FULL PAPER

A review of staging chest CT in trunk and extremity soft tissue sarcoma

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Objectives: To determine the incidence of pulmonary metastases on chest CT in trunk and extremity soft tissue sarcoma based on two size criteria, and to identify factors associated with metastases.

Methods: Retrospective review of chest CT studies in patients with trunk and extremity soft tissue sarcoma over an 18-month period. Data collected included patient age/sex, tumour location, size and relationship to fascia. All chest CTs were reviewed for the presence of metastases which were diagnosed according to two size criteria: multiple nodules > 5 mm in size or multiple nodules > 10 mm in size. Follow-up CT studies were reviewed in cases initially considered indeterminate.

Results: 127 males and 73 females were included (mean age 57.1 years; range 10–90 years). 147 (73.5%) tumours were deep to the fascia and 53 (26.5%) superficial. Tumour size classified according to the 12 AJCC 2019

criteria was: T1 = 52, T2 = 76, T3 = 39, T4 = 33. Based on nodule size >5 mm, 73 (36.5%) patients had no metastases, 42 (21%) had metastases, while 85 (42.5%) studies were indeterminate. Based on nodule size >10 mm, 73 (36.5%) patients had no metastases, 28 (14%) had metastases, while 99 (49.5%) studies were indeterminate. Larger maximum dimension of the primary tumour was a risk factor for pulmonary metastases using both size criteria.

Conclusion: The incidence of pulmonary metastases at presentation in trunk and extremity soft tissue sarcoma is 14–21%. 42.5–49.5% of chest CTs were indeterminate.

Advances in knowledge: The incidence of pulmonary metastases at presentation in trunk and extremity soft tissue sarcoma is 14–21%. Indeterminate pulmonary nodules are also very common.

INTRODUCTION

Soft tissue sarcomas (STS) represent a wide variety of malignant tumours of mesenchymal origin and are currently classified according to the 2020 World Health Organisation Classification of Soft Tissue and Bone Tumours.[1,2] They account for <1.0% of all adult cancers.[3] Current treatment is primarily surgical with or without neoadjuvant or adjuvant radiotherapy.[4,5] The lungs represent the commonest site of metastatic disease and therefore chest CT is recommended at presentation.[6,7]

Several studies have attempted to determine the incidence of pulmonary metastases in trunk and extremity STS but these are now relatively old and relied upon chest radiography and/or suboptimal CT techniques.[8,9] More recent studies have also assessed the value of chest CT in relation to tumour grade[10,11] but pre-date the latest American Joint Committee on Cancer (AJCC) TNM classification of

STS[12] and therefore may no longer be relevant and warrant new analysis. A standardised definition of what constitutes pulmonary metastases is currently lacking, with some studies suggesting that the presence of multiple nodules >5 mm in maximal dimension are likely to represent metastases,[13,14] while others use a minimal nodule size of 10 mm.[15]

The aims of the current study were to determine the incidence of pulmonary metastases at presentation in trunk and extremity STS based on nodule size, to try to determine the relevance of indeterminate pulmonary nodules and to assess patient and tumour characteristics which are more likely to be associated with pulmonary metastases.

METHODS AND MATERIALS

The study was approved by the local Research and Innovation Centre of The Institute of Orthopaedics under the

Integrated Research Application System number 262826, with no requirement for informed patient consent.

This was a retrospective review of all patients diagnosed with a trunk or extremity STS between January 2019 and June 2020 within the setting of a specialist bone and soft tissue oncology service. Patients were added consecutively to a database following each weekly sarcoma multidisciplinary team (MDT) meeting, and therefore no cases were missed. The inclusion criteria were as follows:

(1) Diagnosis of STS by image-guided needle biopsy and/or surgical resection.
(2) A pre-biopsy MRI study.
(3) A pre-treatment staging chest CT study.

Data collected included patient age and gender, location of the STS, relationship to the deep peripheral fascia (superficial or deep according to the definition of Kirchgesner et al[16]) and maximum tumour size from which the tumour was classified as T1 (<5 cm), T2 (5 - </=10 cm), T3 (>10 - </=15 cm) and T4 (>15 cm) according to the 2019 AJCC staging system.[12]

CT studies were performed either prior to referral ($n = 40$; 20%) or following referral at our hospital (The Royal National Orthopaedic Hospital) ($n = 160$; 80%). The latter were obtained on a Philips Ingenuity CT 64-slice Unit with the following protocol: helical scan; collimation 64×0.625; slice thickness 1.5 mm; increment 0.75 mm; KV 120; mA modulated; pitch 0.891; rotation time 0.5 s; reconstructed in axial, coronal and sagittal maximal intensity projection (MIP). All were non-contrast studies and had been reported for clinical purposes by Consultant Musculoskeletal Radiologists working in the setting of a specialist Musculoskeletal Oncology Service. However, for the purposes of this study, they were reviewed by a single Consultant Musculoskeletal Radiologist with 8 years' experience of sarcoma imaging. The CT findings were classified as follows:

- No pulmonary nodules or calcified pulmonary nodules: no metastases.
- Non-calcified pulmonary nodules < 5mm: indeterminate.
- Non-calcified pulmonary nodules > 5 mm but <10mm: metastases for >5 mm criterion but indeterminate for >10 mm criterion.
- Non-calcified pulmonary nodules > 10mm: metastases.
- Increase in size or number of pulmonary nodules on follow-up chest CT irrespective of size: metastases.

All needle biopsy and surgical resections were performed at our hospital and specimens were reported by specialist bone and soft tissue tumour Consultant Histopathologists and classified with regard to tumour subtype according to the 2013 or 2020 WHO Classification of Soft tissue and Bone Tumours.[2] All tumours were further classified according to grade using the Trojani system[17] as low-grade, Grade 2 and Grade 3, the latter two grades finally combined as high-grade STS.

Statistical analysis

Descriptive statistics were used for patient characteristics, tumour locations, maximal tumour size from MRI which was then classified as T-stage according to 12 AJCC 2019 and the classification of chest CT studies. The first set of analyses examined differences in characteristics of patients with and without metastases. The unpaired t-test was used to compare continuous variables while χ^2 test was used for the analysis of categorical variables, with Fisher's exact test preferred for variables where the numbers in some categories were small. A second analysis examined the joint association between the various patient characteristics and metastases in a multivariate analysis. Due to the binary nature of the variables, this analysis was performed using logistic regression. To restrict the number of variables in this stage of the analysis, only those showing some association with outcome in the initial analyses ($p < 0.2$) were included. These

Table 1. Showing details of location of 200 STS

Body region	Location of primary STS	Deep *n* (%)	Superficial *n* (%)
Upper extremity	Shoulder girdle	5 (3.4%)	3 (5.6%)
	Arm	11 (7.5%)	2 (3.8%)
	Elbow	0 (0%)	0 (0%)
	Forearm	5 (3.4%)	3 (5.6%)
	Wrist/hand	5 (3.4%)	1 (1.9%)
Lower extremity	Thigh	61 (41.5%)	18 (34%)
	Knee	5 (3.4%)	3 (5.6%)
	Calf	14 (9.5%)	6 (11.3%)
	Ankle/foot	6 (4.1%)	5 (9.4%)
Trunk	Chest wall	16 (10.9%)	4 (7.5%)
	Abdominal wall	3 (2%)	3 (5.6%)
	Pelvis/groin/buttock	16 (10.9%)	5 (9.4%)
Total		200	147	53

STS, soft tissue sarcoma.

Figure 1. A 61-year-old male with a small mass in the right thigh. (a) Coronal T_1W TSE and (b) axial PDW FSE MR images demonstrate a poorly defined relatively small (T1 AJCC stage) superficial soft tissue mass (arrows) confirmed to be a high-grade leiomyosarcoma on excision. (c) Chest CT study demonstrates a 6 mm nodule (arrow) in the right anterior mid-zone which is a metastasis based on the >5 mm criterion but is indeterminate based on the >10 mm criterion. FSE, fast spin echo; PDW, proton density-weighted; TSE, turbo spin echo.
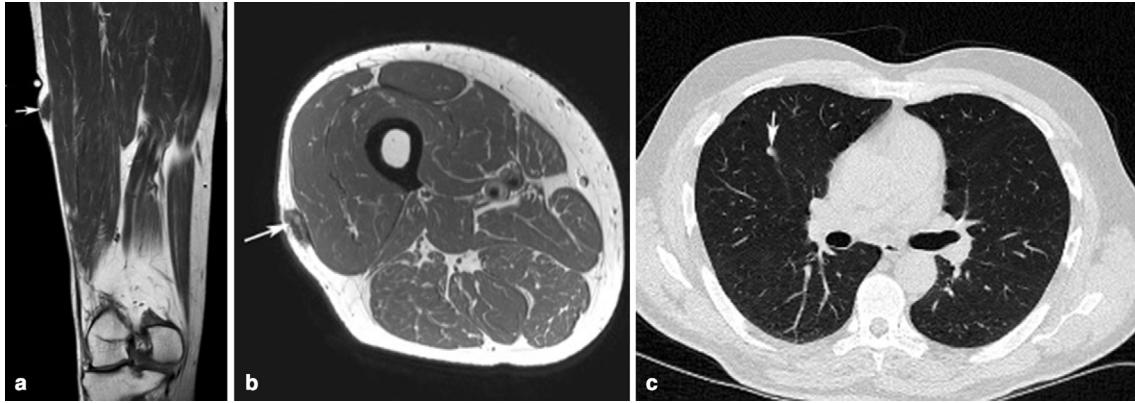
analyses were performed individually for a metastasis cut-off size of 5 and 10 mm.

RESULTS

200 patients fulfilled the inclusion criteria, 127 males and 73 females with mean age 57.1 years (range 10–90 years). 147 (73.5%) tumours were located deep to the fascia and 53 (26.5%) superficial. Details of tumour location are presented in Table 1, the commonest locations being the thigh, chest wall and calf. Overall mean maximal tumour dimension was 93.8 mm (range 12–350 mm), and tumour size classified according to the 12 AJCC 2019 criteria was as follows: T1 = 52 (25.1%), T2 = 76 (38%), T3 = 39 (19.5%), T4 = 33 (16.5%).

Based on initial chest CT and nodule size >5 mm, 73 (36.5%) patients had no metastases and 36 (18%) had metastases

Figure 2. A 61-year-old male with a large mass in the left chest wall. (a) Coronal T_1W TSE and (b) axial PDW FSE MR images demonstrate a large (T3 AJCC stage) soft tissue mass (arrows) confirmed to be a high-grade pleomorphic sarcoma on excision. (c) Chest CT study at presentation demonstrates a tiny nodule (arrow) in the right mid-zone which is indeterminate in nature. (d) Chest CT 3 months later demonstrates new and enlarging nodules (arrows) in the same region consistent with pulmonary metastases. FSE, fast spin echo; PDW, proton density-weighted; TSE, turbo spin echo.
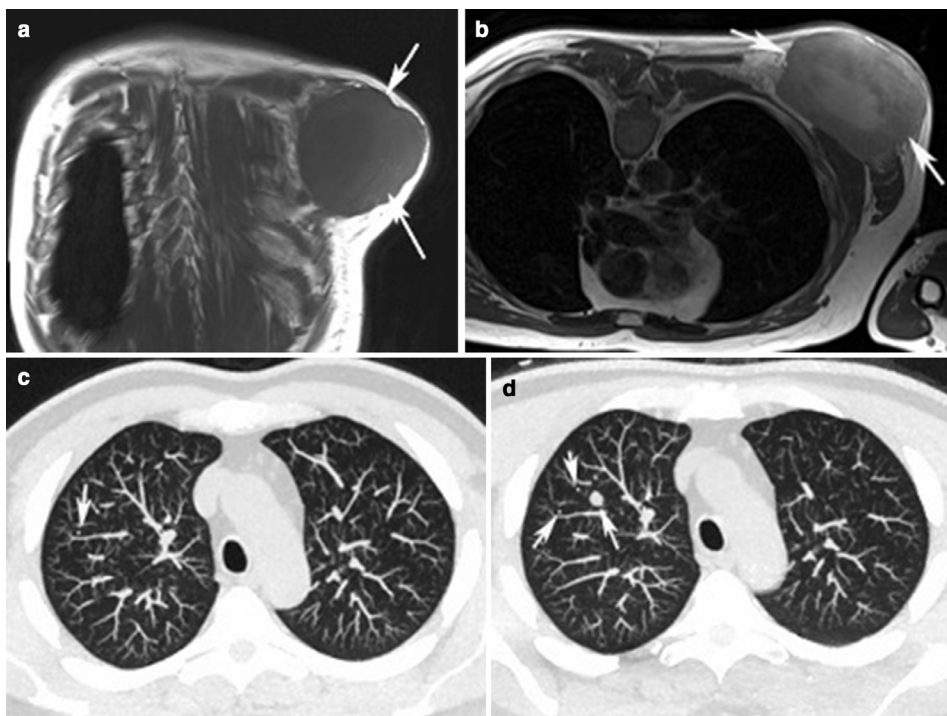
Figure 3. A 74-year-old male with a large mass in the left lateral buttock. (a) Coronal T_1W TSE and (b) axial SPAIR MR images demonstrate a large (T3 AJCC stage) lobular soft tissue mass (arrows) with associated groin and external iliac lymphadenopathy (arrowheads-a) confirmed to be a high-grade extra skeletal myxoid chondrosarcoma on excision. (c) Coronal MIP chest CT study demonstrates multiple nodules (arrows), the largest measuring 17 mm consistent with metastases on both the >5 mm and >10 mm criteria. FSE, fast spin echo; IP, maximum intensity projection; PDW, proton density-weighted; TSE, turbo spin echo.
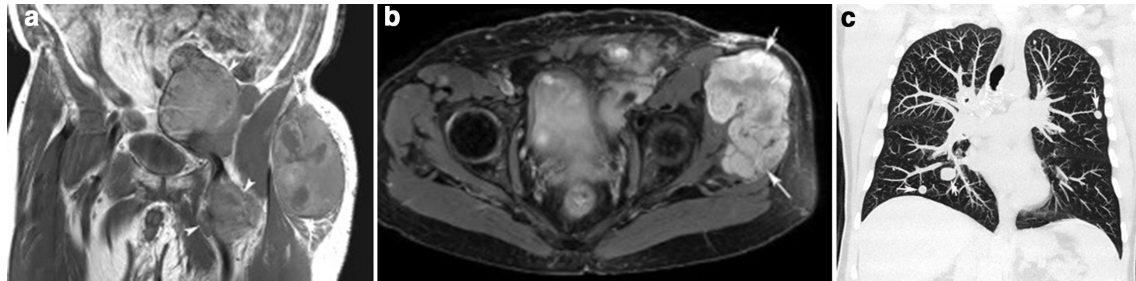
(Figure 1), while 91 (45.5%) CT studies were indeterminate. Of the patients with indeterminate studies, 24 had follow-up chest CT studies at a mean time of 8.2 months (range 3–16 months), 6 of which (25% of the indeterminate scans) were classified as showing metastases due to nodule growth or new nodules (Figure 2), while 18 showed no progression and were still classified as indeterminate. Based on initial chest CT and nodule size

>10 mm, 72 (36.0%) patients had no metastases and 17 (8.5%) had metastases (Figure 3), while 111 (55.5%) studies were indeterminate. Of the patients with indeterminate studies, 33 had follow-up chest CT studies at a mean of 7.5 months (range 1–16 months), 11 of which (33% of the indeterminate scans) were classified as showing metastases due to nodule growth or new nodules while 22 showed no progression and were still classified

Table 2. Showing associations between clinical and STS characteristics and presence of metastases based on >5 mm nodule size

Variable	Category	No metastases or indeterminate ($n = 158$)	Definite metastases ($n = 42$)	*p*-value
Age	–	55.8 ± 18.8	62.0 ± 17.1	0.06
Sex	Female	62 (39%)	11 (26%)	0.12
	Male	96 (61%)	31 (74%)	
Location	Deep	115 (73%)	32 (76%)	0.66
	Superficial	43 (27%)	10 (24%)	
Body region	Abdominal wall	5 (3%)	1 (2%)	0.94
	Ankle/foot	9 (6%)	2 (5%)	
	Arm	10 (6%)	3 (7%)	
	Calf	14 (9%)	6 (14%)	
	Forearm	7 (4%)	1 (2%)	
	Knee	7 (4%)	1 (2%)	
	Pelvis/groin	16 (10%)	5 (12%)	
	Shoulder	6 (4%)	2 (5%)	
	Thigh	64 (41%)	15 (36%)	
	Trunk/chest	14 (9%)	6 (14%)	
	Wrist/hand	6 (4%)	0 (0%)	
Tumour size	T1	43 (27%)	9 (21%)	0.04
	T2	64 (41%)	12 (29%)	
	T3	31 (20%)	8 (19%)	
	T4	20 (13%)	13 (31%)	
Histology	Low grade	18 (11%)	1 (2%)	0.08
	High grade	140 (89%)	41 (98%)	

STS, soft tissue sarcoma.
Summary statistics are: mean ± standard deviation or number (percentage).

Table 3. Showing associations between clinical and STS characteristics and presence of metastases based on >10 mm nodule size

Variable	Category	No metastases or indeterminate ($n = 172$)	Definite metastases ($n = 28$)	p-value
Age	–	55.8 ± 19.0	65.5 ± 13.3	0.001
Sex	Female	67 (39%)	6 (21%)	0.07
	Male	105 (61%)	22 (79%)	
Location	Deep	125 (73%)	22 (79%)	0.51
	Superficial	47 (27%)	6 (21%)	
Body region	Abdominal wall	5 (3%)	1 (4%)	0.58
	Ankle/foot	11 (6%)	0 (0%)	
	Arm	11 (6%)	2 (7%)	
	Calf	18 (10%)	2 (7%)	
	Forearm	7 (4%)	1 (4%)	
	Knee	7 (4%)	1 (4%)	
	Pelvis/groin	16 (9%)	5 (18%)	
	Shoulder	6 (3%)	2 (7%)	
	Thigh	70 (41%)	9 (32%)	
	Trunk/chest	15 (9%)	5 (18%)	
	Wrist/hand	6 (3%)	0 (0%)	
Tumour size	T1	49 (28%)	3 (11%)	0.009
	T2	68 (40%)	8 (29%)	
	T3	32 (19%)	7 (25%)	
	T4	23 (14%)	10 (36%)	
Histology	Low grade	18 (10%)	1 (4%)	0.25
	High grade	154 (90%)	27 (96%)	

STS, soft tissue sarcoma.
Summary statistics are: mean ± standard deviation or number (percentage).

as indeterminate. Therefore, based on a combination of initial and follow-up chest CT, 42 [21%: 95% CI (16–27%)] patients had pulmonary metastases based on nodule size >5 mm, while 28 [14%: 95% CI (10–20%)] patients had pulmonary metastases based on nodule size >10 mm.

The relationship between various patient and STS characteristics with the presence of metastases are presented in Tables 2 and 3. For nodule size >5 mm, the results suggest that tumour size was significantly associated with the presence of metastases (p = 0.04), 50% of patients with T3 or T4 tumours having metastases compared to 33% without metastases. There was also some evidence that patients with metastases were older and had higher-grade tumours than those without metastases, but these results were of borderline statistical significance (p = 0.06 and 0.08 respectively). Sex, location in relation to the fascia and body region were not found to be associated with metastases. For nodule size >10 mm, the results suggest that tumour size was significantly associated with the presence of metastases (p = 0.009), 61% of patients with T3 or T4 tumours having metastases compared to 33% without metastases. Older age was also significantly associated with the presence of metastases (p = 0.001), while male patients were more likely to have metastases, but this

result was of borderline statistical significance (p = 0.07). Location in relation to the fascia, body region and histological grade were not found to be associated with metastases. Table 4 shows the results of logistic regression. A larger tumour size (particularly T4) was associated with an increased risk of metastases for both >5 mm and >10 mm nodule size, while older patient age was also significant for the 10 m nodule size.

Histological diagnosis was based on a combination of needle biopsy and surgical resection specimens in 175 (87.5%) cases and on needle biopsy alone in 25 (12.5%) cases. Details of STS histological subtype and the presence of metastases are presented in Table 5, 181 (90.5%) STS being high-grade (Trojani Grade 2 or 3) and 19 (9.5%) being low-grade. The commonest high-grade tumour subtypes were undifferentiated pleomorphic sarcoma, myxofibrosarcoma, myxoid liposarcoma, undifferentiated spindle cell sarcoma, leiomyosarcoma and synovial sarcoma which together accounted for 80.1% of all high-grade tumours. The commonest low-grade tumour was low-grade fibromyxoid sarcoma. Undifferentiated pleomorphic sarcoma and myxofibrosarcoma were the commonest tumour subtypes associated with metastases.

Table 4. Logistic regression of factors associated with metastases based on >5 mm and >10 mm nodule size

Variable	Category	Odds ratio (95% CI)	*p*-value
>5 mm nodule size			
Tumour size	T1	1	0.04
	T2	0.90 (0.35, 2.31)	
	T3	1.23 (0.43, 3.55)	
	T4	3.11 (1.14, 8.46)	
>10 mm nodule size			
Age	–	1.30 (1.01, 1.68)	0.04
Tumour size	T1	1	0.05
	T2	1.72 (0.43, 6.90)	
	T3	3.04 (0.72, 12.8)	
	T4	5.64 (1.38, 23.0)	

CI, confidence interval.

Of the six patients with indeterminate nodules based on >5 mm size criterion who were finally diagnosed with metastases due to increase in nodule size or number, all were high-grade including three undifferentiated pleomorphic sarcomas, two leiomyosarcomas and one malignant peripheral nerve sheath tumour. One tumour was T1, three were T2, one was T3 and 1 was T4. Of the 11 patients with indeterminate nodules based on >10 mm size criterion who were eventually diagnosed with metastases due to increase in nodule size or number, all were high-grade including five undifferentiated pleomorphic sarcomas, 2 leiomyosarcomas and 1 case each of malignant peripheral nerve sheath tumour, extra skeletal chondrosarcoma, pleomorphic liposarcoma and myxofibrosarcoma. Two tumours were T1, four were T2, three were T3 and 2 were T4.

DISCUSSION
The current study has determined the incidence of pulmonary metastases based on chest CT in STS of the trunk and extremity, 90.5% of which were histologically high-grade tumours. Currently, there are no agreed criteria as to CT features which are definitive of pulmonary metastases in patients with STS. Therefore, we determined the incidence of metastases based on two criteria: minimum nodule size of 5 mm and minimum nodule size of 10 mm. Based on a minimum nodule size of 5 mm, 21% of STS were associated with pulmonary metastases while based on a minimum nodule size of 10 mm, 14% were associated with metastases. For both criteria, the presence of metastases was significantly associated with T3 or T4 tumours, while older age was also a significant feature based on nodule size >10 mm. STS location in relation to body region or the deep fascia were of no relevance.

Previous studies have attempted to determine the incidence of pulmonary metastases at presentation of STS. In a major review of 3149 patients with STS of all locations, Billingsley et al[8] identified 719 patients (22.8%) who presented with or developed metastatic disease. Of these 719 patients, a metastasis was identified at presentation on CXR or CT in 32% while metastatic disease developed either in isolation or in association with local recurrence in a further 36.6%. The trunk and extremities were the source of pulmonary metastatic disease in 65% of cases, and the commonest histological subtypes associated with pulmonary metastases were leiomyosarcoma (21%), malignant fibrous histiocytoma (18%), liposarcoma (12%) and synovial sarcoma (14%). Christie-Large et al[9] determined the incidence of lung metastases at presentation using either CXR or CT in 1,170 patients with STS over a 7.5-year period, finding pulmonary metastases in 8.2% of cases. Pulmonary metastases were diagnosed in the presence of multiple, non-calcified, ovoid or round nodules with no size criterion considered. In four cases, pulmonary nodules identified on CT and reported as metastases were found to be benign at histological examination. They further assessed factors which were more likely to be associated with pulmonary metastases, finding a difference between deep and superficial lesions (9% *vs* 4%), and histological grade (11.8% for high-grade, 7% for intermediate grade and 1.2% for low-grade tumours). The relationship between incidence of lung metastases at presentation and surgical tumour grade has also been assessed. Fleming et al[10] determined the incidence of lung metastases in T1 (<5 cm maximal diameter) extremity STS, finding only 1 case in 125 patients 0.8%. However, only 51 patients (40.8%) underwent CT, and CT studies utilised slice thicknesses of 7–10 mm. The same group reported an incidence of 19.2% based on chest CT in 600 patients with T2 (>5 cm maximal diameter) STS from all locations.[11] In the current study, 11–21% of T1 tumours and 29% of T2 tumours based on the new AJCC criteria had metastases, which would suggest that chest CT is required irrespective of tumour size.

The relevance of pulmonary nodules on chest CT in patients with extra pulmonary malignancies has been the subject of several studies, although many of these studies did not deal specifically with STS. Khokhar et al[18] reviewed 151 patients over a 12-year period, of whom 64 were diagnosed with malignant nodules based on biopsy. Of these, 32 were new lung cancers, 28 were metastases from the primary cancers and 4 were of indeterminate origin. On multivariate analysis, the likelihood of a nodule being malignant increased with nodule size and a history of tobacco exposure. Hanamiya et al[15] reported on the frequency and relevance of pulmonary nodules identified on thin-section (2 mm slice thickness) chest CT in 308 patients with extra pulmonary cancers. One or more non-calcified pulmonary nodules were identified in 75% of cases. Nodules < 10 mm were more likely to be benign, while those >10 mm were more likely to be malignant. With regards to nodule location, 91% of nodules < 10 mm from the pleura were benign, whereas 47% of nodules > 10 mm from the pleura were malignant. Regarding tumour histology, patients with melanoma, sarcoma or testicular cancer were more likely to have malignant nodules. Caparica et al[13] reviewed needle biopsy findings of pulmonary nodules in 228 patients with non-pulmonary cancers over a 36-month period. Of these, 64% had metastatic disease, 26.3% were diagnosed with a new lung cancer and in 9.6% of cases the biopsy yielded a benign diagnosis. On multivariate analysis, findings which were

Table 5. Showing details of STS histological subtype for 200 STS based on low-grade or high-grade histology and the incidence of pulmonary metastases based on >5mm or >10mm nodule size

Diagnosis	Low-grade	Metastases 5 mm: 10 mm	High-grade	Metastases 5 mm: 10 mm
Undifferentiated pleomorphic sarcoma	0	0 (0%): 0 (0%)	33	10 (30.3%): 8 (24.2%)
Myxofibrosarcoma	2	0 (0%): 0 (0%)	28	6 (20%): 3 (15.8%)
Liposarcoma -myxoid	0	0 (0%): 0 (0%)	23	1 (4.3%): 1 (4.3%)
Undifferentiated spindle cell sarcoma	0	0 (0%): 0 (0%)	21	5 (23.8%): 2 (9.5%)
Leiomyosarcoma	2	0 (0%): 0 (0%)	21	5 (21.7%): 2 (8.7%)
Synovial sarcoma	0	0 (0%): 0 (0%)	19	5 (26.3%): 3 (15.8%)
MPNST	0	0 (0%): 0 (0%)	8	4 (50%): 2 (25%)
Rhabdomyosarcoma	0	0 (0%):0 (0%)	6	2 (33.3%): 2 (33.3%)
Low-grade fibromyxoid sarcoma	6	0 (0%):0 (0%)	0	0 (0%): 0 (0%)
Extra skeletal osteosarcoma	0	0 (0%): 0 (0%)	3	0 (0%): 0 (0%)
Epithelioid sarcoma	0	0 (0%): 0 (0%)	3	0 (0%): 0 (0%)
Extra skeletal chondrosarcoma	0	0 (0%): 0 (0%)	2	1 (50%): 1 (50%)
Liposarcoma -pleomorphic	0	0 (0%): 0 (0%)	2	1 (50%): 1 (50%)
Liposarcoma -dedifferentiated	0	0 (0%): 0 (0%)	2	0 (0%): 0 (0%)
Clear cell sarcoma	0	0 (0%): 0 (0%)	2	0 (0%): 0 (0%)
Angiosarcoma	0	0 (0%): 0 (0%)	1	0 (0%): 0 (0%)
Haemangioendothelioma	1	1 (100%): 1 (100%)	1	1 (50%): 0 (0%)
Dermatofibrosarcoma protuberans	2	0 (0%): 0 (0%)	1	0 (0%): 0 (0%)
Ewing sarcoma	0	0 (0%): 0 (0%)	1	0 (0%): 0 (0%)
BCOR-round cell sarcoma	0	0 (0%): 0 (0%)	1	0 (0%): 0 (0%)
CIC-round cell sarcoma	0	0 (0%): 0 (0%)	1	0 (0%): 0 (0%)
Fibrosarcoma	0	0 (0%): 0 (0%)	1	0 (0%): 0 (0%)
Myofibroblastic sarcoma	3	0 (0%): 0 (0%)	1	0 (0%): 0 (0%)
Solitary fibrous tumour	1	0 (0%): 0 (0%)	1	0 (0%): 0 (0%)
Myxoinflammatory fibroblastic sarcoma	2	0 (0%): 0 (0%)	0	0 (0%): 0 (0%)
Total	19		181	

significantly predictive of metastases were multiple nodules > 5 mm in size and the presence of cavitation. Nakamura et al[19] reported on chest CT findings in 124 patients with high-grade STS. Pulmonary nodules were identified at initial presentation in 39.5% of cases, of which almost 70% were benign while 26.5% were metastatic. During follow-up, 24% developed new pulmonary nodules of which 70% were metastatic. Therefore, the relevance of pulmonary nodules is also dependent upon the time point in the patient's disease pathway.

Indeterminate pulmonary nodules on chest CT in sarcoma patients present a diagnostic dilemma and have been the subject of several studies. Rissing et al[14] prospectively studied 331 sarcoma patients to determine if indeterminate pulmonary nodules were of prognostic significance. 71 (21%) had indeterminate pulmonary nodules, 20 (28%) of which progressed indicating metastatic disease. The presence of <5 mm indeterminate nodules was not a prognostic variable, but the presence of

nodules >/=5 mm was associated with worse 3 year disease-free survival compared to patients with normal CT studies or <5 mm indeterminate nodules. Munden et al[20] investigated the relevance of <4 mm indeterminate nodules in oncology patients, finding 28% of such nodules to increase in size and/or number, thereby being consistent with metastases. Mayo et al[21] reviewed chest CT studies in 149 patients with bone and soft tissue sarcoma, of whom 49 (33%) presented with indeterminate lung nodules. 15 (31%) of these progressed indicating that they represented metastases, and nodule progression was associated with tumour size >14 cm at presentation. In the current study, indeterminate pulmonary nodules were identified in 91 and 111 patients based on minimum nodule size of 5 or 10 mm respectively. One of the limitations of this study is that only a relatively small proportion of these patients had follow-up chest CT to determine their significance. This was likely due to the way the scans were initially reported for clinical purposes, which would not have been standardised as to the definition of an indeterminate

nodule. Therefore, the requirement for a follow-up study would have been the decision of the reporting radiologist. Based on the >5 mm nodule criterion, only 6 of 24 (25%) patients with follow-up chest CT showed increase in nodule number or size, while based on the >10 mm nodule criterion 11 of 33 (33.3%) showed increase in nodule number or size. This higher proportion is to be expected, since based on the >10 mm nodule size criterion, indeterminate nodules could measure up to 9 mm in maximal dimension and were therefore more likely to be metastases. Also, this means that the final number of metastases in each group was likely to have been underestimated since only 28% of the 5 mm threshold indeterminate scans were repeated (finding an additional 6 cases of metastases) and only 31% of the 10 mm threshold indeterminate scans were repeated (finding an additional 11 cases of metastases). Therefore, the final number of metastases in the indeterminate group could have been up to 4x greater in the 5 mm group and just over 3x greater in the 10 mm group if all indeterminate scans had been repeated. Increase in nodule number or size was most commonly seen with undifferentiated pleomorphic sarcoma, but due to the small numbers with follow-up chest CT it is not possible to determine the relationship between tumour sub type and the likelihood of indeterminate nodules progressing. There also appeared to be no relationship between STS size and the likelihood of nodule progression. Therefore, no recommendations can be made as to which patients do or do not require follow-up chest CT when indeterminate pulmonary nodules are identified at presentation.

However, in such circumstances it may be worth considering the British Thoracic Society (BTS) guidelines for the investigation and management of pulmonary nodules,[22,23] which include the clinical scenario of pulmonary nodules detected on chest CT in the staging of known extra pulmonary cancers, but not specifically STSs. According to BTS guidelines, solid non-calcified nodules which have typical features of benign lesions such as hamartomas or perifissural nodules, or nodules < 5 mm in size require no follow-up. However, the latter guidance is contentious considering the above literature and the findings of the current study, which clearly show that a small percentage of <5 mm nodules do grow indicating that they likely represent metastases. Nodules < 8 mm in diameter should be subject to CT follow-up while nodules >8 mm in size should be assessed using the Brock model. Regarding timing of follow-up, nodules measuring 5–6 mm in diameter should undergo chest CT in 1 year. However, this delay in a setting of known high-grade sarcoma would be unacceptable to patients, and also the treating clinician if the presence of pulmonary metastases was to have a direct impact on treatment of the primary lesion. According to BTS guidelines, nodules > 8 mm in diameter should have a repeat chest CT in 3 months, which would appear to be a much more acceptable timing for both patients and clinicians.

Another limitation of this study is that none of the pulmonary nodules identified as being metastatic on chest CT had histological confirmation. However, based on the results of previous studies, lung nodules in sarcoma patients that are >10 mm in size are consistent with metastases, while multiple nodules >5 mm in size are also highly likely to be metastatic. In clinical practice, the presence of multiple non-calcified pulmonary nodules >5 mm in size is usually taken to represent the presence of metastatic disease. The vast majority of STS were high-grade and therefore it is difficult to comment upon the requirement for chest CT in patients with low-grade tumours, although only one patient with a low-grade tumour had metastases. Finally, only nodule size was assessed and no consideration was given to location in relation to the pleura.

In conclusion, the current study shows the incidence of pulmonary metastases in patients with trunk and extremity STS to be at least between 14 and 21%, based on which nodule size criterion is used to define a metastasis. Irrespective of size criteria, pulmonary metastases are significantly more common with T3 and T4 tumours but are also identified in a relatively large proportion of patients with smaller tumours. There is no association between the presence of metastases and tumour relationship to the deep fascia. Therefore, the current study would suggest that chest CT should be undertaken at staging in all high-grade STS irrespective of size or location.

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