Original Research
The Effects of Pulsed Electromagnetism on Fresh Fracture Healing: Osteochondral Repair in the Rat Femoral Groove

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ABSTRACT

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.

While pulsed electromagnetic field (PEMF) therapy has become an established treatment for delayed fracture unions, few clinical studies have examined the effects of PEMF stimulation on fresh fractures. Some trials have shown that PEMF favored healing. Hinsenkamp et al examined four different PEMF signals on the healing of tibial fractures held in a Hoffman external fixator. They found that three signal profiles produced no effect, but improvements in healing time and enhanced mechanical consolidation of the fracture repair were found using a 72-Hz repetitive single 32-μs pulse. Brighton has advocated routine electrical treatment of fresh fractures in view of the potential savings in treatment time.

Animal models of fresh fractures treated with PEMF, however, have produced inconclusive results and are not as robust as the claimed clinical efficacy would suggest. Bassett et al studied the effects of PEMF on fibula fractures in beagles. Animals treated with 65-Hz pulses showed enhanced bone repair with improved mechanical qualities 28 days after osteotomy.

Conversely, Law et al were unable to find any PEMF-mediated improvement in the healing of tibial osteotomies in the sheep, and Miller et al found no significant improvement on canine fibula graft incorporation after 2 or 6 months treatment with a 15-Hz pulse-burst PEMF signal; biomechanical strength of the graft/host junction, histological appearance, and time to union were not affected.

Christel et al reported that four different PEMF waveforms were effective in stimulating the healing of rat radial osteotomies; in some cases, an average increase in tensile strength of 30% over control fractures was reported. Three other waveforms, however, were ineffective.

In view of the disparity of reported experimental results concerning the effects of PEMF on fresh fracture repair, this study was undertaken to examine the effects of a 72-Hz square-wave pulsed EM signal on healing in a reproducible osteochondral defect in the rat patellofemoral groove. Results were assessed by macroscopic evaluation of the lesion, histology, and microangiography.

MATERIALS AND METHODS
Ten-week-old female Wistar rats

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were randomly allocated to PEMF-treated (n=9) and mock-treated control groups (n=9). After administering general anesthesia, the joint capsule of the left knee was opened using a medial parapatellar incision and lateral patellar dislocation. A 2×2.5-mm defect was drilled into the center of the articular surface of the femoral groove at the level of insertion of the lateral ligament of the knee; the defect was extended into the cancellous interior of the distal femoral epiphysis. The patella was relocated, the joint closed in layers, and the animals allowed to recover.

Pulsed electromagnetic field stimulation was applied in a 60×40-cm cylindrical solenoid wound coil. The apparatus generated an asymmetrical square-wave pulse, 380 μs in width, with a repetition rate of 72 Hz; the peak magnetic field was approximately 12 G. Animals were not restrained during treatment, but were restricted from the coil walls by being placed in a cardboard box. The treatment coil was placed on a wooden table, distant from any potential field-perturbing metal objects. Animals were placed in the coil for 2 hours per day, 7 days per week. Animals in the control group were placed in the coil but with the current switched off. The rats were sacrificed at 1, 2, 4, and 8 weeks postoperatively.

At each time period, “blind” assessment of the amount of gross callus production, both within and surrounding the defect, was carried out using a devised numerical grading system, based on observations of standard magnified photographs. The mean results from 10 observers were combined for statistical analysis using the nonparametric Wilcoxon’s signed rank test.

The femora of six animals in each group were fixed in formal-saline and decalcified. Sequential 5-μm sagittal sections were taken through the distal end of the femur, passing through the defect; the sections were stained with hematoxylin and eosin, and Mallory’s one-step trichrome stain. Three additional animals in each group were perfused with a barium sulfate/gelatine suspension, injected caudally via the abdominal aorta under terminal general anesthesia. The femora with surrounding muscle were removed, fixed, and decalcified. High-resolution projection angiography was carried out on 2-mm slices cut across the femoral defect site.

**RESULTS**

*Callus Production.* Callus production rapidly occurred within the defect, which in control animals extruded beyond the perimeter of the drill-hole as a pannus. At 1 week, callus production was judged by all observers to be significantly less in PEMF-treated animals (P<.01; Wilcoxon’s signed rank test) compared with control animals. All animals in the PEMF-treated group at 1 week showed reduced external pannus formation. At 2 weeks, there was still significantly less pannus proliferation in the PEMF group (P<.05). There was no significant difference in callus scores at 4 and 8 weeks (Fig 1).

*One Week Postsurgery.* Control defects were characterized by the presence of a large fibrin clot surrounded by loose pluripotential blastema-like mesenchyme. This tissue was becoming denser, with vascular penetration occurring, particularly at the base of the defect where osteogenesis was initiated. Fibrous bridging was taking place at the surface of the defect (Fig 2A).

In all specimens, PEMF treatment appeared to show increased cellular proliferation within the defect compared with controls, with a marked reduction of the fibrin clot (Fig 2B). In some specimens, the fibrin clot was resorbed, and the proportion of loose mesenchyme substantially diminished. Differentiation into vascular dense connective tissue was greatly increased, with osteoid formation and osteogenesis becoming well-established.

*Two Weeks Postsurgery.* The fibrin clot was still present in the control group, surrounded by mesenchyme verging peripherally into dense connective tissue. In PEMF-treated animals, the fibrin clot was resorbed by macrophages, resulting in a matrix packed with primitive mesenchymal cells (Fig 3). Peripherally, osteoid trabecular formation was also advanced compared with the untreated controls.
At both 1 and 2 weeks postsurgery, all PEMF-treated animals showed advanced healing compared with controls. At 2 weeks, scattered islands of chondrogenesis were present in both groups, and the surface was becoming predominantly cartilaginous. There also appeared to be an increased vascular reaction in the PEMF-treated defects, shown both in histological sections and microangiographic preparations. In some cases, the enhanced vascular proliferation was pronounced (Fig 4). Although vascular proliferation was clearly advanced at 2 weeks in PEMF-treated epiphyses, the differences between PEMF-treated and control angiograms were less marked at 4 and 8 weeks.

Four Weeks Postsurgery. The surface region of the control animals were largely filled with a cartilage plug of hyaline appearance. Some residual loose mesenchyme remained in the center, with new bone trabeculae forming in the depths (Fig 5A). In some cases, areas of zonally organized cartilage plaque remained, which were similar in some respects to the structural organization of a growth cartilage. We have termed such structures neogrowth cartilages.

While control specimens at 4 weeks were largely similar, PEMF-treated animals showed more variation. Most specimens showed accelerated healing; the surface of defects in the PEMF groups were well-healed with organized hyaline cartilage, with bone trabeculae occupying most of the defect area (Fig 5B).

In some cases, however, PEMF-treated animals showed abundant residual cartilage, far in excess of that seen in controls, showing not just at the surface but also in the depths of the defect. The PEMF-treated specimen showed a pronounced neogrowth cartilage (Fig 6). These PEMF-irradiated structures, presumably facilitating endochondral bone formation, were greatly enhanced compared with controls, where they occurred only rarely and to a limited extent. This abnormal cartilage production appears, when present, to have retarded bone consolidation in the center of the defect.

Eight Weeks Postsurgery. Articular cartilage restoration varied, often showing some eburation, and generally was not as well preserved in controls as in PEMF-treated animals (Fig 7). Where surface cartilage remained as a prominent feature, the cells were often poorly organized and deficient in chondrocytes. Trabecular bone in controls
Fig 4: Microfocal radiography of the inferior femoral metaphysis, following micropaque injection and subsequent decalcification. Note the arterial filling in a control (A) and a PEMF-treated (B) femur at 2 weeks. Treatment with PEMF has resulted in a particularly florid vascularization.

Fig 5: Control (A) and PEMF-treated (B) defect at 4 weeks. In the control femur, note the loose mesenchymal filling in the depths, together with organized "neogrowth cartilage" (arrow). The surface of the control femur also is filled with a cartilage plug of hyaline appearance while the surface of the PEMF-treated femur has been reformed with organized hyaline cartilage. Bone trabeculae are apparent throughout the PEMF-treated defect area.

Fig 6: PEMF-treated femoral metaphysis showing excessive cartilage organized into pronounced "neogrowth cartilage" (arrow) in this case. This abnormal cartilage proliferation is now retarding normal cellular reorganization.

(Fig 7A) generally appeared sparser and thinner, indeed osteoporotic, compared with PEMF-irradiated animals in whom trabeculae appeared normal.

Figure 7B shows a plaque of cartilage remaining in a PEMF-treated specimen. Limited cartilage plaques also remained in some control specimens, but in general, cartilage was more prevalent as a feature in PEMF-treated animals. In some PEMF-treated animals, cartilage presented as the dominant feature (Fig 8), substantially delaying the repair.

**DISCUSSION**

This qualitative investigation examines the use of PEMF in the treatment of fresh fractures. The model used, although appearing simple, is complicated by the involvement of articular cartilage and bone moieties, both contributing and reacting to the changing microenvironment of the lesion. Furthermore, the loss of articular congruity resulting from imposition of the defect may lead to superimposed changes in the articular surface associated with the development of osteoarthritis. Repair of deep osteochondral lesions largely results from metaplasia of the subchondral granulation tissue, although some hyperplasia of chondrocytes at the defect margins also may contribute to cartilage reformation.12,13

Our observations that early pannus proliferation is suppressed in PEMF-treated animals are similar to those reported13 following the use of pulsing direct current on osteochondral defects in the rabbit femoral condyle. This observation may be of some significance for the preservation of undamaged cartilage surrounding the defect; pannus extrusion is destructive to the joint surface as it secretes proteolytic enzyme as well as depriving the carti-

lage of its normal nutrition.14

The present study demonstrates fibrin clot formation (from the initial hematoma) and its conversion to vascular fibroblastic repair tissue, which changes to a more cellular, fibroblastic network at the articular edge of the defect. At the base of the lesion, bone formation is brisk and extends toward the joint. The granulation tissue differentiates into osteoblasts and chondrocytes; cartilage, under normal conditions, is completely resorbed in the bone domain, and bony continuity is restored.

The repair process is dependent on an adequate blood supply. Hall15 related the pluripotential nature of these processes to the hemodynamic status, suggesting that in ischemic conditions, the cells tend toward fibroblast and chondrocyte production, while hyper-vascularity stimulated production of osteoblast and bone production. In the present study, PEMF treatment produced a clear enhancement of angio-
genesis compared with controls at 2 weeks, when bone formation was clearly advanced over nontreated controls.

At later stages, the results became more variable, and we were unable to clearly relate vascular status to any particular group. This difficulty may be due to variations in cartilage production, particularly seen in PEMF-treated animals from 4 weeks; there may be a reciprocal interaction between angiogenic and chondrogenic stimulation.

Pulsed electromagnetic fields have been shown to have profound effects on connective tissues. In endothelial cell culture, pulsed electromagnetism has stimulated new vessel formation and proliferation,\(^\text{16}\) and this ability may be responsible for the improved revascularization of ischemic rabbit femoral heads reported by Braun and Lemons.\(^\text{17}\) Bassett\(^\text{18}\) has particularly implicated a 72-Hz signal as a potent angiogenic stimulus, and work in our own laboratory supports this contention.\(^\text{19}\)

There is abundant evidence that PEMF can stimulate the synthesis of the major components of bone matrix and cartilage.\(^\text{20,21}\) The results of the present investigation show that pulsed electromagnetism produces an early stimulus to cellular proliferation, and this was also shown in rat tibial osteotomies by Sarker et al.\(^\text{22}\) Hinsenkamp et al\(^\text{23}\) found that an 11-Hz pulse-burst PEMF signal improved mechanical progress of repair of a rat tibial osteotomy, but only in the early stages; by 45 days, all fractures were equivalent. De Haas et al\(^\text{24}\) similarly found that a 1-Hz square-wave PEMF signal stimulated repair of a rabbit radial osteotomy, but healing was only advanced compared with controls over the first 2 weeks.

The authors above concluded that there was no advantage in treating fresh long-bone fractures with PEMF. Our results also suggest that prolonged stimulation fails to improve bone healing compared with untreated controls. Furthermore, although trabeculae often may appear better preserved than in controls, prolonged stimulation may in fact prove detrimental due to continued production of cartilage.

Interestingly, a similar trend was observed using a different treatment modality. Dyson and Brookes\(^\text{25}\) examined the result of applying pulsed ultrasound to healing fibula fractures in the rat. Fracture repair was accelerated when applied during the first 2 weeks, that is, during the inflammatory and proliferative phases. However, treatment applied during the late proliferative repair phase when hard callus was consolidating proved disadvantageous, leading to persistent cartilage growth and delayed fracture healing. This is similar to the events observed in the current study, suggesting that PEMF stimulation is most useful during the period when the fracture site is being cleared of debris, repair stimulating factors are being released, and when cell migration and division are most active.

Cancé et al\(^\text{26}\) found that diaphyseal bore holes in equine metacarpal bones were more responsive to PEMF stimulation than similar holes placed in the metaphysis; in fact, metaphyseal bore holes showed no change in response to PEMF treatment and were sometimes seen to retard healing. The authors argued that PEMF only affected regions of low metabolic activity. It is also worth noting that cancellous metaphyseal bone has the highest blood flow rate, whilst diaphyseal cortex has the lowest flow.\(^\text{27-30}\)

Fracture repair is dependent on the ability of the surrounding tissues to elicit a rapid elevation in the blood supply to the damaged bone. The hemodynamic conditions in metaphyseal (and epiphyseal) bone therefore may already be optimal for efficient fracture repair, while the low flow normally present in compact cortical bone may benefit from the early angiogenic stimulus provided by PEMF. Similar arguments apply to the ischemic environment found in delayed unions where PEMF treatment has been shown to be particularly effective.

**Conclusion**

The present study suggests that PEMF stimulates the early, proliferative phase of fracture repair but may become deleterious if the treatment is prolonged. It may well be that fresh fractures normally heal at their maximum rate and are therefore insensitive to further stimulation. The mechanisms of fracture healing are well-balanced.
and may not be amenable to significant “improvement” in the absence of gross deformity and disturbance to the normal sequence of molecular and heme-dynamic events.

REFERENCES