Crit. Rev Biomed Eng. 1989;17(5):451-529.

Fundamental and practical aspects of therapeutic uses of pulsed electromagnetic fields (PEMFs).

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The beneficial therapeutic effects of selected low-energy, time-varying magnetic fields, called PEMFs, have been documented with increasing frequency since 1973. Initially, this form of athermal energy was used mainly as a salvage for patients with long-standing juvenile and adult nonunions. Many of these individuals were candidates for amputation. Their clearly documented resistance to the usual forms of surgical treatment, including bone grafting, served as a reasonable control in judging the efficacy of this new therapeutic method, particularly when PEMFs were the sole change in patient management. More recently, the biological effectiveness of this approach in augmenting bone healing has been confirmed by several highly significant double-blind and controlled prospective studies in less challenging clinical circumstances. Furthermore, double-blind evidence of therapeutic effects in other clinical disorders has emerged. These data, coupled with well-controlled laboratory findings on pertinent mechanisms of action, have begun to place PEMFs on a therapeutic par with surgically invasive methods but at considerably less risk and cost. As a result of these clinical observations and concerns about electromagnetic "pollution", interactions of nonionizing electromagnetic fields with biological processes have been the subject of increasing investigational activity. Over the past decade, the number of publications on these topics has risen exponentially. They now include textbooks, speciality journals, regular reviews by government agencies, in addition to individual articles, appearing in the wide spectrum of peer-reviewed, scientific sources. In a recent editorial in Current Contents, the editor reviews the frontiers of biomedical engineering focusing on Science Citation Index methods for identifying core research endeavors. Dr. Garfield chose PEMFs from among other biomedical engineering efforts as an example of a rapidly emerging discipline. Three new societies in the bioelectromagnetics, bioelectrochemistry, and bioelectrical growth and repair have been organized during this time, along with a number of national and international committees and conferences. These activities augment a continuing interest by the IEEE in the U.S. and the IEE in the U.K. This review focuses on the principles and practice behind the therapeutic use of "PEMFs". This term is restricted to time-varying magnetic field characteristics that induce voltage waveform patterns in bone similar to those resulting from mechanical deformation. These asymmetric, broad-band pulses affect a number of biologic processes athermally. Many of these processes appear to have the ability to modify selected pathologic states in the musculoskeletal and other systems.(ABSTRACT TRUNCATED AT 400 WORDS)

J Cell Physiol. 1988 Jan;134(1):37-46
Endothelial cell response to pulsed electromagnetic fields: stimulation of growth rate and angiogenesis in vitro.

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The effects of pulsed electromagnetic fields on the repopulation rate of denuded regions of endothelial cell monolayers and on endothelial cell reorganization into complex vessellike structures was monitored in vitro by using human umbilical vein and bovine aortic endothelial cells. A small (20-40%) but statistically significant enhancement in growth rate of partially denuded endothelial cell monolayers as determined by tritiated thymidine incorporation was observed in the presence of pulsed electromagnetic fields. Morphologically, endothelial cells entering the denuded regions were observed to be elongated, often connecting end to end to form a mycelial or "sprouting" pattern when exposed to pulsed electromagnetic fields. This was in contrast to cells outside of the field which had a more cuboidal morphology. Complete disruption of the endothelial cell monolayer by passaging the cells with EDTA-trypsin resulted in reorganization of some of the cells into three-dimensional vessellike structures after as little as 5-8 hours in the presence of the pulsed electromagnetic field. This reorganization occurred in the presence of heparin, endothelial cell growth factor, and a competent fibronectin matrix. Vascularization for comparable cultures outside of the field did not occur during the time-course of the experiments. Discrete stages of neovascularization were observed in the presence of the field that were qualitatively similar to stages of angiogenesis observed in vivo.

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Bone mass is preserved in a critical-sized osteotomy by low energy pulsed electromagnetic fields as quantitated by in vivo micro-computed tomography.
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The effectiveness of non-invasive pulsed electromagnetic fields (PEMF) on stimulating bone formation in vivo to augment fracture healing is still controversial, largely because of technical ambiguities in data interpretation within several previous studies. To address this uncertainty, we implemented a rigorously controlled, blinded protocol using a bilateral, mid-diaphyseal fibular osteotomy model in aged rats that achieved a non-union status within 3-4 weeks post-surgery. Bilateral osteotomies allowed delivery of a PEMF treatment protocol on one hind limb, with the contralateral limb representing a within-animal sham-treatment. Bone volumes in both PEMF-treated and sham-treated fibulae were assessed simultaneously in vivo using highly sensitive, high-resolution micro-computed tomography (microCT) over the course of treatment. We found a significant

reduction in the amount of time-dependent bone volume loss in PEMF-treated, distal fibular segments as compared to their contralateral sham-treated bones. Osteotomy gap size was significantly smaller in hind limbs exposed to PEMF over sham-treatment. Therefore, our data demonstrate measurable biological consequences of PEMF exposure on in vivo bone tissue.

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Pulsed electromagnetic field treatments enhance the healing of fibular osteotomies.

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This study tested the hypothesis that pulsed electromagnetic field (PEMF) treatments augment and accelerate the healing of bone trauma. It utilized micro-computed tomography imaging of live rats that had received bilateral 0.2 mm fibular osteotomies (approximately 0.5% acute bone loss) as a means to assess the in vivo rate dynamics of hard callus formation and overall callus volume. Starting 5 days post-surgery, osteotomized right hind limbs were exposed 3 h daily to Physio-Stim PEMF, 7 days a week for up to 5 weeks of treatment. The contralateral hind limbs served as sham-treated, within-animal internal controls. Although both PEMF- and sham-treatment groups exhibited similar onset of hard callus at approximately 9 days after surgery, a 2-fold faster rate of hard callus formation was observed thereafter in PEMF-treated limbs, yielding a 2-fold increase in callus volume by 13-20 days after surgery. The quantity of the new woven bone tissue within the osteotomy sites was significantly better in PEMF-treated versus sham-treated fibulae as assessed via hard tissue histology. The apparent modulus of each callus was assessed via a cantilever bend test and indicated a 2-fold increase in callus stiffness in the PEMF-treated over sham-treated fibulae. PEMF-treated fibulae exhibited an apparent modulus at the end of 5-weeks that was approximately 80% that of unoperated fibulae. Overall, these data indicate that Physio-Stim PEMF treatment improved osteotomy repair. These beneficial effects on bone healing were not observed when a different PEMF waveform, Osteo-Stim, was used. This latter observation demonstrates the specificity in the relationship between waveform characteristics and biological outcomes.

Chin J Physiol. 1991;34(2):201-11.

Additive effects of prostaglandin E2 and pulsed electromagnetic fields on fracture healing.

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Bone formation of fractured fibulae stimulated by pulsed electromagnetic fields (PEMF), PGE2, and combination of both was assessed with roentgenography and fluorescent

labelling compounds, tetracycline, xylenol orange, and calcein. A total of 72 male New Zealand rabbits was osteotomized by creating a 1 mm-gap at fibulae and randomly divided into 8 groups: one control, one treated with PEMF, three treated with PGE2 of various dosages, and three treated with combined treatments of PEMF and PGE2 of specified dosages. PEMF had positive effects on bone formation. Exogenous PGE2 mimicked the effect of PEMF on linear bone growth. The effect of PGE2 on bone formation or bone remodelling was dose-related (5, 15, 50 micrograms/kg), with 5 micrograms/kg body weight as the optimal dosage in this study. Combination of PEMF and PGE2 exhibited a trend of additive effect on bone formation, especially at 15 micrograms/kg of PGE2. It is hypothesized that PEMF may exert its action on bone healing by increasing the endogenous PGE2. We therefore concluded that external stimulation such as PEMF and PGE2 was beneficial and stimulatory towards bone formation and healing in our animal model. However, the effects were somehow specific in electrical waveforms and dosage. Similar to PEMF, PGE2, therefore, may be a potential agent in promoting bone formation in the clinical treatments of fractures or perhaps non-union.

Orthopedics. 1998 Mar;21(3):297-302.

The effects of pulsed electromagnetism on fresh fracture healing: osteochondral repair in the rat femoral groove.

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Some clinical studies have claimed significant reductions in the healing time of fresh fractures with the use of pulsed electromagnetic fields (PEMFs). Animal models, however, have produced more equivocal results. This investigation examined the effects of PEMF treatment on an osteochondral defect placed in the patellofemoral groove of the rat. The results indicated that PEMF enhances early vascular reaction and suppresses initial pannus proliferation. Early chondrogenesis and bone formation were consistently stimulated, and the restoration of normal bone trabeculae advanced. Pulsed electromagnetic field treatment therefore may be useful in advancing repair during the early proliferative stage. Later results were variable and suggest that prolonged use may have deleterious effects, enhancing chondrogenesis beyond a point observed in normal repair and thus delaying normal subsurface trabeculation.

J Cell Biochem 1993 Apr;51(4):387-93.
Beneficial effects of electromagnetic fields.
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Abstract
Selective control of cell function by applying specifically configured, weak, time-varying magnetic fields has added a new, exciting dimension to biology and medicine. Field parameters for therapeutic, pulsed electromagnetic field (PEMFs) were designed to induce voltages similar to those produced, normally, during dynamic mechanical deformation of connective tissues. As a result, a wide variety of challenging musculoskeletal disorders have been treated successfully over the past two decades. More than a quarter million patients with chronically ununited fractures have benefitted, worldwide, from this surgically non-invasive method, without risk, discomfort, or the high costs of operative repair. Many of the athermal bioresponses, at the cellular and subcellular levels, have been identified and found appropriate to correct or modify the pathologic processes for which PEMFs have been used. Not only is efficacy supported by these basic studies but by a number of double-blind trials. As understanding of mechanisms expands, specific requirements for field energetics are being defined and the range of treatable ills broadened. These include nerve regeneration, wound healing, graft behavior, diabetes, and myocardial and cerebral ischemia (heart attack and stroke), among other conditions. Preliminary data even suggest possible benefits in controlling malignancy.

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