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Meta-analysis of application of minimally-invasive ablation methods and classical surgical approach in osteoid osteoma and osteoblastoma

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Abstract

Osteoblastoma and osteoid osteoma are rare benign bone tumours, sometimes considered variations of the same pathologic process. However, they differ in location, incidence, age group, and size. The gold standard treatment is surgical excision for osteoblastoma and radiofrequency ablation for both. Minimally invasive techniques, including radiofrequency ablation, microwave ablations, cryoablation, ultrasound ablation, and laser ablation, are increasingly used. This meta-analysis aimed to review current treatments, focusing on minimally invasive methods versus traditional surgical excision. A data comparison of 17 original articles from the PubMed database (2014-2024) was conducted, examining treatment methods, patient numbers, success rates, pre/post-operative pain scores, and complication rates. New ablation methods achieve similar clinical results to traditional surgery for treating osteoid osteoma and osteoblastoma while minimizing invasiveness. Most procedures have technical success rates near 100%. Both invasive and non-invasive methods significantly reduce preoperative pain. Classical surgery has higher minor complication rates compared to minimally invasive treatments. Among ablation techniques, magnetic resonance guided focused ultrasound surgery is the least invasive, avoiding radiation and antibiotic-related complications. However, in ablation methods caution is needed to prevent thermal damage to nearby joints and nerves. Protective methods, such as skin protection, hydrodissection, gas dissection, and intraoperative neurostimulation, are recommended. New ablation methods provide less invasive alternatives to surgery, with high clinical and technical success rates and lower complication rates. Among these, magnetic resonance guided focused ultrasound surgery is the least invasive and most promising, though more clinical data is needed due to its recent development.

Running title: Excision vs ablation of osteoblastoma and osteoma

Keywords: osteoblastoma, osteoid osteoma, surgical excision, ablation, minimally invasive techniques

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Introduction

Osteoblastoma (OB) is a primary benign bone neoplasm. It is rare and accounts for 1% of all primary bone tumours and 1-5% of all benign bone neoplasms [1-3]. It affects mainly patients in their second or third decade of life, with male-to-female ratio of 2:1 [2,4]. Both aetiology and risk factors for OB are unknown [1]. In most cases OB presents in the vertebral column, mostly in its posterior parts [1,2,5]. It can extend from vertebral arches and develop on the vertebral bodies, what has been reported in one-third of cases [6]. It also occurs within the long bones, rather in lower than upper extremities [1,3,5]. Nonetheless, there are case reports describing less common locations, such as cuboid bone, hamate bone or patella [2,7,8].

Histopathologically OB resembles another benign bone neoplasm, osteoid osteoma (OO). Some authors even consider these tumours to be variations of the same pathologic process [3]. However, in most cases they are acknowledged as two separate disease entities [1,9].

OO is four times more frequent than OB [4,10]. It usually affects younger people, between 5 and 25 years of age, with male-to-female ratio of 3:1 [11,12]. Unlike OB, the most common site of appearance is the appendicular skeleton, particularly the femur and tibia, where more than half of OOs occur [12,13]. Only around 10% of cases involve the vertebral column [14,15].

The differences in characteristics between OO and OB are presented in **table 1**.

In macroscopic view, OB appears as round or oval bone formation, with diameter larger than 2cm [2,9,16]. Its highly-vascularised nature gives it red or red-brown colouration [1,2]. OB may be asymptomatic or may present with localized pain [1,5,16]. If the lesion is situated in the vertebral column, it may cause painful scoliosis or nerve root compression, which can lead to neurological symptoms such as muscle weakness or paraplegia [1]. In the most aggressive type of osteoblastoma, calcification of the matrix and destruction of cortical bone are visible. Moreover, paravertebral and epidural hypertrophies are observed [17]. Aggressive types of osteoblastomas mimic aneurysmal bone cysts, osteosarcomas, or metastatic bone lesions [18]. On radiographs, OBs are typically radiolucent [1,6]. Computed tomography reveals mineralization of the nidus [6].

Histologically, OB manifests with formation of osteoid and woven bone trabeculae, which are incoherently arranged [1,19]. They are surrounded by layer of osteoblasts and few osteoclasts [19,20]. Osteoblasts present with basophilic nuclei and eosinophilic cytoplasm and usually there is no cellular atypia [19].

There are a few markers that can help differentiate OBs from other types of neoplasms. For instance, β-catenin staining varies between OB and osteosarcoma and can be used to distinguish them [1,21]. Moreover, recent studies show that hypoxia-related microRNA-210, NELL-1 and FOS are also useful markers, although the last one may not be present in every case [1,22–24].

Macroscopic views of OO and OB are comparable, with the former being smaller, not exceeding 2cm in diameter [11,14]. It is also less vascularised and characterized by presence of high levels of prostaglandins and prostacyclin [1,11,15]. For example, concentrations of prostaglandins E2, I2 and F1α were 100-1000 times higher in the area of the tumour [11,25]. OO is not an aggressive tumour [11]. On radiographs it demonstrates with radiolucent nidus surrounded by reactive osteosclerosis [14,15].

The most typical symptom of OO is pain, exacerbated at night and subsiding after administration

TABLE 1 Differences in characteristics of OO and OB

	OSTEOBLASTOMA	OSTEOID OSTEOMA
Incidence	1-5% of all benign bone neoplasms	4 times more frequent than OB
Epidemiology	Mostly men, in their second or third decade of life	Mostly men, between 5 and 25 years of age
Site	Vertebral column, mostly posterior parts	Appendicular skeleton, mostly femur and tibia
Size	More than 2cm	Less than 2cm
Prostaglandins	Absent	Present
Symptoms	Localized pain. If spine involvement, painful scoliosis, nerve root compression	Pain exacerbated at night. If subcutaneous location, swelling and erythema. If close to articulation, synovitis and joint pain.
Histological view	Osteoid and incoherently arranged woven bone trabeculae, osteoblasts and fewer osteoclasts	More organized woven bone trabeculae, osteoblasts and osteoclasts
Vascularization	Higher	Lower

of nonsteroidal anti-inflammatory drugs (NSAIDs) [14,26]. Additionally, it can present with bone deformity or swelling and erythema if the tumour is located subcutaneously. When the lesion is close to the joint the symptoms may be synovitis and joint pain [11,15]. Sometimes the only symptom of OO in children is a limp [15].

Histologically, OB and OO are also similar. OO presents with nidus containing immature woven bone, bordered with osteoblasts and some osteoclasts [12,15,27]. The trabeculae of the woven bone are usually a little more organized than in the OB [1,28]. The osteoblasts of the tumour have similar size and shape, and no pleomorphism in their nuclei [15].

Markers that can be used to distinguish OO from other neoplasms are NELL-1 and FOS [22,24]. It is important to underline that the latter may not be present in every case and it can be found in some osteosarcomas [19]. Markers indicative of both OO and OB are displayed on **figure 1**.

OO and OB can be treated either by surgical excision or minimally-invasive techniques involving various types of ablations such as:

- Radiofrequency ablation (RFA)
- Microwave ablations (MWA)
- Cryoablation (CA)
- Ultrasound ablation
- Laser ablation (LA)

Ethanol ablation, which is a type of chemical ablation, used to be performed in OO treatment, however nowadays it is not utilized due to unpredictable diffusion of alcohol [29]. Aforementioned methods are presented on the **figure 2**.

Materials and methods

Articles relevant for presented meta-analysis were identified by conducting search in PubMed data-base. We limited our studies to articles published in English, between January 2014 to March 2024. Manual search with key words such as "osteoblastoma", "osteoid osteoma", "ablation", "surgical excision", "MRgFUS", "RFA", "cryoablation", "radiofrequency", "ultrasound", "microwave", "laser", "technical success rate", "clinical success rate" or combinations of the above were used to collect applicable papers. We screened abstracts of those to select articles eligible to this research. Clinical terminology, definitions and treatment classification used in this article are standardized according to guidelines approved by Cardiovascular and International Radiological Society of Europe (CIRSE) [30].

Results

Data collected

Articles that suited set requirements were screened for clinical parameters regarding presented treatment methods. Those parameters included primary technical success rate, primary clinical success rate, mean preoperative pain score, mean postoperative pain score (earliest follow-up available is presented), minor complication rate and major complication rate. Most articles used Visual Analogue Scale (VAS) for pain monitoring, while some used unspecified 10 points scale and one used pictorial Wong-Baker FACES pain rating scale. In cases when mean pain score was not available, median

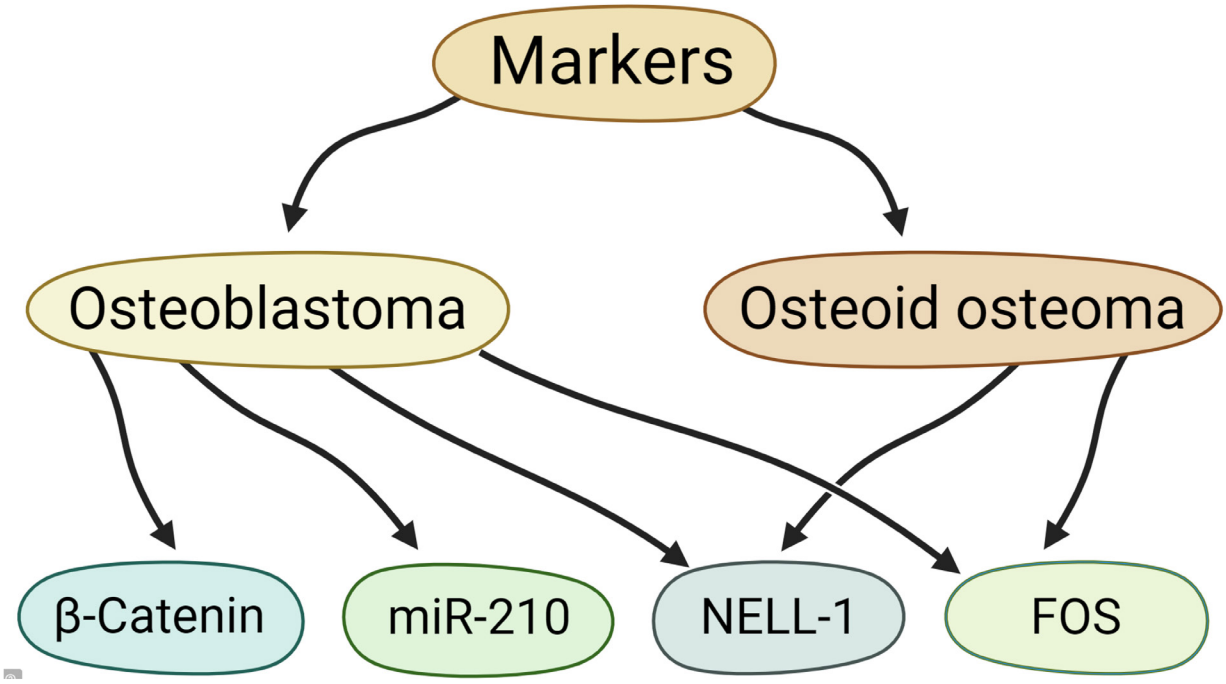

FIGURE 1 Tumour markers characteristic for OO and OB

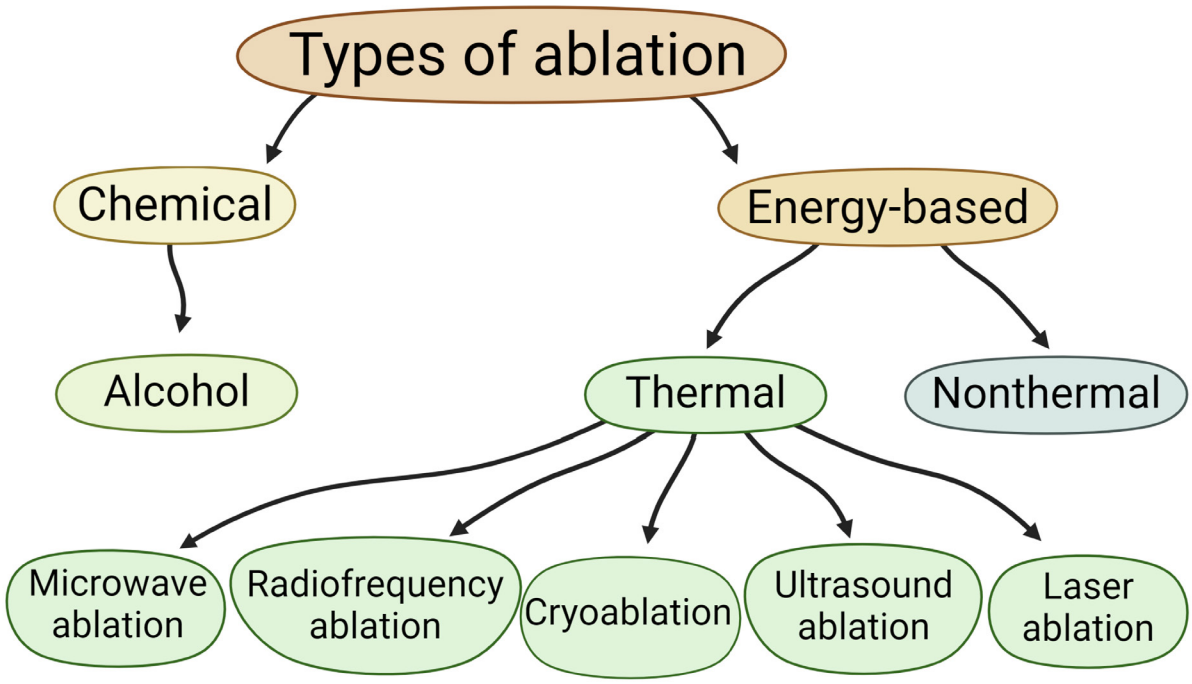

FIGURE 2 Classification of ablation according to guidelines approved by CIRSE

pain score was presented instead. In order to represent authoritative data sample, total of 17 original research articles were selected for data comparison [3,31–46]. Articles discussing application of described methods in paediatric patients were included, however age distribution was not analysed further, as screened articles did not contain sufficient data. Collected information is presented in **table 2**. It should be noted that only one article reporting aforementioned parameters in use of LA was found [43]. Furthermore, clinical data regarding MRgFUS is scarce as it is newly available method.

Surgical excision

Surgical excision of OB has a high technical success rate of around 100% and clinical success rate ranging from 88% to 100% [3,5,44]. The operation involves either intralesional excision or total excision performed under general anaesthesia [3,5]. For some abnormally large OBs the only possible option of treatment is operational removal [47]. At the same time surgical excision of OO has a technical success rate between 95,8%-100% and clinical success rate ranging from 70% to 100%, although it is not currently utilized in OO as it is considered obsolete since late 1990s [37,44,48]. This procedure stopped being the treatment of choice as a result of substantial morbidity and difficulty in conducting complete resection of highly vascularized tumours. Moreover, the small size of OO makes resection harder, which further increases the risk of recurrence due to incomplete excision of the tumour [9]. Surgical excision of OOs and OBs may also be associated with relapse rates of 4,5%-25%. The other complications involve removal of large osseous parts necessitating augmentation, instability secondary to resection and spinal cord or nerve injury [1,44,48]. Despite that surgical excision is still considered to be a gold standard in OB treatment [9,49].

Ablation

Radiofrequency

RFA is a commonly used, minimally-invasive procedure that often is a treatment of choice for OO and OB [30]. Technically RFA can use any electromagnetic field with frequency from 3KHz to 300GHz, but commercially available devices range from 375KHz to 500KHz only [30,50]. In RFA tumour is heated up and subsequently necrosed by electromagnetic field generated by a single electrode (unipolar RFA system) or two electrodes (bipolar RFA system) introduced into the abnormality [5,50,51]. For this, previously inserted needle acting as an access cannula is required [44,52]. Moreover, in unipolar RFA system an additional neutral electrode must be placed onto the skin [13,50,51]. The increase of the temperature is caused by frictional heat [5,29,32]. Furthermore, involvement of the high temperatures imposes need for sedation or analgesia [13,44,51]. It should be mentioned that effectiveness of RFA can be inhibited by variations in impedance of affected tissue, therefore making it impractical in some cases [5,51].

Microwave ablation

MWA uses an electromagnetic field with frequency ranging from 300MHz to 300GHz to destroy the tumour [30]. Therefore, technically it could be clas-

TABLE 2 Clinical parameters of presented methods

Article	Disease	Method	Number of patients	Primary technical success rate	Primary clinical success rate	Mean preoperative pain score	Mean postoperative pain score	Minor complication rate	Major complication rate
arrigoni et. al. [31]	OO	MRgFUS	33	100%	97%	7,6	0,21	0%	0%
Chahal et. al. [32]	OO	RFA	87	89,7%	86,2%	7	NA	2,3%	0%
Coupal et. al. [33]	OO	CA	10	100%	60%	7,4	1,5	0%	0%
Geiger et. al. [34]	OO	MRgFUS	29	100%	90%	8	0,6	0%	0%
Le Corroller et. al. [35]	OO	CA	50	98%	96%	8[a]	0[a]	6%	0%
Masciocchi et. al. [36]	OO	MRgFUS	15	NA	93,3%	8[a, b]	1[a, b]	20%	0%
Masciocchi et. al. [36]	OO	RFA	15	NA	100%	8,5[a, b]	1,5[a, b]	6,6%	0%
Meng et. al [37]	OO	surgery	53	100%	98,1%	6,41	0,78	52,8%	5,7%
Meng et. al. [37]	OO	CA	15	100%	100%	6,33	0,73	20%	0%
Parisot et. al. [38]	OO	MWA	28	96%	93%	7	NA	10,3%	0%
Pusceddu et. al. [39]	OO	CA	9	100%	100%	5,55[a]	1,22[a]	0%	0%
Rehnitz et. al. [40]	OB	RFA	12	100%	91,6%	7	0,25	NA	0%
Rehnitz et. al. [40]	OO	RFA	65	98,5%	96,9%	8,11	0,22	NA	1,5%
Rinzler et. al. [41]	OO	MWA	24	100%	100%	NA	0,2	17%	0%
Santiago et. al. [42]	OO	CA	21	100%	95%	7,95	0,33	14,3%	0%
Tsoumakidou et. al. [43]	OO	LA	57	100%	98,2%	NA	NA	5,3%	0%
Weber et. al. [44]	OB	RFA	19	95%	89,5%	5,4[b]	0,4[b]	0%	10,5%
Weber et. al. [44]	OO	RFA	8	100%	100%	7,75[b]	0,5[b]	0%	0%
Weber et. al. [44]	OB	surgery	8	NA	87,5%	8[b]	0[b]	0%	0%
Weber et. al. [44]	OO	surgery	10	NA	70%	8[b]	1[b]	20%	0%
Yildirim et. al. [45]	OO	MWA	9	100%	77,8%	8,89	0,78	0%	0%
Wu et. al. [3]	OB	surgery	13	100%	100%	6,23	0,54	15,4%	0%
Ayas et. al [46]	OO	surgery	26	100%	100%	4,8	0,2	0%	0%

a – as no mean pain score was available, median pain score is presented instead
b – following records have been taken directly from graphic charts and as such they can be slightly inaccurate

sified as the RFA (as radiofrequency varies from 3KHz to 300GHz). However, the differences in both mechanism of heating and clinical characteristics between those methods resulted in them being classified as separate techniques [30]. The procedure requires insertion of a needle acting as an access cannula for an electromagnetic field generating probe [41,50]. Consequently, it is performed under local or general anaesthesia [41,53,54]. Necrosis of the cancerous cells is effect of agitation of ionic molecules and frictional heat induced by microwaves [29,50,55]. MWA is effective against sclerotic bone lesions as it is not heavily affected by variations in impedance of surrounding tissue [45,55,56]. It should be emphasized that efficacy and safety of MWA in benign spinal bone tumours has not been thoroughly researched, thus its potential use in vicinity of the spine should be approached with caution [55].

Cryoablation

CA uses continuous freezing or alternating freezing-thawing cycles to produce cytotoxic effect that results in death of the cancerous cells [30]. CA can be performed under local or general anaesthesia [37,42,57]. The method itself involves insertion of one or more needles into the nidus of the tumour or into its vicinity. Multiple needles can be simultaneously placed within 1,5-2cm from each other [58,59]. Each needle is used to coaxially introduce a cryoprobe required for the actual procedure [35,37,39]. Gas circulation in non-isolated tip of the cryoprobe forces the temperature change accordingly to set requirements. Freezing phase most commonly employs argon gas to quickly cool the cryoprobe and the surrounding tissue, while thawing phase is usually achieved with helium gas [33]. The goal is to form an enlarging ice-ball, which can be visualized using CT or MRI, as it marks the area where temperature is below 0°C [42]. CA should be performed with extra 3mm safety margin as temperatures below -40°C are sufficient for destruction of the tumour [33,42,60].

Ultrasound ablation

Magnetic resonance guided focused ultrasound surgery (MRgFUS) is a novel procedure used in treatment of OO and OB. In this method external device generates high intensity focused ultrasounds which heat up the neoplastic tissue to ablative temperatures with acoustic energy and therefore cause coagulative necrosis [9,34,61]. Treatment consists series of "sonications", described as acts of delivering a number of ultrasound waves, each lasting 20s. Total amount of energy administered to the tumour site during each sonication ranges from 800J to 1800J. During each sonication temperature of the ablative tissue should not surpass 65°C. Before procedure preliminary low-energy sonication is performed in order to confirm that ultrasound beams are administered into the target area [9,34,62]. MRgFUS is a non-invasive procedure, not only because the ablation of bone lesion occurs without touching patient's skin, but also it is performed without antibiotic prophylaxis and radiation exposure. The procedure is performed under general anaesthesia. The localization of bone tumour and monitoring of its temperature is done with the aid of MRI [34,44,62]. MRgFUS therapy is mainly used for OBs and OOs which are located superficially on bone surface and are within 10cm from skin surface [9,63]. MRgFUS has a 100% technical success rate in OO treatment and clinical success rate ranging from 90% to 97% [34,64]. After ultrasound ablation mean VAS score of both OB and OO patients significantly reduced below 1 point [34,64].

Laser ablation

Laser ablation of OO has a 100% technical success rate and high clinical success rate ranging from 94,7% to 98,2% [9,43]. In most cases it is performed under general anaesthesia, however it can be also conducted with epidural anaesthesia [43,65]. Before the surgery the antibiotic is administered as infection prophylaxis [65,66]. During procedure a needle is used to guide a cannula for laser fibre. Diameter of bare laser fibre is 600μm. Through this fibre the light energy with a wavelength of 1064nm is transferred to the neoplasm. Depending on the tumour size and localization total amount of energy deposited to the lesion ranges from 360J to 4300J. This causes an increase in temperature in tumour area and leads to death of neoplastic cells [66]. Laser ablation has low both minor complication rate and recurrence rate [43,55]. According to Lorenc et al. laser ablation causes noticeable reduction in mean VAS in OO patients [67].

Discussion

Although newly developed ablation methods achieve similar clinical results compared to traditional surgical methods, they appear as an acceptable way of minimalizing invasiveness in treatment of OO and OB.

Technical success rates of all presented procedures, with few exceptions, oscillate around 100%. At the same time average clinical success rates differ slightly between all of the given methods. Preoperative pain scores both after surgical excisions and ablations significantly decline, resulting in mean postoperative pain score values varying between 0 and 1. Furthermore, preoperative pain score values seem to have no impact on choice of type of operation. Major complication rate differs slightly, overall staying around 0%. The major differences can be seen among minor complication rates, which range from 0% to 52,8%. As the 52,8% score is visibly higher than the others and concerns surgery, it may indicate that this method has larger risk of compli-

cations. This corresponds with current tendencies in increased usage of ablations in treatment of OO and OB as they are minimally-invasive techniques. It is important to underline the fact that even between ablation methods the level of invasiveness varies with the MRgFUS being the least invasive of current ablation techniques. Out of all presented procedures MRgFUS is the only one that avoids both risks of radiation exposure and complications stemming from antibiotic exposure.

Various imaging methods, such as MRI and CT, are commonly utilized in all ablation techniques, both preoperatively and intraoperatively [33,34,38,44]. Is should be noted only non-ferromagnetic surgical equipment can be used during MRI. Intraoperative imaging is especially useful in cryoablation, as CT can visualise area occupied by the ice-ball, which corresponds with range of ablated tissue (provided suitable margin is taken into account) [33,42]. Therefore, cryoablation with CT seems to be useful in cases, in which tumour is located near susceptible structures. Furthermore, advances in imaging and visualizing techniques prove to be a novice improvement in ablation. In 2016 Guenette et al. published case of two patients with OO and OB in which advanced 3D computer-based visualizing methods were used in planning of cryoablation, as a way to minimalize risk of complications [68].

Many of minor complications involve secondary tissue damage as a result of excessive ablation. They commonly include thermal injury (burns and frostbites), localized infections and self-resolving haematomas [32,36,56]. Moreover, ablation may result in deterioration of nearby vulnerable structures, such as spinal nerves in spinal OO and OB or joint damage in intra-articular lesions [52,55,56]. Thus, several protection methods can be employed to further lessen the risk of accidental damage and postoperative complications [29,37]. The simplest one is skin protection, which involves subcutaneous fluid injection or external placement of liquid-filled sterile glove as a way of preventing excess thermal exposure of the healthy tissue [33,35,57]. More advanced, frequently deployed method is dissection, which consists of internally insulating tissue from ablation site with fluid. Hydrodissection is performed with water-based solutions (saline, glucose solution, dextrose solution) and can simultaneously involve application of contrast medium [50,59]. Meanwhile, gas dissection uses atmospheric air or carbon dioxide (carbodissection) [35,42,50,59]. It should be mentioned that carbon dioxide demonstrates greater thermoisolating capabilities than air. Finally, intraoperative neurostimulation of adjacent nerves has been suggested as a way to prevent postoperative decline of their function [55]. Presented methods can also be employed in ablation of neoplasms located in non-standard position. In 2019 Basapa et. al. published a case report, where dissection was used to create a pneumothorax as a way of protecting pleura in ablation of costal OO [69].

Conclusions

The OO and OB are rare, benign bone neoplasms. They differ mainly in size, with the latter being bigger. This influences the gold standard of treatments for them, which are sequentially RFA and surgical excision. Newly developed methods of ablation present an opportunity of lessening the invasiveness of the therapy, which can be an interesting alternative, especially for surgery. Even though availability of protection and imaging methods vary across different ablation procedures, they all have high clinical and technical success rates. Moreover, their complication rates are considerably lower than those concerning surgical excision. Of all these methods, MRgFUS is the least invasive one, which makes it the most promising. Yet, as it is quite newly developed, the clinical data considering it still needs to be expanded.

Nonetheless, each method has its own advantages, which can make it a more suitable treatment for an uncommon presentation of OO or OB. In the future more research (especially in the form of randomised clinical trials) is required to further evaluate safety and efficacy of described methods.

Ethical approval
The conducted research is not related to either human or animal use.

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Not applicable.

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Conflict of interest
The authors declare no conflict of interest.

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