Introduction to the diagnosis of lumps and soft tissue sarcoma
9.45am - 10.15am

Mr Myles Smith
Consultant Surgical Oncologist and General Surgeon
The Royal Marsden
Introduction

– Approach to a patient with a lump
– Problems with Soft Tissue Sarcoma (STS) diagnosis
– Extremity sarcoma
– Retroperitoneal sarcoma
  • Extended resection
– Innovations:
  • Robotic GIST resection
  • ILP: the TITAN study
# The Problem

A patient with a lump

<table>
<thead>
<tr>
<th>Is it benign or malignant?</th>
<th>When to refer?</th>
<th>Where to refer?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A patient with a lump.
Getting a correct diagnosis and rapid access to expert care

When to refer:
- >5cm
- Growing
- Deep
- Painful
- Recurrent

Rapid Diagnostic Clinic:
- Clinical examination by expert
- Ultrasound/MRI
- Core biopsy

Diagnosis
Criteria for referral

2006 NICE IOG

- size >5cm
- increasing size
- deep to the deep fascia
- painful
- recurrent after previous excision

- Current NICE guidance is that all should have USS before assessment

A 5cm lump is one that is bigger than a golf ball or the short side of a credit or debit card
### Diagnosis

<table>
<thead>
<tr>
<th>Benign</th>
<th>Intermediate</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal variant</td>
<td>Locally aggressive Non-metastasing</td>
<td>Soft tissue sarcoma</td>
</tr>
<tr>
<td>Benign mass</td>
<td></td>
<td>Lymphoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metastasis</td>
</tr>
</tbody>
</table>
Incidence of STS and Benign Soft Tissue Masses

- 0.5-1% of adult human cancers
- Estimated 5000 cases/year in the UK vs. breast Ca 47,000/yr

Benign soft tissue tumours, especially lipomas, are 100x as common
Anxiety + Discomfort

Soft tissue sarcomas - 1/career
1:7 to 1:4 of large, rapidly growing or deep lumps may represent a locally aggressive non-metastasising lesion (indeterminate)
1:10-20 may be a cancer
New classification lists >100 sarcoma subtypes
Aetiology

- **Sporadic** - majority
- **Inherited** - although there are a few genetic predisposing conditions (e.g. Li Fraumeni syndrome, RB mutations, NF)
- **Environmental** factors: radiation exposure and chronic lymphoedema
Where do soft tissue sarcomas occur?

<table>
<thead>
<tr>
<th>Anatomical sites</th>
<th>10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and neck</td>
<td>10%</td>
</tr>
<tr>
<td>Upper limb and girdle</td>
<td>15 - 20%</td>
</tr>
<tr>
<td>Retroperitoneal/intraperitoneal</td>
<td>15 - 20%</td>
</tr>
<tr>
<td>Chest/Abdominal wall</td>
<td>10%</td>
</tr>
<tr>
<td>Lower limb and girdle</td>
<td>40%</td>
</tr>
</tbody>
</table>
Presentation

Key Signs

Lump
- Rapidly growing
- >5cm
- Deep
- Painful (arising in nerve or compression)
- Recurrent after excision
- Surprise diagnosis after inadvertent excision

Referred via soft tissue lump diagnostic clinic
Problems with diagnosis of STS

**Rare tumours**
- Lack of awareness

**Delays in diagnosis**
- Patient and system factors

**Inappropriate intervention 3x recurrence**
- Suboptimal surgery outside of specialized unit
- Inadvertent surgery
Late diagnosis

UNRECOGNISED SARCOMA
55lb tumour missed for decade

By Nigel Hawkes
Health Editor

FOR nearly ten years Trevor Smithson was told by doctors that he was dangerously obese and had only himself to blame for his constant pain, chronic backache and circulation problems.

"I think everyone just took one look at me and thought I drank 15 pints a day," said Mr Smithson, a 53-year-old aeronautical engineer.

For several months he would often have a distended abdomen and accompanying pain in 1994. He was referred to the hospital by his GP, but when he was seen there he was told he was fat.

When he finally reached the Royal Marsden, he says, the first reaction of Meirion Thomas, his surgeon, was: "So you've not been to see your doctor for years and years, have you?" He had to explain that he had been seeing doctors at regular intervals, with no satisfaction.

Mr Thomas removed what are described in Mr Smithson's discharge notes as "a truly immense intra-abdominal liposarcoma". These are slow-growing malignant tumours that develop in fat tissue, and are often found in the abdominal cavity.

They are soft and can be difficult to diagnose, but Mr Smithson says that he had a range of symptoms that ought to have alerted doctors, including backache, circulation problems in his scrotum and a colon so displaced that it could be felt through the abdominal wall.

He also had excessive body weight while not having any symptoms of obesity anywhere else in his body. "I was constantly shopping for ever-increasing sizes of clothes," he said. "I'm a tall man and when I was also that heavy I wore out my shoes very quickly."

"I went through a difficult time career-wise. I was an aeronautical engineer but I couldn't get a job. Once they had decided I was just obese they didn't take any further action."

Yesterday the hospital said that while they could not discuss individual cases, this particular type of tumour could be difficult to diagnose, and that it might take years to discover.

"If one looked for one thing and didn't have enough information to look for anything else, one might not do tests," a spokeswoman said, making clear that she was talking in general terms and not specifically about Mr Smithson.

"We take complaints very seriously and investigate them thoroughly."
Presentation

Symptomatic mass

Incidental/indirect imaging

My beer belly was a tumour

Doctors remove 3½ stone cancer

Dedifferentiated retroperitoneal liposarcoma
Late diagnosis

PATIENT FACTORS
Malignant Ossifying Myxoid Tumour
Late diagnosis

SYSTEM FACTORS
18 month delay...

71 yo Man

- He initially presented in September 2017 with a 4-5 cm lump in the palmar aspect of his left forearm, about 10 cm from the elbow joint.

- He now presents with a very large tumour in the subcutaneous space which on an MRI scan from December 2018 measured 10 x 8 x cm.

- Unfortunately he did see his GP on multiple occasions between those two dates.

- *At initial presentation it was the size of grape*
MRI of tumour

Axial

There is a large solid lobulated mass arising from the subcutaneous fat within the medial proximal left forearm superficial to the flexor compartment. This process measures 10 cm in craniocaudal diameter and 7.8 x 4.9 cm in cross-section. It is severely distending but not apparently ulcerating the overlying skin and is not involving the underlying musculature.

Opinion:
Large solid heterogeneous mass in the proximal left forearm which is consistent with a sarcoma.

Craniocaudal view

- **Myxofibrosarcoma, at least grade 2**
- **High risk LR, DM**
- **Needs XRT + Reconstruction**
Problems of inappropriate diagnosis and intervention

“The Oculo-Brachial Reflex”
A new pathway with no discernable cortical connections

Cortex

- Normal Pathway
- Oculo-Brachial Pathway

©JM Thomas 1994
Incision biopsy:
Usually unnecessary and potential complications

Early recurrence/progression

Residual leiomyosarcoma
Further recurrence

Scar
Presumed Lipoma: “Extruded In Pieces”

Diagnosis: Myxoid Liposarcoma

How much to resect?
While “whoops” operations can usually be recovered they can be a cause of anxiety for the patient and the doctor.
Definitive Surgery

Wide Excision

End Result
Retroperitoneal Sarcoma

Piecemeal Resection

Early Local Recurrence
Unplanned Excision of Soft Tissue Sarcoma Results in Increased Rates of Local Recurrence Despite Full Further Oncological Treatment

Y. A. Qureshi, J. R. Huddy, J. D. Miller, D. C. Strauss, J. M. Thomas, and A. J. Hayes

Soft Tissue Sarcoma and Melanoma Unit, Department of Academic Surgery, The Royal Marsden Hospital, London, UK

Survival (%)

0 12 24 36 48 60 72 84 96 108 120

P=0.0362

The ROYAL MARSDEN
<table>
<thead>
<tr>
<th>Stage</th>
<th>Category</th>
<th>Total n</th>
<th>LR n</th>
<th>LR %</th>
<th>Median time to LR (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Inadvertent</td>
<td>60</td>
<td>11</td>
<td>18.3%</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Appropriate</td>
<td>74</td>
<td>5</td>
<td>6.7%</td>
<td>24</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Inadvertent</td>
<td>58</td>
<td>15</td>
<td>25.8%</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Appropriate</td>
<td>37</td>
<td>4</td>
<td>10.8%</td>
<td>20</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Inadvertent</td>
<td>16</td>
<td>6</td>
<td>37.5%</td>
<td>10.5</td>
</tr>
<tr>
<td></td>
<td>Appropriate</td>
<td>98</td>
<td>14</td>
<td>14.2%</td>
<td>18</td>
</tr>
</tbody>
</table>
Adherence to National Comprehensive Cancer Network Guidelines is Associated with Improved Survival for Patients with Stage 2A and Stages 2B and 3 Extremity and Superficial Trunk Soft Tissue Sarcoma

Rachel K. Voss, MD¹, Yi-Ju Chiang, MSPH¹, Keila E. Torres, MD, PhD¹, B. Ashleigh Guadagnolo, MD, MPH², Gary N. Mann, MD¹, Barry W. Feig, MD¹, Janice N. Cormier, MD, MPH¹, and Christina L. Roland, MD¹

¹Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; ²Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

FIG. 3 Adjusted survival curves for (a) stage 2A and (b) stages 2B and 3 extremity and superficial trunk sarcomas
FSG study of RPS: Surgical expertise and appropriate surgery on Recurrence

Toulmonde et al Ann Oncol 2014;25:730-4
French Sarcoma Group

NetSarc
- 28 Reference centres
- 2010
- All cases recorded
- Treatment before/after discussion at MDT
  - 26000 cases
- 3X local recurrence in those discussed at MDT after treatment

Surgery after MDT discussion
CTOS 2018

MDT8 without surgery by expert center
The worst case scenario
SOLUTIONS
Clinical Study
Delays in Referral of Soft Tissue Sarcomas

G. D. Johnson,¹ G. Smith,¹ A. Dramis,² and R. J. Grimer²

- 162 Cases STS, 3 month period

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Duration</th>
<th>Month 1</th>
<th>Month 2</th>
<th>Month 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Onset of symptoms to presentation</td>
<td>1.3 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Presentation to 1st referral</td>
<td>2.4 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1st referral to 1st consultant appointment</td>
<td>2.2 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1st consultant appointment to referral to ROH</td>
<td>6.9 w</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 2: The median patient.

- Median delay until presentation to a medical professional by patient:
  - 1.3 weeks

- Median delay in referral to a specialist centre (@DGH):
  - 25 weeks
The 2 week Rule

2006 NICE IOG

- size >5cm
- increasing size
- deep to the deep fascia
- painful
- recurrent after previous excision

- Current NICE guidance is that all should have USS before assessment

A 5cm lump is one that is bigger than a golf ball or the short side of a credit or debit card.
Raising Awareness

- Awareness
  - Education
    - Talks!
  - Media campaigns
    - On the ball
    - Sarcoma awareness week - month

- Appropriate referral and investigation/Central Planning
  - Criteria for referral and outcomes (STWR)
  - Access to MDT
  - Red flags
Home » Get Involved

Sarcoma Awareness Week 2019

88% of people don't know or are not sure what sarcoma is.

Let's change that.
Getting a correct diagnosis and rapid access to expert care

When to refer
- >5cm
- Growing
- Deep
- Painful
- Recurrent

Rapid Diagnostic Clinic
- Clinical examination by expert
- Ultrasound/MRI
- Core biopsy

Diagnosis
Diagnosis - clinical exam, MRI and core biopsy

- FNAC not sufficient
  - Except GIST
- No risk of seeding
- Ideally in the direction of future incision (excised)
Management of STS

- STS is managed (and cured) principally by surgery
  - 50-60% cure

- Local recurrence will happen if an appropriate cancer operation is not undertaken
Surgery for Sarcoma

— Preoperative diagnosis and contemporary planning imaging essential

— The operations are vary varied but all apply the same principles

— Appropriate expertise
  • Technical ability and training
  • Multidisciplinary care (XRT, Physio, ICU, other surgeons)
Principles of STS Surgery

- Resection of the tumour with one uninvolved anatomical plane in all directions
  - WLE ("pushing tumours")
  - Marginal:
    - XRT
    - Good biology (i.e. liposarcoma)
- (Ennenking et al Cancer 1981, 47, 1005)

**Limb**

**Aim is for limb preserving surgery (WLE+XRT)**

**Functional considerations**

**Amputation is rarely necessary** (compare mastectomy)

**Retroperitoneal or visceral**

**Clear margins, extended resection considered**
## Examples of benign tumours and corresponding STS

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adipose tissue</td>
<td>Lipoma</td>
<td>Liposarcoma</td>
</tr>
<tr>
<td>Muscle</td>
<td>Leiomyoma</td>
<td>Leiomyosarcoma, Rhabdomyosarcoma</td>
</tr>
<tr>
<td>Endothelium</td>
<td>Haemangioma</td>
<td>Angiosarcoma, Kaposi sarcoma</td>
</tr>
<tr>
<td>Skin</td>
<td>Dermatofibroma</td>
<td>Dermatofibrosarcoma protuberans (DFSP) incl. fibrosarcoma ex DFSP</td>
</tr>
</tbody>
</table>
Sequencing of therapies for STS

- Radiotherapy (+/- chemotherapy)
- Surgery
- Systemic therapy
- Neoadjuvant
- Adjuvant Palliative Trial
- Dose, infection, limb function
NICE IOG

Key recommendations 2006 onwards

- Surgery
  - Sarcoma surgery performed by appropriately skilled surgeons
    o Via sarcoma MDT or specialist MDT in consultation

- Defined treatment centre volumes:
  - ≥ 100 new cases of soft tissue sarcoma/year (650-700 RMH)
  - ≥50 new bone
  - 25 RPS
    o 65-70 primary/year RMH
OPERATIVE APPROACH
LIMBS
Benign/Indeterminate Lesions
Thigh Liposarcoma
Marginal resection
Quadriceps Tumour Resection

Femoral artery

Femoral nerve
Compartmentectomy:
Triceps resection with preservation of radial nerve
OPERATIVE APPROACH
RETROPERITONEAL SARCOMA
Resection margins?
Retroperitoneal sarcoma
Extended resection

Kidney
Psoas
Colon
Pancreas
Spleen
Overall Survival after Resection by Primary Site of STS, PMH 1975-1990

Survival

Extremities (n=226)
Torso (n=43)
Head and neck (n=52)
Retroperitoneum (n=45)

PMH ’75-’90

**Extent of Resection**

*Does a more aggressive surgical approach improve outcome?*

![Graph showing cumulative incidence of local recurrence by period of surgical resection at our institution.](image)

*Fig 1.* Crude cumulative incidence of local recurrence by period of surgical resection at our institution.

**Early 1985-2001, n=136**  
median f/u 120 mo

**Recent 2002-2007, n=152**  
median f/u 58 mo
Outcome following resection of retroperitoneal sarcoma


Sarcoma Unit, Department of Academic Surgery, The Royal Marsden Hospital NHS Foundation Trust, London, UK
Correspondence to: Mr D. C. Strauss, Department of Academic Surgery, The Royal Marsden Hospital NHS Foundation Trust, Fulham Road, London SW3 6JJ, UK (e-mail: dirk.strauss@rnh.nhs.uk)

- 10 years (Jan 2005-Dec 2014)
- 362 patients, 292 needed multivisceral resection (81%)
  - 30 day mortality 1.4%
  - 30 day morbidity 15.7%
- Grade and incomplete resection predicted worse outcome
Outcome following resection of retroperitoneal sarcoma


Sarcoma Unit, Department of Academic Surgery, The Royal Marsden Hospital NHS Foundation Trust, London, UK

Correspondence to: Mr D. C. Strauss, Department of Academic Surgery, The Royal Marsden Hospital NHS Foundation Trust, Fulham Road, London SW3 6JJ, UK (e-mail: dirk.strauss@rmh.nhs.uk)

- 186 (51.4 per cent) required an anastomosis
  - 4 leaks (rate 2.2%)
  - All left sided colonic anastomosis

- Distal pancreatectomy was performed in 46 patients
  - 8/46 had a leak (17%)

- Nephrectomy was performed in 190 patients, of whom 113 had follow-up renal function tests more than 30 days after the index procedure
  - 1 patient required dialysis for a short period

The ROYAL MARSDEN
ISOLATED LIMB PERFUSION
Mr. Andrew Hayes
How do you resect the “irresectable?”

Sciatic Nerve

Superficial Femoral Artery
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)
Cannulation at superficial femoral level or external iliac level
How do you resect the “irresectable?”

Sciatic Nerve
Superficial Femoral Artery
Isolated limb perfusion result

– Irresectable extremity soft tissue sarcoma, angiosarcoma
Regional chemotherapy with isolated limb perfusion prior to surgery compared with surgery and post-operative radiotherapy for primary, locally advanced extremity sarcoma: a comparison of matched cohorts

HG Smith, J Jakob, MJ Wilkinson, T Pencavel, AB Miah, JM Thomas, PU Tunn, LR Pilz, DC Strauss, P Hohenberger, AJ Hayes
Post-operative outcomes

<table>
<thead>
<tr>
<th></th>
<th>Standard Cohort</th>
<th>ILP Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Resection margin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>65 (81%)</td>
<td>39 (89%)</td>
</tr>
<tr>
<td>R1</td>
<td>15 (19%)</td>
<td>5 (11%)</td>
</tr>
<tr>
<td><strong>Radiotherapy</strong></td>
<td>66 (83%)</td>
<td>12 (27%)</td>
</tr>
<tr>
<td><strong>Follow-up (median)</strong></td>
<td>31 months</td>
<td>36 months</td>
</tr>
<tr>
<td><strong>Local recurrence</strong></td>
<td>13 (16%)</td>
<td>5 (11%)</td>
</tr>
<tr>
<td><strong>Local recurrence or amputation</strong></td>
<td>13 (16%)</td>
<td>7 (16%)</td>
</tr>
<tr>
<td><strong>Distant metastasis</strong></td>
<td>43 (54%)</td>
<td>23 (52%)</td>
</tr>
</tbody>
</table>

Induction ILP followed by radical resection is an alternative management strategy for locally advanced extremity sarcoma and is associated with a reduced requirement for adjuvant radiotherapy.

Consideration should be given to induction ILP particularly in young patients who stand to benefit most from avoiding radiation.
Oncolytic Virus delivered by immune modulators?

Could this improve local disease control?

Could this reduce rates of systemic relapse?
TITAN

(Tumoural Injection of T-VEC and Isolated Limb Perfusion)

A Phase I/II Study of the Safety and Efficacy of Talimogene Laherparepvec (T-VEC) Delivered by Intratumoural Injection in Combination with Isolated Limb Perfusion with Melphalan and Tumour Necrosis Factor-α in Patients with Advanced Extremity Tumours Including Metastatic Melanoma.
The Royal Marsden

Surgical Approach to Gastrointestinal Stromal Tumour and Visceral Sarcoma

Considerations

Oncologically safe approach prerequisite

Anatomic site:
- Stomach > small bowel > rectum

Extent:
- Primary
- Multivisceral

Mode:
- Open
- Laparoscopic
- Robotic Surgery for GIST
- Robotic
Evolution of Surgical Approach to GISTs

Open Surgery
• All cases

Laparoscopic
• <2cm cases
• >5cm
• Favourable site
• Low risk of R1/rupture

Laparoscopic
• >5cm
• Unfavourable sites
• Assistant stapling/hand suture
• Long docking
• Costly

Robotic S/Si
• >5cm
• Better instruments
• Robot stapler
• Barbed sutures
• Quicker to dock
• Less console time
• ERAS < LOS
• Costly

Robotic Xi
• >5cm

Robotic approach preferable to laparoscopic approach due to capabilities of Xi

Robotic Surgery for GIST
Robotic GIST Resections @ RMH
Mr. Myles Smith and Mr. Asif Chaudry

Location of resected GISTs

Gastric only
*Da Vinci Xi*
May 2017-June 2019, n=10

Robotic Surgery for GIST
Summary and Conclusions

**Robotic Surgery for GIST**

**Benefits for patients**
- Early experience suggests that robotic resections appear oncologically safe and expand benefits of minimally invasive surgery to more patients with GIST.
- Main thrust of STS robotic approach.
- Progress with other tumours.

**Benefits for surgeons**
- Ergonomics.
- Better instruments to perform equivalent resections.
- Fluorescence technology.
- Robotic surgery may become the favoured approach in GIST.

**Caveats**
- No tactile feedback (rupture, although not reported).
- Safety.
- Cost vs. benefit to be defined.
- Procedure.
- Operating time.
- Multiple surgeons.
Summary

- Good surgical outcomes require expert multidisciplinary care
- Diagnosis with appropriate referral, core biopsy and imaging
- Balance biology, function and radiation with treatment
- Extended resection of RPLS is safe and gives the best local control
- Advanced extremity tumours consider isolated limb perfusion
- Robotic surgery may be considered in select cases of visceral sarcoma and GIST
Sarcoma, Melanoma and Rare Tumours Surgeons

Mr. Dirk Strauss  Mr. Myles Smith  Mr. Andrew Hayes