Decision-making in Local Management of Extremity Soft Tissue Sarcoma

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Multidisciplinary Local Management – A “Development in Cancer Management”

- Although surgery remains the mainstay of treatment, decisions are not made independently by surgeon
- Collaborative input into radiation and surgical planning
- PMH a leader in this collaborative treatment model
Background

- Soft tissue sarcoma (STS) represents one of the first collaborations in accomplishing structure and function preservation in oncology
- Management involves surgical, radiation oncology, medical oncology, medical imaging and pathology input
- Goal of treatment is local control, function preservation, and usually limb preservation
Objectives

• To present the current paradigm for multidisciplinary decision making for local management of soft tissue sarcomas at PMH

• To highlight the research accomplishments of our group that have led to this management paradigm
Management of Soft Tissue Sarcomas

- **Surgery +/- radiation**
- **COMPLETE** removal of tumor
- Reconstruction of
  - Soft tissues
  - Bone
  - Nerves
  - Blood vessels
- This applies to any anatomic site
  - Extremity
  - Head & neck
  - Retroperitoneum
The Concept of the Surgical Margin

- Originally described for sarcoma by Enneking
- 4 categories
  - Intrallesional
  - Marginal
  - Wide
  - Radical
The Concept of the Surgical Margin

• Intralesional margin is inadequate, associated with unacceptable risk of local recurrence – approximately 40% by 2 years

• Radical margin generally overkill, associated with significant functional implications
Gerrand CH et al, *Classification of positive margins after resection of soft-tissue sarcoma of the limb predicts the risk of local recurrence*, JBJS (Br) 83-B(8), November 2001, pp 1149-1155

Unplanned positive margin, or intralesional excision
Wide Margins

- Depend on the tissue in question
- Generally for skin, fat or muscle, 2 cm is considered a safe wide margin to account for microscopic disease
- This includes tumor and edema
- However 1 mm of fascia, which is a good barrier to tumor spread, is also a wide margin
15 patients underwent resection of sarcoma without neoadjuvant treatment

Edema on T2-weighted images ranged from 0 - 7.1 cm from edge of tumor (mean 2.5 cm)
• In 6 cases malignant cells were found in edema less than 1 cm from tumor margin
• In 4 cases malignant cells were more than 1 cm from tumor margin, with maximum distance 4 cm
Why consider edema in STS?

- Edema contains microscopic disease which may lead to local recurrence if not considered in treatment plan.
- Therefore marginal margins are not adequate if surgery alone is undertaken.
- Treatment of edema may be by wide surgical excision or preoperative radiation.
Imaging in treatment decision making

• If we look at imaging and feel that we can resect tumor
  – with adequate wide margins
  – without sacrificing critical structures or
  – significantly affecting function

• Surgery alone is usually all that is necessary - usually only reserved for small, superficial tumors, irrespective of tumor grade
Imaging in treatment decision making

- If wide resection means
  - sacrifice of critical structures or
  - severe functional consequences
- Radiation will be used – almost always in deep lesions
- Therefore radiation is necessary if marginal margins are anticipated
Imaging in planning margins

- First must ascertain whether sarcoma is superficial or deep to fascia
- This has important ramifications for treatment and prognosis
- This can be determined clinically but MR imaging is essential to confirm the location in relation to the fascia
Superficial sarcomas

- On imaging, if tumor is
  - small
  - superficial to fascia and
  - there is no surrounding edema
- SURGERY ALONE
  resection +/- skin grafting
- This is irrespective of tumor grade
Superficial sarcomas - multinodular

- We can be less certain that 2 cm of skin/fat is an adequate margin in this situation
- Tumor is demonstrating more infiltrative growth pattern
- SURGERY + RADIATION
Superficial sarcoma – subcutaneous edema

• Studies have shown that edema contains microscopic disease
• Once again we can be less certain of our margins in this situation
• SURGERY + RADIATION
Superficial sarcoma – overlying bone

- Bone covered by periosteum, which is not as good a barrier to tumor invasion as muscular fascia
- SURGERY + RADIATION
Superficial sarcoma – extracompartmental area

- Axilla, femoral triangle, popliteal fossa or antecubital fossa are not bounded by fascia
- Inadequate margin between tumor and neurovascular structures
- SURGERY + RADIATION
Deep sarcomas

- Usually impossible to obtain adequate margin without sacrificing critical neurovascular structures or bone
- Radiation will allow for closer margin without increasing risk of local recurrence
“Planned positive” margin

- Sarcomas are frequently adjacent to critical neurovascular structures or bone
- At time of resection, there is often no margin present when dissecting these critical structures off the tumor
“Planned positive” margin

• This “planned positive” margin is not associated with increased risk of local recurrence, provided
  ➢ patient receives radiotherapy and
  ➢ margins are otherwise adequate

• Therefore a “planned positive” margin is akin to a marginal negative margin
Gerrand CH et al, *Classification of positive margins after resection of soft-tissue sarcoma of the limb predicts the risk of local recurrence*, JBJS (Br) 83-B(8), November 2001, pp 1149-1155
Encased Critical Structures

- Essential to establish on preoperative imaging to ensure patient is aware of functional ramifications
- No way to save these structures without gross tumor spillage
Encased Critical Structures

• Generally must be resected
• For major motor nerves, this leaves significant functional deficit but still often better than function after amputation
• In upper extremity, this can be overcome by nerve grafting or distal nerve transfers

- 20 patients underwent resection of sciatic nerve during resection of posterior thigh sarcomas
- Functional outcome on 10 long term survivors
- Mean TESS score 74% (range 46-99%)
- More than 1/3 of patients felt they were not at all compromised in daily activities
- Function superior to high above knee amputation
Encased Vascular Structures

- Encased vessels can be resected and reconstructed
- Reconstructed arteries usually remain patent and function is not affected
- Veins usually occlude and edema often ensues
Compared with a control group of 38 patients without vascular reconstruction, 19 patients with vascular reconstruction had:

- Higher wound complications (68% vs. 32%)
- Higher incidence of DVT (26% vs. 0%)
- Higher likelihood of edema (87% vs. 20%)
- Higher risk of amputation (16% vs. 3%)
- Equivalent function
Bone involvement

- Rare occurrence (5%), often a poor prognostic factor
- Imaging that suggests bone involved will lead to resection and reconstruction
- Essential to know this preoperatively
- Clinical exam also important – mass that is mobile over bone will likely have periosteum as a margin
Patients presenting with bone invasion are more likely to
  - Present with metastases
  - Require amputation

Decreased overall survival
Lymph node involvement

- Rare in soft tissue sarcoma compared to pulmonary metastases
- Generally physical examination is all that is necessary
- Certain histologic subtypes warrant imaging of regional lymph nodes due to higher risk of lymphatic spread
• Of 1066 patients, 39 (3.7%) developed lymph node metastases

• Most common histologic subtypes
  – Epithelioid sarcoma (3/15) 20%
  – Rhabdomyosarcoma (4/21) 19%
  – Clear cell sarcoma (2/18) 11.1%
  – Angiosarcoma (2/18) 11.1%

• Contrary to previous similar studies, synovial sarcoma rarely developed lymphatic mets (4%)
Isolated lymph node metastases

AJCC/UICC stage III

Proportion alive

Followup in months
Follow-up in months from diagnosis of lymphatic involvement.

Proportion alive

Surgical treatment

Palliative treatment
Role for sentinel node biopsy?

- Isolated case reports in clear cell sarcoma, epithelioid sarcoma and rhabdomyosarcoma
- Unclear if prognosis is changed, but warrants further investigation in patients at high risk
The “Whoops” referral

- Excisional biopsy of a lesion (usually superficial) thought to be benign
- Final pathology shows sarcoma with involved margins
- If lesion was resected piecemeal, zone of contamination is likely large
  - probably consider preop RT
- If resected en bloc through reactive zone (marginal excision)
  - re-excise and if margins still close – postop RT
Limb Salvage Surgery

- Possible in 95% + of cases
- Surgery alone is possible if wide margins are achievable (2cm) without sacrificing critical structures (bone, nerves, vessels) based on preop MRI
- Usually only small superficial sarcomas; often need split thickness skin graft
- If not possible, combined treatment with radiation and surgical resection is recommended
Amputation

• Indications all relative
• Usually indicated if patient has more than one of
  – Vascular involvement
  – Motor nerve involvement (or multiple nerves in upper extremity)
  – Infected tumor
  – Poor soft tissue coverage
  – Expected functional outcome poorer than with amputation
• 52 year old male
• Rapidly growing soft tissue mass on dorsum of foot extending up to ankle
• Involvement of extensor tendons, dorsal nerves, vessels, bone invasion
• Below knee amputation – excellent functional outcome
• 19 year old male with NF-1
• Growing mass in calf – MPNST
• Involvement of bone, all 4 compartments of calf, posterior tibial vessels and nerve
• Above knee amputation
90 year old male, local recurrence of previously treated sarcoma in forearm

Involvement of ulna, extensor tendons, ulnar nerve and vessels

Below elbow amputation
• 67 year old male
• Rapidly growing mass right arm just above elbow
• Growing rapidly on radiation
• Involvement of brachial vessels, median & ulnar nerve
• Shoulder disarticulation
Management of Local Recurrences

- Essential to have details on previous treatment – radiation and surgical
- If no previous radiation, lesion may be managed similar to primary tumor, but radiation should be utilized
- Management must be individualized based on
  - Previous radiotherapy and surgery
  - Local anatomy
  - Reconstructive options
  - Probability of complications
  - Functional consequences
- Always be aware of possibility of a new primary
364 lower extremity EBRT at PMH (1986-98) without chemo.

- Females (6% vs. 2%, p = 0.02); > 55 yr (7% vs. 1%, p = 0.004)
- Cox: age, gender, and RT independent factors
- Median fracture time: 44 mos (range, 12 to 153 months)

<table>
<thead>
<tr>
<th>Fracture rates:</th>
<th>Crude rates</th>
<th>5-yr frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>6.3 %</td>
<td>4 %</td>
</tr>
<tr>
<td>High-dose (60-66 Gy)</td>
<td>10 %</td>
<td>7 %</td>
</tr>
<tr>
<td>Low-dose (50 Gy, generally pre-op)</td>
<td>2 %</td>
<td>0.6 %</td>
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</tbody>
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Holt et al. JBJS 2005
Study Purpose

Review the management and outcomes of patients who develop radiation-associated pathologic fractures after treatment of extremity soft tissue sarcomas in a single orthopaedic oncology centre.
Results

1986 - 2005: 1381 patients

946 (68.5%) combined radiation + surgery

32 patients pathologic fracture (3.4%)

34 fractures
## Results

<table>
<thead>
<tr>
<th>Location</th>
<th># Fractures</th>
<th>Healed</th>
<th>Not Healed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetabulum</td>
<td>2 (6%)</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>Prox Femur</strong></td>
<td><strong>12 (35%)</strong></td>
<td><strong>3</strong></td>
<td><strong>9</strong></td>
</tr>
<tr>
<td>Diaph Femur</td>
<td>8 (24%)</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Distal Femur</td>
<td>2 (6%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Prox Tibia</strong></td>
<td><strong>2 (6%)</strong></td>
<td><strong>2</strong></td>
<td><strong>0</strong></td>
</tr>
<tr>
<td>Diaph Tibia</td>
<td>3 (9%)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Metatarsal</td>
<td>2 (6%)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td><strong>Patella</strong></td>
<td><strong>3 (9%)</strong></td>
<td><strong>1</strong></td>
<td><strong>2</strong></td>
</tr>
</tbody>
</table>
Nomogram for Prediction of Femur Fracture in Patients Undergoing Thigh Sarcoma Resection

Points

Sex

Age_at_Sx

Compartment

Diameter

Radiation

Stripping

Total Points

Probability of Fracture