


ONCOLOGY



# Clinical impact of whole-body MRI in staging and surveillance of patients with myxoid liposarcoma: a 14-year single-centre retrospective study

Samir Paruthikunnan<sup>1\*</sup> , Natalia Gorelik<sup>2</sup>, Robert E. Turcotte<sup>3</sup>, Sungmi Jung<sup>4</sup>, Thierry Alcindor<sup>5</sup> and Thomas I. Powell<sup>2</sup>

## Abstract

**Objective** To assess the clinical impact of regular whole-body magnetic resonance imaging (WBMRI) surveillance in myxoid liposarcoma patients.

**Methods** This was a retrospective cohort study of myxoid liposarcoma patients who underwent at least one WBMRI at our institution between October 2006 and December 2020. The effect of WBMRI on clinical management, namely treatment modification or additional diagnostic investigations was studied. A standardised WBMRI surveillance protocol was instituted in 2015. We compared patient outcomes for the metastatic patients who had and had not received regular WBMRI surveillance and performed survival analysis for both subgroups.

**Results** Of the 56 patients (60.7% male, median age: 48.1 years) who underwent 345 WBMRI, 17 (30.3%) had metastases, and 168 WBMRI were performed in this group. The median imaging follow-up for the entire cohort was 35 months; the metastatic group had a median follow-up of 42 months. WBMRI changed the clinical management in 13 (76.5%) metastatic patients, with 33 instances of treatment modification. Thirty-five lesions were labelled 'indeterminate,' 16 (45.7%) had additional investigations/interventions, and 4 (11.4%) were confirmed to be metastatic. Twenty-one metastatic lesions were missed initially on WBMRI and confirmed on subsequent WBMRI, of which 5 (23.8%) were clinically significant. The 5-year survival since the detection of metastasis was better in the regular surveillance subgroup (85.7% vs. 45%), but this was not statistically significant ( $p = 0.068$ ). Five patients (8.9%) developed their first metastasis more than 5 years after diagnosing the primary lesion.

**Conclusion** Regular WBMRI surveillance of myxoid liposarcoma patients considerably impacts clinical management by frequently influencing treatment decisions.

**Clinical relevance statement** WBMRI has been recently recommended as an imaging option for the staging and surveillance of myxoid liposarcoma patients. Our study highlights the impact of regular WBMRI surveillance on the clinical management of these patients and how it affects their survival.

## Key Points

- Current screening recommendations for myxoid liposarcoma patients, including WBMRI, are equivocal.
- WBMRI surveillance modified treatment in about 75% of metastatic myxoid liposarcoma patients and was associated with improved survival.
- A number of delayed metastasis were observed, suggesting the need for extending the period of WBMRI surveillance.

\*Correspondence:

Samir Paruthikunnan  
samir.pm.19@gmail.com

Full list of author information is available at the end of the article

**Keywords** Myxoid liposarcoma, Magnetic resonance imaging, Whole-body imaging

## Introduction

Liposarcomas constitute 17–25% of all soft tissue sarcomas (STS) [1], and myxoid liposarcomas (MLS) represent the second most common type of liposarcomas [2]. However, unlike liposarcomas, MLS demonstrates an unusual predilection for metastasising to the bones and soft tissues compared to the lungs [3–5]. Hence, unlike the other STS, locoregional and chest imaging are insufficient for MLS. Moreover, several studies have reported the inadequacy of bone scintigraphy, computed tomography (CT), and even positron emission tomography (PET)-CT to identify the extrapulmonary metastases associated with myxoid liposarcoma [6, 7]. MLS is also known to be more radiosensitive and chemosensitive than most other STS [8], thus offering the treating clinician the option of surgery for solitary or oligometastatic disease, radiotherapy for metastatic vertebral disease and chemotherapy for multifocal metastases.

Recently, a few studies have proposed using whole-body magnetic resonance imaging (WBMRI) to assess MLS metastases in the bones and soft tissues [3, 9]. However, the present recommendations for staging and surveillance of MLS are equivocal regarding the type of imaging modality and the frequency of screening [7]. For example, the 2021 European Society for Medical Oncology (ESMO) STS guidelines recommend a CT of the thorax and a CT of the abdomen and pelvis for the staging of MLS but also suggest WBMRI as an alternative [10]. Similarly, the 2022 National Comprehensive Cancer Network (NCCN) guidelines for STS recommend an MRI/CT of the primary site for initial staging, a CT of the lungs, abdomen and pelvis, and an MR of the total spine for initial staging and surveillance of MLS. It also recommends considering a WBMRI screening, given the propensity for soft tissue metastases outside the field of view of the CT chest, abdomen and pelvis [11].

To the best of our knowledge, no studies in the literature describe the long-term clinical impact of surveillance of patients of MLS with WBMRI concerning its influence on patient management and the benefits of having a regular WBMRI surveillance protocol. Therefore, our study aims to address this clinical question and assess the clinical impact of regular WBMRI surveillance in MLS patients.

## Materials and methods

### Patient population

This retrospective cohort study received Institutional Review Board (IRB) approval. The IRB waived the requirement for informed consent from the subjects.

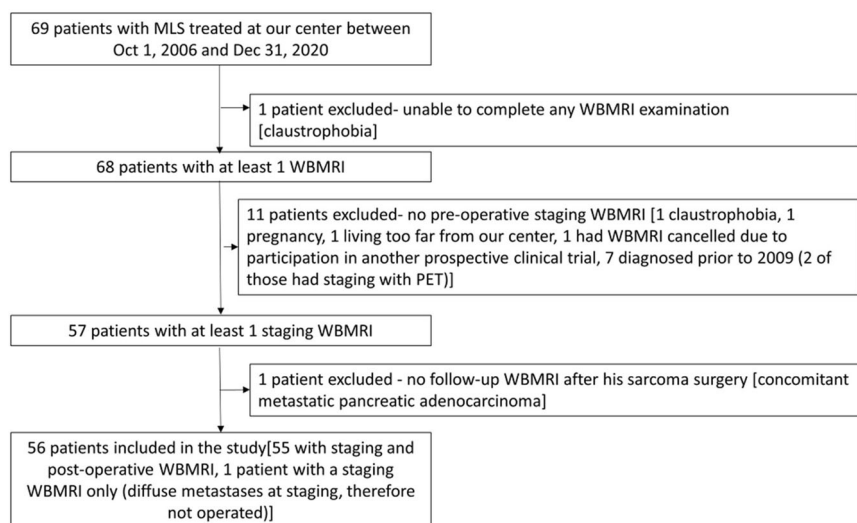
All adult patients with biopsy-proven MLS treated at our quaternary care sarcoma referral centre between October 1, 2006, and December 31, 2020, were identified using an automated search of the institutional radiology reports and the prospective sarcoma tumour registry. All patients with at least one preoperative (staging) and one postoperative (surveillance) WBMRI were included. In addition, one patient with extensive metastatic disease at presentation, who did not survive long enough to undergo any treatment or post-treatment imaging, was also included.

Sixty-nine patients were treated at our centre during the study period. Out of these, one patient could not complete his staging WBMRI due to claustrophobia and refused to undergo further surveillance WBMRI. In addition, 11 patients were excluded as they only had post-treatment surveillance WBMRI but did not have any staging WBMRI, while one patient was excluded as he had concomitant pancreatic adenocarcinoma as a confounding factor with no further imaging or clinical follow-up (Fig. 1). Fifty-six patients (34 males, 22 females; average age 47.1 years, range 21–77 years) were finally included in the study.

### Imaging protocol and analysis

Imaging data were retrospectively collected for the 56 included patients, which included the details of the primary site MRI (site, size, and imaging appearances of the primary tumour), as well as the dates and findings of the staging and surveillance WBMRI, chest CT, and any abdomen and pelvic CT or PET/CT, if performed.

Before 2015, chest CTs were performed for staging and biannual surveillance, but there was no set protocol regarding the routine use of staging and surveillance WBMRI at our centre; WBMRI was infrequently used as an alternative to CT abdomen and pelvis and/or PET/CT, at the discretion of the referring physician. However, since 2015, WBMRI has become the preferred staging and surveillance modality to complement the standard chest CT for MLS. The current staging protocol for MLS includes a CT chest, WBMRI, and an MRI of the primary site, while the surveillance protocol consists of a WBMRI and chest CT every six months for three years. If no metastases are found by year 3, surveillance is continued with WBMRI and chest radiographs performed annually until year 5. If no metastases are detected after year 5, further surveillance imaging includes only annual chest radiographs until year 10. At any point, if metastases are diagnosed, the clock is reset, and the protocol is restarted with six monthly WBMRI and chest CTs.



**Fig. 1** Flow diagram detailing the patient inclusion and exclusion in the study

The WBMRI were performed on a 1.5-Tesla scanner before 2015 (General Electric, 1.5-T SIGNA Excite model). However, our WBMRI protocol changed in 2015, as a new 3-Tesla scanner (Siemens, 3.0-T MAGNETOM Skyra model with Tim Planning Suite) was commissioned. The imaging protocols and parameters before and after 2015 are described in Table 1. Multiple stations cover the entire field of view from the head to the heels, with the average scan time between 40 and 50 minutes on both scanners. In larger or taller patients, the elbows and distal forefeet were occasionally excluded from the field of view.

The primary site MRI, WBMRI, and CT and PET/CT scans were retrospectively reviewed (N.G., S.P.). The primary lesion was considered “superficial” if it did not involve the deep fascia or the underlying muscles and “deep” if it involved these structures. Any lesions identified on the WBMRI were labelled ‘benign,’ ‘malignant,’ or ‘indeterminate’ based on the final report issued by the senior reviewing radiologist (T.P.). The diagnostic pathway followed for defining metastases on WBMRI is depicted in Fig. 2.

Clinical charts were also reviewed, and relevant clinical data were recorded for all patients, including the presence or absence of clinical symptoms at the time of presentation, type of treatment given, histopathological report details such as core and excision biopsies for the grade of tumour, round-cell percentage, surgical margins, and response to treatment; surgical details in cases of Whoops procedures, postsurgical treatment, and clinical follow-up. A tumour with <5% round-cell component was considered ‘low-grade,’ while a tumour with >5% round-cell component was termed ‘high-grade’ [12].

### Statistical analysis

We first compared the metastatic MLS patients with the nonmetastatic patients for the demographic, clinical, imaging, and pathological parameters. Further, amongst the metastatic patients, we defined patients with ‘regular surveillance’ as those with at least two surveillance WBMRI per year for a minimum of 3 consecutive years. We compared this group with those metastatic patients who did not receive ‘regular surveillance’.

Categorical data are expressed as counts (percentages) and continuous variables as medians (interquartile ranges [IQRs]). All tests are conducted as 2-tailed, with  $p$  values less than 0.05 considered statistically significant. The categorical variables were analysed using Fisher’s exact test, while the medians were compared for the continuous variables using nonparametric independent samples median test. R Statistics software version 4.0.0 was used for the statistical analysis. Survival analysis was also performed for all the patients (to assess survival since the diagnosis of the primary lesion) and metastatic patients (to assess survival since the date of diagnosis of the first metastasis), and the log-rank test was used to compare the means of survival times between the metastatic and nonmetastatic groups as well as the regular and non-regular surveillance groups in the metastatic patients.

### Results

#### Comparison between metastatic and nonmetastatic patients

Three hundred and forty-five WBMRI were performed on the fifty-six patients included in our study. The characteristics of metastatic and nonmetastatic groups are presented in Table 2. Of these 56 patients, 17 (30.4%) had

**Table 1** Imaging parameters for WBMRI performed on a 1.5 T scanner before and after 2015

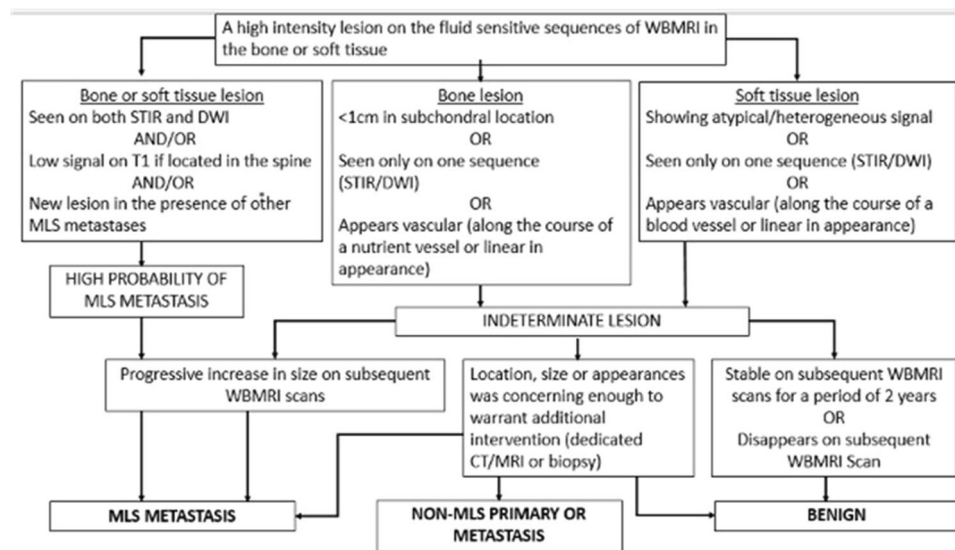
<b>Before 2015</b>				
<b>Parameter</b>	<b>Coronal STIR (whole body)</b>	<b>Axial STIR (whole body)</b>	<b>Sagittal T1 (whole spine)</b>	
No. of stations	4	6–7	2	
TR (ms)	2500–5500	3300–6600	350–450	
TE (ms)	54–68	64–72	14–20	
TI (ms)	140	140	–	
Flip angle (°)	90	90	90	
Matrix size	320 × 192	192 × 320	320 × 224–256	
Field of view (mm)	320–480 × 320–480	350–480 × 350–480	410–480 × 410–480	
Slice thickness (mm)	8	8	5	
Inter-slice gap (mm)	9	9	6	
Pixel bandwidth (Hz)	244	244	122 or 163	
Echo train length	8–12	12	3	
Signal average	1	1	2–3	
<b>After 2015</b>				
<b>Parameter</b>	<b>Coronal STIR (whole body)</b>	<b>Axial STIR (whole body)</b>	<b>Total body DWI b 50–900</b>	<b>Sagittal T1 (whole spine)</b>
No. of stations	6	7	7	3
TR (ms)	9000–14,000	4700–7000	8190–9120	709–850
TE (ms)	53	53	60	9.5
TI (ms)	220	220	240	–
Flip angle (°)	120	120	90	160
Matrix size	256 × 128	256 × 205	134 × 100	384 × 216
Field of view (mm)	500 × 312	500 × 500	500 × 73	390 × 292
Slice thickness (mm)	5	5	5	4
Inter-slice gap (mm)	1	0	0	0.8
Pixel bandwidth (Hz)	300	300	2666	271
Echo train length	13	13	100	3
Signal average	3	3	1 & 8	1
Parallel factor	3	3	2	2

metastases, and 168 WBMRI were performed in this group. Males were predominant in both the metastatic and nonmetastatic groups. More surveillance WBMRI were performed per patient in the metastatic group. A higher proportion of the lesions were deep than superficial in both groups. The metastatic group had a significantly higher proportion of high-grade tumours and a significantly higher proportion of round-cell component (47% having >5% round-cell component compared to 17% in the nonmetastatic group). Two (11.8%) patients in the metastatic group had pulmonary metastases, and both patients developed pulmonary metastases following skeletal metastases. At diagnosis, the median primary tumour size was larger in the metastatic group, but the difference was not statistically significant. Most of the primary tumours underwent neo-adjuvant radiotherapy prior to

definitive surgery. The mean survival duration of the nonmetastatic patients was significantly longer than the metastatic patients.

#### **Comparison between patients with and without regular WBMRI surveillance**

Among the 17 metastatic patients, 7 (41.2%) had regular biannual WBMRI surveillance for at least three consecutive years (Table 3). This group had 112 WBMRI scans compared to the 56 in those who did not receive regular WBMRI surveillance. Six of the seven patients in the regular surveillance subgroup survived at the end of the study period, while eight of the ten of those who did not receive regular WBMRI surveillance died. Survival analysis with Kaplan Meier curves of all the 56 patients demonstrated a 10-year survival rate of 92.3% in the regular surveillance



**Fig. 2** Flow diagram depicting the diagnostic pathway for labelling a lesion as ‘benign’, ‘indeterminate’, or ‘metastatic’ on WBMRI

**Table 2** Comparison of demographic, clinical, imaging and pathology characteristics in patients with and without metastases

Parameter	Patients with metastasis	Patients without metastasis	Total	<i>p</i> value
Number of patients	17 (30.4%)	39 (69.6%)	56	–
Total no. of WBMRI scans	168	177	345	–
Male	13 (76.5%)	21 (53.8%)	34 (60.7%)	0.147
Female	4 (23.5%)	18 (46.2%)	22 (39.3%)	
Median age at diagnosis of primary tumour (IQR, range) in years	50.0 (21.3, 45.5)	47.8 (22.7, 55.5)	48.1 (21.4, 55.5)	0.561
Median WBMRI follow-up duration (IQR, range) in months	42 (52, 113)	33 (30, 120)	35 (39.5, 120)	0.349
Median clinical follow-up duration (IQR, range) in months	90.3 (53.5, 171.2)	78.0 (77.95, 154.8)	84.54 (66.9, 187.9)	0.561
Median no. of WBMRIs (IQR, range)	8 (11, 21)	4 (4, 9)	5 (5, 21)	<b>0.008</b>
Primary tumour location				
Superficial	2 (11.8%)	8 (20.5%)	10 (17.9%)	0.706
Deep	15 (88.2%)	31 (79.5%)	46 (82.1%)	
Primary tumour grade				
Low	4 (23.5%)	29 (74.4%)	33 (58.9%)	<b>0.001</b>
High	13 (76.5%)	10 (25.6%)	23 (41.1%)	
Round-cell component				
Absent or < 5%	4 (23.5%)	25 (64.2%)	29 (51.8%)	<b>0.016</b>
> 5%	8 (47.1%)	7 (17.9%)	15 (26.8%)	
Unknown	5 (29.4%)	7 (17.9%)	12 (21.4%)	
Median primary tumour volume (IQR, range) cm <sup>3</sup>	433.4 (851.4, 2093.5)	242.5 (363.4, 1559.1)	250.7 (397.4, 2138.3)	0.500
Mean survival duration since diagnosis of the primary tumour (95%CI, standard error) in months	114.89 (84.4–145.3, 15.6)	149.1 (136.6–161.6, 6.4)	150.1 (129.7–170.6, 10.4)	<b>0.002</b>
No. of patients treated with neo-adjuvant radiotherapy	14 (82.4%)	33 (84.6%)	47 (83.9%)	1.000
No. of patients treated with adjuvant radiotherapy	5 (29.4%)	11 (28.2%)	16 (28.6%)	1.000

CI confidence interval  
Statistically significant *p* values are in bold

**Table 3** Comparison of demographic, clinical, imaging, and pathology characteristics of metastatic patients who had or did not have regular WBMRI surveillance

	Metastatic patients having regular WBMRI surveillance <i>n</i> = 7	Metastatic patients not having regular WBMRI surveillance <i>n</i> = 10	<i>p</i> value
Total no. of WBMRI scans	112	56	< 0.001
Sex			
Male	5 (71.4%)	8 (80%)	1.000
Female	2 (28.6%)	2 (20%)	
Median duration of WBMRI follow-up primary (IQR, range) in months	64 (59, 71)	32.5 (31.8, 105)	<b>0.015</b>
Median age at diagnosis of primary (IQR, range), in years	55.1 (12.8, 35.1)	47.35 (17.3, 40.2)	0.637
Median duration between the dates of diagnosis of primary and first metastasis (QR, range) in months	9.9 (54.5, 147.9)	39.85 (88.3, 100.1)	0.335
No. of patients developing diffuse metastases* (percentage of total)	3 (42.8%)	3 (30%)	0.644
Location of primary tumour			
Superficial	1 (14.3%)	1 (10%)	1.000
Deep	6 (85.7%)	9 (90%)	
Grade of primary tumour			0.603
Low	1 (14.3%)	3 (30%)	
High	6 (85.7%)	7 (70%)	
Round cell component			0.460
> 5%	2 (28.6%)	6 (60%)	
Absent	2 (28.6%)	2 (20%)	
Not specified	3 (42.8%)	2 (20%)	
Median primary tumour size (IQR, Range) (cm <sup>3</sup> )	437.1 (482.8, 1352.8)	384.8 (1264.4, 2090.2)	0.637
Pre-operative treatment			
Radiotherapy	7 (100%)	7 (70%)	0.485
Chemotherapy	0 (0.0%)	2 (20%)	
None	0 (0.0%)	1 (10%)	
No. of cases with positive surgical margins	2 (28.6%)	3 (30%)	1.000
No. of cases postsurgical radiotherapy	1 (14.3%)	4 (40%)	0.338
No. of patients symptomatic for metastasis	3 (42.8%)	8 (80%)	0.162
No. of patients where the treatment was modified at any point in time following WBMRI	7 (100%)	6 (60%)	0.103
Survival at last follow-up			
Alive	6 (85.7%)	2 (20%)	<b>0.015</b>
Dead	1 (14.3%)	8 (80%)	
Mean survival duration since the detection of the primary malignancy (95%CI, standard error) in months	173.6 (136.0–211.1, 19.2)	93.4 (67.1–119.7, 13.4)	0.093
Mean survival duration since the detection of the metastasis (95%CI, standard error) in months	76.4 (65.2–87.6, 5.7)	53.4 (30.2–76.6, 11.8)	0.068
5-year survival since the time of detection of first metastasis	85.7%	45%	0.068

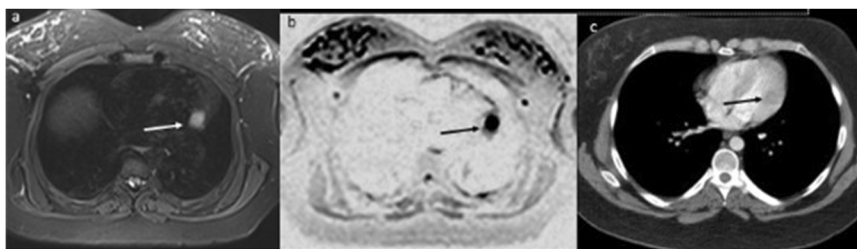
CI confidence interval

Statistically significant *p* values are in bold

\*Diffuse metastases is defined as having &gt; 10 separate metastases on a single WBMRI scan

group and 67.2% in the group not having regular surveillance (Supplementary Figure S1a). The mean survival duration for the regular surveillance group (*n* = 20) was 183.1 months (95%CI: 162.1–204.1, Standard error: 10.7)

compared to 128.7 months (95%CI: 112.9–144.4, Standard error: 8.0) for the nonregular surveillance group (*p* value = 0.301). Survival analysis was also performed for the metastatic patients, and a 5-year survival rate since the



**Fig. 3** A 28-year-old female with primary MLS of the left popliteal fossa diagnosed in 2014 with abdominal and paraspinal soft tissue metastases in 2015 and right popliteal metastasis in 2018. WBMRI scan performed in August 2019 (**a** and **b**) demonstrates a lesion in the left ventricle, which was not well identified on any previous imaging but was confirmed on echocardiography as a mass lesion. This lesion was barely perceptible and missed on the recent CT performed two weeks before the WBMRI (**c**). This lesion was considered metastatic, and the patient underwent localised radiotherapy. Follow-up WBMRI scans demonstrated regression of the metastatic lesion

time of diagnosis of the first metastasis was calculated, which was 85.7% in the regular surveillance group as compared to 45% in the group not receiving regular surveillance ( $p$  value = 0.068) (Supplementary Fig. S1b). The mean survival duration (since the diagnosis of the primary lesion) of the regular surveillance group was 173.6 months as compared to 93.4 months in the nonregular follow-up group ( $p$  value = 0.093) (Table 3).

#### Impact on clinical management of metastatic patients

WBMRI findings changed the management of all patients in the regular surveillance subgroup and > 50% of those who did not receive regular surveillance. Also, fewer patients in the regular surveillance subgroup had symptomatic metastases, but the difference was not statistically significant.

There were 33 instances where WBMRI findings led to a change in clinical management. This included 11 instances of patients receiving additional radiotherapy at the location of the metastasis (Fig. 3), eight instances of patients getting systemic chemotherapy (Fig. 4), four times the patients had a surgical excision, six instances of combined radiotherapy and chemotherapy, three instances of surgery combined with radiotherapy, and one instance of surgery combined with radiation and chemotherapy. Out of 33 instances of treatment modification effected by WBMRI, 24 (72.7%) were seen since regular WBMRI surveillance was started in 2015. On average, there was one treatment modification for every 4.8 WBMRI performed. Figure 5 depicts the timeline of the treatment modifications initiated due to the WBMRI findings.

#### Indeterminate and missed lesions on WBMRI

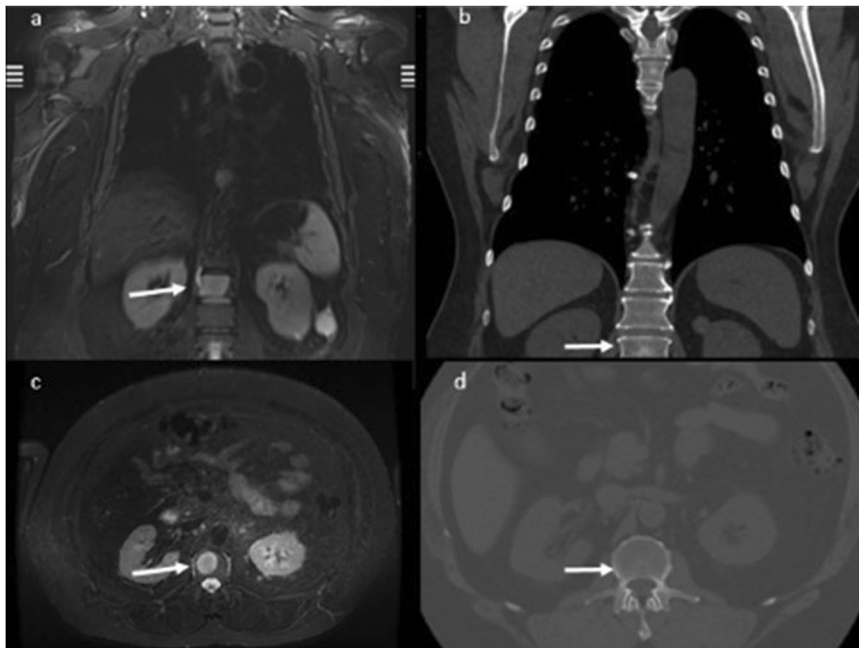
Thirty-five lesions were considered ‘indeterminate’ on 345 WBMRI over 14 years (0.1 indeterminate lesions/WBMRI). Seventeen (48.6%) of these were stable on long-term follow-up by WBMRI over at least 2 years, confirming benignity. Two (5.7%) lesions were not identified

on subsequent MRI scans. Further imaging or intervention was suggested to better characterise the other 16 (45.7%) lesions. Table 4 lists these additional imaging or interventions and the final diagnoses for these lesions. Four of these sixteen indeterminate lesions were confirmed to be metastases from MLS. Two had alternative diagnoses unrelated to MLS (one renal angiomyolipoma and one ovarian mucinous cystadenoma); the remaining 10 cases were benign lesions. WBMRI recommended additional imaging or biopsy to exclude metastases (Fig. 6), which can be considered ‘false positives,’ giving a rate of 0.03 false positives/WBMRI.

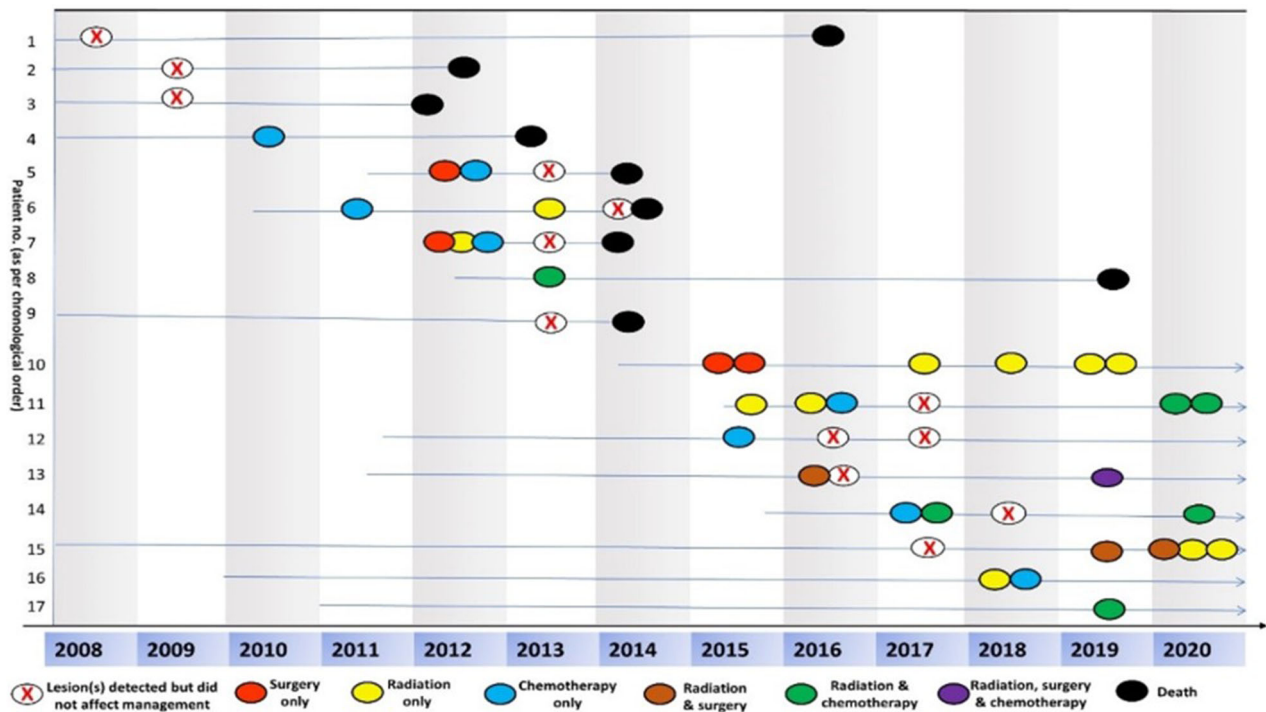
Twenty-one metastatic lesions were missed on a prior WBMRI where they were present but were identified and reported on subsequent WBMRI. These can be considered ‘false negatives,’ giving a rate of 0.06 false negatives/WBMRI. There was an average delay of 9.3 months between the lesions being first missed and then identified on the subsequent WBMRI (Range: 3–29 months). However, only 5 of these 21 lesions (23.8%) were clinically significant to warrant a change in the treatment protocol (Fig. 6). Table 5 lists the locations of these 21 lesions, the time delay in diagnosing these lesions, and any treatment modifications made. Of note, no lesions were missed on the initial staging WBMRI.

#### Delayed presentation with MLS metastases

Our study found that the mean and median times to develop metastasis from an MLS primary were 40.6 months and 28.6 months, respectively. One of the patients developed late-onset metastasis 12.5 years after primary diagnosis and presented with symptomatic vertebral metastasis. Another patient developed metastases 8.3 years after the primary diagnosis and approximately five years after the last surveillance WBMRI. Similarly, another patient was diagnosed 5 years after the primary diagnosis, 26 months after his last surveillance WBMRI. Two other patients were



**Fig. 4** 59-year-old male with primary MLS of the posterior right thigh demonstrating a metastatic lesion in the L1 vertebral body on the staging WBMRI scan (a and c), which was occult on the staging chest CT performed one month prior to the WBMRI scan (b and d). The patient had multiple other bone and soft tissue metastases on the WBMRI scan, for which he received chemotherapy

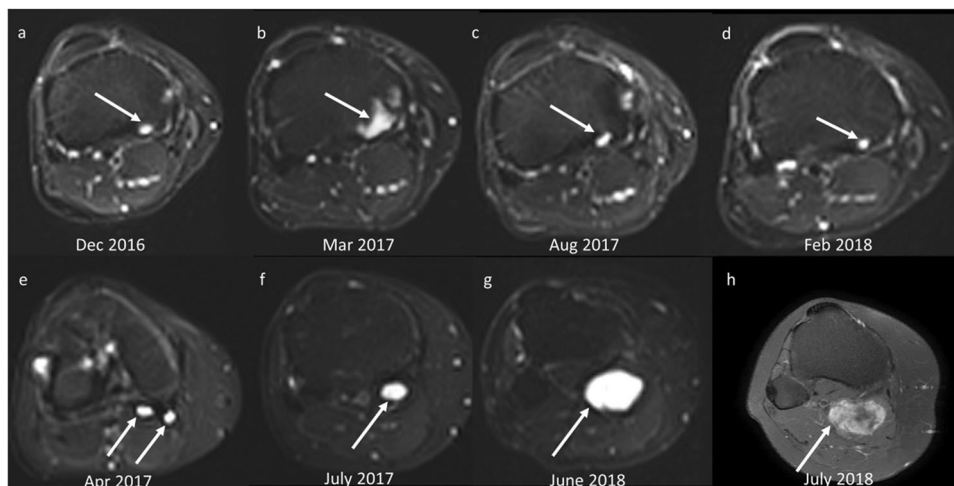


**Fig. 5** Timeline chart of all the metastatic MLS patients with each event of treatment modification. Patients 1–4, 9, and 15 had a diagnosis of the primary lesion before the use of WBMRI imaging in 2008 at our centre



**Table 4** Details of the indeterminate lesions which underwent additional imaging or intervention

Serial no.	Location	Type of Imaging/Intervention	Result of the intervention
1	Right pubic bone	Dedicated MRI	Stress-related changes. Regressed in follow-up WBMRI.
2	Right medial femoral condyle	Dedicated CT	Simple bone cyst
3	Distal left femur	Dedicated MRI	Radiation necrosis
4	Sacrum	CT Biopsy	Negative-regressed on follow-up WBMRI
5	Right proximal humerus	Dedicated MRI	Intraosseous ganglion cyst
6	C1	Bone scan and CT	Sclerotic lesion, probably benign. Stable on follow-up WBMRI.
7	L4 body	CT	Hemangioma (atypical)
8	Left femoral metaphysis	PET-CT and dedicated MRI	No uptake on PET-CT. Dedicated MRI showed synovial herniation pits.
9	Right acetabulum	CT	Degenerative changes with subchondral bone cysts
10	Right kidney	CT	Renal angiomyolipoma
11	Left ovary	Dedicated CT and MRI, followed by surgical excision	Mucinous cystadenoma
12	Left lumbar paraspinal	Surgical resection	Missed in September 2014, detected but indeterminate in July 2015, turned symptomatic in August 2015, resected February 2016-confirmed metastatic
13	Anterior abdominal wall	Surgical resection	Missed in July 2015, detected but indeterminate in October 2015, resected February 2016-confirmed metastatic
14	Popliteal fossa	Dedicated US and MRI	Misdiagnosed as a popliteal cyst in July 2017. Confirmed metastatic on core biopsy in July 2018-localised radiotherapy given.
15	L Proximal femur	Biopsy and excision	Indeterminate in 2011, failed biopsy September 2012, Excised December 2012-confirmed metastatic.
16	Right medial tibial plateau	CT-guided biopsy in 2017	Benign cyst



**Fig. 6 a–d** A 55-year-old male with primary MLS in the left groin. Serial WBMRI scans demonstrate a T2 hyperintense focus in the right posterior medial tibial plateau (**a**), which increased in size on follow-up WBMRI (**b**). The patient underwent a CT-guided bone biopsy in April 2017, which revealed benign findings. Follow-up WBMRI in August 2017 (**c**) and February 2018 (**d**) demonstrate regression of the focus; the lesion was considered a subchondral bone cyst. **e–h** A 28-year-old female with primary MLS of the left popliteal fossa with abdominal and paraspinal soft tissue metastases. Surveillance WBMRI (**e**) demonstrated a T2 hyperintense lesion in the right popliteal fossa, which was presumed to be a popliteal cyst initially, but follow-up WBMRI (**f**) and (**g**) demonstrated interval growth of the lesion. A dedicated MRI of the right knee (**h**) demonstrated that this lesion was solid and suggestive of metastasis. The patient underwent localised radiotherapy for the lesion, following which the lesion regressed

**Table 5** Details of the lesions missed on the initial WBMRI

Lesion number	Year of lesion appearance	Location of missed lesion	Time delay in diagnosis
1	2011	L Sacral ala	1 year 9 months
2	2011	External iliac chain lymph node	10 months
3	2012	Medial L scapula	1 year
4	2013	L1 vertebral body	3 months
5 and 6	2014	Liver lesions (× 2)	3 months
7	2014	Aortopulmonary window	3 months
8	2015	Left L3 paraspinal	10 months
9	2015	Sternum	2 years 5 months
10 and 11	2016	Rib lesions (× 2)	3 months
12 and 13	2016	Thoracic vertebral lesions (v2)	3 months
14	2017	Right deltoid	1 year 6 months
15	2017	Left posterior chest wall	4 months
16	2017	L5 vertebra	8 months
17	2017	Left ilium	8 months
18	2017	Left sacrum	8 months
19	2018	Right popliteal fossa	12 months
20	2019	Left ventricle	10 months
21	2020	Right posterior acetabulum	3 months

diagnosed to have metastases 5.3 and 7.5 years after the primary diagnosis.

### Discussion

Our longitudinal WBMRI surveillance research is a single-centre WBMRI study performed for MLS, spanning fourteen years. It highlights the clinical impact of WBMRI on the surveillance of MLS patients, whereby more than 75% of the metastatic patients had some form of treatment modification as a direct consequence of the WBMRI findings. Most (80%) of the metastatic patients not on regular surveillance tended to present with a higher proportion of symptomatic metastasis, compared to 42.8% in the regular surveillance group. At the end of the study period, 80% of the metastatic patients not getting regular WBMRI surveillance were dead, compared to 14.3% in the regular surveillance group. The 10-year survival rate for all the MLS patients since the primary tumour diagnosis and the 5-year survival rate since the time of diagnosis of the first metastasis were higher in the regular surveillance group. However, these did not reach a statistically significant level. Almost 1/3rd of the metastatic patients (29.4%) developed late-onset extrapulmonary metastases, defined as metastases five years or more after diagnosing the primary tumour.

The peak incidence of MLS is between 40 and 60 years [1, 2, 13–15], and the median age of our study sample (48.1 years) was concordant with this range. Males

predominated our study population (60.7%), consistent with what has been described by multiple other authors [9, 14–17]. None of the patients in our cohort developed local recurrence, which is lower than the reported incidence, ranging between 2.3 and 40% published in the literature [2–4, 12, 15–26]. This could be attributed to the patients receiving preoperative and/or postoperative radiotherapy and a robust sarcoma surveillance program at our centre.

Previous studies have shown a preponderance of MLS metastases to bones and soft tissues rather than the lungs or liver [9, 12, 16–21, 23, 25]. In a study by Visgauss et al, only 16% of the patients had pulmonary-only involvement at the initial metastatic discovery [7]. Similarly, only 2 of the 17 metastatic patients in our study developed pulmonary metastases, and both had pre-existing bone or soft tissue metastases. It has been postulated that abundant fat cells in the bones and soft tissues may be responsible for this atypical metastatic behaviour [22].

Our study demonstrates a lower proportion of symptomatic metastases and potentially better survival in the group having regular WBMRI surveillance. Studies have found the overall 5-year survival to vary between 69 and 96% in MLS patients and the overall 10-year survival between 63 and 85% [12, 27–29]. Comparable with these numbers, our 10-year survival rate since the primary diagnosis and the 5-year survival rate since the diagnosis of the first metastasis almost doubled in the regular

surveillance group. However, the  $p$  values were not statistically significant due to our small sample size.

The treatment protocols (including the chemotherapy and radiotherapy regimens) did not change before or after 2015. However, the 1.5-T protocol followed pre-2015, and the 3-T protocol instituted afterwards could have introduced a confounding variable. Our findings indicate an association between the regularity of the WBMRI surveillance and the survival rates of the metastatic MLS patients, but this would need further validation with prospective randomised control trials on larger study samples.

The WBMRI surveillance at our centre led to additional imaging or intervention for ten indeterminate lesions, which later were confirmed not to be metastatic. This is a relatively low frequency, considering the total number of WBMRI scans performed (345) over 14 years. Our study demonstrates that the number of unnecessary additional imaging/interventions was not exceptionally increased due to indeterminate lesions on WBMRI, and a majority of these indeterminate lesions were characterised as benign or malignant with follow-up WBMRI.

The study also highlights that five (23.8%) metastatic lesions missed or falsely considered benign on a prior WBMRI were significant enough to warrant a treatment change, even if they had been detected in the first instance. These five metastatic lesions were detected within a year of their appearance on the previous WBMRI scans. One underwent surgical excision followed by radiotherapy, while the remaining four were given localised radiation therapy.

Despite recent evidence favouring WBMRI for staging and surveillance for extrapulmonary metastases of MLS [10, 11, 30], there is no consensus regarding the optimal imaging surveillance protocol and duration. The WBMRI protocol at our institute includes surveillance of WBMRI for 5 years after the diagnosis of the primary malignancy in the absence of any metastases. Five patients (8.9% of the entire cohort and 29.4% of all the metastatic patients) developed metastasis beyond 5 years of diagnosing the primary malignancy. Considering the small sample size of our study, further studies will be necessary to validate and justify the duration of WBMRI surveillance for these patients.

The main limitations of our study were the small sample size and its retrospective structure. However, considering that the incidence of MLS is relatively low at 1–2 cases per million patient-years [31, 32], ours is the largest cohort of MLS patients to be surveyed with WBMRI. Furthermore, the number of WBMRI scans performed is also larger than any previous research published in the literature. Future multicentre prospective studies with a

larger sample size will help corroborate our findings. Additionally, before 2015, there was no standardised surveillance protocol and multiple imaging modalities, such as CT, PET-CT, nuclear scintigraphy, and dedicated MRI scans, were used apart from WBMRI for screening and surveillance of MLS. As mentioned above, different imaging protocols before and after 2015 could be confounding. Also, not all metastatic lesions in our study population had histopathological confirmation. However, confirmation with a biopsy was not indicated in the presence of multifocal metastases or interval growth detected by WBMRI. The diagnostic pathway followed by our study offers a pragmatic approach to diagnosing MLS metastases. Another limitation of our study is that it was not possible to differentiate between metastases and synchronous/metachronous tumours by WBMRI. However, the relevance of this distinction concerning clinical management is questionable.

In conclusion, WBMRI led to a change in the management of more than 75% of the metastatic MLS patients in our study. The number of additional investigations or interventions recommended for indeterminate lesions on WBMRI was small, and only a tiny proportion of lesions missed on a prior WBMRI would have affected the ongoing management in retrospect. Our findings suggest an association between regular WBMRI surveillance and a longer survival duration of these patients. However, this needs to be confirmed further with larger multicentre studies. Almost a third of the metastatic patients developed late-onset metastases beyond our institute's standard 5-year surveillance protocol, highlighting the need for further research to determine the optimal duration of WBMRI surveillance for extrapulmonary MLS metastases.

#### Abbreviations

ESMO	European Society for Medical Oncology
MLS	Myxoid liposarcoma
NCCN	National Comprehensive Cancer Network
WBMRI	Whole-body magnetic resonance imaging

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#### Conflict of interest

The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

**Statistics and biometry**

One of the authors has significant statistical expertise.

**Informed consent**

Written informed consent was waived by the Institutional Review Board.

**Ethical approval**

Institutional Review Board approval was obtained.

**Study subjects or cohorts overlap**

Some of our study subjects ( $n = 56$ ) have been previously reported in Gorelik N, Reddy SMV, Turcotte RE, Goulding K, Jung S, Alcindor T, et al Early detection of metastases using WBMRI for initial staging and routine follow-up of myxoid liposarcoma ( $n = 33$ ). *Skeletal Radiol* (Internet). 2018 March 1. The study performed by Gorelik et al aimed to assess how WBMRI helped in the early diagnosis of myxoid liposarcoma metastases, while our study aims to assess the impact WBMRI surveillance has had over the clinical management of myxoid liposarcoma patients, highlights the presence of delayed metastases requiring extended WBMRI surveillance and also evaluates the survival rates in the metastatic patients with and without regular WBMRI surveillance.

**Methodology**

- Retrospective
- Observational
- Performed at one institution

**Author details**

<sup>1</sup>York and Scarborough Teaching Hospitals NHS Foundation Trust, York, United Kingdom. <sup>2</sup>Department of Radiology, McGill University Health Centre, Montreal, Canada. <sup>3</sup>Division of Orthopaedic Surgery, McGill University Health Centre, Montreal, Canada. <sup>4</sup>Department of Pathology, McGill University Health Centre, Montreal, Canada. <sup>5</sup>Department of Medical Oncology, McGill University Health Centre, Montreal, Canada.

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