others of being retrospective, the merits of our study are that all of our 122 patients received the same dose and fractionation, were treated with heterogeneity correction and were followed for at least 6 months.

The published studies have raised multiple possible predictive factors for chest wall pain including dosimetric factors such as total dose, dose per fraction, maximum dose to the chest wall or rib, chest wall volume receiving at least 30 to 70 Gy, size of the planning target volume, and patient related factors such as female gender, location of the tumour in the lungs, age, body mass index, but they have not been consistent. The most commonly reported predictor for chest wall pain remains the $V_{30\,Gy}$, perhaps because it was the first one to be suggested. The wide range of results from the literature may be due to differences in study design and factors such as differences in stereotactic body radiation therapy dose prescriptions (total dose and number of fractions), difficulties and differences in evaluating or scoring chest wall pain, retrospective assessment of chest wall pain, and different follow-up intervals.

5. Conclusion

Chest wall pain (grade 2 or higher) is an infrequent stereotactic body radiation therapy-related toxicity and is less concerning than pain after thoracotomy for which some reports mention incidences of more than 50% of patients still taking pain medication one year after surgery [28]. Considering the wide range of differing results from the literature and the lack of significant predictors found in our current study, a reasonable conclusion is that an ideal constraint for the avoidance of chest wall pain is yet to be defined.

Disclosure of interest

The authors declare that they have no competing interest.

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