

Electrical bone growth stimulator devices



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Nonunion and delayed fractures are prevalent in the United States, accounting for a significant health care cost (Simon & Simon, 2008). Bone is able to remodel and adapt to applied loads and electromechanical stimuli (Smeltzer, Bare, Hinkle, & Cheever, 2009). One method of repairing these types of fractures is with an electric bone growth stimulator, which has been used for over 25 years. There are three types of electric bone growth stimulators, all of which provide an electric current to the bone that causes the bone cells to grow and proliferate. Treatment with bone growth stimulators shortens the recovery time, however cannot be used for large gaps in the bone (Simon & Simon, 2008).

Clinical Significance

Every year in the United States 7.9 million fractures occur (Goldstein, Sprague, & Petrisor, 2010). Approximately 600,000 fractures do not heal properly. Fractures that do not heal properly are usually delayed or nonunion fractures. These fractures require treatment or surgical intervention to heal properly and cost the United States \$3 to 6 billion health care dollars each year (Simon & Simon, 2008).

A delayed union is a fracture that heals very slowly and does not heal within a normal amount of time. Although many factors affect how long it takes for a bone to heal such as which bone is broken and the severity of the fracture, the typical healing time is about three to four months. A delayed union can be caused by several factors including, "poor blood supply, not casting the bone properly, and infection" (Parker, 2010). Sometimes delayed union fractures can heal on their own without intervention or treatment. A nonunion is a fracture that does not heal within twice the expected healing

time, generally six to nine months after the injury. Fibrocartilage also forms between the two pieces of broken bone (Mora, Pedrotti, & Galli, 2006). Figure 1 shows a nonunion fracture of the tibia, the fracture is circled in red and you can see some of the fibrocartilage that formed between the two pieces of bone. Several factors that can cause nonunion are “poor blood supply, not casting the bone properly, infection, and loss of bone or soft tissue” (Parker, 2010). A nonunion fracture will not heal on its own and requires some form of intervention. Some of the options for treating nonunion are “internal and external fixation devices, bone grafts, bone substitutes, biologics like platelet extracts and bone morphogenic proteins, and biophysical stimulation including ultrasound and electrical stimulation” (Simon & Simon, 2008).

Since the repair of delayed and nonunion fractures requires intervention and treatment, the clinical problem is how to provide an intervention that allows “the patient to recover from the injury in the shortest possible amount of time with the fewest complications and the least cost” (Simon & Simon, 2008). The ideal treatment is to repair the fracture without surgery and hospitalization (Goldstein, Sprague, & Petrisor, 2010). Therefore, electrical bone growth stimulators are frequently used to treat delayed and nonunion fractures. Research has shown that electrical stimulation is a prevalent treatment that is utilized to speed up the process of healing in delayed and nonunion fractures. In the United States, electrical bone growth stimulators have treated approximately 400,000 delayed and nonunion fractures (Goldstein, Sprague, & Petrisor, 2010).

Electrical bone growth stimulators, shown in Figure 2, are therapeutic devices that are used to produce and apply electric fields to bone, similar to <https://assignbuster.com/electrical-bone-growth-stimulator-devices/>

the electric fields that occur naturally inside the body but as a result of the injury are either not being produced fast enough or are not being produced at all (Goldstein, Sprague, & Petrisor, 2010). Electrical bone growth stimulators have been shown to be 88% effective for treating delayed and nonunion fractures (Nolte, van der Krans, Patka, Janssen, Ryaby, & Albers, 2001). The typical treatment time with an electrical bone growth stimulator is between three and six months (Simon & Simon, 2008).

Biology and Physiology

“ Humans have 206 bones in their body” (Smeltzer, Bare, Hinkle, & Cheever, 2009). Bone can adapt and remodel as a result of an applied force, an injury or a stimulus. Bone is made up of three types of cells, osteoblasts, osteocytes, and osteoclasts, which are involved in bone formation and remodeling. “ Osteoblasts are cells that form bone” (Smeltzer, Bare, Hinkle, & Cheever, 2009). Osteocytes are formed from osteoblasts and are responsible for maintaining bone, whereas, osteoclasts are cells that absorb bone. These cells play an important role in fracture healing (Smeltzer, Bare, Hinkle, & Cheever, 2009).

The process of healing a fracture, shown in Figure 3, has four major steps. The first step occurs within hours following the injury and lasts for about a week. During this step, the injury causes increased blood flow and bleeding, causing a hematoma to form. This results in inflammation and swelling (Smeltzer, Bare, Hinkle, & Cheever, 2009). The next step begins when fibroblasts reach the injury site then release collagen fibers and form a soft fibrocartilaginous callus between and around the two pieces of bone. The third step begins around week 4, when osteoblasts enter the callus, multiply

and begin to form bone. This forms a harder bony callus that eventually turns into bone. The final stage is remodeling which starts around week 17 and continues until the bone is completely healed. During the remodeling stage, the callus is completely turned into bone by the osteoblasts, and the osteoclasts absorb the extra bone that was produced and not needed (Chiras, 2008).

Market Trends

The market for electrical bone growth stimulators has grown to over \$500 million dollars in the last 25 years, and by 2012 the market is expected to rise to \$690. 1 million (Schenberger, 2007). The consumers of electrical bone growth stimulators are hospitals, orthopedic surgeons and patients with a delayed or nonunion bone fracture. Electrical bone growth stimulators have been used to treat 400, 000 fractures (Simon & Simon, 2008). These devices can be both invasive and noninvasive. The typical cost for a noninvasive electrical bone growth stimulator is between \$3000 and \$7000 and can increase to \$20, 000 for an invasive stimulator that requires two surgeries (Morone & Feuer, 2003). Insurance will cover the cost of the device as long as the patient meets certain criteria, for example the gap between the bones must be less than 1 centimeter (CIGNA , 2010). This cost is much less than the approximately \$27, 000 cost for surgery and hospitalization after a procedure such as internal fixation (Hughes & Anglen, 2010).

Seven companies have received FDA approval (U. S. Food and Drug Administration, 2010) and the five companies that have electric bone growth stimulators on the market are Orthofix, Biomet, DJ Orthopedics (acquired the company Orthologic), Smith and Nephew and DePuy Spine (medcompare, <https://assignbuster.com/electrical-bone-growth-stimulator-devices/>

2010). The only company that has received FDA approval (U. S. Food and Drug Administration, 2010) and that has invasive electric bone growth stimulators on the market is Biomet (medcompare, 2010). Some of the noninvasive stimulators are shown in Figure 4 and two of the invasive stimulators from Biomet are shown in Figure 5.

Bioelectric Principles

Bone that goes through effective growth or repair holds an electronegative potential compared to that of resting bone (Glazer & Glazer, 2001). In bone where a break or fracture has occurred with nonunion or delayed union, it has been found helpful to introduce electric stimuli to the area undergoing complications. The introduction of an electrical current allows the process of bone regeneration to reinitiate. The electrically charged particles within the current act as the missing catalyst for the necessary chemical reactions to stimulate the desired biological response of bone repair at the site of nonunion. Pulsed electrical stimulation can cause changes in the intracellular level of cyclic adenosine monophosphate (cAMP) and thus triggers DNA synthesis within cells (Somjen, Fischler, & Binderman, 1984). The electrical current excites the Na⁺/K⁺ pump of mesenchymal osteoblasts, which causes them to differentiate into osteoblasts that produce a woven matrix of bone (Shapiro, 2008). The electronegative current (DNA synthesis) applied at the surface of the fracture site or at the surface of the skin initiates endochondral bone formation - the synthesis of cartilage, closely followed by bone formation (Shapiro, 2008).

Bone naturally generates an electrical field because of Wolff's Law and piezoelectric properties, which is what the electric bone growth stimulators

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are also based off of. Wolff's law states " that bone changes its external shape and internal (cancellous) architecture in response to stresses acting on it" (Hunt, 2008). Piezoelectricity (Figure 6) is the " stress-generated potentials in bone in which the side of the bone under mechanical compression [becomes] electronegative and the side under tension [becomes] electropositive" (Kim, Won-Ki, & Sung Jac, 1984). The mineral matrix in bone is piezoelectric because of the applied force to the skeletal system from tension (resting bone), and it changes its charge when the bone is under mechanical compression (bone repair/hematoma). The electric field produces electric potentials that cause the bone cells to grow and proliferate (Kim, Won-Ki, & Sung Jac, 1984).

Electrical stimulation creates an increased regulation of osteoinductive growth factors as well as enhancing osteoblastic activity, and decreasing osteoclastic activity through electrochemical reactions. This all leads to the desired reactions of increased bone formation and repair. The electrical stimulation increases the transmembrane calcium translocation, which activates calmodulin, a calcium binding protein involved in inflammation (Hematoma). Electric stimuli also brings about the upregulation of BMP-2, BMP-6, BMP-7, and the BMP receptor ALK-2, which are all bone morphogenic proteins needed to promote bone regeneration (Gan, Fredericks, & Glazer, 2004). At the cathode of the Electric Bone Growth Stimulator, when the electric impulse is applied, three things happen: 1) the local oxygen concentration decreases, causing an increase in the biological process of bone growth, 2) the pH level increases, resulting in a decrease of osteoclastic function, and 3) the release of hydrogen peroxide causing

macrophages to release VEGF, which stimulates the growth of blood vessels in the area of injury. These growth factors enter the tissue matrix and trigger proliferation and differentiation which causes bone to form, thus increasing the healing rate of delayed union or nonunion (Gan, Fredericks, & Glazer, 2004).

History

Device History

The history of Bone Electric Growth Stimulators dates back to the late 1780's when the biologist, Luigi Galvani used electricity on a biological system.

Galvani discovered that a frog could generate muscle spasms throughout its body when an electrical charge was applied to its spinal cord. Alessandro Volta, a colleague of Galvani's, was able to reproduce these (SilcoTek, 2010).

The first documentation of electrical stimulation being used to heal fractures was in 1841 by Dr. Hartshorne, when he reported that a patient with a tibial nonunion was treated with electricity. In 1850, the scientist R. W. Lente was the first to report successful use of Galvanic currents used to treat patients with nonunion. In 1892, the German scientist Wolff was the first to describe how bone formed in response to stress; this description became known as Wolff's Law (Glazer & Glazer, 2001).

The significant gains of healing with electrical stimulation in the 17 & 1800's ends with Wolff's phenomenon description of bone formation. The modern theories that the Electric Bone Growth Stimulators are based off of are from the work that Iwao Yasuda and his colleagues found in the 1950's. In 1938 Yasuda started researching " electrical stimulation of square wave to organic substance" at Kyoto Prefectural University of Medicine (Crenshaw, 1977). In

1953, Yasuda et al discovered that bone in compression was electronegative, and bone in tension was electropositive (Glazer & Glazer, 2001). From 1962 to 1964, the scientists Friedenberg and Brighton furthered Yasuda's research and discovered that bone that is growing or repairing itself shows an electronegative potential, while bone that is not has an electropositive potential. This discovery has encouraged others to research electrical stimuli in relation to bone regeneration (Glazer & Glazer, 2001).

In 1975, Dr. McElhannon published a report stating the technology used to treat fractures in humans with electrical stimulation is not yet advanced enough to promote bone regeneration, but shows promise in animals (Meadows, 2008). Two years later, Dr. Paterson et al performed an experimental model on delayed union fractures of the tibia in adult dogs. The model showed an accelerated healing time where Osteogenesis was normal, and no other abnormalities were found (Meadows, 2008). In 1978, the FDA approved the use of external bone growth stimulators (Haverbush, 2005). In 1983, Dr. Hanaoka performed a study observing "the effects of pulsed micro-electrical currents on internal remodeling in long tubular bone and bone healing" (Meadows, 2008). A group of 14 dogs had electrodes inserted into the femora with pulsed micro-electrical currents applied to the right femora for four weeks. The dogs were split into groups and each group had different electrical currents (Hz) applied. The results showed that bone healing in all cases was promoted (Meadows, 2008). Dr. Ahl et al, in 1984, used a semi-invasive technique for bone healing on 23 patients with nonunion. Ten of those had solid bone regeneration, and the other 13 did not fully unite – these were later determined to have been breaks that were too

far apart (Meadows, 2008). In 1985, Dr. Kondo performed a study on the femur of dogs. The bones in the experimental group observed proliferation of osteoblasts on the third day, which transitioned into bone remodeling and a shortened healing time by the end of the third week (Meadows, 2008). In 1995, Dr. Zamora-Navas et al performed a study on 22 patients with nonunion, with a gap of 0.5 or more, using capacitively-coupled electrical signal for a treatment time of about 26 weeks. In the end, over 70% of the 22 had solid bone union if the gap was 1 cm or smaller (Meadows, 2008). In 1996, the FDA approved the use of Electrical Bone Growth Stimulators, both invasive and noninvasive.

Patent History

On May 31, 1977, Dr. Levy's bone generating device was approved. The stimulator produced electrical pulses applied to the bone, as opposed to "direct current potential", to make the bone grow faster and stronger (Levy, 1977). The device is invasive, and is made of materials that will not poison or react with the surrounding tissue or bone (Levy, 1977).

On November 15, 1983, Hirshorn et al had their patent approved on their implantable bone growth stimulator that uses a direct current output, and constantly transmits pulsed electromagnetic energy to the injury site. The output of energy(rate) is directly proportional to the set current. To make sure that the device is not affected by the pulsing of the transmission, a coil was placed inside the device to deliver a constant current. The device is enclosed in a titanium case, and has a longer shelf life due to an electrical switch that was placed inside the device (Hirshorn, Swift, & Evans, 1983).

On May 19, 1987, Dr. Campbell's patent was approved. His stimulator was circuit adapted, and relied on the tissue (bone) to act as the load to make the circuit work. The storage device controlled the oscillator circuit, which in turn controlled the charge of the current that was issued from the battery and applied directly to the bone at the fracture site (Campbell, 1987).

On May 9, 1995, Kronberg's stimulator was approved. This device was a non-invasive device that used low alternating currents applied to the patient's skin. This particular device is battery powered and was found to generate the "electrical characteristics" found in bones naturally that generate normal bone growth (Kronberg, 1995).

On June 16, 1998, Dr. Erickson's electric bone stimulator was approved. His stimulator came with a hand-held device which transmitted, and received, signals to the implanted stimulator (Erickson, Tepper, Thacker, Varrichio, & Pilla, 1995).

On August 2, 2007, Dr. Nyez's invasive stimulator was approved. The device is controlled by an external remote that sends a wireless signal to the stimulator. The current is circuitry controlled. It was made to be coupled with a hip prosthesis to help with healing and proper function, but can be used to stimulate healthy bone growth in areas of injury (Nyez, 2007).

Device Theory

In 1953, surgeon Iwao Yasuda first demonstrated that callus could be created by applying electric fields to bone (Figure 8). His experiment consisted of wrapping wire around a rabbit femur and sending a small (1 μ A) current to the anode, away from the bone. After three weeks of continuous

current, Yasuda observed that a callus-typically generated during fracture repair- was beginning to form in the direction of the current (Liboff, 2006).

There are three types of electric bone growth stimulators. They are categorized based on invasiveness and type of current. Table 1 gives a brief description of the different devices. Note that there are only two types listed, invasive and noninvasive (Liboff, 2006).

Semi-Invasive Treatment

Semi-invasive systems are semi-implantable: partially internal and partially external. The device provides a constant direct current supplied by an external power supply. The electrodes, on the other hand, are percutaneous and pass through the skin (Electrical Bone Growth Stimulators). These systems, however, are not currently in production, and consequently are not referred to by other scholars and have no relevant data (Clinical Policy Bulletin: Bone Growth Stimulators, 2010).

Invasive Treatment

The invasive treatment option, also known as direct current (DC) stimulation, is fully implanted and utilizes constant direct current. The device requires two surgeries: one to implant the device, and one to remove the device. The anode is placed in the soft tissue, and the cathodes are connected to a power supply (typically a lithium battery) [Cain] and placed at the fusion site. At the fracture site, the electrodes can be arranged in two ways (Figure 9). They can be placed on each side of the fracture as to bridge the defect; or, the electrode can be placed directly in the defect (Liboff, 2006). The although the current setting depends upon the fracture, it is typically set at 20 μA for up to six months (Lyle E. Cain, 2002).

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Noninvasive Treatments

There are both electric and electromagnetic noninvasive EBGs devices. They are completely external and do not require surgery.

Electric Option

The electric noninvasive EBGs device works through capacitive coupling (CC). The CC device uses a 60 kHz alternating sinusoidal signal to produce a current. Two electrodes are placed on the skin, one on each side of the fracture (Figure 10) (Gan, Fredericks, & Glazer, 2004). The power supply (typically a 9-V battery) is worn on the hip, and operated twenty four hours a day. Treatment generally applies 5-10 mA at the skin, and 15-20 μ A at the fracture site. Device maintenance relies on the patient and includes changing the battery daily.

Electromagnetic Options

Pulsed Magnetic Field

The pulsed magnetic field device (PMF or PEMF) follows Faraday's law that "Any change in the magnetic environment of a coil of wire will cause a voltage (emf) to be "induced" in the coil" (Faraday's Law). It applies a sawtooth (nonsinusoidal) voltage to two parallel external coils, one above the fusion site, and one below (see figure #). The applied voltage creates a current through the coils that generates a single, magnetic field through the defect. Because the field is constantly changing, an induced voltage is created, which appears as pulses (Liboff, 2006). The coils can be worn on the skin, or over a cast (if applicable) (Lyle E. Cain, 2002). The device includes an external battery pack and may be operated up to ten hours a day (Lyle E. Cain, 2002), but treatment is typically only three hours daily (Liboff, 2006).

Ion Cyclotron Resonance

The ion cyclotron resonance (ICR) device is similar to the PFM device in that it also uses an external coil system. ICR devices, however, apply a different theory than PMF devices. It was shown in 1985 that “ the results embodied in the so-called calcium efflux effect were in close agreement with the predictions based on the resonance characteristics of certain biological ions subject to the Lorentz force” (Liboff, 2006). The device combines both dc and ac magnetic fields to achieve resonant condition. The theory is that “ ions in resonance are more likely to stimulate the gating mechanism for ion channel transport,” and “ tuning” to these ions can increase growth (Liboff, 2006). The device (Figure 11) also uses an external battery pack, and the unit should only be operated thirty minutes per day (Lyle E. Cain, 2002).

Regulatory Standards

The FDA recognizes the noninvasive bone growth stimulator and the invasive bone growth stimulator under the Title 21-Food and Drugs, of the Code of Federal Regulations (CFR) (Product Classification, 2010). Both are Class III devices, so they must abide by general controls and receive premarket approval. Class III devices “ support or sustain human life, that are of substantial importance in preventing impairment of human health, or that present a potential, unreasonable risk of illness or injury.” Premarket approval (PMA) is “ the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices.” A PMA application must be submitted and reviewed before marketing the products because they are considered “ high-risk” medical devices (Device Classification, 2010).

Device Review

Advantages

Previous treatments for nonunions included rigid fixation, bone grafts, and amputation. The electric bone growth stimulator has several advantages over these more traditional treatments. The treatment is less severe than bone grafting and the hospital stay after the invasive treatment is typically only three to four days, as opposed to ten days of recovery after grafts. Also, the average completion time for a successful union is only four months, compared to six to eight for bone grafts (Anbuselvan, Krishnamurthy, Madhumathi, Manonmani, Aravindan, & Babu, 1995). Moreover, the EBGS is less traumatic than amputation and allows for the retention of limbs.

In regards to the devices, the invasive option is advantageous because it provides constant uniform current and does not require an active patient role. After surgery, the device is self-operated and maintained. Also, the invasive option bypasses tissue resulting in less resistance and better treatment results. The CC device is small, light, and easy to use (Lyle E. Cain, 2002).

Disadvantages

The main disadvantage of the EBGS is that union may be unsuccessful if the fracture gap is too large, typically over one centimeter. Also, before an EBGS is used, it must be determined that the bone is not healing properly on its own. Lastly, these devices have not yet been proven successful for treatment of nonunions in locations other than long bones or spine (Clinical Policy Bulletin: Bone Growth Stimulators, 2010).

In regards to the devices, the invasive option has a higher hospital cost and patient morbidity due to the surgeries necessary for device implantation and removal. The CC device requires patient compliance. The patient must monitor, operate, and maintain the device, which includes changing the battery daily. Also, there may be skin irritation from the electrodes. Also, the PEMF and ICR devices are often larger and heavy than other external devices, which may create difficulties for patients (Clinical Policy Bulletin: Bone Growth Stimulators, 2010).

Product Comparison

Biomet is the only company that produces invasive electric bone growth stimulators. Their products include the OsteoGen Bone Growth Stimulator, the OsteoGen Dual Lead Bone Growth Stimulator for use with bone graft surgery, and the OsteoGen-M Bone Growth Stimulator, which utilizes a mesh cathode. Biomet also produces the following external, noninvasive EBGs devices: EBI Bone Healing System and the OrthoPak 2 Bone Growth Stimulator. The EBI Bone Healing System is more convenient because the actual device is worn like a sports band or brace that wraps around the limb, where as the OrthoPak 2 is a larger device with dermal electrodes that must be carried along with the battery pack. On the plus side, the OrthoPak 2 allows for easier placement of hard-to-reach fracture sites (Biomet, 2010). DJO sells the CMF OL1000 Bone Growth Stimulator. It follows a similar concept as the EBI Bone Healing System, except this device is not fully closed, giving it the ability of being worn over a cast if necessary (Products, 2009).

Literature Review

We assigned the designated sections of the report to each team member to research individually. We attended a research session with librarian Christine Drew to better understand WPI's academic databases and resources. Key terms used in our research included the following: electric bone growth stimulator, bone growth stimulator, bone growth devices, fracture healing, delayed union fracture, non union fracture, Faraday's Law, Wolff's Law, piezoelectricity, bone repair, bone cells, electric bone growth device regulations, cost of bone growth stimulation, FDA class III devices, premarket approval, bone growth device history, Luigi Galvani, electric bone growth studies, companies that sell electric bone growth stimulators, Biomet, Exogen, modern electric growth theory, and bone growth stimulator patent. We searched several databases and reliable search engines including the following: Google Books, Google Scholar, Gale PowerSearch, EBSCOhost, ScienceDirect, PubMed, and Wiley Interscience.