

# The Role for Radiation Therapy in the Management of Sarcoma



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## KEYWORDS

- External beam radiation therapy • IMRT • IGRT
- Preoperative versus postoperative radiation • Radiation treatment planning

## KEY POINTS

- Radiation therapy is an integral component of limb-sparing therapy for extremity soft tissue sarcoma. The benefit of radiation is clearer for high- than low-grade tumors.
- Local recurrence after appropriately delivered radiation and surgery is expected to be less than 10%.
- Radiation therapy can be delivered either before or after definitive surgical resection. Although the decision regarding appropriate sequencing is unique to each case, many tumors are amenable to either schedule, and treatment decisions are subject to institutional bias.
- Image guidance and intensity-modulated radiotherapy has the potential to improve the therapeutic ratio, mainly through the reduction in treatment-related toxicity.
- Retroperitoneal sarcomas are rare tumors with a high propensity for local failure. Retrospective series suggest that the addition of radiation (generally delivered before resection) decreases the incidence of local failure.

## INTRODUCTION

Sarcomas are rare tumors of connective tissue, with diverse histology and site of origin in the body. This article concentrates on the role of radiation in the management of sarcoma of the extremities and retroperitoneum, first with respect to timing and dose. Next the authors focus on practical aspects of treatment planning. Finally, patient set-up and toxicity, acute and late, are addressed.

## AMPUTATION VERSUS LIMB-SPARING SURGERY WITH ADJUVANT RADIATION

Amputation was the standard of care in the management of soft tissue sarcoma (STS) for decades, with local recurrence (LR) rates of less than 20% compared with more

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Disclosures: None.

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Surg Clin N Am 96 (2016) 1127–1139

<http://dx.doi.org/10.1016/j.suc.2016.05.003>

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than 70% after local excision alone (**Table 1**).<sup>1-4</sup> The locally invasive nature of sarcomas along tissue planes and muscle fibers and around vasculature highlights the benefits of amputation over gross local resection alone.

Retrospective data published in the 1960s to 1970s suggested reduced risk of LR when limb-sparing surgery (LSS) was supplemented with adjuvant radiation, although it was not until prospective data were published that this treatment became widely practiced.<sup>5,6</sup>

Published in 1982, the landmark National Cancer Institute (NCI) trial randomized 43 patients to amputation or LSS (defined as resection of gross disease but preservation of neurovasculature necessary for function) followed by adjuvant radiation.<sup>6</sup> All patients received adjuvant chemotherapy (doxorubicin, cyclophosphamide, and methotrexate), delivered concurrently with radiation to 45 to 50 Gy to patients randomized to LSS. Disease-free survival and overall survival at 5 years were similar, 78% and 88% for patients treated with amputation alone versus 71% and 83% for LSS and adjuvant radiation ( $P = .75$  and  $.99$ ). There was a nonsignificant trend toward increased LR for LSS compared with amputation ( $P = .06$ ), although there were only four LRs among patients who had LSS compared with distant-only failures among the amputation group. Distant metastases were found in 3 of 16 and 2 of 27 patients treated with amputation or LSS, respectively. Since that time, LSS essentially became the standard of care in the United States for patients with disease amenable to LSS; amputation rates fell to less than 10%.<sup>7</sup>

#### LIMB-SPARING SURGERY WITH OR WITHOUT ADJUVANT RADIATION

Once amputation fell out of favor, investigation of the benefit of radiation to LSS was necessary. There are two prospective randomized trials that evaluate LSS with or without adjuvant radiation. First, a follow-up trial at the NCI investigated the necessity of adjuvant radiation following LSS.<sup>8</sup> Ninety-one patients with high-grade and 50 patients with low-grade tumor histology received five cycles of adjuvant doxorubicin and cyclophosphamide, of which 44 and 26, respectively, were randomized to concurrent radiation (45 Gy to a wide field with 18 Gy boost to the tumor bed, defined by surgical clips). With median follow-up more than 9 years, only one patient with low-grade lesion treated with chemoradiation had an LR, compared with nine and eight incidents of LR among patients with high- and low-grade lesions who received chemotherapy alone ( $P < .05$  for both groups). However, there was no difference in probability of distant metastases or overall survival at 10 years.

A second prospective trial investigated the necessity of radiation in 164 patients who underwent LSS for extremity STS (more than two-thirds high grade) through randomization of patients to intraoperative brachytherapy (BRT) or no further adjuvant local or systemic therapy.<sup>9</sup> BRT used after-loading catheters placed intraoperatively to

**Table 1**  
Local recurrence rates based on surgical intervention

Author and Year	% Local Excision	% Wide Excision	% Amputation
Shieber & Graham, <sup>1</sup> 1962	87	39	—
Gerner et al, <sup>2</sup> 1975	93	60	8
Markhede et al, <sup>4</sup> 1982	74	8	0
Leibel et al, <sup>3</sup> 1982	30	28	13

Data from Refs. 1-4

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