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## ■ RESEARCH

# Screening and surveillance CT abdomen/pelvis for metastases in patients with soft-tissue sarcoma of the extremity

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## Objectives

The clinical utility of routine cross sectional imaging of the abdomen and pelvis in the screening and surveillance of patients with primary soft-tissue sarcoma of the extremities for metastatic disease is controversial, based on its questionable yield paired with concerns regarding the risks of radiation exposure, cost, and morbidity resulting from false positive findings.

## Methods

Through retrospective review of 140 patients of all ages (mean 53 years; 2 to 88) diagnosed with soft-tissue sarcoma of the extremity with a mean follow-up of 33 months (0 to 291), we sought to determine the overall incidence of isolated abdominopelvic metastases, their temporal relationship to chest involvement, the rate of false positives, and to identify disparate rates of metastases based on sarcoma subtype.

## Results

A total of four patients (2.9%) exhibited isolated abdominopelvic metastatic disease during the surveillance period. In all cases of concomitant chest and abdominopelvic disease, chest involvement preceded abdominopelvic involvement. There was a significant false positive rate requiring invasive workup.

## Conclusions

In the setting of a relative paucity of evidence concerning a rare disease process and in difference to recently published investigations, we add a clinical cohort not supportive of routine cross sectional imaging of the abdomen and pelvis.

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## Article focus

- To determine the utility of CT of the abdomen/pelvis in staging and surveillance of soft-tissue sarcoma of the extremity
- To identify soft-tissue sarcoma types more prone to isolated abdominal metastases
- To identify the rate and effects of false positive CT

## Key messages

- Isolated metastases to the abdomen/pelvis are rare
- Concomitant chest/abdomen metastases affect the chest first
- False positive findings lead to invasive work ups with potential complications

## Strengths and limitations

- Strength: We add a large cohort of a rare condition to a relative paucity of literature supporting the standard of care, which calls for imaging the chest alone, in difference to a recent publication
- Limitation: potential for significant selection bias
- Limitation: inadequate sample size to make conclusions regarding risk of metastases of specific sarcoma types

## Introduction

Soft-tissue sarcoma of the extremity is a rare entity,<sup>1,2</sup> which becomes distantly metastatic in approximately 20% to 30% of patients, uncorrected for tumour grade.<sup>2-4</sup> Most patients who develop metastases will do so

within two to five years of diagnosis, 75% involving the chest,<sup>1,2,5</sup> and with a significant portion presenting symptomatically.<sup>3</sup> The current standard of care for newly diagnosed extremity soft-tissue sarcoma involves imaging of the chest for staging and surveillance for metastatic lesions.<sup>3,6-9</sup> Most sarcomas have been felt to spread first to the lungs prior to extra-pulmonary sites, however, specific sarcoma sub-types have been previously observed to spread to the abdomen initially.<sup>6,10,11</sup> The observation of isolated abdominal metastatic disease is rare,<sup>6,10-12</sup> but leads to many centres routinely imaging the abdomen/pelvis as a measure of screening and surveillance. The utility of this practice has been recently investigated by King et al,<sup>6</sup> and based on a larger than expected rate of abdominal involvement (both isolated and in conjunction with pulmonary disease) the authors were led to consider routine screening and surveillance (CT) of the abdomen/pelvis in all patients with all types of soft-tissue sarcoma of the extremity.

Identification of prognostic factors for development of abdominal disease would benefit clinicians in determining which patients should undergo screening with CT, sparing others excessive radiation, cost, and potential morbidity from false positive findings. However, the current available literature does not provide clear direction in this regard. Given increasing concerns for lifetime radiation exposure,<sup>13,14</sup> costs of potentially unnecessary tests, and the unexpected results of the aforementioned work, we proposed to study the diagnostic utility of CT imaging of the abdomen/pelvis for metastatic disease in primary extremity soft-tissue sarcoma to determine if our experience was supportive of this practice.

We pose the following questions: What is the incidence of chest *versus* abdominopelvic metastatic disease at the time of diagnosis (screening) or in surveillance of patients with soft-tissue sarcoma of the extremities? What is the coincidence and temporal relationship of chest *versus* abdominopelvic metastases? Do specific soft-tissue sarcoma sub-types exhibit disparate rates of metastasis or show propensity for abdomen/pelvis involvement? What is the rate and consequence of false positive results when the modality is routinely employed, and what cost does this impart on the healthcare system?

## Patients and Methods

Following institutional review board approval, by retrospective review of the medical record at a single tertiary care centre with two practicing fellowship-trained musculoskeletal oncologists, we identified potential patients by performing a query of the electronic medical record using ICD-9 codes 171.2 and 171.3 for malignant neoplasm of the upper extremity and lower extremity, respectively. A full chart review was performed on all patients who had undergone CT chest/abdomen/pelvis (C/A/P) to determine the number of abdomen/pelvis CTs obtained, the presence of metastases on a given CT scan,

the temporal relationship of chest to abdominopelvic metastases, and additional work up that was performed due to a positive CT result. Primary endpoints were presence of abdominal or pelvic metastasis on staging or surveillance CT C/A/P and sarcoma type. Secondary endpoints included incidental findings from abdominopelvic imaging, further diagnostic or surgical procedures performed as a result of said findings, and temporal relationship of chest to abdominopelvic metastases.

All patients, including children, adults, and inmates seen clinically between January 2006 and August 2013 were included in the study population, with a mean follow-up of 32.8 months (0 to 291). Mean patient age was 53 years (2 to 88). Malignant tumours of all histological grades were included. From the initial population of queried study subjects, 469 patients underwent initial chart review looking solely at pathology reports for sarcoma type. Patients with benign lesions, bone lesions, metastases, and skin malignancies were excluded, thereby leaving 306 patient charts for review. We chose not to include primary pelvic lesions in our data set. Of these 306 patients, we identified 140 patients who had undergone screening and/or surveillance CT C/A/P. We included all CT scans for which we had electronic or paper reports.

A total of 140 patients were included in the study population. Percent positive values were calculated for any form of metastatic disease, abdominopelvic metastatic disease, pulmonary metastatic disease, and isolated abdominopelvic metastatic disease. These data were further characterised based on time of study collection (screening or surveillance), and the percentage of patients with metastatic disease who had isolated abdomen/pelvis metastases.

Temporality of the diagnosis of chest and abdominopelvic metastases was then examined and presented as percentage of patients with both chest and abdomen/pelvis involvement presenting simultaneously or in the chest or abdomen/pelvis at disparate time points. Time to diagnosis of chest and abdominal metastases were calculated in those who had positive abdominal imaging. Total rate of metastatic disease of the chest and abdomen/pelvis at screening and surveillance was then recorded by tumour tissue type. Finally, percentages of positive CT scans not representing metastatic disease were tabulated as the false positive rate. Charts of those patients undergoing further diagnostic work up were identified and invasive tests and associated complications were recorded and described.

## Results

Of 140 patients, 55 (39%) with primary soft-tissue sarcoma of the extremity had metastatic disease identified on either chest or abdominal imaging. In total 51 patients' (36.4%) metastatic disease involved only the chest, whereas four (2.9%) exhibited isolated abdominal

**Table 1.** Patients with metastatic disease of the abdomen/pelvis

Patient	Sarcoma	Age (yrs)	Chest mets staging	A/P mets staging	Time to chest mets surveillance (mths)	Time to A/P mets surveillance (mths)	Location
14366	Kaposiform hemangioendothelioma	27	No	No	50	50	Pelvic lymph nodes, abdominal
16481	Epithelioid sarcoma	23	No	No	8	18	Liver
33917	Epithelioid sarcoma	27	No	No	4	5	Iliopsoas
34482	Spindle cell sarcoma	73	No	No	8	20	Mesenteric
34981	Clear cell sarcoma of tendon sheath	40	No	No	N/A	18	Inguinal lymph nodes
40729	Spindle cell sarcoma	23	No	No	6	6	Bony
43768	Synovial sarcoma	18	No	No	97	97	Peritoneal
45974	Leiomyosarcoma	74	Yes	No	-	4	Liver
46259	Rhabdomyosarcoma	71	No	No	N/A	4	Inguinal lymph nodes
59750	Pleomorphic liposarcoma	56	Yes	No	-	7	Multiple
61489	Myxoid liposarcoma	64	No	No	N/A	8	Inguinal lymph nodes
80066	Pleomorphic sarcoma	76	No	No	N/A	6	Liver
88902	Leiomyosarcoma	63	Yes	Yes	-	-	Liver
97186	Pleomorphic sarcoma	48	No	No	6	9	Inguinal lymph nodes, pelvic sidewall

A, abdomen; P, pelvis; Mets, metastases

metastases, and ten (7.1%) had metastases of both the chest and abdomen/pelvis. A total of 14 patients (10%) had abdominal or pelvic metastases identified by abdominal CT scan, one (0.7%) at diagnosis and 13 (9.3%) on surveillance imaging (Table 1).

Isolated abdominal metastatic disease represented 7% of patients with any metastases and 28.6% of the subset with abdominal metastases. Of ten patients with metastases to both the chest and abdomen/pelvis, none developed evidence of disease of the abdomen/pelvis prior to evidence of chest involvement. Whereas six of ten (60%) patients developed evidence of metastases to the chest prior to the abdomen/pelvis, four (40%) were found to have both pulmonary and abdominopelvic metastases at the same time. Of those with abdominopelvic metastases, the average time to diagnosis of chest or abdomen/pelvis metastases was 17 (n = 10) and 19 (n = 14) months, respectively. Those with isolated abdominal metastases had an average disease-free interval of 12 months (n = 4).

A total of 11 of 21 sarcoma types represented in the cohort developed extra-pulmonary metastases (Table II). Relatively prevalent sarcoma types (n > 5) within the cohort that when metastatic disease had a higher percentage (> 20%) of abdominal or pelvic involvement, were epithelioid sarcoma, leiomyosarcoma, liposarcoma, spindle cell sarcoma, and synovial sarcoma. Isolated abdominal metastases were observed in one each of clear cell sarcoma, pleomorphic sarcoma, myxoid liposarcoma, and rhabdomyosarcoma. Three of 24 patients with liposarcoma of any type developed metastases. One of 14 myxoid liposarcoma developed metastatic disease,

which was isolated to the pelvis, and two of ten patients with other liposarcoma developed abdominal disease.

Of 19 patients (13.6%) with positive CTs of the abdomen/pelvis, 14 (73.7%) had metastatic disease. There were six false-positive results necessitating further diagnostic work, four of which were invasive with a significant complication in one of four. Based on the 2013 Medicare fee schedule for bundled CPT 74177 (CT abdomen/pelvis with contrast), the cost of a single CT of the abdomen and pelvis is \$483.<sup>15</sup> A total of 212 such diagnostic studies were performed in this cohort of patients, estimating a total cost to the healthcare system of \$102 500, or \$25 625 to identify a single patient with isolated metastases of the abdomen/pelvis.

## Discussion

The diagnostic utility of routinely obtaining CTs of the abdomen/pelvis in the screening and surveillance of patients with extremity soft-tissue sarcoma for the development of metastatic disease is in question.<sup>6</sup> Approximately one third of patients will develop metastatic disease, 75% involving the chest,<sup>1,2</sup> and therefore most authors endorse routine imaging of the chest alone, unless further imaging is indicated clinically.<sup>3,7,8,9</sup> The observation of isolated abdominal metastatic disease is rare,<sup>6,12</sup> but has led to many centres routinely imaging the abdomen/pelvis as a measure of screening and surveillance. Identification of prognostic factors for development of abdominal disease would benefit clinicians in determining which patients should undergo screening with CT, sparing others excessive radiation, cost, and potential morbidity from false positive findings. However, the current available literature does not provide clear direction.

**Table II.** Metastatic disease by sarcoma type

Sarcoma type	Pts	Total patients with Mets	Chest mets staging	Chest mets surveillance	A/P mets staging	A/P mets surveillance
Pleomorphic sarcoma	25	10	2	7		1
Leiomyosarcoma	19	10	4	6	1	1
Myxoid Liposarcoma	14	1				1
Pleomorphic sarcoma not otherwise specified	14	7	1	6		1
Epithelioid Sarcoma	12	4		4		2
Synovial Sarcoma	12	4	1	3		1
Liposarcoma, other	10	2	1	1		1
Spindle cell	8	6		5		2
Chondrosarcoma	5	2		2		
Extraskeletal osteosarcoma	3	2		2		
Fibrosarcoma	3	1		1		
Rhabdomyosarcoma	3	1				1
Alveolar soft part	2	2	1	1		
Clear cell	2	1				1
MPNST	2	1		1		
Angiosarcoma	1					
Extraskeletal Ewing	1					
Kaposiform hemangioendothelioma	1	1		1		1
Malignant myopericytoma	1					
Myxoid sarcoma	1					
Post-radiation sarcoma	1			1		
Total (%)	140	55 (39)	10 (7)	41 (29)	1 (1)	13 (9)

Pts, patients; Mets, metastases; A, abdominal; P, pelvic; MPNST, malignant peripheral nerve sheath tumour

By retrospectively reviewing our own experience, we sought to determine if the occurrence of abdominopelvic metastatic disease in our population with primary soft-tissue sarcoma of the extremity warranted routine imaging of the abdomen/pelvis.

Our study is retrospective and, thus, prone to the weaknesses of this type of investigation. Foremost is the risk of sampling bias as it could be hypothesised that patients who developed metastatic disease in any form would be more likely to undergo imaging of the abdomen/pelvis in this cohort. As a standardised protocol was not in place prospectively, the decision to image the abdomen/pelvis was made clinically by the involved practitioners. This may add additional selection bias due to the possibility that a perception of a higher risk of metastatic disease may have led to a higher likelihood that the abdomen/pelvis would be imaged. Similarly, observations of temporality are limited by the relative propensity to image the chest more commonly than the abdomen, which may also negatively skew our observed incidence of isolated abdominal metastatic disease. Finally, our sample size of 140 patients was not large enough to perform formal differential statistical analysis based on sarcoma sub-type. Despite these limitations, a relatively large sample of patients with an average follow-up period of 33 months is presented.

The overall rate of metastases to distant sites of 39% observed in the current study is comparable with some prior reports<sup>7,10</sup> and slightly higher than others.<sup>1,4,6,11</sup> In total 10% of the current cohort experienced metastatic disease to the abdomen or pelvis based on either screening or surveillance imaging, which is comparable with

prior investigations.<sup>6</sup> Only one had evidence of abdomen/pelvic metastatic disease at diagnosis, whereas there were 13 positive exams on surveillance imaging, suggesting that surveillance imaging may have a higher diagnostic yield than screening when a diagnosis of soft-tissue sarcoma is known prior to staging. Based solely on these rates, one may consider routine imaging of the abdomen and pelvis as warranted.

However, when considering the incidence of isolated abdomen/pelvis metastases and the temporal relationship of development of chest *versus* abdomen/pelvis lesions in patients with both, it is harder to support routinely imaging the abdomen/pelvis in all patients with primary soft-tissue sarcoma of the extremity. Only 2.9% of patients developed isolated abdominal metastases, which represented 7% of those with metastatic disease of any type. Of those patients who developed both chest and abdominal/pelvic metastases in the current population, none developed evidence of abdominal disease prior to its discovery in the chest. King et al<sup>6</sup> reported similar findings, with 5% isolated abdominal disease and no cases of abdominal involvement preceding chest involvement when both were present.

Based on the results of previous authors<sup>1,4,10,14</sup> and nationally endorsed guidelines as summarised by King et al,<sup>6</sup> a rational approach may be to image the chest in all patients with primary soft-tissue sarcoma of the extremity at diagnosis and during the follow-up period. Additional imaging of the abdomen/pelvis should be considered for large tumours of high grade in deep locations or in those with clinical signs warranting further investigation.<sup>1-5,7,11</sup>

This strategy would be improved if sarcoma sub-types more prone to metastasising to the abdomen/pelvis could be reliably identified. However, low sample sizes, and disparate observations make this difficult.<sup>2,6,12</sup> Similar to previous work, in this study we identified a higher rate of abdominopelvic involvement (when metastatic) with epithelioid sarcoma, leiomyosarcoma, liposarcoma, spindle cell sarcoma, and synovial sarcoma. However, consistent with King et al<sup>6</sup>, only three of 24 liposarcomas were observed to spread to the abdomen/pelvis in contrast to the findings of Cheng et al<sup>10</sup> and Zanarini and Sugarbaker<sup>12</sup> only one myxoid liposarcoma developed isolated abdominal metastatic disease. Our and other sample sizes make reliable statistical analysis unreliable and larger sample sizes collected in a prospective fashion based on a standardised protocol will be required to make more reliable conclusions in this regard.

Finally, when exploring whether or not to employ a specific diagnostic modality, the potential morbidity resulting from its use and its cost must be weighed against its diagnostic yield. No definite conclusions may be drawn from our dataset. However, relative to results that would significantly affect treatment (very few), a large radiation exposure, cost, and high false positive rate with the potential complications of expensive and invasive testing as a result of non-malignant findings should not be ignored.

The routine use of CT of the abdomen and pelvis in the staging and surveillance of all patients with primary soft-tissue sarcoma of the extremity for metastases is not necessarily supported by the current study. As the majority of metastatic disease in this cohort involved the chest either prior to or alongside abdominal/pelvic involvement, routine imaging of the chest should be performed with the decision to image the abdomen/pelvis being based on previously described tumour characteristics and clinical findings (as presented by previous publications and discussed above). Insufficient data exist to base this decision on sarcoma subtype. Radiation exposure, cost, and the consequences of false positives should not be ignored when deciding whether or not to image the abdomen/pelvis routinely during staging or surveillance

protocols. Further prospective controlled studies with large sample size using a standardised clinical protocol and longer follow-up, are needed.

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### Author contributions:

- M. J. Thompson: Data analysis, Writing the paper, Data collection
- J. Ross: Data collection, Data analysis, Writing the paper, Second corresponding author
- G. Domson: Data collection, Attending surgeon, Paper writing oversight
- W. Foster: Data collection, Attending surgeon, Paper writing oversight

### ICMJE Conflict of Interest:

- None declared

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