وبالله فائق
Role of radiotherapy in sarcomas

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Management

- requires a **MULTIDISCIPLINARY TEAM (MDT)**

- Treatment goals include:
  
  complete eradication of tumor with optimal **function preservation** and **minimal** treatment related **toxicities**
Management (surgery)

- In almost all cases, appropriate surgical resection is a prerequisite for curative treatment of STS

- procedures include:
  - marginal resection or excisional biopsy “shell-out”
  - wide resection (conservative surgery-limb sparing surgery)
  - radical resection or amputation
Management (surgery)

- LR rates after marginal resection range from 50% to 93%.

- Radical resection, which involves removal of all of the muscles and neurovascular structures within the compartment where the tumor resides or amputation (LR rate = 0-18%).
Uses of Radiotherapy:

- Curative
- Adjacent
- Neo-adjacent
- Palliative
Types of Radiation Therapy:

- **External**
- **Internal**
  - "Brachytherapy"
INDICATIONS-PORT

1. All deep seated tumors
2. All high grade tumors, size > 5 cm
3. Intermediate grade tumor size > 5 cm
4. Repeated margin positivity
5. Tumor > 5 cm superficial
6. Close margin Intermediate/High grade
Randomized Clinical Trials of RT

- **Rosenberg et al. (NCI) (n= 43) (1982)**
  

- **Randomized Prospective Study of NCI (n= 141) (1998)**
  

- **20-year follow-up of NCI study (2014)**
  

- **Memorial phase III RCT about role of BRT (n= 164) (1996)**
  

- **NCIC SR2 phase III Preop vs. postop RT outcome (n= 190) (2002)**
  

- **Preop vs. Postop RT late morbidity (NCIC SR2 update) (2005)**
  
Management (conservative surgery and RT)

- Three sentinel RCTs have been performed and have established RT combined with CS as the standard management for most (high-grade) STS of the extremities and trunk:

1- The first of these trials was conducted by Rosenberg et al. at the NCI:

- LR rates were 0% (0 of 16) and 15% (4 or 27)
- There was no significant difference in survival
Management (conservative surgery and RT)

2- NCI (1998) ➔

LR rates for the high-grade tumors were 20% (9 of 44) for CS and chemotherapy compared to 0% (0 of 47) for CS, chemotherapy, and RT (P = .003)

For the low-grade tumors, LR rates were 33% (8 of 24) for CS alone and 4% (1 of 26) for CS and RT (P = .016)

An update of this trial confirmed the lack of survival difference with 20-year OS of 64% for CS alone and 71% for CS and RT (P = .22)
Management (conservative surgery and RT)

3- MSKCC (BRT) ➔

LR rates for high-grade tumors were 30% (19 of 63) for CS alone compared with 9% (5 of 56) for CS plus BRT (P = .0025).

No difference in LR rates by treatment was seen for low-grade tumors; rates were 26% (6 of 23) and 36% (8 of 22) for patients treated with CS alone and CS plus BRT, respectively.
NCI Randomized Prospective Study 1998

N=141

Eligibility Criteria
- HG (91) and LG (50)
- Limb STS
- 1983-1991

*with med f/u of 9.6 yrs, Adj. RT decreased LRR significantly ($22 \rightarrow 0\%$) ($P = 0.003$) for HG

10 yr OAS 74% vs 75% (not significant)

Adj. RT decreased LRR significantly ($P = 0.016$) for LG
NCI Study Update 2014

Eligibility Criteria

- HG (91) and LG (50)
- Limb STS
- 1983-1991

Received adj. RT
70
HG (44); LG (26)

Surgery alone
71
HG (47); LG (24)

N=141

*with med f/u of 17.9 yrs 10 yr OAS 82% for adj RT vs 77% (not significant p= 0.22)

20 yr OAS 64% for adj RT vs 71% (not significant)
NCIC SR2 Phase III RCT 2002

N=190

Eligibility Criteria
- Extremity STS
- age > 15
- without mets.

Preop RT 94
Postop RT 96


*with med f/u 3.3 yrs wound complication 35% for preop vs. 17% for postop (p= 0.01)

OAS was slightly better in patients who had preop RT than in postop (p=0.048)

LRR, DRR and PFS didn’t differ between groups
Which is better, pre op RT or post op RT?
<table>
<thead>
<tr>
<th>PREOP RT</th>
<th>PORT</th>
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</thead>
<tbody>
<tr>
<td>Treatment volume smaller-No need to cover operated field</td>
<td>Treatment volume larger</td>
</tr>
<tr>
<td>Reduce seeding during surgery</td>
<td>More seeding</td>
</tr>
<tr>
<td>Tumor regression and better resectability</td>
<td></td>
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<tr>
<td>Decreased risk of recurrence</td>
<td></td>
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<tr>
<td>Less toxic</td>
<td>More toxic</td>
</tr>
<tr>
<td>No hypoxia-Blood supply uninterrupted</td>
<td>Hypoxia in tumor bed may adversely affect outcome</td>
</tr>
<tr>
<td>Disadv-Poor wound healing-No complete HPR</td>
<td>Adv-Complete HPR available</td>
</tr>
<tr>
<td></td>
<td>Pre op RT</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Local control</td>
<td>93%</td>
</tr>
<tr>
<td>Metastatic free relapse</td>
<td>67%</td>
</tr>
<tr>
<td>survival</td>
<td></td>
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<tr>
<td>5yr overall survival</td>
<td>73%</td>
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<tr>
<td>5yr cause specific</td>
<td>78%</td>
</tr>
<tr>
<td>survival</td>
<td></td>
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</tbody>
</table>
Preoperative versus postoperative RT:

- the authors suggested that:
  - these patients preferentially receive preoperative RT
Preoperative versus postoperative RT:

- Patients for whom **postoperative radiation may be preferred** include:
  - infiltrative **subcutaneous myxofibrosarcomas**
  - surgery alone might represent appropriate treatment
  - **Obese or diabetic** patients with subcutaneous tumors
Management (conservative surgery and RT)

- BRT is typically not recommended for low-grade STS.

- BRT as monotherapy is only recommended for high-grade tumors resected with negative margins.

- In the setting of positive resection margins, a combination of external beam RT and BRT or external beam RT alone is preferred.
Brachytherapy:

- For treatment combining external beam RT with BRT as a boost, doses are typically **45 to 50 Gy** for external beam, **15 to 25 Gy** for a LDR BRT boost, and **12 to 20 Gy** (in 2- to 4-Gy bid fractions) for a HDR BRT boost

- **Total** of approximately **65 Gy**
Principles of Treatment Planning

- There continue to be exciting technologic advances for treatment, which include:
  
  IMRT dose painting
  
  IGRT
  
  adaptive RT
  
  particle-beam radiotherapy (protons, carbon ions)
  
  stereotactic body RT (SBRT)
Conventional RT
Conformational RT
Doses

- **Posoperative:**

  - Treatment usually commences about 4 to 6 weeks following surgery and once the wound is fully healed.

  - Recommended total doses are **60 to 66 Gy** (delivered in 1.8- or 2-Gy fractions) for the case of **negative margins** and **66 to 68 Gy** for **positive margins**.
Doses

- Posoperative:
  - The **first course** of treatment is typically treated to a dose of 45 to 50 Gy and the balance of the dose is given in one reduced field.
Positioning the Patient:

- The **first step** of RT planning is to determine the appropriate positioning of the patient.

- It is important for the patient to be **comfortable** to ensure setup **reproducibility**.
RADIOThERAPY PLANNING

- Positioning & Immobilisation
- Planning CT Scan 3-5 mm cuts with iv contrast
- Co register Preoperative MRI /CT
- 3DCRT/IMRT preferred
Radiation Therapy

Ideal position for treating STS of hand, forearm or distal upper arm.
Radiation Therapy
Target Volumes and Treatment Fields

- **Preoperative Radiation Therapy:**

  - Current **standard** of care target volumes for preoperative RT include gross tumor volume (GTV) defined as the gross tumor delineated by the T\(_1\) postgadolinium MRI.

  - **Fusion** of the diagnostic MRI and planning CT for optimal target definition is strongly encouraged.
Preoperative Radiation Therapy:

- Clinical target volume (CTV) is defined as the GTV plus:
  - 4-cm margins in the longitudinal directions
  - 1.5-cm margins radially

These margins can be truncated if they extend beyond the compartment or beyond an intact fascial barrier, bone, or skin.
An unclassified pleomorphic high-grade sarcoma of the medial proximal right thigh in a 30-year-old woman that was treated with preoperative IMRT (50 Gy). A: Axial T₁ postgadolinium image of the magnetic resonance imaging (MRI) scan. B: Coronal T₁ postgadolinium image of the MRI scan.
planning CT scan showing the gross tumor volume (GTV, cyan), clinical target volume (CTV, purple), and planning target volume (PTV, red).
Target Volumes and Treatment Fields

- Postoperative Radiation Therapy:
  - There is actually no “gross tumor.”
  - It can be helpful to draw a GTV in the location where the gross tumor was preoperatively, as sometimes this volume is used for cone-down volumes.
  - It is also helpful to contour the operative bed.
Target Volumes and Treatment Fields

- Postoperative Radiation Therapy:
  - The CTV should encompass all the tissues handled during the surgery including the incision and any drain sites (Postoperative changes seen on MRI help define the operative bed.)
  - An additional longitudinal margin of 4 cm and a radial margin of 1.5 cm is generally added to the operative bed to form the CTV.
- Preoperative Radiation Therapy:
  - The planning target volume (PTV) is defined as the CTV plus 5 to 10 mm based on institution setup uncertainty.
Principles of Treatment Planning

- Basic tenets for treating the extremity are:
  - to “spare a strip” of the limb circumference (to prevent subsequent lymphedema and pain)
  - to avoid treating the whole thickness of bone to high doses (to diminish risk of fracture)
  - to avoid treating an entire joint to high doses (to decrease joint stiffness).
Pink: tumor; Green: ovaries

Dose Lines:
100% Yellow
90% Blue
40% Brown
6% Green
RADIATION THERAPY
TOXICITIES
Pre op RT - complications

- wound dehiscence,
- wound necrosis
- persistent drainage,
- infection,
- seroma formation,
- ulceration,
- and cellulitis
Chronic effects of RT

- > 1 yr after RT
- fibrosis/contractures,
- Lymphedema,
- neurologic injury,
- osteitis, and
- fractures
Radiation Therapy Toxicities

- **Chronic Radiation Therapy Toxicities:**
  - The *most significant* chronic toxicities following RT to the *extremities* include:
    - Edema
    - subcutaneous fibrosis
    - decreased muscle strength
    - decreased range of motion
    - pain
    - and, less commonly, bone fractures
osteosarcoma

- Radiation therapy has no major role in osteosarcoma
- Radiation therapy may be useful in some cases where the tumor cannot be completely removed by surgery. E.g. in pelvic bones or in the bones of the face.
Post-operative Radiation Therapy

- For gross or microscopic positive margin
- For marginal Resection
- For wide-resection with Poor Histological response to Neoadjuvant Chemotherapy (>10% viable tumor cells in the specimen)
EWINGS SARCOMA
radiation responsive tumor.

- **Definitive Radiation Therapy:**
- Tumors where Resection is Impossible
- For skull, face, vertebra, or pelvic primary
- Patient with poor Surgical risk
- Patient refusing surgery
- Note: Surgery is the preferred arm where wide or marginal resection is possible