Soft Tissue Sarcoma

Principles of Radiotherapy & Toxicity

Dr SAJAL KAKKAR

MD, FUICC (USA), FAROI (Fr)

Director, Radiation Oncology

Max Super Speciality Hospital, Mohali

The Sarcomas

- Osteosarcoma
- Ewing's family of tumors
  - Ewing's sarcoma of bone and soft tissue
  - Peripheral Primitive neuroectodermal tumor
- Soft tissue sarcomas
  - Non-rhabdomyosarcoma STS
  - Rhabdomyosarcoma
    - Embryonal rhabdomyosarcoma
    - Alveolar rhabdomyosarcoma
    - Other variants

Natural History

- **50% in extremities, 30% intraabdominal**
- **Intra compartmental extension**
- **Centrifugal growth**
- **Pseudocapsule formation**

- **Hematogenous metastases (Lung, bone, liver)**
- **Lymphatic Spread**
  (14%-20% risk in Synovial, Epithelliod, Angiosarcoma, ERMS)

Work -Up

Family History

Prior therapeutic irradiation

Size

Location

Distal Neurovascular deficits

Biopsy

- **Incisional (preferred) or Tru-cut**
- **Site and Technique**

Work -Up

Imaging

MRI

CT Chest

FDG PET

- **Sarcoma vs Benign tumor**
- **Low grade vs High grade**
- **To plan biopsy**
- **Response to chemotherapy**
- **Detection of recurrence**

Treatment

- Surgical Oncologist
- Radiation Oncologist
- Medical Oncologist
- Rehabilitation

Surgery

Organ Preservation

Negative margins

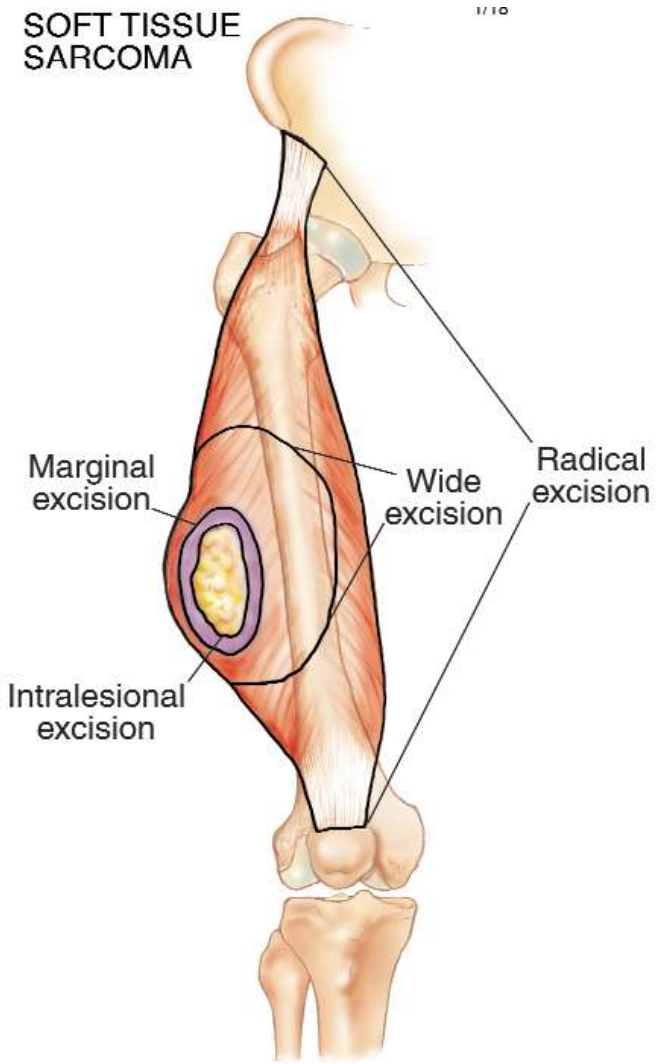
Surgery

Intralesional

Marginal

Wide Excision

Radical Excision



Radiation Therapy

- Indications
- Pre-op vs Post-op
- EBRT/Brachytherapy/IORT
- RT Planning/Dose

PERGAMON

European Journal of Cancer 39 (2003) 1872–1880

European Journal of Cancer

www.ejconline.com

Does adjuvant radiation therapy increase loco-regional control after optimal resection of soft-tissue sarcoma of the extremities?

K. Khanfir[a], L. Alzieu[b], P. Terrier[c], C. Le Péchoux[a], S. Bonvalot[d], D. Vanel[e], A. Le Cesne[f,*]

[a]*Department of Radiotherapy, Institut Gustave Roussy, Villejuif 94805, France*

Retrospective Analysis (1975-96)

133 pts – 52% PORT, 48% no RT

mR < 10mm, oR >10mm

Local Control

Better in RT arm, p=0.01

Trend for superficial STS, p=0.06

RT beneficial in mR

No benefit in oR

Survival

Tumor Grade

No influence of RT

Adjuvant RT indicated in close margin status
? Role in negative margins

Khanfir et al, Eur J Cancer 2003

Long-Term Outcomes in Extremity Soft Tissue Sarcoma After a Pathologically Negative Re-resection and Without Radiotherapy

METHODS. A review of the prospective sarcoma database identified 200 patients with primary, nonmetastatic, extremity STS treated with limb-sparing surgery between June 1982 and December 2002 who had a pathologically confirmed negative re-resection. None of the patients had adjuvant RT. Univariate and multivariate analyses were performed to determine clinicopathologic factors associated with LR.

RESULTS. With a median follow-up of 82 months the 5-year actuarial LR rate was 9%. Factors associated with higher LR rates on univariate and multivariate analysis were older age, stage III presentation, and histology. The 5-year LR rate was 5% for those <50 compared with 15% for those ≥50 ($P = .001$). For patients with stage III the LR rate was 26% versus 7% for those with stage I/II ($P < .001$). On multivariate analysis only age ≥50 (relative risk [RR] 3.3; $P = .02$) and stage III disease (RR 3.4; $P = .01$) remained significant predictors for LR. When the cohort of patients was divided into 3 groups based on the number of risk factors present, the 5-year LRs were as follows: no risk factors (stage I/II and <50 years old) 4%, 1 risk factor (stage III or ≥50) 12%, and 2 risk factors (stage III and ≥50) 31% ($P < .01$).

T size> 5cm, Age>50yrs predictors of local rec

MSKCC Group, Cancer 2008

Randomized Prospective Study of the Benefit of Adjuvant Radiation Therapy in the Treatment of Soft Tissue Sarcomas of the Extremity

By James C. Yang, Alfred E. Chang, Alan R. Baker, William F. Sindelar, David N. Danforth, Suzanne L. Topalian, Thomas DeLaney, Eli Glatstein, Seth M. Steinberg, Maria J. Merino, and Steven A. Rosenberg

91 pts, high grade lesions
RT – 47 pts
No RT – 44 pts

Median f/u 9.6 yrs

Significant decrease in local rec, p=0.028

No OS difference

50 pts, low grade lesions
RT – 26 pts
No RT – 24 pts

Median f/u 9.6 yrs

Lower probability of local rec

Prospective QOL assessment

Significantly lower functional parameters in RT arm (ms edema, strength, joint motion)

RT improves local control rates in high grade sarcoma
RT may lead to lower QOL in short term

Yang JC, JCO 1998

Long-Term Results of a Prospective Randomized Trial of Adjuvant Brachytherapy in Soft Tissue Sarcoma

By Peter W.T. Pisters, Louis B. Harrison, Denis H.Y. Leung, James M. Woodruff, Ephraim S. Casper, and Murray F. Brennan

164 pts, extremity or superficial trunk sarcoma

Localised, completely resected

No major bone or neurovascular resection

No violation of tumor during surgery

BRT OR no BRT

Technique

2cm isotropic margin

Afterloading catheters

42Gy-45Gy, 4-6 days

Median f/u 6yrs:

Significant local control in BRT arm, p=0.04

Significant local control in high grade lesions, p=0.0025

No difference in low grade lesions

No OS difference

Local control benefit in high grade lesions
Simple, convenient, short course treatment

Peter WT et al, JCO 1996

RT Indications

High Grade

Stage II/III tumors

Margins close (<1cm)

Histology (Myxofibrosarcomas, Myxoid LPS)

When NOT to give?

- **Low grade, T size< 5cm, superficial tumor with wide margins**
- **Unplanned excisions or non-oncologic resections**

What is adequate margin?

- Lack of consensus
- Variability of site, feasibility of wide negative margins
- Close margin at periosteum, fascia vs muscle, adipose tissue, skin

R1/R2 resection – always discuss with the surgeon for re-resection and negative margins

Close or positive margins near critical structure (major nerve, vessel, bone) warrants RT

RT Timing

Preoperative

Advantages:
Decreased risk of i/o seeding
Smaller target volume
Reduced risk of late tox
Tumor shrinkage

Disadvantages:
Delay of Sx
Major wound complications

Post operative

Advantages:
Accurate HPE
Immediate surgery
No wound healing complications

Disadvantages:
Large treatment volumes
Irreversible S/E – lymphedema, fibrosis
Decreased range of motion, fracture

Preoperative versus postoperative radiotherapy in soft-tissue sarcoma of the limbs: a randomised trial

Lancet 2002

Brian O'Sullivan, Aileen M Davis, Robert Turcotte, Robert Bell, Charles Catton, Pierre Chabot, Jay Wunder, Rita Kandel, Karen Goddard, Anna Sadura, Joseph Pater, Benny Zee

190 pts, b/w 1994-97

Non-metastatic extremity sarcoma

Primary end point – Major wound complication

Sx & RT 3-6 weeks apart

RT – 50Gy+/- 16-20Gy

Median f/u 3.3yrs

O'Sullivan et al, Lancet 2002

	Preoperative (n=88)	Postoperative (n=94)
Wound complications*		
Yes	31 (35%)	16 (17%)
Secondary operation for wound repair	14 (45%)	5 (31%)
Invasive procedure for wound management†	5 (16%)	4 (25%)
Deep wound packing deep to dermis in area of wound at least 2 cm with or without prolonged dressings >6 weeks from wound breakdown‡	11 (35%)	7 (44%)
Readmission for wound care§	1 (3%)	0
No complications	57 (65%)	78 (83%)

More wound complications in pre-op group, p=0.01

Most complications in thigh pts

No difference in local rec or PFS rates

Higher risk of wound complications in preoperative RT
Similar local control rates

O'Sullivan et al, Lancet 2002

Radiotherapy and Oncology 75 (2005) 48–53
www.elsevier.com/locate/radonline

Phase III randomised trial

Late radiation morbidity following randomization to preoperative versus postoperative radiotherapy in extremity soft tissue sarcoma

Aileen M. Davis[a,j,*], Brian O'Sullivan[b,j], Robert Turcotte[c], Robert Bell[b,d,j],

129 pts evaluated for late toxicities
Jt. Stiffness, edema, fibrosis at 2 yrs
EORTC/RTOG Criteria
Musculoskeletal Tumor Rating Scale (MSTS)
Toronto Extremity Salvage Score (TESS)

≥ Grade 2 Toxicity	Joint Stiffness	Edema	Subcut.Fibrosis
Pre-op RT	17.8%	15.1%	31.5%
Post-op RT	23.2%	23.1%	48.2%, p=0.07

- **Significantly lower function scores on MSTS/TESS in > Grade 2 toxicities**
- **Field size sig. predictor for fibrosis and joint stiffness**

Phase 2 Study of Preoperative Image-Guided Intensity-Modulated Radiation Therapy to Reduce Wound and Combined Modality Morbidities in Lower Extremity Soft Tissue Sarcoma

Cancer 2013

Brian O'Sullivan, MD[1,2]; Anthony M. Griffin, MSc[3]; Colleen I. Dickie, MSc[1]; Michael B. Sharpe, PhD[1,2]; Peter W. M. Chung,

Phase II prospective study, 2005-09
70 pts, lower extremity STS
Pre-op IG-IMRT
Pri. End Point – Acute wound complication (WC)

IG-IMRT reduces the risk & severity of WCs

Dose: 50Gy/25 frs
RT Avoidance – skin & s/c tissue required to close future resection site (virtual skin flap)

Results –
30.5% developed WCs vs 42% in Canada SR2 trial
93% primary closure vs 71%
33% secondary Sx for WC vs 43%

VOLUME 33 · NUMBER 20 · JULY 10 2015

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Significant Reduction of Late Toxicities in Patients With Extremity Sarcoma Treated With Image-Guided Radiation Therapy to a Reduced Target Volume: Results of Radiation Therapy Oncology Group RTOG-0630 Trial

Dian Wang, Rush University Medical Center, Chicago, IL; Qiang Zhang, NRG Oncology Statistics and Data Manage-

Dian Wang, Qiang Zhang, Burton L. Eisenberg, John M. Kane, X. Allen Li, David Lucas, Ivy A. Petersen,

Phase II prospective study
79 pts, extremity STS
Pre-op IG-IMRT
Pri. End Point – RT morbidity at 2yrs (s/c fibrosis, edema, joint stiffness)
Margins:
•Int/High Grade Tm or T≥ 8cm: Longitudinal – GTV+3cm, radial – 1.5 cm
•Low Grade or T < 8cm - GTV+2cm, radial – 1 cm
Median fu 3.6 yrs

Results –
•5 local failures, all in-field
•10.5% at least one ≥ Grade 2 toxicity vs 37% in Canada SR2 trial
•26/71 pts at least one major WC, all in lower extremity and common in distal

Preoperative vs Postoperative RT

Localised extremity/truncal STS, pre-op RT is recommended over post-op RT

Initial surgery recommended in special situations like uncontrolled pain, bleeding, fungation followed by post-op RT

Following an unplanned excison, pre-op RT recommended before oncologic resection, where RT indicated

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RT Techniques

Key points

Compartmental Anatomy

Extent of tumor

Tumor behavior

Centrifugal spread, pathway of least resistance

Delineate scar, drain sites

Clip Placement

Natural Barriers –

Synovium, articular cartilage, periosteum,

tendinous origin & insertion of muscles

Poor Barriers –

Fat, muscles

Positioning

Comfortable

Reproducible

Assess multiple limb positions

Rotate the extremity to minimise dose to surrounding tissue

Mind the diameter of CT SIM bore

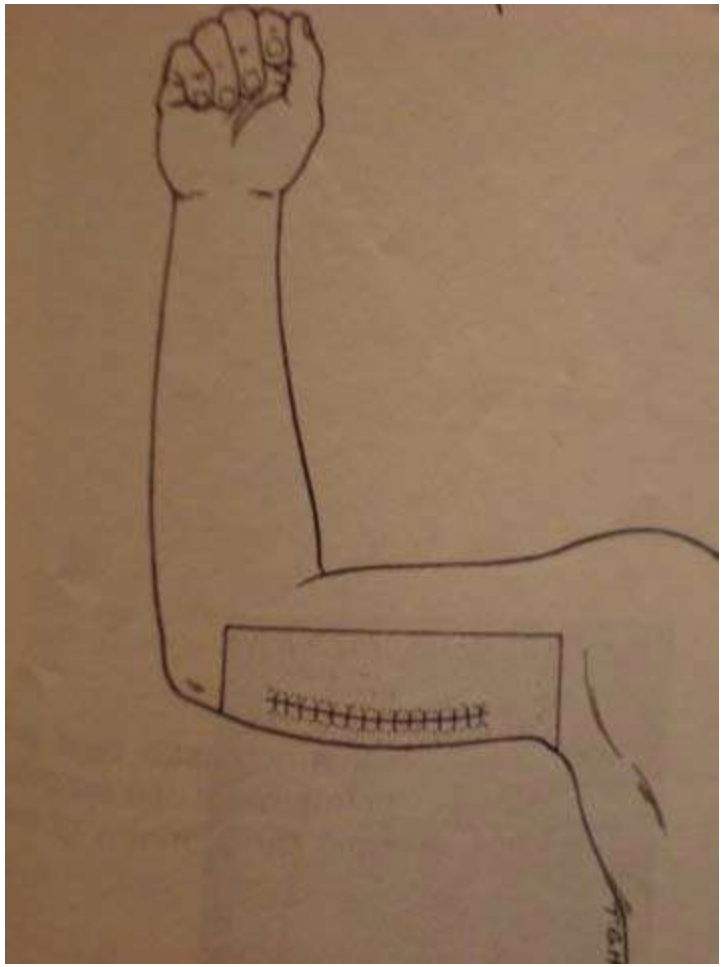
FROG-LEG position

Separates ant. Thigh from post. & medial compartments

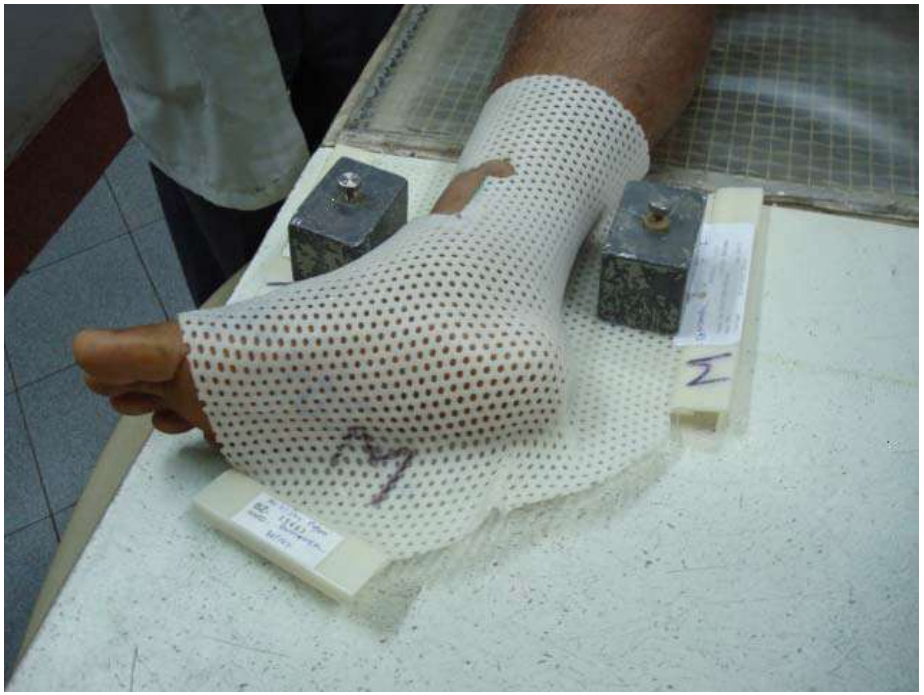
ARM

‘ THROWING ’ position
Shoulder 90 abduction & max ext rotation

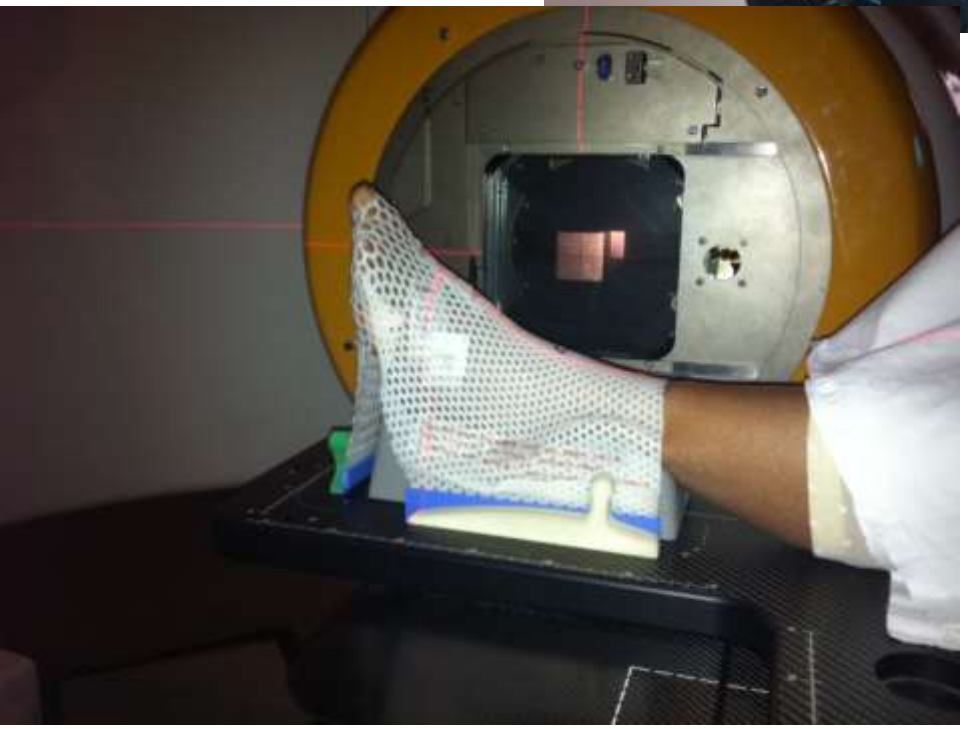
Adequately separates Biceps compartment from Triceps



POST-MEDIAL Compartment



2D Simulator Planning



Field Placements

Keep uninvolved compartment out of radiation portal

Avoid joints as far as possible

Spare half circumference of uninvolved bone

Spare at least 1.5 - 2.0cm of limb circumference

Margins not extend beyond natural barriers (Bone,fascial planes)

Cover surgical scar & drain sites

Pergamon

Int. J. Radiation Oncology Biol. Phys., Vol. 32, No. 4, pp. 977–985, 1995

0360-3016/95 $9.50 + .00

0360-3016(95)00111-5

● *Clinical Original Contribution*

CONSERVATIVE SURGERY AND ADJUVANT RADIATION THERAPY IN THE MANAGEMENT OF ADULT SOFT TISSUE SARCOMA OF THE EXTREMITIES: CLINICAL AND RADIOBIOLOGICAL RESULTS

ARNO J. MUNDT, M.D.,* AZHAR AWAN, M.D.,* GREGORY S. SIBLEY, M.D.,* MICHAEL SIMON, M.D.,† STEVEN J. RUBIN, M.D.,* BRIAN SAMUELS, M.D.,‡ WILLIAM WONG, M.D.,* MICHAEL BECKETT, B.S.,* S. VIJAYAKUMAR, M.B., B.S., D.M.R.T.* AND RALPH R. WEICHSELBAUM, M.D.*

*Department of Radiation and Cellular Oncology, University of Chicago/Michael Reese Hospitals,

Methods and Materials: Sixty-four consecutive adult patients with soft tissue sarcoma of the extremities (40 lower, 24 upper) who underwent conservative surgery and adjuvant irradiation (7 preoperative, 50 postoperative, 7 perioperative) between 1978 and 1991 were reviewed. The initial radiation field margin surrounding the tumor bed/scar was retrospectively analyzed in all postoperative patients. Initial field margins were < 5 cm in 12 patients, 5–9.9 cm in 32 and ≥ 10 cm in 6. Patients with negative pathological margins were initially treated with traditional postoperative doses (64–66 Gy); however, in later years the postoperative dose was reduced to 60 Gy. Thirteen cell lines were established prior to definite therapy, and radiobiological parameters (multitarget and linear-quadratic) were obtained and correlated with outcome.

Results: Postoperative patients treated with an initial field margin of < 5 cm had a 5-year local control of 30.4% vs. 93.2% in patients treated with an initial margin of ≥ 5 cm ($p = 0.0003$). Five-year local control rates were similar in patients treated with initial field margins of 5–9.9 cm (91.6%) compared with those treated with ≥ 10 cm margins (100%) ($p = 0.49$). While postoperative patients receiving < 60 Gy had a

Target Volumes

Table 6 Target delineation guidelines for extremity and superficial truncal STS target volumes[65,75,83,94]

Target	Delineation Guidance
Preop RT extremity or truncal CTV	CTV = GTV + 1.5 cm radial and 3-4 cm longitudinal anatomically constrained expansion with inclusion of peritumoral edema and biopsy tract (when feasible)
Preop RT subcutaneous tumor CTV (for tumor not involving fascia)	CTV = GTV + 3-4 cm circumferential margins with expansion of 0.5-1 cm into underlying non-involved muscle with inclusion of peritumoral edema and biopsy tract (when feasible)
Postop RT extremity or truncal CTV1	CTV1 = tumor bed (defined by clips/preop MRI) + 1.5 cm radial and 3-4 cm longitudinal anatomically constrained expansion + the operative field, surgical scar, and drain sites (when feasible)
Postop RT extremity or truncal CTV2	CTV2 = tumor bed (defined by clips/preop MRI) + 1.5 cm radial and 2 cm longitudinal expansion
Postop subcutaneous tumor CTV1	CTV1 = tumor bed (defined by clips/preop MRI) + 3-4 cm circumferential margins with expansion of 0.5-1 cm into uninvolved muscle + the operative field, scar, and drain sites (when feasible)
Postop subcutaneous tumor CTV2	CTV2 = tumor bed (defined by clips/preop MRI) + 1.5-2 cm circumferential margins and 0.5 cm into uninvolved muscle
Extremity or truncal PTV expansion	PTV expansion of 0.5 cm may be used with daily image guidance however >1.0 cm may be needed without daily image guidance. For preop RT, dose coverage to the PTV can be trimmed 3-5 mm from skin to reduce wound healing complications if achievable without unacceptable compromise of CTV coverage and if surgeon plans to resect overlying skin and subcutaneous tissue[73]

Abbreviations: CTV = clinical target volume; GTV = gross tumor volume; MRI = magnetic resonance imaging; preop = preoperative; postop = postoperative; PTV = planning target volume; RT = radiation therapy; STS = soft tissue sarcoma.

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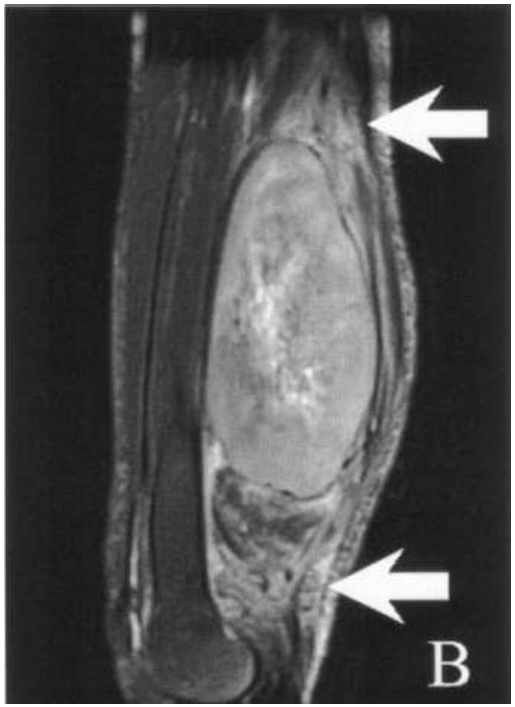
Defining The Target...

10-20% local recurrences after wide excision

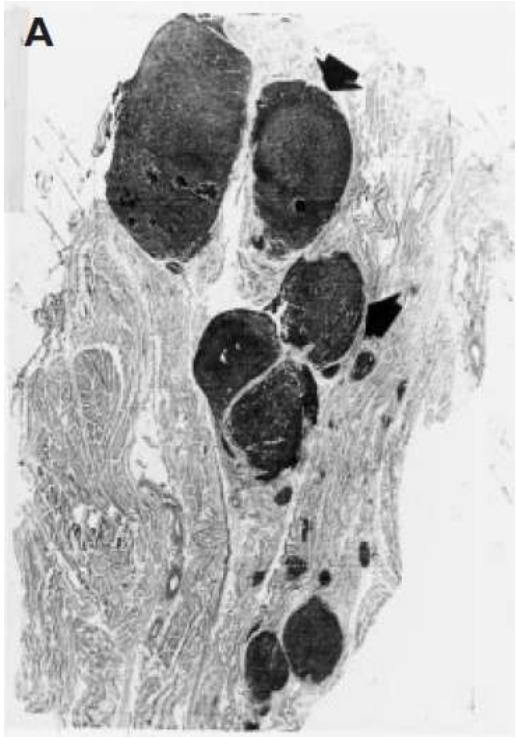
‘Reactive Zone’ or ‘Risk Zone’

region surrounding the lesion, situated between the tumor margin/pseudocapsule and more remote normal tissues

Radiologically, T2 weighted changes -> peritumoral edema



T2 w & T1 contrast MR scans



Section of high grade sarcoma with skip mets and intervening normal tissue

Int. J. Radiation Oncology Biol. Phys., Vol. 61, No. 3, pp. 1439–1445, 2005

0360-3016/05/$–see front matter
doi:10.1016/j.ijrobp.2004.08.036

CLINICAL INVESTIGATION Sarcoma

HISTOLOGIC ASSESSMENT OF PERITUMORAL EDEMA IN SOFT TISSUE SARCOMA

Lawrence M. White, M.D.,* Jay S. Wunder, M.D.,† Robe
Brian O'Sullivan, M.D.,‡ Charles Catton, M.D.,‡ Peter
Martin Blackstein, M.D., Ph.D.,§ and Rita A. Kan

Explains the reason for local relapse after Sx alone
Influences surgical/radiation margins
Cautious use of high precision techniques

Prospective study
15 pts, extremity/truncal STS, post Sx
Pre-op MRI: maximal extent of peritumoral edema measured
Soft tissue beyond the tumor sampled for path. assessment

Results:

- **Peritumoral edema/Reactive changes seen in MRI of all pts**
- **Extent: 0-7cm (mean 2.5 cm), mostly in sup-inf plane**
- **10/15 pts tumor cells beyond margin/pseudocapsule with intervening normal tissue in between**
- **6/10 such pts, tumor cells < 1cm from tumor margin and 4/10 pts > 1cm (max 4 cm)**

Satellite tumor cells seen in the region of edema as per MRI

cancers

MDPI

Article

Analysis of the Peritumoral Tissue Unveils Cellular Changes Associated with a High Risk of Recurrence

Cancers 2023

Audrey Michot [1,2,3,*], Pauline Lagarde [2,3], Tom Lesluyes [2], Elodie Darbo [1,3], Agnès Neuville [2], Jessica Baud [1],

Molecular profiling of pseudocapsule
To identify biomarkers to predict recurrence post surgery

Prospective study
20 pts of STS
Peritumoral tissue infiltrated with M2 macrophages & low in healthy tissue expression -> greater risk of relapse

Elective Nodal Radiation?

NO

Targets and OARs		
3. For patients with primary, localized extremity and truncal STS receiving preoperative RT, an anatomically constrained CTV is recommended. (Table 6)	Strong	Moderate 17,65,73,75
4. For patients with primary, localized extremity and truncal STS receiving postoperative RT, an initial dose to an anatomically constrained CTV1 and additional dose to a reduced volume CTV2 is recommended. (Table 6)	Strong	Moderate 17,88,94,95
5. For patients receiving either preoperative or postoperative RT for primary, localized extremity and truncal STS, volumetric contouring of the OARs and use of appropriate dose constraints are recommended.	Strong	Moderate 65,66,73,75,94,96,97
6. For patients with primary, localized extremity and truncal STS, elective nodal RT is **not** recommended.	Strong	Moderate 17,65,73,75,88,94,95

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Dose

Table 5 Dose-fractionation schedules and target volumes for EBRT in extremity and superficial truncal adult STS

KQ3 Recommendations	Strength of Recommendation	Quality of Evidence (refs)
Radiation Dose and Fractionation		
1. For patients with primary, localized extremity and truncal STS receiving preoperative RT, 5000 cGy in 25 once daily fractions is recommended.	Strong	Moderate [16,17,65,73,75]
2. For patients with primary, localized extremity and truncal STS receiving postoperative RT, 5000 cGy in 25 once daily fractions or 5040 cGy in 28 once daily fractions to CTV1 and additional dose to a reduced volume CTV2 is recommended. *(see Table 6 for target volume definitions)* Implementation remark: Additional dose to CTV2 of 1000 to 1600 cGy is used for negative margins and 1600 cGy for microscopic positive margins.	Strong	Moderate [11,17,50,88-93]

ASTRO Clinical Practice Guidelines, Pract Radiat Oncol 2021

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2023
Soft Tissue Sarcoma

NCCN Guidelines Index
Table of Contents
Discussion

Pre-op RT –
50-50.4 Gy
R1 resection – 14-20 Gy boost

Post –op RT –
Phase 1 : 50-50.4 Gy
Phase 2 : Tumor bed 10-20Gy

Unresectable Disease – 50 Gy + Boost till 63 Gy
(higher doses 70-80 Gy can be considered)

RT Complications

Fibrosis

Atrophy

Fracture

Decreased range of movements

Peripheral nerve injury

Dependent edema

Int. J. Radiation Oncology Biol. Phys., Vol. 75, No. 4, pp. 1119–1124, 2009

0360-3016/09/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2008.12.006

CLINICAL INVESTIGATION **Sarcoma**

BONE FRACTURES FOLLOWING EXTERNAL BEAM RADIOTHERAPY AND LIMB-PRESERVATION SURGERY FOR LOWER EXTREMITY SOFT TISSUE SARCOMA: RELATIONSHIP TO IRRADIATED BONE LENGTH, VOLUME, TUMOR LOCATION AND DOSE

COLLEEN I. DICKIE, B.SC., MRT(T)(MR),* AMY L. PARENT, B.SC., MRT(T),*
ANTHONY M. GRIFFIN, M.SC.,†‡ SHARON FUNG, M.SC.,§ PETER W. M. CHUNG, M.D., F.R.C.P.C.,*‡
CHARLES N. CATTON, M.D., F.R.C.P.C.,*‡ PETER C. FERGUSON, M.D., F.R.C.S.C.,†‡
JAY S. WUNDER, M.D., F.R.C.S.C.,†‡ ROBERT S. BELL, M.D., F.R.C.S.C.,†‡
MICHAEL B. SHARPE, PH.D.,*‡ AND BRIAN O'SULLIVAN, M.D., F.R.C.P.C.*‡

*Radiation Medicine Program, Princess Margaret Hospital, Toronto, ON, Canada; †Division of Orthopaedic Surgery, University Musculoskeletal Oncology Unit, Mount Sinai Hospital, Toronto, ON, Canada; ‡University of Toronto, Toronto, ON, Canada; and §Medical Biostatistics Department, The University Health Network, Toronto, ON, Canada

Methods and Materials: Of 691 LE-STS patients treated from 1989 to 2005, 31 patients developed radiation-induced fractures. Analysis was limited to 21 fracture patients (24 fractures) who were matched based on tumor size and location, age, beam arrangement, and mean total cumulative RT dose to a random sample of 53 nonfracture patients and compared for fracture risk factors. Mean dose to bone, RT field size (FS), maximum dose to a 2-cc volume of bone, and volume of bone irradiated to ≥40 Gy (V40) were compared. Fracture site dose was determined by comparing radiographic images and surgical reports to fracture location on the dose distribution.

Results: For fracture patients, mean dose to bone was 45 ± 8 Gy (mean dose at fracture site 59 ± 7 Gy), mean FS was 37 ± 8 cm, maximum dose was 64 ± 7 Gy, and V40 was 76 ± 17%, compared with 37 ± 11 Gy, 32 ± 9 cm, 59 ± 8 Gy, and 64 ± 22% for nonfracture patients. Differences in mean, maximum dose, and V40 were statistically significant ($p = 0.01$, $p = 0.02$, $p = 0.01$). Leg fractures were more common above the knee joint.

Conclusions: The risk of radiation-induced fracture appears to be reduced if V40 <64%. Fracture incidence was lower when the mean dose to bone was <37 Gy or maximum dose anywhere along the length of bone was <59 Gy. There was a trend toward lower mean FS for nonfracture patients.

Radiotherapy and Oncology 93 (2009) 125–130

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Radiotherapy and Oncology

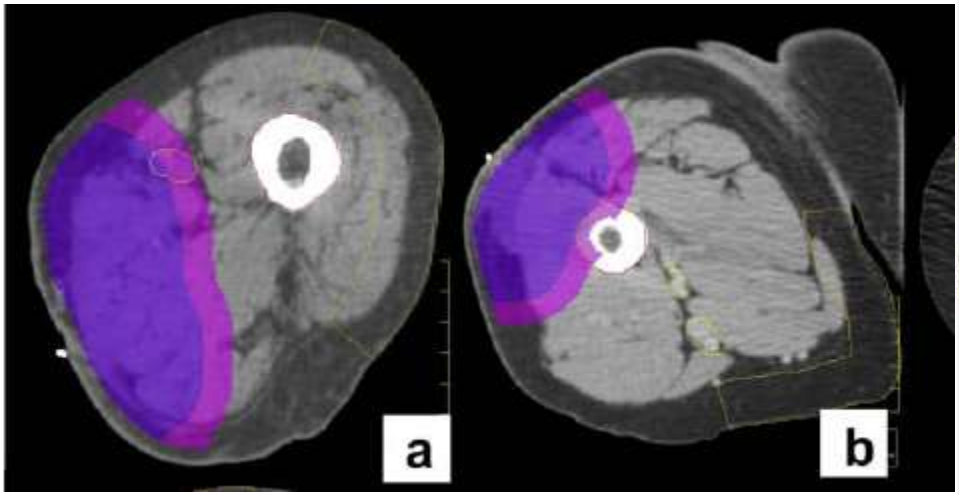
journal homepage: www.thegreenjournal.com

RT of soft tissue sarcoma

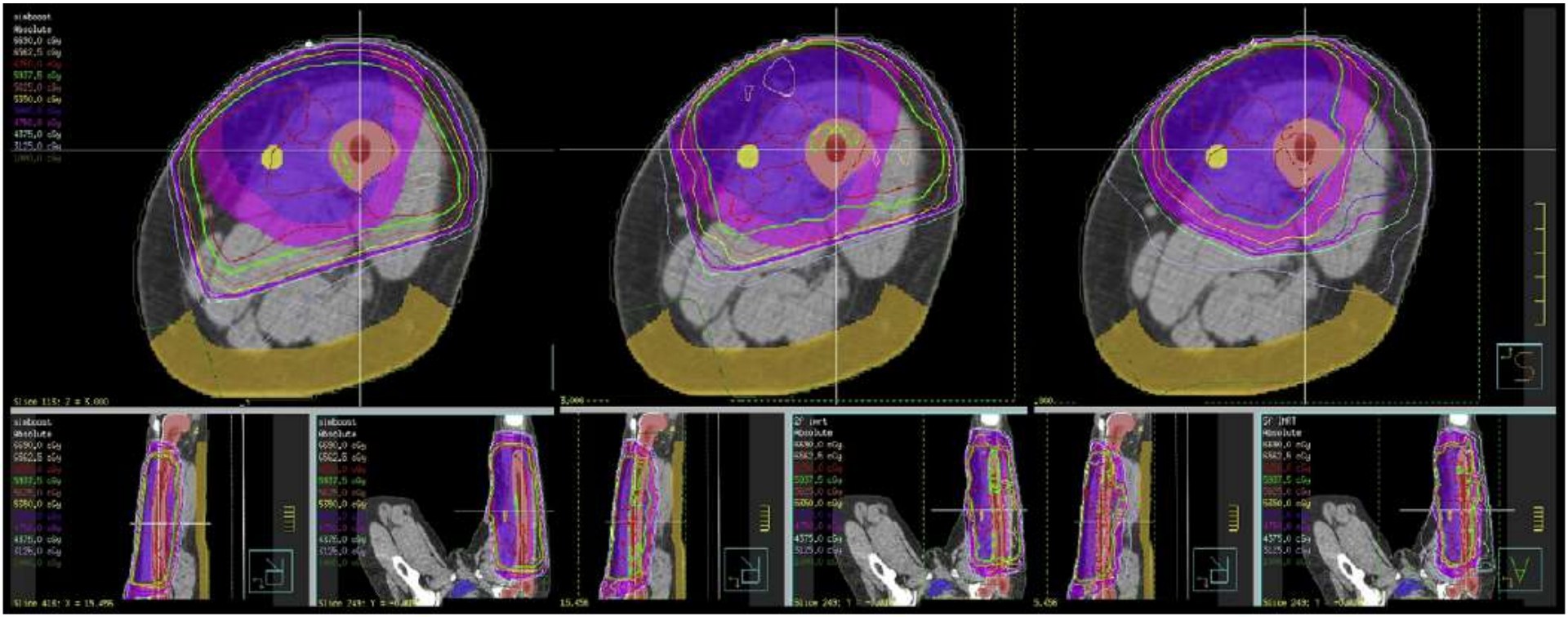
Comparison of conventional radiotherapy and intensity-modulated radiotherapy for post-operative radiotherapy for primary extremity soft tissue sarcoma

Alexandra J. Stewart [a,*], Young K. Lee [b], Frank H. Saran [c]

The neurovascular bundle was contoured manually from pelvic brim to mid knee joint. The whole femur was contoured using an auto contour setting and then checked and modified manually if necessary. The minimum skin corridor was defined as volume of a 2 cm thick band that covered 30% of the limb circumference at 180 degrees from the centre of the PTV_1 over the length of PTV_1, see Fig. 1 to demonstrate skin corridor (defined by yellow line) in each patient. A circumference of 30% was chosen since clinical experience has shown that a skin corridor of 20–30% is likely to give a minimal risk of lymphoedema in the future. Normal tissue was defined as the volume of ipsilateral limb lying outside PTV_1



Target	Volume (%)	Primary dose constraint
PTV_2	99%	90% (56.2 Gy)
	95%	95% (59.4 Gy)
	50%	100% (62.5 Gy)
	5%	105% (65.6 Gy)
	1%	110% (68.8 Gy)
PTV_1	99%	90% (45.0 Gy)
	95%	95% (47.5 Gy)
	50%	100% (50.0 Gy)
Organs-at-risk		
Femur	0–50% bone circumference within PTV	100% bone cortex under 52 Gy 50% of cortex of bone must not receive over 45 Gy in 2 Gy per fraction or equivalent
	50–99% bone circumference within PTV	Aim to spare 1/3 of bone circumference if it is at least 1 cm from the PTV
	100% bone circumference within PTV	Aim for central sparing of cortex/bone marrow
Joint	<50% of any joint within the field	
Contralateral leg	No beams entering or exiting through contralateral leg if possible	
Genitalia	Exclude where possible	Max. dose to testes 6 Gy Max. dose to ovaries 8 Gy
Skin corridor	Aim for 0 Gy	
Soft tissue outside PTV	Less than 55 Gy in 2 Gy per fraction	
Neurovascular bundle	56 Gy in 2 Gy per fraction	



Significantly lower V45 femur, V55 normal tissue

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CLINICAL INVESTIGATION **Sarcoma**

INTENSITY MODULATED RADIATION THERAPY FOR PRIMARY SOFT TISSUE SARCOMA OF THE EXTREMITY: PRELIMINARY RESULTS

KALED M. ALEKTIAR, M.D.,* LINDA HONG, PH.D.,† MURRAY F. BRENNAN, M.D.,‡
CESAR DELLA-BIANCIA PH.D.,† AND SAMUEL SINGER, M.D.‡

*Departments of Radiation Oncology, †Medical Physics, ‡Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY

Results: Median follow-up time was 23 months. Grade 1 RT dermatitis developed in 71% of patients, Grade 2 in 16%, and Grade 3 in 10%. Infectious wound complications developed in 13% and noninfectious complications in 10%. Two patients (6.4%) developed fractures. Grade 1 neuropathy developed in 28% of patients and Grade 2 in 5%. The rates of Grade 1 and 2 joint stiffness were each 19%. Grade 1 edema was observed in 19% of patients and Grade 2 in 13%. The 2-year local control, distant control, and overall survival were 95%, 65%, and 81%, respectively.