Int. J. Radiation Oncology Biol. Phys., Vol. 82, No. 2, pp. 974–980, 2012

0360-3016/$ - see front matter

doi:10.1016/j.ijrobp.2010.12.002

CLINICAL INVESTIGATION **Thoracic Cancer**

PREDICTION OF CHEST WALL TOXICITY FROM LUNG STEREOTACTIC BODY RADIOTHERAPY (SBRT)

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Purpose: To determine patient, tumor, and treatment factors related to the development of late chest wall toxicity after lung stereotactic body radiotherapy (SBRT).

Methods and Materials: We reviewed a registry of 134 patients treated with lung SBRT to 60 Gy in 3 fractions who had greater than 1 year of clinical follow-up and no history of multiple treatments to the same lobe ($n = 48$). Patients were treated as per Radiation Therapy Oncology Group Protocol 0236 without specific chest wall avoidance criteria. The chest wall was retrospectively contoured. Thirty-two lesions measured less than 3 cm, and sixteen measured 3 to 5 cm. The median planning target volume was 29 cm^3.

Results: With a median follow-up of 18.8 months, 10 patients had late symptomatic chest wall toxicity (4 Grade 1 and 6 Grade 2) at a median of 8.8 months after SBRT. No patient characteristics (age, diabetes, hypertension, peripheral vascular disease, or body mass index) were predictive for toxicity, whereas there was a trend for continued smoking ($p = 0.066$; odds ratio [OR], 4.4). Greatest single tumor dimension ($p = 0.047$; OR, 2.63) and planning target volume ($p = 0.040$; OR, 1.04) were correlated with toxicity, whereas distance from tumor edge to chest wall and gross tumor volume did not reach statistical significance. Volumes of chest wall receiving 30 Gy (V30) through 70 Gy (V70) were all highly significant, although this correlation weakened for V65 and V70 and maximum chest wall point dose only trended to significance ($p = 0.06$). On multivariate analysis, tumor volume was no longer correlated with toxicity and only V30 through V60 remained statistically significant.

Conclusions: Tumor size and chest wall dosimetry are correlated to late chest wall toxicity. Only chest wall V30 through V60 remained significant on multivariate analysis. Restricting V30 to 30 cm^3 or less and V60 to 3 cm^3 or less should result in a 10% to 15% risk of late chest wall toxicity or lower.

Stereotactic body radiotherapy, SBRT, Chest wall toxicity, Lung cancer, Stage I.

INTRODUCTION

Stereotactic body radiotherapy (SBRT) provides excellent local control for patients with medically inoperable Stage I non–small-cell lung cancer, as well as select patients with pulmonary oligometastases (1–15). In general, treatment is very well tolerated with a low incidence of acute and late toxicity. Late chest wall toxicity has been described in the literature, including skin changes (erythema, ulceration and fibrosis) (16), chest wall pain (focal or neuropathic), and rib fracture (symptomatic and asymptomatic) (1, 4, 5, 7, 8, 10–12, 17–20).

Chest wall toxicity is typically mild or moderate and treated effectively by oral anti-inflammatory medication, gabapentin, or narcotics. Skin changes may be seen 3 to 6 weeks after treatment (16), whereas chest wall pain and rib fracture typically occur substantially later, with a median time to onset of greater than 6 months after SBRT (17–21). At present, few data exist to guide informed consent and treatment planning with respect to symptomatic chest wall toxicity after SBRT. We have previously noted a greater incidence of chest wall toxicity in peripheral lesions treated to 60 Gy in 3 fractions as opposed to 50 Gy in 5 fractions (18% vs. 4%) (19). Meanwhile, in two separate dose–volume analyses, a Swedish study found the strongest association between individual rib dose–volume histogram parameters and fracture risk in the small-volume/high-dose region (18) whereas a second study found strong correlations with both the volume of chest wall receiving 30 Gy (V30) and small-volume/high-dose regions, such as V60 (17).

These studies differ in terms of the selection criteria and length of follow-up of patients, SBRT fractionation used, and dosimetric volume of interest studied. We present an analysis of patient, tumor, and treatment factors and their correlation with late chest wall toxicity in patients treated

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Conflict of interest: none.

Received April 14, 2010, and in revised form Nov 28, 2010. Accepted for publication Dec 7, 2010.

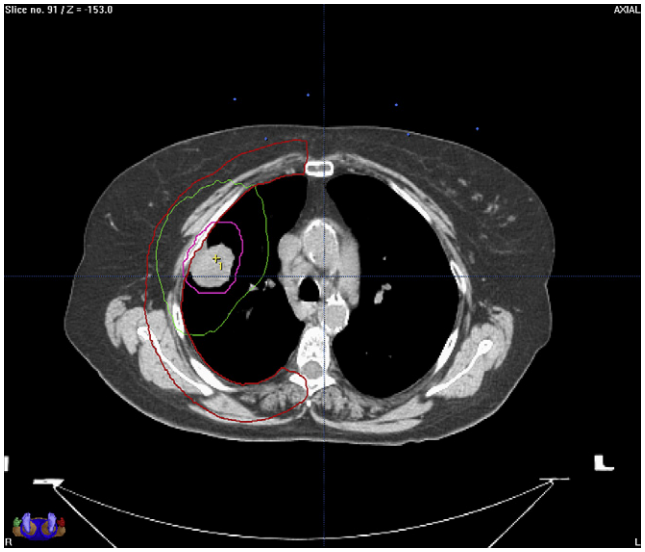

Fig. 1. Chest wall contour.

with thoracic SBRT. All patients were treated with a uniform treatment regimen of 60 Gy in 3 fractions and have sufficient follow-up to detect most chest wall events. Our aim is to both help predict the risk of toxicity for individual patients and assist with establishing treatment planning parameters to minimize this risk.

METHODS AND MATERIALS

Patient selection and evaluation

This is a retrospective review of an institutional review board–approved registry of 134 patients treated between February 2005 and February 2008 with SBRT for isolated lung lesions measuring less than 5 cm. We limited our analysis to patients who either had chest wall toxicity before 1 year or had no toxicity with clinical follow-up of at least 1 year (n = 117) and were treated to 60 Gy in 3 fractions (n = 51). Patients with previous radiation or multiple SBRT treatments to the same lobe were then excluded (n = 3), leaving a final population of 48 patients who were analyzed for this study (40 with primary non–small-cell lung cancer and 8 with oligometastatic lesions). Oligometastatic patients had only a single metastatic lesion in the lung with greater than 2 years from their primary diagnosis in all cases.

Patient factors analyzed included age, gender, smoking history, smoking status, body mass index (BMI), and the presence of diabetes, hypertension, or peripheral vascular disease at the time of consultation. Tumor factors included greatest tumor dimension on computed tomography (CT), gross tumor volume (GTV), closest distance from tumor periphery to chest wall on planning CT scan, and planning target volume (PTV). Treatment factors included chest wall dosimetry (absolute volume in cubic centimeters receiving 30 Gy through 70 Gy, in 5-Gy increments), maximum chest wall point dose, heterogeneity index (maximum point dose divided by prescription dose), and conformality index (prescription volume/PTV). Chest wall was contoured as the arc of all ipsilateral soft tissue outside of lung tissue from the edge of the sternum circumferentially to the edge of the vertebral body including the spinal nerve root exit site (Fig. 1). All mediastinal tissue was excluded. Although all the patients were originally planned without heterogeneity correction, for the purposes of this analysis, all plans were recalculated with heterogeneity corrections enabled to better approximate the true dose delivered.

Patients were followed up 6 to 8 weeks after SBRT, and then every 3 months thereafter, with CT imaging at each visit. Positron emission tomography scans were obtained when imaging or clinical findings suggested the possibility of recurrence. Chest wall toxicity was defined clinically according to a modified version of the Common Terminology Criteria for Adverse Events version 3.0 including all symptomatic skin ulceration, focal chest wall pain, and neuropathic pain: Grade 1, mild pain, no need for narcotics; Grade 2, moderate pain, narcotics indicated; Grade 3, severe pain/pain or treatment interferes with activities of daily living, long-acting or scheduled narcotics indicated; and Grade 4, disabling. Asymptomatic rib fractures were not scored. Patients whose toxicity level changed over time were scored at the time of greatest toxicity.

Treatment procedure

Patients were simulated supine in a vacuum bag restriction system (Bodyfix; Elekta, Stockholm, Sweden). An abdominal compression device was applied to reduce respiratory movement and adjusted under fluoroscopy. A planning axial CT scan with 3-mm slice thickness was taken during quiet breathing, full inspiration, and full expiration. Treatment plans were generated by BrainScan 5.31 planning software (BrainLAB, Feldkirchen, Germany) referenced to the free-breathing study. Patients were treated on the Novalis system (BrainLAB) by use of orthogonal films and the ExacTrac stereotactic body system (BrainLAB) for positioning. Target volume and critical structure definitions, as well as planning goals and restrictions, were strictly as per Radiation Therapy Oncology Group Protocol 0236 (22). No planning decisions were made based on proximity to chest wall, and no chest wall dosimetric constraints were used. Patients received 60 Gy in 3 fractions over a period of 8 to 14 days delivered via 6-MV photons by use of one to seven dynamic arcs.

Statistical analysis

The primary endpoint was development of clinical chest wall toxicity during the follow-up interval. Logistic regression analysis was used to correlate patient, tumor, and treatment factors to clinical chest wall toxicity in both univariate and multivariate models. Statistical analyses were performed with StatView 5.0 (SAS Institute, Cary, NC), and $p < 0.05$ was considered statistically significant. Finally, by use of the logistic regression models, probability curves for chest wall toxicity were created for the tumor and dosimetric parameters of interest. The probability of chest wall toxicity was based on the odds ratios:

$$\text{Probability of Chest Wall (CW) toxicity by Variable} = \frac{e[\text{coefficient of constant} + (\text{Natural Log (LN) Odds ratio} * \text{Variable})]}{1 + e[\text{coefficient of constant} + (\text{LN Odds ration} * \text{Variable})]}$$

RESULTS

Forty-eight lesions in forty-five patients met all inclusion criteria. Two patients had synchronous bilateral lesions, whereas one patient had a synchronous unilateral upper and lower lobe lesion. No patient with multiple lesions had toxicity. Patient characteristics are shown in Table 1. Thirty-two lesions measured less than 3 cm, whereas sixteen measured 3 to 5 cm. The overall median size was 2.15 cm,

and the median PTV was 29 cm^3. Dosimetric characteristics are shown in Table 2.

Median follow-up was 18.8 months (range, 5.6–30.7 months), and 10 patients reported toxicity at a median of 8.8 months (range, 3.7–12.0 months) after SBRT. Toxicity was Grade 1 (mild pain, no need for narcotics) in 4 patients and Grade 2 (moderate pain, narcotics indicated) in 6 patients. No patient had Grade 3 toxicity (severe pain/pain or treatment interferes with activities of daily living, long-acting or scheduled narcotics) or Grade 4 toxicity (disabling). Individual patients' V30 and V60 values are plotted in Fig. 2 with patients having toxicity highlighted.

No patient factors were associated with late chest wall toxicity (Table 3); however, continued smoking showed a trend ($p = 0.066$; odds ratio [OR], 4.4). Diabetes, hypertension, peripheral vascular disease, and higher BMI all had odds ratios greater than 1; however, p values did not approach statistical significance for correlation with toxicity ($p = 0.68$, $p = 0.57$, $p = 0.68$, and $p = 0.28$, respectively). Tumor factors associated with toxicity included greatest tumor dimension ($p = 0.047$; OR, 2.63) and PTV ($p = 0.040$; OR, 1.04). GTV–to–chest wall distance and GTV ($p = 0.16$ and $p = 0.12$) were not statistically significantly correlated (Table 3). Dosimetric factors were strongly correlated with toxicity, as shown in Table 4. All volumetric chest wall dosimetric measurements at each increment were correlated with toxicity, whereas maximum chest wall point dose showed a trend ($p = 0.064$; OR, 1.46). Heterogeneity and conformality index did not show substantial correlation ($p = 0.42$ and $p = 0.46$, respectively).

Tumor volume and volumetric chest wall dosimetry were further analyzed for correlation with chest wall toxicity by use of multivariate models. Chest wall V30 and V60 were chosen to represent chest wall dosimetry. Two separate analyses (Table 5) showed chest wall V30 ($p = 0.040$) and V60 ($p = 0.016$) to remain predictive of toxicity whereas PTV was no longer statistically significant ($p = 0.51$ vs. V30 and $p = 0.95$ vs. V60) after accounting for dosimetry.

Probability plots of lesion size (Fig. 3) and chest wall dosimetry (Fig. 4) compared with chances of chest wall toxicity were generated. V30 values of 10, 20, 40, 60, 80, and 100 cm^3 were associated with a 6%, 9%, 19%, 35%, 55%, and 74% risk of toxicity, respectively, and V60 values of 1, 2, 5, 10, 15, and 20 cm^3 were associated with a 6%, 8%, 16%, 39%, 69%, and 88% risk of chest wall toxicity, respectively. The dose–volume relationships resulting in a 15% risk of late chest wall toxicity are shown in Fig. 5.

$$\text{Probability of CW toxicity by PTV (cc)} = \frac{e[-2.793 + (0.038 * \text{PTV})]}{1 + e[-2.793 + (0.038 * \text{PTV})]}$$

$$\text{Probability of CW toxicity by Tumor Size (cm)} = \frac{e[-3.626 + (0.965 * \text{size})]}{1 + e[-3.626 + (0.965 * \text{size})]}$$

$$\text{Probability of CW toxicity by PTV (cc)} = \frac{e[-3.151 + (0.042 * \text{V30})]}{1 + e[-3.151 + (0.042 * \text{V30})]}$$

$$\text{Probability of CW toxicity by V30 (cc)} = \frac{e[-2.793 + (0.038 * \text{PTV})]}{1 + e[-2.793 + (0.038 * \text{PTV})]}$$

$$\text{Probability of CW toxicity by V60 (cc)} = \frac{e[-2.927 + (0.247 * \text{V60})]}{1 + e[-2.927 + (0.247 * \text{V60})]}$$

DISCUSSION

The purpose of our study was to identify patient, tumor, and treatment factors associated with the development of chest wall toxicity after lung SBRT. The reported incidence of late chest wall toxicity after SBRT has varied widely,

Table 1. Patient characteristics ($n = 45$)

Characteristic	Data
Age [median (range)] (y)	72 (50–89)
Gender (female)	69%
Size ($n = 48$)	
<3 cm	32
3–6 cm	16
Tumor size [median (range)] (cm) ($n = 48$)	2.15 (0.8–4.0)
Smoking [median (range)] (pack-years)	50 (0–140)
Continued smoking	19%
Diabetes	25%
Hypertension	73%
PVD	25%
BMI	26.6 (13.8–42.5)

Abbreviations: PVD = peripheral vascular disease; BMI = body mass index.

Table 2. SBRT dosimetry ($n = 48$)

Characteristic	Median (range)
GTV (cm^3)	6.3 (0.8–35.2)
PTV (cm^3)	29.2 (9.9–84.5)
PTV coverage (%)	99.9% (95.6–100%)
Heterogeneity index	1.35 (1.06–1.67)
Conformality index	1.50 (1.13–1.87)
CW V30 (cm^3)	25.4 (0–147.1)
CW V40 (cm^3)	10.8 (0–70.1)
CW V50 (cm^3)	5.6 (0–43.8)
CW V60 (cm^3)	3.5 (0–29.7)
CW V70 (cm^3)	0.4 (0–20.3)
Maximum CW dose (Gy)	24.5 (6–28.3)

Abbreviations: SBRT = stereotactic body radiotherapy; GTV = gross tumor volume; PTV = planning target volume; CW = chest wall; V30 = volume receiving 30 Gy; V40 = volume receiving 40 Gy; V50 = volume receiving 50 Gy; V60 = volume receiving 60 Gy; V70 = volume receiving 70 Gy.

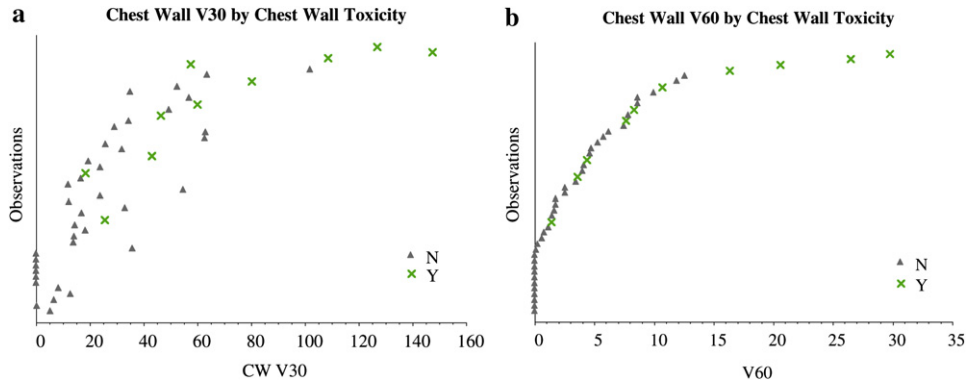

Fig. 2. Individual patient dosimetry and chest wall (CW) toxicity: volume of chest wall receiving 30 Gy (V30) (a) and volume of chest wall receiving 60 Gy (V60) (b).

ranging from less than 5% to as high as 25% (1, 4, 5, 7, 8, 10–12, 16–21). A number of factors may account for such a range of outcomes, including differences in patient populations, follow-up interval, SBRT dose prescriptions, and treatment techniques. "Chest wall toxicity" itself is a broad term, which may include neuropathic pain referable to the treated site, rib fracture, or focal soft-tissue changes. Although particular factors may contribute more or less to each of these specific symptoms, we chose to address these together because they all represent focal toxicity experienced by patients after SBRT and likely have more overlap than discordance in etiology. We limited our analysis to symptomatic lesions because consequences from otherwise asymptomatic rib fractures are likely minimal.

In defining our study population, we chose to focus on patients treated with a single fractionation schedule to avoid uncertainties regarding conversions of biologically equivalent doses, which may confound analysis with high doses delivered per fraction, where the linear quadratic model may diverge from observed results (23). We also limited our analysis to patients with at least 1 year of clinical follow-up, given that the median time to development of chest wall pain is typically greater than 6 months (17–20) and toxicity may develop later in patients with shorter follow-up. In our cohort 10 patients (21%) reported mild to moderate chest wall symptoms, although all symptoms were limited to Grade 1 or Grade 2. Toxicity in this cohort was in keeping with reported the SBRT literature (1, 4, 5, 7, 8, 10–12, 16–21). Of note, surgical literature describes up to a 50% incidence of post-thoracotomy pain syndrome, with 30% of patients reporting chronic pain in a series by Karmakar and Ho (24), although most cases were likewise described as mild or moderate. The emergence of data on the causes of chest wall toxicity after thoracic SBRT will allow radiation oncologists to begin to modify treatment to further minimize this complication in the future.

No patient factors were statistically significantly correlated with the development of chest wall toxicity. It is of interest that patients with toxicity had a numerically higher BMI and greater incidence of diabetes, hypertension, and peripheral vascular disease, although none of these differences reached statistical significance. Diabetes and peripheral vascular disease have been associated with late radiation toxicity in other settings (25). Hypertension may be difficult to study, given a range of potential inclusion criteria. We also noted a trend between continued smoking and development of late toxicity, which has previously been reported for the

Table 3. Univariate analysis of patient and tumor factors

Characteristic	*p* Value	OR (95% CI)
Gender	0.50	1.64 (0.39–6.95)
Age	0.46	0.97 (0.90–1.05)
Continued smoking	0.07	4.4 (0.91–21.30)
Diabetes	0.68	1.38 (0.29–6.48)
Hypertension	0.57	1.63 (0.30–8.93)
PVD	0.68	1.38 (0.29–6.48)
BMI	0.28	1.06 (0.95–1.18)
Tumor size	0.05	2.63 (1.01–6.80)
GTV	0.12	1.07 (0.98–1.17)
PTV	0.04	1.04 (1.01–1.08)
Distance to CW	0.16	0.21 (0.02–1.87)

Abbreviations: OR = odds ratio; CI = confidence interval; PVD = peripheral vascular disease; BMI = body mass index; GTV = gross tumor volume; PTV = planning target volume; CW = chest wall.

Table 4. Univariate analysis of dosimetric factors

Characteristic	*p* Value	OR (95% CI)
GTV (cm^3)	0.11	1.07 (0.98–1.17)
PTV (cm^3)	0.040	1.04 (1.01–1.08)
Heterogeneity index	0.42	0.09 (0.0–33.0)
Conformality index	0.46	0.25 (0.01–10.5)
CW V30 (cm^3)	0.0040	1.04 (1.01–1.07)
CW V40 (cm^3)	0.0037	1.08 (1.03–1.15)
CW V50 (cm^3)	0.0035	1.16 (1.05–1.27)
CW V60 (cm^3)	0.0053	1.28 (1.08–1.52)
CW V65 (cm^3)	0.0083	1.35 (1.08–1.68)
CW V70 (cm^3)	0.014	1.40 (1.07–1.82)
Maximum CW dose (Gy)	0.06	1.46 (0.98–2.17)

Abbreviations: OR = odds ratio; CI = confidence interval; GTV = gross tumor volume; PTV = planning target volume; CW = chest wall; V30 = volume receiving 30 Gy; V40 = volume receiving 40 Gy; V50 = volume receiving 50 Gy; V60 = volume receiving 60 Gy; V65 = volume receiving 65 Gy; V70 = volume receiving 70 Gy.

Table 5. Multivariate analysis

Characteristic	*p* Value	OR (95% CI)
Multivariate 1		
PTV	0.51	0.97 (0.89–1.06)
CW V30	0.040	1.06 (1.002–1.11)
Multivariate 2		
PTV	0.95	1.002 (0.95–1.06)
CW V60	0.016	1.27 (1.05–1.54)

Abbreviations: OR = odds ratio; CI = confidence interval; PTV = planning target volume; CW = chest wall; V30 = volume receiving 30 Gy; V60 = volume receiving 60 Gy.

development of fibrosis and telangiectasia after breast radiation (26). The influence of patient comorbidities may be more subtle than tumor location or treatment dosimetry, given the large dose gradients involved in SBRT, and may require a larger sample size to detect significant interactions. Although no firm conclusions can be drawn at present, each of these factors merits further study in a larger population.

With respect to tumor factors, proximity to the chest wall and tumor size have previously been reported to be associated with late chest wall toxicity. A study of 50 patients from Memorial Sloan-Kettering previously reported that a distance from tumor to posterior skin of less than 5 cm was correlated with acute skin reaction after lung SBRT (44–48 Gy in four fractions) (16). Similarly, Princess Margaret Hospital reported rib fractures to occur in tumors with a median distance from the chest wall of 0.4 cm (range, 0–1.8 cm) (20). Patients with toxicity in our study also had tumors close to the chest wall (median distance, 0 cm; range, 0–0.7 cm). Patients with tumors more than 1 to 2 cm from the chest wall and 5 cm from the posterior skin therefore seem to be at very low risk of toxicity. Conversely, 21 patients in our study had lesions directly against the chest wall, although toxicity developed in only 7 of these patients (33%). The reasons why two-thirds of these patients with chest wall within the PTV (and thus full dose to chest wall) did not have toxicity develop are as interesting as those that predispose other patients to toxicity and are not yet fully elucidated.

We have previously reported larger median tumor size in patients in whom chest wall toxicity is developing (19), and in this study both the single greatest tumor dimension and volume were associated with toxicity. On multivariate analysis, however, tumor volume was no longer a significant predictor of toxicity whereas chest wall dosimetry remained statistically significant. Patients in this study were all treated with rotational arc therapy; however, there was variation in the number of arcs (one to six), range of each individual arc, weighting of each arc, and orientation of arcs with respect to each other. Hoppe *et al.* (16) previously reported that patients treated with three beams or fewer were more likely to have skin toxicity develop than patients treated with four or more beams, and they likewise noted that Grade 2 or higher skin toxicity developed in 4 of 5 patients treated with three posterior beams over a narrow angular range. One explanation for chest wall dosimetry being dominant over tumor size on multivariate analysis therefore could be that concentrating dose over a small volume of chest wall leads to toxicity. During the treatment planning process, care should be taken to examine the shape of the dose distribution, as well as the chest wall dose–volume histogram in addition to that of target and other critical structures. Comparing the chest wall dose–volume histogram of a treatment plan with plots generated from studies such as ours should allow for estimates of risk of toxicity after treatment planning, as well as the potential to modify this risk before treatment, so long as this does not result in undertreatment of target or violation of other normal tissue constraints.

Every measure of volumetric dosimetry (chest wall V30–V70) was correlated to toxicity. Maximum point dose was also correlated but only trended toward statistical significance ($p = 0.06$). This is consistent with the two previously reported studies in which all dosimetric levels showed some correlation to toxicity (17, 18). Whereas Dunlap *et al.* (17) found the greatest correlation of V30 to toxicity, we found roughly equal correlation of V30–V60. One possible explanation is that many of the patients in their study were treated only to 50 Gy and thus likely have relatively small chest wall V60 values, although they still found V60 to correlate to toxicity as well. In our study correlation of dosimetry to toxicity also becomes less strong at dose–volume points exceeding prescription dose, as is noted by a slightly weaker correlation

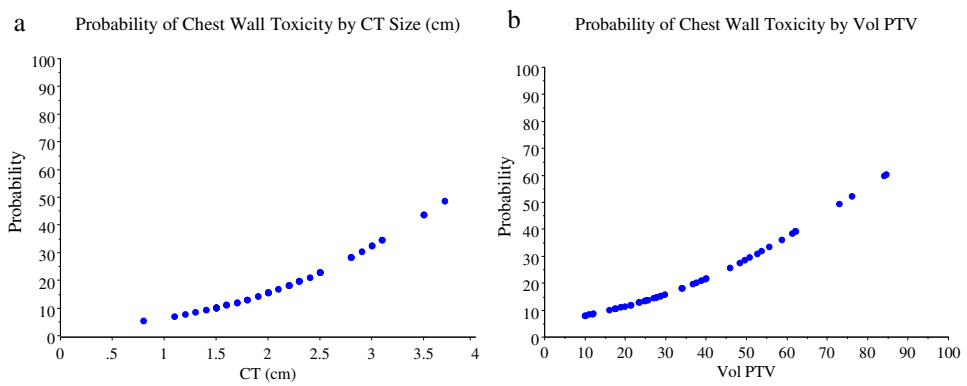

Fig. 3. Predicted toxicity by tumor volume: computed tomography (CT) size (a) and planning target volume (PTV) (b).

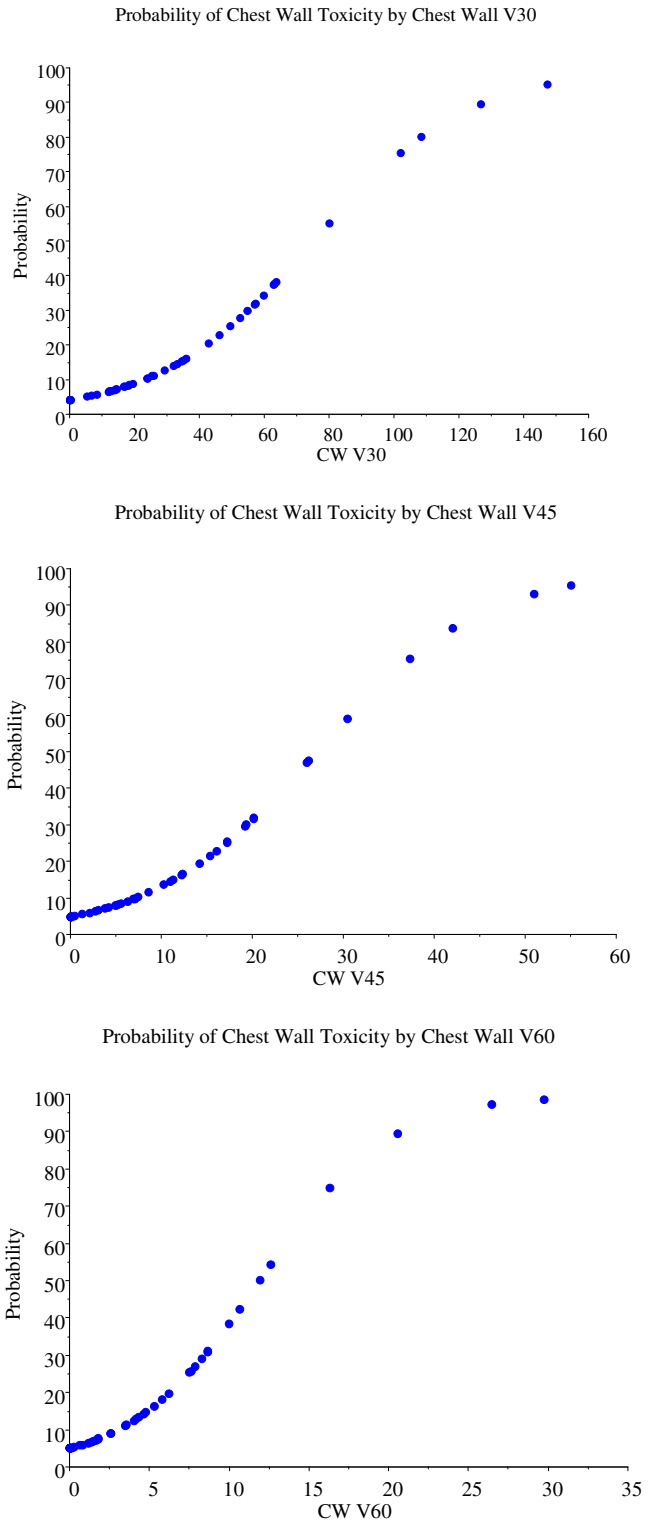

Fig. 4. Predicted toxicity by chest wall dosimetry: volume of chest wall receiving 30 Gy (V30) (a), volume of chest wall receiving 45 Gy (V45) (b), and volume of chest wall receiving 60 Gy (V60) (c).

of V70 and the fact that maximum point dose only trends toward correlation ($p = 0.06$). This may be because of small variations in daily setup or intrafraction respiratory motion such that high point doses suggested by the treatment planning system are spread over a larger area during treatment.

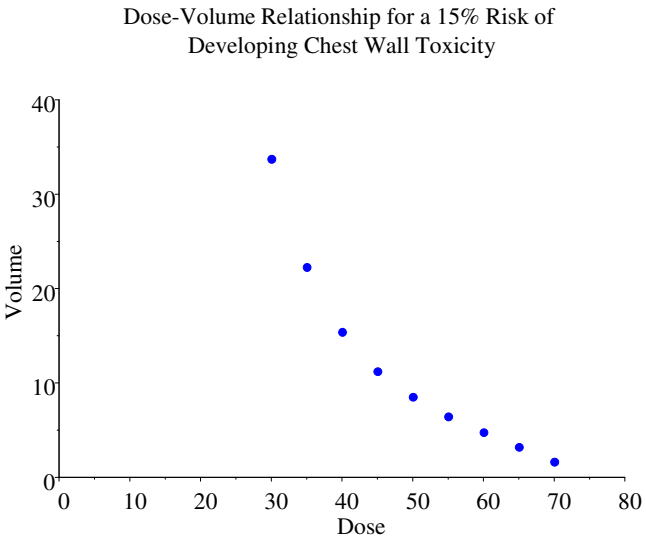

Fig. 5. Dose–volume relationship for 15% risk of chest wall toxicity.

The study by Pettersson *et al.* (18) finds the strongest correlation in the high-dose/small-volume dosimetry measurements but with the qualification that the volume is at least 2 cm^3, which is close to the median V60 in our population. The dosimetric variables studied are not truly independent variables because treatment plans with high V30 values are more likely to have high V60 values as well. Given the ability of treatment planning algorithms to constrain multiple dose–volume relationships, we believe that it is important to consider both low and high dose/volume constraints and have focused on both V30 and V60 at this point.

Another interesting difference between our study and that of Dunlap *et al.* (17) was that whereas they found the risk of chest wall toxicity to saturate around 50% for all dose–volume levels, this did not appear to be the case in our analysis because risk of toxicity approached 100% as volume receiving a particular dose was increased. This was particularly true of V60, with toxicity developing in all 4 patients with V60 greater than 15 cm^3 (Fig. 2). In addition, although other authors have documented rib fractures at point doses as low as 20 to 26 Gy (though typically at higher doses) (7, 10, 20), we did not see clinical toxicity in patients with a minimum absolute chest wall point dose of less than 67.5 Gy.

A strength of our study population is that all patients were treated with the same dose and fractionation schedule. Combining dosimetric data from different fractionation schedules likely requires corrections for biologically equivalent doses rather than absolute doses. This is complicated by limitations of the linear quadratic equation to predict biologically equivalent doses in the fraction sizes used in lung SBRT (23). Furthermore, we have previously seen substantially greater chest wall toxicity in patients receiving 60 Gy in 3 fractions compared with 50 Gy in 5 fractions (18% vs. 4%). This difference may reflect substantial differences in biological effect of these fractionation schedules. To generalize our model to patients treated with other dose and fractionation regimens, further study with advanced biological modeling is required.

CONCLUSIONS

1. Tumor size is correlated to risk of chest wall toxicity.
2. Chest wall dosimetry is correlated to risk of chest wall toxicity.
3. Restricting V30 to less than 30 cm^3 and V60 to less than 3 cm^3 should result in a less than 10% to 15% risk of chest wall toxicity. However, tumor coverage and other normal tissue constraints should not be compromised.

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