Regence

Medical Policy Manual Durable Medical Equipment, Policy No. 83.12

Ultrasonic Bone Growth Stimulators (Osteogenic Stimulation)

Effective: June 1, 2024

Next Review: April 2025
Last Review: April 2024

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Low-intensity pulsed ultrasound devices are used to transmit energy through tissue as acoustical pressure (sound) waves as a treatment to promote healing of bone fracture sites.

MEDICAL POLICY CRITERIA

I. Low-intensity pulsed ultrasound treatment may be considered **medically necessary** when either of the following Criteria are met:

A. Treatment of fracture nonunion of bones of the appendicular skeleton when all of the following Criteria (1.- 6.) are met:

1. Patient is skeletally mature (see Policy Guidelines); and
2. At least 3 months have passed since the date of injury or treatment; and
3. Radiographic evidence on at least 2 serial imaging studies during the most recent 3-month period showing evidence of nonunion or nonhealing; and
4. The fracture gap is less than or equal to 1 cm; and
5. The patient is not a tobacco user OR there is clinical documentation that the patient has been abstinent from tobacco use for at least six weeks prior to

stimulation; and

6. The patient can be adequately immobilized.

B. As an adjunct to closed reduction and immobilization in the treatment of certain fresh fractures (defined as within 14 days of the fracture) when all of the following Criteria (1. - 3.) are met:

1. Patient is skeletally mature (see Policy Guidelines); and
2. The patient is not a tobacco user OR there is clinical documentation that the patient has been abstinent from tobacco use for at least six weeks prior to stimulation; and
3. The fracture is one of the following types:
   a. Jones fracture; or
   b. Scaphoid; or
   c. Talar neck; or
   d. Tarsal navicular.

II. The replacement or revision of all or part of an existing stimulator is considered **medically necessary** when the existing stimulator is malfunctioning, cannot be repaired, and is no longer under warranty.

III. Replacement or revision of all or part of an existing stimulator is considered **not medically necessary** when Criterion II. is not met.

IV. Low-intensity pulsed ultrasound treatment is considered **not medically necessary** for any of the following:

A. Fracture nonunion that does not meet Criterion I.A.;

B. Fresh fractures that do not meet Criterion I.B.;

C. Fractures or nonunion of bones of the axial skeleton (skull and vertebrae);

D. Stress fractures (defined as a fatigue-induced fracture resulting from repeated stress over time);

E. Fractures due to bone pathology or tumor/malignancy;

F. Failed joint fusion following arthrodesis.

V. Low-intensity pulsed ultrasound treatment is considered **investigational** for all other conditions, including but not limited to treatment of any of the following: distraction osteogenesis, osteotomy, congenital pseudoarthrosis, or osteonecrosis.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

- Skeletally mature refers to a system of fused skeletal bones, which occurs when bone growth ceases after puberty; for females, this generally occurs around age 16, and for males, around age 18.

- Fractures that have undergone surgical treatment and no longer require surgical intervention should be considered for ultrasound bone growth stimulation applying the Criteria for Fracture Nonunions.

LIST OF INFORMATION NEEDED FOR REVIEW

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

1. History and Physical/Chart notes documenting policy criteria.
2. Documentation of nonunion location, serial radiographs documenting no progressive signs of healing over most recent three months, fracture gap measurement, and documentation supporting skeletal maturity and non-smoking status of the patient.

CROSS REFERENCES

1. Electrical Bone Growth Stimulators (Osteogenic Stimulation), Durable Medical Equipment, Policy No 83.11

BACKGROUND

Ultrasound is a form of mechanical energy that can be transmitted through tissue as acoustical pressure (sound) waves. As low-intensity waves generated by the device pass over the surface of the skin overlying the fracture, the tissues in the callus may be mechanically stimulated and generate a biochemical response to the stimulation. This may increase blood flow to the fracture site, expression of genes involved in bone healing, secretion of growth factors, and bone matrix ossification, all of which may contribute to fracture healing or nonunion.[1]

REGULATORY STATUS

In 1994, the Sonic Accelerated Fracture Healing System (SAFHS®; renamed Exogen 2000® and since 2006, Exogen 4000+; Bioventus) was approved by the U.S. Food and Drug Administration through the premarket approval process for treatment of fresh, closed, posteriorly displaced distal radius (Colles) fractures and fresh, closed, or grade I open tibial diaphysis fractures in skeletally mature individuals when these fractures are orthopedically managed by closed reduction and cast immobilization. In February 2000, the labeled indication was expanded to include the treatment of established nonunions, excluding skull and vertebra. The AccelStim™ Bone Growth Stimulator (Orthofix US) was FDA approved in 2022 for accelerating time to healed fracture for fresh, closed, posteriorly displaced distal radius fractures and fresh, closed, or Grade I open tibial diaphysis fractures and for established non-unions in skeletally mature adults. Food and Drug Administration product code: LOF.

BONE FRACTURES

An estimated 178 million new fractures were reported worldwide in 2019.[2]. Most bone fractures heal spontaneously over several months following standard fracture care (closed reduction if necessary, followed by immobilization with casting or splinting). However, approximately 5% to 10% of all fractures have delayed healing, resulting in continued morbidity and increased utilization of health care services.[3] Factors contributing to a nonunion include

which bone is fractured, fracture site, the degree of bone loss, time since injury, the extent of soft tissue injury, and patient factors (eg, smoking, diabetes, systemic disease).[4]

FRESH (ACUTE) FRACTURE

While there is no standard definition of a “fresh” fracture, the most common definition is within seven days after the fracture occurs.[5, 6] Other studies have defined fresh as less than five days after fracture and as up to 10 days postfracture, and other studies have suggested even more variable timeframes based on fracture location.[7-9] Most fresh closed fractures heal without complications using of standard fracture care (i.e., closed reduction and cast immobilization).

FRACTURE NONUNION

There is no consensus on the definition of nonunions applicable to all fractures, given variations in the bone tissue and fracture characteristics.[4] A 2005 AHRQ Technology Assessment review found that nonunion is most commonly defined as the absence of signs of healing for an additional three months after assessment is made that healing is delayed.[1] These definitions do not reflect the underlying conditions in fractures that affect healing, such as the degree of soft tissue damage, alignment of the bone fragments, vascularity, and quality of the underlying bone stock. There also is variability in the specific radiographic and clinical criteria used to diagnose nonunion. A review of the literature found that 79% of surgeons use radiographic evidence of cortical continuity as the primary means of defining fracture nonunion, and 42% also used weight-bearing and 37% used pain at the fracture site during palpation.[10]

EVIDENCE SUMMARY

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of low-intensity pulsed ultrasound (LIPUS) for bone healing, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

LOW-INTENSITY PULSED ULTRASOUND

Systematic Reviews

Searle (2023) published a Cochrane Review assessing the effects of low-intensity ultrasound (LIPUS), high-intensity focused ultrasound (HIFUS) and extracorporeal shockwave therapies (ECSW) as part of the treatment of acute fractures in adults.[11] A total of 21 studies, involving 1,543 fractures in 1,517 participants were included, two were quasi-RCTs. Twenty studies tested LIPUS versus control (1,459 participants). The authors reported very low-certainty evidence for the effect of LIPUS on Health-related quality of life (HRQoL) measured by SF-36 at up to one year after surgery for lower limb fractures (mean difference [MD] 0.06, 95% confidence interval [CI] -3.85 to 3.97, favors LIPUS; three studies, 393 participants). There may be little to no difference in time to return to work after people had complete fractures of the upper or lower limbs (MD 1.96 days, 95% CI -2.13 to 6.04, favors control; two studies, 370 participants; low-certainty evidence). There is probably little or no difference in delayed union or non-union up to 12 months after surgery (RR 1.25, 95% CI 0.50 to 3.09, favors control; seven studies, 746 participants; moderate-certainty evidence). Although data for delayed and non-union included both upper and lower limbs, we noted that there were no incidences of delayed or non-union in upper limb fractures. In upper limb fractures, MDs ranged from 0.32 to 40 fewer days to fracture union with LIPUS. In lower limb fractures, MDs ranged from 88 fewer days to 30 more days to fracture union. Little to no difference was found in incidents of skin irritation. Time to fracture union and pain at one-month post-surgery was not evaluated due to statistical heterogeneity. No studies reported data for functional recovery. Data for treatment adherence were inconsistently reported across studies but was generally described to be good. Data for costs were reported for one study, with higher direct costs, as well as combined direct and indirect costs, for LIPUS use. The authors conclude that they are uncertain of the effectiveness of ultrasound therapy for acute fractures for patient-reported outcomes (PROMS) and that LIPUS makes little to no difference in the treatment of delayed union or non-union. All studies had unclear or high risk of bias in at least one domain. The certainty of the evidence was downgraded for imprecision, risk of bias and inconsistency.

A systematic review (SR) by Schandelmaier (2017) provides a comprehensive overview and analysis of the existing evidence, including 26 RCTs that used LIPUS for bone healing.[12] Given the substantial overlap in the studies included in this SR and others, summarized below, we will primarily focus on the findings of Schandelmaier (2017), which include analyses that highlight the results of RCTs identified as of higher quality. The recently published meta-analysis by Seger (2017) analyzed healing index and average time to union following use of LIPUS in cases of scaphoid nonunion, but it did not report control group comparisons.[13] The systematic review by Lou (2017), focused on fresh fractures and the review by Leighton (2017) focused on nonunions.[14, 15] All systematic reviewers acknowledged that the evidence for the use of LIPUS has methodologic limitations.

The study populations in RCTs included by Schandelmaier (2017) examined multiple types of fractures including fresh fractures surgically managed (n=7), fresh fractures not surgically managed (n=6), distraction osteogenesis (n=5), nonunion fractures (n=3), osteotomy (n=3), and stress fractures (n=2). The RCTs had a median population size of 30 patients (range, 8-501 patients). The outcomes examined by this SR emphasized those reported by patients to be most important: functional recovery (eg, time to return to work, time to full weight-bearing); pain reduction; and number of subsequent operations. Additional outcomes included time to radiographic healing because this may be used by physicians to influence clinical decision making and adverse events associated with LIPUS.

In this SR, two reviewers independently assessed the quality of selected RCTs, using GRADE, a modified Cochrane risk of bias tool. Generation of randomization sequence, concealment of

allocation, and blinding of patients, caregivers, and outcome reporting were evaluated in each trial. Each outcome within each trial was assessed for blinding of outcome assessors, loss to follow-up, and additional limitations. Trial authors were contacted if there was uncertainty in the quality assessment. Of the 26 included trials, six were considered to have a low-risk of bias, with the remaining 20 trials considered to have a high-risk of bias. Reasons for high-risk of bias designation included failure to report a method for allocation concealment (15 trials), high or unclear numbers of patients excluded from the analysis (13 trials), unblinded patients (10 trials), and unblinded caregivers or outcome assessors (10 trials). Of the six trials rated to be at low-risk of bias, four were conducted in individuals with fresh fracture, three of which were operatively managed tibial fractures.

LOW-INTENSITY PULSED ULTRASOUND FOR FRACTURE NONUNION

Systematic Review

Leighton (2017) reported the results of a SR and meta-analysis of published literature that explored the use of low-intensity pulsed ultrasound as a treatment of nonunions.[15] A total of 13 eligible papers, including one RCT, reporting the results of LIPUS for the treatment of 1441 nonunions of the tibia, humerus, radius, ulna and femur, were evaluated. The date range of the literature search was not specified. The quality of the studies was scored using the Methodological Index for Non-Randomized Studies. Quality scores ranged from 5 to 12, with an “ideal” score for a nonrandomized trial being 16. The pooled estimate of effect size for heal rate was 82% (95% CI: 77 to 87%) for any anatomical site and fracture age of at least three months, although statistical heterogeneity was identified across all primary studies (Q=41.2 [df=12], p<0.001, Tau2=0.006, I2=71). With a stricter definition of nonunion as fracture age of at least eight months duration, the pooled estimate of effect size rose to 84% (95% CI: 77% to 91.6%) although heterogeneity remained present: Q=21 [df=8], p<0.001, Tau2=0.007, I2=62). No statistically significant difference was detected between upper and lower extremity long bone nonunions in heal rate. Favorable results of LIPUS intervention were obtained when LIPUS was used as an alternative rather than as an adjuvant to surgery.

Seger (2017) published a SR with meta-analysis including five studies focused on scaphoid nonunions in which healing index and average time to union following LIPUS were analyzed.[13] Among the 166 nonunions in the analysis, 78.6% (range, 33%-100%) were reported to show healing following LIPUS, with an average time to union of 4.2 months (range, 2.3-5.6 months). These results lead the authors to conclude that LIPUS may serve as a nonoperative alternative to scaphoid nonunion in certain cases.

Randomized Controlled Trials

Schofer (2010), published the results of a multicenter, double-blinded, sham-controlled RCT of LIPUS in 101 adult patients who had sustained a tibial shaft fracture that subsequently showed inadequate progress toward healing.[16] This RCT was included in the SR by Leighton. Delayed union was defined as a lack of clinical and radiologic evidence of union, bony continuity, or bone reaction at the fracture site for no less than 16 weeks from the index injury or the most recent intervention. Patients were randomized to LIPUS (n=51) or to an inactive sham device (n=50), to be administered 20 minutes a day for 16 weeks. The primary outcome was change in bone mineral density assessed by computed tomography attenuation coefficients. Gap area was a secondary outcome. Intention-to-treat analysis showed that low-intensity pulsed ultrasound improved mean bone mineral density by 34% (90% CI, 14% to 57%) compared with sham treatment. The mean reduction in bone gap area was -0.13 mm^2 in the low-intensity

pulsed ultrasound group and -0.10 mm^2 in the sham group (effect size, -0.47; 95% CI, -0.91 to -0.03 mm^2). At the end of 16 weeks, physicians judged 65% of patients in the low-intensity pulsed ultrasound group healed and 46% of the patients in the sham group healed (p=0.07). This trial did not report functional outcomes or pain assessment, limiting the utility of results.

Ricardo (2006) published a blinded RCT evaluating 21 subjects with scaphoid nonunion who were treated with low-intensity pulsed ultrasound or a sham device following a pedicled vascularized bone graft.[17] Time to healing was defined as the number of days from the operation to healing both clinically (solid and not causing tenderness or pain) and radiographically (bridging cortices). All patients were males, with an average age of 26.7 years (range 17 to 42 years) and an average interval between injury and surgery of 38.4 months (range 3 months to 10 years). Follow-up averaged 2.3 years (range 1-4 years). Although all patients achieved fracture union (active and placebo groups) compared with the placebo device (n=11), the active device (n=10) accelerated healing by an average of 38 days (56+/-3.2 days compared with 94+/-4.8 days, p<0.0001).

Nonrandomized Studies

Nolte (2016) conducted a retrospective comparison of patients with metatarsal fractures treated by low-intensity pulsed ultrasound and by surgical techniques.[18] For the comparative analysis, patients from a U.S. Food and Drug Administration (FDA) required LIPUS registry (n=594) were propensity-matched 1:1 with patients treated surgically from a health claims database. The overall heal rates for all types of fractures combined were comparable for LIPUS (97%) and surgery (95%) (p=0.07). After exclusion of registry patients who received surgery, heal rate with LIPUS alone (97.4%) was significantly better (p<0.0097) than the heal rate for matched patients in 2011 (94.2%).

Rutten (2007) published an analysis of 76 individuals with tibial nonunions. Included in the analysis were 71 individuals who were at least 3 months from the last surgical intervention and did not show any healing improvements in the 3 months before ultrasound treatment (average fracture age: 257 days; range: 180-781).[19] All individuals were followed up (average 2.7 years) by questionnaire, or by phone, if needed. There was an overall healing rate of 73%, at an average 184 days to healing (range: 52-739). No difference in healing rate for open or closed fractures was observed.

Section Summary: Fracture Nonunion

The evidence for the use of LIPUS in the treatment of fracture nonunion includes 14 studies, two of which are RCTs, and two additional nonrandomized studies. Two systematic reviews with meta-analyses have evaluated data on LIPUS for fracture nonunion. Shorter healing times compared to sham or no treatment have been identified across these studies, and favorable outcomes in reduction of bone gap size and mineral density have been found with treatment with LIPUS compared to sham treatment. There is sufficient evidence to determine that treatment of fracture nonunion with LIPUS provides improvement in health outcomes in skeletally mature patients.

FRESH FRACTURES

Systematic Review

Lou (2017) conducted a SR with meta-analysis focusing on fresh fractures in adults.[14] The literature search, conducted through November 2016, included 12 studies (n=1099), all of

which were included in the Schandelmaier (2017) meta-analysis, except for a small abstract (n=20). The evidence was considered to be of moderate-to-high quality. The pooled results revealed that low-intensity pulsed ultrasound significantly decreased the time to fracture union (standard mean difference [SMD]: 0.65; 95% confidence interval [CI], 1.13 to 0.17), improved the quality of life (SMD: 0.20; 95% CI, 0.03 to 0.37) without affecting the time to full weight bearing (SMD: 0.76, 95% CI: 1.92 to 0.4), the time to resuming work (SMD: 0.06; 95% CI, 0.14 to 0.27), or the incidence rate of delayed union and nonunion (RR: 1.02; 95% CI, 0.60 to 1.74). A subgroup analysis demonstrated that the reduction in healing time with low-intensity pulsed ultrasound was not reflected in individuals who underwent surgical intervention. While the authors concluded that individuals with fresh fractures may benefit from the use of low-intensity pulsed ultrasound, there were several methodologic limitations in the trials, including but not limited to the inadequate concealment of treatment allocation, the high loss of follow-up, the unclear age baseline, smoking, or gender status.

Hannemann (2014) published a SR with meta-analysis of 13 RCTs (n=737) comparing pulsed electromagnetic fields (PEMF) or low-intensity pulsed ultrasound (LIPUS) bone growth stimulation with placebo for fresh fractures.[20] Three hundred and fifty-five participants were treated with LIPUS (n=209) or PEMF (n=146), and 382 participants were treated with a placebo device. No significant differences were found in time to radiological union between PEMF or LIPUS and placebo (mean difference = -13.32, 95% CI= -32.71 to 6.06, p=0.18), however, in pooled data analyses, heterogenous results that significantly favored PEMF or LIPUS treatment specifically in non-operatively managed fractures were identified (mean difference = -26.65, 95% CI-50.35 to -2.91, p=0.03). In addition, pooled analysis of the three studies comparing PEMF or LIPUS with placebo of the upper limb found heterogenous results of significantly reduced time to radiological union in this group compared to control (mean difference=-20.23, 95% CI -32.68 to -7.77, p=0.001). There was considerable heterogeneity in the outcome parameter of time to radiological union, which is considered a limitation of the study. The authors concluded that bone growth stimulation with LIPUS or PEMF decreases healing time to radiological union for fresh fractures undergoing non-operative treatment and fractures of the upper limb.

Surgically Managed

Randomized Controlled Trials

Gopalan (2020) conducted a single-blind RCT of LIPUS plus open reduction and internal fixation compared to surgery alone in 40 patients with mandibular fracture at a single surgical center in India.[21] Patients who were randomized to the intervention group received LIPUS therapy at 4, 8, 14, and 20 days postoperatively for 20 minutes daily. Postoperative examinations were performed 5, 9, 15, and 21 days to assess wound healing, pain, and teeth mobility. Assessment of orthopantomograms and ultrasound scans were blinded. Patients were not blinded, and it is unclear whether pain assessments were conducted by blinded outcome assessors. Pain scores were significantly lower in the treatment group compared to the control group at all assessment time points. Ultrasound assessments of fracture healing were significantly better in the treatment group at weeks 4, 8, and 12, but radiographic assessments of fracture healing did not differ between groups at any time point. Wound healing was significantly greater in the intervention group on postoperative day 5, 9, and 1, but the difference was not significant on day 21. This study was limited by its small sample size, single center design, and lack of blinding of patients.

Included in the SR by Lou was a double-blinded, sham-controlled RCT, the Trial to Re-evaluate Ultrasound in the Treatment of Tibial Fractures (TRUST) published by Busse (2016). This RCT evaluated LIPUS for the treatment of patients who underwent intramedullary nailing for fresh tibial fractures.[22] This is the largest RCT to date, enrolling 501 patients; 250 received a LIPUS device, and 251 received a sham device. Treatment was self-administered for 20 minutes a day until there was radiographic evidence of healing. Coprimary endpoints were radiographic healing and return to function (as measured by the 36-Item Short-Form Health Survey [SF-36] Physical Component Summary score). Both radiographic and functional assessments had to show a clinically important effect for the results to be considered positive. All patients, clinicians, investigators, data analysts, and the industry sponsor were blinded to allocation until data analysis was complete. Patient compliance was considered moderate, with 73% of patients administering over half of all recommended treatments. There was no difference in time to radiographic healing between the treatment groups (hazard ratio, 1.07; 95% CI, 0.86 to 1.34; p=0.55). Additionally, there was no difference in the SF-36 Physical Component Summary scores (mean difference, 0.55; 95% CI, -0.75 to 1.84; p=0.41). A previously conducted pilot double-blind RCT by Busse et al (2014), including 51 subjects not assessed in the 2016 study, also did not find any statistically significant differences in pain reduction, number of subsequent operations, or radiographic healing time.[23]

Tarride et al (2017) provided additional analyses using data from the TRUST trial, comparing health care resource use among patients using low-intensity pulsed ultrasound with patients using the sham device.[24] There were no significant differences between groups (11% in patients receiving low-intensity pulsed ultrasound vs. 10% in patients receiving sham) in need for secondary procedures (eg, removal of lock screw, implant exchange or removal). There were also no statistically significant differences in use of physical therapy (44% vs. 46%), use of anticoagulants (42% vs. 36%), or use of nonsteroidal anti-inflammatory drugs (28% vs. 35%) among patients receiving Low-intensity pulsed ultrasound compared with patients receiving sham, respectively.

Nonsurgically Managed

Randomized Controlled Trial

Lubbert (2008) performed a multicenter, double-blind RCT (n=101) of LIPUS treatment of fresh (<5 days) clavicle shaft fractures.[9] This trial also was included in the SR by Lou. Patients used the low-intensity pulsed ultrasound devices for 20 minutes once daily for 28 days and recorded their subjective feeling as to whether the fracture healed (the primary outcome measure), pain on a visual analog scale, level of daily activities (hours of work, household work, sport), and analgesic use. Patient perception of the day the fracture healed was determined in 92 patients (47 active, 45 placebo); mean time to heal was 26.77 days in the active group and 27.09 days in the placebo group (p=0.91). Between-group differences regarding analgesic use and mean visual analog scale scores for pain also did not differ significantly.

Section Summary: Fresh Fractures

Evidence for LIPUS for fresh fractures includes 12 RCTs reporting outcomes from a number of fracture sites including the tibia, radius, lateral malleolus, scaphoid, fifth metatarsal, and clavicle. A SR of these studies concluded that in a pooled analysis, LIPUS decreased the time to fracture union only in non-surgically managed patients, but did not improve time to full weight bearing, time to resuming work, or the incidence rate of delayed union or nonunion. A number of limitations to the trials also were noted, including inadequate concealment of

treatment allocation, high loss of follow-up, the unclear age baseline, and unclear smoking or gender status.

STRESS FRACTURES

Gan (2014) evaluated the effectiveness of LIPUS for the improvement of lower limb bone stress injuries.[25] In this prospective, randomized, double-blind, placebo-controlled trial, individuals with a magnetic resonance imaging (MRI)-diagnosed grade II-IV bone stress injury of either the postero-medial tibia, fibula or second, third, or fourth metatarsal were randomized to either active treatment or placebo device for 20 minutes daily for four weeks. A total of 30 participants were initially recruited; 23 participants were included in the final analysis. Six clinical parameters including night pain, pain at rest, pain on walking, pain with running, tenderness, and pain with single leg hop were compared prior to and after the intervention. The investigators reported no significant differences between the treatment and placebo groups for measurements of the six clinical parameters. Regardless of the relatively short duration of four weeks and the small sample size consisting of primarily female participants, low-intensity pulsed ultrasound was found to be ineffective for the healing of lower limb bone stress injuries.

Rue (2004) reported on a double-blind RCT that examined the effects of 20 minutes of daily LIPUS on tibial stress fracture healing outcomes such as pain, function, and resumption of professional and personal activities in 26 military recruits.[26] The delay from onset of symptoms to diagnosis was 32 days in the low-intensity pulsed ultrasound group and 28 days in the placebo group. This trial found no significant difference in healing times between LIPUS treatment and sham, with a mean time of return to duty of 56 days for both groups. The trial was rated with a high-risk of bias in the Schandelmaier (2017) meta-analysis.

LOW-INTENSITY PULSED ULTRASOUND FOR OTHER CONDITIONS

Open Fractures

There is limited and inconsistent data addressing the efficacy of LIPUS for the treatment of open fractures. Emami (1999) conducted a randomized study of 32 individuals with a fresh tibial fracture that was fixed with an intramedullary rod. Patients underwent additional treatment with an active or inactive ultrasound device.[6] The time to healing was not significantly different in the two groups. These observations are consistent with the meta-analysis conducted by Busse (2002) whose analysis supported the use of LIPUS for fractures treated nonoperatively but no clear benefit in operatively treated fractures.[22] In contrast, Leung (2004) reported a RCT of 30 fractures in 28 individuals with complex tibial fractures treated with internal or external fixation to receive or not receive additional treatment with LIPUS.[27] Based on radiologic assessment, the time to callus formation was significantly less in those in the ultrasound treatment group; however, two individuals in the control group experienced delayed union (12%). Due to the inconsistent results in these two small randomized studies, and the negative results of the meta-analysis, LIPUS is considered not medically necessary for open fractures.

Osteotomy Sites

Goshima (2022) published a retrospective study comparing 45 individuals treated with low-intensity pulsed ultrasound with 45 individuals who did not receive low-intensity pulsed ultrasound following open-wedge high tibial osteotomy.[28] The study included patients treated

between 2012 and 2017 at a hospital in Japan. Treatment was applied for 20 minutes daily and continued for three months postoperatively or as judged sufficient by the study investigator. The lateral hinge united at six weeks in 73.3% of knees in the low-intensity pulsed ultrasound group and 75.6% in the control group. The visual analogue pain scores were statistically improved in the low-intensity pulsed ultrasound group compared with control at six weeks and three months, but the numerical differences were small (32.2 vs. 38.7 and 27.5 vs. 36.4 at six weeks and three months, respectively). Mean Japanese Orthopaedic Association scores were not significantly different between groups at any time point. The authors concluded that their study does not support the use of low-intensity pulsed ultrasound in patients after open-wedge high tibial osteotomy.

Urita (2013) published a small (n=27) quasi-randomized study (alternating assignment) of LIPUS after ulnar-shortening osteotomy for ulnar impaction syndrome or radial-shortening osteotomy for Kienböck disease.[29] Patients in the LIPUS group received daily 20-minute treatment for at least 12 weeks postoperatively. Blinded evaluation of radiographic healing showed that LIPUS reduced the mean time to the cortical union by 27% (57 days vs. 76 days) and endosteal union by 18% (121 days vs. 148 days) compared with sham treatment. At the time of endosteal healing, the osteotomy plus LIPUS group and the osteotomy-only group had similar results, as measured using the Modified Mayo Wrist Score and no pain at the osteotomy site. The study was rated at high-risk of bias in the meta-analysis by Schandelmaier (2017).

Distraction Osteogenesis

Song (2019) reported on a retrospective observational study of 30 patients who underwent tibial lengthening procedures at a single institution between October 2009 and October 2015.[30] Fifteen patients who received low intensity pulsed ultrasound during distraction osteogenesis were compared to 15 patients who underwent the same procedure but did not receive low intensity pulsed ultrasound. During the distraction phase, calluses of the low intensity pulsed ultrasound group were more cylindrical, more homogeneous, and denser than those of the control group. At the time of external fixator removal, however, there were no significant differences between the groups in callus shape and type. There were no significant differences in external fixation index between the groups, however, significant differences were found in healing indexes of the anterior and medial cortices ($p<0.001$ and $p=0.002$, respectively). There were six complications in the group who received low intensity pulsed ultrasound and five in the control group. No complications related to the low intensity pulsed ultrasound procedure were reported.

Salem (2014) evaluated the use of LIPUS compared to control in a nonblinded, randomized trial of 21 individuals undergoing callus distraction for posttraumatic tibial defects.[31] Outcomes were examined clinically and radiologically, analyzing callus maturation with a computer-assisted measurement. Use of LIPUS shortened healing by 12 days/cm and the total fixator time by 95 days. The results of this study are limited by the small number of participants and nonblinded study design. Larger randomized, sham-controlled trials of homogeneous study populations are needed to evaluate the efficacy of low-intensity pulsed ultrasound as an adjunct to distraction osteogenesis procedures for any indication.

Dudda (2011) investigated the effect of LIPUS in a prospective RCT of 36 participants (n=16 treatment group, n=20 control group) who underwent distraction osteogenesis (>2 cm) to the lower extremities.[32] The authors did not specify the location of the bone distraction beyond

“right” and “left” lower leg” in either the treatment or control group. Fixation devices included Regazzoni, Ilizarov, and hybrid fixators. Evaluation was performed by standard radiographs every 3 to 4 weeks. Treatment outcomes were reported in measures of the length of the “fixator gestation period”, the distraction consolidation index (the ratio of fixator gestation time in days over the distraction gap size in cm), and the Paley index (ratio of fixator gestation period in months over the distraction gap size in cm). The investigators reported a shorter fixation gestation period by 43.6 days for the treatment group versus the control group, 218.6 versus 262.2 days, respectively, but the statistical significance of this outcome was not reported. The mean distraction consolidation index for the treatment group was 32.8 days/cm and 44.6 days/cm for the control group (p=0.116). The mean Paley index for the treatment versus the control group was 1.09 months/cm and 1.49 months/cm, respectively (p=0.116). The difference between the treatment and control groups in these measures did not reach statistical significance. Limitations of this study include the small number of callus distractions performed, heterogeneity of the population (highly variable patterns of injury and medical treatments performed), and the lack of blinding to treatment.

There are no controlled studies identified in the published literature that specifically address the use of LIPUS as a treatment of fresh fractures of the axial skeletal system, fractures due to bone malignancy, congenital pseudoarthroses, or as an adjunct to spinal fusion. There are no studies in the peer-reviewed literature specifically focused on improved healing rates following uncomplicated bunionectomy procedures (first metatarsal osteotomy) as compared to a period of immobilization and limited weight bearing; in addition, these surgeries are not considered at high risk for post-surgical nonunion.

PRACTICE GUIDELINE SUMMARY

The American Academy of Orthopedic Surgeons (AAOS) published a 2020 update to their clinical practice guideline on the management of distal radius fractures.[33] Although the Academy issued a limited recommendation for the use of low-intensity pulsed ultrasound for adjuvant treatment of distal radius fractures in its prior (2010) guidelines,[34] low-intensity pulsed ultrasound was not mentioned in the updated guidelines.

Similarly, a 2022 AAOS guideline on management of hip fracture in older adults does not mention low-intensity pulsed ultrasound.[35]

In 2023, the AAOS published a guideline on the treatment of clavicle fractures. The guideline includes a moderately strong recommendation that low-intensity pulsed ultrasound should not be used for acute mid-shaft clavicle fracture, based on a lack of data supporting its efficacy for accelerated healing or improved non-union rates. The only randomized trial that was available at the time of guideline development showed no difference in these outcomes compared to placebo.[36]

The 2018 National Institute for Health and Care Excellence (NICE) guidelines for low-intensity pulsed ultrasound to promote healing of fresh fractures at *low* risk of non-healing state, “the evidence for low-intensity pulsed ultrasound to promote healing of fresh fractures at low risk of non-healing raises no major safety concerns. However, current evidence does not show efficacy. Therefore, this procedure should not be used for this indication.”[37]

The 2018 NICE guidelines for low-intensity pulsed ultrasound to promote healing of fresh fractures at *high* risk of non-healing state, “the evidence for low-intensity pulsed ultrasound to promote healing of fresh fractures at high risk of non-healing raises no major safety concerns.

The current evidence on efficacy is very limited in quantity and quality. Therefore, this procedure should only be used in the context of research."[38]

The 2018 NICE guidelines state "the evidence for low-intensity pulsed ultrasound to promote healing of delayed-union and non-union fractures raises no major safety concerns. The current evidence on efficacy is inadequate in quality. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research."[39]

In 2013, NICE published guidance on Exogen for the treatment of long-bone fractures with nonunion and delayed fracture healing.[40] NICE concluded that use of the Exogen bone healing system to treat long-bone fractures with nonunion is supported by "clinical evidence" and "cost savings … through avoiding surgery." For long-bone fractures with delayed healing, defined as no radiologic evidence of healing after three months, there was "some radiologic evidence of improved healing." However, due to "substantial uncertainties about the rate at which bone healing progresses without adjunctive treatment between three and nine months after fracture" and need for surgery, "cost consequences" were uncertain. In 2019, the Exogen guidance was updated with a review of studies published after June 2012. The review decision stated, "Overall the additional clinical evidence identified since the guidance was published in 2013 supports the current recommendations." In 2019, the Exogen guidance was updated with a review of studies published after June 2012. The review decision stated, "Overall the additional clinical evidence identified since the guidance was published in 2013 supports the current recommendations." The reviewers did not consider the Schandelmaier (2017) systematic review because it pooled fresh fractures and distraction osteogenesis alongside non-unions.

SUMMARY

FRACTURE NONUNION

It appears that low-intensity pulsed ultrasound may improve health outcomes for individuals with certain types of fracture nonunion. Evidence-based clinical practice guidelines consider the evidence for the use of low-intensity pulsed ultrasound for the treatment of fracture nonunion to be limited, however, use of low-intensity pulsed ultrasound for the treatment of certain fracture nonunion is widely used. Therefore, the use of low-intensity pulsed ultrasound for the treatment of fracture nonunion is considered medically necessary when Criteria are met.

For patients who do not meet the policy criteria for fracture nonunion, low-intensity pulsed ultrasound is considered not medically necessary because the technology is not considered clinically effective or appropriate for these individuals.

FRESH FRACTURE

It appears that low-intensity pulsed ultrasound may improve health outcomes for individuals with certain types of fresh fractures. Evidence-based clinical practice guidelines consider the evidence for the use of low-intensity pulsed ultrasound for the treatment of fresh fractures to be limited, however, use of low-intensity pulsed ultrasound for the treatment of certain fresh fractures is widely used. Therefore, the use of low-intensity pulsed ultrasound for the treatment of fresh fractures is considered medically necessary when Criteria are met.

For patients who do not meet the policy criteria for fresh fracture, low-intensity pulsed ultrasound is considered not medically necessary because the technology is not considered clinically effective or appropriate for these individuals.

DEVICE REPLACEMENT

In certain situations, an osteogenic stimulator may no longer be able to perform its basic function due to damage or wear. When a stimulator is out of its warranty period and cannot be repaired adequately to meet the patient's medical needs, replacement of the device may be medically appropriate. Therefore, replacement of all or part of a low-intensity pulsed ultrasound stimulator may be considered medically necessary when device replacement Criteria are met.

When a stimulator is in its warranty period or can be repaired or adapted adequately to meet the patient's medical needs, replacement of the device is not medically appropriate. Therefore, replacement of all or part of a low-intensity pulsed ultrasound stimulator is considered not medically necessary when device replacement Criteria are not met.

STRESS FRACTURES

The evidence for the use of low-intensity pulsed ultrasound for the treatment of stress fractures has not demonstrated the added benefit of the technology on health outcomes. Evidence-based clinical practice guidelines do not recommend the use of low-intensity pulsed ultrasound for the treatment of stress fractures. Therefore, low-intensity pulsed ultrasound for the treatment of stress fractures is considered not medically necessary.

FRACTURES DUE TO BONE PATHOLOGY AND FAILED JOINT FUSIONS

The use of low-intensity pulsed ultrasound for the treatment of fractures due to bone pathology or tumor/malignancy or failed joint fusions is not considered clinically appropriate. Evidence-based clinical practice guidelines do not recommend the use of low-intensity pulsed ultrasound for the treatment of fractures due to bone pathology or tumor/malignancy failed joint fusions. Therefore, low-intensity pulsed ultrasound for the treatment of fractures due to bone pathology or tumor/malignancy or failed joint fusions is considered not medically necessary.

OTHER INDICATIONS

There is not enough evidence to determine if low-intensity pulsed ultrasound improves health outcomes in the treatment of any other conditions. Evidence-based clinical practice guidelines do not recommend the use of low-intensity pulsed ultrasound for any other condition. Therefore, low-intensity pulsed ultrasound is considered investigational for the treatment of all other conditions, including but not limited to distraction osteogenesis, osteotomy, congenital pseudoarthrosis, or osteonecrosis.

REFERENCES

1. Schoelles K, Snyder D, Kaczmarek J, et al. *The Role of Bone Growth Stimulating Devices and Orthobiologics in Healing Nonunion Fractures.* 2005. PMID: 25879121

2. Collaborators GF. Global, regional, and national burden of bone fractures in 204 countries and territories, 1990-2019: a systematic analysis from the Global Burden of Disease Study 2019. *Lancet Healthy Longev.* 2021;2(9):e580-e92. PMID: 34723233
3. Einhorn TA. Enhancement of fracture-healing. *The Journal of bone and joint surgery American volume.* 1995;77(6):940-56. PMID: 7782368
4. Buza JA, 3rd, Einhorn T. Bone healing in 2016. *Clin Cases Miner Bone Metab.* 2016;13:101-05. PMID: 27920804
5. Heckman MM, Whitesides TE, Jr., Grewe SR, et al. Compartment pressure in association with closed tibial fractures. The relationship between tissue pressure, compartment, and the distance from the site of the fracture. *The Journal of bone and joint surgery American volume.* 1994;76(9):1285-92. PMID: 8077257
6. Emami A, Petren-Mallmin M, Larsson S. No effect of low-intensity ultrasound on healing time of intramedullary fixed tibial fractures. *Journal of orthopaedic trauma.* 1999;13(4):252-7. PMID: 10342350
7. Mayr E, Rudzki MM, Rudzki M, et al. [Does low intensity, pulsed ultrasound speed healing of scaphoid fractures?]. *Handchirurgie, Mikrochirurgie, plastische Chirurgie : Organ der Deutschsprachigen Arbeitsgemeinschaft fur Handchirurgie : Organ der Deutschsprachigen Arbeitsgemeinschaft fur Mikrochirurgie der Peripheren Nerven und Gefasse* 2000;32(2):115-22. PMID: 10857066
8. Zura R, Xu ZJ, Della Rocca GJ, et al. When Is a Fracture Not "Fresh"? Aligning Reimbursement With Patient Outcome After Treatment With Low-Intensity Pulsed Ultrasound. *Journal of orthopaedic trauma.* 2017;31(5):248-51. PMID: 28134628
9. Lubbert PH, van der Rijt RH, Hoorntje LE, et al. Low-intensity pulsed ultrasound (LIPUS) in fresh clavicle fractures: a multi-centre double blind randomised controlled trial. *Injury.* 2008;39:1444-52. PMID: 18656872
10. Bhandari M, Guyatt GH, Swiontkowski MF, et al. A lack of consensus in the assessment of fracture healing among orthopaedic surgeons. *Journal of orthopaedic trauma.* 2002;16(8):562-6. PMID: 12352564
11. Searle HK, Lewis SR, Coyle C, et al. Ultrasound and shockwave therapy for acute fractures in adults. *Cochrane Database Syst Rev.* 2023;3(3):Cd008579. PMID: 36866917
12. Schandelmaier S, Kaushal A, Lytvyn L, et al. Low intensity pulsed ultrasound for bone healing: systematic review of randomized controlled trials. *BMJ.* 2017;356:j656. PMID: 28348110
13. Seger EW, Jauregui JJ, Horton SA, et al. Low-Intensity Pulsed Ultrasound for Nonoperative Treatment of Scaphoid Nonunions: A Meta-Analysis. *Hand (N Y).* 2017:1558944717702470. PMID: 28391752
14. Lou S, Lv H, Li Z, et al. The effects of low-intensity pulsed ultrasound on fresh fracture: A meta-analysis. *Medicine (Baltimore).* 2017;96:e8181. PMID: 28953676
15. Leighton R, Watson JT, Giannoudis P, et al. Healing of fracture nonunions treated with low-intensity pulsed ultrasound (LIPUS): A systematic review and meta-analysis. *Injury.* 2017;48(7):1339-47. PMID: 28532896
16. Schofer MD, Block JE, Aigner J, et al. Improved healing response in delayed unions of the tibia with low-intensity pulsed ultrasound: results of a randomized sham-controlled trial. *BMC Musculoskelet Disord.* 2010;11:229. PMID: 20932272
17. Ricardo M. The effect of ultrasound on the healing of muscle-pediculated bone graft in scaphoid non-union. *International orthopaedics.* 2006;30(2):123-7. PMID: 16474939

18. Nolte P, Anderson R, Strauss E, et al. Heal rate of metatarsal fractures: A propensity-matching study of patients treated with low-intensity pulsed ultrasound (LIPUS) vs. surgical and other treatments. *Injury.* 2016;47(11):2584-90. PMID: 27641221
19. Rutten S, Nolte PA, Guit GL, et al. Use of low-intensity pulsed ultrasound for posttraumatic nonunions of the tibia: a review of patients treated in the Netherlands. *J Trauma.* 2007;62:902-8. PMID: 17426546
20. Hannemann PF, Mommers EH, Schots JP, et al. The effects of low-intensity pulsed ultrasound and pulsed electromagnetic fields bone growth stimulation in acute fractures: a systematic review and meta-analysis of randomized controlled trials. *Archives of orthopaedic and trauma surgery.* 2014;134(8):1093-106. PMID: 24895156
21. Gopalan A, Panneerselvam E, Doss GT, et al. Evaluation of Efficacy of Low Intensity Pulsed Ultrasound in Facilitating Mandibular Fracture Healing-A Blinded Randomized Controlled Clinical Trial. *J Oral Maxillofac Surg.* 2020;78(6):997 e1-97 e7. PMID: 32145206
22. Busse JW, Bhandari M, Einhorn TA, et al. Re-evaluation of low intensity pulsed ultrasound in treatment of tibial fractures (TRUST): randomized clinical trial. *BMJ.* 2016;355:i5351. PMID: 27797787
23. Busse JW, Bhandari M, Einhorn TA, et al. Trial to re-evaluate ultrasound in the treatment of tibial fractures (TRUST): a multicenter randomized pilot study. *Trials.* 2014;15:206. PMID: 24898987
24. Tarride JE, Hopkins RB, Blackhouse G, et al. Low-intensity pulsed ultrasound for treatment of tibial fractures: an economic evaluation of the TRUST study. *Bone Joint J.* 2017;99-B:1526-32. PMID: 29092994
25. Gan TY, Kuah DE, Graham KS, et al. Low-intensity pulsed ultrasound in lower limb bone stress injuries: a randomized controlled trial. *Clinical journal of sport medicine : official journal of the Canadian Academy of Sport Medicine.* 2014;24(6):457-60. PMID: 24667169
26. Rue JP, Armstrong DW, 3rd, Frassica FJ, et al. The effect of pulsed ultrasound in the treatment of tibial stress fractures. *Orthopedics.* 2004;27(11):1192-5. PMID: 15566133
27. Leung KS, Lee WS, Tsui HF, et al. Complex tibial fracture outcomes following treatment with low-intensity pulsed ultrasound. *Ultrasound in medicine & biology.* 2004;30:389-95. PMID: 15063521
28. Goshima K, Sawaguchi T, Horii T, et al. Low-intensity pulsed ultrasound does not promote bone healing and functional recovery after open wedge high tibial osteotomy. *Bone Jt Open.* 2022;3(11):885-93. PMID: 36373863
29. Urita A, Iwasaki N, Kondo M, et al. Effect of low-intensity pulsed ultrasound on bone healing at osteotomy sites after forearm bone shortening. *The Journal of hand surgery.* 2013;38(3):498-503. PMID: 23375786
30. Song MH, Kim TJ, Kang SH, et al. Low-intensity pulsed ultrasound enhances callus consolidation in distraction osteogenesis of the tibia by the technique of lengthening over the nail procedure. *BMC Musculoskelet Disord.* 2019;20(1):108. PMID: 30871538
31. Salem KH, Schmelz A. Low-intensity pulsed ultrasound shortens the treatment time in tibial distraction osteogenesis. *International orthopaedics.* 2014;38(7):1477-82. PMID: 24390009
32. Dudda M, Hauser J, Muhr G, et al. Low-intensity pulsed ultrasound as a useful adjuvant during distraction osteogenesis: a prospective, randomized controlled trial. *J Trauma.* 2011;71:1376-80. PMID: 22071933
33. American Academy of Orthopaedic Surgeons. Management of Distal Radius Fractures Evidence-Based Clinical Practice Guideline. [cited 04/18/2024]. 'Available from:'

https://www.aaos.org/quality/quality-programs/upper-extremity-programs/distal-radius-fractures/.
34. Lichtman DM, Bindra RR, Boyer MI, et al. Treatment of distal radius fractures. *J Am Acad Orthop Surg.* 2010;18:180-9. PMID: 20190108
35. O'Connor MI, Switzer JA. AAOS Clinical Practice Guideline Summary: Management of Hip Fractures in Older Adults. *J Am Acad Orthop Surg.* 2022;30(20):e1291-e96. PMID: 36200817
36. Wright M, Della Rocca GJ. American Academy of Orthopaedic Surgeons Clinical Practice Guideline Summary on the Treatment of Clavicle Fractures. *J Am Acad Orthop Surg.* 2023;31(18):977-83. PMID: 37432981
37. National Institute for Health and Care Excellence (NICE). Low-intensity pulsed ultrasound to promote healing of fresh fractures at low risk of non-healing [cited 4/18/2024]. 'Available from:' https://www.nice.org.uk/guidance/ipg621.
38. National Institute for Health and Care Excellence (NICE). Low-intensity pulsed ultrasound to promote healing of fresh fractures at high risk of non-healing. [cited 4/18/2024]. 'Available from:' https://www.nice.org.uk/guidance/IPG622/chapter/1-Recommendations.
39. National Institute for Health and Care Excellence (NICE). Low-intensity pulsed ultrasound to promote healing of delayed-union and non-union fractures. [cited 4/18/2024]. 'Available from:' https://www.nice.org.uk/guidance/IPG623/chapter/1-Recommendations.
40. National Institute for Health and Care Excellence (NICE). EXOGEN ultrasound bone healing system for long bone fractures with non-union or delayed healing. [cited 4/12/2023]. 'Available from:' https://www.nice.org.uk/guidance/mtg12.

CODES

Codes	Number	Description
CPT	20979	Low intensity ultrasound stimulation to aid bone healing, noninvasive (nonoperative)
HCPCS	E0760	Osteogenesis stimulator, low intensity ultrasound, non-invasive

Date of Origin: *April 2020*