Management of Soft Tissue Sarcoma

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Disclosure

Employer:
• Brigham and Women’s Hospital

Leadership Position:
• ASTRO Scientific Committee Sarcoma Track Vice-Chair

I have no financial conflicts of interest to disclose.
Learning Objectives

For extremity and retroperitoneal sarcoma, to understand:

• Patterns of spread
• Prognostic factors
• Optimal treatment approaches
• Risk factors for RT complications
Overview

- Incidence and Epidemiology
- Diagnosis and Staging
- Prognostic Factors
- STS Extremity and Trunk
- Retroperitoneal Sarcoma
Soft Tissue Sarcoma Incidence

• < 12,000 cases in the US for 2016
• STS represents ~ 1% of all cancers
Pathogenesis

• Most have no clear etiology (>95%)

• Associated Genetic Syndromes
  – e.g. Li-Fraumeni, Familial Adenomatous Polyposis (FAP), NF 1

• Associated Environmental Factors
  – e.g. Radiation exposure, Lymphedema
Histopathologic Types

- ~25 major categories of STS
- ~60 types when subcategories are considered
- >300 synonyms for these 60 types!

More Common Types:

- Pleomorphic sarcoma
- Liposarcoma
- Leiomyosarcoma
- Desmoid tumor
- Rhabdomyosarcoma
- Synovial sarcoma
- Malignant peripheral nerve sheath tumor
- Angiosarcoma
- Ewing Sarcoma
- Extraskeletal osteosarcoma
- Myxofibrosarcoma
- Solitary fibrous tumor
Difficulties with Pathology

• Rarity
• Diversity
• Change in diagnosis after specialist review: 30 - 70%*
• Disagreement among specialists: 25 - 40%**

** Coindre 1986, Hasegawa 2002
Anatomic Sites of STS

- Lower Extremity 46%
- Upper Extremity 15%
- Superficial Trunk 15%
- Retroperitoneal 15%
- Head & Neck 8%

Natural History

- Invade along muscle fibers, fascial planes
- LN involvement uncommon (5% overall)

Exceptions “CARE” (15-20%)
- Clear cell sarcoma
- Cutaneous Angiosarcoma
- Rhabdomyosarcoma
- Epithelioid sarcoma

- Distant spread most commonly to lung
Patterns of Local Growth
- along paths of least resistance -
Diagnosis
Most STS present as asymptomatic soft tissue mass

Diagnostic Approach
• Core biopsy, Incisional biopsy
• Mass < 3 cm: excisional biopsy
Staging Evaluation

• H + P

• Evaluation of primary
  – MR (extremity/ superficial trunk)
  – CT (retroperitoneum)

• Evaluation of distant disease
  – Chest CT
  – Bone or PET scan usually *not* necessary
Prognostic Factors for Survival

- Grade* (most important)
- Size
- Depth (Superficial/Deep to fascia)
- Site (Extremity vs Trunk/RP)
  (Distal vs Proximal)
- LN Involvement
- Age (young better than old)
Prognostic Factors for LR

- Marginal Resection
- Positive Margin
- Locally Recurrent disease
- Older age
- H & N and RP location
Management by Multimodality Team

Radiology
Pathology
Surgery: Oncologic/Orthopedic, Plastic
Radiotherapy
Medical Oncology
Physical Therapy
Social Work
Management at Experienced Center

• Associated with better outcome

Paszat, *Sarcoma* 2002
STS of Extremity and Trunk
Treatment for Low Grade STS

Generally surgery alone
Wide resection, Neg margins → LR <15%
Survival rate typically > 90%
Treatment for Low Grade STS

Generally surgery alone

Wide resection, Neg margins $\implies$ LR $<15\%$
Survival rate typically $> 90\%$

Indications for RT

– Positive margins
– LR s/p prior surgery alone
– Location not amenable to salvage surgery
Treatment for High Grade (G2/3) STS of Extremity and Trunk

Limb-Sparing Surgery (LSS) and RT
Treatment for High Grade (G2/3) STS of Extremity and Trunk

Limb-Sparing Surgery (LSS) and RT

Outcome

• Local Recurrence < 15%
• Survival varies by size, grade 2 vs 3
STS Extremity/Trunk

3 classic randomized trials established the role for LSS + RT for high grade (G2/3) STS
NCI (Rosenberg Ann Surg 1982)
- Amputation vs LSS + RT
- LR with LSS + RT: 15%; Equivalent OS

NCI (Yang, JCO 1998)
- LSS alone vs LSS + RT
- Improved local control with RT; Equivalent OS

MSKCC (Harrison, IJROBP 1993)
- LSS alone vs LSS + BRT (brachytherapy)
- Improved local control with BRT; Equivalent OS
NCI Randomized Trial: Local Control (all pts)

Radiation

No Radiation

P₂ = .0001
MSKCC Randomized Trial: Local Control (all pts)

Brachytherapy

No Brachytherapy

Tick mark (I) indicates last follow-up

- Brachytherapy (78 Pts. 65 Censored)
- No Brachytherapy (86 Pts. 61 Censored)

p = 0.04
Treatment Technique
Principles of RT Planning

• **Determine appropriate patient position**
  – Reproducible
  – Patient comfort
  – Supine, neutral positions preferred
    • Exceptions: tumors of back, prone

• **Rigid immobilization (custom cast)**
  – Immobilize foot for LE, hand for UE
Principles of RT Planning

• Position patient keeping in mind:
  – Spare strip of limb circumference (<20 Gy)
  – Minimize dose to bone and joint
  – Minimize subcutaneous hot spots
Immobilization
Immobilize Hand for UE

Immobilize Foot for LE

Note supine, neutral, comfortable positions
Treatment Volumes
Pre-op RT Volumes

GTV

- Use MR T1 post-gadolinium images
Pre-op RT Volumes

GTV

- Use MR T1 post-gadolinium images

CTV

- Expand GTV per guidelines
- Include T2 peri-tumoral edema if feasible
RT Volume for Pre-op RT

**CTV**
- GTV + 4 cm proximal/distal,
- 1.5 cm radial
- Edit CTV at bone

**PTV**
- CTV + 5-10mm per institutional standard

*Haas, IJROBP 2012; 84:572*
EXAMPLE:
Target Volumes, Dose Distributions
7 x 6 x 7 cm G3 leiomyosarcoma deep to L gluteal muscles

MR: Axial T1 post-gadolinium

Coronal T1 post-gadolinium
GTV, CTV, PTV
IMRT Isodose Distributions

- Conformal
- Spare
  - hip joint
  - subcutaneous tissue
Reduced RT Volume for Pre-op RT
RTOG 0630*

• Prospective, multi-center Phase II trial
• 50 Gy pre-op RT
• Daily image guidance: kV, MV or CBCT

*Wang JCO 33:2231; 2015
Reduced RT Volume for Pre-op RT
RTOG 0630*

IGRT to reduced target volume

- G2/3, tumor ≥ 8cm:
  - CTV sup/inf margins 3cm, radial 1.5 cm
  - Also cover edema on T2 MR

- G2/3, tumor < 8cm
  - CTV sup/inf margins 2cm, radial 1 cm
  - Also cover edema on T2 MR
Reduced RT Volume for Pre-op RT
RTOG 0630

- 79 patients, 57 assessed for 2-yr late toxicity
- Median FU 3.6 yrs
- 84% Grade 2/3
- 75% IMRT, 25% 3D
Reduced RT Volume for Pre-op RT

RTOG 0630

- 79 patients, 57 assessed for 2-yr late toxicity
- Median FU 3.6 yrs
- 84% Grade 2/3
- 75% IMRT, 25% 3D

2 yr Local Control: 94% (all LF were within CTV)

> Grade 2 late toxicity: 10.5%

Compared to 37% for NCIC pre-op arm

Fibrosis 5.3%, Joint Stiffness 3.5%, Edema 5.3%
Reduced RT Volume for Pre-op RT
RTOG 0630

Authors’ Conclusion:
“The significant reduction of late toxicities and absence of marginal-field recurrences suggest the target volumes used in RTOG-0630 are appropriate for pre-op IGRT for extremity STS”

This may be practice changing, confirmatory data are awaited
RT Volumes for Post-op RT
RT Volumes for Post-op RT

First Course-
• Contour GTV and operative bed
• CTV = op bed + 1.5 cm radially, 4 cm longitudinally

Cone Down
• CTV = GTV + 1.5 cm radially and 2 cm longitudinally

CTV to PTV expansion = 5-10 mm

*Haas, IJROBP 84:572; 2012
RT Doses

Pre-operative RT (2 Gy)
- Pre-operative volume: 50 Gy

Post-operative RT (1.8 - 2 Gy)
- First Course: 45-50.4 Gy
- Cone Down: 16-20 Gy
- Total Dose: 60-66 Gy
Post-op Dose and Margins

Positive Margins (M+) \(\rightarrow\) higher LR

DeLaney, (MGH) IJROBP, ’07

For patients with positive margins:

<table>
<thead>
<tr>
<th>Dose</th>
<th>5-yr Local Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose &gt; 64 Gy</td>
<td>85%</td>
</tr>
<tr>
<td>Dose &lt; 64 Gy</td>
<td>66% p&lt;.05</td>
</tr>
</tbody>
</table>

• We recommend 66-68 Gy
Post-op Dose and Margins

Negative Margins

• I give 63 Gy

• 60-66 Gy is acceptable
Pre-op vs Post-op RT
Pre-op vs Post-op RT: Dose + Volume

PRE-OP RT
Lower Dose: 50 Gy
Smaller Irradiated Volume: CTV = GTV + 4 cm longitudinal margins

POST-OP RT
Higher Dose: 60-66 Gy
Larger Irradiated Volume: CTV = operative bed + 4 cm longitudinal margins
Pre-op vs Post-op RT: Efficacy

EQUIVALENT

• Several non-randomized trials have shown similar local control rates

• Canadian RCT* 7 yr update showed:
  – Similar LC rates (92%, 93%)
  – Similar DFS and OS rates

Pre-op vs Post-op RT: Toxicities

DIFFERENT

PRE-OP

• More acute wound complications
  (35% vs 17%*)
• Usually reversible

POST-OP

• More long-term edema, fibrosis, decreased ROM
• Usually irreversible

*O’ Sullivan Lancet 2002;359:2235
Pre-op vs Post-op RT

• Equivalent efficacy
• Different Toxicities
• Treatment approach should be individualized
• We prefer Pre-op RT for most situations
  – lower dose, smaller treatment volume \(\rightarrow\) less irreversible long-term toxicity
RT Technique: 3D vs IMRT
IMRT

Goals:

• Maintain or improve local control rates achieved with 3D

• Reduce morbidities
  – Edema, joint stiffness, fibrosis, wound complications, fracture, etc
## Local Control Rates for Modern Series
### 3D Conventional and IMRT: Similarly Excellent

<table>
<thead>
<tr>
<th>Study</th>
<th>5-yr LR</th>
<th>RT Modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCIC RCT, 2004</td>
<td>6%, 7%</td>
<td>3D (100%)</td>
</tr>
<tr>
<td>O’ Sullivan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BWH/DFCI, 2013</td>
<td>10%</td>
<td>3D (84%)</td>
</tr>
<tr>
<td>Baldini</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSKCC, 2014</td>
<td>15.1%</td>
<td>3D (100%)</td>
</tr>
<tr>
<td>Folkert</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MGH, 2010</td>
<td>11.5%</td>
<td>3D (88%)</td>
</tr>
<tr>
<td>Kim</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PMH, 2013</td>
<td>11.8%</td>
<td>IMRT (flap sparing, 100%)</td>
</tr>
<tr>
<td>O’ Sullivan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSKCC, 2014</td>
<td>7.6%</td>
<td>IMRT (100%)</td>
</tr>
<tr>
<td>Folkert</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RTOG 0630, 2015</td>
<td>11.4%</td>
<td>IMRT (75%)</td>
</tr>
<tr>
<td>Wang</td>
<td>(2-yr)</td>
<td></td>
</tr>
</tbody>
</table>
Comparison of Local Control: 3D vs IMRT

- MSKCC retrospective series
- 1996-2010

<table>
<thead>
<tr>
<th></th>
<th>3D RT</th>
<th>IMRT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>154</td>
<td>165</td>
</tr>
<tr>
<td>Median FU</td>
<td>90 mos</td>
<td>42 mos</td>
</tr>
<tr>
<td>5-yr LR</td>
<td>15.1%</td>
<td>7.6%</td>
</tr>
</tbody>
</table>

Folkert JCO 2014;32:3236
Comparison of Local Control: 3D vs IMRT

• Multivariate analysis: IMRT independent favorable predictor for LC
  – HR for LR 0.46, p=0.02

• Patients who received IMRT had more unfavorable features:
  – older, more high grade tumors, close/positive margins, and nerve manipulation
## Late Toxicity Results

<table>
<thead>
<tr>
<th>Institution</th>
<th>PMH*</th>
<th>MSKCC**</th>
<th>RTOG 0630&amp;</th>
<th>Pre-op Arm NCIC#</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Modality</td>
<td>100% IMRT (sparing flap)</td>
<td>100% IMRT (79% post-op)</td>
<td>75% IMRT</td>
<td>100% 3D</td>
</tr>
<tr>
<td>&gt; Grade 2:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subcutaneous Fibrosis</td>
<td>9.3%</td>
<td>NS</td>
<td>5.3%</td>
<td>31.5%</td>
</tr>
<tr>
<td>Joint Stiffness</td>
<td>5.6%</td>
<td>14.5%</td>
<td>3.5%</td>
<td>17.8%</td>
</tr>
<tr>
<td>Edema</td>
<td>11.1%</td>
<td>7.9%</td>
<td>5.3%</td>
<td>15.1%</td>
</tr>
</tbody>
</table>

• Use of IMRT may be the main reason for reduced toxicity

*O’ Sullivan Cancer 2013, 119:1878; **Folkert JCO 2014, 32(29):3236
3D vs IMRT

• Local control is at least similar and may be better with IMRT

• Late toxicities appear to be lower with IMRT
Treatment Complications
Wound Complications: NCI Canada randomized trial

Major Wound Complications

<table>
<thead>
<tr>
<th>Pre-op RT (31/88)</th>
<th>35%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-op RT (16/94)</td>
<td>17% p=0.01</td>
</tr>
</tbody>
</table>

O’ Sullivan Lancet 2002;359:2235
# Wound Complications: NCI Canada randomized trial

## Major Wound Complications

<table>
<thead>
<tr>
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<th>Pre-op RT (31/88)</th>
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</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>17%     p = 0.01</td>
</tr>
</tbody>
</table>

## Predictors for Wound Complication (MVA):

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-op RT</td>
<td>3.08</td>
<td>.004</td>
</tr>
<tr>
<td>Size &gt; 10cm</td>
<td>1.11</td>
<td>.0005</td>
</tr>
<tr>
<td>LE vs UE</td>
<td>10.4</td>
<td>.03</td>
</tr>
</tbody>
</table>
## Wound Complications

Dana Farber/Brigham and Women’s

| Major Wound Complications | 35% |

### Predictors for Wound Complication (MVA):

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>5.6</td>
<td>.03</td>
</tr>
<tr>
<td>Size &gt; 10cm</td>
<td>6.2</td>
<td>.001</td>
</tr>
<tr>
<td>Tumor &lt; 3mm from skin</td>
<td>3.9</td>
<td>.03</td>
</tr>
<tr>
<td>Vascularized flap</td>
<td>6.4</td>
<td>.002</td>
</tr>
</tbody>
</table>

Baldini Ann Surg Oncol 2013; 20:1494
### Pre-op vs Post-op RCT: Late Effects

NCI Canada randomized trial

<table>
<thead>
<tr>
<th>Condition</th>
<th>Post-op RT</th>
<th>Pre-op RT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrosis</td>
<td>48%</td>
<td>32%</td>
<td>0.07</td>
</tr>
<tr>
<td>Edema</td>
<td>23%</td>
<td>15%</td>
<td>NS</td>
</tr>
<tr>
<td>Joint Stiffness</td>
<td>23%</td>
<td>18%</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Davis Radiother Oncol 2005, 75:48*
Pre-op vs Post-op RCT: Late Effects
NCI Canada randomized trial

<table>
<thead>
<tr>
<th>&gt;= Grade 2</th>
<th>Post-op RT</th>
<th>Pre-op RT</th>
<th>p-value</th>
</tr>
</thead>
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<tr>
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<td>Joint Stiffness</td>
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<td>18%</td>
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</tr>
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Larger field size correlated with:

- fibrosis ($p<0.01$), joint stiffness ($p<0.01$), & edema ($p=0.06$)
Bone Fracture: MSKCC

- 205 pts w/ STS of thigh treated with S + RT
- 9 pts (0.04%) developed femur fracture

Risk factors for fracture:
- Periosteal stripping (5-yr fracture rate: 29%)
- Female gender
- Chemotherapy

Lin, Cancer 1998, 82:2356
Bone Fracture: Princess Margaret

74 LE STS Matched pair analysis

Lower risk of bone fracture if:

- V40 < 64%
- Mean bone dose < 37 Gy
- Max bone dose < 59 Gy

Dickie IJROBP, 2009: 75:1119
Retroperitoneal Sarcoma (RPS)
Patterns Of Failure:
- Predominantly LR: 50-80%
- DR to liver and lung

Poor Outcome:
- 5-yr OS ~ 30-60%
RPS

• Difficulties of Surgery
  – Proximity to critical organs, major neurovascular structures
  – “Radical (R0) resection” very difficult

• Difficulties of RT
  – Large tumor size
  – Normal tissue sensitivities
CT of Retroperitoneal Liposarcoma
Favorable Prognostic Factors

• Complete resection (R0)
• Low grade
• Primary presentation (vs recurrent)
RPS

• Surgery is mainstay and only curative treatment

• Roles of RT and CT unproven

• No series of randomized trials to guide treatment
  – One randomized trial (IORT)
Is there a role for Radiation?

• Non-randomized trials have assessed post-op RT, pre-op RT, +/- IORT or BRT

• Some suggest a benefit with RT, but none are definitive

• … There is no clear role for RT
NCDB Case-Control Analysis

- 9,068 pts National Cancer Data Base
- Primary RPS: pre-op RT, post-op RT, no RT
- Case-control propensity score-matched analysis

*Nussbaum, Lancet Oncol 2016; 17(7):966*
NCDB Case-Control Analysis

- 9,068 pts National Cancer Data Base
- Primary RPS: pre-op RT, post-op RT, no RT
- Case-control propensity score-matched analysis

- Both pre-op RT and post-op RT associated with significant survival benefits
  - Pre-op RT: HR 0.70 (p<0.0001)
  - Post-op RT: HR 0.78 (p<0.0001)

*Nussbaum, Lancet Oncol 2016; 17(7):966
NCDB Case-Control Analysis

Limitations

- Retrospective, possible selection bias
- No details about resections
- No data for LR
- No data for histologic sub-types

*Nussbaum, Lancet Oncol 2016; 17(7):966*
Variability in Patterns of Recurrence after Resection of Primary RPS

• N = 1,007 pts
• Resection RPS by high volume surgeons
• 8 Sarcoma Centers
• Use of RT/CT variable (18%, 32%)

Findings for RT

• N = 1,007 patients

• Multivariate analysis:
  – Reduced local recurrence for RT
    HR 0.58, p< 0.001

• No difference in DR, OS with RT

• Same limitations (retrospective, etc)

Randomized Trial for Pre-op RT
EORTC 62092 (STRASS)

• Accrual recently completed (n=256)
Current Standard of Care: RPS

- Definitive resection– only proven treatment
- Many centers: no RT, pre-op RT
- Few centers: post-op RT, CT
Radiation Therapy for RPS

Extrapolating from extremity data …

• Equivalent efficacy for:
  
  50 Gy pre-op RT  
  60-66 Gy post-op  

  (Tolerable for RP)  
  (Too toxic for RP)

• If RT is given, most prefer pre-op RT

• Post-op RT is discouraged
Post-op RT for RPS is discouraged by Expert RT and Surgeon Panels*

- **Too toxic**
  - To give effective dose (60-66 Gy)
  - A lot of normal tissue falls into RT field

- **If lower tolerable doses are given**
  - Likely not effective
  - May render future surgery, RT more difficult

---

Since Many Centers Give Pre-op RT, How Should it be Delivered?

• There were no standard guidelines

• An expert panel was convened to develop guidelines

Baldini  IJROBP 2015; 92:603
CTV Definition

Perform 4D CT for tumors above iliac brim
Expand GTV-4D symmetrically by 1.5 cm
CTV Definition

Perform 4D CT for tumors above iliac brim

Expand GTV-4D symmetrically by 1.5 cm

Edit CTV:

• Bone, RP Compartment, Kidney, Liver: 0 mm
• Bowel and Air Cavity: 5 mm
• Skin Surface: 3-5 mm
• If tumor extends through inguinal canal, add 3 cm distally (as per extremity STS)
Dose

50 – 50.4 Gy

1.8 - 2 Gy fractions
RPS Contours

Uniform
1.5 cm expansion (green)

Edits along bowel, vertebral body, RP cavity (blue)

Final CTV (blue)
Dose-Painting Boost to High Risk Margins

CONCEPT:

• Deliver boost to areas at risk for positive margins after resection

• Along posterior abdominal wall, para-vertebral space, major vessels
Dose-Painting Boost to High Risk Margins

• Efficacy is unproven
• Technique is under investigation
• **Consensus recommendation:** best considered only on protocol or by experienced centers
Bowel Constraint: Dana-Farber/BWH/MGH

- 56 pts treated with pre-op RT for RPS
- Delivered doses to bowel bag compared to constraints in literature (GI/GYN)
  - 75% exceeded constraint: V15 > 830 cc
  - 70% exceeded constraint: V25 > 650 cc
  - 75% exceeded constraint: V45 > 195 cc

Mak, Pract Radiat Oncol 2016; 6:360
Bowel Constraint: Dana-Farber/BWH/MBH

- 56 pts treated with pre-op RT for RPS
- Delivered doses to bowel bag compared to constraints in literature (GI/GYN)
  - 75% exceeded constraint: V15 > 830 cc
  - 70% exceeded constraint: V25 > 650 cc
  - 75% exceeded constraint: V45 > 195 cc
- Acute GI toxicity: \( \geq \) Grade 3: 5%
- Above constraints likely too conservative

Mak, Pract Radiat Oncol 2016; 6:360
As we seek to optimize treatment for RPS

Important to recognize “RPS” is a group of diseases with distinct behaviors
RPS: Histologies (2,025 cases)

- Malignant Peripheral Nerve Sheath Tumor
- Solitary Fibrous Tumor
- Leiomyosarcoma
- Dedifferentiated Liposarcoma
- Well differentiated Liposarcoma

Tan Ann Surg 2016;263:593-600;
Two Important Papers* in *Annals of Surgery*, 2016

Histologic sub-type is the dominant predictor of patterns of recurrence for RPS following resection

- Dedifferentiated liposarcoma (DD LPS)
- Well differentiated liposarcoma (WD LPS)
- Leiomyosarcoma (LMS)

Tan Ann Surg 2016;263:593
Overall Survival by Histology

8-yr Overall Survival
WD LPS: ~85%
DD LPS G1-2: ~50%
LMS: ~45%
DD LPS G3: ~30%

Local Recurrence by Histology

8-yr Local Recurrence
DD LPS G1-2: ~48%
DD LPS G3: ~37%
WD LPS: ~35%
constant rate of LR

LMS: ~10%

Distant Recurrence by Histology

8-yr Distant Recurrence

LMS: ~50%

DD LPS G3: ~32%

DD LPS G1-2: ~9%

WD LPS: ~0%

Both Studies Show:

• **WD LPS**
  - Constant LR, high over time, despite this
  - High survival, low DR

• **LMS**
  - Low LR
  - Lowest survival, highest DR

• **DD LPS**
  - Outcomes in between WD LPS and LMS
  - Moderate LR, DR, Survival
Going forward,

- We should tailor RPS treatment strategies to histologic sub-type, grade and other patient factors

- Prospective studies should stratify by histology
Conclusions
Extremity/Trunk
RT Indications

Low Grade Sarcomas (G1)

• Locally recurrent
• Positive margins
• Locations not amenable to salvage surgery
RT Indications

Low Grade Sarcomas (G1)
• Locally recurrent
• Positive margins
• Locations not amenable to salvage surgery

High Grade Sarcomas (G2/3)
• Most extremity/truncal lesions unless on protocol for treatment with surgery alone
RT Technique

• Careful, reproducible immobilization

• GTV → CTV expansion:
  – 4 cm longitudinal (perhaps soon 3cm)
  – 1.5 cm radial

• Pre-op or Post-op RT acceptable
  – Associated with different morbidities
  – Wound complications vs fibrosis, edema
  – (Most prefer pre-op)
3D-CRT vs IMRT

• Both acceptable, IMRT preferred
  – Similar Efficacy (maybe IMRT is better)
  – Probably less toxicity with IMRT
Complications

Wound Complication Risk Factors
- Pre-op RT, lower extremity, large tumor, large field size, tumor <3mm from skin, flap closure

Bone Fracture Risk Factors
- Periosteal stripping, chemo, high dose

Fibrosis, Edema, Joint Stiffness
- Large field size, high dose, post-op RT
Conclusions

Retroperitoneum
Standard of Care for RPS:
• Best attempt at R0 resection

Role of RT: unproven
• Best assessed on trial (EORTC)

If RT Given off Trial → Give Pre-op
• Follow expert consensus guidelines
  – 50 Gy; CTV: GTV-4D + 1.5cm margins
• Boost to high risk margins best on protocol
• Post-op RT is discouraged
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