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American Brachytherapy Society consensus statement for soft tissue sarcoma brachytherapy

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ABSTRACT

PURPOSE: Radiation therapy represents an essential treatment option in the management of soft tissue sarcomas (STS). Brachytherapy represents an important subset of radiation therapy techniques used for STS, with evolving indications and applications. Therefore, the purpose of this guideline was to update clinicians regarding the data surrounding brachytherapy (BT) and provide recommendations for the utilization of BT in patients with STS.

METHODS AND MATERIALS: Members of the American Brachytherapy Society with expertise in STS, and STS BT in particular, created an updated guideline for the use of BT in STS based on a literature review and clinical experience.

RESULTS: Guidelines are presented with respect to dose and fractionation and technical features to improve outcomes and potentially reduce the risk of toxicity. Brachytherapy as monotherapy can be considered in low-risk cases or in situations where re-irradiation is being considered. Brachytherapy boost can be considered in cases at higher risk of recurrence or where BT alone cannot adequately cover the target volume. To limit wound complications, the start of BT delivery should be delayed until final wound closure, or if after immediate reconstruction, started after postoperative Day 5.

CONCLUSIONS: The current guidelines have been created to provide clinicians with a review of the data supporting BT in the management of STS as well as providing indications and technique guidelines to ensure optimal patient selection and clinical outcomes.

Keywords: Soft tissue sarcoma; Brachytherapy; Retroperitoneal sarcoma; Radiation

Introduction

Soft-tissue sarcoma (STS) describes a heterogeneous group of malignant entities, consisting of various pathologies, histologic grades, and sites of origin. Treatment historically consisted of radical resections and amputation, which were associated with a significant detriment in structural function and quality of life. This led to a shift in STS treatment paradigms to a multidisciplinary approach using marginal resection and adjuvant radiation, in hopes of maintaining comparable disease control while improving the patient's quality of life (1–4). The first randomized trial to show equivalent disease-specific survival between amputation and limb-sparing surgery with adjuvant radiotherapy (RT) was over three decades ago (2). Now, limb-sparing treatment is the current standard of care.

There are selected cases that can be adequately controlled with wide local excision (WLE) alone (5–7). In sarcoma patients with a higher risk of recurrence (i.e., size >5 cm, deep, high grade, recurrent, or closely resected margins), the addition of RT can improve local control (LC). In randomized trials, the addition of external beam radiation therapy (EBRT) (8) or brachytherapy (BT) (9–11) can offer an absolute LC benefit of ~20–30% in the setting of limb preserving WLE. Radiation can be administered as EBRT

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alone, BT alone, or as a combination of EBRT with a brachytherapy boost (EBRT-BT). Treatment with EBRT can be administered in either the preoperative or postoperative setting. Initial trials used postoperative EBRT, but preoperative EBRT has become popular after randomized evidence showed similar LC with the potential for improved late complications (8,12−14).

Brachytherapy is primarily delivered intraoperatively or postoperatively. During surgical resection, catheters are implanted in the tumor bed, allowing high radiation dose to the surgical bed with a rapid dose drop to the surrounding normal tissue. This rapid fall off in dose is because of the low energy radiation used in BT, with a limited dose penetration that is in proportion to the inverse square law ($1/r^2$) (15). Historically, BT can better spare normal tissue than EBRT, which may translate to a lower rate of complications (i.e., lymphedema, subcutaneous fibrosis, or bone fractures) (8,11,16). Brachytherapy offers a relatively short and convenient adjuvant treatment, delivered in the inpatient or outpatient setting, usually spanning <1−2 weeks in duration. BT alone is useful when avoiding normal tissue radiation is paramount but is limited in its volume coverage. EBRT can deliver dose to a large volume at risk with increased homogeneity than BT but can increase both low and high radiation dose volumes to normal tissue. The combination of EBRT and BT provides microscopic disease coverage over a sizable volume, which BT alone lacks, and provides faster boost delivery to the surgical bed and a steeper dose gradient, which EBRT alone lacks. In this review, we will discuss BT in STS, focusing on treatment considerations, BT procedures, and patient outcome.

Methods and materials

The American Brachytherapy Society (ABS) board of directors appointed a group of physicians with expertise in sarcoma BT to provide a consensus statement. The previous ABS guideline (17) was updated with recent studies on the topic. Literature review was conducted with inclusion of all human clinical studies available in English language evaluating BT and STS. The goal of these guidelines is to provide an adequate description of treatment considerations, procedural instructions, radiation dosing, outcomes, and complications. Before publication, the consensus statement was approved by the ABS Board of Directors.

Results

Treatment considerations

Patient workup

STS has a relatively low incidence in the United States, with an estimated 11,930 new cases in 2015 (18), which is best served by a multidisciplinary sarcoma team (19). In addition to staging, preoperative workup should be aimed at assessing extent of disease, resectability, neighboring critical structures, and whether a patient can tolerate treatment (i.e., comorbidities, performance status, previous radiation, etc.). During the history and physical examination, it is important to determine whether a patient is a surgical candidate, what their limb function is before surgery, and their risk for wound complications (i.e., diabetes, peripheral vascular disease, smoking history, previous radiation or surgery to the site of disease, tumor location, baseline edema, etc.) (20).

Preoperative imaging of the primary tumor can aid in delineating gross disease, surrounding edema, and determining disease extent. Imaging can also identify the lesion's relationship to surrounding structures (i.e., visceral organs, bone, nerves, blood vessels, etc.) and determine tumor resectability. Therefore, preoperative imaging is essential to planning the surgical approach, surgical extent, and utility of BT. Imaging of the extremity, trunk, and pelvis are best served with an MRI, whereas CT is adequate for abdominal and retroperitoneal disease. Nodal evaluation should be considered for histologies with >10% incidence of nodal involvement, most notably the "SCARE" subtypes (synovial, clear cell, angiosarcoma, rhabdomyosarcoma [RMS], and epitheloid sarcoma) (21−23).

The most common mode of distant metastasis in STS is hematogenous spread to the lung. For all STS, chest imaging should be included as a part of staging. Chest CT is the most common chest imaging used, but chest x-ray may be adequate in low-risk patients (i.e., low-grade T1 disease) (24). Abdominal and pelvic CT is recommended in myxoid/round cell liposarcoma, epithelioid sarcoma, angiosarcoma, and leiomyosarcoma (19). Total spine MRI should be considered for myxoid/round cell liposarcoma, and CNS imaging should be considered for alveolar sarcomas and angiosarcomas. Positron emission tomography (PET)−CT may be useful for staging, prognostication, and determining response to neoadjuvant chemotherapy (25−27).

Tissue biopsy is required to confirm stage, histology, and tumor grade. A carefully planned core needle or incisional biopsy along a planned future resection axis is recommended. It is preferable that the surgeon planning to perform the definitive resection perform the biopsy. Incisions should be made in the longitudinal orientation to help with closure and avoid circumferential radiation. To reduce tumor contamination, care should be taken to minimize dissection during biopsy, with meticulous attention to hemostasis.

Primary treatment

Historically, surgery alone was the primary treatment of choice, with LC dependent on the extent of resection. Retrospectively, local recurrence rates were much higher with local surgical excision (30−60%) than amputation (5−20%) (28−33). To improve this disease control deficit, the addition of RT to local surgical excision was prospectively evaluated and showed comparable DFS and OS to amputation (2).