

# Radiotherapy Considerations in Extremity Sarcoma

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# Role of RT in STS

- Local tumour eradication while allowing successful limb preservation leading to good functional outcome with minimum toxicity
- How?
  - Reducing the risk of local recurrence by “extending” the surgical margin
- Expect 90% local control in conjunction with conservative surgery



# Evidence for RT

- Overall survival not compromised by WLE + RT vs. amputation

*Rosenberg et al Ann Surg, 1982*

- Local control better with WLE + BRT vs WLE for high grade tumours

*Pisters et al JCO, 1996*

- Local control better with WLE + EBRT vs. WLE regardless of grade

*Yang et al JCO, 1998*



*Ballo and Lee Curr Opin Oncol,  
2003*



Orientation and geometry of  
brachytherapy catheters  
influenced by the surgical incision  
and reconstruction

## Brachytherapy requires:

- Pre-procedure planning and coordination
- Experience in performing these procedures
- Multidisciplinary collaboration between radiation and surgical oncologists together with medical imaging



# BRT results

TABLE 3. Local control

Variable	n	5-y LC (%)	P value	95% CI
Size (cm)				
≤50	60	86	.3	76-96
>50	142	83		76-90
Depth				
Superficial	27	88	.5	77-99
Deep	175	83		77-89
Site				
Upper extremity	56	66	<.001	52-80
Lower extremity	146	91		86-96
Location				
Central	25	57	<.001	38-78
Noncentral	177	88		82-94
Margin				
Negative	165	86	.04	81-93
Positive	37	74		58-90

LC, local control; CI, confidence interval.

Cohort of extremity STS  
202 pts  
Adjuvant BRT

146 pts  
Lower extremity

56 pts  
Upper extremity

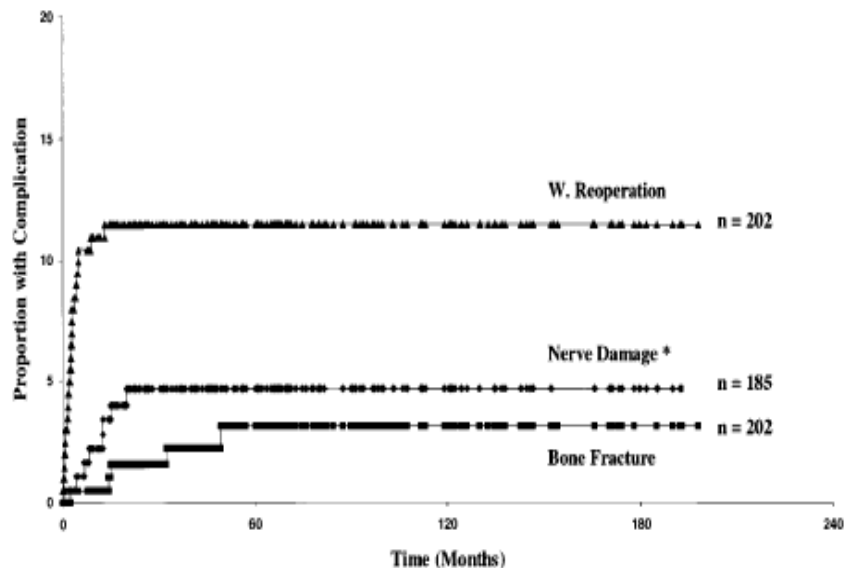
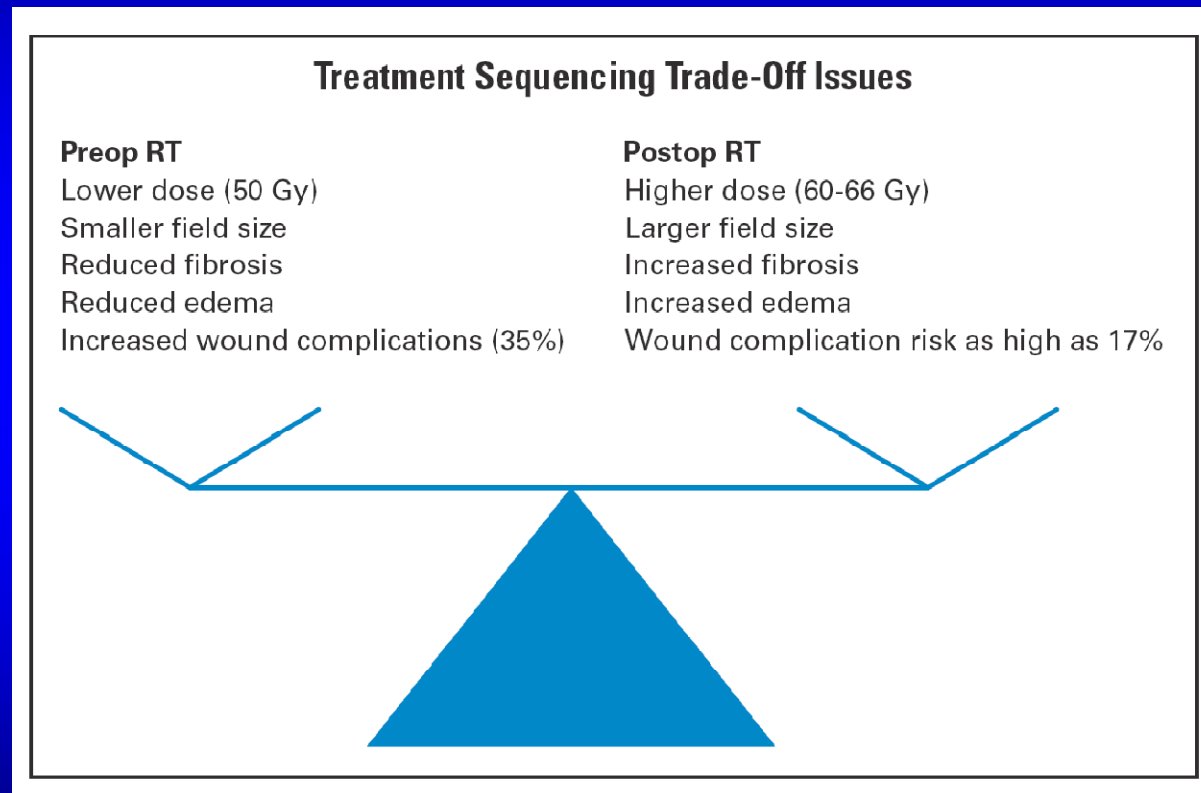


FIG. 5. Actuarial complications for primary high-grade sarcoma treated with brachytherapy. \*Only patients who did not have nerve resection were included.



# EBRT Timing

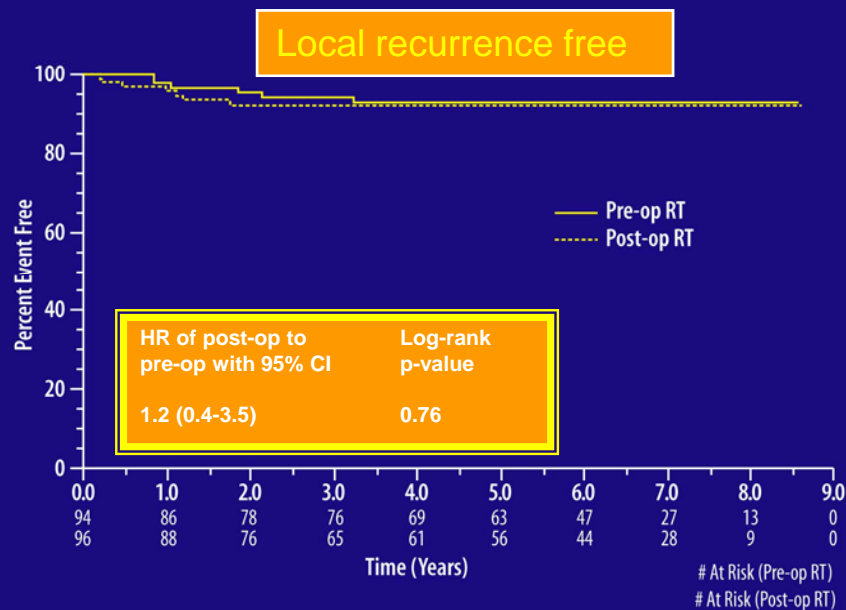


*Pisters, O'Sullivan and Maki et al JCO, 2007*



\*O'Sullivan et al Lancet, 2002

# NCIC 'SR2'



EXTREMITY STS  
180 Pts\*  
WLE

Postop RT  
92 Pts  
66 Gy

Preop RT  
88 Pts  
50 Gy

\*Designed to compare toxicity  
Volume 5cm/2cm longitudinal/radial margin to 50 Gy then 2cm margin to 66 Gy

Acute wound healing complications  
17% (postop) vs. 35% (preop),  
p=0.01 (seen more in lower extremity)

O'Sullivan et al ASCO, 2004



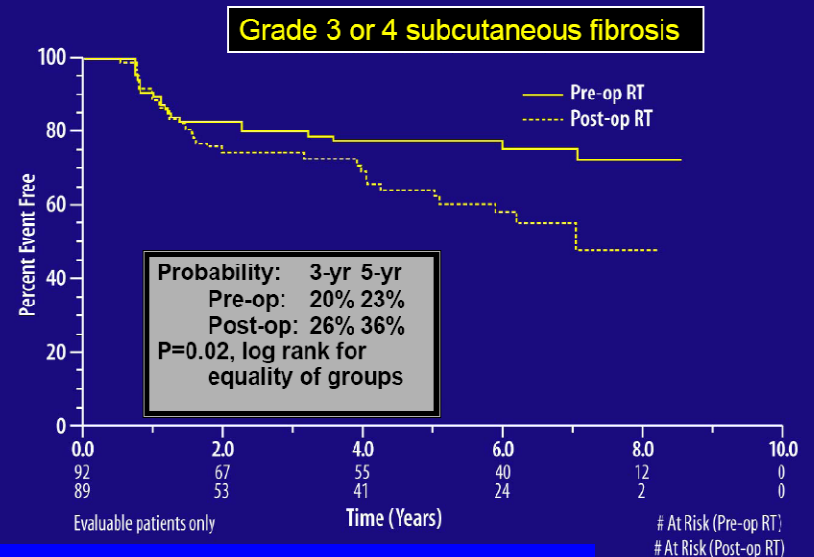
# Toxicity

- Disadvantage to pre-op RT in early stages ( 6 weeks) of recovery following limb preservation
- With time (1 year) scores are similar for both treatment groups:
  - TESS (physical disability),
  - MSTS (clinical measures) Davis et al JCO, 2002
  - SF-36 bodily pain

## 2-year Late Complications ( $\geq$ grade 2)

	Pre-op RT	Post-op RT	<i>p</i>
<b>Fibrosis</b>	31.5%	48.2%	0.07
<b>Stiffness</b>	17.8%	23.2%	0.51
<b>Edema</b>	15.1%	23.2%	0.26

Davis et al Radiother Oncol, 2005



O'Sullivan et al ASCO, 2004

Correlates with increasing field size and dose



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# FRACTURES FOLLOWING RADIOTHERAPY AND LIMB-SALVAGE SURGERY FOR LOWER EXTREMITY SOFT-TISSUE SARCOMAS

A COMPARISON OF HIGH-DOSE AND LOW-DOSE RADIOTHERAPY

364 lower extremity EBRT alone at PMH (1986-98)

Fracture rates:	Crude rates	5-yr frequency
Overall	6.3 %	4 %
High-dose (60-66 Gy)	10 %	7 %
Low-dose (50 Gy, mostly pre-op)	2 %	0.6 %

Females (6% vs. 2%,  $p = 0.02$ ); > 55 yr (7% vs. 1%,  $p = 0.004$ )

Age, gender, and RT independent factors

Median fracture time: 44 months (range 12-153)





“Randomised trial of Volume of post-operative Radiotherapy given to adult patients with Extremity soft tissue sarcoma”

NCRI UK

Post-op  
(64-66 Gy)

Sx

2 cm  
longitudinal  
margin

5 cm  
longitudinal  
margin

End-points: Local control and function (TESS)



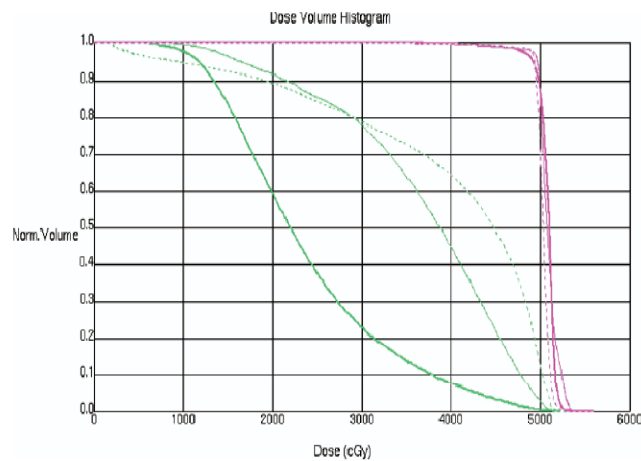
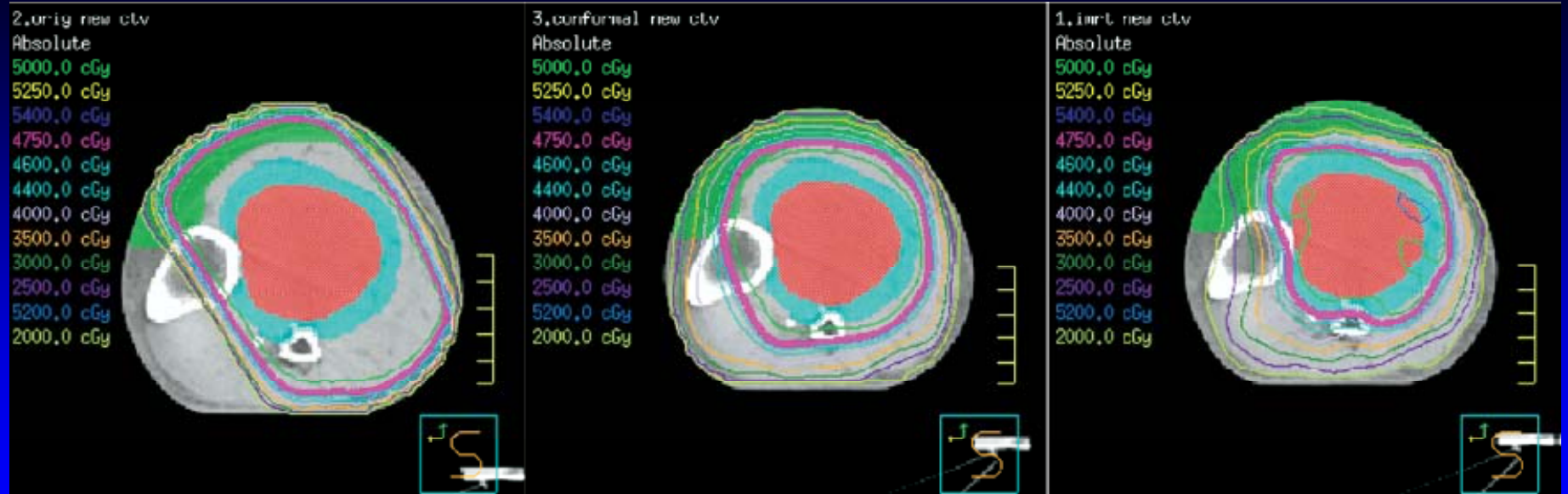


Fig. 2. Dose-volume histogram displaying dose to flaps (green lines) and clinical target volume (purple lines) for original (dashed line), conformal (thin solid line), and intensity-modulated radiotherapy (IMRT) (thick solid lines) plans for Patient 8. Roughly 22% of flaps received  $\geq 30$  Gy for this IMRT plan compared with almost 80% in original and conformal plans.

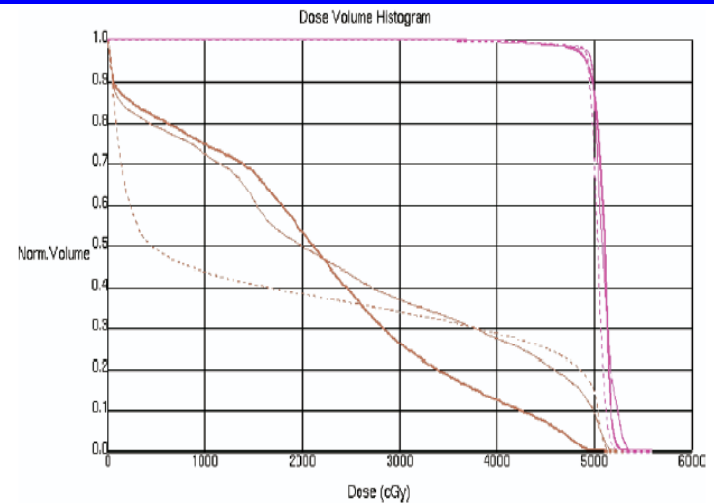


Fig. 3. Dose-volume histogram displaying dose to bone (brown lines) and clinical target volume (purple lines) for original (dashed line), conformal (thin solid line), and intensity-modulated radiotherapy (IMRT) (thick solid lines) plans for Patient 8. Almost 30% of bone received  $\geq 40$  Gy in original and conformal plans compared with 12% in IMRT plan.

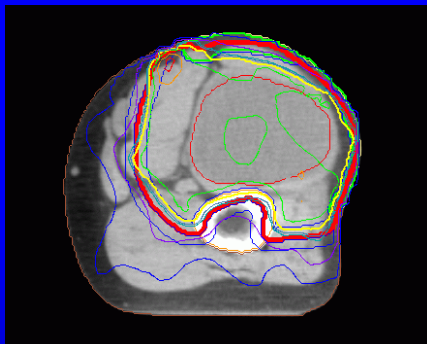
# Modern Imaging and RT Opportunities

Courtesy O'Sullivan/Ferguson

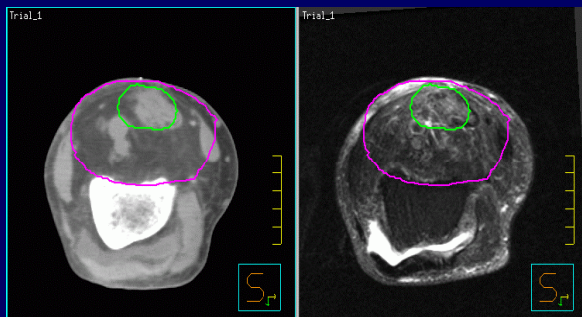
## IMRT

- Smaller PTVs
- Bone + skin flap avoidance
- Steep dose gradients

## Pre-op IMRT

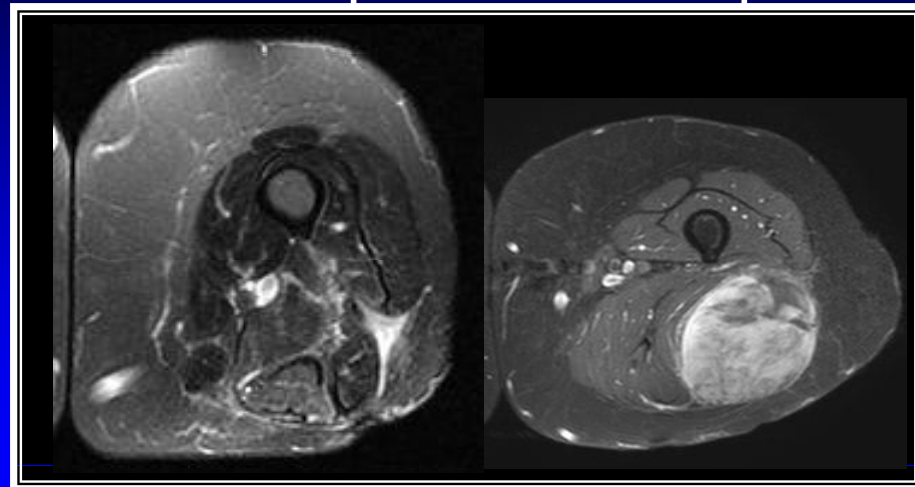


## IMAGE FUSION



Post-op

Pre-op



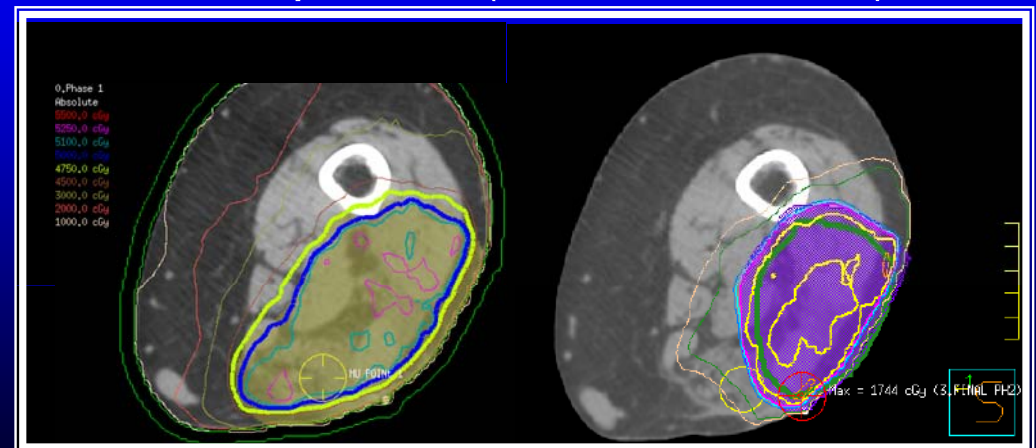
Older patient



Avoid wound problems

Phase 1  
Post-op IMRT (bone avoidance)

Phase 2



# Ongoing trial: “Flap-sparing” IMRT

- Phase II preop IMRT study commenced July 2005 at PMH
- Primary endpoint: Acute wound healing complications (reduce to the base line level of the NCIC SR2)
- 59 patients planned



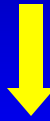


Positioning  
Immobilization  
Documentation

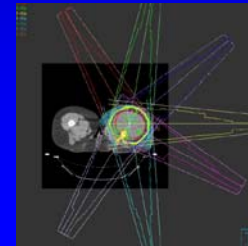
Multidisciplinary treatment decision for pre-op RT



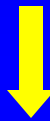
CT Simulation



Generation of IMRT Distribution

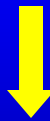
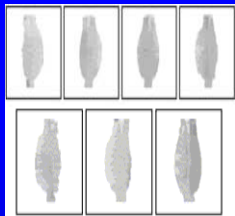


Contouring  
Beam placement  
Plan review



Treatment unit Preparation

Physics QA  
Final approval



Treatment delivery with daily image guidance

Fusion with CT  
Shift to iso  
Documentation



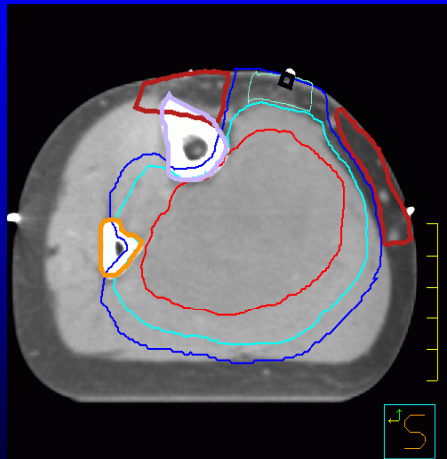
Integrate RT target back to the surgical approach

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# Considerations

- Anatomically diverse presentations
- Tumour size
- Volume changes during treatment course
- Position of unaffected limb
- Shifts from stable setup point to planned isocentre



## Critical structures:

- Bone
- Subcutaneous tissues

## Target structures:

- GTV, CTV, PTV
- Contaminated Biopsy

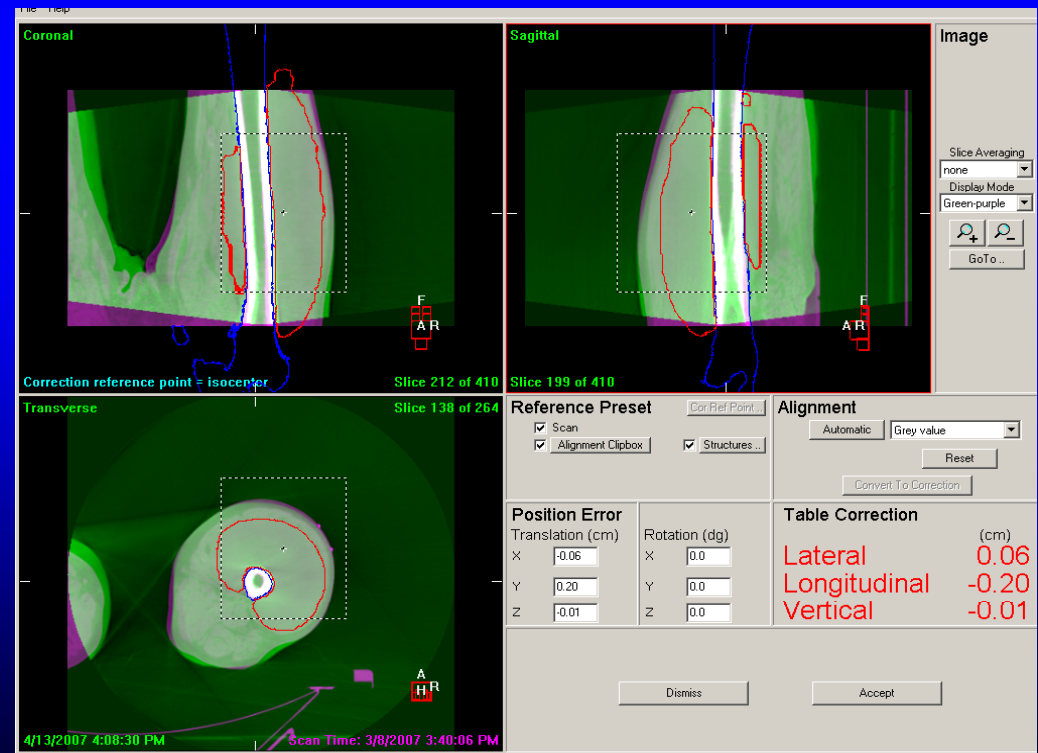
## Deviation in setup:

- Geographic miss
- Critical structures enter high dose region



# 3D image guidance for RT

- Verify the isocentre position
- Identify changes in limb position
- Soft tissue delineation
- Daily assessment of volume changes



Correction reference point = isocenter

Position Error

Translation (cm)		Rotation (dg)	
X	-0.06	X	0.0
Y	0.20	Y	0.0
Z	-0.01	Z	0.0

Table Correction (cm)

Lateral	0.06
Longitudinal	-0.20
Vertical	-0.01

# Conclusion

- Radiotherapy in extremity STS requires multidisciplinary collaboration
- The goal of functional limb preservation with local control and minimal toxicity is achievable
- “Advanced” RT is enhanced by modern imaging both for treatment planning and delivery



# Acknowledgement

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Doug Moseley, Mike Sharpe, Fannie Sie, Tim Craig, Radiation Physics, Radiation Treatment Planners and Therapists



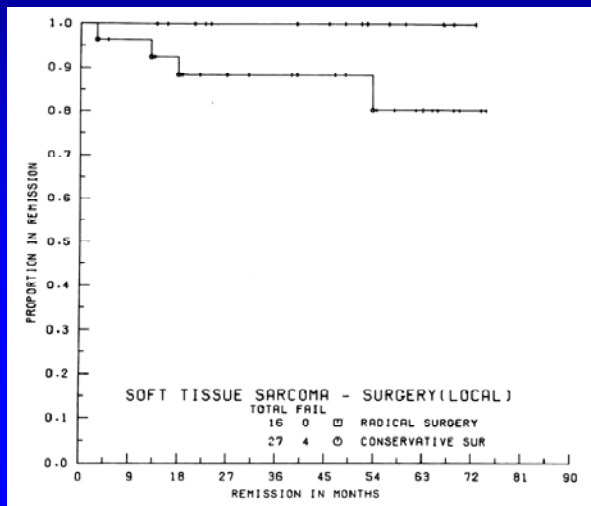


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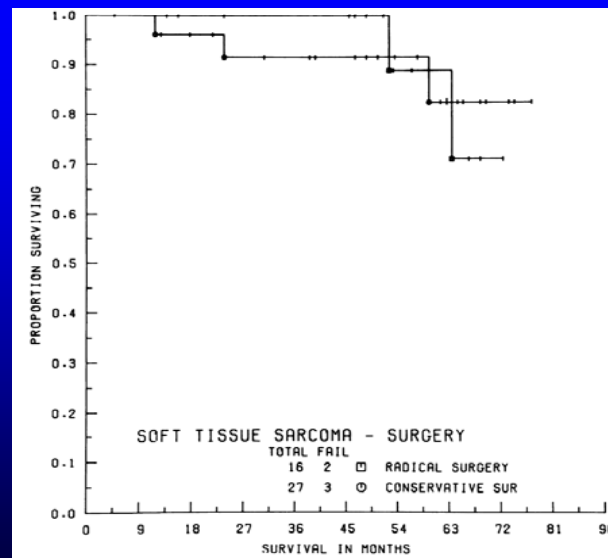


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# Amputate or not



Local control



Overall survival

43 pts  
High grade STS

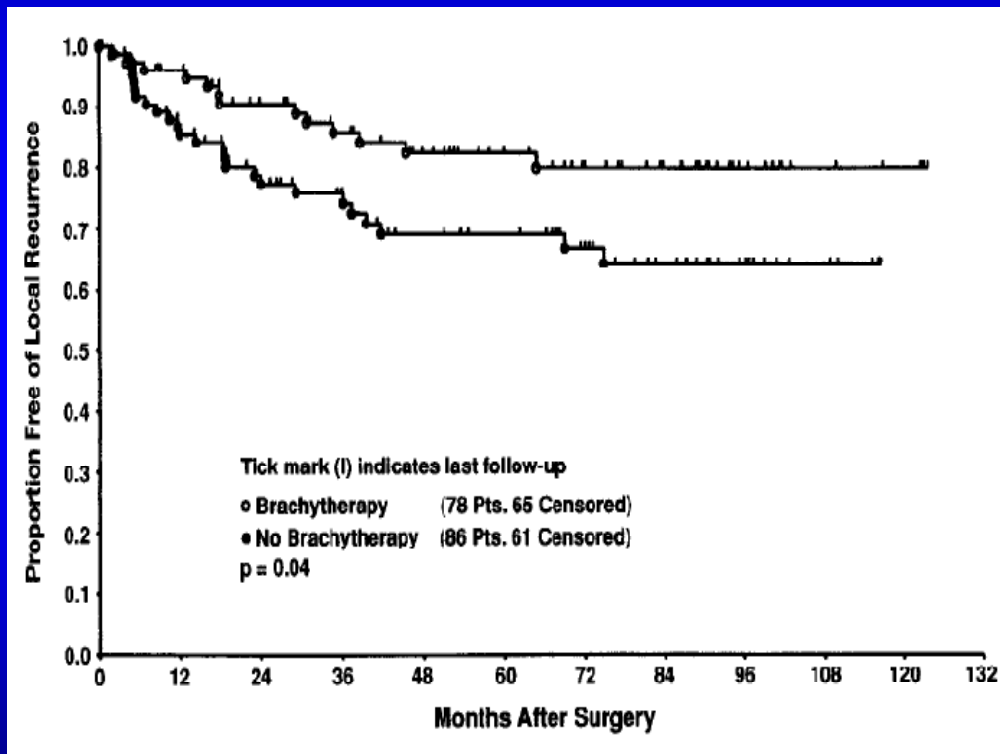
16 pts  
Amputation

27 pts  
WLE + RT

*Rosenberg et al Ann Surg, 1982*



# Limb preservation with BRT



EXTREMITY/TRUNK STS  
164 Pts  
WLE

BRT  
86 Pts

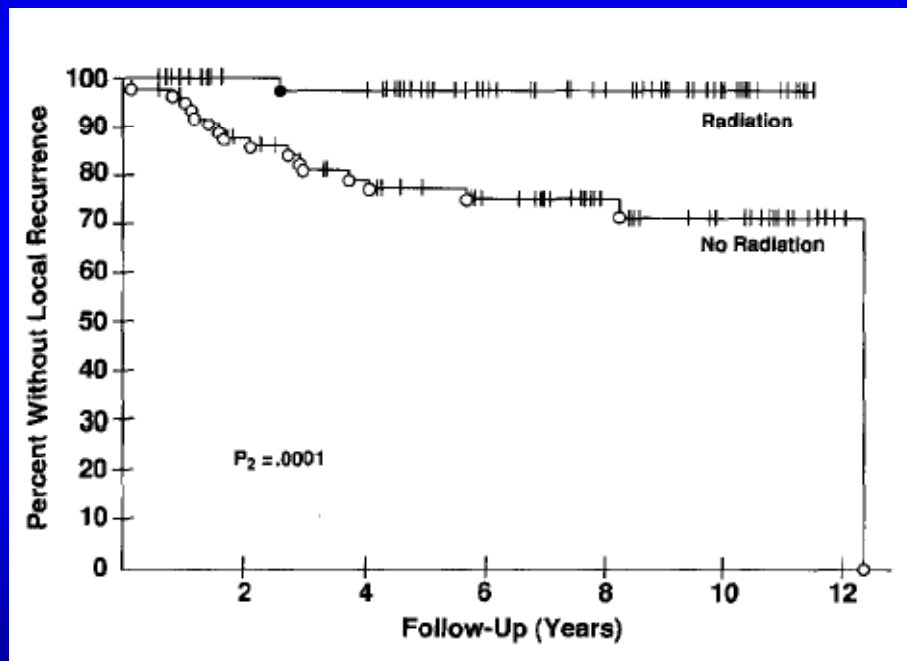
No BRT  
78 Pts

*Pisters et al JCO, 1996*



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# Limb preservation with EBRT



EXTREMITY STS  
91 Pts  
WLE  
(+ CT for high grade)

Adjuvant RT  
47 Pts

No Adjuvant RT  
44 Pts

*Yang et al JCO, 1998*



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