Medical Policy

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Title: Low Intensity Pulsed Ultrasound Fracture Healing Device

Related Policies:	▪ *Electrical bone growth stimulation of the appendicular skeleton* ▪ *Electrical stimulation of the spine as an adjunct to spinal fusion procedures*

Professional / Institutional
Original Effective Date: February 11, 2011 / December 11, 2014
Latest Review Date: May 28, 2025
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Populations	Interventions	Comparators	Outcomes
Individuals: • With fresh fractures (surgically managed and nonsurgically managed)	Interventions of interest are: • Low-intensity pulsed ultrasound as an adjunct to routine care	Comparators of interest are: • Routine care without low-intensity pulsed ultrasound	Relevant outcomes include: • Symptoms • Morbid events • Functional outcomes • Quality of life
Individuals:	Interventions of interest are:	Comparators of interest are:	Relevant outcomes include: • Symptoms

Populations	Interventions	Comparators	Outcomes
• With fracture nonunion or delayed union fractures	• Low-intensity pulsed ultrasound as an adjunct to routine care including surgery, if appropriate	• Routine care including surgery, if appropriate, without low-intensity pulsed ultrasound	• Morbid events • Functional outcomes • Quality of life
Individuals: • With stress fractures, osteotomy sites, or distraction osteogenesis	Interventions of interest are: • Low-intensity pulsed ultrasound as an adjunct to routine care	Comparators of interest are: • Routine care without low-intensity pulsed ultrasound	Relevant outcomes include: • Symptoms • Morbid events • Functional outcomes • Quality of life

DESCRIPTION

Low-intensity pulsed ultrasound (LIPUS) has been investigated as a technique to accelerate healing of fresh fractures, surgically treated closed fractures, delayed unions, nonunions, stress fractures, osteotomy sites, and distraction osteogenesis. LIPUS is administered using a transducer applied to the skin surface overlying the fracture site.

OBJECTIVE

The objective of this evidence review is to evaluate whether, compared with routine care without low-intensity pulsed ultrasound, low-intensity pulsed ultrasound improves the net health outcome when used as an adjunct to routine care to treat fractures (including fresh fractures, surgically treated closed fractures, delayed unions, nonunions, stress fractures, osteotomy sites, and distraction osteogenesis).

BACKGROUND

Bone Fractures

An estimated 178 million new fractures were reported worldwide in 2019.[1,] 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.[2,] 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).[2,]

Fracture Nonunion

There is no standard definition of a fracture nonunion.[3,] The U.S. Food and Drug Administration (FDA) has defined nonunion as when "a minimum of 9 months has elapsed since injury, and the fracture site shows no visibly progressive signs of healing for a minimum of 3 months." Other definitions cite 3 to 6 months of time from the original injury, or simply when serial radiographs fail to show any further healing. 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.

Delayed Union
Delayed union is generally considered a failure to heal between 3 and 9 months post-fracture, after which the fracture site would be considered a nonunion. The delayed union may also be defined as a decelerating bone healing process, as identified in serial radiographs. (In contrast, nonunion serial radiographs show no evidence of healing.) It is important to include both radiographic and clinical criteria to determine fracture healing status. Clinical criteria include the lack of ability to bear weight, fracture pain, and tenderness on palpation.

Treatment
Low-intensity pulsed ultrasound (LIPUS) has been proposed to accelerate healing of fractures. Low-intensity pulsed ultrasound is believed to alter the molecular and cellular mechanisms involved in each stage of the healing process (inflammation, soft callus formation, hard callus formation, and bone remodeling). The mechanism of action at the cellular level is not precisely known, but it is theorized that LIPUS may stimulate the production or the activities of the following compounds that contribute to the bone healing process: cyclooxygenase-2, collagenase, integrin proteins, calcium, chondroblasts, mesenchymal cells, fibroblasts, and osteoblasts.

LIPUS treatment is self-administered, once daily for 20 minutes, until the fracture has healed.

REGULATORY STATUS
In 1994, the Sonic Accelerated Fracture Healing System (SAFHS®; renamed Exogen 2000® and Exogen 4000+, now Exogen® Ultrasound Bone Healing System; Bioventus) was approved by the FDA through the premarket approval process for treatment of fresh, closed, posteriorly displaced distal radius (Colles) fractures and fresh, closed, or grade 1 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. FDA product code: LOF.

Table 1 summarizes the FDA cleared or approved LIPUS devices.

Table 1. U.S. Food and Drug Administration-Approved Low-Intensity Pulsed Ultrasound Devices

Device	Indication	Manufacturer	Date Approved	PMA No./Device Code
Exogen® Ultrasound Bone Healing System	• Treatment of fresh, closed, posteriorly displaced distal radius (Colles) fractures and fresh, closed, or grade 1 open tibial diaphysis fractures in skeletally mature individuals when these fractures are orthopedically managed by closed reduction and cast immobilization. • Expanded to non-invasive treatment of established nonunions[a], excluding skull and vertebra.	Bioventus	1994;2000	P900009;P900009/S006
AccelStim™ Bone Growth Stimulator	• 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	Orthofix	2022	P210035

[a] The device was formerly named Sonic Accelerated Fracture Healing System Model 2A (SAHFS®)
[b] A nonunion is considered to be established when the fracture site shows no visibly progressive signs of healing.

POLICY

A. Low-intensity pulsed ultrasound is considered **not medically necessary** as a treatment of fresh fractures (surgically managed or nonsurgically managed).

B. Low-intensity pulsed ultrasound is considered **not medically necessary** as a treatment of fracture nonunion and delayed union fractures.

C. Low-intensity pulsed ultrasound is considered **not medically necessary** as a treatment of stress fractures, osteotomy, and distraction osteogenesis.

POLICY GUIDELINES

A. Fresh (Acute) Fracture
   1. There is no standard definition for a "fresh" fracture. A fracture is most commonly defined as fresh for 7 days after the fracture occurs, but there is variability. For example, one study defined fresh as less than 5 days after fracture, while another defined fresh as up to 10 days post-fracture. Most fresh closed fractures heal without complications with the use of standard fracture care, (i.e., closed reduction and cast immobilization).

B. Delayed Union
   1. Delayed union is defined as a decelerating healing process as determined by serial radiographs, together with a lack of clinical and radiologic evidence of union, bony continuity, or bone reaction at the fracture site for no less than 3 months from the index injury or the most recent intervention.

C. Nonunion
   1. There is not a consensus for the definition of nonunions. One definition is failure of progression of fracture-healing for at least 3 consecutive months (and at least 6 months following the fracture) accompanied by clinical symptoms of delayed/nonunion (pain, difficulty weight bearing).

   2. The definition of nonunion in FDA labeling suggests that nonunion is considered established when the fracture site shows no visibly progressive signs of healing, without giving any guidance regarding the timeframe of observation. However, it is suggested that a reasonable time period for lack of visible signs of healing is 3 months. The following individual selection criteria are consistent with those proposed for electrical stimulation as a treatment of nonunions:
      a. at least 3 months have passed since the date of the fracture,
         AND
      b. serial radiographs have confirmed that no progressive signs of healing have occurred,
         AND
      c. the fracture gap is 1cm or less,
         AND
      d. the individual can be adequately immobilized and is of an age when he/she is likely to comply with non-weight bearing.

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

RATIONALE

The evidence review was created with searches of the PubMed database. The most recent literature update was performed through January 30, 2025

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, 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 technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 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. Randomized controlled trials 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

Numerous systematic reviews have evaluated the use of LIPUS for various types of fracture including those with nonunion or delayed union. Select systematic reviews are summarized in Tables 1 and 2. A systematic review by Schandelmaier et al (2017) provides the most comprehensive and rigorous overview and analysis of the existing evidence, including 26 RCTs that used low-intensity pulsed ultrasound for bone healing.[4,] However, because there is a substantial degree of overlap in the studies included in these reports (Table 2), we will primarily focus on the findings of Schandelmaier et al (2017), which include analyses that highlight the results of RCTs identified as of higher quality. The meta-analysis by Seger et al (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.[5,] The systematic review by Lou et al (2017)[6,] focused on fresh fractures and the review by Leighton et al (2017)[7,] focused on nonunions. Leighton et al (2021) conducted an additional systematic review/meta-analysis looking at non-union in the specific populations of those with instrumented, infected, or fragility-related non-unions.[8,] All systematic reviewers acknowledged that the evidence for the use of the positions on LIPUS has methodologic limitations (Table 2).

Table 2. Systematic Reviews Assessing Use of Low-Intensity Pulsed Ultrasound to Treat Fractures

Study	No. of Studies	Study Designs	No. of Subjects	Types of Fractures	Main Conclusions on LIPUS
Searle et al (2023)[9,]	21	RCT; Quasi-RCT	1517	Multiple types	Uncertain effectiveness, but it is possible that LIPUS makes little to no difference
Leighton et al (2021)[8,]	29 (20 included in quantitative analysis)	CS, cohort, RCT, case report	NR	Instrumented non-unions, fragility fracture non-union, infected non-union	Healing rates of patients with instrumented, infected, or fragility non-unions is similar to the general non-union population
Schandelmaier et al (2017)[4,]	26	RCT	1593	Multiple types	Based on moderate- to high-quality evidence in fresh fracture, LIPUS does not improve outcomes important to patients and is unlikely to affect radiographic bone healing
Seger et al (2017)[5,]	5	CS Registry	166	Nonunion	Encouraging results for consideration as nonoperative alternative in select cases
Lou et al (2017)[6,]	12	RCT; Quasi-RCT	1099	Fresh fracture	Positive results though strength of the evidence is limited
Leighton et al (2017)[7,]	13	RCT; CS Cohort Registry	1441	Nonunion	Potential benefit of LIPUS ; however, no evidence that LIPUS can be used instead of surgery. May be useful in patients for whom surgery is high-risk.
Busse et al (2009)[10,]	13	RCT	563	Multiple types	Promising results but moderate- to low-quality evidence

CS: case series; LIPUS: low-intensity pulsed ultrasound; NR: not reported; RCT: randomized controlled trial.

The study populations in RCTs included by Schandelmaier et al (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 to 501 patients).[4,] The outcomes examined by this systematic review 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 systematic review, 2 reviewers independently assessed the quality of selected RCTs, using Grading of Recommendations Assessment, Development and Evaluation (GRADE), a modified Cochrane risk of bias tool.[4,] 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, 6 were considered to have a low-risk of bias, with the remaining 20 trials considered to have a high-risk of bias. Reasons for a 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 6 trials rated to be at low-risk of bias, 4 were conducted in individuals with fresh fracture, 3 of which were operatively managed tibial fractures.[11,12,]

Schandelmaier et al (2017) acknowledged that their findings could be less applicable to underrepresented clinical subgroups.[4,] However, they noted that in subgroup analyses, the effect of LIPUS on days to radiographic healing did not differ significantly across clinical subgroups (interaction p=.13) or between high and moderate compliance with treatment (interaction p=.99). They also noted that qualitative subgroup effects (such as no benefit in 1 subgroup and important benefit in another) are unusual.

Studies included in these systematic reviews can be compared in Appendix Table A1.

Meta-analysis results are summarized in Tables 3 and 4. Variation in results was observed for days to full weight-bearing, pain, and radiographic healing. When only trials with low risk of bias were included, there was no difference between treatment and control groups (Table 3).

Table 3. Summary of Low-intensity Pulsed Ultrasound Results from the Schandelmaier Meta-Analysis

Outcomes	**No. of Trials and Results (95% CI)**						**Heterogeneity**	
	High Risk of Bias		***Low Risk of Bias***		***Total***		***p***	***I^2***
	n	*Results*	*n*	*Results*	*n*	*Results*		
Percent difference in days to return to work	Not reported separately		Not reported separately		3	2.7 (-7.7 to 14.3)	.76	0%
Percent difference in days to full weight-bearing	1	-40.0 (-48.4 to -30.3)	2	4.8 (-4.0 to 14.4)	3	-16.6 (-44.9 to 26.1)	<.001	95%
Mean difference in pain reduction on 1 to 100 VAS (follow-up, 4 to 6 wk)	1	-28.1 (-37.1 to -19.2)	3	-0.9 (-2.5 to 0.6)	4	-6.9 (-15.4 to 1.6)	<.001	91%
RR of subsequent operations (follow-up, 8 wk to 44 mo)	Not reported separately		Not reported separately		7	0.8 (0.6 to 1.2)	.67	0%

Outcomes	No. of Trials and Results (95% CI)						Heterogeneity	
Percent difference in days to radiographic healing	12	-32.8 (-39.5 to -25.3)	3	-1.7 (-11.2 to 8.8)	15	-27.3 (-34.7 to -19.0)	<.001	85%
Risk difference in adverse events	Not reported separately		Not reported separately		9	0.0 (-0.0 to 0.03)	.40	4%

CI: confidence interval; RR: relative risk; VAS: visual analog scale.
Adapted from Schandelmaier et al (2017).[4,]

Table 4. Summary of Findings and Quality of Evidence from the Schandelmaier Meta-Analysis

	Outcomes	QOE	LIPUS Effect on Outcome
1	Percent difference in days to return to work	Moderate[a]	Probably little or no impact
2	Percent difference in days to full weight-bearing	High	No impact
3	Mean difference in pain reduction on 1 to 100 VAS (follow-up, 4 to 6 wk)	High	No impact
4	Relative risk of subsequent operations (follow-up, 8 wk to 44 mo)	Moderate[a]	Probably little or no impact
5	Percent difference in days to radiographic healing	Moderate[a]	Probably little or no impact
6	Risk difference in adverse events	High	No impact

LIPUS: low-intensity pulsed ultrasound; QOE: quality of evidence: VAS: visual analog scale.
Adapted from Schandelmaier et al (2017).[4,]
[a] Due to serious imprecision.

FRESH FRACTURES

Clinical Context and Therapy Purpose

The purpose of LIPUS in individuals who have fresh fractures (either surgically managed or non-surgically managed) is to provide an adjunctive treatment option to standard of care.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is patients with fresh fractures (either surgically or non-surgically managed). A fracture is most commonly defined as fresh for 7 days after the fracture occurs.

Interventions

The therapy being considered is LIPUS. LIPUS is believed to alter the molecular and cellular mechanisms involved in each stage of the healing process (inflammation, soft callus formation, hard callus formation, and bone remodeling). The mechanism of action at the cellular level is not precisely known, but it is theorized that LIPUS may stimulate the production or the activities of

the following compounds that contribute to the bone healing process: cyclooxygenase-2, collagenase, integrin proteins, calcium, chondroblasts, mesenchymal cells, fibroblasts, and osteoblasts. LIPUS would be an adjunctive therapy following setting and immobilizing the bone. The patient takes the LIPUS device home and self-administers the treatment. Recommended time of treatment administration is 20 minutes/day.

Comparators
The comparator is standard fresh fracture management without LIPUS as an adjunctive therapy.

Outcomes
The general outcome of interest is time to healing, which may be measured radiologically and assessed by an orthopedic surgeon. Clinically meaningful measures for healing would involve functional outcomes such as assessment of pain, use of analgesics, the need for secondary procedures, and ability to return to activities of daily living.

Follow-up should extend for months, the duration of time required for fracture healing.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for randomized controlled trials (RCTs);
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews
Lou et al (2017) conducted a meta-analysis focusing on fresh fractures.[6,] The literature search, conducted through November 2016, included 12 studies, all of which were included in the Schandelmaier et al (2017) meta-analysis, except for a small study (n=20) by Strauss et al (1999), which only appeared in a conference abstract.[13,] Studies included patients that had been surgically and conservatively managed. Results from the Lou et al (2017) meta-analysis showed that time to fracture union was significantly lower in patients receiving LIPUS than in patients not receiving LIPUS (standard mean difference (SMD), -0.65; 95% confidence interval [CI], -1.13 to -0.17). However, subgroup analysis showed that this significant reduction in healing time with LIPUS was seen only among patients conservatively managed, while there was no difference in healing time among patients surgically managed. Reviewers concluded that patients with fresh fractures might benefit from the use of LIPUS but warned that there were methodologic limitations in the trials. Separate analyses using only low-risk of bias trials were not conducted in the Lou et al (2017) meta-analyses.

Surgically Managed - Randomized Controlled Trials
Busse et al (2016) reported on results from a concealed, blinded, sham-controlled, randomized Trial to Re-evaluate Ultrasound in the Treatment of Tibial Fractures (TRUST) evaluating LIPUS for the treatment of patients who underwent intramedullary nailing for fresh tibial fractures.[14,] 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=.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=.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.[14,]

Tarride et al (2017) provided additional analyses using data from the TRUST trial, comparing health care resource use among patients using LIPUS with patients using the sham device.[15,] There were no significant differences between groups (11% in patients receiving LIPUS 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 LIPUS compared with patients receiving sham, respectively.

Emami et al (1999) conducted a double-blind, sham-controlled trial that randomized 32 patients who had a fresh tibial fracture fixed with an intramedullary rod to additional treatment with an active (n=15) or inactive (n=17) LIPUS device.[16,]LIPUS treatment began within 3 days of surgery (1 patient began treatment within 7 days of injury) and was self-administered for 20 minutes a day for 75 days. Radiographs were taken every third week until healing. Results showed that LIPUS did not shorten healing time based on any of the following measures: time to first visible callus (mean, 40 days for low-intensity pulsed ultrasound vs. 37 days for sham; p=.44); time to radiographic healing assessed by radiologist (mean, 155 days [median, 113 days] for LIPUS vs. mean, 125 days [median, 112 days] for sham; p=.76); and time to radiographic healing assessed by orthopedic surgeon (mean, 128 days, for LIPUS vs. mean, 114 days for sham; p=.40).

Gopalan et al (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.[17,] 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 at 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 days 5 and 9, 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.

Nonsurgically Managed - Randomized Controlled Trial
Lubbert et al (2008) performed a multicenter, double-blind RCT (N =101) of LIPUS treatment of fresh (<5 days) clavicle shaft fractures.[18,] Patients used the LIPUS 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 (VAS), 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=.91). Between-group differences regarding analgesic use and mean VAS scores for pain also did not differ significantly.

Section Summary: Fresh Fractures
Evidence for the use of LIPUS following fresh fractures includes one meta-analysis and five RCTs - four involving surgically managed patients and one involving nonsurgically managed patients. A 2017 meta-analysis, which encompassed both surgically and conservatively managed patients, revealed that LIPUS significantly reduced the time to fracture union compared to patients not receiving the treatment (SMD, -0.65; 95% CI, -1.13 to -0.17). However, subgroup analysis indicated that this reduction in healing time was significant only for conservatively managed patients, with no observed difference for surgically managed patients. This meta-analysis concluded that patients with fresh fractures might benefit from the use of LIPUS but cautioned about the methodological limitations across the included studies. One RCT involving 40 patients with mandibular fractures showed improved wound healing and pain scores in those who received LIPUS after surgical fixation compared to those who underwent surgery alone. However, this study was limited due to lack of blinding and its small sample size. The other RCTs found no statistically significant differences in radiographic healing, physical component score of the SF-36, use of physical therapy, need for secondary procedures, use of nonsteroidal anti-inflammatory drugs, and time to first visible callus.

FRACTURE NONUNION OR DELAYED UNION FRACTURE

Clinical Context and Therapy Purpose
The purpose of LIPUS in individuals who have fracture nonunion or delayed union fracture is to provide an adjunctive treatment option to standard of care.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is patients with fracture nonunion or delayed union fracture. There is not a consensus definition of nonunion or delayed union. In general, these conditions are considered if serial radiographs either do not show progressive healing or show a decelerating healing process after 3 months since the fracture occurrence.

Interventions
The therapy being considered is LIPUS. LIPUS is believed to alter the molecular and cellular mechanisms involved in each stage of the healing process (inflammation, soft callus formation, hard callus formation, and bone remodeling). The mechanism of action at the cellular level is not precisely known, but it is theorized that LIPUS may stimulate the production or the activities of the following compounds that contribute to the bone healing process: cyclooxygenase-2, collagenase, integrin proteins, calcium, chondroblasts, mesenchymal cells, fibroblasts, and

osteoblasts. LIPUS would be an adjunctive therapy following setting and immobilizing the bone. The patient takes the low-intensity pulsed ultrasound device home and self-administers the treatment. Recommended time of treatment administration is 20 minutes/day.

Comparators
The comparator is standard nonunion or delayed union fracture management without LIPUS as an adjunctive therapy.

Outcomes
The general outcome of interest is time to healing, which may be measured radiologically and assessed by an orthopedic surgeon. Clinically meaningful measures for healing would involve functional outcomes such as assessment of pain, use of analgesics, the need for secondary procedures, and ability to return to activities of daily living.

Follow-up should extend for months, the duration of time required for fracture healing.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews
The meta-analysis by Seger et al (2017) included 5 studies focused on scaphoid nonunions and analyzed healing index and average time to union following LIPUS.[5,] Among 166 cases in the analysis, 78.6% (range, 33% to 100%) were reported to show healing following LIPUS , with an average time to union of 4.2 months (range, 2.3 to 5.6 months). Comparative results were not conducted.

The meta-analysis by Leighton et al (2017) included 13 studies, one of which was an RCT.[7,] The date of the literature search was not provided. Quality of the studies was assessed using the Methodological Index for Non-Randomized Studies. Quality scores ranged from 5 to 12 (an "ideal" is 16 for nonrandomized trials). While the pooled estimate of effect size for the healing rate was 82% (95% CI, 77% to 87%), significant heterogeneity was detected (I^2=62). A separate analysis, excluding studies with quality scores of 6 or lower, resulted in a comparable heal rate of 80% (95% CI, 74% to 85%).

The systematic review by Schandelmaier et al (2017) included 3 RCTs of nonunion fractures operatively managed. Because all the RCTs were rated at high-risk of bias, the authors could not adequately assess the efficacy of LIPUS for nonunion fractures.[4,] Two of the RCTs are discussed below (Schofer et al, 2010; Ricardo, 2006); one is not discussed below because it was published only as a thesis.

Leighton et al (2021) included patients with instrumented, infected, or fragility-related non-union in a systematic review of LIPUS.[8,] The study found non-union healing rates of 82% in patients with instrumentation or infection and 91% in patients with fragility fractures. Although the authors concluded the healing rates were comparable to a standard population of patients with non-union, the analysis consisted primarily of small case series limiting its role in the overall body of evidence.

Randomized Controlled Trials

White et al (2024) conducted a Canadian multicenter, prospective, double-blinded RCT (Scaphoid Non-union and Low-intensity Pulsed Ultrasound, SNAPU; NCT02383160) trial to assess whether active LIPUS using the Exogen Ultrasound Bone Healing System (relative to sham LIPUS) accelerates the time to union following surgery for scaphoid nonunion.[19,] After surgery, patients self-administered activated or sham LIPUS units beginning at their first postoperative visit. The primary outcome was the time to union on serial CT scans starting 6 to 8 weeks postoperatively. Secondary outcomes included patient-reported outcome measures, range of motion, and grip strength. A total of 142 subjects completed the study (69 in the active LIPUS group and 73 in the sham group). There was no difference in time to union (p =.854; hazard ratio [HR], 0.965; 95% CI, 0.663 to 1.405). Likewise, there were no differences between the active LIPUS and sham groups with respect to any of the secondary outcomes, except for wrist flexion at baseline (p =.008) and at final follow-up (p =.043). The investigators conducted a priori subgroup analyses to analyze union rates based on device compliance, defined by total number of treatments and 80% compliance with a minimum of 30 treatments. No differences were observed in the rates of union or the time to union between the compliance subgroups.

Schofer et al (2010), reported on a multicenter, randomized, double-blind, sham-controlled trial of LIPUS in 101 patients with delayed union of the tibia (Table 5).[20,] 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. Roughly one-third of patients had an open fracture. 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 LIPUS 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 LIPUS 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 that 65% of patients in the LIPUS group were healed and 46% of the patients in the sham group were healed (p=.07) (Table 6). 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 LIPUS or a sham device following a pedicled vascularized bone graft (Table 5).[21,] 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). Additional outcomes included pain, wrist range of motion, radiographic evidence of union, carpal height index, and scapholunate-capitolunate angles; however, the authors did not report these outcomes by treatment arm. The authors reported a statistically significant reduction in time to radiographic healing (-40.4%; 95% CI, -48.7% to -30.8%) with low-intensity pulsed ultrasound (Table 6).

Table 5. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	***Comparator***
White et al (2024); NCT02383160[19,]	Canada	6	2014 to 2020	Patients had to have had an established scaphoid fracture for a minimum of 3 months, with at least 1 feature of a scaphoid nonunion: collapse, humpback deformity, sclerosis at the fracture site, or cystic changes.	LIPUS (n=69)	Sham device (n=73)
Schofer et al (2010)[20,]	Germany	6	2002 to 2005	Patients with tibial delayed unions	LIPUS (n=51)	Sham device (n=50)
Ricardo (2006)[21,]	Cuba	1	1999 to 2004	Patients with scaphoid nonunion fractures treated with pedicled vascularized bone grafts from the distal radius	LIPUS (n=10)	Sham device (n=11)

LIPUS: low-intensity pulsed ultrasound; RCT: randomized controlled trial.

Table 6. Summary of Key RCT Results

Study	Healing		p-value
	Low-intensity pulsed ultrasound	***Sham device***	
White et al (2024); NCT02383160[19,]	Of the 59 scaphoid unions, 47 (79.7%) united by <26 weeks postoperatively, whereas the remaining 12 united at ≥26 weeks In patients whose fractures united at ≥26 weeks, union was detected at a mean (and SD) of 86 ± 58 weeks postoperatively	Of the 55 scaphoid unions, 50 (90.9%) united by <26 weeks postoperatively, and 5 united at ≥26 weeks. In patients whose fractures united at ≥26 weeks, union was detected at a mean of 71 ± 53 weeks postoperatively	.854
Schofer et al (2010)[20,]	Physician assessed 65% healed	physician assessed 46% healed	.07
Ricardo (2006)[21,]	56 + 3 days	94 + 5 days	<.0001

RCT: randomized controlled trial; SD: standard deviation

The purpose of the limitations tables (Tables 7 and 8) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each

table and provides the conclusions on the sufficiency of the evidence supporting the position statement.

Table 7. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
White et al (2024); NCT02383160[19,]	4. Recruitment was not equal across the sites.				
Schofer et al (2010)[20,]				2. Primary outcome was bone mineral density and secondary outcome was gap area. Physicians judged patients as healed/not healed, but no description of criteria used by physician	
Ricardo (2006)[21,]					

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 8. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
White et al (2024); NCT02383160[19,]						
Schofer et al (2010)[20,]				1. Drop out rate for LIPUS group was 10% and drop out rate for sham device was 24%		

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Ricardo (2006)[21,]	No description of randomization procedure				1. Power calculations not reported and sample size is small (N=21)	4. Only time to healing was compared statistically; additional outcomes (pain, return to activities) were not reported by treatment group

LIPUS: low-intensity pulsed ultrasound
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

Observational Study

Nolte et al (2016) conducted a retrospective comparison of patients with metatarsal fractures treated by LIPUS and by surgical techniques.[22,] For the comparative analysis, individuals from a 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=.07). A subgroup analysis of patients with delayed or nonunion metatarsal fractures (n=226) also showed comparable rates of healing among the LIPUS group (96%) and the surgery group (96%).

Section Summary: Fracture Nonunion or Delayed Union Fracture

The evidence for low-intensity pulsed ultrasound treatment of fracture nonunion consists of systematic reviews, RCTs, and uncontrolled studies. There are 2 meta-analyses (2017) without controlled comparative results. A third meta-analysis, which included all types of fractures, identified 3 RCTs of patients with nonunion; however, all 3 trials were considered at high-risk of bias. One meta-analysis specific to individuals with instrumented, infection, or fragility-related non-union found few RCTs and results were largely based on case series. A Canadian multicenter, prospective, double-blinded RCT (SNAPU) trial evaluated whether active LIPUS accelerates the time to union following surgery for scaphoid nonunion, involving 142 subjects (69

in the active LIPUS group and 73 in the sham group). The study found no significant differences in the time to union (p =.854) or any secondary outcomes, except for wrist flexion at baseline (p =.008) and final follow-up (p =.043). Subgroup analyses based on device compliance showed no differences in union rates or time to union between compliance subgroups. Of the earlier 2 published RCTs, the larger one had primary and secondary outcomes that were physiological assessments, rather than functional measures. It is unclear how healing status was determined in this study, as the outcome was described as "physician-assessed." Limitations of the second earlier published RCT include no description of the randomization process and small sample size.

STRESS FRACTURES, OSTEOTOMY SITES, OR DISTRACTION OSTEOGENESIS

Clinical Context and Therapy Purpose

The purpose of LIPUS in individuals who have stress fractures, osteotomy sites or distraction osteogenesis, is to provide an adjunctive treatment option to standard of care.

The following PICO was used to select literature to inform this review.

Populations

The population of interest consists of patients with stress fractures, osteotomy sites, or distraction osteogenesis.

Interventions

The therapy being considered is LIPUS. LIPUS is believed to alter the molecular and cellular mechanisms involved in each stage of the healing process (inflammation, soft callus formation, hard callus formation, and bone remodeling). The mechanism of action at the cellular level is not precisely known, but it is theorized that LIPUS may stimulate the production or the activities of the following compounds that contribute to the bone healing process: cyclooxygenase-2, collagenase, integrin proteins, calcium, chondroblasts, mesenchymal cells, fibroblasts, and osteoblasts. LIPUS would be an adjunctive therapy following setting and immobilizing the bone. The patient takes the LIPUS device home and self-administers the treatment. Recommended time of treatment administration is 20 minutes/day.

Comparators

The comparator is standard stress fracture, osteotomy sites, or distraction osteogenesis management without LIPUS as an adjunctive therapy.

Outcomes

The general outcome of interest is time to healing, which may be measured radiologically and assessed by an orthopedic surgeon. Clinically meaningful measures for healing would involve functional outcomes such as assessment of pain, use of analgesics, the need for secondary procedures, and ability to return to activities of daily living.

Follow-up should extend for months, the duration of time required for fracture healing.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;

- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Stress Fractures

Rue et al (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.[23,] The delay from onset of symptoms to diagnosis was 32 days in the LIPUS 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 et al (2017) meta-analysis.[4,]

Osteotomy Sites

Urita et al (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.[24,] 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 et al (2017).[4,]

In a retrospective study, Goshima et al (2022) compared 45 individuals treated with LIPUS with 45 individuals who did not receive LIPUS following open-wedge high tibial osteotomy.[25,] The study included patients treated between 2012 and 2017 at a hospital in Japan. Treatment was applied for 20 minutes daily and continued for 3 months postoperatively or as judged sufficient by the study investigator. The lateral hinge united at 6 weeks in 73.3% of knees in the LIPUS group and 75.6% in the control group. The VAS pain scores were statistically significantly improved in the LIPUS group compared with control at 6 weeks and 3 months, but the numerical differences were small (32.2 vs. 38.7 and 27.5 vs. 36.4 at 6 weeks and 3 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 LIPUS in patients after open-wedge high tibial osteotomy.

Distraction Osteogenesis

The Schandelmaier et al (2017) systematic review also included 6 trials of LIPUS for distraction osteogenesis following surgery. Four of 6 studies were rated at high-risk of bias.[4,] Four studies were in the tibia.[11,12,] No clinically meaningful results were reported for the mandible studies in the meta-analysis.[4,] The remaining studies in the tibia were all unblinded. No statistically significant difference was noted in subsequent operations (relative risk, 0.63; 95% CI, 0.13 to 2.99) in the meta-analysis.[4,] Four of the studies[26,27,28,29,] were included in the meta-analysis[4,] for time to radiographic healing with mixed results, 3 not reporting statistically significant results.

Lou et al (2018) conducted a systematic review and meta-analysis on the use of LIPUS for the treatment of patients with distraction osteogenesis.[30,] The literature search, conducted in May 2018, identified 7 RCTs (172 patients) for inclusion. The Cochrane risk of bias tool was used to assess trial quality. Three of the trials were considered low-risk of bias and 4 were considered to have high-risk of bias. Main limitations in the trials were related to the lack of treatment allocation details and outcome assessors' knowledge of treatment. Pooled results did not find statistically significant differences in treatment time, radiological gap fill area, histological gap fill length, or bone density.

Song et al (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.[31,] Fifteen patients who received LIPUS during distraction osteogenesis were compared to 15 patients who underwent the same procedure but did not receive LIPUS. During the distraction phase, calluses of the LIPUS 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. There were 6 complications in the group who received LIPUS and 5 in the control group. No complications related to the LIPUS procedure were reported.

Section Summary: Stress Fractures, Osteotomy Sites, or Distraction Osteogenesis
The evidence for LIPUS treatment of stress fractures, osteotomy sites, or distraction osteogenesis consists only of lower quality RCTs and a retrospective comparative observational study with a high risk of bias. Results do not generally include functional outcomes and results across various outcomes, primarily including time to radiographic healing, are inconsistent. A meta-analysis of 3 trials on the use of low-intensity pulsed ultrasound for patients with distraction osteogenesis reported no statistically significant differences in treatment time, gap fill, or bone density.

SUPPLEMENTAL INFORMATION
The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

National Institute for Health and Care Excellence
In 2013, NICE published guidance on Exogen for the treatment of long-bone fractures with nonunion and delayed fracture healing.[32,][The 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 3 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 3 and 9 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.[32,] 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 et al (2017) systematic review because it pooled fresh fractures and distraction osteogenesis alongside non-unions.

In 2018, NICE published guidance on the use of LIPUS in 3 clinical circumstances, The guidance made the following conclusions:

- To promote healing of fresh fractures at low-risk of non-healing: "Current evidence does not show efficacy. Therefore, this procedure should not be used for this indication."[33,][To promote healing of fresh fractures at high-risk of non-healing: "Current evidence on efficacy is very limited in quantity and quality. Therefore, this procedure should only be used in the context of research.[34,]
- To promote healing of delayed and nonunion fractures: "Current evidence on efficacy is inadequate in quality. Therefore, this procedure should only be used with special arrangements for clinical governances, consent and audit or research.[35,]

American Academy of Orthopaedic Surgeons
In 2020, the American Academy of Orthopaedic Surgeons (AAOS) published updated guidelines on the treatment of distal radius fractures.[36,] Although the Academy issued a limited recommendation for the use of LIPUS for adjuvant treatment of distal radius fractures in its prior 2009 guidelines, LIPUS was not mentioned in the updated guidelines.

Similarly, a 2021 AAOS guideline on management of hip fracture in older adults does not mention LIPUS.[37,]

In 2022, the AAOS published a guideline on the treatment of clavicle fractures.[37,]The guideline includes a moderately strong recommendation that LIPUS 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. This 2022 guideline for the treatment of isolated clavicle fractures was developed with input from representatives from the American Shoulder and Elbow Surgeons, the Orthopaedic Trauma Association, and the American Society of Shoulder and Elbow Therapists.[38,]

U.S. Preventive Services Task Force Recommendations
Not applicable.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 9.

Table 9. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Unpublished			
NCT03382483[a]	A Prospective, Patient-centric, Observational, Consecutive Enrollment, Non-interventional Study of Patients At Risk for Fracture Non-union Treated with EXOGEN Compared to a National Healthcare Claims Database Control	12,387	May 2022 (unknown status; Last Update Posted, Feb 2021)

NCT: national clinical trial.
[a] Denotes an industry-sponsored or cosponsored trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS	
20979	Low intensity ultrasound stimulation to aid bone healing, noninvasive (nonoperative)
E0760	Osteogenesis stimulator, low intensity ultrasound, noninvasive

REVISIONS	
11-12-2014	Policy added to the bcbsks.com web site on 11-12-2014. Update effective for Professional on 11-12-2014. Effective for Institutional on 12-11-2014.
02-16-2015	In Coding section: ▪ Added ICD-10 diagnosis codes, effective October 1, 2015.
04-28-2015	Updated Description section.
	In Policy section: ▪ In Policy Guidelines, Item 1 A, added "There is no standard definition for a "fresh" fracture." and ",(1-3) but there is variability. For example, 1 study defined fresh as less than 5 days after fracture,(4) while another defined fresh as up to 10 days after fracture.(5)"
	Updated Rationale section.
	Updated References section.
10-12-2016	Updated Description section.
	In Policy section: ▪ In Item A, added "pulsed" to read "Low-intensity pulsed ultrasound treatment may be considered medically necessary when used as an adjunct to conventional management (i.e., closed reduction and cast immobilization) for the treatment of fresh, closed fractures in skeletally mature individuals. Candidates for ultrasound treatment are those at high risk for delayed fracture healing or nonunion. These risk factors may include either locations of fractures or patient comorbidities and include the following:" ▪ In Item A 2, added "e) Tibial diaphysis fracture that is closed or grade I open (skin opening is ≤1 cm with minimal muscle contusion)" ▪ In Item B, added "pulsed" to read "Low-intensity pulsed ultrasound treatment may be considered medically necessary as a treatment of delayed union of bones, including delayed union of previously surgically-treated fractures, and excluding the skull and vertebra. (See Policy Guidelines for definition of delayed union.)" ▪ In Item C, added "pulsed" to read "Low-intensity pulsed ultrasound treatment may be considered medically necessary as a treatment of fracture nonunions of bones,

REVISIONS	
	including nonunion of previously surgically-treated fractures, and excluding the skull and vertebra. (See Policy Guidelines for definition of nonunion.)" ▪ In Item D, added "pulsed" and "and" to read "Other applications of low-intensity pulsed ultrasound treatment are experimental / investigational, including, but not limited to, treatment of congenital pseudarthroses, open fractures, fresh surgically-treated closed fractures, stress fractures, and arthrodesis or failed arthrodesis." ▪ In Policy Guidelines Item 3 B, removed "3) the fracture gap is 1 cm or less, AND"
	Updated Rationale section.
	Updated References section.
03-01-2018	Updated Description section.
	In Policy section: ▪ Removed previous policy language, "A. Low-intensity pulsed ultrasound treatment may be considered medically necessary when used as an adjunct to conventional management (i.e., closed reduction and cast immobilization) for the treatment of fresh, closed fractures in skeletally mature individuals. Candidates for ultrasound treatment are those at high risk for delayed fracture healing or nonunion. These risk factors may include either locations of fractures or patient comorbidities and include the following: 1. Patient comorbidities: a) Diabetes b) Steroid therapy c) Osteoporosis d) History of alcoholism e) History of smoking 2. Fracture locations: a) Jones fracture b) Fracture of navicular bone in the wrist (also called the scaphoid) c) Fracture of metatarsal d) Fractures associated with extensive soft tissue or vascular damage e) Tibial diaphysis fracture that is closed or grade I open (skin opening is ≤1 cm with minimal muscle contusion) B. Low-intensity pulsed ultrasound treatment may be considered medically necessary as a treatment of delayed union of bones, including delayed union of previously surgically-treated fractures, and excluding the skull and vertebra. (See Policy Guidelines for definition of delayed union.) C. Low-intensity pulsed ultrasound treatment may be considered medically necessary as a treatment of fracture nonunions of bones, including nonunion of previously surgically-treated fractures, and excluding the skull and vertebra. (See Policy Guidelines for definition of nonunion.) D. Other applications of low-intensity pulsed ultrasound treatment are experimental / investigational, including, but not limited to, treatment of congenital pseudarthroses, open fractures, fresh surgically-treated closed fractures, stress fractures, and arthrodesis or failed arthrodesis." and added, "A. Low-intensity pulsed ultrasound is considered not medically necessary as a treatment of fresh fractures (surgically managed or nonsurgically managed). B. Low-intensity pulsed ultrasound is considered not medically necessary as a treatment of fracture nonunion and delayed union fractures. C. Low-intensity pulsed ultrasound is considered not medically necessary as a treatment of stress fractures, osteotomy, and distraction osteogenesis."
	Updated Rationale section.
	In Coding section: ▪ Removed diagnosis codes.
	Updated References section.
	Added Appendix section.
04-11-2018	Updated Description section.
	Updated Rationale section.
	Updated References section.
	Removed Appendix section.
04-24-2019	Updated Rationale section.
	Updated References section.

REVISIONS	
05-07-2021	Changed Policy Title from "Ultrasound Accelerated Fracture Healing Device" to "Low Intensity Pulsed Ultrasound Fracture Healing Device"
	Updated Description section.
	In Policy Guidelines: • Added PG 3.b.iii
	Updated Rationale section.
	Updated References section.
07-12-2022	Updated Description Section
	Updated Rationale Section
	Updated References Section
04-25-2023	Updated Description Section
	Updated Rationale Section
	Updated Coding Section ▪ Removed ICD-10 Diagnoses box
	Updated References Section
04-23-2024	Updated Description Section
	Updated Rationale Section
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05-28-2025	Updated Description Section
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