Radiation Therapy for Soft Tissue Sarcomas

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NCI: limb salvage vs. amputation

- 43 patients randomized 2:1 to
  - WLE + XRT or amputation
- Local recurrence 4/27 WLE vs 0/16 amp
  (p=0.06)
  Positive margins correlated with local recurrence
- No difference in overall survival or DFS

NCI: limb salvage vs. amputation

NCI: XRT vs No XRT

- 91 patients high-grade: WLE (44) vs WLE + XRT (47)
  - All received adjuvant chemotherapy
- 50 patient low-grade: WLE (24) vs WLE + XRT (26)
- Median f/u 9-10 yrs
- Local recurrence
  - High-grade: 17/44 (39%) WLE vs 1/47 (2%) WLE + XRT (p=0.0028)
  - Low-grade: 8/24 (33%) WLE vs 1/26 (4%) WLE + XRT (p=0.016)
- No difference in overall survival or DFS

NCI: XRT vs No XRT

MSKCC: brachy vs No brachy

- 164 patients: WLE (86) vs WLE + brachy (78)
- Median f/u 76 months
- Local control at 5 years
  - WLE 69% vs WLE + XRT 82% (p=0.04)
  - High-grade: WLE: 66% vs WLE + XRT 89% (p=0.0025)
  - Low-grade: WLE: 76% vs WLE + XRT 83% (p=0.6)
- No difference in overall survival or DFS

Pisters JCO 1996; 14:859-868
MSKCC: brachy vs No brachy

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NCIC: pre-op vs post-op XRT

- 190 patients randomized:
  - pre-op 50 Gy (94) vs post-op 66 Gy (96)
- Median f/u 76 months
- Wound complications: pre-op (35%) vs post-op (17%) p=0.01
- No difference in local control
- Grade 2 or higher fibrosis
  - Pre-op 31% vs post-op 48% (p=0.07)
- Edema
  - Pre-op 15% vs post-op 23% (p=NS)
- Joint stiffness
  - Pre-op 18% vs post-op 23% (p=NS)

O’Sullivan Lancet 2002; 359:2235
Davis Radiother Oncol 2005; 75:48
Local Control After Radiation
Radiation Therapy Techniques

- Rigid immobilization
- Spare > 1 cm strip of skin
  - To prevent edema
- Minimize dose to whole bone (< 50 Gy)
- Do not cross joint space
- Bolus scar unless tangential beams used
- CT planning essential
- Use beam modifiers
  - Wedges
  - Filed-within-field
- Use 6MV for extremities
Radiation Therapy Techniques

Pre-op

• Gross tumor plus
  – 5 cm proximal and distal
  – 2 cm radial (except where near bone or crossing joint space)

• Cone down (if used)
  – GTV plus 2-3 cm all around
Radiation Therapy Techniques
Post-op

• First course - larger volume of:
  – All tissue handled (tumor bed, drain, scar) + 2cm
  – Tumor bed + 5 cm proximal/distal and 2 cm radial
    (except where near bone or crossing joint space)
• Cone down #1
  – Tumor bed + 2-3 cm all around
• Cone cone #2 (if given)
  – Tumor bed + 1-2 cm margin all around
Radiation Therapy Dose

- **Pre-operative XRT:**
  - Pre-op volume to 50 Gy
  - Post-op boost (positive margins) 16-20 Gy
- **Post-operative XRT**
  - First course 45-50 Gy
  - Cone down #1 10-15 Gy
  - Cone down #2 6-10 Gy
  - Total dose:
    - 60 Gy (- margins)
    - 66 Gy (+ margins)
    - 70+ Gy (gross disease)
Radiation Therapy Dose
Positive margins

• Recommend 66 Gy
Radiation therapy techniques

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Field-within-field
Complications

- Impaired wound healing 15-40%
- Edema 20%
- Fibrosis, decreased ROM 20%
- Bone fracture 2-10%
- Peripheral nerve injury 1-10%
Complications: Lower Extremities

- **Acute Would complications** 27%
  - Pre-op (34%) vs post-op 16% p<0.001
  - Size > 5 cm (31%) vs < 5 cm (17%) p=0.04

- **Chronic limb complications** 13%
  - Groin/thigh (16%) vs other sites (4%) p=.008
  - Prior acute wound complication
    - Yes (20%) vs none (10%) p=.003
  - Dose > 60 Gy (18%) vs < 60 Gy (9%) p=0.04
  - Bone fracture 1.2%

Cannon Cancer 2006
Complications: Bone Fracture

- 205 patients with STS of thigh
  - Treated with surgery + XRT
- 9 patients (0.04%) developed femur fracture
- High-risk patients included:
  - Periosteal stripping
  - Female
  - chemotherapy

Lin Cancer 1998
Complications: Bone Fracture

- 364 patients with STS of lower extremity
  - Treated with surgery + XRT
- 4% fractures at 5 years
  - High-dose (60-66 Gy) 7%
  - Low dose (50 Gy) 0.6% p=.007
  - Female 6%
  - Male 2% p=.02
  - Age > 55 years 7%
  - Age < 55 years 1% p=.004

How can we decrease toxicity and maintain excellent local control?

Answer:?
Intensity Modulated Radiation Therapy (IMRT)
Intra-Operative Radiation Therapy (IORT)
Goals:

- Maintain excellent local control
- Reduce morbidity
  - Edema
  - Joint stiffness
  - Wound complications
  - Fractures
Is IMRT better than 3D?

Comparison of 3D vs IMRT plans for 10 cases of STS close to femur

• Definitions
• CTV = GTV + 1.5 cm radially, or at bone interface
• CTV = GTV + 5-10 cm sup/inf
• PTV = CTV + 5mm

Hong IJROBP 2004
QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.
IMRT vs 3D for STS

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IMRT
IMRT for STS

**Appeal:**
- Spare more normal tissue
- Reduce morbidity

**Concerns:**
- Reduction in local control
  - Marginal misses
- Potential increased risk of 2nd malignancies
  - Due to increase volume receiving low dose
- Other unforeseen morbidities
NCI: IORT for Retroperitoneal Sarcomas

N=35
15 IORT
20 no IORT
Median f/u 8 years

Randomize

Surgery + 20 Gy IORT
+ post-op XRT (35-40 Gy)

Surgery
+ post-op XRT (50-55 Gy)
Peripheral neuropathy developed in IORT patients only when large IORT Fields were used to cover tumor beds in the area of the sacral nerve plexis

NCI: Retroperitoneal Sarcomas

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IORT for extremity sarcomas

- German retrospective review of 153 patients
- Median IORT dose 15 Gy
- Mean EBRT dose 43 Gy (40-50.4 Gy)
- Median f/u 33 m
- Local control (5 yr) 78%
- Acute grade 2-4 toxicity 23%
- Late grade 2-4 toxicity 17%

Oertel et al. IJROBP 2006, 64:1416
IORT for extremity sarcomas: UCSF experience


- Indications for IORT included: tumors whose proximity to critical structures resulted in the expectation of close or microscopically positive surgical margins, and recurrent tumors within previously irradiated fields.

- The median IORT dose was 12.5 Gy (range 10-17.9 Gy).
IORT for extremity sarcomas: UCSF experience

- Median follow up of 22 months
- 2- and 5-year estimated rates of local control were 79% (95% CI 62-89%) and 76% (58-87%), respectively;
- Distant metastasis-free survival were 75% (59-86%) and 68% (50-81%), respectively;
- Overall survival were 85% (69-93%) and 70% (50-83%), respectively.
IORT for extremity sarcomas: UCSF experience

• The two-year local control rate for tumors with positive or close margins (≤1 mm) was 76%, compared with 83% for margins > 1 mm.
• The two-year local control rate for patients who did not receive adjuvant EBRT was 65%, and 87% for those who did (median dose 56 Gy).
• The two-year local control rate was 91% versus 47% for primary versus recurrent tumors (p=0.01).
• Patients with primary tumors had a two-year local control rate of 100% if the margin was >1mm, and 83% for positive/close margins.
• Eight patients (14.3%) developed grade 3 wound healing complications; 7 of these patients had received adjuvant EBRT.

Tsuji abstract ASTRO 2007
IORT for extremity sarcomas: UCSF experience

Conclusions:

- IORT offers a viable method of delivering local therapy
- Excellent local control in primary tumors (91%)
  - 100% LC in primary tumors with margins > 1mm
  - 83% LC in primary tumors with close/positive margins
- Reduced dose of post-op XRT (median dose 56 Gy)
  - May translate to less toxicity
- Low wound healing complications (14%)
- Good local control for recurrent tumors in previously radiated fields (47%)

Tsuji abstract ASTRO 2007
IORT for extremity sarcomas: UCSF experience

**Doses**

- IORT 12-15 Gy
- Post-op XRT
- - margins:
  - 50 Gy to large field
- Expected + margin (in IORT field)
  - 50 Gy to large field + 6-10 Gy boost: total dose 56-60 Gy
- Unexpected + margin (not in IORT field)
  - 50 Gy to large field + 16 Gy boost: total dose 66 Gy
Surgery for lung metastases

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Radiosurgery for lung metastases
Radiosurgery for lung metastases
Radiosurgery for lung metastases

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