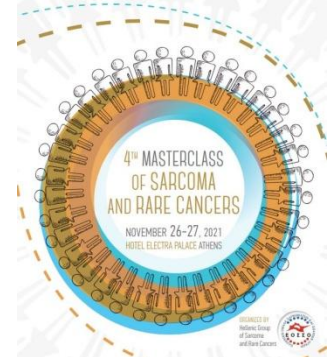




HELLENIC REPUBLIC

**National and Kapodistrian
University of Athens**



Interventional Radiology techniques for sarcoma metastatic disease

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Medical School, National and Kapodistrian University of Athens

SARCOMA

- **FINANCIAL DISCLOSURES**
 - FOCUSED CRYO: Advisory Board
 - IMACTIS: Advisory Board
 - ECO MEDICAL, NANJING: Proctor
 - MEDTRONIC: Advisory Board, Proctor
 - CANNON: Advisory Board

SARCOMA

- Soft tissue sarcomas: rare and heterogeneous mesenchymal neoplasms - **>70 histological subtypes**; unknown etiology - several genetic syndromes and environmental risk factors
- **Most powerful prognostic factors:** Depth, size, histology
- Incidence: <6/100.000 cases (**1–2%** of adult / 15% of pediatric cancer) – 27.908 new cases per year in Europe

SARCOMA

- Most common: undifferentiated pleiomorphic sarcoma, GIST, liposarcoma or leiomyosarcoma
- The 10-year relative survival rate for patients >20 years old was 70% - 50% of patients >65 years old
- **Oligometastatic disease:** surgery or interventional radiology improve local control and survival

DEFINING TERMS

- **Oligometastatic disease**

- <3-5 lesions, <3-5cm diameter

- » Gangi et al. Quality Improvement Guidelines for Bone Tumour Management. CVIR 2010 33:706–713

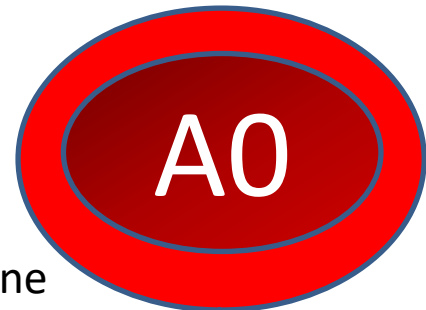
- the presence of 1 and 5 distant metastases in <2 organs, although the exact number of metastases that should be considered remains debatable

- deSouza et al. Strategies and technical challenges for imaging oligometastatic disease. EJCANCER 2017; XX:1-11

- **Ablation with curative intent**

- Ablation volume – Safety margin (A0)

 tumor
Ablation zone



SARCOMA

Electromagnetic - Thermal

- Radiofrequencies (RFA)
- Microwaves (MWA)
- Laser (LITT)

Mechanical - Thermal

- High Intensity Focused Ultrasound (HIFU)

Thermal

- Cryoablation (CWA)

ABLATION FOR SARCOMA

Rational:

Minimally
invasive
approach

Well-tolerated
even in patients
with co-
morbidity

Overall morbidity
of the procedure
is low

Preservation
of long-term
function with
low damage to
healthy
parenchyma
around the
metastases

SARCOMA

Falk et al. Effect on Survival of Local Ablative Treatment of Metastases from Sarcomas: A Study of the French Sarcoma Group

281 oligometastatic (at the onset) sarcoma patients (1-5 lesions)
pulmonary (71.5%), hepatic (10.6%)

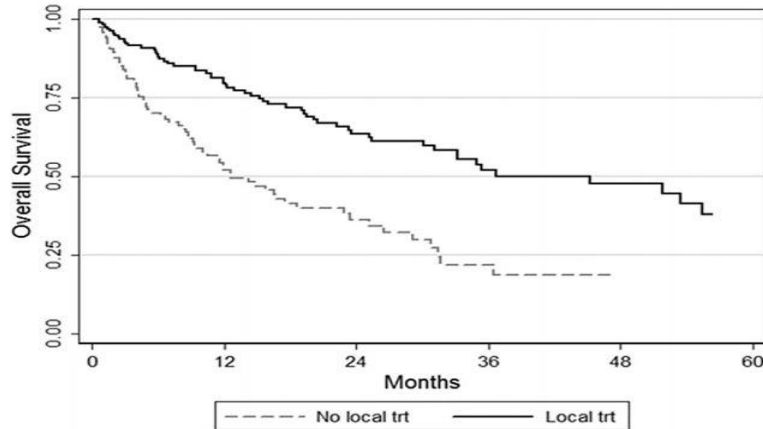
extra pulmonary and extrahepatic metastases (19.2%)

164/281 (77.9%) local treatment incl. surgery

35 (16.4%) RFA

25.7 mo fu

paradigm shift regarding the treatment of
oligometastatic cancer
supports the evidence for sarcomas



Original Article

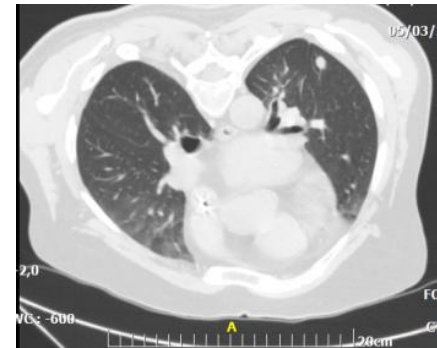
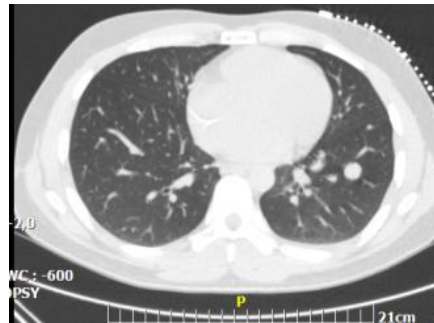
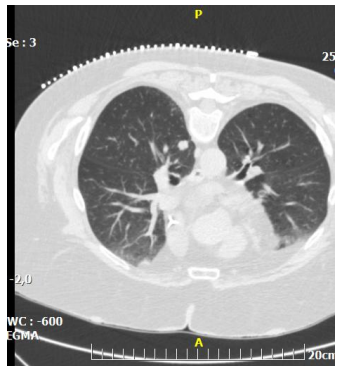
Effect on Survival of Local Ablative Treatment of Metastases from Sarcomas: A Study of the French Sarcoma Group

A.T. Falk ^{*}, L. Moureau-Zabotto [†], M. Ouali [‡], N. Penel [§], A. Italiano [¶], J.-O. Bay ^{||**}, T. Olivier ^{††}, M.-P. Sunyach ^{††}, P. Boudou-Roquette ^{§§}, S. Salas ^{¶¶}, C. Le Maignan ^{||||}, A. Ducassou ^{***}, N. Isambert ^{†††}, E. Kalbacher ^{†††}, C. Pan ^{§§§}, E. Saada ^{*}, F. Bertucci [†], A. Thyss ^{*}, J. Thariat ^{*} for the Groupe Sarcome Français-Groupe D'etude Des Tumeurs Osseuses

SARCOMA @ LUNG

- Pulmonary metastases in **20–50%** of patients with soft-tissue and bone sarcomas
- Overall median survival with lung metastases: **15 months**

S.M. Thompson et al.: Image-Guided Thermal Ablative Therapies in the Treatment of Sarcoma. Curr. Treat. Options in Oncol. 2017



SARCOMA @ LUNG

deBaere et al: Radiofrequency ablation is a valid treatment option for lung metastases: experience in 566 patients with 1037 metastases

- Mean diameter 17.4 mm - Median follow-up 35.5 months
- Median OS was 62 months, and 1-, 2-, 3-, 4- and 5-year OS rates were 92.4% [standard error (SE) = 1.2], 79.4% (SE = 1.9), 67.7% (SE = 2.4), 58.9% (SE = 2.8) and 51.5% (SE = 3.3), respectively
- Location of primary disease, disease-free interval (DFI), size >2 cm, and three or more metastases were associated with OS in univariate analysis and remained independently associated with OS in multivariate analysis.

Table 1. Rates (standard error) of overall survival, progression-free survival and treatment failure according to the primary

	Primary				
	Colon (N = 191)	Rectum (N = 102)	Kidney (N = 68)	Sarcoma (N = 51)	Other (N = 154)
Overall survival					
1 year	92.9% (1.9)	93.6% (2.5)	95.5% (2.6)	94.1% (3.3)	89.0% (2.6)
3 years	76.1% (3.7)	64.9% (6.3)	73.5% (6.5)	58.0% (8.2)	59.1% (4.6)
5 years	56.0% (6.0)	49.6% (8.4)	53.8% (9.1)	41.5% (9.3)	49.4% (6.4)
Progression-free survival					
1 year	37.6% (3.6)	30.4% (4.8)	39.7% (5.9)	43.0% (7.0)	49.0% (4.1)
3 years	17.0% (3.0)	8.6% (3.2)	13.8% (4.9)	26.5% (6.6)	17.6% (3.4)
5 years	14.8% (3.0)	6.4% (3.0)	9.2% (5.0)	15.9% (6.2)	7.6% (3.9)
Treatment failure					
1 year	10.9% (2.4)	14.5% (3.7)	7.4% (3.2)	6.1% (3.4)	9.9% (2.5)
2 years	16.2% (3.0)	30.7% (5.7)	13.0% (5.0)	8.3% (4.0)	16.4% (3.5)
3 years	16.2% (3.0)	30.7% (5.7)	25.1% (9.3)	8.3% (4.0)	16.4% (3.5)



Radiofrequency ablation is a valid treatment option for lung metastases: experience in 566 patients with 1037 metastases

T. de Baère^{1*}, A. Aupérin², F. Deschamps¹, P. Chevallier³, Y. Gaubert⁴, V. Boige⁵, M. Fonck⁶, B. Escudier⁵ & J. Palussière⁷

Departments of ¹Image Guided Therapy; ²Biostatistics, Gustave Roussy Cancer Campus, Villejuif; ³Department of Imaging, Hôpital Archet 2, Nice; ⁴Department of Imaging, Hôpital de la Timone, Marseille; ⁵Department of Medical Oncology, Gustave Roussy Cancer Campus, Villejuif; ⁶Departments of ⁷Medical Oncology; ⁷Imaging, Institut Bergonié, Bordeaux, France

SARCOMA @ LUNG

- osteosarcoma oligometastatic lung metastases (post-surgical recurrences)
- 11 children - 26 lung metastases
- 2–16 mm (mean = 6.7 mm)
- **100% local control rate**
- 5/11 patients remained in complete remission after median follow-up of 37.5 months
- 5/11 patients developed new metastases – 2/5 patients were retreated and are still in remission after subsequent treatment

TABLE 1 Patient demographics

Patient	Age (years)	Sex	Wt (kg)	Timing of metastases	Histological subtype	Progression on chemotherapy	Tumor necrosis (%)	Prior Thoracotomies	# Recurrence pre-ablation
1	12.5	M	34	Synchronous	Fibroblastic	No	100	1	2
2	12.8	F	31	Synchronous	Anaplastic	No	<90	4	3
3	8.0	F	31	Synchronous	Indeterminate	No	<90	2	2
4	13.6	M	40	Metachronous	Fibroblastic	No	99	1	2
5	9.8	M	26	Synchronous	Osteoblastic	No	92	3	3
6	16.4	F	49	Synchronous	Indeterminate	No	<90	4	5
7	15.5	F	47	Synchronous	Osteoblastic	No	90	2	3
8	12.4	F	35	Synchronous	Chondroblastic	No	91	1	2
9	17.6	M	53	Metachronous	Indeterminate	No	98	1	2
10	12.9	M	56	Synchronous	Osteoblastic	Yes	<90	2	3
11	7.1	M	19	Synchronous	Osteoblastic	Yes	92	2	3

M male, F female

TABLE 2 Percutaneous ablation treatment information

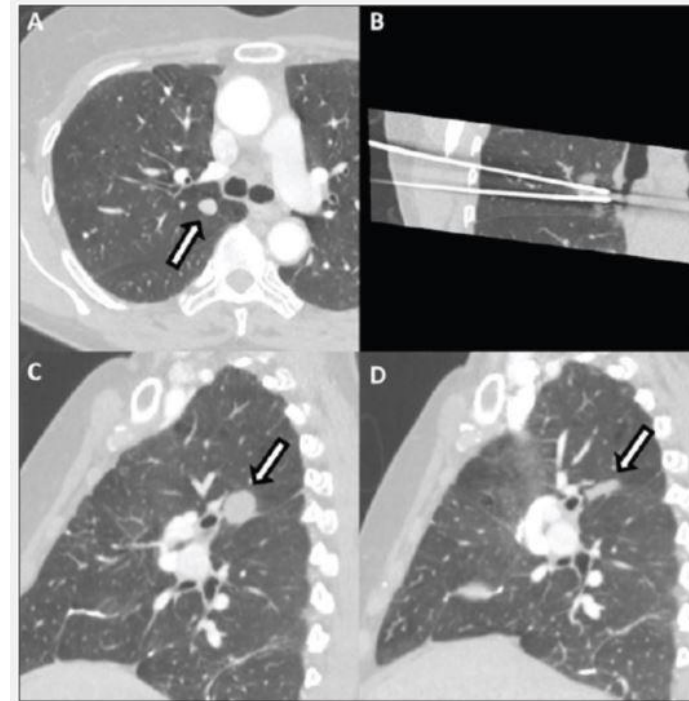
Patient	Modality	Nodules ablated	Laterality	Nodule size (mm)	Post-ablation imaging follow-up (months)	Post-ablation recurrence	Time to recurrence (months)	Post-ablation time to death (months)
1	RFA	1	Right	3	41.8	–	–	–
2	RFA	2	Right	9, 8	40.9	–	–	–
3	RFA	4	Right	3, 3, 3, 5	37.5	–	–	–
4	RFA	2	Left	5, 14	37.9	Cranium	9.5	–
5	RFA	3	Bilateral	3, 5, 16	5.6	Right lung	2.3	8.7
6	RFA	2	Bilateral	10, 16	4.8	Bilateral lungs	4.7	6.7
7	RFA	2	Left	5, 5	5.2	Bilateral lungs	5.0	8.8
8	RFA	2	Left	2, 3	24.7	–	–	–
9	RFA	1	Left	2	4.1	–	–	–
10	RFA	5 ^o	Bilateral	5, 6, 8, 10, 11	8.8	Bilateral lungs	0.9 ^a	–
11	Cryo	2	Bilateral	5, 9	0.7	Lumbar	0.7	1.0

RFA radiofrequency ablation, Cryo cryoablation

SARCOMA @ LUNG

Bourgouin et al: Comparison of Percutaneous Image-Guided Microwave and Cryoablation for Sarcoma Lung Metastases: 10-Year Experience

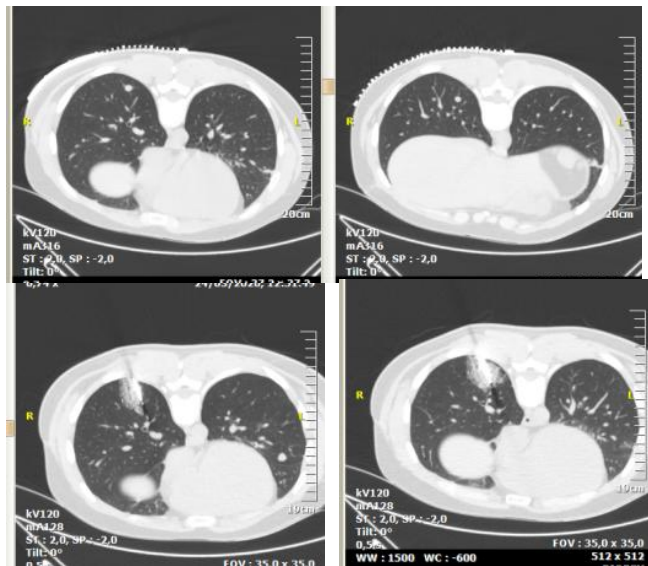
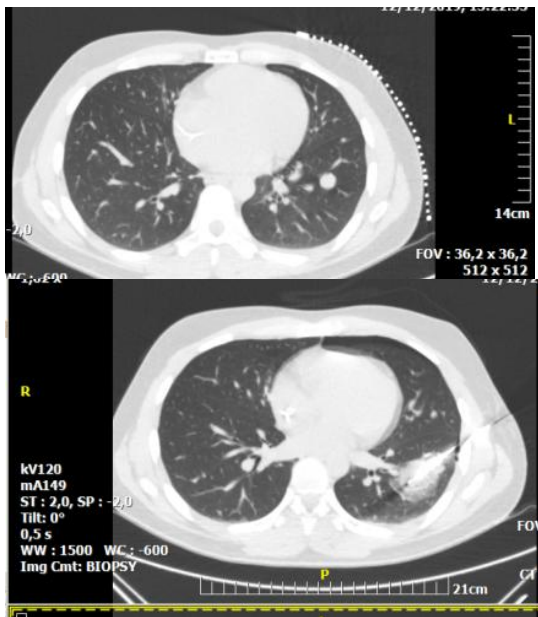
- 27 patients – 39 ablation
- 21 MWA, 18 cryoablation; 1-4 sessions per patient
- Primary technical success was 97% for both modalities
- Median follow-up was 23 months
- Tumor size ≤ 1 cm was associated with decreased cumulative incidence of local progression ($p = .048$)
- Ablation modality and tumor location were not associated with progression ($p = .86$; $p = .54$)



CASE EXAMPLE



CASE EXAMPLE



SARCOMA @ LUNG

Author	Type of ablation	Number of patients (N)	Mean size (mm)	Mean follow up (months)	Mean overall survival rate	Median progression-free survival rate	Complications
Koeblinger et al	RFA	22	9	20	2- and 3-year time were 94% and 85 % (51 months)	1- and 2-year were 53 and 23 %, (12 months)	2 pt with grade 3 complications
Nakamura et al	RFA	20	14 ± 9	18	1 and 3 year were 58% and 29% (12.9 months)		38% needed pneumothorax tube
Palussiere et al	RFA	29	9	50	1 and 3 year were 92.2% and 65.2%	7 months	68.7% pneumothorax
Sato et al.	RFA	46	13.5 ± 9.0	16.9	1-, 2-, and 3-year were 80.6, 70.1, and 47.1% (31.7 months)	Primary and secondary efficacy rates were 83.5 and 90.0% at 1 year and 76.3% and 81.4% at 2 years	73% grade 1 33% grade 2
Yevich et al.	RFA+ CRYO	11	6.7	16.7			3 pneumothoraxes
Saumet et al.	RFA	10		24		None had recurrence/ Seven patients were in complete remission	3 hemoptysis and pneumothorax
Gravel et al.	Percutaneous thermal ablation	30	18.2	34.6	48.3 months 1, 3 and 5-year overall survival rates were 96.7%, 62.0% and 28.3% respectively	Local control rate at 1 year was 95.2% and at 3 years was 89.4%.	

Thermal ablation of lung metastasis from sarcoma

SARCOMA @ LIVER

- Limited literature on percutaneous ablation: rarity of the disease - studies reporting data on diverse histologic subtypes without sarcoma-specific analyses
- **Gastrointestinal stromal tumor (GIST)** is the most common primary sarcoma to metastasize to the liver
- Imatinib mesylate, a selective tyrosine kinase inhibitor (TKI) targeting c-KIT, is the current standard of care for metastatic GIST tumors

SARCOMA @ LIVER

- adjuvant percutaneous RFA after TKI
- 17 patients – 27 GIST liver meta
- 2.5 ± 1 cm (range 0.9–4.5 cm)
- **100% technical success**
- **no local recurrences** during a mean follow-up period of 49 months
- No major complications

Table 1 Patient and tumor characteristics

No	Sex/age (year)	Group	Primary site	Extrahepatic disease	No. of liver metastases treated by RF	Tumor maximum size	Complication
1	M/45	C	Small bowel	Peritoneal metastasis	1	17	No
2	F/57	A	Colon	No	1	30	No
3	F/65	A	Colon	No	2	18/45	No
4	F/66	A	Colon	No	1	27/29	No
5	M/53	A	Small bowel	No	2	15/23	No
6	M/40	B	Small bowel	No	3	12/25	No
7	F/65	C	Small bowel	No	1	42	No
8	M/50	C	Stomach	No	1	28	No
9	M/59	C	Stomach	No	1	36	Minor
10	F/63	A	Abdomen	No	1	11	No
11	F/52	A	Stomach	No	1	31	No
12	F/62	B	Stomach	No	3	9/23/37	No
13	M/42	B	Small bowel	No	2	29	No
14	F/72	B	Rectum	No	2	20/35	Minor
15	M/61	A	Stomach	No	1	26/36	No
16	F/45	B	Small bowel	No	3	10/18/41	No
17	M/51	C	Stomach	No	1	15	No

Table 2 Progression-free survival

	Progression-free survival rate (95 % confidence interval)				Median FU (mo)
	6 months	12 months	18 months	24 months	
Group A	58.7 % (49–97)	42.9 % (16–75)	28.6 % (8–64)	28.6 % (8–64)	74.5
Group B	100 %	100 %	100 %	75 % (30–95)	29.6
Group C	80 % (38–96)	60 % (23–88)	20 % (4–62)	20 % (4–62)	53.9

SARCOMA @ LIVER

- **2-year progression-free survival 75%** in patients who continued TKI therapy post ablation
- <30% in patients who discontinued TKI therapy post ablation.
- Conclusion: adjuvant RFA of GIST liver metastases is **effective at achieving local tumor control**
- should be performed once the patient achieves **best morphologic response on TKI therapy**

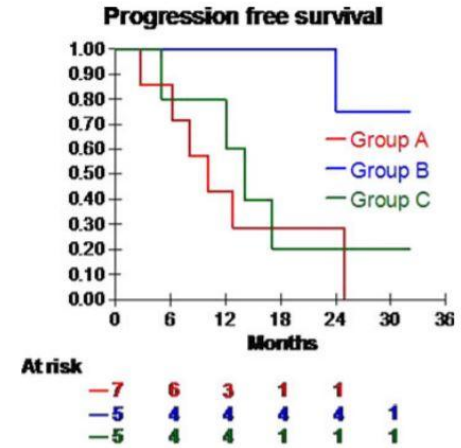


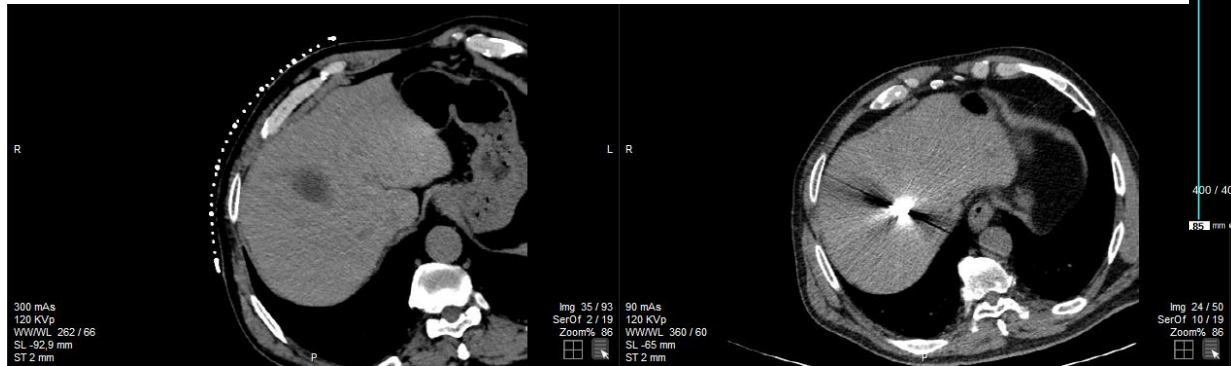
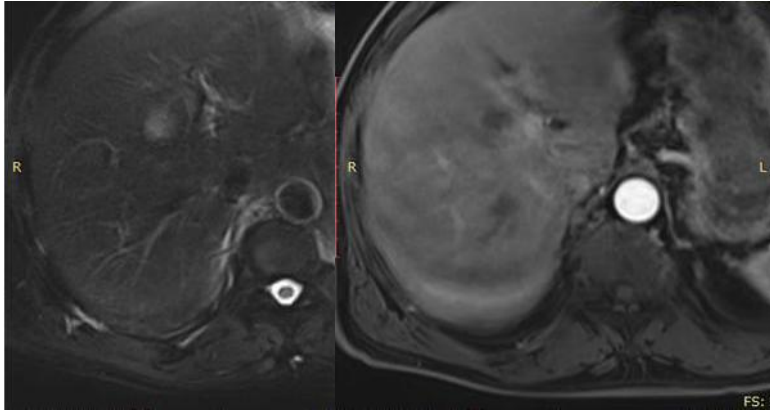
Fig. 4 Kaplan-Meier curve for PFS

SARCOMA @ LIVER

Authors	Type of ablation	Type of sarcoma	Number of patients (N)	Mean lesion size	Mean follow up (months)	Median time to progression	Overall survival rate/time	Complications
Jones et al.	RFA	GIST Other sarcoma	13 7	-	21	28 months	2-year overall survival was 77%	3 patients with sepsis
Jung et al.	RFA	GIST	29	1.3 cm	33.1	6% showed local recurrence at 3.2 and 10.5 months	90.2 months	1 patient with bleeding at the ablation site & 1 peritoneal seeding near the ablation tract
Hakime et al.	RFA	GIST	17	2.5 ± 1 cm	49	Two-year progression-free survival (PFS) after RFA was 29 % in group A, 75 % in group B, and 20 % in group C.	Only two patients (both in group C) died at 20 and 48 months	11% minor complications

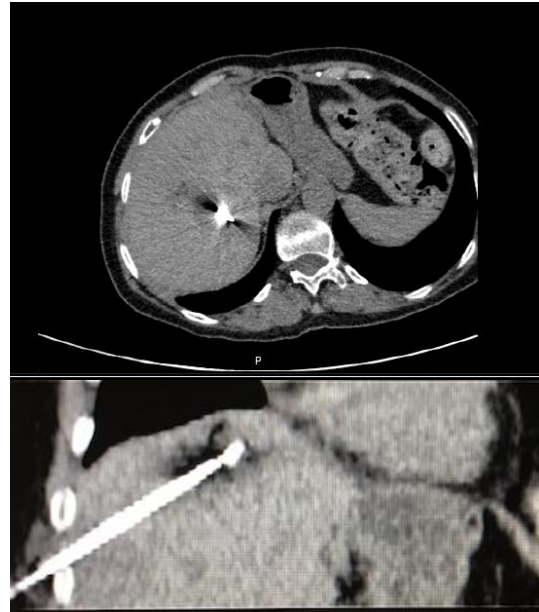
Thermal ablation of liver metastasis from sarcoma

CASE EXAMPLE



leiomyosarcoma

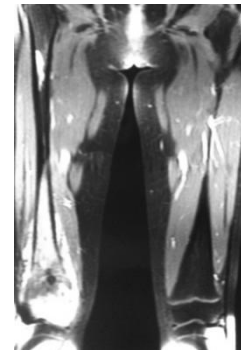
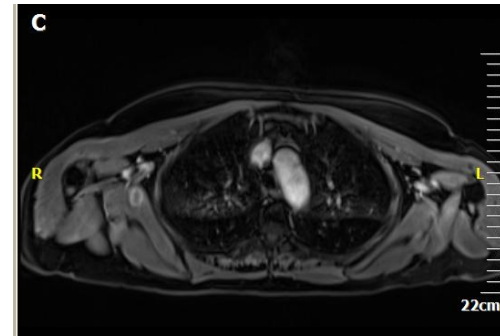
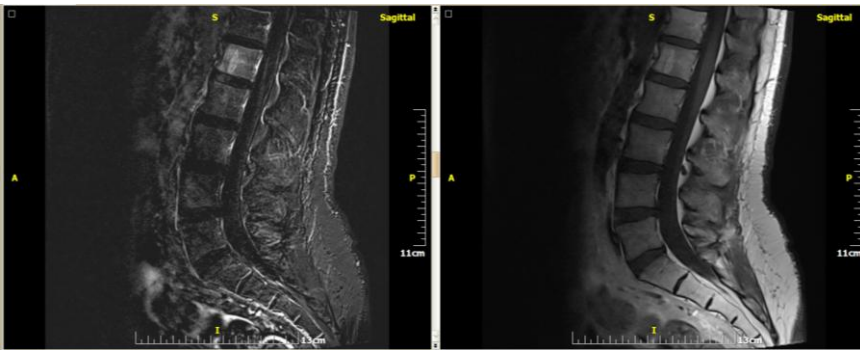
CASE EXAMPLE



GIST META

SARCOMA @ MSK

- Literature is scarce
- Series often combined sarcomas and non-sarcomatous bone tumours



S.M. Thompson et al.: Image-Guided Thermal Ablative Therapies in the Treatment of Sarcoma. *Curr. Treat. Options in Oncol.* 2017
G.D. Demeti et al. Efficacy and safety of imatinib mesylate in advanced gastrointestinal stromal tumors. *N Engl J Med.* 2002

SARCOMA @ BONE/SPINE

- Ablation is an effective option for local tumor control and pain palliation of MSK sarcoma meta
- Treatment in the setting of oligometastatic disease offers potential for remission

	≥3 months	≥6 months	≥9 months	≥1 year
Overall local tumor control (n = 64)	88% (35/40)	80% (24/30)	78% (21/27)	70% (19/27)
Local tumor control in the setting of oligometastatic disease	100% (12/12)	100% (11/11)	100% (10/10)	100% (10/10)
Local tumor control in the setting of chemoradiation	100% (10/10)	100% (6/6)	100% (6/6)	100% (4/4)
Total number of treated tumors with disease progression of untreated metastases	78% (31/40)	70% (21/30)	67% (18/27)	67% (18/27)
Local tumor control in the setting of progression of untreated metastases	84% (26/31)	71% (15/21)	67% (12/18)	67% (12/18)
Total cases without follow-up	24	10	3	0
<i>Reason</i>				
Death/Hospice	19	7	1	0
No clinical indication for imaging follow-up	1	1	0	0
Lost to follow-up	4	2	2	0

SARCOMA @ BONE/SPINE

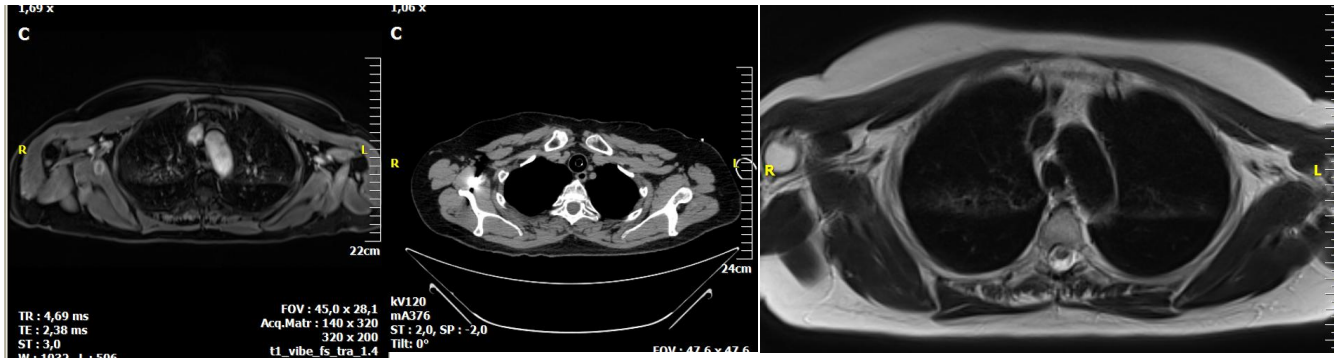
Authors	Type of ablation	Primary Site	Number of patients	Follow up (months)	Outcomes	Complications
Yamakado et al.	RFA	Bone and soft-tissue sarcomas	52	25.5	Residual tumors were found in 59.6 % (31/52), Overall survival rates were 73.4 % at 1 year, 39.3 % at 3 years, and 34.3 % at 5 years in all patients	Major complications 0.9 %.
Saumet et al.	RFA	Osteosarcoma (pediatric population)	16 (7 with bone lesions)	14.9	Complete remission (N = 3) Local tumor control (N = 3) Pain relief (N = 1)	First-degree burn (N = 1) Soft tissue infection (N = 1) Tibial fracture 6-months post ablation in the treatment zone (N = 1)

Thermal ablation of bone metastasis from sarcoma

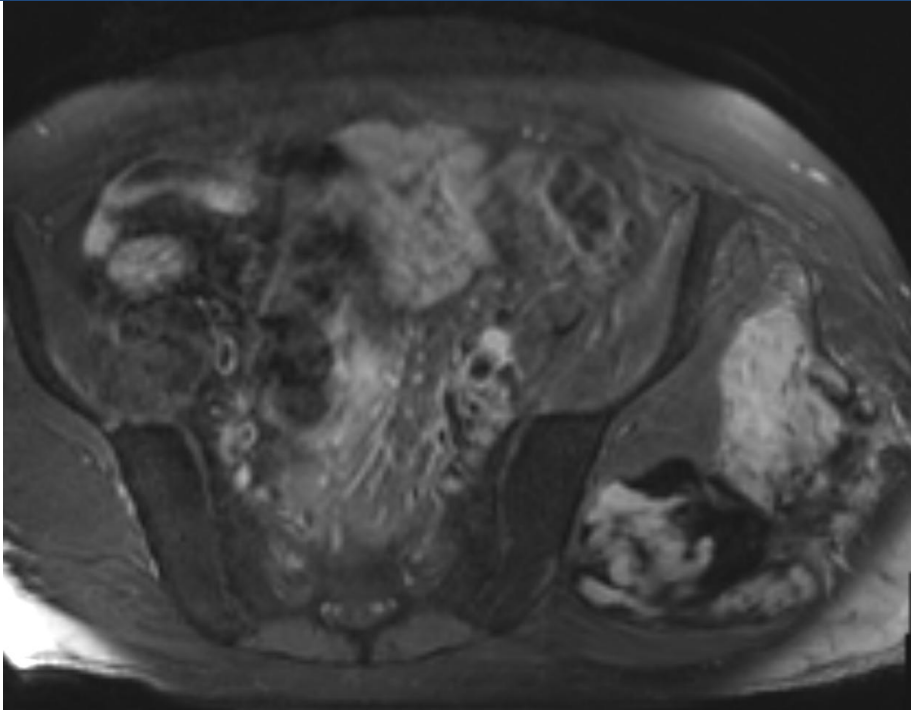
SARCOMA @ BONE/SPINE

Author (year)	Number sarcoma patients	Number of tumors	Age range	Sarcoma type	Sarcoma subtypes	Ablation device
Bone						
Li (2015)	12	12	11–24	Primary bone tumor	OGS—juxta-articular around knee	Adjuvant cryoablation + joint-preserving transephysis tumor resection
Li (2015)	11	11	9–16	Primary bone tumor	OGS—juxta-articular around proximal tibia	Adjuvant MWA + joint-preserving transephysis tumor resection
Saumet (2015)	7	>9	6–25	Primary bone tumor	OGS	RFA
Yu (2015)	27	27	11–56	Primary bone tumor	OGS	HIFU
Kurup (2012)	5	8	31–80	Primary bone tumor	Chordoma	Cryoablation
Chen (2010)	80	80	5–89	Primary bone tumor	OGS pOGS PS ChSA ES mGCT	HIFU (N = 14) HIFU + chemotherapy (N = 66)
Li (2010)	13	13	9–72	Primary bone tumor	OGS MFH	HIFU
Soft tissue						
Fan (2016)	39	50	25–73	Soft tissue sarcoma Recurent retroperitoneal	LPS FS LMS MFH Meso	Cryoablation
Schmitz (2016)	18	26	9–77	Soft tissue sarcoma Desmoid tumor	EAD	Cryoablation
Jiongyuan (2014)	19	19	18–79	Soft tissue	DFSP	Cryoablation
Havez (2013)	13	17	15–74	Soft tissue sarcoma Desmoid tumor	EAD	Cryoablation
Bone/soft tissue						
Yamakado (2014)	16 (Bone) 36 (Soft tissue sarcoma)	1 (N = 12) 2–6 (N = 18) ≥7 (N = 22)	10–87	Recurent bone and soft tissue sarcoma	LMS OGS LPS MFH ChSA Other	RFA
Littrup (2013)	Sarcoma (N = 12)	28 (sarcoma)	18–91		OGS	Cryoablation

CASE EXAMPLE

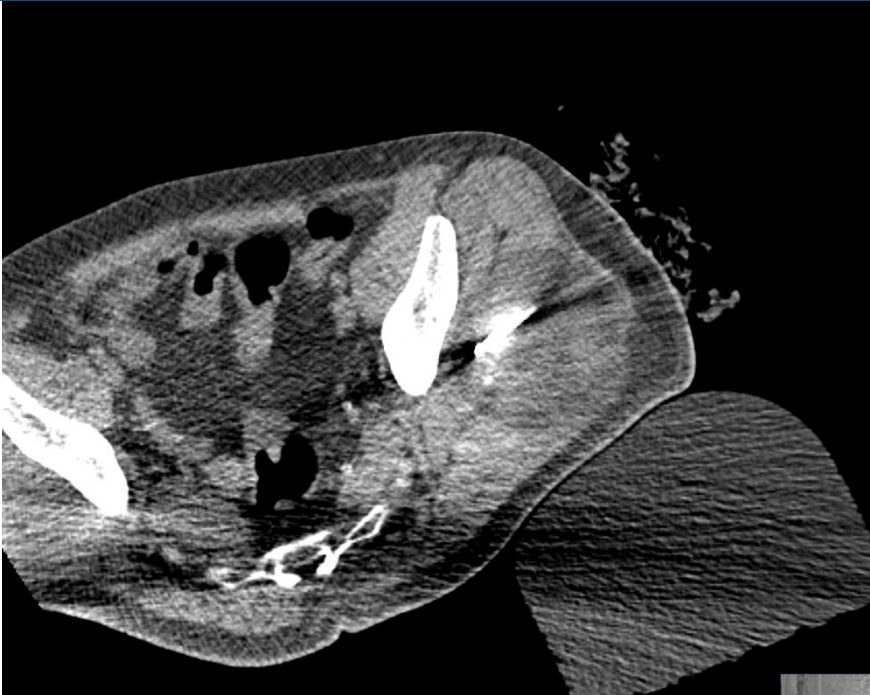


DESMOIDS



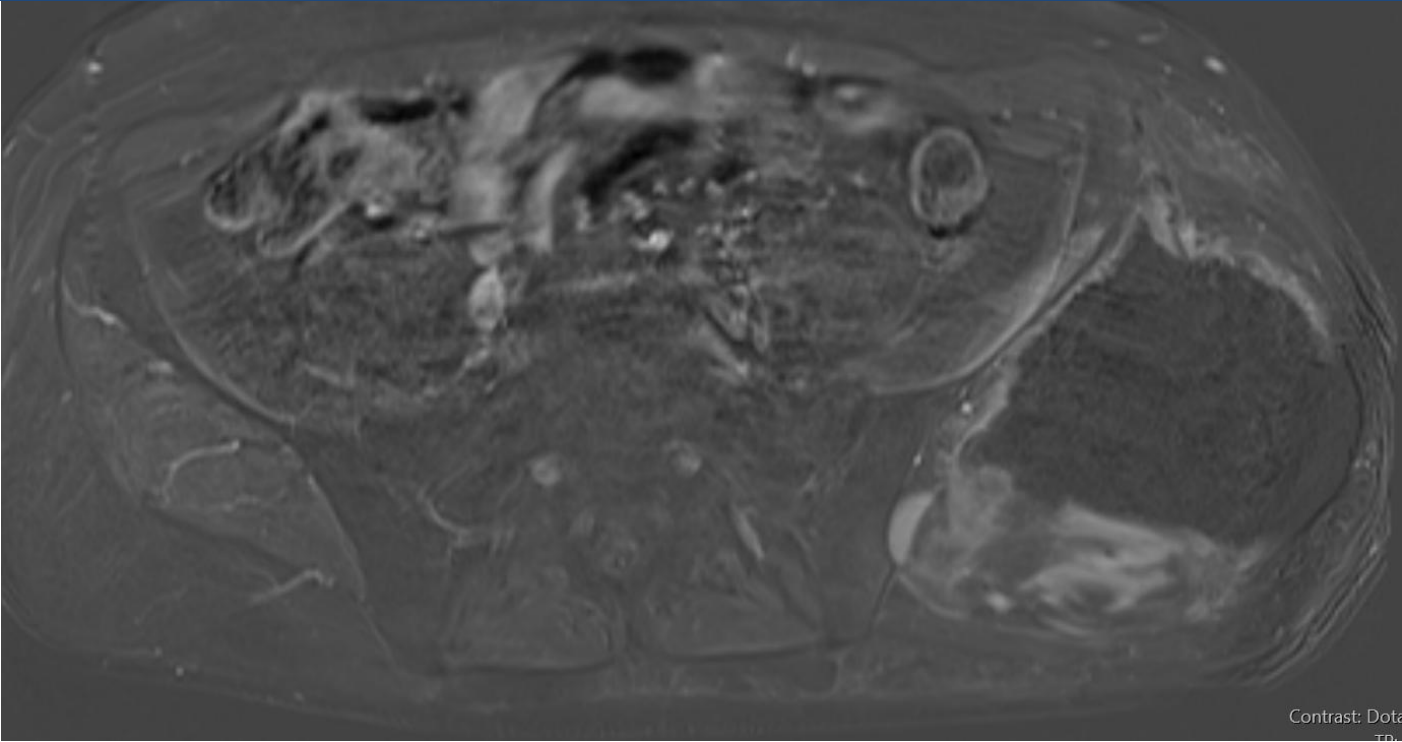
48 yom with painful left gluteal desmoid tumor

DESMOIDS



First ablation (12 probes)

DESMOIDS



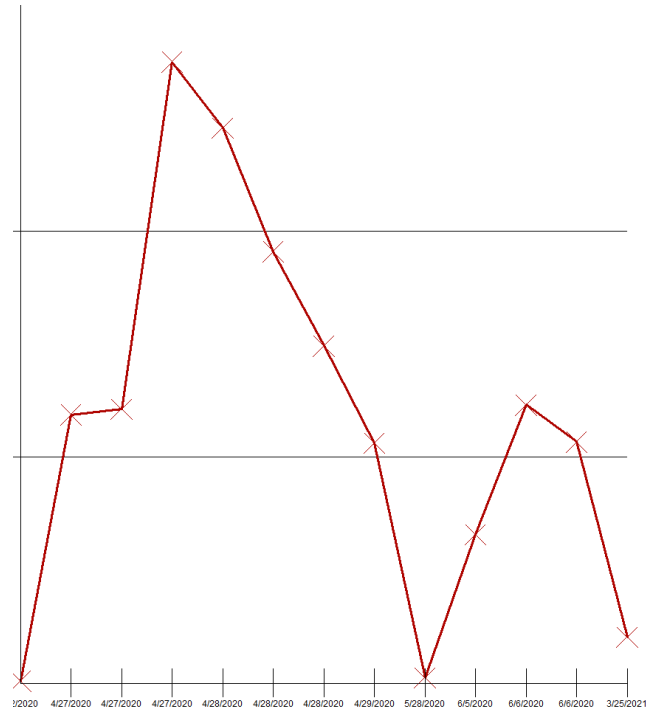
First ablation Post MRI (T1FS subtraction images)

DESMOIDS



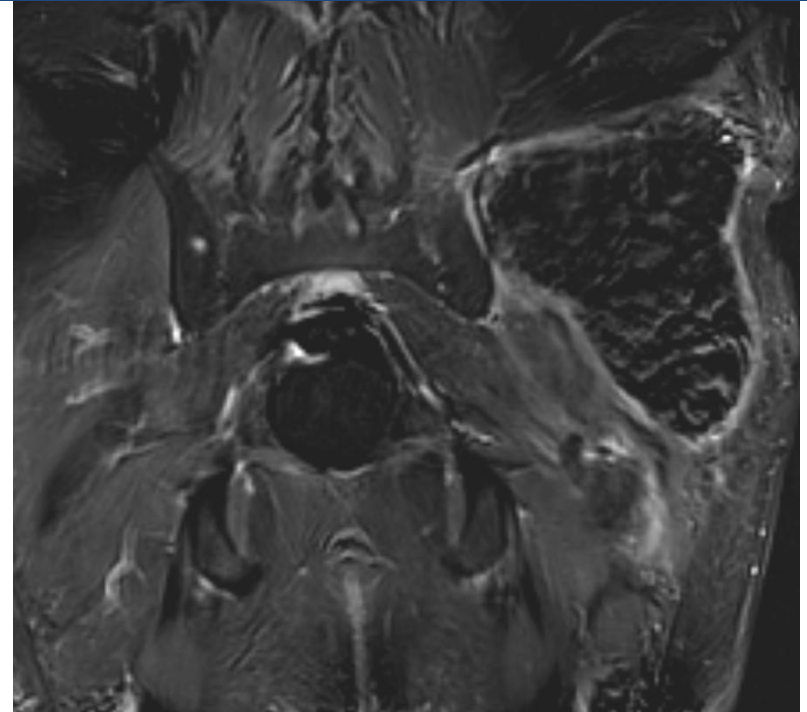
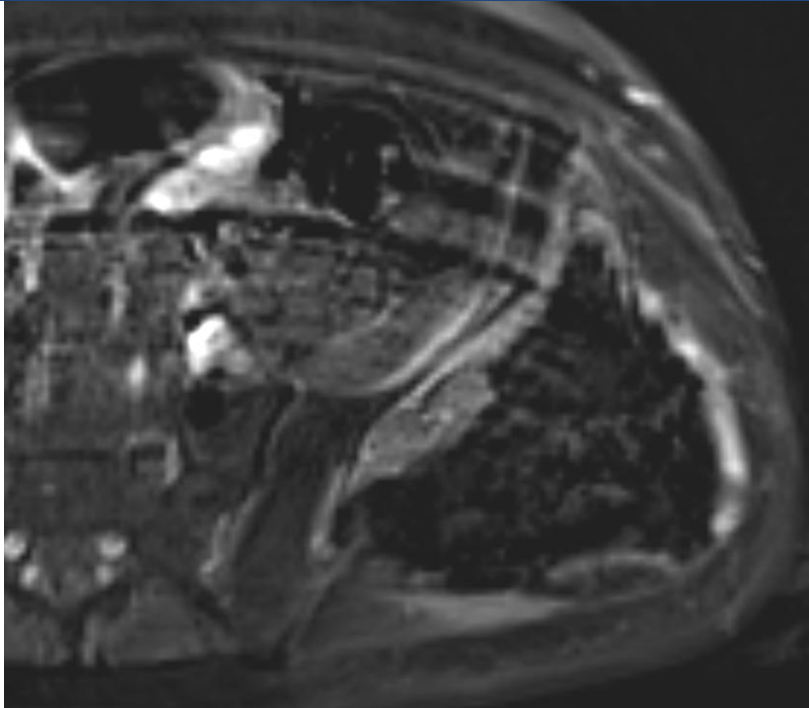
Second ablation (10 probes)

DESMOIDS



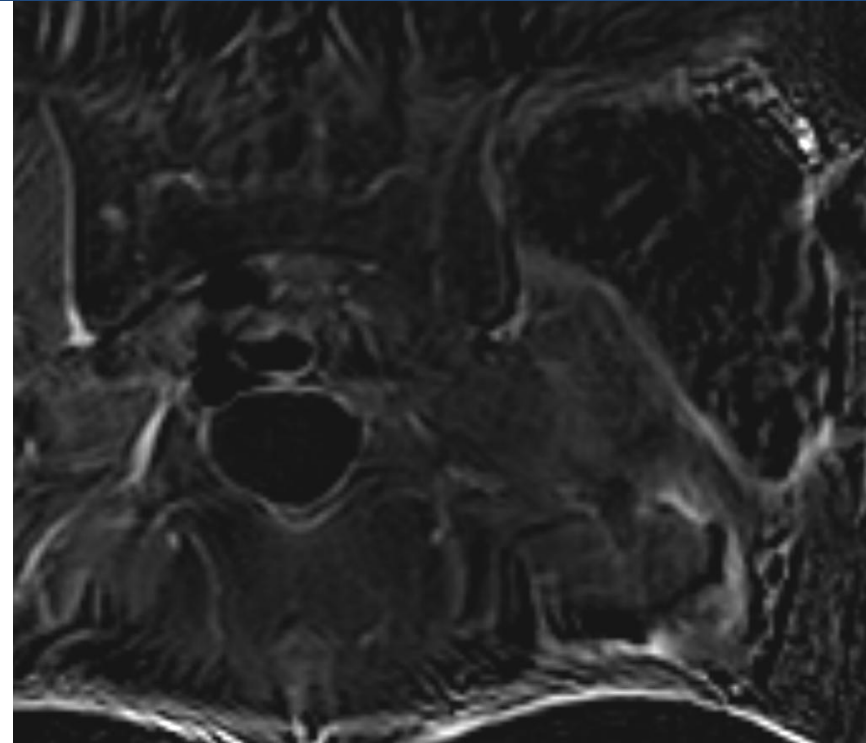
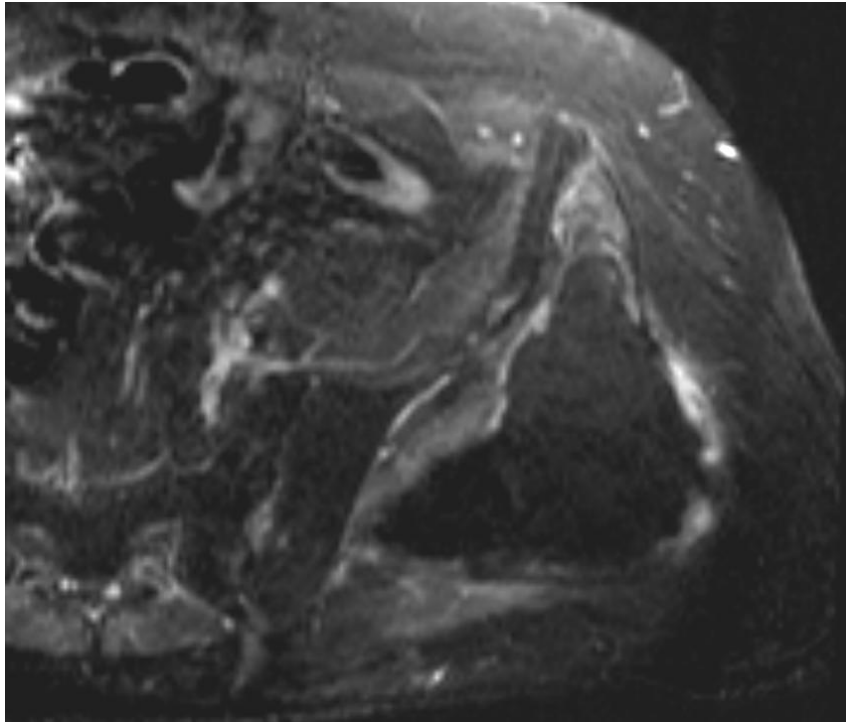
CK elevation with rhabdomyolysis (planned admission for IV fluids and Cr and CK monitoring)

DESMOIDS



Post Second ablation 4 mos

DESMOIDS



Post Second ablation 10 mos

TAKE HOME MESSAGE....

- **Focal treatment** whenever possible should be recommended at tumour board discussion; ideally should be performed in referral centers - Ablation for oligometastatic disease of sarcomas in lung, liver, bone/spine and soft tissue appears **safe and effective**
- **Comparison of results is challenging due to rarity of sarcomas and differences in studied patient population**
- **Personalized treatment** and development of specific targeted therapy


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Cardiovasc Intervent Radiol
<https://doi.org/10.1007/s00270-019-02259-w>



REVIEW

Basic Knowledge in Soft Tissue Sarcoma

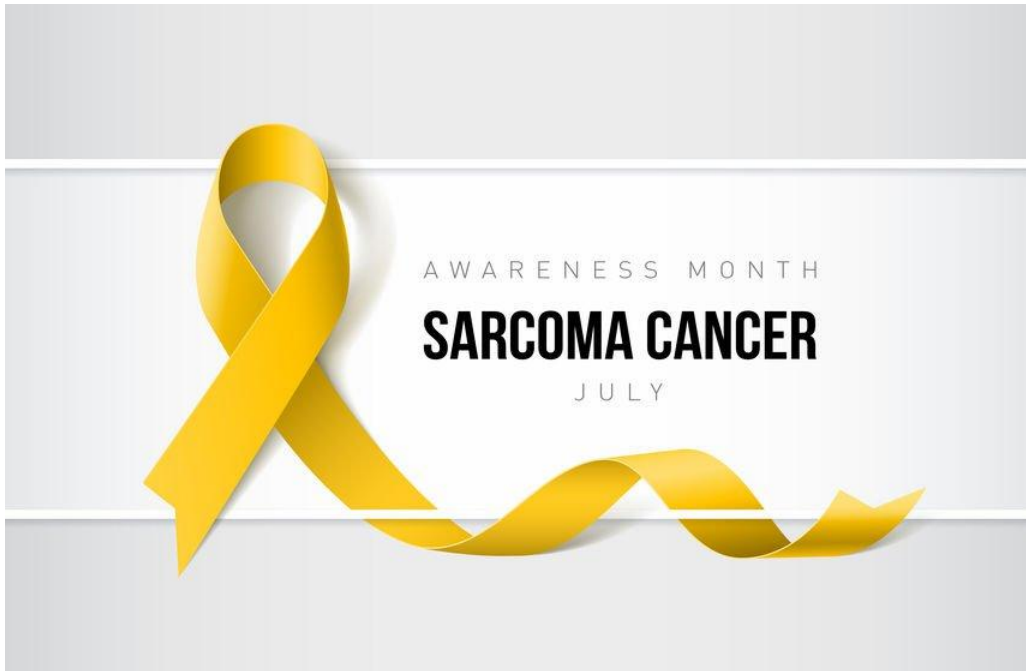
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Abstract Sarcoma is rare and heterogenous with various subtypes having a different prognostic. Desmoid is a tumour with a local aggressiveness; GIST with KIT mutation responds massively to target treatment as IMATINIB, whereas soft tissue sarcoma and leiomyosarcoma are very aggressive with poor response to systemic therapies. Interventional radiology plays an important role in the diagnosis of sarcomas with image-guided percutaneous core needle biopsy being the most commonly used biopsy technique in the diagnosis of sarcomas. Biopsy access routes discussed with the surgeon, and skin access is tattooed. Surgery is a mainstay of sarcoma treatment; the resection can be large. Indeed, resection objective is R0 because quality of surgical margins impacts local control and survival. Radiotherapy is possible in neoadjuvant or in

adjuvant treatment to improve local control rate. Recently radiotherapy enhancer injected percutaneously in soft tissue sarcoma has proven benefit in increasing the rate of R0 complete surgical resection. Several studies showed better local control rate linked with post-operative radiotherapy. In patients affected by oligometastatic disease, complete surgical resection of all metastatic sites is in fact considered the primary treatment because complete remission is critical for cure. The decision making to use local therapies is complex, depends upon diverse presentations and histologies, and should always be taken in a multidisciplinary discussion. Today, percutaneous image-guided treatments with ablation technologies (radiofrequency ablation, cryotherapy, microwaves ablation) provide high rate of durable local control for small-sized malignant deposit in many organs including lung, liver and bones. Sarcoma must be managed by multimodality treatment in expert reference centres. Such management has a considerable impact on the prognosis.

Keywords Sarcoma · Soft tissue sarcoma · Stromal tumor · Interventional oncology

THANK FOR YOUR ATTENTION



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