Image-guided ablation of bone tumors: revoir of current techniques

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Résumé
Ablation des tumeurs osseuses sous contrôle de l'imagerie : revue des techniques actuelles
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De nombreuses techniques de radiologie interventionnelle permettent la destruction percutanée des tumeurs osseuses : alcoolisation, ablation par laser, ablation par radiofréquence, ablation par micro-ondes, ablation par ultrasons, cryoablation. Plusieurs indications sont déjà validées, telles que l’ablation par radiofréquence de l’ostéome ostéoidé et des métastases osseuses qui offrent des résultats supérieurs aux techniques traditionnelles. D’autres applications devraient s’établir au cours des prochaines années.

Le but de cet article est de rappeler les principes des différentes techniques d’ablation, de résumer leurs indications et leurs résultats et de discuter leur mise en œuvre ainsi que leur éventuelle association aux techniques de cimentation osseuse.


Abstract
Multiple interventional radiology techniques are available for percutaneous ablation of bone tumors: alcohol, laser, radiofrequency, microwave, ultrasound, and cryogenic ablation. Several indications have already been validated, including radiofrequency ablation of osteoid osteoma and bone metastases, with results superior to conventional treatment. More indications should be added over the coming years.

The purpose of this article is to review the principles of the different ablation techniques, summarize their respective indications and results and discuss their implementation and the eventual combination with cementoplasty techniques.


Several image-guided techniques are available for percutaneous tumor ablation: alcohol, laser, radiofrequency, microwave, high-intensity focused ultrasound, and cryogenic ablation. These are mainly used for ablation of hepatic, renal or pulmonary tumors. They offer multiple advantages. They are minimally invasive, allow targeted tumor destruction, have a low rate of complications, and can be performed under sedation. They provide a therapeutic option to patients with advanced metastatic disease. Most of these techniques require only short hospital admissions, therefore offsetting the equipment cost by reducing the admission costs (daily hospital rate between 1,000-1,200 €) (1, 2).

These techniques may be applied to the management of bone tumors and their use for that purpose should increase in the future (3-5). The purpose of this review is to describe the different image-guided techniques available for percutaneous tumor ablation, and review the current indications and results for bone tumors.

General principles

These percutaneous tumor ablation techniques are performed using varied needles or probes (generic term describing the device placed into the tumor) with diameter usually less than 10G (2.6 mm). A coaxial technique provides a simplified means of progressing through the different steps of the procedure while protecting the needle path. Different image-guiding modalities are available. CT is more commonly used because it is widely available and allows precise depiction of deeper seated or smaller lesions. In addition to the radiation exposure, CT provides low contrast resolution, insufficient to visualize some tumors or post-treatment necrosis without the injection of intravenous contrast material. The intermittent nature of the image guidance also is a limitation. This may in part be remedied by the careful use of the very irradiating CT-fluoroscopy (6). US and fluoroscopy are complementary techniques that may be combined with CT to provide real-time image-guidance and improved spatial orientation (7). MRI is the ideal imaging modality during ablation procedures because of its superior contrast resolution and ability to measure temperature changes and other physicochemical parameters within the lesions during treatment. The use of MR guidance is limited by the low number of available units (especially open or wide bore), the need for expensive MR-compatible equipment (titanium or nickel alloy), and interference between coils and ablation systems. Currently, the ablation of similar lesions under CT and MR are longer to perform under MR and are more expensive, but without exposure to ionizing radiation (8-10).
While only minimally invasive in nature, these procedures must be performed under strict sterile technique, especially given that the target organ is bone, a structure with limited defenses against infections. The skin must be prepped and draped in a sterile fashion, and sterile gloves, gowns, and masks must be worn. The type of anesthesia: local, regional (block, spinal or epidural), sedation, or general anesthesia depends on the nature of the lesion, the selected ablation technique and general state of the patient. Local anesthesia along the needle path and periosteum is always desirable. The injection of fast and short acting local anesthetics (lidocaine for example) is necessary in cases where local anesthesia is used alone or in combination with sedation, but unnecessary when regional or general anesthesia are used. The injection of longer acting anesthetics (ropivacaine for example) as a mixture initially or alone towards the end of a procedure is useful to reduce the intensity of post-treatment pain and discomfort. Regional anesthesia is frequently used during ablation of benign bone tumors such as osteoid osteoma but rarely for cases of bone metastases. The selection between sedation and general anesthesia usually depends on the volume of the target lesion, the patient, and the experience of the anesthesiologist and radiologist. General anesthesia with immobile patients is usually preferable for lesions that are difficult to access or near critical structures (11).

In order to perform percutaneous ablation of a bone tumor, adequate knowledge and familiarity with the principles of action of the technique (which may be gained from experience using the technique for ablation in other tissues, such as the liver for example), specific features of bone tissues, pathophysiology of bone tumors and management are required. Comprehensive pre-ablation work-up is mandatory, which often requires the use of multiple imaging modalities. MR is used for improved evaluation of soft tissue components and is invaluable for spine tumors with possible extension to the spinal canal. CT easily demonstrates the lytic or blastic nature of the lesion and allows quantification of bone loss. This is most important for weight-bearing bones where a complementary strengthening procedure (injection of a bone cement or surgical osteosynthesis) may reduce the risk of pathological fracture. Different criteria are used to identify lesions with high risk of fracture: cortical destruction more than 50%, lytic lesion larger than 3 cm in diameter and pain during weight-bearing (12). Finally, patient selection for percutaneous image-guided ablation requires a multidisciplinary approach. Comprehensive patient follow-up to evaluate treatment efficacy and detect potential complications is important for both customizing optimal patient treatment and assess overall efficacy of the technique compared to conventional therapy (13).

Technique of tumor ablation

Tumor ablation is defined as the direct application of chemical or physical therapies to a specific focal tumor in an attempt to achieve eradication or substantial tumor destruction (14). This definition excludes other vascular interventional radiology techniques such as chemooembolization (15). Nonetheless, several studies have demonstrated the synergy of these techniques when used in combination as well as used in combination with radiation therapy, chemotherapy, chemooembolization, embolization or vascular clamping (16).

Alcohol ablation

Alcohol ablation (fig. 1) is the simplest tumor ablation technique to undertake. After fine needle placement into the tumor, a mixture of iodinated contrast material (25%) and lidocaine 1% (75%) is injected to assess the area of diffusion and provide local anesthesia. In the absence of vascular intravasation or contact with vital structures, absolute alcohol is then injected. Alcohol causes coagulation necrosis secondary to cellular dehydration and ischemia secondary endothelial necrosis and vascular thrombosis. Alcohol ablation has been used to treat bone metastases (17, 18) and rarely osteoid osteoma (19). Alcohol ablation is a simple and inexpensive technique (material cost less than 30 €), but alcohol diffusion into the tu-
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Laser ablation

Infrared laser ablation (fig. 2) has been used to treat several types of tumors (20). A neodymium:yttrium aluminum garnet (Nd:YAG) type generator or diode is used at lower power for thermal effect (photocoagulation) or at higher frequency (vaporization and cavitation). The light energy is transmitted to the tumor by a bare-tipped optical fiber, 400 μm in diameter, and converted into thermal energy when diffusing into tissues. Tissue diffusion varies with the wavelength. The increased temperature induces denaturation of proteins indispensable to normal cellular function, resulting in cellular coagulation necrosis. Tumor necrosis is well-limited and proportional to the amount of deposited energy, up to 15 mm in diameter for 1 200 J. Multiple fiber application is necessary for larger lesions. The procedure lasts about 10 minutes (21).

Photocoagulation is mainly used in the treatment of osteoid osteomas (22). The technique is accurate and reliable, allows treatment of difficult to access lesions, and is MR compatible. It is not adequate for treatment of very large lesions. The generator cost ranges between 15,000 and 30,000 € depending on the power, and each optical fiber is about 150 €.

Radiofrequency (RF) ablation

RF ablation (fig. 3) is a technique that is widely used for numerous indications. An RF generator produces an alternating current (460 kHz frequency) at the tip of an active electrode placed into the tumor, and the applied current exits through return grounding pads placed on the skin. Passage of the current through the tissues

causes ionic agitation resulting in tissue heating. The thermal effect depends on the electrical conduction properties of the given tissue. With temperatures over 60°C, immediate and irreversible cell damage occurs due to protein denaturation (coagulation necrosis). Temperatures over 100°C result in tissue carbonization and vaporization that degrade electrical and thermal conduction due to their grounding properties. The target therapeutic temperature is between 60-100°C for 5-10 minutes. With a single tip electrode, tumor ablation and necrosis is less than 15 mm in diameter. Different variations allow larger areas of necrosis up to 50 mm, by using internally-cooled electrodes (cooling system, pulsed mode), improving tissue conductivity (perfused electrode), or increasing the electrode tip coverage (umbrella electrodes, multipolar arrays) (2). With bipolar arrays, active and return electrodes are placed in the target tissue, and return surface grounding pads are not necessary. Heat is generated not only around the active electrode, but also around the ground needle and in the region between the two closely spaced electrodes. This results in larger zones of coagulation necrosis, and improved protection of surrounding tissues. This technique is valuable for high-risk lesions, including spinal and paraspinal tumors (23). On weight-bearing bones, RF ablation may be complemented by cement injection (24).

RF ablation can be used for benign tumors, including osteoid osteoma, and bone metastases (25).

This technique is versatile and effective with multiple indications. The cost for the generator ranges between 20 000 and 50 000 € and each electrode costs between 500 and 1 000 €.

Microwave ablation

Microwave ablation (fig. 4) is relatively new. The microwave generator produces an electromagnetic wave (frequency of about 900 MHz) from the tip of an antenna placed into the tumor. Electromagnetic microwaves agitate water molecules in the surrounding tissue, producing friction and heat, thus inducing cellular death via coagulation necrosis. Compared to other techniques, microwave ablation is less sensitive to variations in tissue composition as well as carbonization or vaporization phenomena, allowing higher intratumoral temperatures, larger tumor ablation volumes, and faster ablation times. The only commercially available system in the USA is composed of three microwave antennae in a triangular configuration with a 2 cm distance between each antenna. Grounding skin pads are not required. Microwave ablation is performed at 45 W for 10 minutes.

Indications for bone tumors are potentially multiple, especially since microwave drilling systems could be available to drill through cortical bone (27). This technique has been used to facilitate surgery for bone sarcomas by Chinese groups (28), but follow-up is insufficient for percutaneous applications.

Cryoablation

Cryoablation (fig. 5) is an older surgical technique (29). Current percutaneous applications arose from technological advances in probe manufacturing and use of argon gas as a cryogen. The argon gas is circulated in the probe causing freezing of tissues at ~100°C around the active probe (formation of ice balls). Temperatures below ~20°C induce cellular death via protein denaturation and rupture of cell membranes. The volume of tissue necrosis can be up to 3 cm in diameter and is slightly smaller than the ice ball. Several probes may be placed simultaneously for larger lesions. A typical cryoablation cycle usually includes a freezing phase (10 minutes), a thawing phase (5 minutes) with helium gas, and a second freezing phase (10 minutes). The probe must be allowed to warm up before it is removed. This cycle must be used to ensure complete and irreversible tumor destruction. The main advantage of cryoablation is the possibility to visualize the ice ball corresponding to the future zone of necrosis with all available imaging technique, including CT. In addition, cryoablation is not affected by the type of tissue and could potentially be used to treat sclerotic bone lesions without reduced efficacy. Unlike RF ablation, cryoablation possesses intrinsic anesthetic
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Fig. 8: Palliative monopolar RF ablation of a symptomatic scapular metastasis in a 67 year old patient with pharyngeal carcinoma.

a  Localizing CT images.
b  Placement of the RF electrode.
c  Tumor necrosis with gas production.

Fig. 9: Palliative bipolar RF ablation of a symptomatic iliac metastasis in a 54 year old patient with bronchogenic carcinoma.

a  Localizing CT images showing the left iliac wing lesion.
b-d  Placement of parallel electrodes in the deep and superficial portions of the tumor; the cecum is displaced away from the tumor by injecting a glucose solution to prevent the risk of complications.

Effects allowing the procedure to be performed under local anesthesia or milder sedation. It also preserves the tissue structure and does not cause collagen fiber retraction. The main pitfalls are the length of the procedure (about 30 minutes) and the cost of the equipment (3, 30).

Cryoablation has recently been used to treat bone metastases (31) and osteoid osteoma (32).

High-intensity focused ultrasound (HIFU) ablation

HIFU ablation (fig. 6) is an old previously abandoned technique (33) that is being reintroduced. A transducer is used to generate an US wave (frequency range between 1-20 MHz) and the mechanical energy is transformed into thermal energy in the tissues. The focused beam can generate high temperatures in the tissues resulting in coagulation necrosis. Cavitation (generation of gas bubbles) may contribute to the lesion by increasing mechanical and thermal energy. HIFU ablation results in well-defined areas of necrosis, about 15 mm in diameter along the axis of the beam, and about 1.5 mm in transverse diameter. The procedure can be performed under MR or US guidance. Image guidance is more delicate for moving organs and gas-containing structures are a natural barrier to the use of US (34). The main advantage of the technique...
is its non-invasive nature, but interstitial applicators are currently being developed (35).
HIFU ablation has been used to treat bone metastases (36, 37) and sarcomas (38).

**Indications**

Therapeutic indications are classically divided into palliative when the purpose of treatment is to provide symptomatic relief and curative when the purpose of treatment is complete tumor destruction. There is some overlap since many patients with metastatic disease have prolonged remissions due to increasingly effective chemotherapy regimens, where complete destruction of a few metastases would be desirable.

**Palliative treatment of bone metastases**

Bone metastases are a frequent source of pain and overall compromise in the patient’s quality of life. Pain is due to a variety of mechanisms: periosteal stretching by tumor, release of chemical mediators by tumor cells, osteolysis and fractures, nerve root infiltration and compression of nerves (39).

In addition to systemic therapy for the underlying malignancy (chemotherapy, hormonotherapy), the management of bone metastases relies on bisphosphonates, pain medication, external beam radiation therapy and surgery (40). Surgery is usually limited to the prevention and treatment of fractures and related complications, and sometimes resection of an isolated metastasis (41). External beam radiation therapy remains the gold standard treatment for bone metastases in spite of several pitfalls. Its efficacy is variable (partial relief for about 90% of patients but insufficient in 20-30% of these patients, complete relief in only 54% of cases), delayed (only 50% experience relief within the first month) and transient (12 weeks on average) without possibility of additional treatment due to dose constraints. Several sessions are often required (even though mono-fractionation appears effective as well) and the effects on bone are variable and delayed with regards to bone strengthening (42-45).

Bisphosphonates reduce bone pain and prevent skeletal complications due their inhibition of osteoclast activity (46, 47).
Finally, opiates are effective but have dose-dependent side effects (constipation, nausea, impaired mentation) (48).

Bone ablation techniques are an interesting alternative in patients with refractory pain or intolerance to other treatments. They provide faster symptomatic relief compared to external beam radiation and a reduction in the need for pain medications. Alcohol ablation was the first technique used successfully, providing significant improvement in 73% of cases (fig. 7) (17, 49). It was supplanted by RF ablation providing significant symptomatic improvement in 95% of patients during the first week (50, 51).

RF ablation can be used for most tumor locations, even spinal lesions (fig. 8 and 9)
Fig. 11: Palliative combined RF ablation and cement vertebroplasty of a symptomatic T11 metastasis in a 62 year old patient with breast carcinoma.

a Localizing CT showing a lytic lesion of the pedicle and posterior vertebral body.
b Placement of a temperature monitoring device in the epidural space to monitor the intraspinal temperature.
c Placement of the RF electrode via the vertebroplasty trocar.
d The trocar is advanced into the vertebral body prior to cement injection.
e Post-treatment CT.

Fig. 12: Palliative combined RF ablation and cement injection of a symptomatic iliac wing lesion in a 65 year old patient with multiple myeloma.

a, b Localizing CT showing the lytic lesion of the iliac wing and pathological fracture.
c, d Placement of the RF electrode via the vertebroplasty trocar and coagulation of the lesion.
e The trocar is advanced and the cement is injected.
f Post-treatment CT.
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(23, 52, 53). Smaller lesions can be completely eradicated. Complete ablation of larger tumors is not mandatory since treatment at the interface between tumor and periosteum is sufficient to provide symptomatic relief (54, 55). In patients with metastases from well-defined thyroid carcinoma, the goal is to completely eradicate the lesions to reduce the dose of therapeutic radioactive iodine (56). Ablation of sclerotic metastases is possible using reduced power to avoid early increase in impedance. RF ablation tends to be painful and usually is performed using deep sedation or general anesthesia. Pain secondary to tumor necrosis is usually present during the first three days requiring the administration of opiates and NSAIDS.

Good symptomatic relief has recently been reported using cryoablation (fig. 10) (31) and HIFU ablation (37).

One of the goals in ablation of bone metastases is to identify lesions at risk for pathological fracture (mainly the spine and acetabulum) to then consider combining the ablation procedure with the injection of cement to increase the pain relieving effects and prevent bone collapse (fig. 11 and 12) (18, 52, 57-59).

Finally, plasma-mediated RF ablation is a recent technique allowing decompression prior to injection of cement for vertebroplasty in patients with advanced metastases and compromised spinal canal (fig. 13). Unlike conventional RF ablation, this modified technique causes tissue dissolution at low temperature (60).

Curative treatment of primary bone tumors

The management of primary bone tumors has classically been surgical. Oncologic procedures are well known (need to confirm the histological diagnosis prior to resection, large or radical resection based on tumor stage, confirmation of diagnosis on the surgical specimen) and percutaneous ablation techniques are typically contraindicated. However, surgery is associated with a non-negligible rate of failure or complication for some benign bone tumors and percutaneous ablation techniques may become valuable. Osteoid osteoma is an excellent example. The small tumor size (less than 15 mm) allows CT guidance and complete RF or laser ablation (fig. 14). These techniques may thus be recommended as a first line treatment for osteoid osteoma. The main pitfall is the unavailability of histological confirmation of diagnosis given the small size of the needles used. Fortunately, characteristic clinical symptoms and imaging features usually provide a high degree of diagnostic confidence (61, 62).

RF ablation has also been used to treat other benign tumors (fig. 15) some as chondroblastoma (63, 64) and osteoblastoma. These are mainly cases of tumors that were mistaken for osteoid osteomas or tumors in locations unfavorable to surgical management.

Ablation of malignant tumors may be considered in patients with non-resectable local recurrence. Several patients with recurrent sacral chordoma were successfully treated with RF ablation (65-67).
Conclusion

Several ablation techniques are available to treat bone tumors. RF ablation is most frequently used for bone metastases and osteoid osteoma. In these patients, results are excellent and superior to results from conventional management. Additional indications should emerge in future years.

References


Fig. 15: RF ablation of an eosinophilic granuloma of the iliac wing in a 28 year old patient.
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