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# Systematic Review of MRg-HIFU as a Treatment for Osteoid Osteoma: Evaluating its Effectiveness and Clinical Applicability

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## ABSTRACT

**Introduction:** Osteoid osteoma is a small size, primary bone tumor associated with localized pain worsen at night disturbing sleep and affect life quality. Magnetic resonance-guided focused ultrasound (MRgFUS) has been recently used for osteoid osteoma and claimed to be superior to other treatment methods. However, its feasibility and efficiency still need to be precisely evaluated on a large scale to confirm its superiority and feasibility. This systematic review aimed to assess the MRgFUS feasibility and efficiency for osteoid osteoma ablation based on the success rate and complication in addition to its suitability to the different age groups.

**Methods:** A detailed search in websites including PubMed, Web of science, and Cochrane Library databases was conducted to screen the related literature to analyze data according (PRISMA) This analysis included the success rates (absence of pain at end of follow-up period), tumor recurrence rate, secondary intervention rate and ratio of complications if present in addition to the patients median age.

**Results:** Out of identified 217 studies in the data base a total of 12 studies published between 2013 and 2021 were assigned for inclusion. These studies varied between prospective, retrospective, clinical trials, case series and clinical observational cohort and included 503 patients. The period of post-treatment follow-up ranged between 4 weeks to 3 years, the ages of the treated patients varied from children to aged patients over 80 years and the majority of the osteoid osteoma distribution was 51.8 % in the femur followed by 14.5%, 11.39%, 10.88%, and 51.8% in the tibia, hand/foot, ankle and humorous respectively. The success rate of the combination was 91.4% (95% CI: 88.8%–93.5.7%) with a minor complications incidence (heat burn at the ablation site probe paths) in a rate was 0.65% with absence of recorded major complications.

**Conclusion:** MRgHIFU is a promising technique and can be an excellent clinical and feasible choice for osteoid osteoma ablation based on its high acoustic absorption of the bone tissue and its superiority over other therapeutics, being noninvasive, associated with high success rate and minor complication especially.

**Keywords:** *Osteoid osteoma, MRgFUS, Systematic Review.*

## 1. INTRODUCTION

Osteoid osteoma is a small size, benign tumor that prevalently affect the long bones diaphysis or metaphysis mostly of the femur and tibia. This type of tumor affect people in the 2nd and 3rd decades of their life with higher incidence in men [1,2]. Although its malignant transformation probability is null [3], this primary bone tumor is associated with intermittent, localized pain that is worsen at night to the extent that awaken the patient, disturbing his sleep and hence seriously affect his life quality. This severe pain is produced by the localized increased secretion of COX and prostaglandin E 100 to 1000 times more than that of the normal bone tissue associated with increased surrounding capillary permeability leading to the development of edema [4, 5]. This edema make a localized pressure stimulate the localized nerve fibers producing the common osteoid osteoma-associated pain [3]. Owing to its COX and prostaglandin-based inflammatory state, osteoid osteoma pain is well relieved by non-steroidal anti-inflammatory drugs [6]. Anatomically, osteoid osteoma is classified into cortical, medullary, and subperiosteal, with cortical type being the predominant form affecting long bones [7]. A well-circumscribed tumor about 1.5-2 cm in diameter, osteoid osteoma is a soft friable composition and red in color that decrease to the nidus center with time due to osseous maturation [8]. A central nidus surrounded by peripheral sclerosis is the common presented osteoid osteoma form [9]. It is composed of a central nidus, consists of growing interwoven bone sheaths rimmed with osteoblasts and dispersed osteoclasts in the connecting tissue separating the osteoid trabeculae, and vascular spaces [10]. The peripheray of osteoid osteoma nidus lesion is surrounded with a zone of solid, mature bone [8].

After enchondroma and non-ossifying fibroma, osteoid osteoma comes in the third category of the most prevalent benign bone tumor [11], representing 2-3% of all primary bone tumors and accounts for 10-14% of all nonmalignant tumors of the bone [12, 13, 14]).

About 70% of osteoid osteoma affects people in the 2nd decade of their life [15; 16], while 13% and 3% occurs in people older than 30 years and younger than 5 years respectively [17, 18], with incidence rate of 2-3 in males vs 1 in females [14, 8]. More than 50% of osteoid osteoma are encountered in the appendicular skeleton mainly the lower extremities especially, the femur and tibia [19], while spinal osteoid osteoma accounts for 7%–20% of all lesions [20] whereas 10% occur in the hand and wrist [21], of which 6% were recently reported to affect the proximal phalanges, 22% affect the middle phalanges, and 11% affect the metacarpal bone [22].

Although there is no agreement on the osteoid osteoma specific pathogenesis [23], however, based on a previous history of trauma in a significant percentage of the cases, osteoid osteoma was suggested to be a sort of an inflammatory process or due to unusual healing of post-traumatic state but a repored history of trauma was documented in only one third of the cases [24]. The inflammatory pathway being the background of the osteoid osteoma pathogenesis was augmented by the reported high localized levels of COX and prostaglandin E2 in the osteoid osteoma tissue [25]. However, due to its histological similarity to osteoblastoma, osteoid osteoma was believed by most pathologist to be an osteoblast-derived benign tumor [23]. The tumor's nature of osteoid osteoma was further reinforced by the cytogenic study that revealed the involvement of clonal cytogenetic abnormalities, associated with chromosome 22q changes, a same region that enclose some genes usually encountered in cell abnormal growth occurred in other types of neoplastic proliferation [26].

Classically, osteoid osteoma is monitored by X-ray radiograph as the initial diagnostic method a that is usually followed by computed tomography (CT) scan that represents the ideal way to precisely identify the lesion which usually appear as a deeply dense sclerotic area enclose a hypodense tumor focus ([27, 28]. Among the different diagnostic methods, the dynamic enhanced Magnetic resonance imaging (MRI) is of an important role to explore the osteoid osteoma due to the nidus enhancement nature that strongly supports the diagnosis ([29]). However a good metabolic exploration of the lesion is of an additional importance to differentiate the lesion from other similar disease by bone scintigraphy [30, 31]. In most case, the clinical symptoms combined with X-ray, CT and MRI are considered efficient to attain a confirmatory diagnosis [32].

To attain a very effective non-recurrent, minimal invasive techniques, a variety of ways has been tried for otsteoid osteoma treatment. As osteoid osteoma is associated with pain that became stronger at night to the extent of impairing the sleep quality, it is usually treated conservatory with non-steroidal anti-inflammatory drugs (NSAIDs). However, the use of NSAIDs cannot be extended time for being intolerable for most of the patient and its undesirable side effect. Permanently getting off the osteoid osteoma associated pain in those patients who cannot tolerate NSAIDs for long time has been undertaken by surgical removal of the lesion [9].

The difficulty of precise localization of Osteoid osteoma nidus in open surgical removal and high probability of unnecessary removal or damage of the surrounding bone tissue has led to the urgent search for other methods to achieve a less invasive with a lower destruction.

For its minimal invasive implementation, safety, shorter hospital stay and efficiency, percutaneous thermal ablation technique was the next approach for osteoid osteoma treatment in the last decades [33]. This percutaneous thermal ablation techniques is a collective name including cryoablation (CA), microwave ablation MWA, interstitial laser ablation (ILA) and radiofrequency thermal ablation (RFA) [7]. In spite of the high success rate obtained by different percutaneous thermal ablation techniques for soteoid osteoma treatment, it still invasive that necessitate the drilling from the skin and soft tissue by the probe to attain the osteoid osteoma nidus to burn it with a risk of the invasive-associated complication even if its possibility is low. In the same context, osteoid osteoma ablation by CT-guided radiofrequency in spite of achieving a nearly an absolute success rate [34,35, 36], it has a high risk of exposing the patients and the physician to the ionising radiation [37]. CT-guided radiofrequency also due to the incorrect positioning of needle, may fail to achieve complete nidus ablation due to radiofrequency overshooting beyond the precise nidus position or inaccurate angulation of the needle to the nidus postion [6].Therefore the search is continuous for inventing of new noninvasive techniques to ablate the osteoid osteoma with minimal or no complication. This may be achieved in the newly developed Magnetic Resonance-guided High Intensity Focused Ultrasound (MRg-HIFU) that we aimed to study in this systematic review hopping to summarize the available previous reports that have implemented this technique and to evaluate its effectiveness in osteoid osteoma ablation.

## 2. Methodology:

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and standard practises in the field. Using magnetic resonance imaging-guided high-intensity focused ultrasound (MR-HIFU) therapy to manage and treat osteoid osteoma was the purpose of this review.

Several bibliographical databases, including MEDLINE, PubMed, Google Scholar, CINAHL, and Scopus, were queried between January 2012 and 30 April 2023 to identify eligible articles. Osteoma AND Osteoid AND (therapy, treatment, OR management) AND (MR-HIFU OR Magnetic resonance imaging-guided high-intensity focused ultrasound) AND (MR-HIFU OR Magnetic resonance imaging-guided high-intensity focused ultrasound) AND (guidelines, consensus, practice, OR recommendation OR interventional OR study OR trial). Two researchers independently conducted a literature search and data extraction from each qualifying study. In the analysis, all reviews, expert opinions, and studies were included. Manuscripts that did not list the authors' names were excluded. From the reference lists of the retrieved articles, additional articles were uncovered.

The screening procedure consisted of two phases: title and abstract screening followed by full-text screening of possibly eligible publications. Disagreements between the two researchers were resolved through dialogue and consensus. Using the Cochrane Risk of Bias tool for randomised controlled trials (RCTs) and the Newcastle-Ottawa Scale for non-randomized research, the quality of the included studies was evaluated. The extracted data included study characteristics (e.g., study design, sample size, and follow-up period), patient characteristics (e.g., age, sex, and comorbidities), interventions (e.g., MR-HIFU parameters, duration of treatment, and number of sessions), outcomes (e.g., pain relief, reduction in size of the osteoma or osteoid, and adverse events), and conclusions. This systematic review did not require ethical approval because it did not involve any human or animal subjects.

## 3. Results:

The initial search identified 216 studies, which were vetted based on their titles and abstracts, resulting in the elimination of 127 research. After deleting duplicates, 89 studies were found appropriate for further examination. Of these, 79 papers were omitted for different reasons, including 37 studies that were not relevant based on the title and abstract, 12 studies that did not address the issue of this study, 5 studies that were replies of authors, 6 book, and 19 reviews. At the completion of the screening process, 10 publications were included in the qualitative synthesis of the present study (Figure 1). These 10 studies were examined for their quality and relevance to the topic of MR-HIFU therapy for osteoma and osteoid osteoma, and the data were consolidated and given in a table, which highlights the various features of MR-HIFU therapy, including efficacy, safety, and practicality.

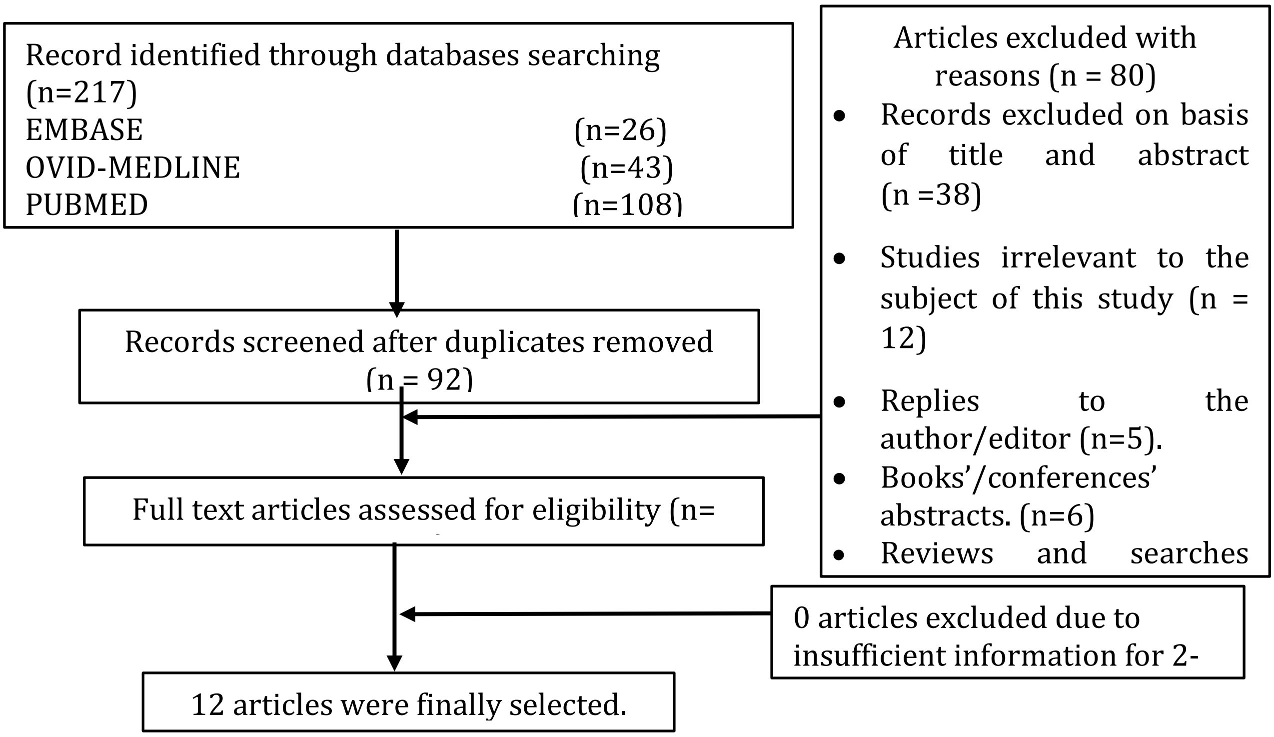


**Figure 1**The PRISMA figures showing the steps to choose the studies for systematic review.

Ten studies evaluated the use of MR-guided focused ultrasound (MRgFUS) or MR-guided high-intensity focused ultrasound (MR-HIFU) for the treatment of bone lesions, such as osteoid osteomas and bone metastases. The designs and sample sizes of the research varied, with the greatest containing 167 lesions and the smallest only four patients.

Table 1 shows the study design, sample size, patient demographics, lesion site, intervention, and outcome measures for the included studies. Pain alleviation, complete response, technical success, clinical success, complications, and feasibility are mentioned in Table 2 as outcome measures utilized in the investigations. In the included studies, Table 3 presented the treatment outcomes, including the intervention, outcome measures, and results. Table 4 detailed the success rates for lowering pain, while Table 5 gave a review of the intervention's characteristics.

***Characteristics of the included studies:***

The included investigations were done between 2013 and 2021 using diverse study approaches, including prospective cohort, case series, clinical trials, and a phase III clinical trial. Across studies, sample sizes ranged from 4 to 167 participants, and participants' ages and genders varied. The spine/sacrum, pelvis, limbs, ribs, and sternum were all affected. MRgFUS, MR-HIFU, and a combination of MR-HIFU with hydro-dissection or radiofrequency ablation were employed as therapies (RFA) (Table 1).

**Table 1:** Characteristics of the included studies

| Study | Design | Sample Size | Age | Gender | Lesion Location | Intervention | Outcome Measures |
|---|---|---|---|---|---|---|---|
| **Napoli et al., 2013 [38]** | Prospective | 6 patients | Mean age 21 years | 5 men, 1 woman | Not located in vertebral body | MR-guided focused ultrasound ablation | Feasibility, safety, and clinical efficacy |
| **Geiger et al., 2014 [39]** | Prospective multicenter | 30 patients | Mean age 25 years | 21 men, 9 women | Nonspinal osteoid osteomas | MRgFUS | Technical success, complications, and clinical success through one year of follow-up |
| **Hurwitz et al., 2014 [40]** | Phase III trial | 112 | 61.7 year | Male 51 Female 61 | Painful bone metastases | MRgFUS | Self-reported pain score, Numerical Rating Scale for pain, morphine equivalent daily dose intake, Brief Pain Inventory-QoL |
| **Bazzocchi et al., 2015 [41]** | Case series | 7 | 33.5±12.4 years | 6 male, 1 female | Superficial OO of the lower limb | MRgFUS | Visual analogue scale score, Qol |
| **Masciocchi et al., 2016 [42]** | Active control trial | 15 patients in MRgFUS group, 15 patients in RFA group | 23 (19-30) | Male 10 Female 5 | Osteoid osteoma | MRgFUS or RFA | Pain relief and motor functional recovery |
| **Rovella et al., 2016 [43]** | Retrospective | 4 patients | 14 to 18 years | Male 3 female 1 | Not specified | MR-guided focused ultrasound | Pain resolution, recurrence, treatment duration, sonication time, energy, and image analysis |
| **Napoli et al., 2017 [44]** | Prospective study | 45 | 18 years ( 16–25) years | 38 male 7 female | Femur 16, hand and foot 13, tibia 6, ankle 4, humerous 3 and elbow 1 | MR imaging–guided HIFU | The feasibility, safety, and clinical effectiveness of MR imaging–guided HIFU were considered primary outcomes. |
| **Sharma et al., 2017 [45]** | Clinical trial | 9 | 16±6 years | 7 male, 2 female | Symptomatic osteoid osteoma | MR-HIFU | Analgesic requirement, visual analog scale pain score, sleep quality |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Bing et al., 2018 [46]** | retrospective | 167 lesions (115 metastases and 52 OOs) | Not specified | Not specified | Spine/sacrum (54), pelvis (43), limbs (50), ribs (17), sternum (3) | MRgHIFU alone or with hydro-dissection | Suitability for MRgHIFU, matrix of treatable tumors, and combination with minimally-invasive thermo-protective techniques |
| **Yarmolenko et al., 2018 [37]** | Clinical trial | 8 | 7-24 yrs ( Mean 15.8±5.9 yrs) | Male 6 Female 2 | OO lesions and adjacent periosteum | MR-HIFU ablation | Temperature and tissue perfusion changes, ablated volumes, treatment time |
| **Arrigoni et al., 2019 [47]** | Case series | 33 | 13.8 years | Male 23 Female 10 | Femur (17) Tibia (6) Ankle (5) Hand and foot (2) Fibula (2) | MRgFUS | Primary and secondary success, complications |
| **Arrigoni et al., 2021 [48].** | clinical, observational, cohort | 116 | 5-60 years | 76 male 40 female | Femur (30) Ankle (5) Humorous (5) Hand and foot (3) Elbow (2) | RFA or MRgFUS | Pain relief and motor functional recovery |
| **Total** | | **503** | | | | | |

***Outcome measures:***

This study included a total number of 503 patients whose basic data are shown in Table 1. The majority of the included studies were young adults, with only two studies investigated complete mature adults [41, 44] and other two studies included some old patients over 50 years old [48] or very old patients over 60 years [40]. The total included studies had a median sample size of 30 (range 4–167). The median period follow-up of patients was 12 months, and a range of 2 weeks to 36 months.

Moreover out of twelve studies, eight studies have specified the prediction site of the osteoid osteoma being mainly in the femur 100 lesion out of total 193 with nearly 52 % of the predilection site occurring in the femur followed by the tibia (14.5%), ankle 14.5% then hand and foot 11.4 % followed by humorous 0.5% and finally a minor distribution in the acetabulum/hip, elbow, pelvis and fibula. Table 2.

**Table (2)** Osteoid osteoma tumor distribution allover the skeleton.

| Author, year | Pelvis | Acetabulum/hip | Femur | Tibia | Fibula | Ankle | Elbow | Humo-rous | Hand/foot |
|---|---|---|---|---|---|---|---|---|---|
| **Geiger et al., 2014 [39]** | 0 | 0 | 17 | 7 | 0 | 2 | 1 | 0 | 2 |
| **Bazzocchi et al., 2015 [41]** | 0 | 0 | 6 | 1 | 0 | 0 | 0 | 0 | 0 |
| **Masciocchi et al., 2016 [42]** | 0 | 1 | 8 | 2 | 0 | 2 | 0 | 2 | 0 |
| **Napoli et al., 2017 [44]** | 2 | 0 | 16 | 6 | 0 | 4 | 1 | 3 | 13 |
| **Sharma et al., 2017 [45]** | 0 | 0 | 3 | 3 | 0 | 2 | 0 | 0 | 1 |
| **Yarmolenko et al., 2018 [37]** | 0 | 0 | 3 | 3 | 0 | 1 | 0 | 0 | 1 |
| **Arrigoni et al., 2019 [47]** | 0 | 1 | 17 | 6 | 2 | 5 | 0 | 0 | 2 |
| **Arrigoni et al., 2021 [48]** | 0 | 1 | 30 | 0 | 0 | 5 | 2 | 5 | 3 |
| **Total = 193** | **2** | **4** | **100** | **28** | **2** | **21** | **4** | **10** | **22** |

Depending on the study, outcome assessments included suitability for MRgFUS, technical success, clinical success, complications, pain alleviation, motor functional recovery, feasibility, and quality of life. The most prevalent outcome measure was pain alleviation, and the most common definition of success was complete response (Table 3). Out of 12 studies, 8 studies (66.6%) employed pain alleviation as an outcome measure, with a reported utilization rate of 100 % (Sharma et al., 2017 [45, 39, 41, 40, 47, 44]. One out of twelve research (8.3%) utilized complete response as an outcome measure [42]. In 27% of research, technical success was employed as an outcome measure, whereas clinical success was used in 45% of studies). The stated use rate of technical success was 64%, while the utilization rate of clinical success was 80% [39, 38, 37 ]. Complications were utilized as an outcome measure in 4 of 12 (33.3 %) trials, with a reported usage rate of 33% (Napoli et al., 2013 [38, 39, 47, 44]). Out of 12 research, 5 studies (33.3%) utilized feasibility, with a reported use rate of 60% [38, 37, 46, 43]. (Table 3).

**Table 3:** Outcome Measures Used in Studies on MRgFUS and MR-HIFU Treatments

| Study | Pain Relie f | Complete Response | Technical Success | Clinical Success | Complications | Feasibility |
|---|---|---|---|---|---|---|
| **Napoli et al., 2013 [37]** | N/A | N/A | Yes | Yes | N/A | Yes |
| **Geiger et al., 2014 [39]** | Yes | N/A | Yes | Yes | Yes | N/A |
| **Hurwitz et al., 2014 [40]** | Yes | N/A | N/A | Yes | Yes | N/A |
| **Bazzocchi et al., 2015 [41]** | Yes | N/A | N/A | N/A | N/A | N/A |
| **Masciocchi et al., 2016 [42]** | Yes | N/A | N/A | N/A | N/A | N/A |
| **Rovella et al., 2016 [43]** | N/A | N/A | N/A | N/A | N/A | Yes |
| **Napoli et al., 2017 [44]** | yeas | N/A | N/A | N/A | Yes | Yes |
| **Sharma et al., 2017 [45]** | Yes | N/A | N/A | Yes | N/A | N/A |
| **Bing et al., 2018 [46]** | N/A | N/A | N/A | N/A | N/A | Yes |
| **Yarmolenko et al., 2018 [37]** | Yes | N/A | Yes | N/A | N/A | Yes |
| **Arrigoni et al., 2019 [47]** | N/A | N/A | N/A | Yes | No | N/A |
| **Arrigoni et al., 2021 [48]** | Yes | N/A | N/A | Yes | Yes | N/A |

The success rate of the12 studies was 91.4% (95% CI: 88.8%–93.5.7%), except for 1 study that did not mention the success rate [48]. Four studies (involving 148 patients) reported a mean VAS score of 0.62 (9.5% CI: 0.28–0.96) with high heterogeneity ($I2 = 75\%$, $P < 0.05$) at 1 week post-treatment [42, 44, 47, 48]. Four studies (involving 111 patients) reported mean VAS scores with high heterogeneity ($I2 = 98\%$, $P < 0.05$) of 0.37 (9.5% CI: 0.07–0.68) at 1 month post-treatment [38, 39, 42, 44]. One of the studies (involving 7 patients) evaluated the VAS scores at 12 weeks after the treatment getting a score of 0.30 (95% CI: 0.26–0.86) [41]. The VAS score was evaluated at 36 months after the treatment in a study including (involving 45 patients), in which the VAS score was 0.07 (95% CI: 0.01–0.15) [44]. Generally there was a progressive decrease of the VAS score from the time of RFA or MRgFUS application on the osteoid osteoma lesion to the end of the follow up period.

The need for secondary intervention was reported in 7 studies (involving 12 patients) representing 4.3 % of the of patients' total number included in these studies [41, 39, 42, 43, 44, 47, 48]. Exceptionally, the study by Masciocchi et al., [42], reported some complication as MRgFUS- associated heat damage or burning of the skin and surrounding tissue to the OO due to high energy delivered to these tissue. Moreover, in other study, the success rate was only 64% and the treatment-related adverse event as sonication pain, occurred in 32.1% of MRgFUS patients while two patients had pathological fractures, one patient had third-degree skin burn, and one patient suffered from neuropathy [40] Table 4 and the Success rate depending on pain relief of each study as shown in table 5

**Table 4:** Treatment outcomes in the included studies

| Study | Intervention | Outcome Measures | Results |
|---|---|---|---|
| **Napoli A et al., 2013 [38]** | MR-guided focused ultrasound ablation | Feasibility, safety, and clinical efficacy | Mean number of sonications was 4, with a mean energy deposition of 866 J. No treatment or anesthesia-related complications occurred. Mean pre- and post-treatment VAS scores significantly differed. |
| **Geiger et al., 2014 [39]** | MRgFUS | Technical success, complications, and clinical success through one year of follow-up | Technical success observed for all 29 patients. Complete clinical success rate of 90% demonstrated without adverse events. |
| **Hurwitz et al., 2014 [40]** | MRgFUS | Self-reported pain score, Numerical Rating Scale for pain, morphine equivalent daily dose intake, Brief Pain Inventory-QoL | Response rate for the primary endpoint was 64.3% in the MRgFUS arm and 20.0% in the placebo arm (P < .001). MRgFUS was also superior to placebo at 3 months on the secondary endpoints assessing worst score NRS (P < .001) and the BPI-QoL (P < .001). The most common treatment-related adverse event (AE) was sonication pain, which occurred in 32.1% of MRgFUS patients. Two patients had pathological fractures, one patient had third-degree skin burn, and one patient suffered from neuropathy. |
| **Bazzocchi et al., 2015 [41]** | MRgFUS | Visual analogue scale score, Qol | Mean VAS dropped to 0 after 1 month, and in 6 patients (86%) VAS remained 0 during the follow-up. No intra-operative complications or short/mid-terms adverse events were observed. |
| **Masciocchi et al., 2016 [42]** | MRgFUS or RFA | Pain relief and motor functional recovery | Similar proportion of subjects treated by MRgFUS (94%) or RFA (100%) experienced complete response 12 weeks after treatment, with no significant difference. However, heat damage or burning of the skin and surrounding tissue to the OO due to high energy delivered to these tissue occurred in |
| **Rovella et al., 2016 [43]** | MR-guided focused ultrasound | Pain resolution, recurrence, treatment duration, sonication time, energy, and image analysis | Complete pain resolution with no recurrence in 3 patients, 1 patient had recurrence of symptoms after 2 weeks and underwent a new successful treatment with increased energy levels. |
| **Napoli et al., 2017 [44]** | MR imaging–guided HIFU | Pain resolution, recurrence, treatment duration | Out of 45 patients, 42 patients (93%) had significant improvement in pain score after treatment and did not require further clinical management. Most of them (39 patients (87% achieved a general VAS score of 0 within the 36 months of follow up. Moreover, normal sleep cycle pattern and normal physical activities were restored in 41 patients |
| **Sharma et al., 2017 [45]** | MR-HIFU | Analgesic requirement, visual analog scale pain score, sleep quality | Median pain scores significantly decreased 4 weeks within treatment (6 vs 0, P < .01). Total pain resolution and cessation of analgesics were achieved in 8 of 9 patients after 4 weeks. Comparable clinical response with standard of care treatment. |
| **Bing et al., 2018 [46]** | MRgHIFU alone or with hydro-dissection | Suitability for MRgHIFU, matrix of treatable tumors, and combination with minimally-invasive thermo-protective techniques | 50% of OOs suitable for MRgHIFU alone, 32.7% suitable for MRgHIFU with hydro-dissection. 35.7% of metastases suitable for MRgHIFU alone, 37.4% suitable with hydro-dissection and/or consolidation. |
| **Yarmolenko et al., 2018 [37]** | MR-HIFU ablation | Temperature and tissue perfusion changes, ablated volumes, treatment time | MR-HIFU ablation was feasible in all eight cases. Post ablation contrast-enhanced MRI showed ablated volumes ranging 0.46–19.4 cm3 extending further into bone (7 ± 4 mm) than into soft tissue (4 ± 6 mm, p = 0.01, Mann–Whitney). Treatment time ranged 30–86 min for sonication and 160 ± 40 min for anesthesia. Complete pain relief with no medication occurred in 7/8 patients within 28 days following treatment. |

| | | | |
|---|---|---|---|
| **Arrigoni et al., 2019 [47]** | MRgFUS | Primary and secondary success, complications | Primary success of 97%. One case alone was submitted to repeat treatment because the first one failed (secondary success). No major or minor complications were recorded. |
| **Arrigoni et al., 2021 [48]** | RF; MRgFUS | Pain relief and motor functional recovery | Primary success of 94%–98% with very few serious adverse events (0%–2%). |

**Table 5:** Success rate depending on pain relief

| Study | Intervention | Outcome Measures | Results |
|---|---|---|---|
| **Geiger et al., 2014 [39]** | MRgFUS | Pain reduction as measured with a visual analog scale (VAS), recurrence, and long-term complications through twelve months | Complete clinical success rate of 90% demonstrated without adverse events. |
| **Hurwitz et al., 2014 [40]** | MRgFUS | Success rate of achieving the primary endpoint response | The response rate for the primary endpoint was 64.3% in the MRg-FUS arm. |
| **Bazzocchi et al., 2015 [41]** | MRgFUS | Success rate of achieving a visual analog scale score of 0 after 1 month and during follow-up | In all patients, the VAS score dropped to 0 after 1 month. In 6 patients (86%), the VAS score remained 0 during the follow-up |
| **Masciocchi et al., 2016 [42]** | MRgFUS, RFA | Success rate of experiencing complete response 12 weeks after treatment | A similar proportion of subjects treated by MRgFUS (94%) or RFA (100%) experienced complete response 12 weeks after treatment |
| **Napoli et al., 2017 [44]** | MRg-HIFU | Success rate of achieving a visual analog scale score of 0 after 1 month and during follow-up and restoration of the normal sleep cycle pattern and normal physical activities 36 months following treatment. | Out of 45 patients, 42 patients (93%) experienced complete response after 36 months of follow up. Of this number (39 patients (87% achieved abolishment of pain at the 36 months of follow up. Returning to normal sleep cycle and normal physical activities were achieved in 41 patients |
| **Sharma et al., 2017 [45]** | MR-HIFU | Success rate of achieving total pain resolution and cessation of analgesics after 4 weeks | 8/9 patients (89%) achieved total pain resolution and cessation of analgesics after 4 weeks |
| **Yarmolenko et al., 2018 [37]** | MR-HIFU ablation | Success rate of complete pain relief with no medication within 28 days following treatment | 7/8 patients (87.5%) experienced complete pain relief with no medication within 28 days following treatment |
| **Arrigoni et al., 2021 [48]** | MRgFUS, RFA | Pain relief and motor functional recovery | Primary success of 94%–98% of success with very few serious adverse events (0%–2%). |

## 4. Discussion:

Osteoid osteoma-associated pain is a nightmare affecting the quality of sleep and need to be consistently controlled. In spite of the availability of abolishing this pain by the use of the NSAIDs, unfortunately it can be linked to deleterious side effects besides being intolerable for most of the patient. Permanently getting off the osteoid osteoma associated pain in those patients who cannot tolerate NSAIDs for long time has been undertaken by surgical removal of the lesion [9]. However, the difficulty of precise localization of osteoid osteoma nidus in open surgery and high probability of unnecessary removal or damage of the surrounding bone tissue, motivated the surgeons to invent a less invasive methods to reduce the osteoid osteoma surrounding tissue damage during its surgical removal. Indeed many progressively less invasive techniques have been developed. of these, the percutaneous thermal ablation, is a minimal invasive technique that has been implemented for the last decades and achieved the safety, the shorter hospital stay and the efficiency [33]. Different types of this percutaneous thermal ablation have been implemented and achieved high success rates, of which, cryoablation (CA), microwave ablation MWA, interstitial laser ablation (ILA) and radiofrequency thermal ablation (RFA) [7]. However because the percutaneous thermal ablation is still invasive requiring the skin and soft tissue drilling by the probe to reach the osteoid osteoma nidus, it may be associate with thermal burn in the drilling path and surrounding tissues. Compared to this, the currently investigated MRgFUS and MR-HIFU techniques have achieved the goal of being non-invasive as they uses a strong magnetic field to precisely pointing the ultrasound beams on the targeted tumor and therefore avoiding the normal surrounding tissue destruction during the tumor ablation [49]. Consisted with this, the result of the data meta-analysis in the current study assures the superiority of the MRgFUS over the percutaneous thermal ablation due to absence of postoperative complications and the high rate of success. Indeed, MRgFUS has been approved to be fairly efficient for controlling metastatic bone lesion [50]. Moreover, treatment of 10,000 patients with a claimed perfect efficacy and feasibility has been achieved using the MRgFUS as a deeply trusted therapeutic podium [46]. Many proofs have accumulated to augment the consideration of MRgFUS as an excellent alternative for abolishing osteoid osteoma-associated bone pain [42, 41, 45]. Therefore, it may be a must to precisely evaluate the efficiency and feasibility of MRgFUS for osteoid osteoma treatment. In the current study, collective analysis of the previous reports that implemented MRgFUS in osteoid osteoma treatment presented a high success rate that has been achieved in a short postoperative period with and minor complication. Based on these facts, MRgFUS can be considered the golden option for abolishing the osteoid osteoma-associated pain.

Moreover, osteoid osteoma ablation has been undertaken by CT-guided radiofrequency achieving a high rate of success [35, [36]. But unfortunately, CT-guided radiofrequency was described to be associated with a great risk of the deleterious effect of ionising radiation on the patients and surgeons [37]. Additionally, affecting the feasibility of the CT-guided radiofrequency techniques, the possibility of the radiofrequency overshooting beyond the precise nidus position or inaccurate angulation of the needle to the nidus postion resulting in the incorrect positioning of needle and the resulting incomplete ablation of the osteoid osteoma nidus [6]. The currently discussed (MRg-HIFU) show the high success rate of osteoid osteoma associated with high precision, no risk of any radiation exposure of the patients or the surgeons with very minute complications. These data again augment the consideration of the (MRg-HIFU) superior over the other techniques types of osteoid osteoma ablation including the percutaneous thermal ablation techniques and the CT-guided radiofrequency in addition to the open surgical removal or the extended periods of the NSAIDs use. Worth to noting, the variability between the included studies in the current systematic review was noticeable concerning the rate of success and the complication rates. This may be attributed to the variability of the patients ages with a high rate of success in the young ages [47] compared to older ages patients [41] indicating the expected higher success rate in the lower ages patients. This proposed effect of the age on the success rate is further assured by the reported low success rate of 65.7% in the old age patients with a median age of 61.7 years [40]. In the same context, the variation in age of the treated patient groups in different studies affect the rate of complication with higher rate in the older age of patients included in the studies [40] compared to the lower complication rate of the younger age of patients included in other studies [47]. Moreover, the patients numbers included in the different studies may affect the success rate percentage calculation with higher calculated success rate in the higher number of patients [47]) compared to lower calculated success rate in the lower number of patients included in other study [45]. In the current study, it was noted the great variation of the follow up period between the different studies in a way that significantly affected the success rate calculation with a low success rate in the short follow up periods of four weeks and a success rate of 87.5% [37] compared to 2 years of follow up with a 97% calculated success rate [47]. Therefore, it may be worthy recommending that the patients who underwent osteoid osteoma ablation by MRg-HIFU are to be followed up for considerable periods not less than one year before being completely evaluated. Importantly, the success rate of the MRg-HIFU mediated bone tumors ablation was affected by the bone tumor nature whether it is benign or metastatic with the trending of excellent success rates were mostly reported especially in the younger age groups of benign bone tumors patients as osteoid osteoma [44, 45, 47]). Meanwhile the inclusion of metastatic types of bone tumors patients in the studies that used MRg-HIFU mediated bone tumors ablation were mostly reported to negatively affect the success rate [46]. MRgHIFU was suggested to be the ideal palliative technique for osteoid osteoma ablation [38, 39, 42], or bone metastatic tumor [40].

There are some limitations to draw an assured final decision. This is attributed to most of the included studies uses low number of patients and short period of patients follow up so that they were invalid to completely evaluate the long-term feasibility and safety of the MRgFUS technique for osteoid osteoma ablation. Secondly, the included studies did not discuss the effect of the age and sex on the efficacy of the MRgFUS on the osteoid osteoma ablation therefore more studies are required taking in consideration the effect of age and sex on the MRgFUS safety and the efficacy.

## 5. Conclusion:

The result of the current systematic review indicates the promising future of the use of the MRgHIFU as the excellent clinical and feasible choice for osteoid osteoma ablation based on its high acoustic absorption of the bone tissue and its superiority over other therapeutics, invasive or even radiotherapy in respect to the high success rate, efficiency and feasibility beside its association with lower rate of recurrence and complications especially when guided by imaging. However more prospective precisely planned studies are still needed to more accurately evaluate its efficiency and feasibility with consideration of extending the post-treatment follow up period.

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