

# Development + Diagnosis of Metastasis, Disease-Specific Patterns and Local Treatment Options

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# NCCN Guidelines for Metastatic Soft Tissue Sarcomas

**Disseminated  
metastases or  
unresectable**



## **Options:**

**Observation, if asymptomatic**

**Best supportive care**

**Chemotherapy**

**Palliative surgery**

**Radiation**

**Ablation procedures**

**RFA**

**Cryotherapy**

**Embolization procedures**

# Advanced/ Metastatic Disease

- Median overall survival 12-19 months<sup>1,2</sup>
- Limited treatment options
  - Toxic
- Increasing range of therapies
- Improved survival over time
  - More systemic therapy options
  - Improved palliative care
  - Better confirmation of diagnosis
  - Multi-disciplinary care

<sup>1</sup>Ryan CW et al. JCO 34(32); 3898-3905: 2016

<sup>2</sup>Tap WD et al. JAMA 323(13); 1266-1276: 2020

# Management of Metastatic Disease: Principles

- Heterogeneity
  - Differential sensitivity
  - Between subtypes
  - Within a specific subtype: Leiomyosarcomas
    - Extremely aggressive versus indolent
- Active surveillance
  - Indolent subtype
  - Low volume disease
  - No symptoms
- Solitary/ oligo metastatic disease
  - Local treatment modalities
- Keep systemic therapy in reserve
  - Quality of life

# What does the oncologist think?

- Thoughtful approach to the management of metastatic disease
  - Symptoms
  - Disease burden
  - Disease tempo
  - Histological subtype
- Use treatments wisely and strategically

# Systemic therapy in Soft Tissue Sarcomas

- Chemotherapy:
  - Mainstay of treatment for unresectable metastatic disease
- Previously “one size fits all” approach to therapy
  - Anthracyclines
  - Ifosfamide
  - Others (DTIC, navelbine, cisplatin)
- Gemcitabine plus docetaxel
- **Recently approved agents:**
  - Pazopanib
  - Trabectedin
  - Eribulin
  - Tazemetostat
  - NTRK inhibitors
  - Ripretinib + avapritinib for GIST

# Aim of Systemic Therapy

- Downstage advanced disease
  - Chemosensitive subtype
  - Combination doxorubicin + ifosfamide
  - Performance status
  - Co-morbidities
- Palliation of metastatic disease
  - Chemosensitive
  - Sequential therapy
  - Maintain quality of life

# Different drugs for different diseases

- Localized

- Osteosarcoma
- Ewing
- Rhabdomyosarcoma
- GIST

MAP  
VDC/ IE  
VAC  
Imatinib

- Metastatic

- Dermato fibrosarcoma protuberans
- Giant cell tumor of bone
- Alveolar soft part sarcoma
- Inflammatory myofibroblastic tumor
- PEComas
- Endometrial stromal sarcoma
- Chordoma
- Ewing/ Rhabdomyosarcoma
- Ewing/ Rhabdomyosarcoma
- Solitary fibrous tumor

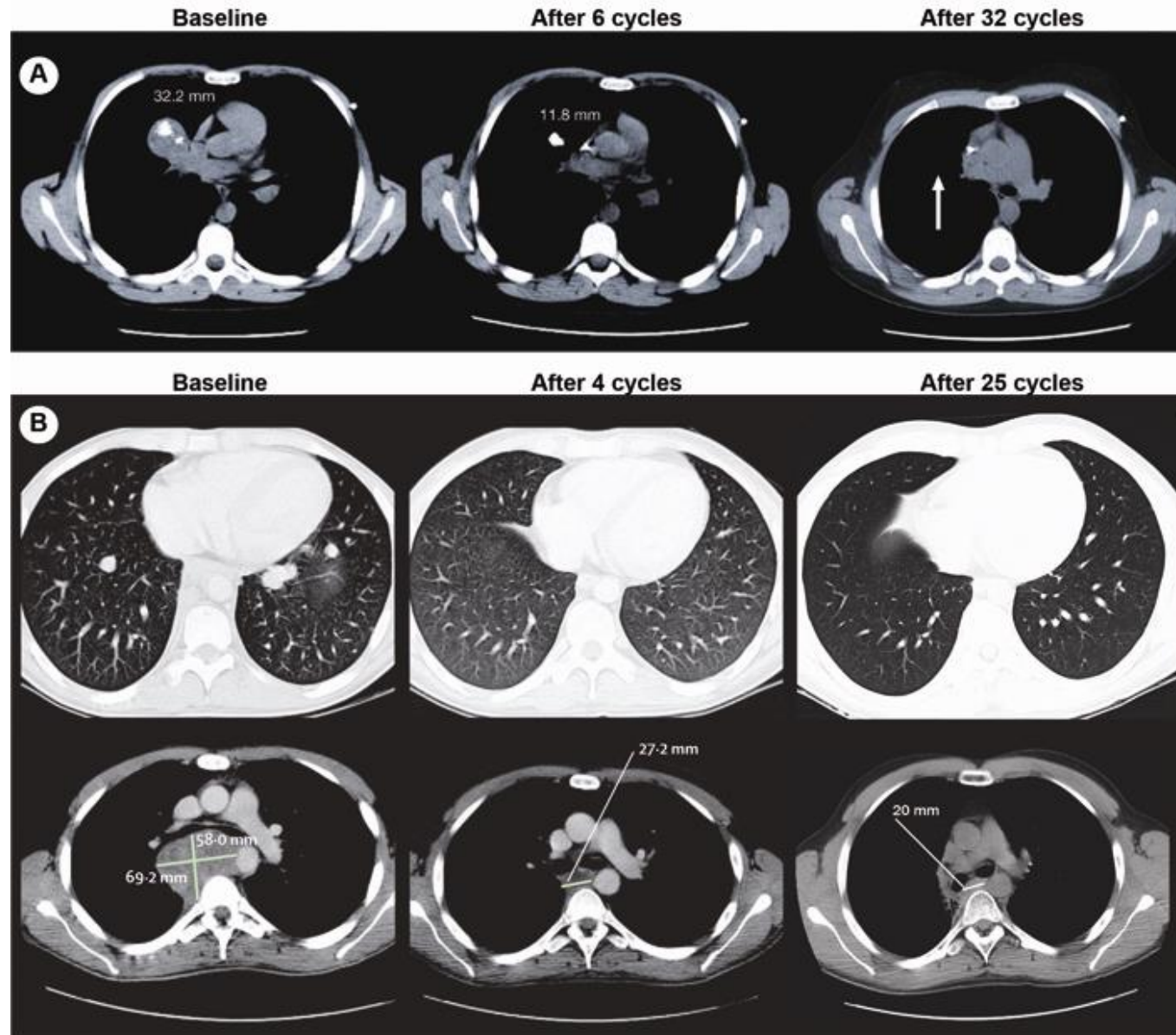
Imatinib  
Denosumab  
Cediranib/ sunitinib  
ALK inhibitors  
mTOR inhibitors  
Aromatase inhibitors  
Imatinib/ mTOR Inhibitors  
Cyclo/ topotecan  
Irinotecan/ temozolamide  
Anti angiogenic agents



# Clinical Trials

- Chemo resistant histological subtype
  - Toxicity of conventional chemotherapy
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- Importance of obtaining prospective data
- Phase 1 trials
  - Biological basis for treatment
  - Logistics – time commitment

# Phase 1 trial: Radiological Response



### **Doubt about effectiveness of lung metastasectomy for sarcoma**

Tom Treasure, MD, MS, FRCS, FRCP,<sup>a</sup> and Fergus Macbeth, MA, DM, FRCR, FRCP(Glas),  
FRCP(Lon), MBA<sup>b</sup>

- Studies on lung metastasectomy
  - Retrospective, inherent selection bias
  - No control data
  - No description of reference population
  - No denominator
- No information on
  - Lung function
  - Patient reported outcomes
- “For patients having sequential treatments, the patient needs to be alive to have the next treatment, which might be confused with the patient is alive *because of* the previous treatment.”

# **The Effect of Metastasectomy: Fact or Fiction?**

Torkel Åberg, M.D., Kjell-Åke Malmberg, M.D.,  
Bert Nilsson, M.D., and Enn Nõu, M.D.

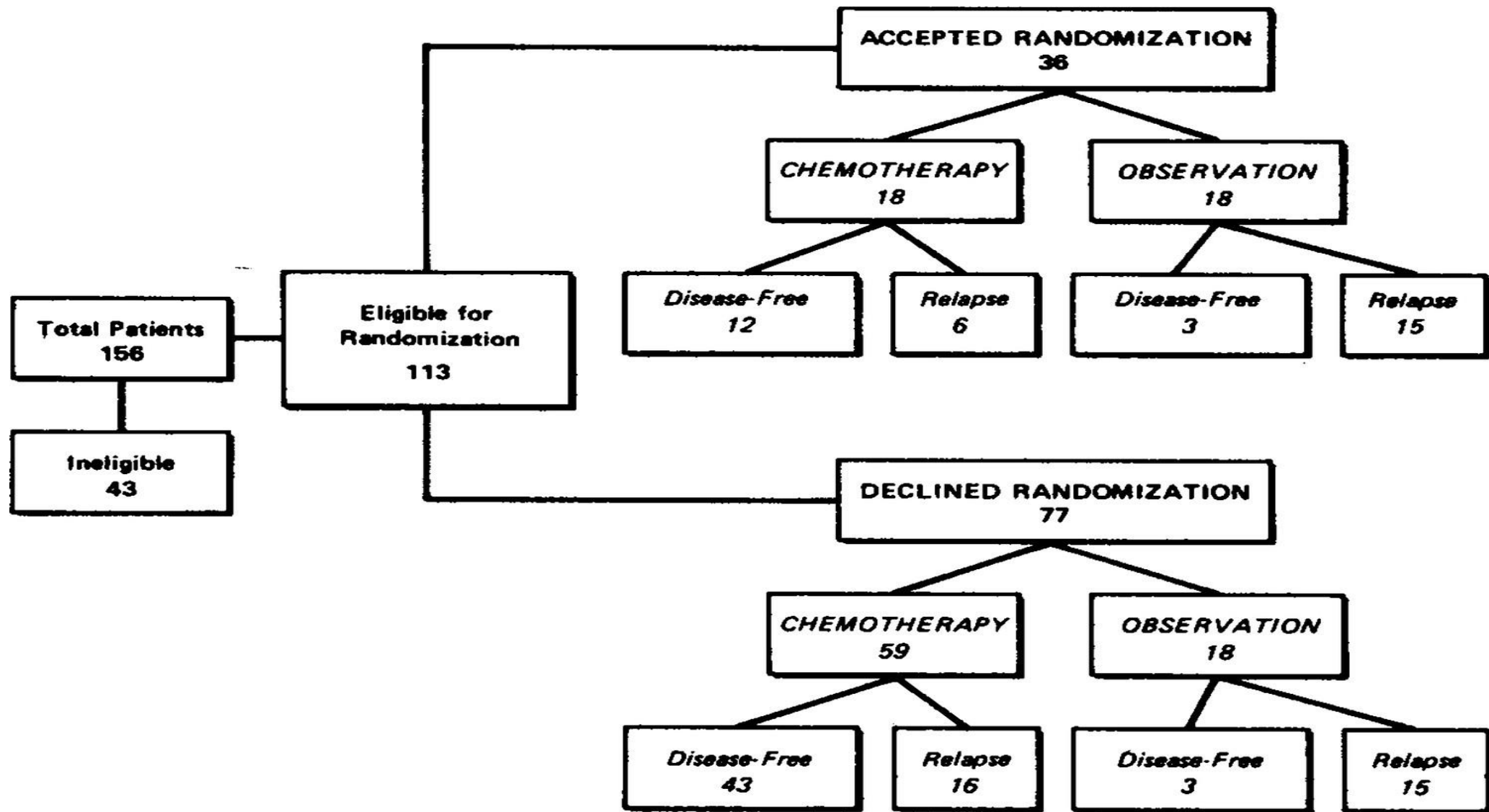
From the Departments of Thoracic Surgery and Lung  
Medicine, University Hospital, Uppsala, Sweden.

Accepted for publication Jan 18, 1980.

Address reprint requests to Dr. Åberg, Department of  
Thoracic Surgery, University Hospital, 750 14 Uppsala 14,  
Sweden.

- Metastasectomy
  - Patient selection critical
  - Evidence base: retrospective
- Is a randomized trial feasible?
- Equipoise.....?

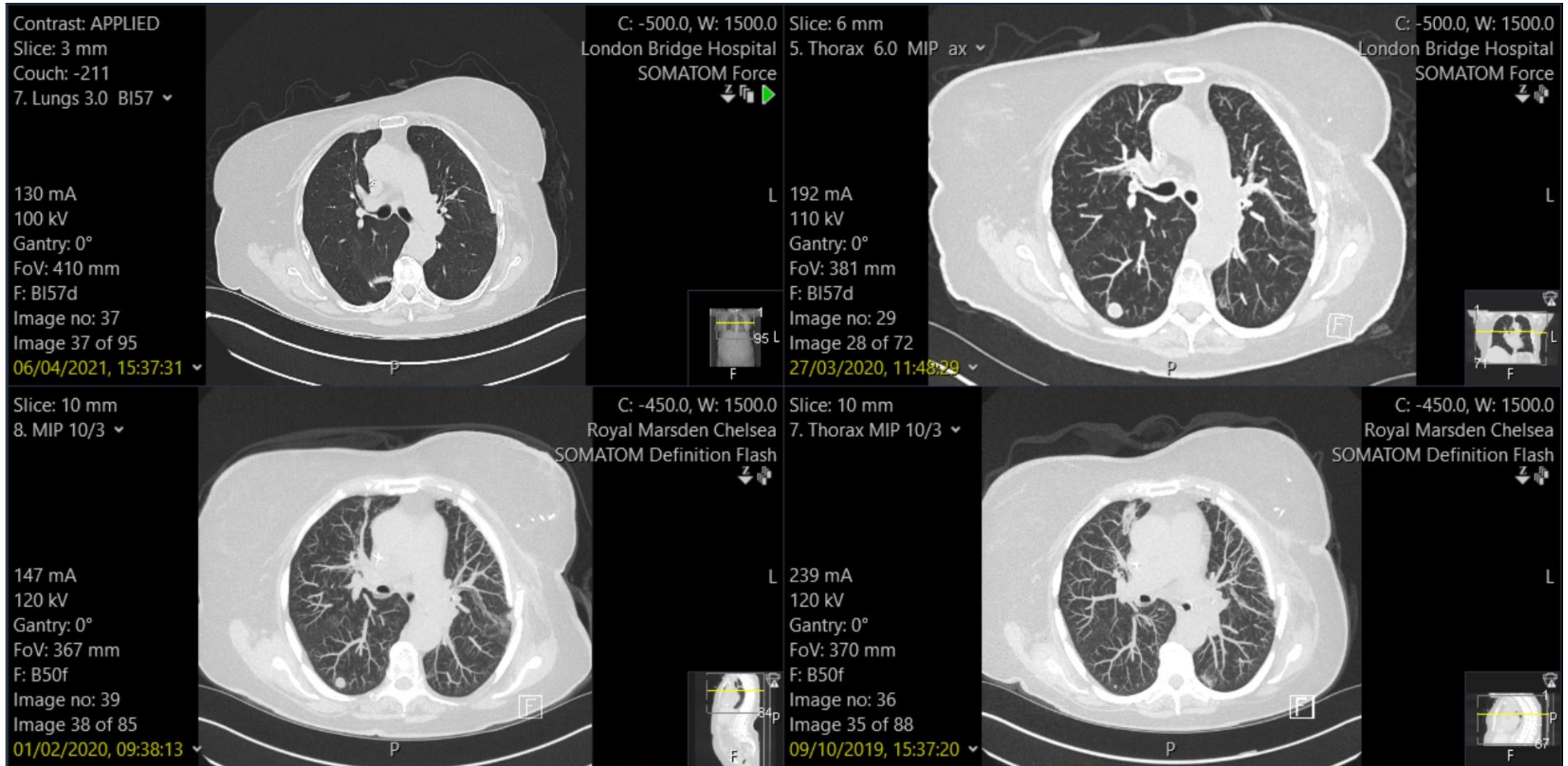
# MIOS Osteosarcoma Trial



# Surgery for metastatic disease

- **2010**: Left breast conserving surgery and radiation for breast carcinoma
- **Feb 2019**: Resection of radiation-associated high grade pleomorphic sarcoma left chest
- **Oct 2019**: Small pulmonary metastasis: right lower lobe
- **June 2020**: Resection right lung metastasis

# Surgery for metastatic disease



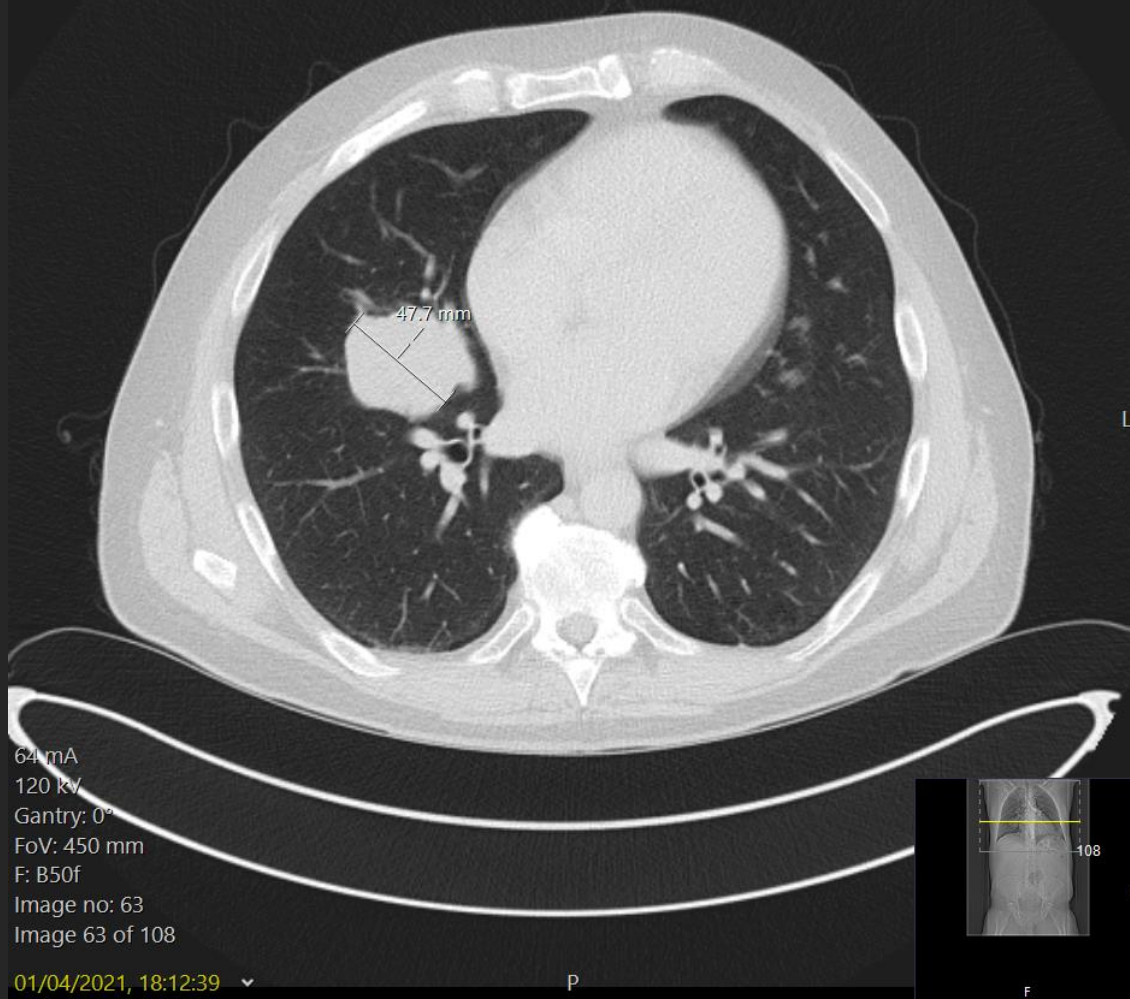
# Active Surveillance

- **2004**: Resection left buttock clear cell sarcoma
- **Mar 2006**: Resection of locally recurrent disease
- **Jun 2016**: Wide excision primary tumour site + left inguinal lymphadenectomy (4 positive lymph nodes)
- **Feb 2010, Aug 2011, Apr 2012 & Jan 2017**: Resection of in-transit deposits
- **Mar 2018**: CT: Low volume lung disease + left buttock nodules
- **Jun – Sep 2018**: BOSTON Phase I clinical trial
- **Nov 2018 – June 2019**: Gemcitabine + dacarbazine



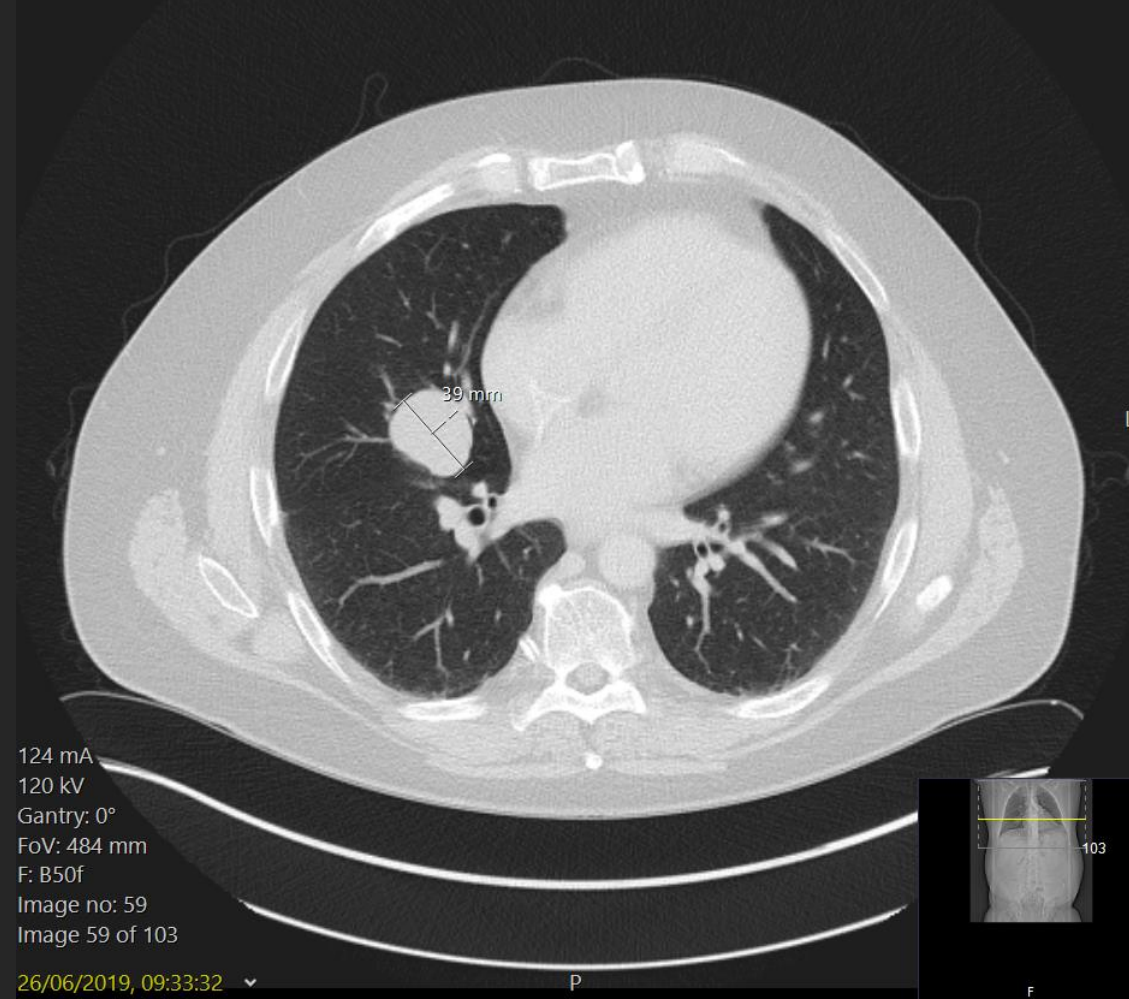
Contrast: Omnipaque 300  
Slice: 3 mm  
Couch: 184.6  
7. TAP IV 3/3 lung ▾

C: -450.0, W: 1500.0  
The Royal Marsden Hospital (London)  
SOMATOM Definition Flash  
Z R L



Contrast: Omnipaque 300  
Slice: 3 mm  
Couch: 286.1  
7. TAP IV 3/3 lung ▾

C: -450.0, W: 1500.0  
Royal Marsden Chelsea  
SOMATOM Definition Flash  
Z R L



# Multi-disciplinary Approach

- Solitary metastatic disease
- Solitary progression:
  - Local therapy can allow continuation of systemic therapy
- Other approaches



Available online at [www.sciencedirect.com](http://www.sciencedirect.com)



**EJSO**  
the Journal of Cancer Surgery

[www.ejso.com](http://www.ejso.com)

EJSO 36 (2010) 477–482

# Radiofrequency ablation is a feasible therapeutic option in the multi modality management of sarcoma

R.L. Jones<sup>a,\*</sup>, J. McCall<sup>a,b</sup>, A. Adam<sup>c</sup>, D. O'Donnell<sup>c</sup>, S. Ashley<sup>a</sup>, O. Al-Muderis<sup>a</sup>,  
K. Thway<sup>a</sup>, C. Fisher<sup>a</sup>, I.R. Judson<sup>a</sup>

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Available online 8 January 2010

# Safety and Efficacy Outcomes of Embolization in Hepatic Sarcomas

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Elizabeth T. Loggers<sup>2</sup>  
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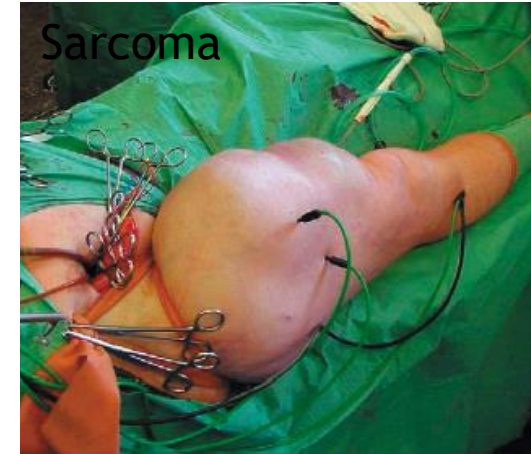
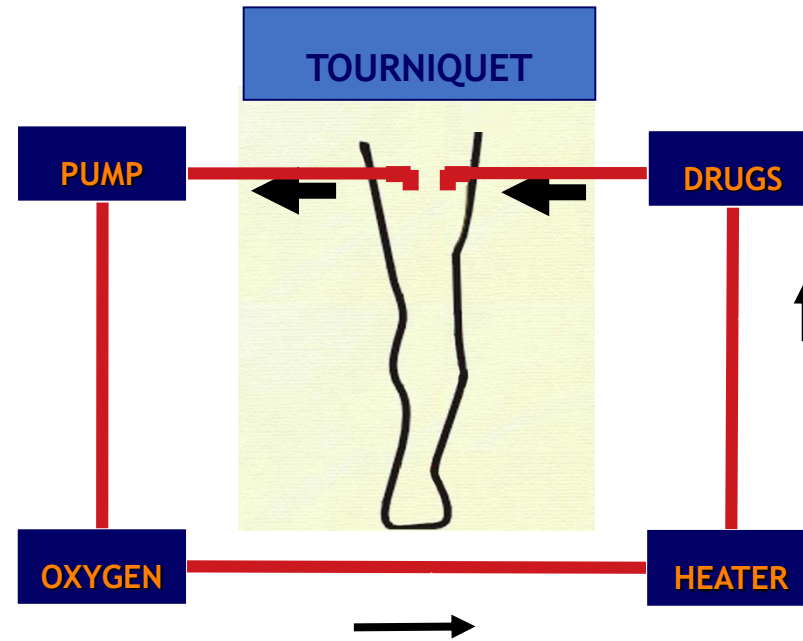
**OBJECTIVE.** The outcome for patients with unresectable hepatic sarcoma is poor with a median survival period of 12–16 months. The purpose of this study was to evaluate liver-directed transcatheter therapies for the treatment of hepatic sarcomas.

**MATERIALS AND METHODS.** In a retrospective study, the cases of patients with primary and metastatic hepatic sarcoma treated by transcatheter embolization, chemoembolization, and <sup>90</sup>Y radioembolization between 2004 and 2015 were identified. Response Evaluation Criteria in Solid Tumors version 1.1 response was assessed for the target tumor. Survival was assessed by means of Kaplan-Meier analysis.

**RESULTS.** Twenty-eight patients (17 [61%] men, 11 [39%] women; median age, 47 years) were included. Eighteen patients were treated electively. Two of the electively treated patients

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# Isolated limb perfusion (ILP)



- Allows delivery of high dose chemotherapy and biological agents whilst avoiding severe systemic toxicity
- Melphalan+TNF-alpha (not licenced in the US)



# Isolated limb perfusion result

- Irresectable extremity soft tissue sarcoma: angiosarcoma



Angiosarcoma  
Pre ILP

3 years  
Post ILP

5 years  
Post ILP

# Conclusions

- Number of options for patients with metastatic sarcomas
- Multi-disciplinary input
- Thoughtful and strategic approach to management
- Clinical trial participation
  - Laboratory studies
  - Quality of life studies

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