Evolving Paradigms in Management of Sarcomas

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Evolution of Radiotherapy Use in STS

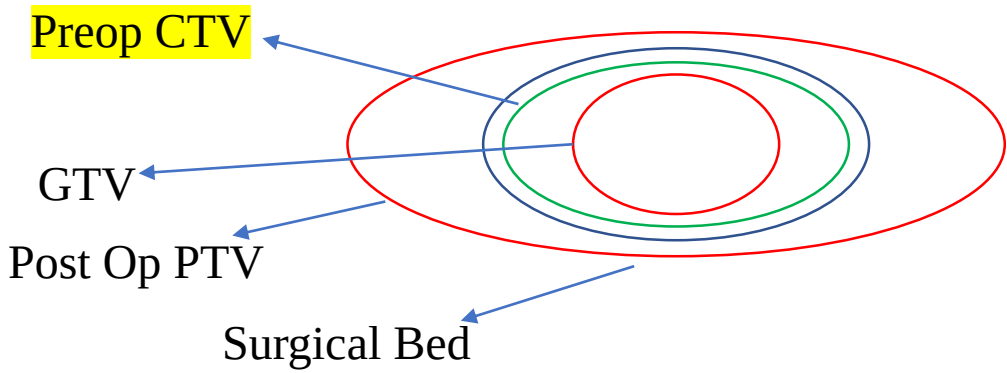
- Limb-sparing surgery + Radiation **offers similar outcomes** to amputation
- 5 yr local control: 71% vs 78%

- Limb-sparing surgery + Radiation **offers better outcomes** than limb-sparing surgery alone
- 10 yr local control: 100% vs 81%
- **Worse QoL noted with RT**

Rosenberg et al., *Ann Surg.*, 1992
Yang et al., *JCO*, 1998

Evolution of radiation in STS

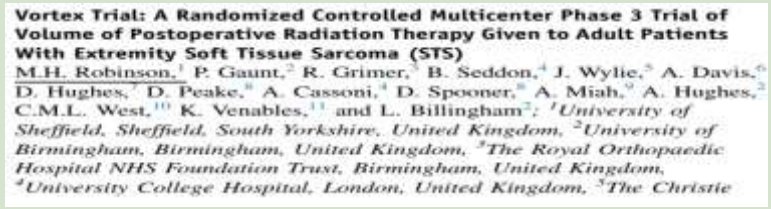
Trial	Prox-Dist Extent	Radial Extent	Rx
NCIC SR2 O'Sullivan et al., Lancet, 2002	5 cm	Not well defined	50 Gy in 25 fx
RTOG 0630 Wang et al., JCO, 2015	2-3 cm	1-1.5 cm	50 Gy in 25 fx
Candian IMRT O'Sullivan et al., Cancer, 2013	4 cm	1.5 cm	50 Gy in 25 fx



- Local recurrence rates only 7-11%
- Late grade 2+ toxicity rates only 10-14%
- Persistent wound healing toxicity rates of 30-37% in the pre-operative setting

Adjuvant vs Neoadjuvant RT

	Adjuvant RT	Neoadjuvant RT
Level of evidence	I	I
Dose	60-66 Gy (LC: 66% vs 85%)	50 Gy
CTV	Operative area+4 cm	MR T1 post Gd + 4*cm (newer trials: 1.5-2 cm)
LC rate	93%	92%
Toxicity	Long term ROM, fibrosis 48 vs 32%; edema15% *v*23% joint stiffness and18%*v*23% Grade 2+ radiation dermatitis Pre vs post: 36% vs 68%	Acute wound complication high (35 vs 17%, SS) [Predictor: LE (HR 10.4); DM (HR 5.6), Size (HR 6.2); Flap (HR 60.4)]



Vortex Trial: A Randomized Controlled Multicenter Phase 3 Trial of Volume of Postoperative Radiation Therapy Given to Adult Patients With Extremity Soft Tissue Sarcoma (STS)

M.H. Robinson,[1] P. Gaunt,[2] R. Grimer,[3] B. Seddon,[4] J. Wylie,[5] A. Davis,[6] D. Hughes,[7] D. Peake,[8] A. Cassoni,[4] D. Spooner,[6] A. Miah,[9] A. Hughes,[2] C.M.L. West,[10] K. Venables,[11] and L. Billingham[2]; [1]*University of Sheffield, Sheffield, South Yorkshire, United Kingdom,* [2]*University of Birmingham, Birmingham, United Kingdom,* [3]*The Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham, United Kingdom,* [4]*University College Hospital, London, United Kingdom,* [5]*The Christie*

3DCRT vs IMRT/VMAT

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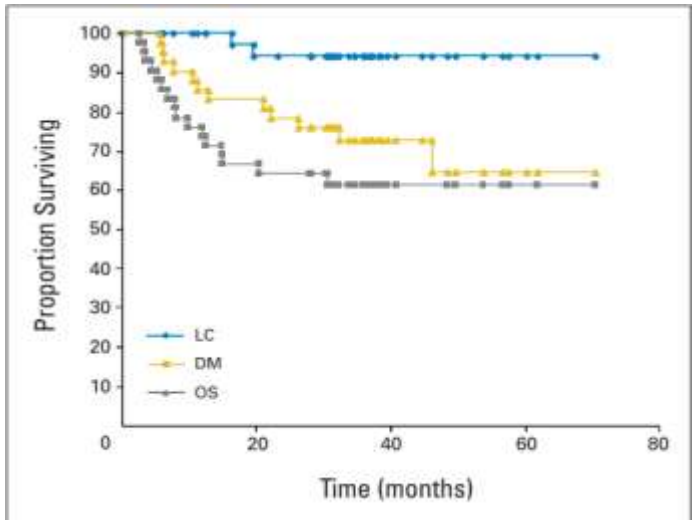
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Impact of Intensity-Modulated Radiation Therapy on Local Control in Primary Soft-Tissue Sarcoma of the Extremity

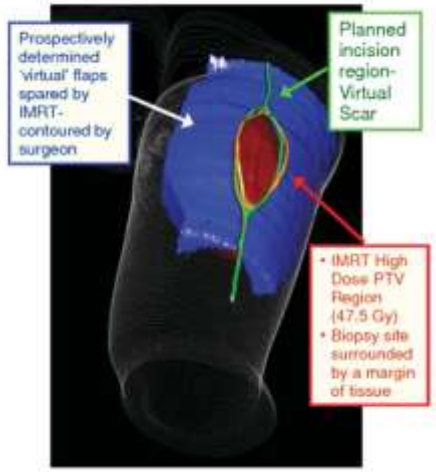
Kaled M. Alektiar, Murray F. Brennan, John H. Healey, and Samuel Singer



Ann Surg Oncol
https://doi.org/10.1245/s10434-019-07182-5
Annals of SURGICAL ONCOLOGY
ORIGINAL ARTICLE – SARCOMA

Femoral Fracture in Primary Soft-Tissue Sarcoma of the Thigh and Groin Treated with Intensity-Modulated Radiation Therapy: Observed versus Expected Risk

Michael R. Folkert, MD[1], Dana L. Casey, MD[2], Sean L. Berry, PhD[3], Aimee Crago, MD[4], Nicola Fabbri, MD[5], Samuel Singer, MD[4], and Kaled M. Alektiar, MD[3]



- Observed crude risk of fractures was 6.5% vs 25 expected risk from the nomogram
- Median time to fracture was 23 months (range, 6.9–88.6)
- > 60 year

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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, Qiang Zhang, Burton L. Eisenberg, John M. Kane, X. Allen Li, David Lucas, Ivy A. Petersen, Thomas F. DeLaney, Carolyn R. Freeman, Steven E. Finkelstein, Ying J. Hitchcock, Manpreet Bedi, Anurag K. Singh, George Dundas, and David G. Kirsch

Dian Wang, Rush University Medical Center, Chicago, IL; Qiang Zhang, NRG Oncology Statistics and Data Management Center, Philadelphia, PA; Burton L. Eisenberg, HoagUniversity of Southern California Norris Cancer Center, Los Angeles, CA; John M. Kane and Anurag K. Singh, Roswell Park Cancer Institute,

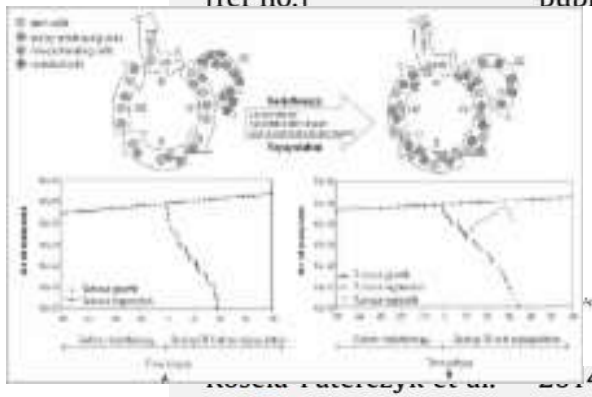
A B S T R A C T

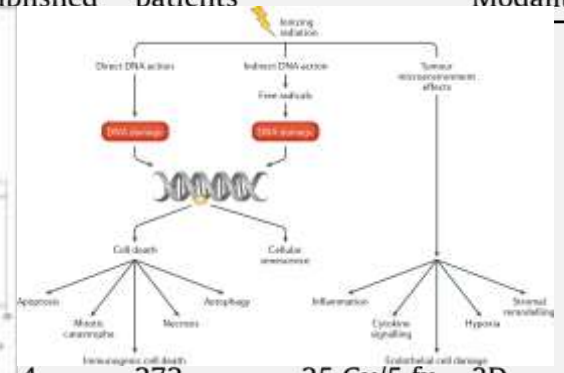
5-year LC 94% (regardless of margin status), 5-year DM-free 61%, 5-year OS 64%
Toxicity: Dermatitis Grade III- 10%. Fractures 6%. Joint stiffness Grade II- 19%. Edema Grade II- 13%
Femur V100 decreased by 57% (SS), femur D5 reduced 67% (SS).
Ipsilateral soft tissues V100 decreased by 78% (SS), D5 decreased 13%

1956

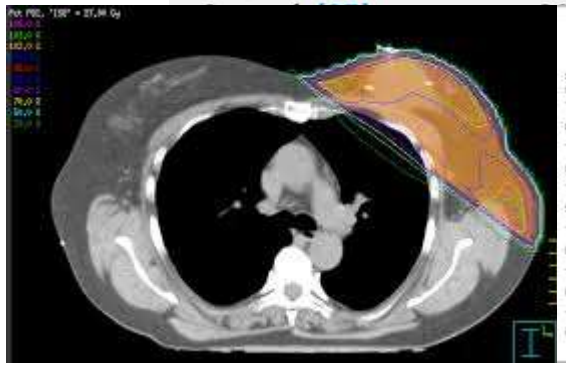
2021

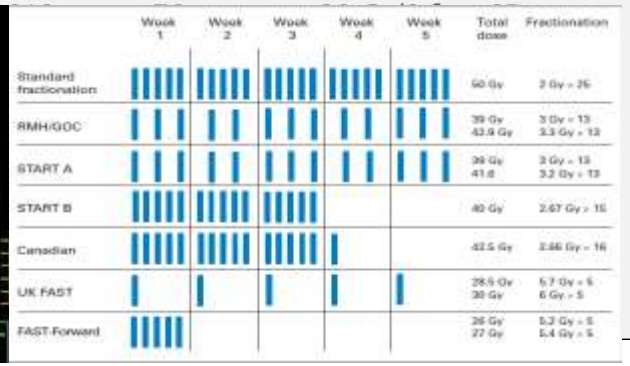
Hypofractionation in STS





First author [ref no.]	Year published	No. patients	Dose	RT Modality	Time to surgery	Preoperative or concurrent ChT	LC	FU	Wound complications
					4 weeks	Yes	89%	5 years	NR
					4–6 weeks	Yes	81.5%	32.1 months	41.8%
					4–8 weeks	Yes	89%	5 years	17.2%*
[26]	2014	272	25 Gy/5 fx	3D	3–7 days	Yes, selected patients	81%	3 years	32.4%
					2–3 weeks	Yes	87.2%	4.3 years	32%
					1–2 weeks	Yes	83%	5.9 years	NR
					2–6 weeks	No	94.3%	29 months	32%
					7 days	Metastatic patients only	100%	10.7 months	31%
					4–8 weeks	Yes	95%	29 months	33%





Neoadjuvant CTRT in STS

VOLUME 24 · NUMBER 4 · FEBRUARY 1 2006
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Phase II Study of Neoadjuvant Chemotherapy and Radiation Therapy in the Management of High-Risk, High-Grade, Soft Tissue Sarcomas of the Extremities and Body Wall: Radiation Therapy Oncology Group Trial 9514

William G. Kraybill, Jonathon Harris, Ira J. Spiro,† David S. Ettinger, Thomas F. DeLaney, Ronald H. Blum, David R. Lucas, David C. Harmon, G. Douglas Letson, and Burton Eisenberg

3-year rate for LRF 17.6% if amputation is considered a failure and 10.1% if not.

3-year rates for disease-free, distant [illegible]-free, and OS are 56.6%, 64.5%, and 75.1%

Phase II trial of Preop Hypo fractionated RT with or without CT in STS

Clinical Investigation

Combined Preoperative Hypofractionated Radiotherapy With Doxorubicin-Ifosfamide Chemotherapy in Marginally Resectable Soft Tissue Sarcoma: Results of a Phase 2 Clinical Trial

Mateusz J. Sp[illegible]hD,* Hanna Kosela-Paterczyk, MD, PhD,* Aneta Bor[illegible] Michał Wągrodzki, MD, PhD,† Anna Szumera-Ciećk[illegible]hD,†,‡ Anna M. Czarnecka, MD, PhD,†,§ P[illegible]eda-Wysocka, MD,‖ Iwona Kalinowska, MD,* [illegible]czuk, MSc, PhD,¶,# Edyta Dąbrowska-Szewczyk, MSc,**,†† [illegible]j Cieszanowski, MD, PhD,‖ and Piotr Rutkowski, MD, PhD*

en bloc R0 resections was 71.7%

Wound complications that fulfill definitions described by O'Sullivan et al 34%

Radiotherapy and Oncology 159 (2021) 161–167
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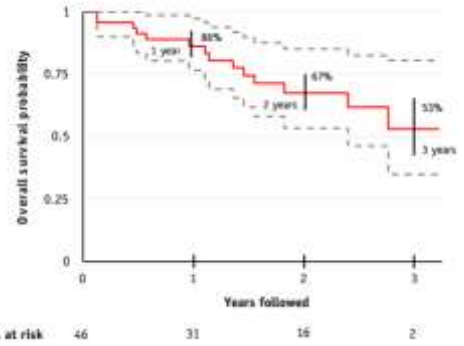
Original Article

Neoadjuvant hypofractionated radiotherapy and chemotherapy for extremity soft tissue sarcomas: Safety, feasibility, and early oncologic outcomes of a phase 2 trial



Summary

- Small, High-grade Sarcomas: For stage II (T1G2-3) tumors, surgery + radiation is generally recommended

- Select patients **may** receive surgery alone based on prospective data
  - De novo T1 G2-3 STS resected with a **minimum 1 cm margin****
  - 5 year and 10 year local recurrence rates of 7.9% and 10.6%
  - 10-year **local recurrence rate for high grade STS is 16.7%**

- Resectable, High-risk (T2-4 G2-3) Sarcomas:Treated with surgery with pre- or post-operative radiotherapy
  - **Toxicity profile differed considerably**

- **IMRT/IGRT considered standard of care**

- **Hypofractionated RT +/- Conc CT is being investigated and initial results are promising**