The Royal Orthopaedic Hospital NHS
NHS Trust

Ewing's sarcoma Local Recurrence - Predictable or preventable?

Royal Orthopaedic Hospital, Birmingham

Chandrasekar CR
Simon Carter
Roger Tillman
Robert Grimer
Seggy Abudu
Jeys LM

THE ROYAL ORTHOPAEDIC HOSPITAL BIRMINGHAM

Ewing's sarcoma Local Recurrence - Background

- The outcome for patients with Ewing's sarcoma recurrence is poor <20% five years survival
- Local recurrences occur in 8%-25% of patients with Ewing's sarcoma
- The aim of the study was to analyze the patients who had a local recurrence to identify factors predicting the local recurrence and if it could be prevented

Ewing's sarcoma
Treatment guidelines as specified in Euro-Ewing's 99 and EICESS 92 protocols

- Definitive surgery to follow 6 courses of chemotherapy.
- In all cases complete surgical removal is desirable [wide/radical margin].
- Surgery should be combined with adjuvant radiotherapy in case of insufficient margins and/or poor histological response [>10%viable tumour cells in the Resection specimen]

Ewing's sarcoma Local Recurrence - Predictable or preventable?

- **A retrospective analysis of 650 patients who had a diagnosis of Ewing's sarcoma treated between 1975 and 2009 was performed and 64 patients (10%) who had a local recurrence were identified and analysed.**

Ewing's sarcoma Local Recurrence - Predictable or preventable?

- 37 male 27 female
- Age 5 - 67 years (31 under the age of 16)
- Fifteen patients had metastases at diagnosis
- Twenty patients had chemotherapy and radiotherapy only while 44 had chemotherapy and surgery +/- post op radiotherapy.
- Thirteen patients who were suitable for post –operative radiotherapy did not receive the treatment

Ewing's sarcoma Local Recurrence

Local recurrence 64/650 [10%]

Site					
	31/246	Axial	12%	33 /404	Appendicular 8%
	3/7	Spine	43%	3/11	radius 27%
	2/7	Ribs	29%	8/52	fibula 15%
	24/160	Pelvis	15%	7/82	tibia 9%
	2/16	Scapula	13%	8/140	femur 6%

2/3 Patients with LR had tumour volume > 200cc.

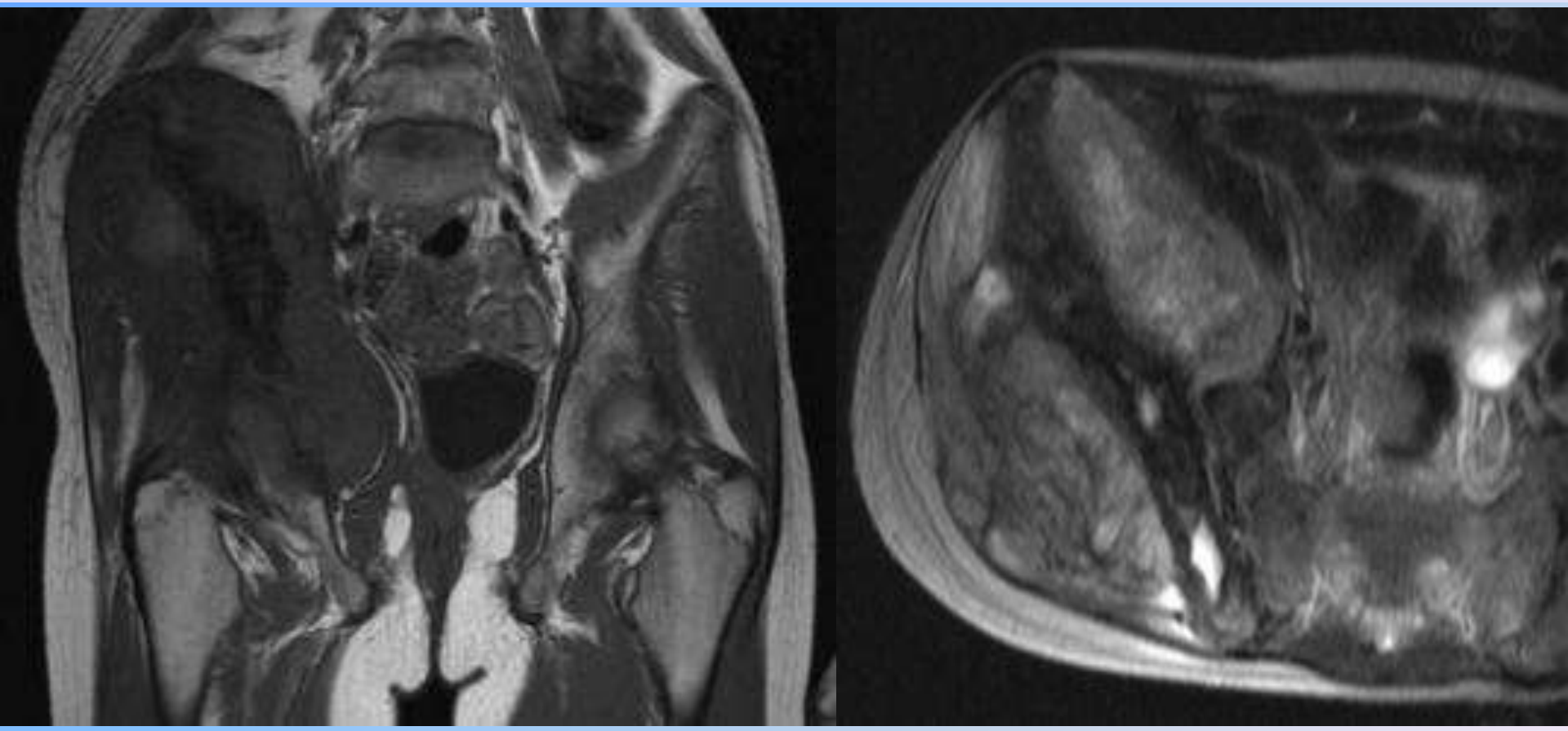
Time to LR Mean – 22months [3–175 months],

Median 17 months [83% < 2 yrs]

Ewing's sarcoma Local Recurrence - Predictable or preventable?

- **Surgical margins and LR**
- **23% of the patients who developed a LR had surgery with recorded wide margins - Limb salvage surgery with wide margins can still leave microscopic residual disease behind!**
- **7 patients who developed a LR had a wide margin and chemo necrosis > 90% [3 with 100% chemo necrosis]**
- **Is there a role for extending adjuvant radiotherapy for Limb salvage patients with wide margins and good response to chemotherapy??**

Pelvic Ewing's



Wide margin not possible and LSS with marginal margins can leave microscopic tumour. Wound problems delay adjuvant RT = High risk of local recurrence

Ewing's sarcoma Local Recurrence - Predictable or preventable?

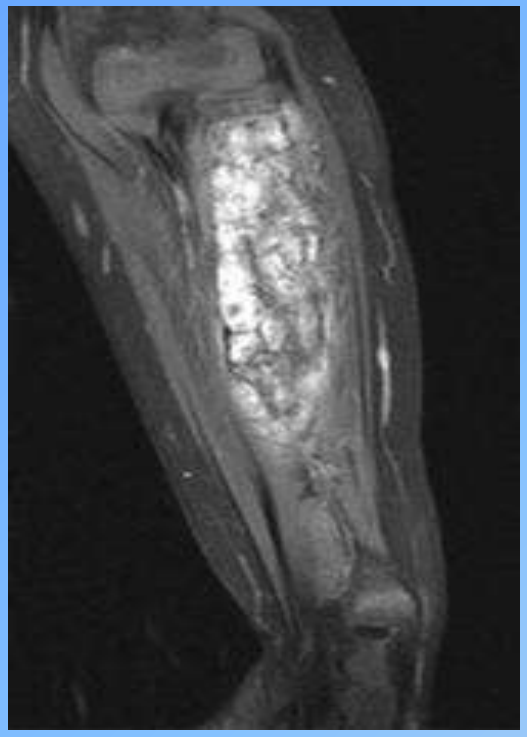
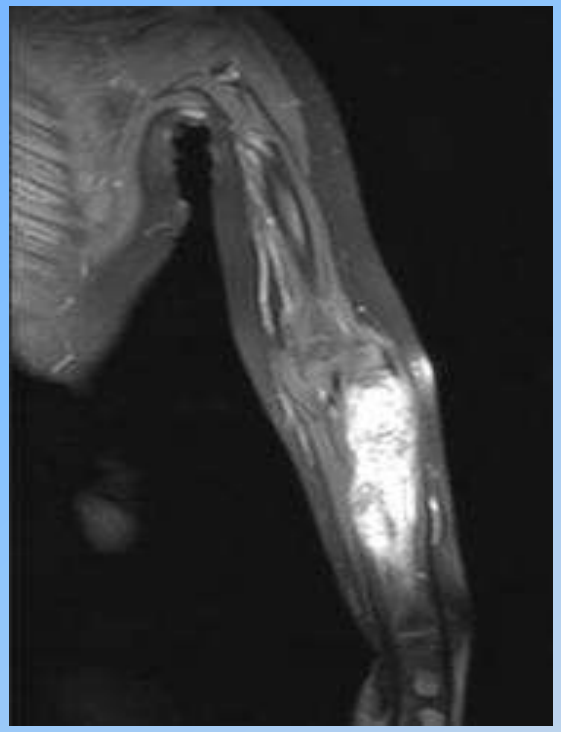
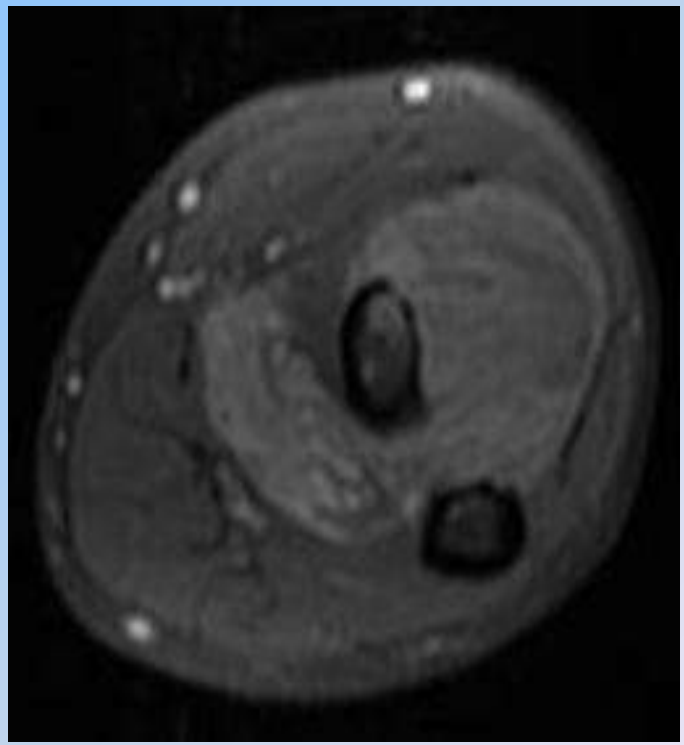
- **Chemo necrosis and local recurrence**
- **56% of patients who had a local recurrence had chemo necrosis >90%**
- **33% had chemo necrosis of 100%**
- **What is the reason for LR if there is 100% response?**

  Differential chemo response of residual micro/macroscopic tumour?

  Sampling problem at pathology?

  Failure to offer adjuvant RT due to good chemo response?

Ewing's Radius
Age - 3 yrs - LSS 75% Necrosis

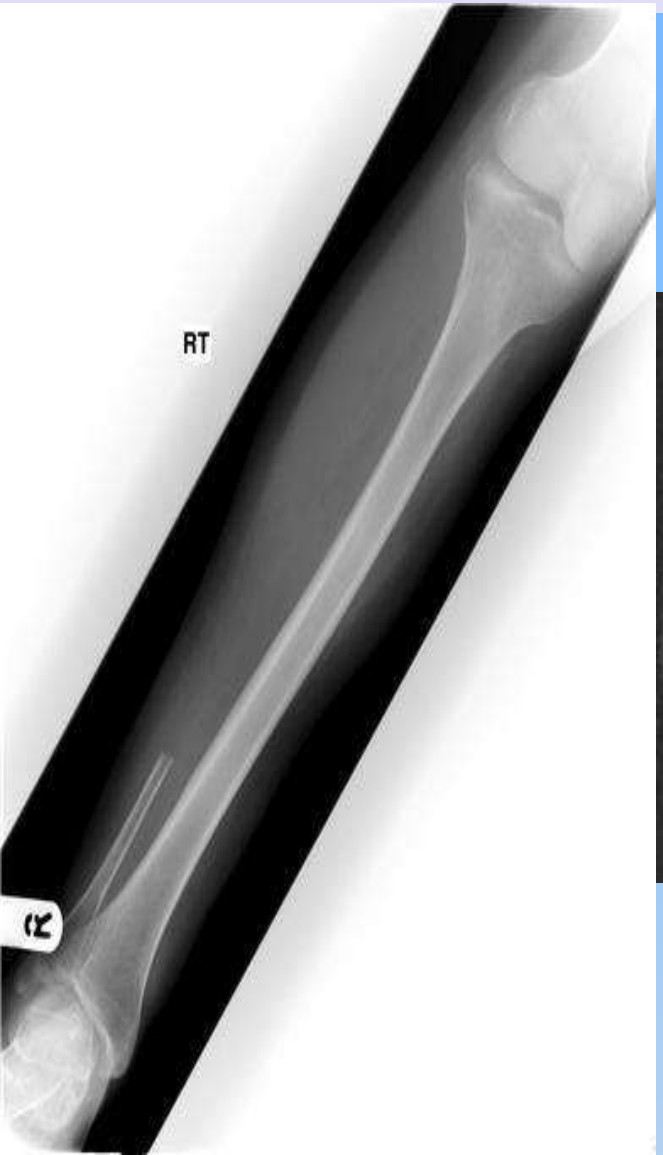




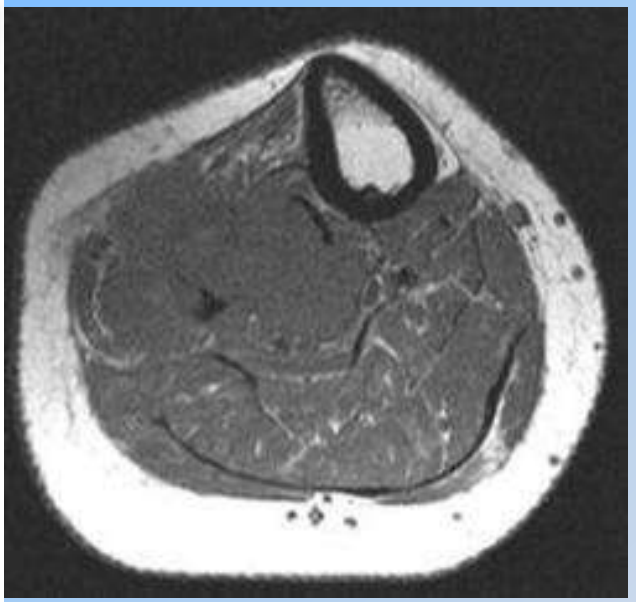
?Radical surgery for fibula/radial tumours if margins are doubtful

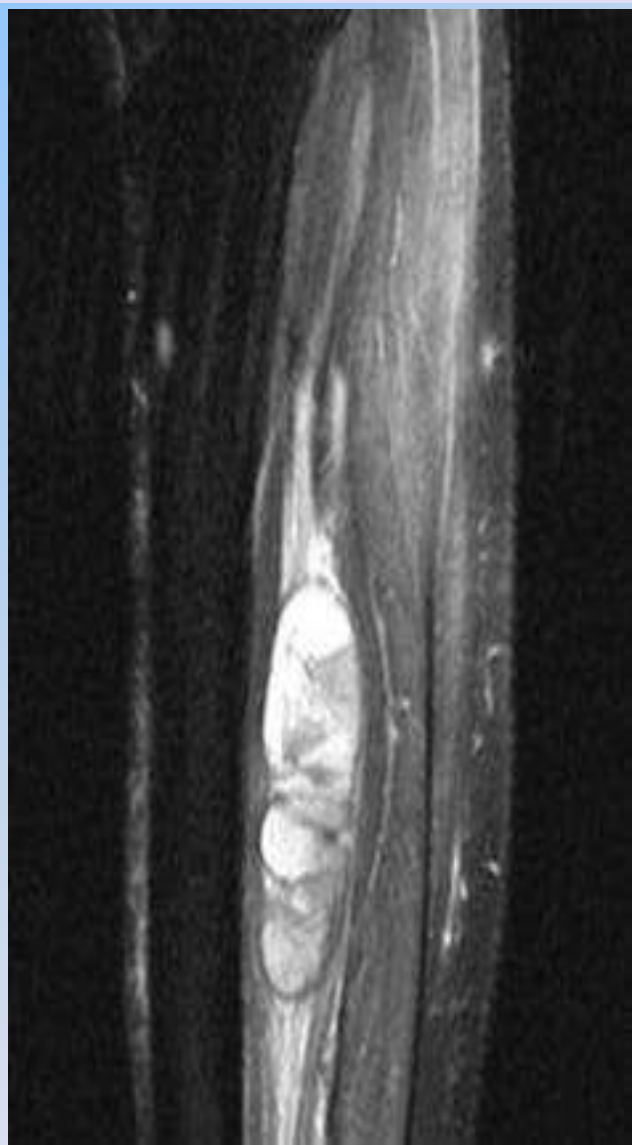
Ewing's sarcoma Local Recurrence - Predictable or preventable?

- **Radiotherapy should be applied if complete surgery is impossible, and should be discussed where histological response in the surgical specimen was poor (i.e. >10% viable tumour cells) [IV, C]. Radiotherapy is applied at doses of 40–45 Gray for microscopic residues and 50–60 Gray for macroscopic disease [III, B]. [ESMO Guideline]**
- **Post op radiation often not given though there was a clinical indication for 13 patients**
- **Biological reconstructions like fibular graft, ECR**
- **Risk of infection after use of endoprosthesis**
- **Risk of radiation induced malignancy in young children**
- **Wound problems and inability to have spacer protection for pelvic Ewing's sarcoma**

LR after limb salvage – Fibula 100% chemonecrosis!





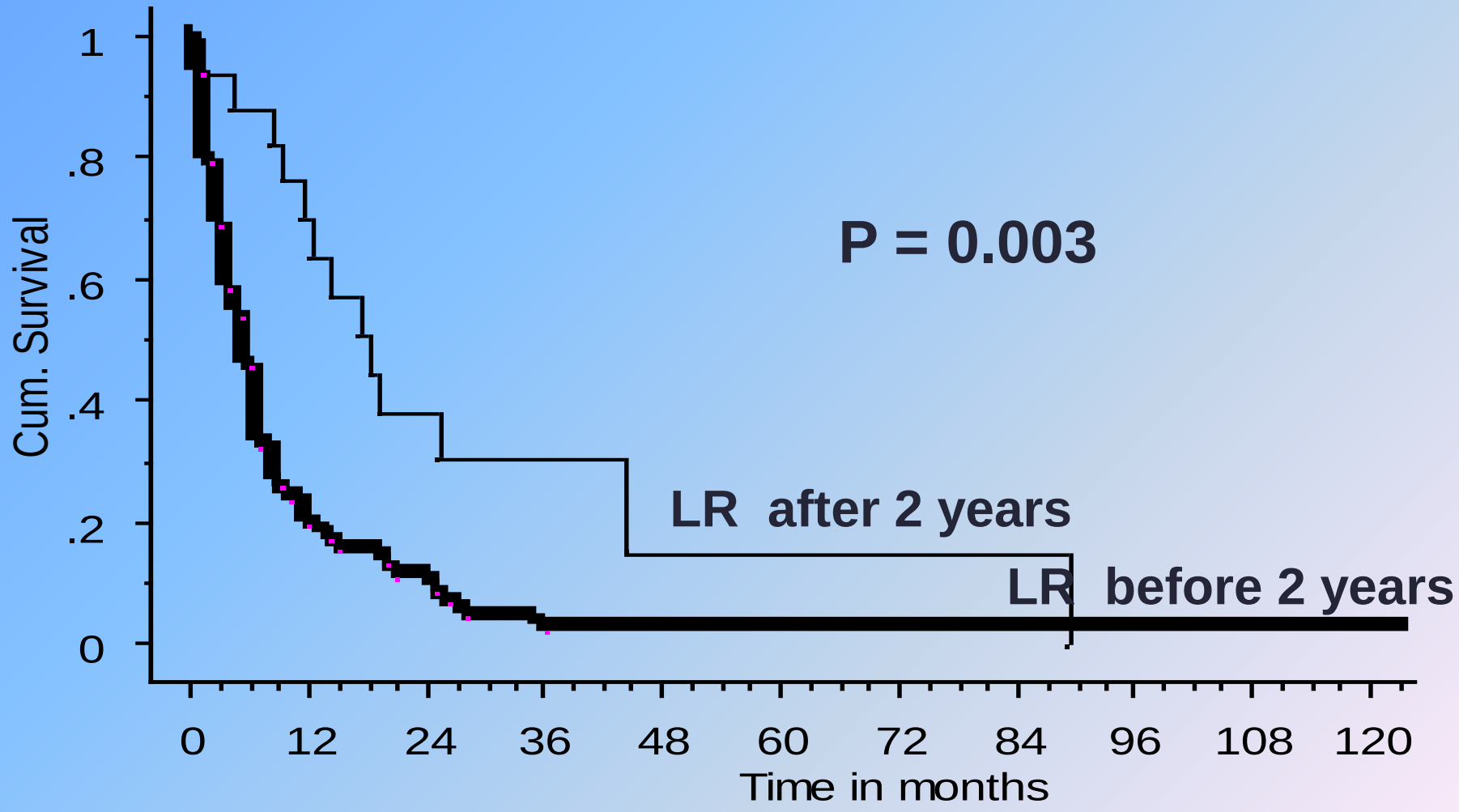


Ewing's sarcoma Local Recurrence - Predictable

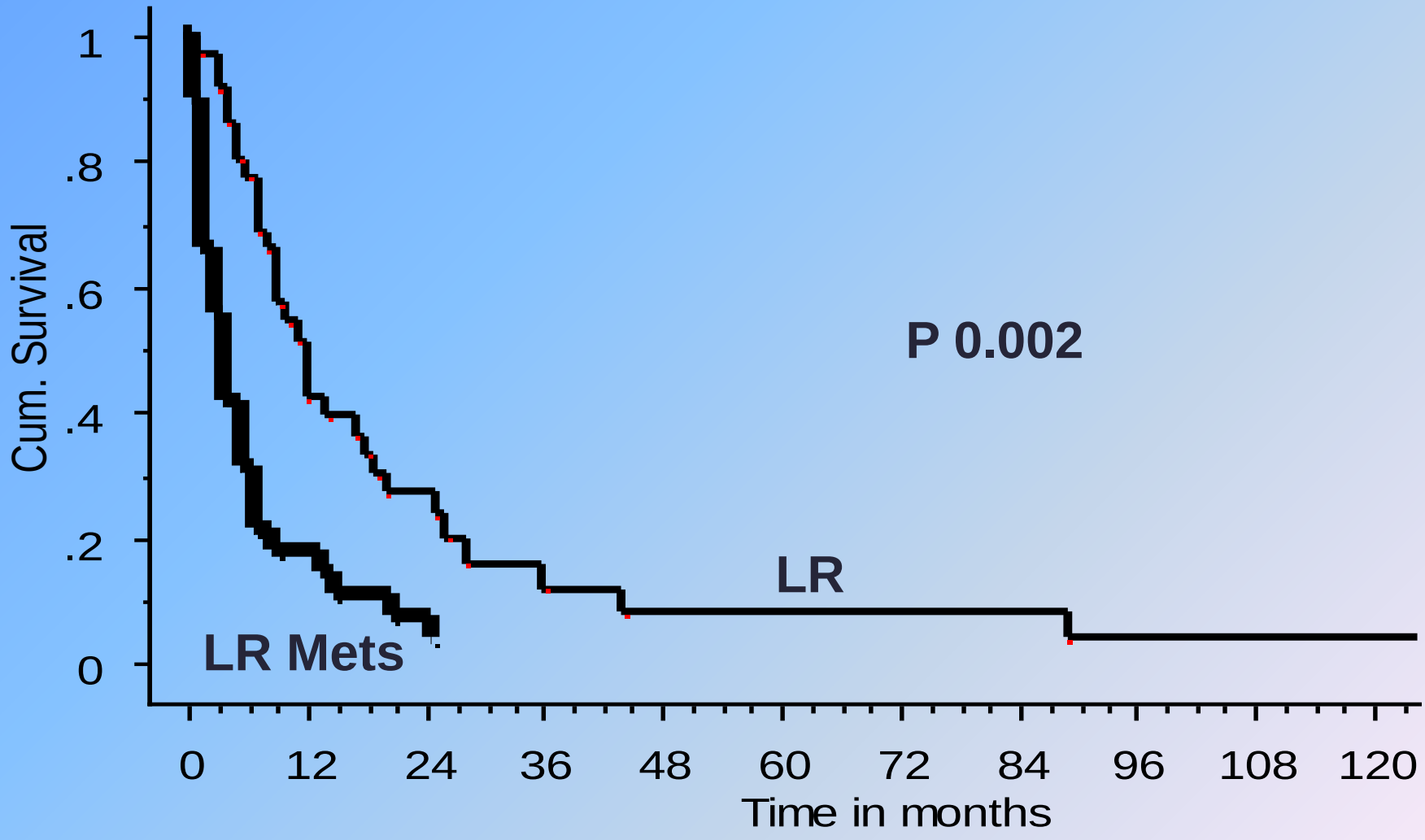
- The risk of local recurrence is higher if the tumour is located in the axial skeleton, fibula and radius, treatment with chemotherapy and radiotherapy alone [location and size of the tumour precluding surgery – three times more likely to develop a LR].
- One out of three patients who have good response to chemotherapy still went on to develop a LR.
- Post operative radiotherapy not given when there was an indication -The use of biological reconstruction and younger age group often resulted in deferral of post-operative radiotherapy.

Survival after LR

The estimated 5 years survival for the patients after LR was 15% [including 15 patients with metastases at diagnosis]



Survival after LR vs LR Mets



Ewing's sarcoma Local Recurrence - Predictable or preventable?

Problems

- Limb salvage surgery often results in close but clear margins and there is no way of identifying microscopic residual disease
- Biological reconstructions and post operative radiotherapy
- Ideal post treatment monitoring to detect early relapse – availability of resources and cost/benefit of routine PET-CT/, whole body MRI, High resolution chest CT instead of Chest X ray
- Role for repeat biopsy during chemotherapy and alter chemo protocol if there is poor chemo response in inoperable tumours

Ewing's sarcoma Local Recurrence - Predictable or preventable?

Problems

Non invasive growers = no MRI post op =? Late diagnosis of LR and poor planning of local surgery for LR – use PET CT

Inability of MRI/ Bone scan to differentiate early LR from scar tissue/infection

Ideal post treatment follow up for the first 2 years –

Who? Medical oncologist ? Orthopaedic Oncologist?

What tests ? Local clinical assessment+ chest x ray / whole body MRI/ PET CT

How often? 3monthly for 2 years?

Conclusions

- Tumour location, type of treatment offered can predict risk of local recurrence.
- > 90% chemo necrosis and wide margins don't eliminate LR - Role for adjuvant radiotherapy?
- ? Radical surgery for radius / fibular tumours if margins are close
- Most LR seen within 2 years – proactive imaging to detect early recurrence

James EWING

- Born on Christmas day 1866
- Was bed bound with osteomyelitis of femur for 2 years when he was14, won a microscope in a competition
- Studied in Boston and New York
- Appointed Prof. of pathology at Cornell university at the age of 33 and held the post for 33 years
- Described ‘endothelioma of bone’ in 1920
- Died from bladder cancer 1943