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REVIEW ARTICLE

Imaging applications in multicatheter brachytherapy for soft tissue sarcomas

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Abstract

Multicatheter brachytherapy can be applied as a monotherapy or in combination with external beam radiotherapy as an adjuvant treatment for soft tissue sarcoma. Successful application of brachytherapy in the treatment of soft tissue sarcoma requires implementation of multiple imaging modalities during preoperative and postoperative planning. Preoperative imaging is essential in planning local therapy for soft tissue sarcoma in that it defines the proximity of the tumor to adjacent critical structures, predicts the likelihood of close or positive surgical margins, and aids in defining the target volume for a brachytherapy implant. In the postoperative setting, imaging is utilized to assess the accuracy of target volume coverage and integrity of the implant, as well as in three-dimensional treatment planning.

Keywords: *Sarcoma; brachytherapy; radiotherapy treatment planning; magnetic resonance imaging; computed tomography.*

Introduction

Soft tissue sarcomas (STS) represent a heterogeneous group of rare malignancies that arise from mesenchymal tissues. Although STS can originate at any site harboring connective tissue, these tumors have a propensity to develop in the muscle groups of the extremities. The natural history of high-grade STS is one of early development of predominately pulmonary metastasis and extensive local invasion, invading adjacent bone and neurovascular structures. Historically, limb amputation was the primary surgical option, because of the challenges in maintaining a functional limb and high rates of local recurrence with limited surgical excision. Investigators at the National Cancer Institute conducted a randomized trial comparing amputation with limb-sparing resection and adjuvant external beam radiotherapy (EBRT). This landmark study demonstrated equivalent disease-free and overall survival outcomes for those undergoing limb preservation compared with those receiving amputation and represented one of the earliest successes in applying limited surgery and radiotherapy in an organ-preservation approach[1].

A prospective randomized clinical trial of brachytherapy (BRT) as adjuvant treatment for STS following limb-sparing surgery has also demonstrated excellent rates of local control[2]. No prospective trials have compared EBRT with BRT as adjuvant treatments for extremity STS. Thus, the choice of modality is often based on the expertise of the treating clinicians. The combination of EBRT and BRT as an adjuvant treatment has also been reported to afford good rates of local control and acceptable toxicity[3]. In the setting of isolated local recurrence of STS, EBRT and/or BRT have been shown to improve local control[4].

EBRT utilizes a linear accelerator to generate megavoltage photons, and BRT involves the delivery of radiation from a radioactive source placed within the tumor or tumor bed. BRT confers the following advantages over EBRT: shorter treatment times, shorter interval from surgery to initiation of radiotherapy, direct intraoperative visualization of the target volume, and reduced volume of normal tissue irradiated.

Low-dose-rate and high-dose-rate BRT can be used as a monotherapy or in combination with EBRT for close or positive margins[5]. Dose rate is the time interval over which a therapeutic dose of radiation is delivered and is dependent on the activity of the radioactive source. The isotope most commonly used for both low-dose-rate and high-dose-rate applications in the treatment of

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STS is iridium-192[6]. Low-dose-rate BRT implants use a ribbon of radioactive sources and deliver the dose over a 4- to 6-day period. This requires the patient to be isolated in a shielded room during treatment and involves some radiation exposure to health care providers. High-dose-rate BRT implants utilize a single source that is advanced by a source wire through catheters within the target volume, delivering the dose over several minutes, then retracting back into a shielded vault. The dose is delivered in a fractionated regimen, usually twice daily, over 5–7 days. The advantage conferred by high-dose-rate BRT is that patients are exposed to radioactivity only during those minutes of treatment, thus avoiding prolonged periods of isolation, accommodating outpatient treatment, and decreasing exposure to health care providers. However, most of the clinical data supporting the efficacy and describing the toxicity of BRT for STS is derived from experiences with low-dose-rate BRT.

During the intraoperative portion of the BRT procedure, the target volume is delineated by direct visualization and multiple catheters are placed percutaneously, in a single plane, uniform, parallel array along the tumor bed. The catheters serve as conduits through which the radioactive source(s) is passed, creating a plane of dose that conforms to the tumor bed. Postoperatively, patients undergo computerized, image-based treatment planning. The dose is prescribed 5 mm to 10 mm from the plane of the implant. Treatment is initiated no sooner than 5 days following wound closure. The delay in initiating treatment is incorporated to minimize the risk of wound complications commonly incurred in the treatment of STS[7]. Following treatment, the catheters can be removed at the bedside.

Successful application of BRT in the treatment of STS requires implementation of multiple imaging modalities for preprocedure planning, postoperative assessment of the accuracy of target volume coverage and integrity of the implant, as well as in three-dimensional treatment planning. This article describes the preoperative and postoperative components of BRT planning and present examples of the roles of imaging, through illustrative cases.

Brachytherapy planning in STS

Preoperative imaging is essential in planning local therapy for STS in that it defines the proximity of the tumor to adjacent critical structures, predicts the likelihood of close or positive surgical margins, and aids in defining the target volume for a BRT implant. Magnetic resonance imaging (MRI) is the modality most commonly used for preoperative imaging of extremity STS as a result of its superior soft tissue contrast and capacity for multiplanar image acquisition. These functions are critical to surgical planning, which requires accurate delineation of tumor, bone, joint, and neurovascular relationships. To directly compare the accuracy of local staging by computed tomography (CT) and MRI, the Radiology Diagnostic Oncology Group performed a comparative study of the two modalities in a cohort of 316 patients with bone and soft tissue sarcoma and found the modalities to be equivalent[8]. However, MRI has been reported to be superior to CT for staging the local extent of STS in retrospective analyses of single institution experiences[9,10]. The accuracy of preoperative radiographic staging in STS may directly affect clinical outcomes. For example, in their clinical analysis of 83 patients with isolated local recurrence of STS, Moureau-Zabotto *et al.*[4] attribute the high rate of further local recurrences (45%) to the low rate of preoperative MRI acquisition (30%).

Postoperative CT imaging is used to assess the accuracy of a BRT implant's target volume coverage and the integrity of an implant. This procedure is termed a CT simulation and is typically performed on postoperative day 1. The CT images aid in determining the relationship of the BRT catheters to the landmarks used intraoperatively, under direct visualization, to define the target volume. These landmarks can be anatomic structures or radioopaque markers, such as surgical clips. The CT simulation also serves as a quality assurance measure in which the integrity of the implant can be assessed. The geometry of BRT implant is very susceptible to distortion during subsequent portions of the operative procedure such as insetting the overlying flap, closing the abdomen (for intraabdominal cases), awaking the patient from anesthesia, or transferring the patient from the operating room table. Thus, postoperative verification of catheter placement and patency is critical. As a result of the physical properties of BRT sources, the dose from a radioactive BRT source falls off exponentially with distance from the source. This characteristic property of therapeutically applied radioisotopes is described by the inverse square law. If the catheters are physically displaced from the target during closure, then the prescribed dose cannot be delivered to that volume. The catheters, hollow flexible plastics tubes, can also be bent in such a way as to preclude the placement of the radioactive sources within them. The patency of the catheter lumen is assessed at the time of CT simulation by placing temporary radioopaque markers into the catheters. If these markers cannot be advanced through the lumen of the BRT, then the catheter will not accommodate a radioactive source and that catheter cannot be used for treatment. The loss of a functional catheter has detrimental dosimetric consequences.

The CT data set obtained at the time of CT simulation is also used in the development of a radiation therapy treatment plan. The postoperative CT provides a three-dimensional rendering of the single plane of catheters and defines the relationships of the catheters to each other, the target volume, and adjacent critical structures. In the application of high-dose-rate BRT, the composite dose distribution is determined by where a radioactive source is positioned along the course of the catheter,

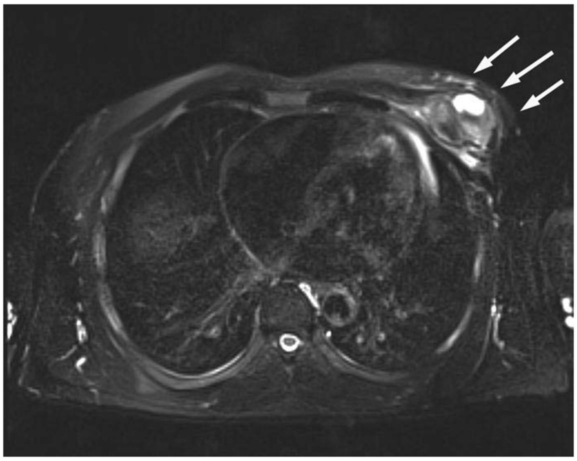

Figure 1 **T2-weighted axial chest MRI reveals no invasion by tumor of the underlying ribs or intercostal muscles, but a widely negative deep margin cannot be achieved without chest wall resection.**

known as a dwell position and the duration of time the source stays in that position, the dwell time. The dose distribution can be tailored using these two variables. The treatment planning software performs thousands of computations per second to provide a three-dimensional composite graphical representation of the dose distribution on the CT images. Modern CT-based treatment planning systems also allow for graphical optimization, whereby a radiation oncologist can drag and drop the isodose lines on the CT dataset to the desired location and immediately observe the composite dose distribution and its relationship to the target volume and adjacent normal structures. CT-based three-dimensional planning also provides volumetric data on the dose to the target volume and normal tissue, which is important for predicting toxicity.

The following cases highlight the role of MRI and CT imaging in the implementation of BRT for STS.

Case 1

A 50-year-old man presented with a 2-month history of an enlarging left breast mass. An MRI of the chest revealed a well-circumscribed mass with heterogeneous T2 signal arising from the left pectoralis major muscle (Fig. 1). This lesion was histologically confirmed to be a poorly differentiated sarcoma. Exemplifying the utility of MRI in preoperative planning, the MRI delineated the proximate relationship of the tumor and chest wall, which precluded a widely negative deep margin without chest wall resection. Therefore, a multicatheter BRT implant was planned to address the deep margin following wide local excision. Thirteen BRT catheters were placed percutaneously in a medial to lateral orientation to cover the tumor bed. A left latissimus dorsi rotational flap was mobilized and the catheters were advanced through the flap, with careful attention to avoid its vascular pedicle (Fig. 2a). The catheters were advanced through the skin and soft tissue by a sharp trocar to create a parallel, uniformly spaced array along the chest wall (Fig. 2b). The patient developed a pneumothorax following the procedure as a result of a small perforation in the chest wall by the trocar. The iatrogenic pneumothorax resolved with placement of a chest tube and there were no additional acute complications from the procedure. The patient has no evidence of local or distant recurrence in 12 months of follow-up.

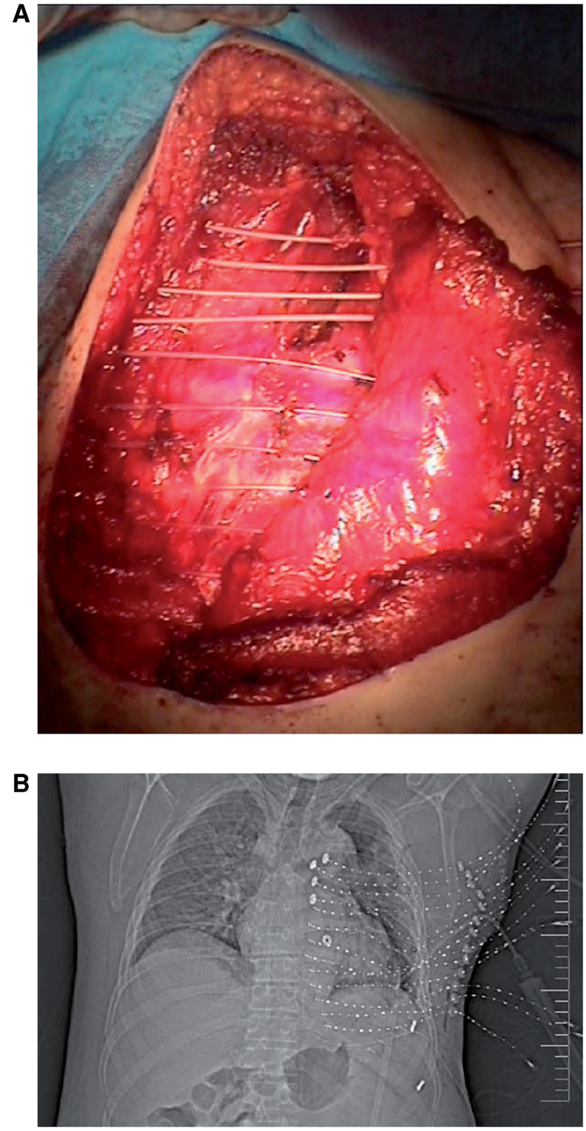

Figure 2 **(a) An intraoperative image of the brachtherapy catheters lining the deep margin along the chest wall and a latissimus dorsi rotational flap being inset to fill the soft tissue deficit that measured 16 × 18 cm. (b) Anteriοposterior CT scout image of the brachytherapy implant with radioopaque markers placed within catheters.**

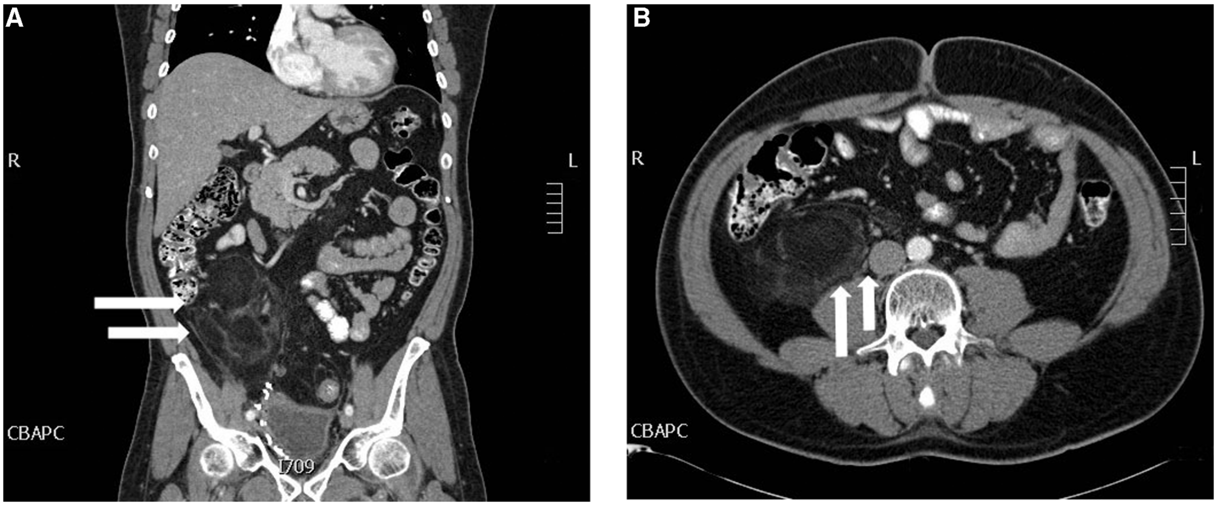

Figure 3 **(a) Abdominal CT with contrast reveals a fat density mass in the right lower quadrant. (b) Axial abdominal contrast-enhanced CT revealing the density mass to be closely associated with the right psoas muscle and inferior vena cava.**

Case 2

A 52-year-old man with a history of a well-differentiated right retroperitoneal liposarcoma presented with an isolated local recurrence in the right lower quadrant (Fig. 3a,b). The patient previously received adjuvant EBRT to the pelvis following surgical resection at the time of initial presentation. During preoperative planning for the recurrence, an abdominal CT confirmed the tumor's proximity to the inferior vena cava and right psoas muscle, thus illustrating the value of CT in pretherapy planning. The previous course of EBRT delivered the maximum tolerated dose to the bowel and limited the further application of that modality. BRT was planned to address the close deep margin. The intraoperative assessment of the tumor extent confirmed the preoperative CT findings. Intraoperatively, closed end catheters were placed in a medial to lateral orientation along the tumor bed and pulled through the lateral abdominal wall such that the open end was accessible for BRT source placement after the abdomen was closed. The target volume for the BRT implant was delineated intraoperatively; the anatomic boundaries of the tumor were determined by direct visual inspection. The medial border of the caudal target volume was the right ureter, in which a stent was placed preoperatively to aid in its identification and minimize the risk of injury. The lateral border of the target volume was the abdominal wall and the deep margin was at the level of the psoas muscle and inferior vena cava. The physical properties of BRT sources can be exploited to reduce the volume of normal tissue irradiated, but in this case the bowel was at risk for acute and late toxicity because of its proximity to the BRT implant as well as the previous administration of EBRT. To minimize this risk of injury, the bowel was displaced from the BRT implant intraoperatively, by mobilizing an omental flap and insetting it between the BRT and the bowel. On postoperative day 1, the patient underwent CT simulation. The CT images confirmed the integrity of the BRT implant by documenting that the catheters were in still in a parallel array and covered the intraoperatively delineated target volume after the abdomen had been closed (Fig. 4a,b). The CT-based three-dimensional treatment planning also confirmed that the omental flap had afforded enough distance between the BRT implant and bowel to achieve significant sparing of an at risk normal tissue (Fig. 5). BRT was initiated on postoperative day 5 and following completion of therapy, the BRT catheters were removed at the bedside without complication. The patient has been followed for 13 months without evidence of tumor recurrence or bowel complications.

Case 3

A 26-year-old woman at 27 weeks' gestation, presented with acute abdominal pain. An MRI, rather than a CT scan, was used in her initial diagnostic evaluation, because MRI avoids the dose of ionizing radiation to a fetus conferred by CT. The imaging confirmed the clinical diagnosis of acute appendicitis and described the incidental finding of a $5.8 \times 8.3 \times 3.2$ cm mass in the region of the right hip (Fig. 6). The patient elected to delay surgical management of the mass until after delivery. A biopsy confirmed this mass to be a high-grade malignant myoepithelioma. Adjuvant radiotherapy was anticipated due to the high-grade histology. However, the preoperative MRI had delineated the tumor's proximity to the right hip joint space, which placed the patient at significant risk for joint fibrosis and pathologic fracture as a

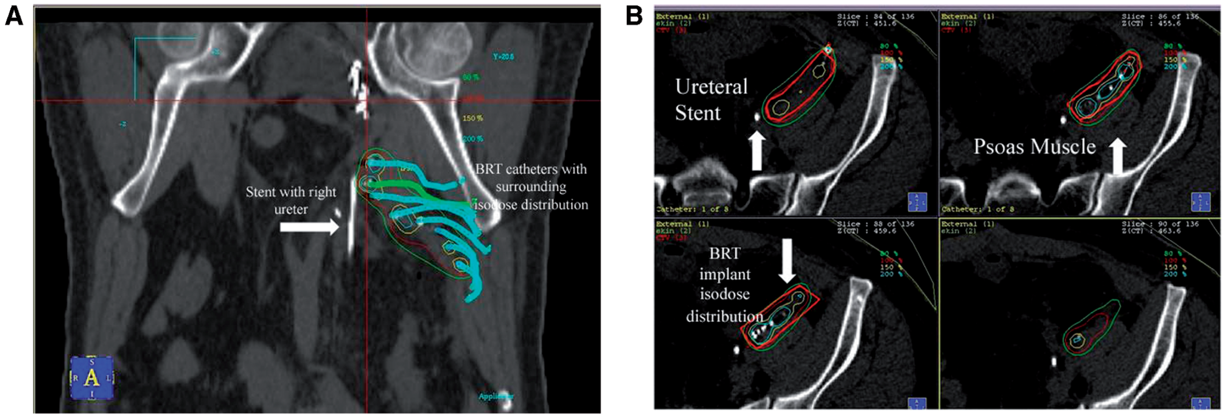

Figure 4 **(a) Coronal CT simulation image, obtained in feet first orientation, confirms the BRT catheters maintained their intraoperative position after the abdomen was closed. The catheters abut the stented right ureter, which represented the median border of the caudal target volume and ensures the prescribed dose can be delivered to that target volume. (b) Axial CT simulation image confirming that the implant and resultant isodose distribution cover the caudal region of target volume. The catheters cover the deep margin of the tumor bed along the psoas muscle and the medial margin at level of the ureteral stent.**

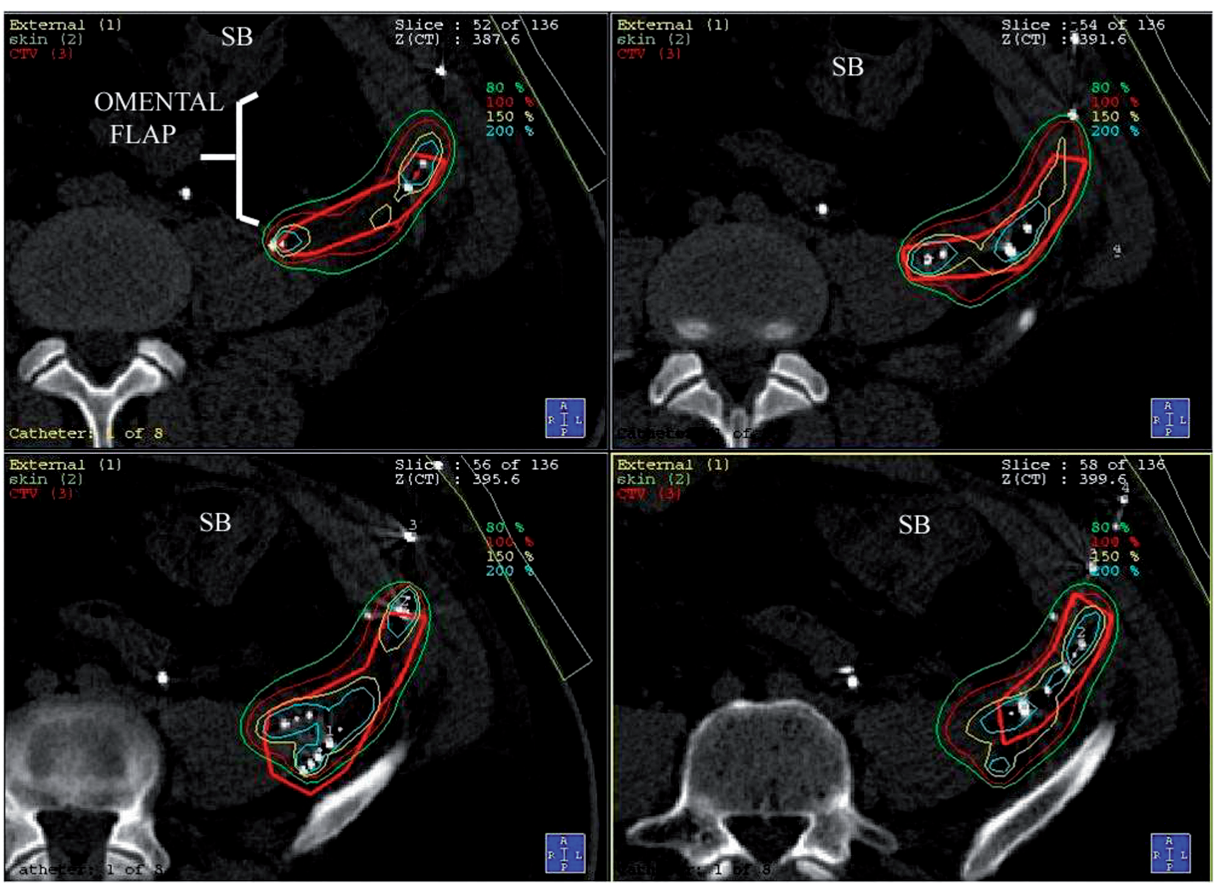

Figure 5 **Sequential axial CT-based treatment planning images documenting the displacement of the small bowel (SB) from the BRT implant by an omental flap and resultant dose-sparing to the SB.**

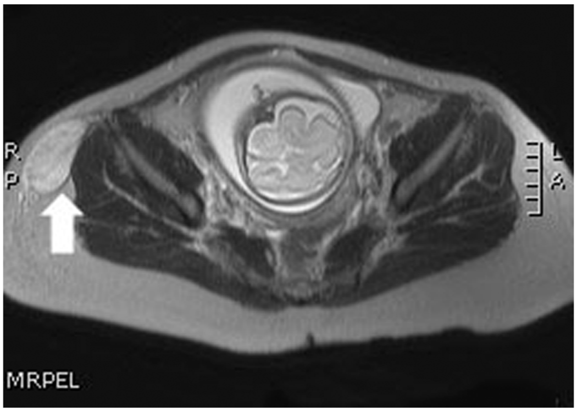

Figure 6 **Axial T2-weighted abdominal MRI defining the proximity of the mass to the hip joint and its medial most extent is lateral to the wing of the ilium.**

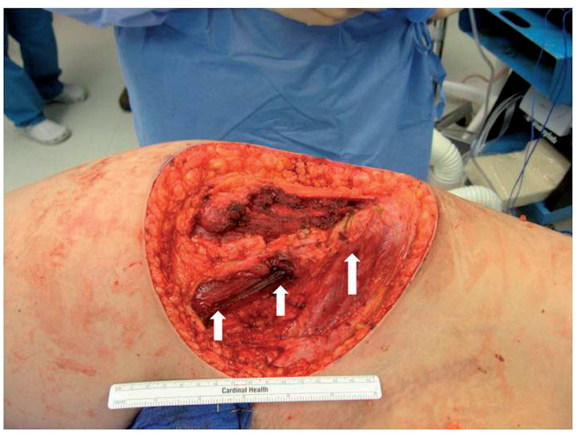

Figure 7 **Intraoperative image of patient in the left lateral decubitus position. Arrows denote the wing of the ilium, the medial extent of tumor.**

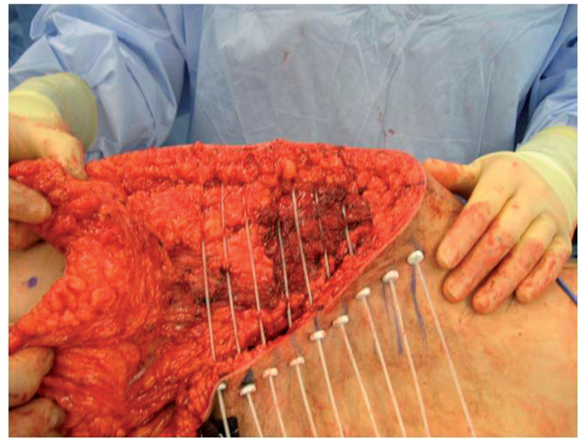

Figure 8 **Multicatheter BRT implant used to reapproximate the lax skin and subcutaneous connective tissue to the level of the wing of the ilium, while V-Y advancement flap is being inset.**

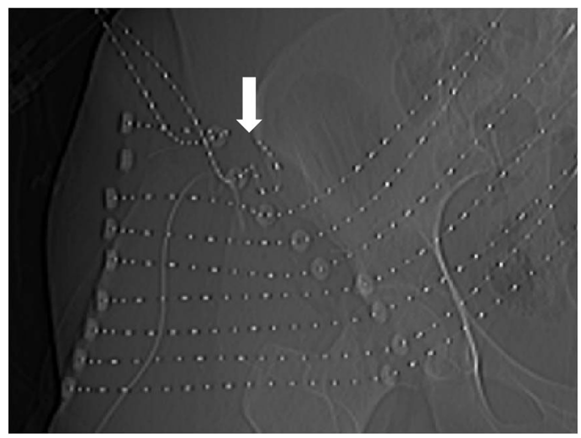

Figure 9 **Anterioposterior CT simulation scout image confirming the second catheter in the implant was bent during the perioperative period. The radioopaque marker could not be advanced through the lumen of the second catheter.**

consequence of the required high postoperative EBRT dose[11]. Therefore, a BRT boost was planned to ensure adequate dose delivery to the tumor bed while limiting the dose to the right hip joint and proximal femur. In preparation for surgical excision, the patient was positioned in a left lateral decubitus position and a wide local excision was performed. The skin and subcutaneous connective tissue of the abdomen were markedly lax as the result of a recent full-term pregnancy. When the tumor was extirpated, the lax skin and subcutaneous connective tissue produced a much larger soft tissue deficit than was originally anticipated (Fig. 7). This resulted in significant anatomic distortion of the operative site and initially, confounded the definition of the tumor bed, the target volume that would be implanted with BRT catheters. Fortunately, a preoperative MRI had identified the medial-most extent of tumor as lateral to the wing of the ilium (Fig. 6). That landmark could clearly be identified intraoperatively and was used to define the medial border of the implant (Fig. 7). The catheters were placed percutaneously, in a parallel, medial to lateral orientation and were used to aid in reapproximating the skin and subcutaneous connective tissue to the level of the wing of the ilium. Subsequently, the soft tissue deficit was filled with a V-Y advancement flap (Fig. 8). In this case, the preoperative delineation of tumor extent on MRI was essential to overcoming the intraoperative anatomical distortions and obtaining accurate target volume coverage by the BRT implant. On postoperative day 1, the patient underwent a CT simulation. However, the radioopaque markers in the second BRT catheter could not be advanced (Fig. 9). The damaged catheter was removed at the bedside. Once damaged, the catheter cannot be replaced.

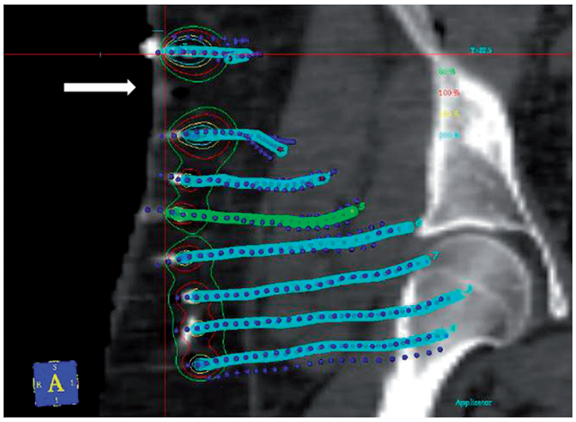

Figure 10 **CT-based three-dimensional treatment planning image demonstrating the dosimetric consequences of damaging one of the catheters. The loss of the second catheter resulted in a compromised dose distribution. Note the cold spot in the isodose distribution denoted by the arrow.**

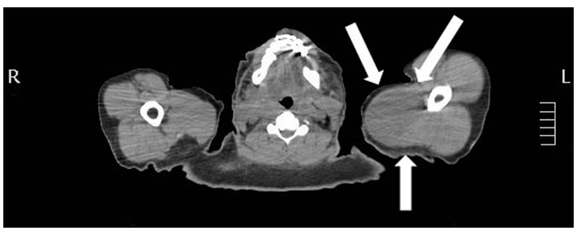

Figure 11 **Axial CT image that identifies a left shoulder mass that appears to arise from the insertion of pectoralis minor muscle.**

Without a catheter in that space to harbor the radioactive isotope, dose could not be delivered to that volume of the implant without markedly increasing the dose to normal tissue (Fig. 10). The postoperative treatment planning CT played a critical role in quality assurance, by documenting that the integrity of the implant had been compromised, prior to prescribing the dose to the patient. The events of the perioperative period after the implant were reviewed. It was determined that the catheter was likely bent during the extubation when the patient, not fully alert, attempted to sit up and flexed at the hip. The patient has no evidence of recurrence with 21 months of follow-up.

Case 4

A 73-year-old man presented with a slowly enlarging left shoulder mass. A CT of the chest revealed a 5.8 × 7.9 cm heterogeneous hypoattenuating soft tissue mass arising from the insertion of the left pectoralis minor muscle (Fig. 11). The mass was histologically confirmed to be a liposarcoma. Radiographically, the mass abutted the proximal humerus and gleno-humeral joint, portending a close or positive margin at the time of surgical resection.

Figure 12 **Intraoperative image of BRT implant at left shoulder tumor bed. The BRT implant was covered with a pectoralis major rotational flap.**

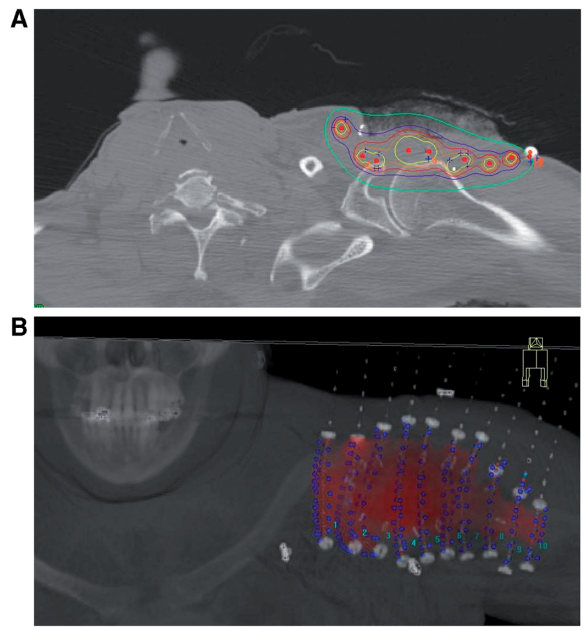

Figure 13 **(a) Axial CT simulation image documenting the prescribed dose covering the area of close margin at the gleno-humeral joint and the humeral head. (b) Coronal CT simulation image documenting the distribution of the prescription dose, represented by a red dose cloud.**

BRT was planned to address the deep margins at the surface of the bone. Ten BRT catheters were implanted (Fig. 12) and a pectoralis major rotational flap was mobilized to cover the implant. The flap was then covered by a split thickness skin graft. A CT simulation was performed on postoperative day 1. The dose was prescribed to 5 mm beyond the plane of the catheters. However, the three-dimensional dose distributions were optimized based on the CT data set, to ensure appropriate dosimetric coverage of the highest risk region, the gleno-humeral joint and humeral head (Fig. 13a,b). The patient now has

12 months of follow-up with no evidence of local recurrence. However, a CT positron emission tomography (PET) scan revealed pulmonary nodules that are suspicious for metastatic disease. A biopsy to confirm these findings pathologically is currently underway.

Conclusions

The successful application of BRT in the treatment of STS is dependent on multiple imaging modalities. Imaging is critical in the preoperative setting to define the proximity of the tumor to adjacent critical structures, predict the likelihood of close or positive surgical margins, and delineate the target volume for a BRT implant. In the postoperative setting, imaging is required to assess the integrity of implanted BRT catheters, the accuracy of a BRT implant's target volume coverage, as well as to develop a three-dimensional treatment plan.

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