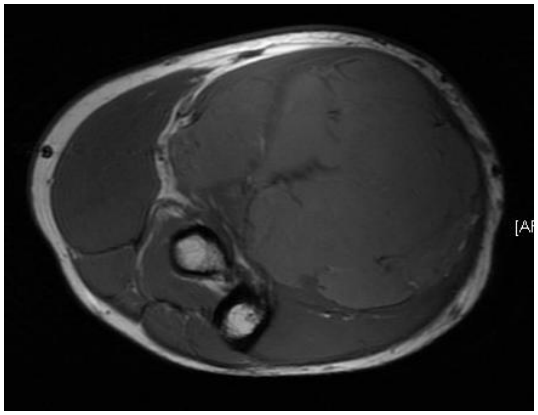
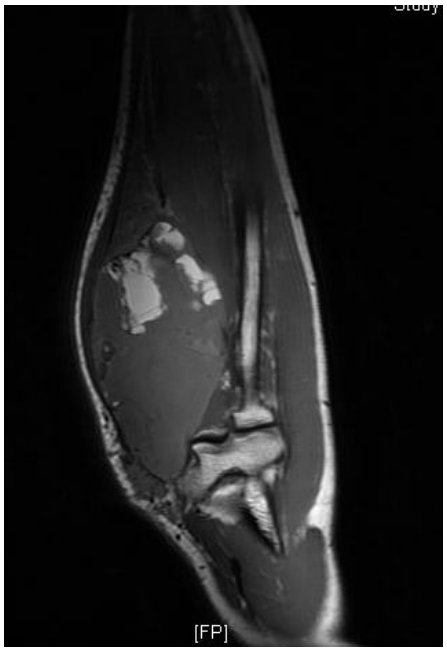
What’s new in bone and soft tissue sarcoma Treatment and Guidelines 2012?

Rob Grimer

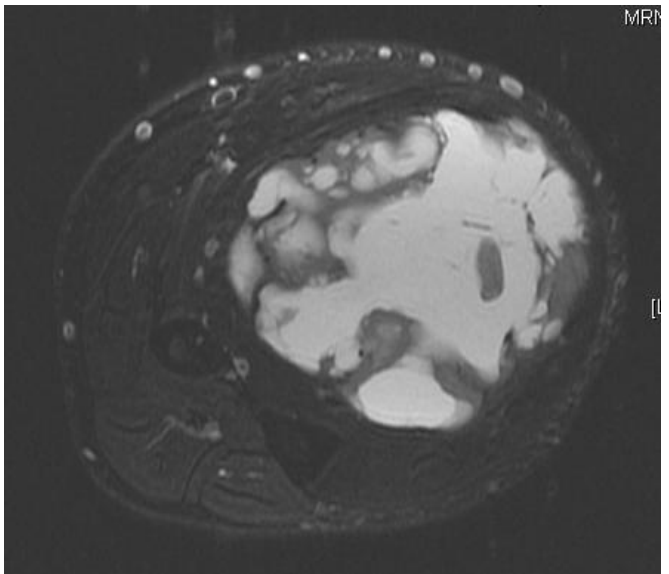
- ESMO conference 2012
- Top Oncologists in world (~ 400)
- Lots of sarcoma basic science – key messages:
  - 40% of STS diagnoses altered by second opinion (8% with Rx consequences)
  - Neoadjuvant chemotherapy gaining popularity for big (>10cm) tumours
  - Lots of new agents targeted at specific disease types

Neoadjuvant Rx - CT

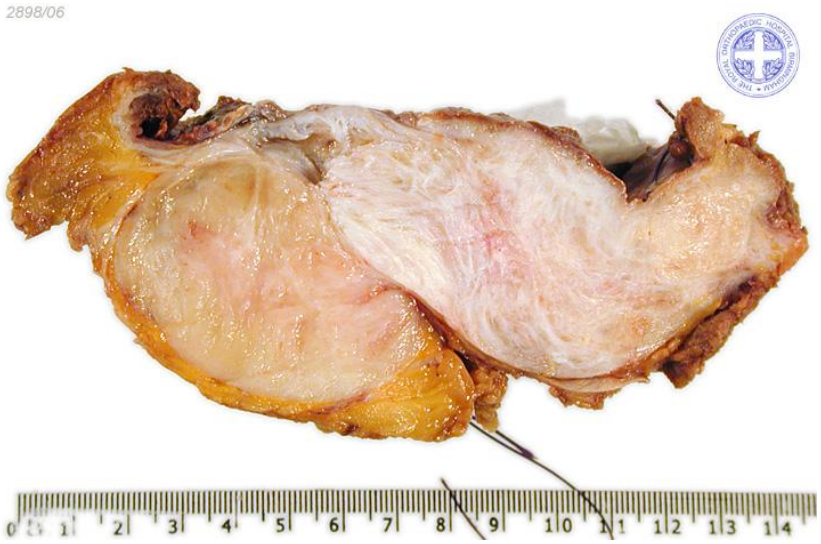


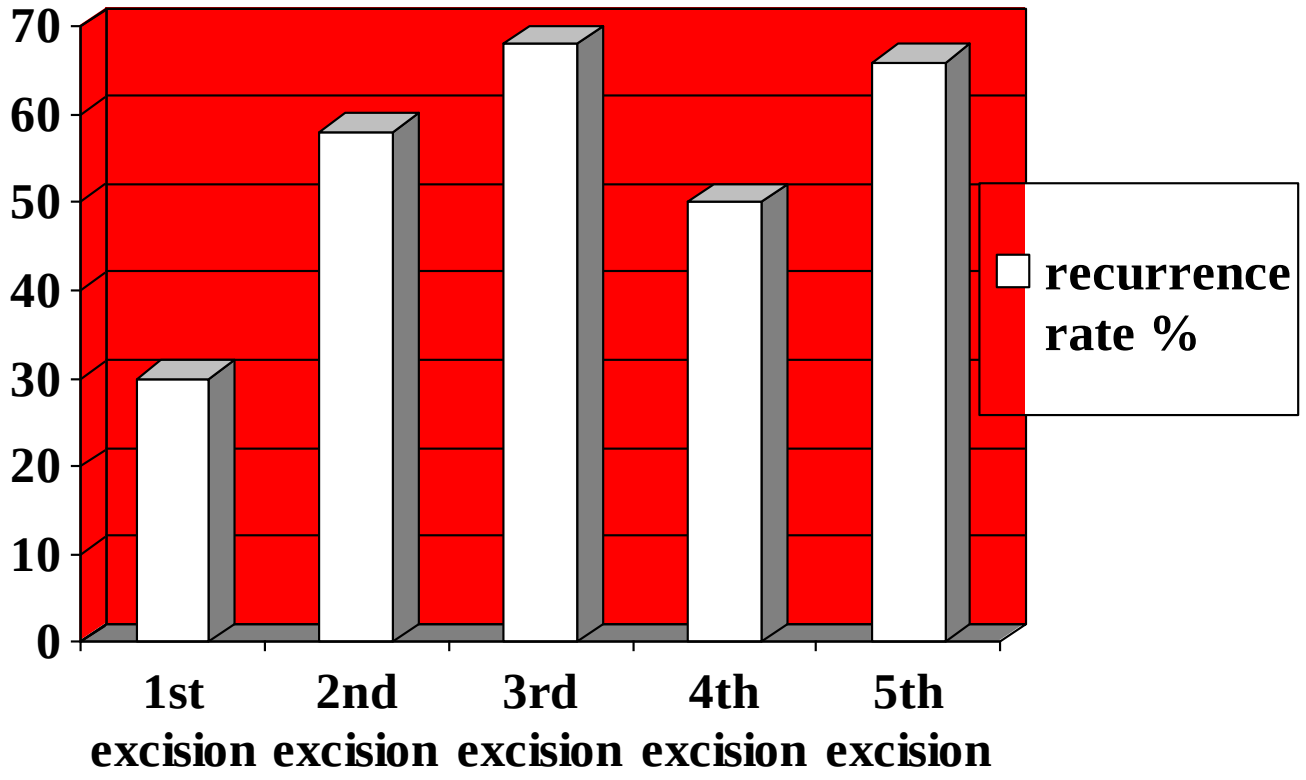


- To improve resectability of ‘difficult’ STS
- Start with Adria/Ifos
- PET after one cycles useful in assessing response (>35% decrease in FDG uptake)
  - Benz 2009
- If NO response move to R/T



Fibromatosis - the recurring nightmare !





- Fibromatosis is now a medical problem not surgical
  - Observation for many
  - Sequential NSAID, Hormones, Chemo eg Caelyx, MTX + Vinblastine, R/T
  - Surgery for symptoms
  - Age, size and site predict aggressiveness as does expression of Beta Cateinin

Advanced disease (mets)

- Loads of trials of chemotherapy for advanced STS
- Mostly rather dismal outcomes
- Median survival 12 months
- 8% alive at 5 years
- First line Rx = Doxorubicin +/- Ifosfamide
- Second line = Trial (standard of care)

Diagnosis and classification

- New WHO textbook out later this year
- Precise nomenclature awaited

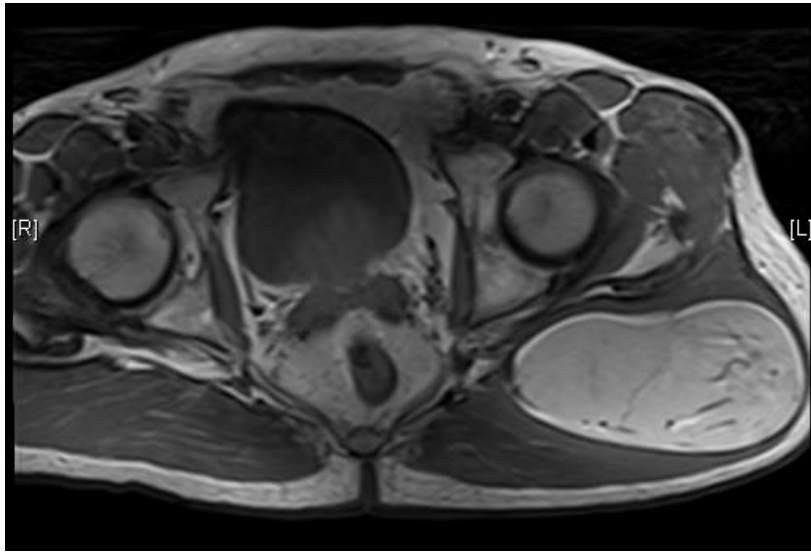
- UPS is the new ‘diagnosis’

= Undifferentiated Pleomorphic Sarcoma

ie all those things previously called Sarcoma NOS, spindle cell sarcoma, MFH etc

Will liposarcomas be resolved?

- At the moment all Atypical Lipomatous Tumours have a ICD -0 code 8851/3
- aka Well Differentiated Liposarcoma
- Therefore they are malignant
- Need to hit targets
- GP told they have cancer
- Patient told they have Ca
- But
  - Outside abdo they never kill
  - 1% will dedifferentate



Staging

- General acceptance that it is needed
- Agreement that although not perfect the AJCC system should be used
- Latest version 7

Staging with AJCC v7 (2011)

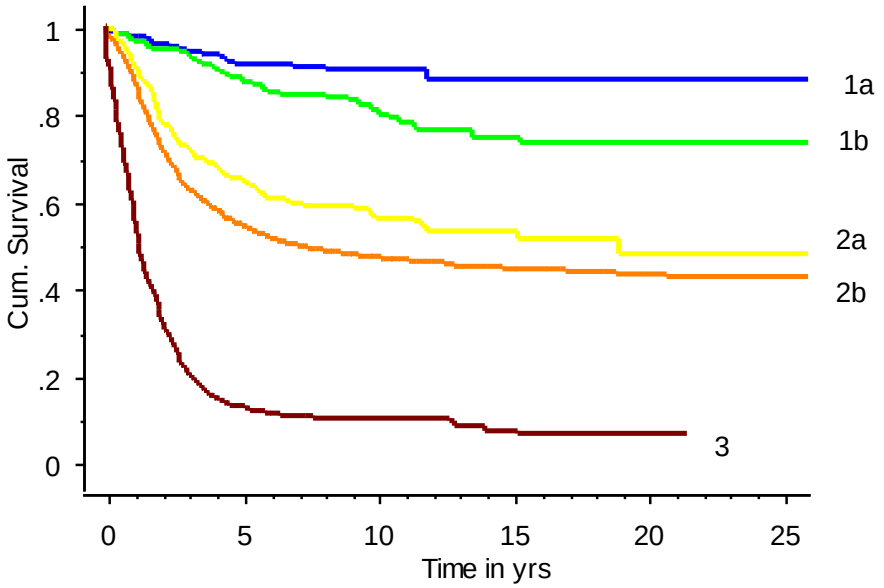
		Bone			STS	
	Size	Grade		Size	Grade	Depth
1A	≤ 8	G1		≤ 5	G1	s/d
1B	>8	G1		>5	G1	s/d
2A	≤ 8	G2		≤ 5	G2-3	s/d
2B	>8	G2		>5	G2	s/d
3	skip	any		>5	G3 Any N1	s/d
4	mets	any		mets		

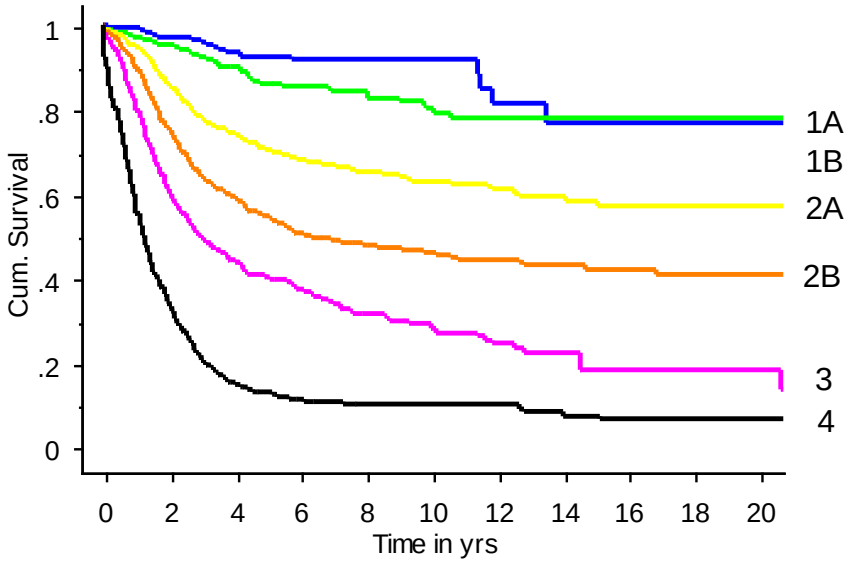
Enneking system

- **Enneking** staging was introduced by Bill Enneking in 1980 as a system to stage musculoskeletal sarcomas.* It has stood the test of time and has been well validated. It is simple to use.
  - 1a = low grade, intracompartmental
  - 1b = low grade, extracompartmental
  - 2a = high grade, intracompartmental
  - 2b = high grade, extracompartmental
  - 3 = any stage with metastases at presentation

*** Enneking WF, Spanier SS, Goodman MA. A system for the surgical staging of musculoskeletal sarcoma.** Clin Orthop Relat Res. 1980 Nov-Dec;(153):106-20.

Enneking vs AJCC v7
All tumours





Enneking gives a nice spread and identifies a very good group – but AJCC identifies a very poor group!

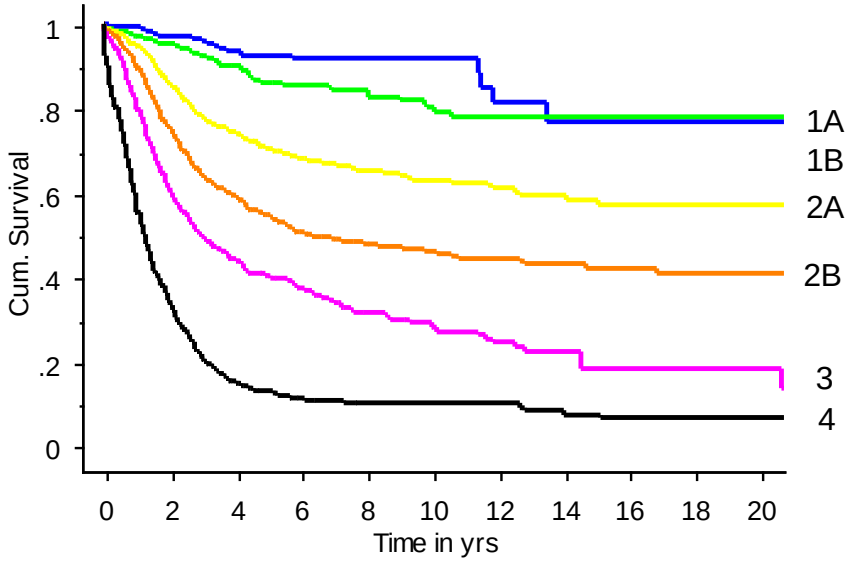
What are the main prognostic factors for sarcomas ?

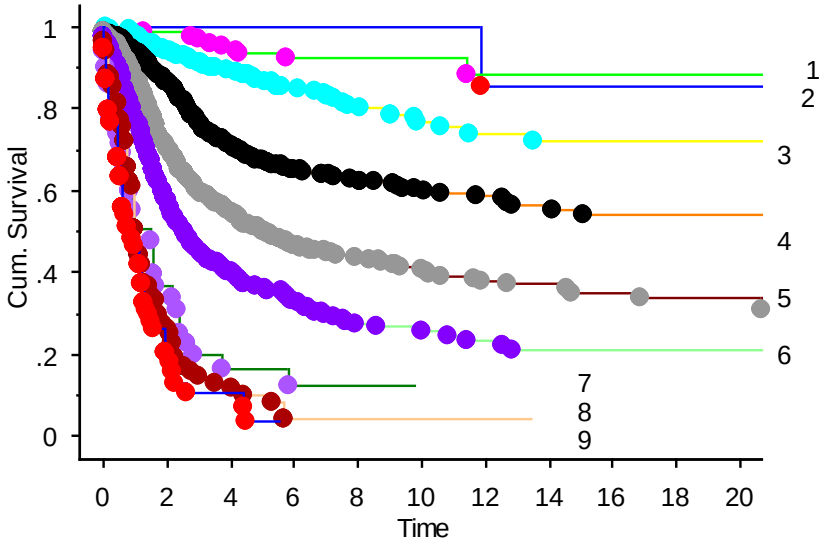
- Mets at diagnosis p <0.0001 HR 4.2
- Grade
  - High p <0.0001 HR 5.0
  - Intermediate p <0.0001 HR 3.5
- Age p <0.0001 HR 1.016
- Size p <0.0001 HR 1.05
- Depth p <0.0001 HR 1.96
- Compartment p =0.0002 HR 1.38

A simple scoring system?

- Grade
  - Low – 1
  - Intermediate – 2
  - High -3
- Size - big 1
- Depth (soft) – deep 1, sc 0
- Extra compartmental (bone) -1, intra 0
- Age > 50 -1, <50 - 0
- Mets at diag 3

AJCC v7 vs Numerical





The more factors you add in the more curves you can get….

MTPPE (Mepact) for OS

- The immune modulator muramyl tripeptide added to postoperative chemotherapy was associated with a statistically significant advantage in overall survival and a non-significant trend in event-free survival in one large randomized trial. Muramyl tripeptide has been approved in Europe for patients under 30 years of age with completely resected localized osteosarcoma.
- There is no consensus in the sarcoma community on the use of this drug, because of weaknesses in the single trial available . Further studies are definitely needed to identify the subgroup of patients who could benefit.
- Whenever possible, patients with osteosarcoma should receive chemotherapy in the context of prospective trials, which is regarded as standard of care.
- Recently approved by NICE - Got through after price reduction to around £36,000 / QALY

Metastatic osteosarcoma

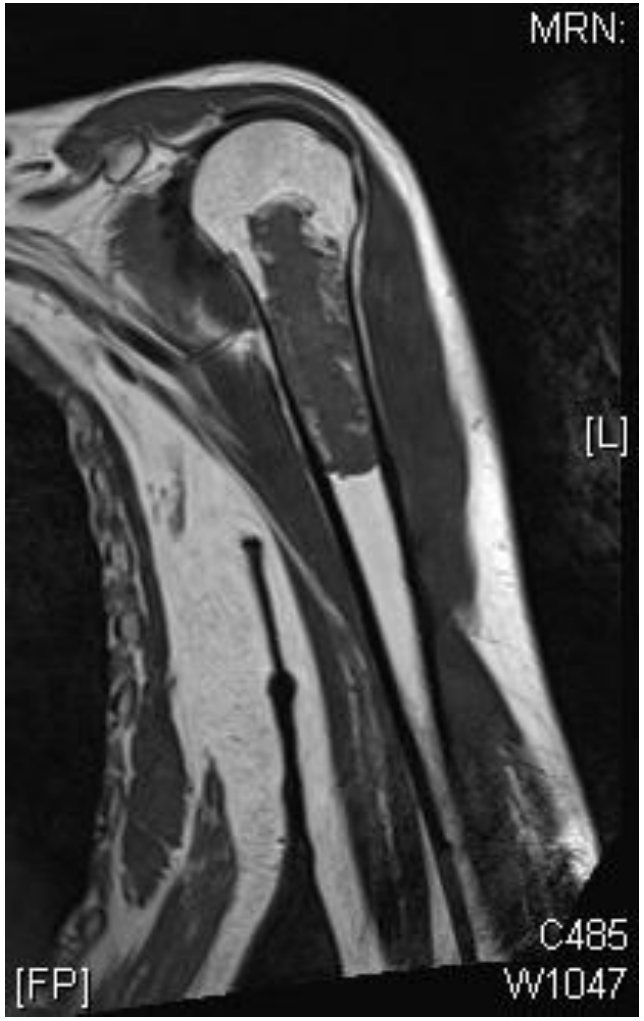
- Agree that optimum treatment is surgical excision
- Role for chemotherapy unclear if complete surgical resection
- Consider ifosfamide ± etoposide ± carboplatin

Ewings sarcoma

- Decisions by MDT
- Surgery when possible
- RT for poor response or involved margin ?all?

- Role of high dose therapy and BMT unclear
- New EWS trial being produced
- UK National EWS MDT now in action
- ALL new cases of EWS should be discussed there.

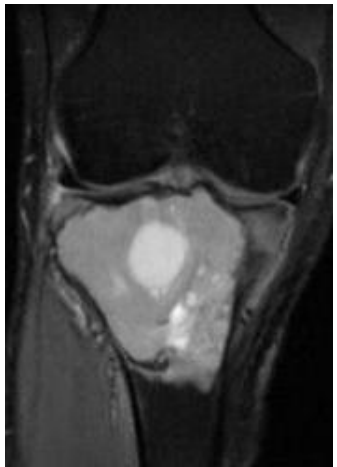
When is a chondroid lesion a chondrosarcoma?

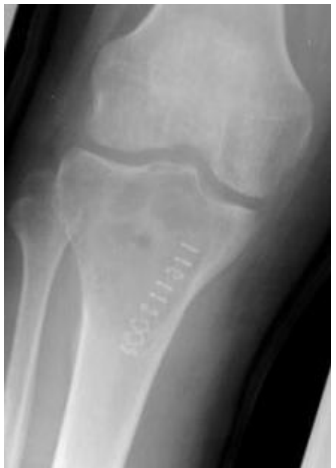


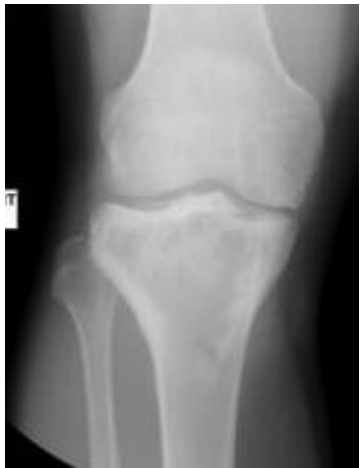
- Many chondroid lesions discovered incidentally
- Which are malignant?
- Is observation safe?
- Histology NOT helpful
- Pelvis – always malignant
- Worrying features:
  - Pain
  - Cortical erosion
  - Hot on BS
  - Dynamic MRI
    - Parlier-Cuau C, 2011

Giant cell tumour of bone

- Aggressive borderline tumour
- Hi rates of recurrence with curettage
- Impressive results with Denosumab
- Not yet licensed
- Results this summer
- Currently available at ROH (trial basis)







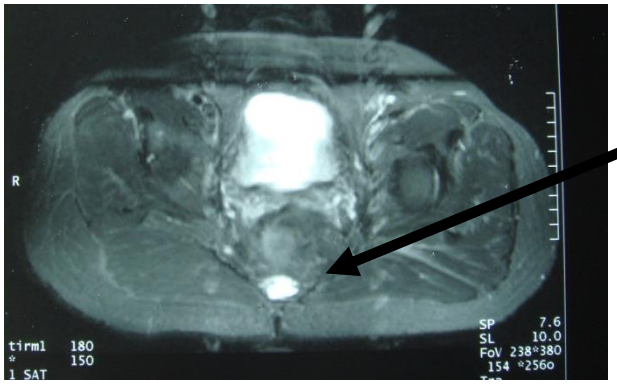
GCT Prox tibia – curetted but early OA at 5 yrs.

PVNS now known as Diffuse Tenosynovial Giant Cell Tumour

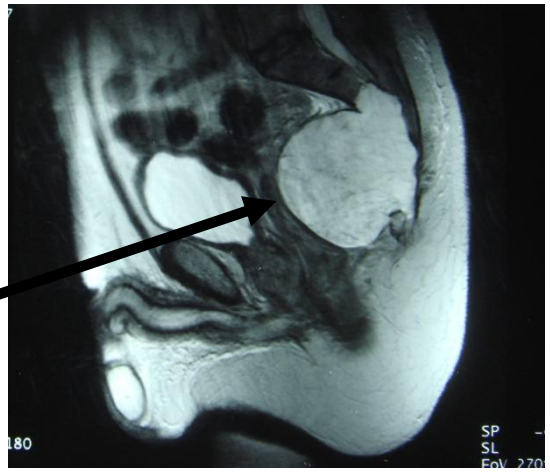
- Localised type easy to control – excise
- Diffuse type much more difficult
- Options:
  - Surgery
  - Yttrium
  - R/T
  - Imatinib – good response
  - Monitor with PET

Chordoma – 20/yr

- Traditional treatment – surgery
- 50% recur no matter what margin, 37% mets
- Average survival 10 yrs
- Conventional RT – limited, if any, role
- Increasing evidence of role of Protons or Carbon Ion Therapy



Staging MRI in 1999 for Ca prostate showed abnormal mass in sacrum. Noted but ignored. Back pain in 2003 led to new MRI = 9cm tumour.



Proton results

- MGH: 29 spine/sacrum chordomas
  - Post-op IMRT and protons, 72 – 77.4Gy
  - 23/23 primary chordomas controlled
  - 3/6 recurrent chordomas controlled

DeLaney et al, Red J, 2009;74:732-739

- PSI, Switzerland: 40 spine/sacrum chordomas (47% R2 resection)
  - Protons 72.5 (59.4 – 75.2) Gy
  - 19/19 no SS controlled, 100% LC at 5 years
  - 12/21 SS failed, 30% LC at 5 years

Staab et al, Red J, 2011;81:e489-496

Carbon ions

- 4 centres world-wide
- Chiba Cancer Centre, Japan:
  - 95 patients unresectable sacral chordoma
  - 1996 – 2007
  - 84 patients primary presentation, 11 patients recurrent after primary resection
  - Dose 70.4 (52.8 – 73.7) GyE

Imai et al, Br J Radiol, 2011; Mar 22 (Epub)

Carbon ions

- 5 year overall survival 86%
- 5 year local control rate 88% *(awesome!)*
- 2 pts severe skin toxicity, 15 pts sciatic nerve damage
- ‘possibly the best charged particle therapy’

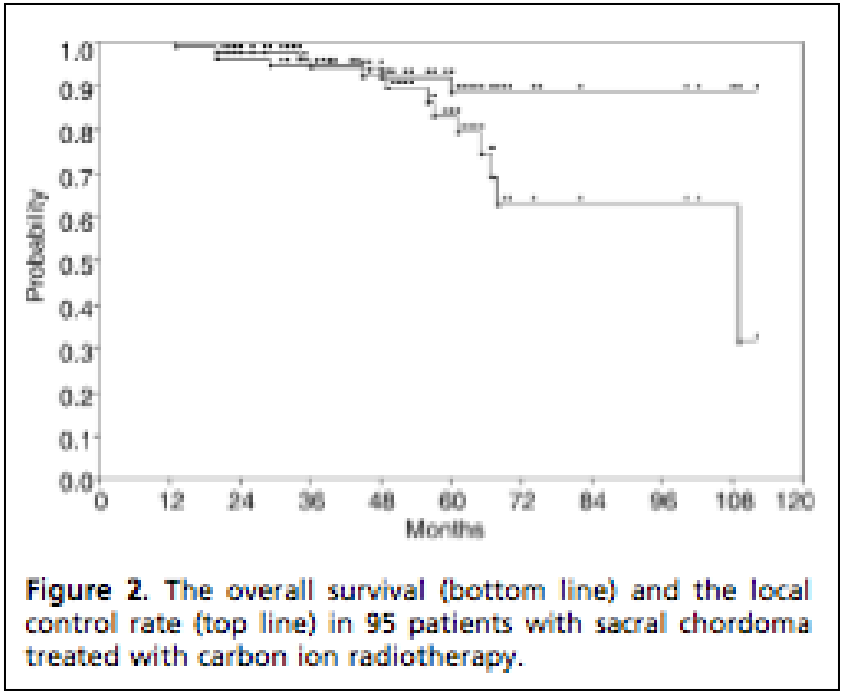


Figure 2. The overall survival (bottom line) and the local control rate (top line) in 95 patients with sacral chordoma treated with carbon ion radiotherapy.

Imai et al, Br J Radiol, 2011; Mar 22 (Epub)

Chordomas – refer to experts!

- Local control is still everything!
  - Early diagnosis
  - Wide excision in experienced centre
  - Adjuvant dose-escalated radiotherapy – IMRT, protons, carbon ions
- Inoperable/metastatic disease:
  - Dose-escalated radiotherapy (heavy particle RT if possible)
  - Targeted therapies – helpful, but only short term benefit….

Conclusion

- Sarcoma care is becoming much more personalized
- Sarcoma centres MUST be up to date with latest therapies
- If in doubt – refer on
- BSG website will be identifying centres with special expertise