Image-Guided Percutaneous Ablation of Bone and Soft Tissue Tumors

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ABSTRACT

Image-guided percutaneous ablation of bone and soft tissue tumors is an effective minimally invasive alternative to conventional therapies, such as surgery and external beam radiotherapy. Proven applications include treatment of benign primary bone tumors, particularly osteoid osteoma, as well as palliation of painful bone metastases. Use of percutaneous ablation in combination with cementoplasty can provide stabilization of metastases at risk for fracture. Local control of oligometastatic disease and treatment of desmoid tumors are emerging applications.

KEYWORDS: Percutaneous, ablation, bone, soft tissue, osteoid osteoma, painful, metastases

Objectives: Upon completion of this article, the reader should be able to identify the role of image-guided percutaneous ablation therapies in the treatment of primary bone tumors such as osteoid osteoma, as well as for palliation of painful bone metastases. The reader should also be able to assess aspects of patient selection, procedure technique, and clinical outcomes.

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Primary bone tumors and metastatic bone and soft tissue tumors present treatment challenges requiring a multidisciplinary approach, including orthopedic surgeons, radiation oncologists, medical oncologists, and interventional radiologists. Over the last decade, image-guided percutaneous ablation has emerged as an important minimally invasive alternative to conventional therapies, including surgery for benign primary bone tumors, primarily osteoid osteoma,^{1–5} as well as surgery, radiation therapy, and chemotherapy for metastases to bone and soft tissues.^{6–8} These ablation methods may be utilized with curative intent in the case of osteoid osteoma, to potentially provide local control (and possibly delay progression and increase survival) with oligometastatic dis-

ease, or to palliate painful metastases. This article will discuss the different ablative technologies applied to bone and soft tissue tumors, summarize the data supporting effectiveness of percutaneous ablation of primary and metastatic tumors in bone and soft tissue, and describe a rational approach to the treatment of these tumors based on tumor type, location, and goals of treatment.

ABLATION TECHNIQUES

Several different image-guided ablation techniques have emerged in the treatment of both primary bone tumors and secondary tumors to bone and soft tissue. The most widely used techniques include thermal

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ablation methods, such as radiofrequency ablation (RFA), cryoablation (or cryotherapy), microwave ablation, and laser ablation (or laser interstitial thermal therapy). Additional techniques include alcohol ablation, cementoplasty, and magnetic resonance imaging-(MRI-) guided focused ultrasound. These techniques differ in the type of energy delivered, image-guidance methods, treatment monitoring, and patient experience. These differences may influence which technique is best suited for a particular case, given lesion type, location, and goals of therapy.

GENERAL PRINCIPLES

The treatment of bone and soft tissue tumors with ablative techniques requires careful consideration of the perilesional anatomy. Adjacency of critical structures, including nerves, blood vessels, and bowel, influences patient selection and requires use of techniques to protect and monitor these structures. For example, thermal sink effects should be considered in approaching lesions in proximity to major blood vessels. Thermocouples may be used to monitor many different adjacent critical structures, and monitoring of motor evoked potentials may be used when adjacent to spinal cord or to major motor nerves. Methods to insulate the spinal cord or displace bowel have also been described.^{9,10} Finally, the targeted lesion must be accessible percutaneously and sufficiently separate from the spinal cord, major motor nerves, brain, artery of Adamkiewicz, bowel, and bladder. The required margin of safety depends on the ability to visualize, displace, and monitor adjacent critical structures and the experience of the interventional radiologist.

Tumor ablation typically requires regional anesthesia, moderate intravenous sedation, or general anesthesia to place the applicators and to treat patients' intraprocedural discomfort. The level of anesthesia used for treatment of these patients varies by practice. Regional anesthesia may be adequate for RFA of some osteoid osteomas, whereas technically challenging metastatic lesions often require general anesthesia.

The area targeted for treatment depends on the lesion type and goals of therapy. Treatment of osteoid osteomas requires ablation of the central nidus. Achieving local control of oligometastatic disease depends upon complete tumor inclusion in the ablation zone with an adequate margin. Palliation of painful metastases relies on adequate coverage of the bone / tumor interface.

All ablative techniques rely on adequate image guidance for applicator placement and monitoring. Ultrasound provides excellent, real-time visualization of soft tissue tumors, allowing precise applicator placement without radiation exposure. However, the use of ultrasound for applicator placement is only effective for relatively superficial masses and efficient placement of multiple applicators can be difficult to achieve. More-

over, the gas produced by RFA and ice produced by cryoablation prevents accurate intraprocedural monitoring of the ablation zone. Fluoroscopy provides high spatial and temporal resolution with low radiation risk and is widely used for vertebroplasty. MRI has superior contrast resolution in imaging most bone and soft tissue tumors without radiation exposure. Moreover, real-time guidance and temperature monitoring MRI sequences have been developed. Although promising for the treatment of patients with ablative methods, MRI-compatible devices are limited, and the MRI environment is often difficult or impractical for procedures in many clinical practices. Computed tomography (CT) is the most widely used imaging modality for these skeletal procedures for many reasons, including the relatively rapid, precise placement of devices using CT-fluoroscopy and near real-time monitoring of cryoablation with noncontrast CT imaging.

RADIOFREQUENCY ABLATION

RFA is the most widely adopted thermal ablation method with high success rates in the treatment of liver,¹¹ lung, and kidney tumors, and more recently, for the treatment of bone and soft tissue tumors outside the liver, lungs, and kidneys. Rosenthal and colleagues first described successful RFA treatment of osteoid osteomas.² RFA has now replaced surgery as the first-line therapy for osteoid osteoma with equivalent success rates, decreased morbidity, and earlier convalescence compared with surgical curettage. More recently, several trials have shown excellent palliation of painful bone metastases using RFA.^{6,7,12-14}

RFA involves direct percutaneous insertion of 15- to 17-gauge straight or expandable electrodes. These electrodes deliver high-frequency (375–500 kHz) alternating current into the tumor, which causes ionic agitation within the tissues leading to frictional heat. Grounding pads are placed on the patient so that the applied electrical current may exit the body. Local tissue temperatures reach 60 to 100°C, producing protein denaturation and coagulation necrosis. At temperatures >100°C, tissue vaporization and carbonization occur, impeding conductance of the thermal energy and limiting the size of the ablation zone. RF electrodes have different strategies to limit the temperatures reached, including internal cooling with chilled water or diffusion of water along the electrode tines. RFA is limited by perfusion-mediated tissue cooling effects due to adjacent high-flow vascular structures, which prevent achievement of lethal temperatures.

CRYOABLATION

Cryoablation is the oldest thermal ablation method, but previously relied on direct application of liquid nitrogen

to the surgical field. Current generation percutaneous cryoprobes deliver room temperature argon gas through a sealed, segmentally insulated probe. Due to rapid gas expansion within the distal tip of the cryoprobe causing rapid cooling (Joule-Thomson effect), temperatures as low as -100°C are reached within a few seconds. Cryoprobes are 1.2 to 2.4 mm in diameter, or ~ 11 to 17 gauge, and are insulated along their shafts to allow the percutaneous use of these devices. Helium gas is infused into the cryoprobes instead of argon to achieve active thawing. The diameter of the cryoprobe, length of the uninsulated tip, and the time of freezing determine the size of the ablation zone, or ice ball, generated. A single cryoprobe typically provides an oblong ice ball of ~ 3.5 cm diameter. Multiple cryoprobes (up to 25) may be used simultaneously with current cryoablation systems and placed in the geometric configuration that best provides coverage of the tumor. In general, probes are placed ~ 2 cm apart within the tumor and 1 cm from the outer tumor margin.

Two freezes of 10 minutes each are typically performed for each lesion, separated by a 5-minute-long passive thaw. Shorter or longer freeze times may be used depending on the adequacy of lesion coverage by the ice and the proximity of adjacent critical structures. Monitoring may be performed as frequently as every 2 minutes with limited noncontrast CT, although the ablation zone may also be seen with MRI. With CT monitoring, the ablation zone is identified as a well-marginated, low attenuation region along the distal shaft of the cryoprobe. The outer edge of the ice as seen on body window and level settings (window = 400, level = 40) corresponds to 0°C , with cell death reliably occurring 3 mm deep to the edge. Cell death is the result of membrane rupture and osmotic changes due to intra- and extracellular ice crystal formation, as well as protein denaturation. The probes are actively thawed for 10 to 15 minutes until they reach $\sim 25^{\circ}\text{C}$, and may then be removed. Like RFA, cryoablation is subject to perfusion-mediated thermal energy loss by adjacent vascular structures.

Cryoablation may be used to treat large, complex lesions while preserving adjacent normal critical structures. Careful monitoring of the cryoablation margin is possible due to the visibility of the ice ball on CT, a key advantage of cryoablation over other methods.¹⁵ The ice is also able to penetrate deeply into bone, unlike RF energy, which may allow better treatment of a painful osteoblastic metastasis. Finally, patients do not experience increased pain in the immediate posttreatment period following cryoablation in contrast to the significant increased immediate pain following RFA.

MICROWAVE ABLATION

Microwave ablation utilizes 14.5-gauge antennae applicators to deposit electromagnetic microwaves (at least

900 MHz), which cause ionic agitation and frictional heating. No grounding pads are necessary, unlike RFA. In theory, microwaves should be less influenced by tissue impedance variables and perfusion-mediated tissue cooling, potentially reaching higher intratumoral temperatures.¹⁶ This is reported to cause larger, more uniform ablation zones. A few limited reports of treatment of patients with metastatic disease have appeared with promising results.^{17,18}

LASER ABLATION

Laser ablation, also termed laser photocoagulation or laser interstitial thermal therapy (LITT), uses optical fibers to transmit infrared light energy into a tumor to produce heat and coagulation necrosis. A unique feature of laser ablation equipment is MRI compatibility. Laser ablation is primarily used in the treatment of osteoid osteomas.¹⁹⁻²² The ablation size obtained using LITT is relatively small per applicator, and as a result requires the use of multiple fibers for treatment of larger lesions. Primary success rates for treatment of osteoid osteoma as high as 98% have been reported with a 100% secondary success rate.^{19,23}

ALCOHOL ABLATION

Alcohol ablation of bone and soft tissue tumors is simple and inexpensive. Ethanol causes necrosis through cellular dehydration and indirectly leads to vascular thrombosis and ischemia. A fine needle (20-25 gauge) is directed into the tumor.²⁴ Iodinated contrast and lidocaine may be injected to demonstrate the extent of diffusion and provide analgesia, respectively. Ethanol is then instilled into the tumor directly. This method is limited by the unpredictable diffusivity of ethanol through the tumor and peritumoral tissues, particularly in cortical bone.

CEMENTOPLASTY

Cementoplasty, termed vertebroplasty when performed in the spine, refers to the instillation of polymethylmethacrylate (PMMA) cement into bone. This technique has been used for benign vertebral compression fractures and is increasingly used to treat painful bone metastases.²⁵ It may be performed in isolation, given direct cytotoxic effects of the PMMA on tumor cells and sensory nerves, or as an adjunctive procedure to other ablation methods to stabilize weight-bearing bones in the spine and pelvis and minimize the risk of pathologic fracture. The rationale for pain relief includes a direct effect on nociceptors as well as stabilization of painful microfractures within metastases. Most operators will treat up to three vertebral levels at a single setting.¹⁰ To prevent cement embolization and injury to neural tissue,

it is important to monitor cement instillation to avoid cement leakage into veins, epidural space, and neural foramina. When used as an adjuvant therapy, it is commonly performed the day following RFA or cryoablation when general anesthesia is employed to minimize duration of anesthesia and because moderate intravenous sedation is sufficient for performance of cementoplasty.

MRI-GUIDED FOCUSED ULTRASOUND

MRI-guided focused ultrasound has been shown to be effective in the treatment of symptomatic uterine fibroids and is being investigated in the treatment of tumors in the breast, liver, and brain. This technique involves the use of MRI guidance for the delivery of focal elevated temperatures delivered with focused ultrasound energy. Thermal monitoring imaging sequences allow the visualization of thermal ablation while avoiding adjacent critical structures. A recent report by Liberman and colleagues of a prospective trial of the use of this technique in the treatment of painful skeletal metastases showed significantly improved pain scores in 72% of the 25 patients with 3 months or greater follow-up.²⁶

TREATMENT OF PRIMARY BONE TUMORS

Osteoid osteomas are common, small (<2 cm), painful, benign bone tumors that occur in children and young

adults, with 90% of cases in patients younger than 25 years.¹⁹ Classically, these tumors may cause severe pain, worse at night, relieved with salicylates. They have a lucent nidus composed of vascular osteoblastic tissue, usually in the metaphysis or diaphysis of the long bones. Rosenthal and colleagues first described the application of RFA to osteoid osteomas.² As they described, the nidus should be targeted using CT imaging and the tumor treated using a noncooled RFA electrode for 6 minutes at 90°C (Fig. 1). Since then, others have reported successful ablation of osteoid osteomas using RFA, alcohol, and laser ablation.²⁷ Furthermore, reports and small series of percutaneous ablation of other primary bone tumors, including chondroblastomas and eosinophilic granuloma, have appeared in the literature.²⁸⁻³¹

Rosenthal et al reported a series of 263 patients treated with RFA resulting in 112 patients (89%) of the 126 cases with 2-year follow-up experiencing complete pain relief.³ Gangi et al reported early complete pain relief in 112 out of 114 patients with osteoid osteomas treated with laser photocoagulation, with another patient experiencing pain relief after treatment of reflex sympathetic dystrophy for 2 months, and a single patient failure.¹⁹ Six patients experienced recurrence of their symptoms 6 to 27 months following ablation and were successfully retreated. Of note, several of these treated tumors were within 8 mm of the spinal cord or nerve root with no neurologic deficit.

Figure 1 Radiofrequency ablation (RFA) of osteoid osteoma. (A) Coronal reformatted computed tomography (CT) image shows cortical thickening (arrow) in proximal tibial metadiaphysis of 16-year-old boy. (B) Axial CT image shows 0.5 × 1.2 cm centrally calcified lucent nidus of tumor (arrow). (C) Axial CT image shows RF electrode through nidus. Tumor successfully treated at 90°C for 6 minutes with resolution of patient's night pain.

RFA of chondroblastoma has shown promising results in several small series, although care must be taken to avoid damage to the nearby articular cartilage.^{28,32–34}

TREATMENT OF PAINFUL BONE AND SOFT TISSUE METASTASES

Indications

Bone and soft tissue metastases are a common problem in oncology patients. Autopsy studies have shown that up to 85% of patients with breast, prostate, and lung cancer have bone metastases at the time of death.³⁵ Complications due to skeletal metastases, including intractable pain, fracture, and decreased mobility, can reduce performance status and quality of life and lead to depression and anxiety.³⁵

Palliation of painful bone and soft tissue metastases utilizes localized therapies (surgery and radiation), systemic therapies (chemotherapy, hormonal therapy, radiopharmaceuticals, and bisphosphonates), and analgesic medications (opioids and nonsteroidal antiinflammatory agents). Radiation therapy (RT) is the standard of care for localized pain due to bone metastasis, although it has limitations. Meta-analysis data shows that one month following RT, more than 40% of patients experience a 50% reduction in pain, and less than 30% experience complete pain relief.³⁶ Relief from pain is frequently transient, with recurrence of pain in 57% of patients at a median of 15 weeks after completion of RT.³⁷ Unfortunately, patients who experience recurrent pain at a previously irradiated metastatic site are usually not eligible for further RT secondary to limitations in normal tissue tolerance.

Surgery is typically reserved for recent or impending pathologic fractures and may not be a suitable option in cancer patients who are debilitated with poor functional status and advanced disease. In patients with oligometastatic disease, surgery may be beneficial, but the long convalescence makes minimally invasive strategies more attractive. Targeted pharmacologic therapy, including chemotherapy, bisphosphonates, or radionuclides, have limited application in treatment of most of these tumors. Systemic analgesics are often the only option given to these patients, are frequently insufficient in management of pain, and carry significant side effects, such as constipation, nausea, and sedation.

Pain relief from bone tumor ablation is likely multifactorial. Destruction of periosteal sensory nerve fibers, decompression of tumor volume, decrease in nerve-stimulating cytokines released by the tumor, and inhibition of osteoclast activity all likely contribute.^{7,38}

Patient Selection

The appropriate application of percutaneous tumor ablative technology to the treatment of painful bone and soft tissue metastases begins with patient and lesion selection. The location and severity of pain should be determined by physical examination and validated pain scales. Patients should have at least moderate pain (≥ 4 on a 10-point scale for worst pain in a 24-hour period) because it is difficult to alleviate mild pain (0–3) with ablation, and these patients are often well treated with analgesic medications. As these are localized therapies, patients should have pain localized to one or two sites with corresponding abnormalities on cross-sectional imaging. Diffuse painful skeletal metastases should be treated with systemic therapies rather than a focal approach. Also, when numerous lesions are present, it is difficult to localize the source of a patient's pain accurately, preventing selection of an appropriate lesion to treat. In addition, lesions should be osteolytic, mixed osteolytic / osteoblastic, or primarily soft tissue in composition (Fig. 2). Osteoblastic lesions, frequently multifocal when present, may also be treated but require a bone biopsy device or drill for access and placement of ablation applicators.

Outcomes in Ablation of Painful Metastases

Several single-center and multicenter trials and series have reported excellent outcomes and safety in the ablation of bone and soft tissue metastases with RFA and cryoablation, with fewer studies evaluating alcohol ablation and MRI-focused ultrasound.

Of the percutaneous tumor ablation technologies, RFA has been evaluated most carefully. A multicenter study found that RFA significantly reduces pain in patients who present with pain due to metastatic disease refractory to standard treatments.^{7,8,13} Fifty-nine of 62 patients (95%) experienced a clinically significant drop in pain (≥ 2 point drop in worst pain in a 24-hour period). A recent American College of Radiology Imaging Network (ACRIN) single-arm prospective trial of RFA to palliate painful bone metastases in 55 patients showed decreased pain severity at one month (14.0 odds ratio) and 3 months (8.0 odds ratio) in those patients with at least 3-month follow-up.¹⁴

RFA has significant limitations despite its effectiveness in reducing pain from bone metastases. These include the inability to visualize the ablation margin with CT or ultrasound monitoring, the need for sequential overlapping ablation sessions to cover large lesions, and significantly increased pain during and immediately following the procedure. Although up to three RFA probes may be used simultaneously, adequate treatment is often limited by adjacent normal critical structures. Multiple overlapping ablations are required to treat a tumor that cannot be adequately covered with three

Figure 2 Cryoablation of painful soft tissue metastasis. (A) Contrast-enhanced computed tomography (CT) image shows 2.6-cm enhancing mass medial to scapula in 51-year-old man with metastatic esophageal sarcoma status postsurgery and radiation. (B) Longitudinal ultrasound image showing cryoprobe placement through metastasis. (C) Unenhanced CT image during cryoablation shows low attenuation ice ball completely encompassing the metastasis.

RFA probes. These overlaps are subject to potential incomplete tumor ablation at the margins of the overlapping treatments. Furthermore, the RFA procedure may be associated with significant intraoperative pain, and patients frequently experience increased pain in the immediate posttreatment period, requiring a period of weeks before significant pain reduction is achieved.

Interim analysis of our single center prospective clinical trial using cryoablation to treat painful metastatic disease in 14 patients showed encouraging results.⁶ Using the Cleeland Brief Pain Inventory,^{39,40} mean score for worst pain in a 24-hour period decreased from 6.7/10 to 3.8/10 over 4 weeks. All patients who were prescribed narcotic medications prior to the procedure reported a reduction in these medications (8 out of 8). No serious complications were seen. Pain relief from cryoablation appears to be durable with 4 of 5 patients (80%) reporting excellent pain control in the treated area during the 24-week follow-up period. Cryoablation resulted in significant pain reduction, with a 43% mean reduction in worst

pain in 4 weeks, which is considered to be clinically significant.⁴¹ Patients' reported pain relief 4 weeks following cryoablation ranged from 50 to 100%, which compares favorably to the reported RT response.

Percutaneous cementoplasty is also effective at palliation of pain due to metastatic disease, and has been studied in isolation, as an adjunct to RT, and in combination with RFA and cryoablation (Fig. 3).⁴²

Treatment for Local Control

Studies showing clinical benefit from achieving local control of bone and soft tissue metastases in patients with oligometastatic disease are lacking. However, patients would theoretically benefit in similar fashion to patients described in the literature of surgical metastasectomy. Moreover, the potential inflammatory responses seen following percutaneous tumor ablation may provide greater benefit than surgical excision if the host immune response to the tumor cells may be heightened. This area requires further study. Cryoablation is an ideal technique

Figure 3 Cryoablation and cementoplasty of painful bone metastasis. Coronal reformatted computed tomography (CT) image (A) shows 2.1-cm lytic renal cell carcinoma metastasis in right proximal femur in 69-year-old man. Single cryoprobe placed into tumor for cryoablation (B) resulted in ice ball (arrows) encompassing tumor (C). Final image (D) demonstrates cement filling ablation cavity following cementoplasty.

for this purpose as tumors may be treated aggressively, given the conspicuity of the ice ball during intraprocedural CT monitoring.

Treatment of Soft Tissue Desmoid Tumors

Extraabdominal desmoid tumors are nonmalignant, aggressive, invasive lesions involving the fascia, septae, and aponeuroses adjacent to muscle. These tumors usually affect young adults, are slightly more common in woman than men, and are relatively rare. The most common locations are the shoulder or upper extremity, chest wall or paraspinal region, and head and neck. The etiology is likely multifactorial with proposed genetic, endocrine, and traumatic cases. Surgical resection is currently recommended, although local recurrence is common, seen in ~40% of cases. Chemotherapy and radiation are considered alternative or adjuvant therapies. Kujak and colleagues report preliminary data from cryoablation of five extraabdominal desmoid tumors that had failed conventional therapy, with local control of disease in three patients at latest follow-up.⁴³ Two patients with large masses in whom the desmoids could not be completely treated due to proximity or encasement of

nerves showed in one patient reduction in size of the mass and in the second enlargement following partial treatment. Ilaslan and colleagues report RFA of five desmoid tumors in four patients with no recurrences after 4 to 68 months of follow-up.⁴⁴ Two patients experienced complications, including cellulitis and soft tissue necrosis. Another report of percutaneous chemical ablation with acetic acid in two patients showed complete response in one and partial response in the other.⁴⁵

CONCLUSION

The image-guided percutaneous ablation of bone and soft tissue tumors offers a minimally invasive approach that is effective, durable, and repeatable. Percutaneous ablation of osteoid osteomas has supplanted surgical excision as the preferred therapy. Similarly, promising results have been reported with ablation of painful bone metastases. Prospective comparison studies between different ablation techniques and standard therapies, such as RT, would be extremely useful to distinguish the relative benefits of these therapies for palliation of painful metastatic lesions. Further research is also needed to define the role of ablative therapies in obtaining local control of

bone and soft tissue tumors in patients with oligometastatic disease.

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