

How Sarcoma/ GIST Research and Expert Care are Organized in the UK

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Disclosures

- Consultant for:
 - Adaptimmune
 - Blueprint
 - Clinigen
 - Eisai
 - Epizyme
 - Daichii
 - Deciphera
 - Immunedesign
 - Lilly
 - Merck
 - Pharmamar

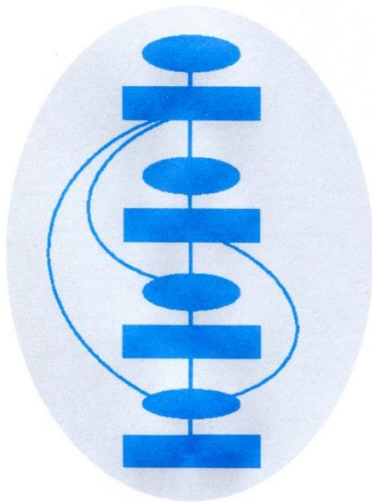
Importance of Centralised Care

- Rarity
- Heterogeneity
- Diverse anatomic primary sites
- Cumulative experience required for expertise in all aspects of care

Guidance on Cancer Services

Improving Outcomes for People with Sarcoma

The Manual



- Consultation exercise lead to publication of guidance in 2006 covering early referral, diagnosis, centralisation of care and all aspects of multidisciplinary management

<http://guidance.nice.org.uk/CSGSarcoma>

March 2006

NICE IOG: Key Recommendations

- All sarcoma patients must be managed by a sarcoma MDT
- Designated Diagnostic Centres
- Provisional sarcoma diagnosis must be reviewed by specialist sarcoma pathologist
- Treatment Centre must manage:
 - ≥ 100 new cases of soft tissue sarcoma a year
 - 50 for bone sarcomas
 - Implications for numbers of surgeons and other staff
- Sarcoma operations must be done by appropriately experienced surgeons
 - In sarcoma MDT or specialist MDT in consultation

IOP specifies need for all sarcoma patients to be referred to a specialist MDT

- X-ray
- MRI
 - Extremity
 - Head and neck
 - Chest wall
- CT
 - Abdomen and pelvis
 - Chest: evaluate for metastatic disease
 - Bone

Criteria for urgent referral for a patient with a suspicious lump

- >5cm
- Increasing size
- Deep to deep fascia
- Painful

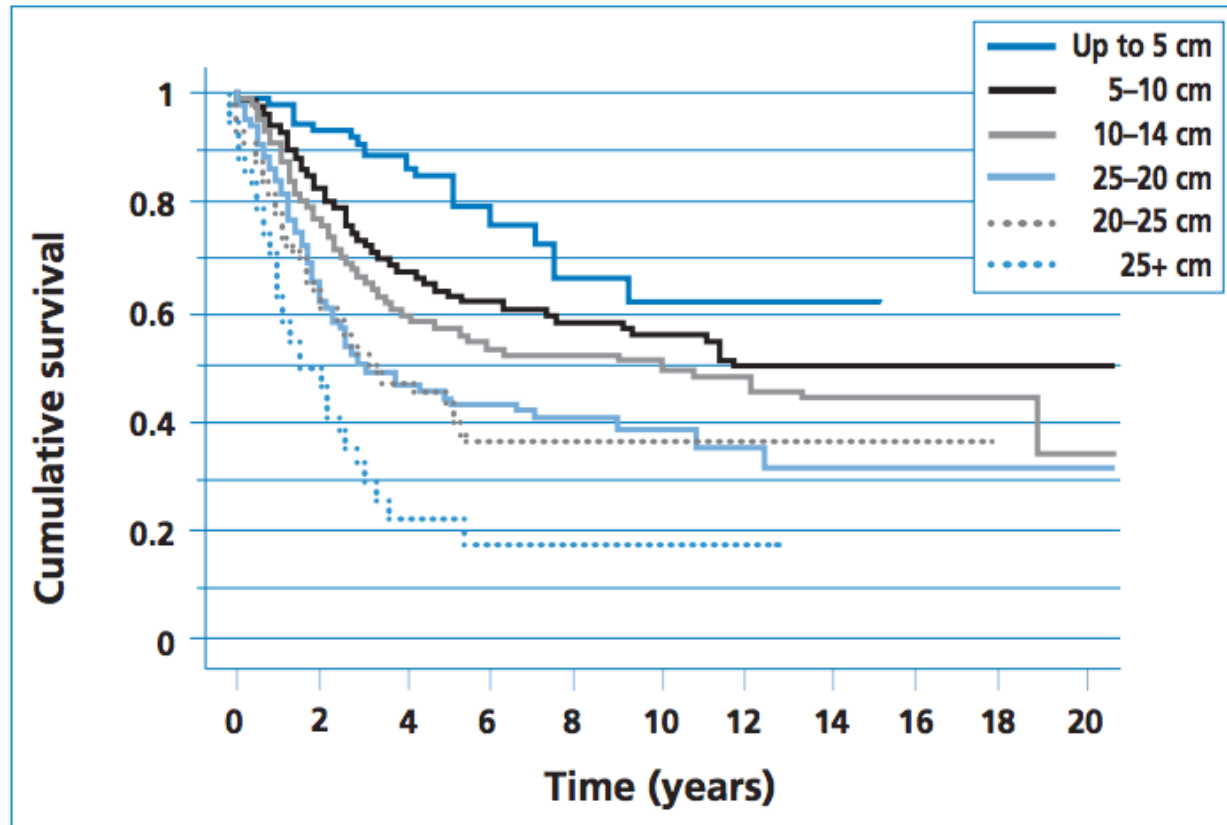
Early Referral:

Impact of tumour size on survival in STS

Figure 1. Survival of all sarcomas without metastases at diagnosis, split by size category at diagnosis

*Improving Outcomes for
People with Sarcoma*

Background

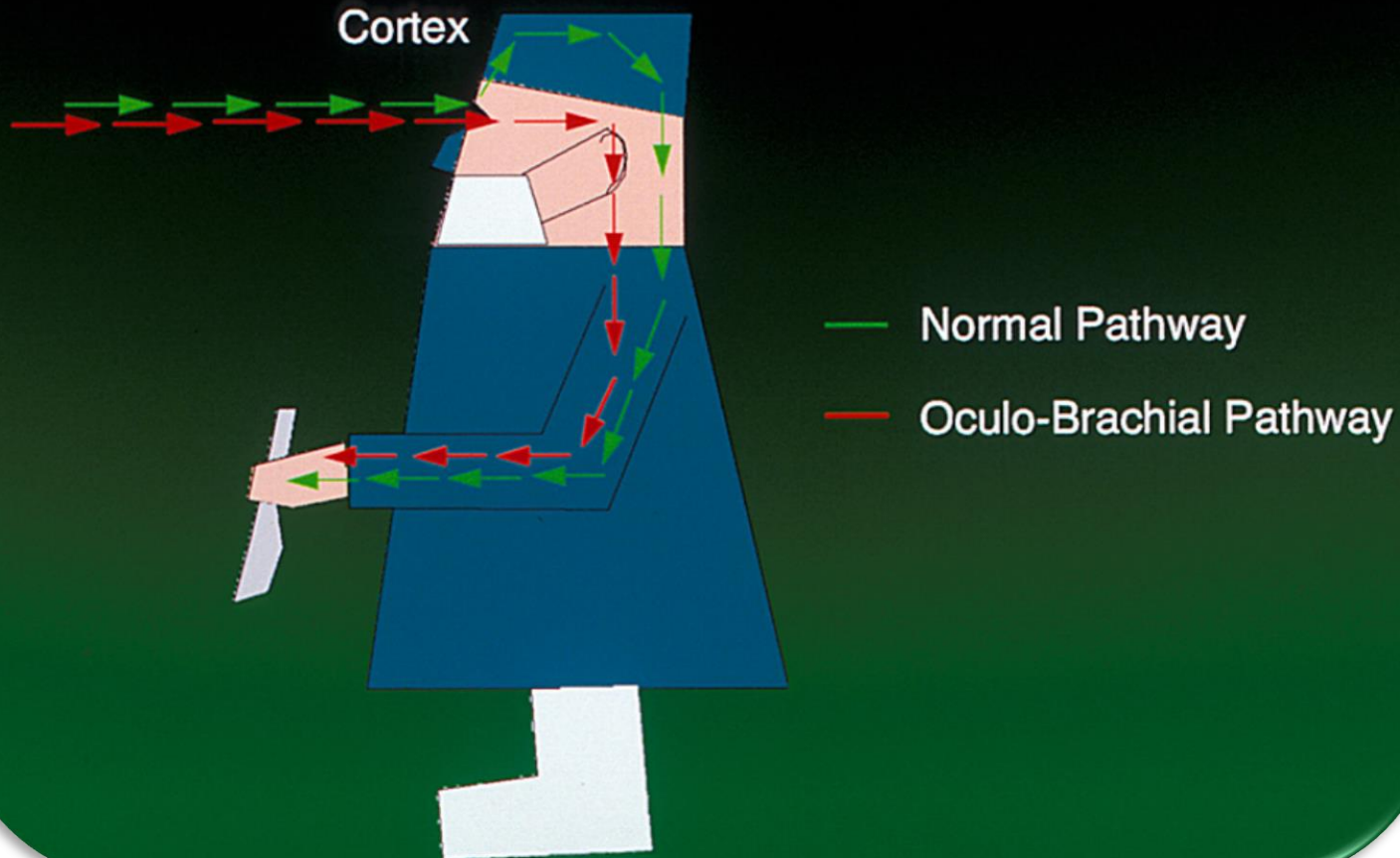


Source: Royal Orthopaedic Hospital: unpublished data 2005.

Problems of inappropriate diagnosis and intervention

“The Oculo-Brachial Reflex”

A new pathway with no discernable cortical connections



Pathology: Discrepancies Sarcoma Diagnosis

Year	Author	Country	Number	Diagnosis	Grade
1978	Baker et al	USA	130	32	-
1984	Tetu et al	Canada	260	35	-
1986	Presant et al	US SECSG	216	28	24
1986	Coindre et al	FR Panel	25	30	25
1989	Alvegaard et al	SSG	240	25	40
1989	Shiraki et al	US ECOG	488	26	-
1991	Harris et al	UK	376	24	-
1995	Prescott et al	UK	17	29	-
1999	Meis-Kindblom et al	SSG	1000	20	25
2004	Randall et al	US	104	37	25
2004	Van Dalen et al	NE rpl	143	24	36
2009	Thway et al	UK	349	22	23
2010	Lurkin et al	France	366	25	19
2012	Ray-Coquard et al	France/ Italy	1463	44	-
2014	Thway et al	UK	348	28	11

IOG specifies need for all sarcoma patients to be referred to a specialist MDT

- *The MDT needs to comprise all diagnostic and treatment disciplines*
- Suspicious masses on cross-sectional imaging
 - Referred for biopsy at specialist centre
- Optimal diagnostic procedure
 - Core needle biopsy
 - Image-guided if necessary
- All suspected sarcoma histology reviewed by a
 - Sarcoma specialist pathologist

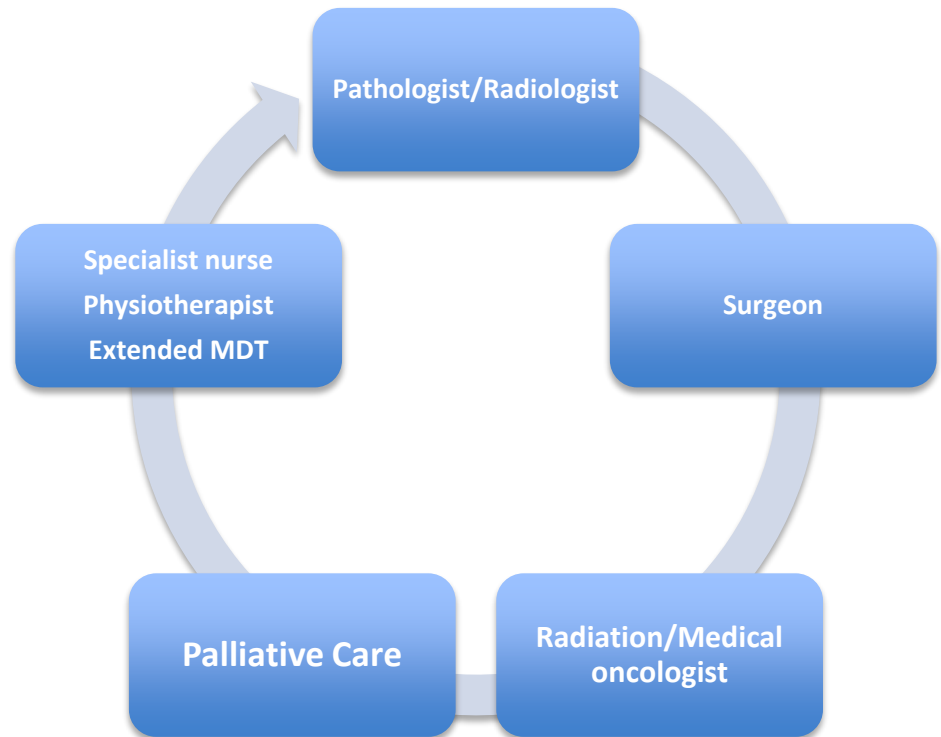
Surgery: Impact of Referral to Specialist Centers

- Canadian study
 - Limb STS patients referred to centre within 3 months of diagnosis
 - Had improved OS and reduced risk amputation
- Swedish study
 - Limb/ trunk STS patients referred to specialist centre before surgery had
 - Improved DSS but not OS
- Five studies
 - 1 UK, 1 France and 3 Sweden compared surgical margins
 - 4 found adequate margins more likely for patients treated at specialist centres
- Consistent evidence of reduced risk of local recurrence at specialist centres



NICE IOG: *Key recommendations*

- **Surgery**
 - Sarcoma surgery performed by appropriately skilled surgeons
 - Via sarcoma MDT or specialist MDT in consultation
 - **Defined treatment centre volumes:**
 - ≥ 100 new cases of soft tissue sarcoma/year
 - 25 RPS
 - 55-60 primary/year RMH



Networks

- NETSARC:
- Impressive organisational structure
- Importance MDT discussion prior to first surgery¹
 - Pre-operative imaging + biopsy
 - Local recurrence free survival
- Multi institutional Tumour Boards²:
 - Collaboration
 - Shared care
 - Rare cancers
 - UK Ewing Tumour Board
- Low/ middle income countries:
 - Logistical hurdles
 - Specialist surgical/ radiation expertise
 - Cost of novel systemic therapies
 - Available resources

¹Blay JY et al. Ann Oncol 28; 2852-2859: 2017

²Attia S et al. CTOS 2015

European Reference Networks (ERNs)

- EU directive: 2011/24
- Tackle rare diseases requiring specialist care
- Reference centres:
 - Knowledge/ research hubs for other EU countries
- Rights of EU patients to cross-border healthcare
- Ensure availability treatment facilities

Value of Guidelines

- Guidelines cover referral pathways, diagnosis and management
 - Early referral
 - The larger the tumour the worse the outcome
 - Accurate diagnosis
 - Surgery
 - Radiation
 - Chemotherapy
 - Follow-up

Radiation

- Adjuvant radiotherapy (RT) reduces
 - Local recurrence in limb/ limb girdle soft tissue sarcomas
- High doses required
 - Typically 60-66 Gy
- IMRT may reduce long term morbidity
- Special techniques required for difficult sites
- Pre-operative RT may be advantageous at certain sites
 - Planned close margins
 - Retroperitoneal sarcomas
 - Myxoid liposarcoma

Yang J, Chang A, et al. J Clin Oncol 16;197: 1998
O'Sullivan B, et al. Lancet 359; 2235: 2002

Systemic therapy

- Role in the neoadjuvant/ adjuvant setting
- Importance of clinical trials
- Palliation of advanced/ metastatic disease
- Part of multi-disciplinary discussion

Importance of Phase I trials

- Sarcoma patients
 - About 1% adult cancers
 - About 10% of patients enrolled in Phase I trials
- Reflecting limited number therapeutic options
- Outcome sarcoma patients similar to general Phase I population
 - OS (median 7.6 months [95%CI, 4.8–10.4])
 - 90-day mortality: 30/ 178 (17%)
 - PFS (median 2.1 months [95%CI, 1.7–2.5])
- Response rate
 - Lower than general Phase I population

Multi Disciplinary Care

- Key Worker
 - Single point of contact
 - Liaison with primary care/ patient groups
- Physiotherapy
- Pharmacy/ nursing staff
 - Ifosfamide
 - Methotrexate
- AYA Services
- Survivorship

Surgery for Metastatic Disease

- Studies from 1970s onwards
- Selection bias
 - Disease biology
- Small numbers
- Short follow-up
- Few data on
 - Lung function
 - Quality of life
- Role in multi-disciplinary management

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

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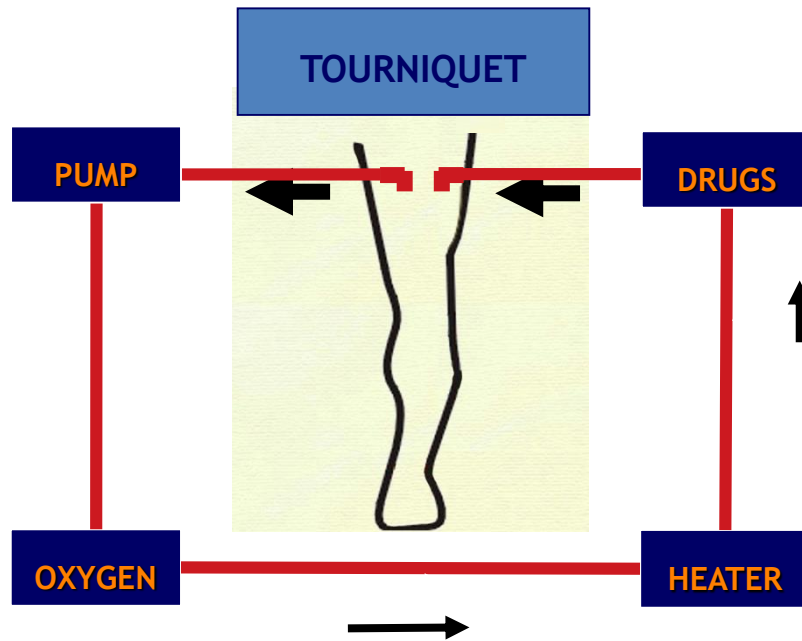
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Accepted 21 December 2009

Available online 8 January 2010

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- Effective in lung metastases
 - Importance of multi-disciplinary care

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 Reponse

- Irresectable extremity angiosarcoma



Angiosarcoma
Pre ILP

3 years
Post ILP

5 years
Post ILP

Sarcoma Treatment in UK

- Centralization of care
- Resources
 - Benign soft tissue masses: sarcomas = 100:1
- Publically funded system
 - Rationing
 - High cost drugs: availability
 - Specialist services
- Clinical trials

Differences in Healthcare

- USA
- Insurance companies
 - Complexity
- Geography
 - Vast areas
- Physician autonomy
- Referral base
- UK
- Government funded
 - Free at point of service
- Geography
 - Small distances
- Standardization
- Centralized referral



"Let me put it this way. If this were America you couldn't afford to be as ill as you are."



Conclusions

- Centralization
 - Improve patient care
 - Research
- Collaboration

Thank you – any questions?



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