HOW PEMF WORKS
Orthofix Pulsed Electromagnetic Field Technology

CERVICAL-Stim®
Osteogenesis Stimulator

SPINAL-Stim®
Osteogenesis Stimulator
How PEMF affects spinal fusion?

A successful spinal fusion depends on many complex healing processes. In patients with conditions and risk factors that can lower fusion success rates, pulsed electromagnetic field (PEMF) stimulation helps create an environment conducive to healing. PEMF stimulation is a safe, noninvasive treatment prescribed by a physician to promote spine fusion success, or to treat a failed lumbar fusion with the goal of avoiding a revision surgery. The Orthofix Cervical-Stim® and Orthofix Spinal-Stim® devices help promote spinal fusion by providing, 360 degrees of PEMF coverage that reaches up to five vertebral levels.

Orthofix Spine Fusion Stimulators use a unique PEMF signal to create a conducive environment for spinal fusion.*
PEMF impacts bone healing at a molecular, cellular, and tissue level.

Within 10 minutes of PEMF exposure, signaling pathways are activated.⁷

PEMF stimulates bone cells to proliferate, differentiate, and mineralize.⁸

PEMF has been shown to improve the quality of bone tissue and enhance bone preservation.⁹,¹⁰

PEMF has been clinically proven to be a safe and effective noninvasive treatment to improve healing rates.⁴,⁵
HOW PEMF WORKS:

MOLECULAR LEVEL

Research on the molecular impact of PEMF demonstrates:7, 8, 11, 12

• Exposure of a bone-forming cell (osteoblast) to PEMF generates an electric field gradient across the cell membrane.11

• Following this activation, bone cells recognize PEMF with an immediate intracellular response.7

• Similar to growth factors (PTH and Insulin), PEMF activates signaling pathways within minutes.12

• Activating these signaling pathways with PEMF (P13-mTor-p70-s6)7 results in cell growth, proliferation, and differentiation.8, 12

Within 10 minutes of PEMF exposure, signaling pathways are activated.*7

PEMF Activates mTOR Signaling Pathway7
HOW PEMF WORKS:

CELLULAR LEVEL

Research at The Cleveland Clinic and New York University have significantly advanced our understanding of how PEMF facilitates bone growth at the cellular level.⁷, ⁸, ¹²

- PEMF treatment causes a significant increase in expression for genes involved in proliferation, differentiation, and mineralization⁸

- The use of PEMF and BMP-2 together has been documented to have an additive effect on cell growth and proliferation, which suggests that each intervention utilizes a separate intracellular signaling pathway.⁷, ⁸, ¹²

PEMF stimulates bone cells to proliferate, differentiate, and mineralize.*⁸

PEMF activates signaling pathways⁷

Bone cell growth and proliferation is enhanced⁸
The application of PEMF has been documented to have a significant effect on bone tissue in animal studies completed at the Cleveland Clinic.9,10

**PEMF Increases Bone Volume and Quality**9

- In a fibular fracture model (rat osteotomy), the group treated with PEMF was shown to have a 2-fold increase in bone volume 13-20 days postoperatively compared with the control group. A histological comparison between osteotomy sites revealed the bone quality was better in sites treated with PEMF.

**PEMF Slows Bone Resorption in a Pre-Clinical Disuse Model**10

- A separate study also utilizing a fibular fracture model (rat osteotomy) reported the group treated with PEMF experienced a 75% preservation of bone volume at the distal fibular end in comparison to controls.

PEMF has been shown to improve the quality of bone tissue and enhance bone preservation.9,10

**HOW PEMF WORKS:**

**TISSUE LEVEL**

![Graph showing Twice as Fast Callus Formation](image)

<table>
<thead>
<tr>
<th>Rate of Hard Callus Formation (NCV/day x 10⁷)</th>
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<tr>
<td>SHAM</td>
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<td>PEMF</td>
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Notes:
- Significantly faster rate of callus formation for PEMF
- NCV = Normalized Callus Volume
Clinical studies have validated the effectiveness of Orthofix PEMF devices.1-5

Patients undergoing interbody lumbar spinal fusion treated with PEMF in a prospective, double-blinded, randomized, controlled trial had significantly higher fusion rates than patients without adjunctive PEMF treatment.1,4

- 195 patients (98 PEMF group/97 placebo control group): Among consistent users,* fusion success rates were 92% in the PEMF group compared with 68% in the control group (P<0.001).

PEMF is a safe and effective alternative to surgical treatment for patients with established pseudarthrosis.2

- A prospective, multi-center, open trial was conducted on 100 patients where at least 9 months elapsed following spine fusion surgery with 3 months of no progressive healing shown on radiographs. These patients had risk factors such as revisions, multilevel fusions, and smoking. An overall fusion success rate of 67% was reached in this population of previously failed patients.

Patients undergoing cervical fusion treated with PEMF in a prospective, controlled, randomized clinical trial had significantly higher fusion rates than patients without adjunctive PEMF treatment.3,5

- 323 patients (163 PEMF group/160 control group): There was a fusion success rate of 84% in the PEMF group compared with 69% in the control group (P= 0.0065). The fusion success rate in patients age 50 and above in the PEMF group was 81% compared with 56% in the control group (P=0.004).

*Consistent users were patients wearing the device 2 or more hours per day.

PEMF has been proven to be a safe and effective noninvasive treatment to improve overall fusion healing success rates.1-5
Phase 1: Hematoma

- When a bone breaks, blood vessels in the bone and periosteum are torn and hemorrhage, and a hematoma (blood clot) forms at the fracture site.
- Tissue at the site becomes swollen and painful in response to inflammatory factors.
- New blood vessels begin to form to reestablish the blood supply.

PEMF Benefit
- PEMF stimulates an increase in vessel production.\textsuperscript{13}

Phase 2: Formation of Soft Callus

- Inflammatory factors attract cells to the site.
- Cells remove the hematoma and bone debris.
- For healing to progress at this stage, the inflammatory response must cease.
- Cells begin reconstructing the bone by laying down matrix. Proteins and mineralization factors produced by the osteoblasts (bone forming cells) begin to consolidate into what is known as a soft callus.

PEMF Benefit
- PEMF amplifies calcium flux, which activates signal transduction pathways.\textsuperscript{14, 15}
- Activated pathways increase the production of growth factors.\textsuperscript{14}
- These growth factors promote healing by increasing the number and activity of osteoblasts.\textsuperscript{14}
Phase 3: Formation of Hard Callus
• Osteoblasts mineralize the matrix, converting soft callus into hard callus.

PEMF Benefit
• PEMF treatment increases mineralization of this matrix and calcification of fibrocartilage.\textsuperscript{9,14}

Phase 4: Remodeling
• Woven bone is remodeled into stronger lamellar bone by the orchestrated action of osteoblast bone formation cells and osteoclast bone resorption cells.
• Eventually, the fracture callus is remodeled into a new shape which closely duplicates the bone’s original shape and strength.

PEMF Benefit
• PEMF stimulates remodeling activity by increasing the rate of osteoblast activity.\textsuperscript{14}
REFERENCES


10. Ibiwoye MO, Powell KA, Grabiner MD. Bone mass is preserved in a critical-sized osteotomy by low energy pulsed electromagnetic fields as quantitated by in vivo micro-computed tomography. J Orthop Res. 2004;22(5):1086-93


15. Spadaro J, Bergstrom W. In Vivo and In Vitro Effects of a Pulsed Electromagnetic Field on Net Calcium Flux in Rat Calvarial Bone. Calcif Tissue Int. 2002; 70:496-502

*The results of preclinical studies may not be indicative of human clinical trials.
GLOSSARY

• **OSTEOBLASTS** - bone forming cells

• **OSTEOCLASTS** - cells that break down bone, involved in remodeling

• **GROWTH FACTOR** - a substance (typically a protein or a hormone) that stimulates growth of a cell population and stimulates maturity of the cell.

• **PROLIFERATION** - increase cell population/number of cells

• **DIFFERENTIATION** - maturity of the cells; only mature cells can be active/result in bone formation.

• **CYTOKINE** - protein signaling molecules involved in the inflammatory response.
Brief Prescribing Information:

Full prescribing information can be found in product labeling on our patient education website www.bonestimulation.com or by calling Patient Services at 1-800-535-4492.

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.

Cervical-Stim®
The Cervical-Stim is indicated as an adjunct to cervical fusion surgery in patients at high risk for non-fusion; there are no known contraindications.

Do not use this device if you have a cardiac pacemaker or defibrillator. Remove the device prior to any imaging procedures. The safety of this device for use on patients who are pregnant or nursing has not been established. Adverse effects may include increased pain, numbness and tingling, headache, migraines and nausea; these effects may or may not be directly related to use of the device.

Spinal-Stim®
The Spinal-Stim is indicated as a spinal fusion adjunct to increase the probability of fusion success and as a nonoperative treatment of salvage of failed spinal fusion, where a minimum of nine months has elapsed since the last surgery.

Cardiac pacemakers may be adversely affected by exposure to pulsed electromagnetic fields. Use of this device is contraindicated where the individual has an implanted cardiac pacemaker. The safety and effectiveness of this device has not been established for individuals lacking skeletal maturity. The safety of this device for use on patients who are pregnant or nursing has not been established. Rare instances of reversible minor discomfort have been reported.

1.800.555.4492
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