Bone Stimulation For Nonunions: What The Evidence Reveals

Numerous methods of bone stimulation have emerged in recent years but how effective are they at facilitating healing? These authors take a critical look at the evidence on the efficacy of electrical stimulation, low-intensity pulsed ultrasound and extracorporeal shockwave therapy.

Bone stimulators currently represent a $500 million market in the United States alone. They are becoming an increasingly popular conservative treatment option for delayed unions and nonunions. Numerous studies have estimated that 5 to 10 percent of fractures occurring in the United States annually have impaired healing.1-11

Impaired bone healing not only causes chronic pain and disability for the patient, but also leads to considerable socioeconomic costs including healthcare costs and lost wages. When impaired healing occurs, it presents a frustrating problem for both the patient and the surgeon. Both parties desire a non-surgical option to stimulate bone healing. Bone stimulators present an attractive option to augment healing due to the conservative nature and relative ease of operation.

In regard to research on bone stimulation, Griffin and colleagues reviewed 49 studies and found that electromagnetic stimulation is an effective adjunct to conventional therapy when it comes to managing nonunions of long bone fractures. However, when one is determining whether to use bone stimulators, it is important to consider several factors including cost, length of treatment and the current body of evidence on the efficacy of bone stimulators.

Currently, there are three main types of bone stimulators: electrical stimulation, low-intensity pulsed ultrasound and extracorporeal shockwave therapy (ESWT).

A Closer Look At The Evidence On Electrical Stimulation

The oldest and most studied method of bone stimulation is electrical stimulation. The first report of utilizing electricity to induce healing was in 1841.12 In that paper, Hartshorne described a patient who underwent treatment in 1812 for a tibial nonunion with “shocks of electric fluid passed daily through space between the ends of the bones.” Subsequent work by Lente in 1850 further recognized the potential for electricity to heal bone.13

However, there was little work done in this regard until 1953 when Yasuda published his work on rabbit femurs and demonstrated new bone growth near the cathode.14 The first work involving human patients was in 1971 when Friedenberg and colleagues used direct current for the management of a nonunion of femurs and demonstrated new bone growth near the cathode. The first work involving human patients was in 1971 when Friedenberg and colleagues used direct current for the management of a nonunion of femurs and demonstrated new bone growth near the cathode.14 The first work involving human patients was in 1971 when Friedenberg and colleagues used direct current for the management of a nonunion of femurs and demonstrated new bone growth near the cathode.14 The first work involving human patients was in 1971 when Friedenberg and colleagues used direct current for the management of a nonunion of femurs and demonstrated new bone growth near the cathode.14

In regard to research on bone stimulation, Griffin and colleagues reviewed 49 studies and found that electromagnetic stimulation is an effective adjunct to conventional therapy when it comes to managing nonunions of long bone fractures. However, when one is determining whether to use bone stimulators, it is important to consider several factors including cost, length of treatment and the current body of evidence on the efficacy of bone stimulators.

Proponents of electrical stimulation frequently reference a 1994 study by Scott and King.15 The study compared 10 patients with long bone nonunions treated with electrical stimulation and saw no unions in the control group. They achieved union in six of the 10 patients with the electrical stimulation device and saw no unions in the control group.

However, Novicoff and colleagues in 2008 published a literature review investigating the efficacy of electrical stimulation on bone healing. The authors found there were few randomized clinical trials (including the trial by Scott and King) to support commonly practiced modalities. Novicoff and
In 1991, Valchanou and Michaliov presented the first clinical report of ESWT on 82 human fracture nonunions. The authors found that shockwave stimulated osteogenesis in 70 of 82 patients and that healing rate in 52 of 71 patients and added that ultrasound treatment shows a statistically significant higher healing rate in comparison with the rate of spontaneous healing. They concluded that low-intensity pulsed ultrasound is an effective treatment for established tibial nonunions and can be “a good, safe, and cheaper alternative to surgery.”

In 2008, Griffin and colleagues published a systematic review of literature on low intensity pulsed ultrasound for the purposes of bone healing. Corradi and Cozzolino discovered in 1952 that continuous wave ultrasound was able to stimulate bone formation in radial fractures of rabbits. The first clinical use of low-intensity pulsed ultrasound is credited to the same authors in 1953 when they demonstrated an increase in periosteal callus in the treatment of eight patients with fracture nonunions.

In 1994, the Food and Drug Administration (FDA) approved the first low-intensity pulsed ultrasound device for the treatment of fresh fractures of the tibial diaphysis and distal radius. In 2000, the FDA approved the use of low-intensity pulsed ultrasound on nonunions.

For many years, physiotherapists have used ultrasound as a therapeutic device for soft tissues at an intensity of 100 to 300 W/cm². Researchers have also investigated the use of ultrasound at far lower intensities (>30 W/cm²) for its effect on bone healing. The exact physical mechanism of action is not completely understood. Many believe that the low level mechanical forces acting on the site with impaired healing mimic mechanical forces applied to bone while the patient is weightbearing and are similar to the effect of electrical stimulation. It may be that low-intensity pulsed ultrasound has a direct effect on cells, increasing the incorporation of calcium ions in cartilage and bone cells and increasing the expression of genes required for healing. These genes include aggrecanase, insulin-like growth factor (IGF) and transforming growth factor beta (TGF-β).

Research has also shown that low intensity pulsed ultrasound has its most profound effect on the chondrocytes, increasing the rate of soft callus formation and endochondral ossification.

In 2007, Rutten and colleagues studied 71 patients who received ultrasound treatment between January 2000 and February 2003. The authors noted an overall healing rate in 52 of 71 patients and added that ultrasound treatment shows a statistically significant higher healing rate in comparison with the rate of spontaneous healing. They concluded that low-intensity pulsed ultrasound is an effective treatment for established tibial nonunions and can be “a good, safe, and cheaper alternative to surgery.”

In 2008, Griffin and colleagues published a systematic review of literature on low intensity pulsed ultrasound for acute long bone fractures. They concluded there may be utility in treating fresh fractures with low-intensity pulsed ultrasound due to a statistically significant decreased healing time. However, the authors also noted that the decrease in healing time may not be clinically relevant. They also questioned the usefulness of low-intensity pulsed ultrasound in patients with a fracture that is likely to heal anyway. The authors also noted this was not a true systematic review as they felt a meta-analysis was inappropriate due to study differences and variability among the selected studies.

However, Busse and co-workers in 2009 reported different results. The authors’ systematic review of the literature found 13 trials that met inclusion criteria. They reported a moderate to low quality of available evidence to support the use of low-intensity pulsed ultrasound on acute long bone fractures. In fact, the authors found conflicting results and that one can make no direct conclusions on the effects of ultrasound on the healing of fresh fractures. They did not investigate the effects of low-intensity pulsed ultrasound for nonunions.

In addition, Busse and co-workers noted that although the overall results of low-intensity pulsed ultrasound are promising, establishing the role of the technology in the management of fractures requires large, blinded trials that directly address important outcomes including the patient’s return to function.

Currently, there is no direct comparison in the literature of electrical stimulation and low-intensity pulsed ultrasound on fracture/nonunion healing. In a review of eight trials, Walker and co-workers attempted to compare the efficacy of the two bone stimulation methods but the authors were unable draw any direct conclusions. This is primarily because the authors of the ultrasound studies reported success in terms of days to healing while the electrical stimulation authors reported success in terms of the percentages of the groups with united fractures.

How Effective Is ESWT At Stimulating Bone Growth?

The newest method of bone stimulation undergoing study is ESWT. Physicians have used shockwave for years for breaking down calculi in the kidney, ureter and gall bladder.

Mordan and Yeaman began investigating the effects of ESWT on bone in the U.S. in the late 1980s. In 1991, Valchanou and Michaliov presented the first clinical report of ESWT on 82 human fracture nonunions. The authors found that shockwave stimulated osteogenesis in 70 of 82 patients and contributed to union “within a reasonable period of time.” More investigation is continuing in the area of ESWT and bone healing.

As podiatrists are aware, extracorporeal shockwave therapy involves the use of shockwaves or pressure impulses via a spark discharge from an electrode. Shockwaves enter the human body relatively...
unhindered due to the different impedances. When the pressure impulses encounter bone, the impulses destroy the edges of bone and form microfractures, producing small bony fragments and the formation of new trabeculae.25,29

Schleberger and Senge noted that in three of four cases, using ESWT was successful in treating nonunion of diaphyses.29 The authors pointed out that the shockwaves induced callus formation in the soft tissue of the nonunion in approximately six weeks and this transformed into bony union in all cases but one.

In 2002, Birnbaum and colleagues reviewed the literature and found 10 publications that met inclusion criteria.30 The authors noted that ESWT is noninvasive and has low complications, and noted that the use of shockwave seems justifiable. However, they concluded that, "proof of the positive effect of ESWT in the treatment of nonunions by prospective, randomized study is missing."

Zelle and co-workers published a literature review in 2010 on the efficacy of ESWT on the healing of nonunions.31 They found 10 studies that met their inclusion criteria with 294 patients. All studies were level 4 evidence. There were no controls and no clearly defined exclusion criteria based on previous/concurrent treatment. The review excluded corrective osteotomies and arthrodeses. The study authors noted a 76 percent overall union rate.

In Conclusion
Clearly, more research in this area is necessary based on the current body of evidence. Current evidence is lacking homogeneity as well as universal definitions of success. Future investigations should be prospective, randomized and double blinded with clearly defined protocols for therapy. Such investigations should be homogeneous in treatment modalities for the study groups with clear definitions of success. Despite bone stimulators offering a relatively conservative option and a demand for these modalities from both patients and physicians, the current evidence is inconclusive as to the benefit of this technology. Cost to benefit studies are lacking as well. While external bone stimulators may help increase the healing rate and decrease healing time, the current evidence is lacking to support their use.

Dr. Wienke is a third-year resident at Trinity Regional Medical Center in Fort Dodge, Iowa.
Dr. Dayton is the Director of Podiatric Surgical Residency at Trinity Regional Medical Center. He is a Fellow of the American College of Foot and Ankle Surgeons. Dr. Dayton is also in private practice at Trilmark Physicians Group in Fort Dodge, Iowa.

References
23. Griffin XL, Costello I, Costa ML. The role of low intensity pulsed ultrasound therapy in the management


For further reading, see “Understanding The Benefits Of Electrical Bone Stimulation” in the December 2007 issue of Podiatry Today or “A Closer Look At Bone Stimulators For Charcot” in the December 2006 issue.