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Percutaneous bone lesion ablation

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Abstract Benign tumors and metastatic bone lesions can be treated by ablation techniques performed either alone or in combination with other percutaneous techniques. Ablation techniques include ethanol or acetic acid injection and thermal ablation by means of energy deposition [including laser, radiofrequency, microwave, cryoablation, radiofrequency ionization and magnetic resonance (MR)-guided high-intensity focused ultrasound (HIFU)]. Goal definition of the therapy is crucial: ablation techniques can be proposed as curative treatments in benign bone tumors or oligometastatic disease (<3 lesions). Alternatively, these techniques can be proposed as palliative treatments aiming at reduction of pain, local control of the disease and tumor decompression. Depending on the lesion's location ablation can be combined with cementation with or without further metallic augmentation; local tumor control can be enhanced by combining ablation with transarterial bland embolization or chemoembolization. Thermal ablation of bone and soft tissues is characterized by high success and relatively low rates of potential complications, mainly iatrogenic thermal damage of surrounding sensitive structures. Successful thermal ablation requires a sufficient ablation volume and thermal protection of the surrounding vulnerable structures. This article will describe the general principles governing ablation and the mechanism of action for each technique and in addition will review the literature about safety and effectiveness of percutaneous imaging-guided ablation for benign and malignant (primary and metastatic) lesions.

Keywords Bone · Ablation · Thermal · Chemical · Benign · Malignant

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Introduction

Pain is a common complaint in oncologic patients. Osseous metastasis is the most common source of pain (80 %) in cancer patients with ~25 % meeting no relief from analgesics [1, 2]. External beam radiotherapy achieves only partial pain relief in the vast majority of patients [1, 2]. In addition, osteonecrosis or neural damage might complicate radiotherapy sessions or the results on pain reduction might delay up to 4 weeks [1, 3]. Primary malignant bone tumors are not so common, with cumulative risk for developing bone cancer ranging from 0.7 to 0.9 % [4]. Benign bone tumors are by far more common than malignant forms [4].

Ablation techniques aim at generating cytotoxic temperatures (>60 and <−20 °C) (Table 1). Percutaneous ablation techniques include injection of chemical substances such as ethanol or acetic acid, delivery of energy (radiofrequency, microwave, laser) aiming at temperature increase, application of extreme cold (cryoablation) and high-intensity focused ultrasound (usually performed under magnetic resonance (MR) guidance which totally lacks any invasive character) [5–11]. Indications for imaging-guided ablation in bone tumors include curative and palliative treatments. Curative treatments aim at total necrosis of benign lesions (osteoid osteoma, osteoblastoma <3 cm in diameter, etc.) or of specific malignant tumors (slow-growing cancers with <3 lesions of <3 cm in diameter

Table 1 Review of the literature concerning different indications and techniques

Pathology	References	Technique	Indication
Osteoid osteoma	Gangi et al. [28]	Laser ablation	Curative treatment
	Mahnken et al. [24]	RFA (bipolar)	Curative treatment
	Dasenbrock et al. [25]	Coblation	Curative treatment
	Mahnken et al. [29	RFA (monopolar)	Curative treatment
	Basile et al. [27]	MWA	Curative treatment
	Napoli et al. [11]	MR-guided HIFU	Curative treatment
Other primary benign tumors	Tutton et al. [37]	Ethanol and cryoablation	Curative treatment
	Becce et al. [38]	RFA	Curative treatment
	Cable et al. [36]	RFA	Curative treatment
	Corby et al. [35]	RFA	Curative treatment
	Ramnath et al. [34]	RFA	Curative treatment
Bone and soft tissue metastasis	Callstrom et al. [42]	RFA	Pain reduction and local control
	Carrafiello et al. [44]	RFA	Pain reduction and local control
	Pusceddu et al. [49]	MWA	Pain reduction and local control
	Callstrom et al. [46]	Cryoablation	Pain reduction and local control
	Napoli et al. [11]	MR-guided HIFU	Pain reduction and local control
Primary malignant tumors	Li et al. [50]	US-guided HIFU	Curative treatment
	Rosenthal et al. [66]	RFA + surgery	Curative treatment

RFA radiofrequency ablation, *MWA* microwave ablation, *MR* magnetic resonance, *HIFU* high-intensity focused ultrasound

each) [5]. Palliative treatments aim at pain reduction and tumor debulking [5]. Occasionally, ablation should be combined with osteoplasty to prevent impending pathologic fractures [5–9].

This article will describe the general principles governing ablation and the mechanism of action for each technique and in addition will review the literature on safety and effectiveness of percutaneous imaging-guided ablation for benign and malignant (primary and metastatic) lesions.

General principles

Ablation of bone lesions requires some kind of anesthesia (usually sedation or general anesthesia are preferred). The presence of anesthesiologist will increase technical and clinical efficacy and at the same time decrease potential complication rates. Similar to all interventional techniques in the musculoskeletal system, ablation is performed under extended sterility measures and antibiotic prophylaxis [5, 6]. Imaging is necessary for exact positioning of the ablation device inside the lesion. Whenever there is intact cortex surrounding the target, a trocar is used for a coaxial approach. Once the ablation device is in position, the trocar should be withdrawn outside the expected ablation zone to avoid energy transmission with subsequent skin and soft tissue burns. Protective techniques for preventing iatrogenic damage to surrounding nerves and other sensitive structures should be applied whenever the ablation zone is expected to extend to a distance <1 cm. These techniques include skin protection, temperature measurement, monitoring of nerve root function and dissection of sensitive structures away from the ablation zone by means of gas (room air or CO_2) or fluid [12–14]. Knowledge of where a sensitive structure is located is a prerequisite for a safe and efficacious ablation session.

Ablation techniques

Chemical ablation

During ethanol or acetic acid injection, cellular dehydration, vascular thrombosis and ischemia occur resulting in target necrosis [5]. A major disadvantage of the technique is the unpredictable diffusion of the injectate. Chemical ablation was used mainly in osteolytic lesions not only for tumor necrosis but for pain reduction as well (due to the neurolysis effect) [5]. A spinal needle (usually 22 Gauge in diameter) is inserted in the lesion and the chemical agent mixed with contrast medium (for improved visualization) is injected. Depending on the size of the lesion to be treated 3–25 ml of sterile 95 % ethanol is administrated in a single or repeated sessions [5]. The mean success rate for pain reduction is 74 % with optimum results achieved within 24 h post-injection [5].

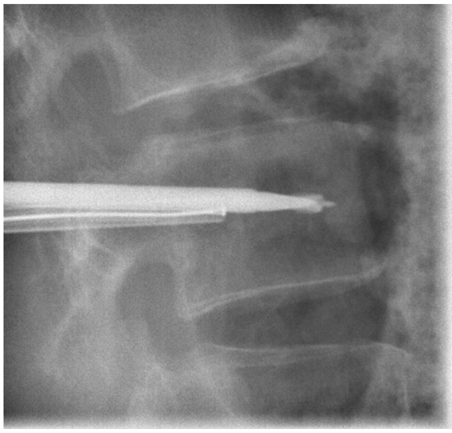

Fig. 1 Lateral fluoroscopic view. Patient with carcinoma of the prostate gland and painful osteoblastic metastases in the spine. Bilateral transpedicular access. A coblation electrode was coaxially inserted in order to decompress the tumor and create bone channels necessary for the subsequent polymethyl methacrylate (PMMA) injection

Fig. 2 Computed tomography (CT) axial scan: patient with hepatocellular carcinoma and a large soft tissue mass infiltrating the right iliac bone. Microwave ablation was performed due to the large size of the mass, followed by PMMA injection

Radiofrequency ablation

During radiofrequency ablation (RFA) a closed circuit is formed consisting of the generator, the patient, the RFA probe and the grounding pads. Radiofrequency energy is dispersed between the cathode of the circuit (RF probe) and the grounding pads. Energy released from the probe via molecular movement and agitation causes temperature increase resulting in coagulation necrosis [15]. Radiofrequency ablation is sensitive to “heat sink” effect, a term used to describe heat loss due to cooling from the flowing blood inside a nearby vessel of a diameter >3 mm [15]. Electrodes used during RFA include monopolar (single tip or multitined expandable, internally cooled, perfusion) or bipolar ones [15]. A separate group of radiofrequency ablation includes coblation (radiofrequency ionization used mainly for tumor decompression) (Fig. 1). In case of intact cortex, a trocar can be used to gain access to the lesion and then the electrode is inserted coaxially.

Microwave ablation

During microwave ablation (MWA), energy radiates from an antenna into the tissue resulting in direct heating of tissue volume surrounding the antenna. The heat in microwave ablation results from dielectric hysteresis [16, 17]. Unlike RFA, MWA is not limited by tissue conductivity and impedance; in addition, microwaves penetrate charred or desiccated tissue [16, 17]. Microwaves are not governed by “heat sink effect” and they produce a larger ablation zone in a shorter period of time (Fig. 2). For large-sized lesions, multiple antennae can be inserted to create the necessary ablation zone. Once again whenever osseous cortex is intact, a trocar is required to gain access. As in RFA, this trocar has to be removed outside the expected ablation zone prior to initiation of energy deposition.

Laser ablation

During laser ablation, a fiber transmits infrared light energy which results in cytotoxic temperature [5]. In general practice, laser fibers of wavelength near the infrared spectrum are used [neodymium–yttrium–aluminum–garnet (Nd:YAG) diode laser 800–1,000 nm] [5]. A trocar is required for the laser fiber to gain access to the lesion. Laser ablation results in a small-sized ablation zone and therefore is indicated for osteoid osteoma, small-sized lesions and in patients with a contraindication to radiofrequency ablation (metallic implants, pacemakers, etc.). To increase the diameter of the ablation zone one, multiple laser fibers can be used [5].

Cryoablation

During cryoablation extreme cold is applied to induce ischemia, protein denaturation and breakdown of cellular membrane. Energy delivery occurs by means of gas (helium and argon) expansion which is governed by the Joule–Thompson law [18]. Argon expansion occurs during cooling and helium expansion occurs during thawing [18]. During cryoablation the formed ice ball is visible under imaging guidance (thus enhancing efficacy and safety) while the technique seems to be characterized by significantly lower peri- and post-procedural pain (Fig. 3). On the other hand, the required consecutive circles of freezing and thawing are time-consuming and an increased number of probes is required for adequate ablation zone, thus

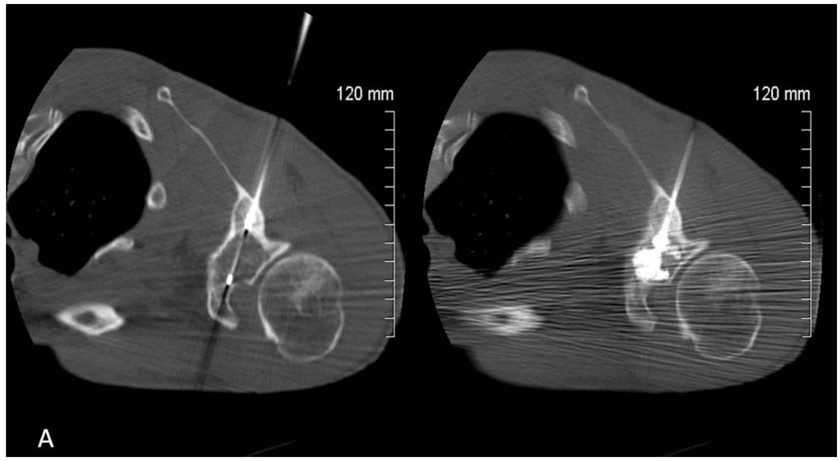

Fig. 3 CT axial scan: patient with scapular hemangioma treated with cryoablation followed by PMMA injection

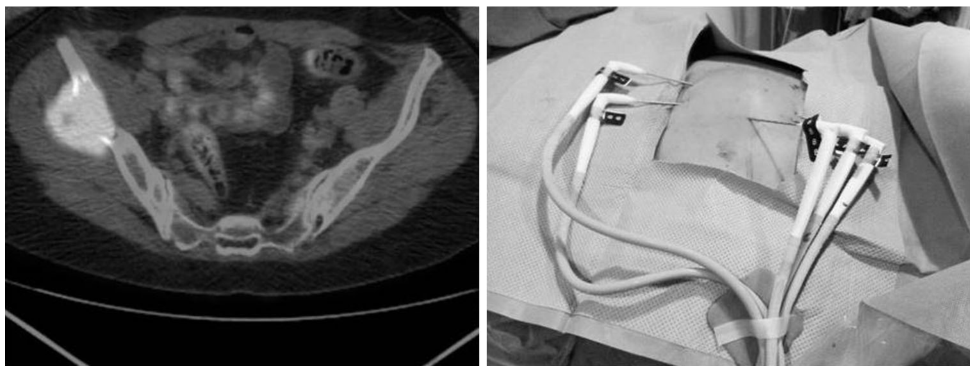

Fig. 4 Patient with melanoma and a metastatic lesion in the right iliac bone [shown on positron-emission tomography (PET)-CT scan]. Patient was treated with cryoablation followed by screw placement and PMMA injection. For the whole lesion to be covered by the ice ball, five cryoprobes were inserted

increasing the cost (Fig. 4). To ensure total tumor necrosis, the visible ice ball must cover the whole lesion and in addition include a safety margin of at least 5 mm. A specific complication associated to cryoablation is the cryoshock phenomenon which seems to be related to large-sized ablation volumes [5].

MR-guided HIFU

During MR-guided HIFU, focused ultrasound energy is delivered at the target resulting in focal elevated temperatures and coagulation necrosis [11]. In addition to targeting, MR guidance also provides real-time thermal monitoring. Planning of the treatment is essential and requires combined coronal, axial and sagittal sequences to be rendered three dimensional. Furthermore, planning of the treatment calculates the required energy that has to be delivered in the lesion through the skin. Treatment initially starts with sub-therapeutic sonications and post-verification continues at full therapeutic dose.

Osteoid osteoma

Osteoid osteoma is a benign bone tumor representing 11–14 % of all bone nonmalignant tumors, the third most common biopsied benign tumor and 2–3 % of all excised primary bone tumors [19]. The tumor is more common in males (M:F 1.6–4:1) with the majority of patients aged between 10 and 20 years and the majority of lesions occurring at metaphysic or diaphysis of long bones [19–21]. Patients typically complain of pain which exaggerates at night and is characteristically relieved by salicylates and nonsteroidal anti-inflammatory drugs (NSAID). Rosenthal et al. [22, 23] in 1992 first reported computed tomography (CT)-guided RFA as a treatment technique for osteoid osteomas comparing its efficacy to surgical operation. Nowadays, the therapeutic armamentarium for osteoid osteoma includes almost all thermal ablation techniques (RFA, MWA, laser, coblation and MR-guided HIFU) [24–31]. A recent systematic review of the literature for all ablation techniques performed to treat osteoid osteoma reports a 95 % success rate for pain relief and a 5 % failure rate [32]. In addition, the same systematic review reports level III evidence for recurrence prevention with guidelines including biopsy performance prior to ablation and multiple ablation sessions in large osteoid osteomas [32]. A key element in each ablation session for osteoid osteoma is a temperature of 90 °C for a prolonged ablation time [32].

Percutaneous ablation of osteoid osteoma is performed under axial imaging guidance (CT or MR), extended local

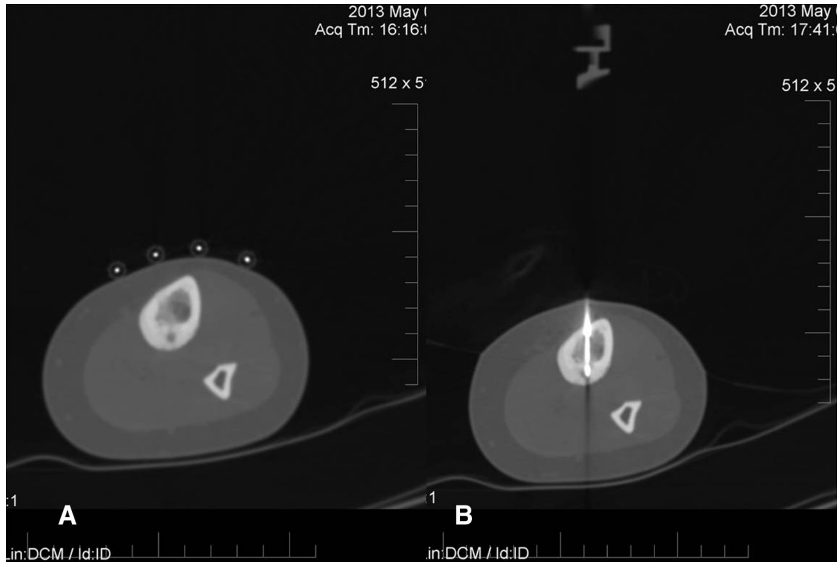

Fig. 5 CT axial scans: osteoid osteoma in the tibia. Entry point in the patient's skin was marked with a metallic mesh, a trocar was used for gaining access to the nidus and a radiofrequency electrode was inserted coaxially. Ablation protocol specifically for osteoid osteoma was performed

Fig. 6 During radiofrequency (RF) ablation (coaxial access of the RF electrode through a trocar) a sterile glove filled with cold water is placed over the patient's skin for protection against skin burn, due to proximity of the expected ablation zone to the skin

sterility measures and antibiotic prophylaxis [5, 6, 33]. A trocar is required in most of cases to gain access to the nidus of the osteoid osteoma; once the trocar is in position, the ablation device is inserted coaxially (Fig. 5). The ablation protocol is performed according to the manufacturer's guidelines for each device (Fig. 6). Imaging-guided ablation of osteoid osteoma is a safe technique with a very low rate of potential complications, including iatrogenic damage to the surrounding nerve root or tissues due to electrode placement, heat effect and size of bone necrosis [8].

Other benign tumors

A recent state-of-the-art review on interventional oncology of musculoskeletal lesions reports that "essentially any small well defined lesion at imaging can be treated with RF ablation" [8]. Usually, benign tumors to be treated by ablation include osteoblastoma (<3 cm in diameter) and chondroblastoma [5]. Throughout the literature there are reports of ablation in tumor-induced osteomalacia caused by mesenchymal benign tumors, intraosseous spinal glomus tumor, hemangiomas, chondromyxoid fibroma, intracortical chondroma, aneurysmal bone cyst, giant cell tumor and eosinophilic granuloma [8, 34–39].

Malignant tumors

Most common cancer locations include lung, colon, breast and prostate which have metastatic lesions in 20 % of the cases at presentation, while specifically for lung, breast and prostate 85 % of patients present bone metastatic lesions at the time of death [40]. Percutaneous thermal ablation can be used as curative therapy in oligolesional disease (<3 lesions). In most cases, ablation is used as a palliative therapy aiming at pain reduction and mobility improvement, tumor reduction and decompression [5–8]. The therapeutic armamentarium for these lesions includes surgery, embolization, chemotherapy, osteoplasty, ablation, radiotherapy and palliative analgesics. Surgical options in stage IV disease raise concerns concerning future life quality while chemotherapy has little effect on pain reduction [40]. Radiotherapy provides partial pain relief in most cases, it is limited for many sites and occasionally complicated by osteonecrosis or neural damage [3, 41].

Pathophysiologic explanations for pain reduction after ablation include necrosis of the interface between tumor and the pain-sensitive periosteum, tumor decompression, decrease in nerve-stimulating cytokines released by the tumor, and inhibition of osteoclastic activity [5, 7–10, 42]. A strict definition of therapeutic goal is required in ablation of a malignant lesion. Concerning pain palliation, ablation should focus at the tumor–bone interface. Whenever local control is the goal, the ablation zone should extend beyond the tumor margins. In weight-bearing areas where stabilization is additionally required ablation should be combined with cementoplasty with or without further augmentation.

Contraindications include uncorrected coagulopathy disorders, skin infection, immunosuppression and the absence of a safe path to the lesion [46]. Ability for informed consent provision is required. Tumor board meetings for decisions on local control are desirable. Ablation of malignant lesions should be performed under extended local sterility measures and antibiotic prophylaxis. Thermal protection techniques are optional and could be applied whenever the ablation zone is expected to extend close to critical or sensitive structures (e.g., nerve root, skin, etc.). So far, all ablation techniques seem to be equally effective with high efficacy rates and minimal complications [5, 7–10, 43–49]. Several published studies on the ablation of bone and soft tissue lesions report excellent results concerning safety and efficacy [11, 40–49]. The mean success rate when pain reduction is concerned is around 75–87 % [5, 9]. Ablation is a local therapy and therefore cannot be applied in patients with numerous painful lesions who should be treated with systemic therapies; in addition, in certain cases it is difficult to define few lesions responsible for the symptoms in these patients. There is a lack of studies illustrating the clinical benefit of local control by ablation which should, however, be similar to that of surgical metastasectomy [9]. Concerning primary malignant tumors, ablation can be performed as curative treatment in selected cases of osteosarcoma or soft tissue sarcoma and can provide limb salvage either performed alone or in combination with surgery [8, 50].

Combined techniques for malignant lesions

In cases of hypervascular lesions (metastatic lesions most usually originating from thyroid, renal cell or hepatocellular carcinomas), local tumor control can be enhanced by combining ablation with transarterial chemoembolization or bland embolization [51]. Triple therapies with chemoembolization, ablation and cementation have been described as well [52].

In the spine, due to weight bearing on one hand and the resultant post-ablation osteonecrosis on the other, any ablation technique should be followed by cementation [5–7]. Polymethyl methacrylate (PMMA) has been widely tested with success in the weight-bearing forces of the spine including metastatic lesions treated with ablation and cementation [53–55]. In peripheral bones, however, due to shearing forces applied during weight bearing, PMMA alone might be insufficient; in such cases combination of ablation with PMMA injection and further augmentation with metallic instruments has shown promising preliminary results [56–58].

Ablation in the spinal column

As previously mentioned, due to weight bearing, ablation in the spinal column should be accompanied by cement augmentation. Another critical issue is the presence of nearby critical structures which are sensitive to extremely high or low temperatures. During ablation in the spinal column the temperature close to nerve roots and inside the spinal canal increases despite the decreased heat transmission by the cancellous and cortical bone [59]. Heating nervous tissue at 45 °C for 10.8 min has been shown to cause 50 % damage which is more extensive as the time and temperature increase, and the same is valid for peripheral nerves as well [60, 61]. Heat transfer due to ablation in the spine is affected by the active tip of the ablation device, the ablation protocol and the presence of intact bone cortex [62, 63]. Extreme cold during cryoablation can also result in neural damage with temporary neuropraxia occurring at -20 °C and permanent neurologic damage at ≤ -40 °C [5]. Due to the sensitivity of nerves in extremely high or low temperatures and their proximity to ablation zone when spine is involved it seems rational to use all necessary and available protective techniques. These techniques include the use of thermo sensors for temperature measurement and the use of electrostimulation, evoked potentials or other monitoring techniques for the evaluation of nerve function during ablation session [5, 14, 64]. In addition, room air or carbon dioxide can be used to displace nontarget structures. Carbon dioxide is preferable since its higher solubility and its lower thermal conductivity can act as an excellent insulator in addition to increasing the distance between the ablation zone and sensitive structures. The combination of gas dissection and continuous temperature measurement close to sensitive structures is a safe and cost-effective technique which can increase the number of lesions to be treated by percutaneous imaging-guided approaches [65]. In addition, when skin is close to the expected ablation zone, increase in the distance can be achieved by local anesthetic or 5 % dextrose injection in the subcutaneous tissues and extra care can be performed by placement of a sterile glove containing warm or cold normal saline depending on the ablation technique.

Conclusions

Percutaneous imaging-guided ablation techniques include chemical ablation (injection of ethanol or acetic acid) and thermal ablation by means of energy deposition (radiofrequency or microwave ablation, coblation, cryoablation, laser ablation, high-intensity focused ultrasound). Imaging guidance improves visualization of the lesion and enhances exact positioning of the ablation device thus resulting in high technical and clinical efficacy rates as well as low potential complication rates. Anesthesiologic control, extended local sterility measures and prophylactic antibiosis constitute prerequisites. Percutaneous ablation techniques in bone lesions constitute curative therapies in benign tumors and oligometastatic disease; specifically for osteoid osteoma thermal ablation is considered the method of choice. In addition, percutaneous ablation techniques can be proposed as palliative therapies aiming at pain reduction and tumor decompression. Depending on lesion location, ablation can be combined with cementation with or without further metallic augmentation; local tumor control can be enhanced by combining ablation with transarterial bland embolization or chemoembolization. Protective techniques are optional but should be used to avoid iatrogenic damage of surrounding sensitive or critical structures whenever these structures are at risk close to the ablation zone.

Conflict of interest The Authors declare no conflict of interest.

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