Prevention of Osteoporosis by Pulsed Electromagnetic Fields*

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ABSTRACT: Using an animal model, we examined the use of pulsed electromagnetic fields, induced at a physiological frequency and intensity, to prevent the osteoporosis that is concomitant with disuse. By protecting the left ulnae of turkeys from functional loading, we noted a loss of bone of 13.0 per cent compared with the intact contralateral control ulnae over an eight-week experimental period. Using a treatment regimen of one hour per day of pulsed electromagnetic fields, we observed an osteogenic dose-response to induced electrical power, with a maximum osteogenic effect between 0.01 and 0.04 tesla per second. Pulse power levels of more or less than these levels were less effective. The maximum osteogenic response was obtained by a decrease in the level of intracortical remodeling, inhibition of endosteal resorption, and stimulation of both periosteal and endosteal new-bone formation. These data suggest that short daily periods of exposure to appropriate electromagnetic fields can beneficially influence the behavior of the cell populations that are responsible for bone-remodeling, and that there is an effective window of induced electrical power in which bone mass can be controlled in the absence of mechanical loading.

CLINICAL RELEVANCE: Our data suggest a potential role for the use of pulsed electromagnetic fields in the prevention of loss of bone in immobilized patients; in the aging, postmenopausal population; and in astronauts who are subjected to prolonged exposure to the microgravitational milieu. Structurally deleterious loss of bone may be slowed or prevented by appropriate use of non-invasive electromagnetic stimulation.

Osteoporosis is characterized by the loss of mineralized tissue, which results in structural failure despite continued functional demands. Recent clinical surveys have demonstrated that adult bone mass diminishes at a mean rate of 1.1 per cent per year, and it can reach a loss of 2 per cent per year after menopause. As the probability of fracture is closely related to a person's effective bone mass, a modality that could prevent or retard loss of bone might provide a substantial reduction in the incidence of skeletal morbidity.

Several prophylactic measures to prevent loss of bone are available; these include estrogen therapy, supplemental dietary calcium, calcitonin, vitamin D, and exercise. There also are treatment regimens that stimulate formation of bone, such as sodium fluoride and parathyroid hormone. While discussion of these forms of treatment is beyond the scope of this report, the recent article by Riggs and Melton is an excellent review. Although these regimens have been shown to be effective in the treatment of osteopenia, limitations, cautions, and dangers are inherent in their extended use. Even exercise, which provides the only endogenous stimulus to maintain normal bone mass, is potentially dangerous, as it may precipitate the fracture that it is supposed to prevent. The clinical potential for increasing bone mass, or simply preventing loss of bone, by alternative non-invasive means is therefore substantial.

One non-invasive technique is the induction of low-intensity electrical fields into the bone and surrounding tissues. Interest in the use of electricity to influence the regulation of bone mass was aroused in 1954, when Yasuda demonstrated that bone, under load, can generate an electrical potential. Relatively large potentials (1.0 to 1.5 millivolts), arising from the impact loading of wet bone, were subsequently measured by Bassett and Becker, leading to the hypothesis that strain-generated electrical potentials, produced during functional activity, may in fact be the signal that is responsible for the regulation of specific cellular processes in bone. More recently, the use of electricity as a treatment for delayed unions and non-unions of bone has received attention. While these studies identified electricity as a possible means of stimulating cellular activity in the skeleton, it remains unclear which aspects of the electrical field are responsible for regulating these cellular events. Also, there is only sparse evidence of a dose-response effect of electricity on inhibiting osteopenia, none of which, to our knowledge, has focused on the non-invasive use of electromagnetic fields.

For the studies that are reported here, we initiated a systematic series of experiments in which we identified a specific parameter of the induced electrical field, power,
and monitored the skeletal changes that were associated with this parameter in an established in vivo model for adaptive bone-remodeling.

Materials and Methods

This functionally isolated ulna model was developed initially to study mechanically induced structural adaptation in bone. The ulnae in the turkeys that were used in this protocol were approximately fifteen centimeters long and 1.5 centimeters wide, which is close to twice the length and width of a human metacarpal bone. Unlike the bones of small rodents, the ulna of the turkey normally undergoes secondary haversian remodeling, a process that makes the bone applicable as a model for the osteopenias that are concomitant with aging in the human. In addition, the ulna’s position in the wing of the bird means that it can be retained in situ, but deprived of normal mechanical function without causing distress or suffering to the animal. In this study, the course, progress, and balance of the remodeling response to functional deprivation, together with the modulating effect of pulsed electromagnetic-field stimulation, was monitored by postmortem histological studies, microradiography, stereology, and the distribution of fluorescent (tetacycline) labels that had been administered biweekly throughout the experimental period.

The left ulnae of forty-one skeletally mature male turkeys were isolated from functional load-bearing by proximal and distal metaphyseal osteotomies, performed under general anesthesia with halothane. These animals, which reach skeletal maturity (ulnar epiphyses fused) at approximately nine months, were between twelve and fifteen months old and weighed between eighteen and twenty-three kilograms. The diaphyseal face at the ends of each ulnar osteotomy was covered with a stainless-steel cap to prevent osseous union. The preparation, therefore, consisted of a 110-milimeter diaphyseal section of mature bone that was deprived of mechanical function but had undisturbed musculature and nutrient and neural supplies (Fig. 1). The contralateral ulna was left intact and served as a control. The data in this report reflect differences in area between a transverse section of the bisected middle of the diaphyseal shaft of the functionally isolated ulna and a section taken from the identical location in the intact contralateral (control) bone. We assumed that the control ulna represented the cross-sectional morphology of the experimental ulna before remodeling changes ensued, and in this paper we refer to these differences as indicative of the changes that occurred in the isolated bone over only the experimental period of eight weeks.

The differences in remodeling activity between the isolated and control ulnae, over the eight-week experimental period, were evaluated for disuse alone (Group 1), for exposure to inactive induction coils (Group 2), and for exposure to one of five pulsed electromagnetic fields (Groups 3 through 7). These five pulsed electromagnetic fields consisted of similar pulse patterns of thirty-millisecond bursts at a repetition rate of 1.5 hertz, each burst containing 120 repetitions of an asymmetrical pulse (Fig. 2). These signals were chosen because they were thought to approximate the
fundamental frequencies and intensities that have been postulated to develop under normal physiological loading conditions. The characteristics of the pulse waveforms were determined using a search coil constructed such that a one-millivolt output signal corresponded to a rate of change of the magnetic flux density of 0.7 tesla per second. Since the pulse patterns were similar for all five waveforms, the average power of the induced electrical fields was proportional to the square of the time rate of change of the magnetic flux density and the flux rise time: (tesla per second)$^2 \times T$. The units that are used in this report are T$^2$s$^{-1}$. As the magnitude of the induced electrical field at the level of the osseous tissue is unknown, the relative power has been estimated from the amplitude and duration of the pulses that were induced in the search coil. The five waveforms in this study induced electrical fields with average powers proportional to 0.002, 0.01, 0.04, 0.10, and 0.15 T$^2$s$^{-1}$.

The isolated ulnae were exposed to the pulsed electromagnetic fields using small (ten-centimeter-diameter) aircore coils with integral waveform generators and battery packs. When the coils were strapped to the wing using Velcro fasteners, the coils approximated a Helmholtz configuration (a paired-coil configuration in which the separation of the coil is equal to its radius). Starting two days postoperatively, one of the six signal types was applied for one hour a day, five days a week. Four birds were exposed to inactive coils, and thirty-four birds were treated with one of the five coils that generated pulsed electromagnetic fields. In three birds, the left ulna was functionally isolated, as has been described, but no coil treatment of any sort was administered.

After eight weeks of treatment, the animals were killed, and undecalcified 100-micrometer transverse sections were taken from the middle of the diaphyseal shaft of each pair of ulnae (Fig. 3, a). The sections of the experimental ulna were compared with sections from the identical region of the contralateral (control) ulna. Microradiographs of these sections were made, and the sectional properties were calculated by projecting the radiographs onto a forty by forty-centimeter (0.1-millimeter-resolution) digitizing tablet. The periosteal and endosteal envelopes, as well as intracortical porosity, were traced onto the tablet, and total area was calculated.

**Results**

In the animals in which the functionally isolated ulna was exposed to the inactive coil (Group 2), the cross-sectional area was reduced by 10.8 per cent (standard error, 4.8 per cent) as compared with the contralateral ulna (Table I). It should be emphasized that both the microradiographs and the fluorescent sections of the contralateral control ulna showed little, if any, remodeling or modeling activity, reflecting little osseous turnover. This lack of remodeling supports our assumption that the control ulna reflects the morphology of the experimental ulna before remodeling, stimulated by disuse or by electrical treatment, has begun. In addition, this result with the inactive coil was not significantly different from the 13.0 per cent (standard error, 3.4 per cent) loss of bone that was seen with disuse alone (Group 1). In both cases, this loss of bone was produced by endosteal resorption and intracortical porosis (Fig. 3, b), and it closely resembled the age-related osteopenic changes in the human metacarpal.

The comparison of the geometric properties of the sections from the experimental and control ulnae of the thirty-four birds that were exposed to active coils are shown in Figure 4. The digitized areas of the ulnae exposed to pulsed electromagnetic fields at the low and high ends of the power spectrum showed no significant difference from the response that was generated by simple disuse or by disuse and exposure to the inactive coils (Table I). However, pulsed electromagnetic fields of 0.01 and 0.04 T$^2$s$^{-1}$ were associated
Transverse microradiographs of the middle of the diaphyseal shaft of the ulna of the turkey after eight weeks of treatment.

a: Intact control, showing a quiescent, uniformly mineralized cortex (scale mark, 2.0 millimeters).
b: Ulna that was functionally isolated and was exposed to a dummy coil. Compared with its intact contralateral control (a), the functionally isolated ulna has lost 13.1 per cent of its bone. Activity in the cortex shows remodeling that is typical of disuse osteoporosis: cortical thinning by endosteal resorption and porosis caused by incompletely infilled haversian remodeling.
c: Ulna that was functionally isolated and was treated with one hour a day of a pulsed electromagnetic field, engendering an average power proportional to 0.04 tesla's\(^{-1}\). There is an increase in bone mass of 23 per cent. This remodeling activity represents a net increase, compared with the functionally isolated ulna that was exposed to inactive coils, of approximately 33 per cent. While there is substantial periosteal and endosteal new-bone formation, there is very little remodeling activity in the cortex. Despite the increase, osteoporosis has been prevented and bone mass has increased.

with increases in bone mass of 12.3 and 9.7 per cent (standard errors, 3.3 and 3.4 per cent). This represents a 23 and 20 per cent increase, respectively, compared with the ulnae that were exposed to inactive coils (loss of tissue of 10.8 per cent). In addition, the sections from the ulnae that were exposed to 0.01 and 0.04 T\(^{s^{-1}}\) demonstrated little or no evidence of endosteal resorption or intracortical porosis, and the new bone that was generated was firmly attached to the osseous surface, was well mineralized, and consisted principally of primary osteons (Fig. 3, c).

Discussion

In the United States, more than two million fractures in people who are more than forty-five years old can be attributed to osteoporosis annually, amounting to more than six billion dollars in medical costs\(^{35}\). While the pathophysiology of the different osteopenias may not be similar\(^{35}\), the primary clinical objective of research in this area remains the development of a means of retaining bone mass in the presence of factors that tend to produce resorption. The loss of skeletal mass is substantial; once loss of bone begins, in the fourth decade of life, women lose 50 per cent of the trabecular bone mass and 25 per cent of the cortical bone mass, while men lose approximately two-thirds those amounts\(^{19,23,24}\). Not only do the pain, loss of vertebral height, fractures, and post-fracture complications impair the quality of life, but the treatment imposes an inerous burden on the medical services of the country. Those fractures are frequently the precipitating events leading to permanent infirmity and terminal decline; 70 per cent of patients who enter nursing homes for treatment of a fracture of the hip die within the first year\(^{13}\). The clinical, social, and economic impact of reducing the incidence of such fractures in elderly and non-ambulatory people would be considerable.
Disuse osteoporosis represents an uncoupling between formation of bone and the bone resorption that is induced by decreased mechanical loading. Several investigators have applied the principles of imposed electrical currents to prevent this osteopenia. McElhaney et al. used a rat model of disuse osteoporosis to show that capacitively coupled thirty-hertz sinusoidal fields were effective in preventing loss of bone, while three-hertz fields at the same driving voltage were not. Bassett et al. demonstrated that seventy-hertz pulsed (325-microsecond) magnetic fields were as effective in slowing osteoporosis as were trains of pulses (twenty 325-microsecond pulses, separated by 200 microseconds) at ten hertz. Subsequent experiments by Kenner et al., using a rabbit model of disuse osteoporosis, showed that directly coupled five-hertz pulsed fields significantly reduced loss of bone during disuse. Martin and Gutman, also using the rat model for osteoporosis, showed that the effect of a capacitively coupled thirty-hertz field was not dependent on the duration of stimulation, as exposure for two hours a day was as effective as exposure for eight hours a day. In contrast, Brighton et al., using a model of sciatic denervation osteopenia in the rat, demonstrated that capacitively coupled electrical stimulation, delivered at sixty kilohertz, could prevent the loss of bone caused by disuse only if the signal was applied for twenty-four hours a day, and even then at an amplitude of ten volts peak to peak. Interestingly, this group also reported that the capacitively coupled electrical signal, delivered at sixty kilohertz, could reverse the loss of bone due to disuse, but needed a daily twenty-four-hour signal of only 0.5 volt peak to peak. This is extremely important, as it represents the first in vivo evidence of influence of electrical fields on osteogenesis, describing some specific dose-response effects in the modeling skeleton.

However, while these studies are valuable contributions to the understanding of how electricity affects skeletal tissues, it is not clear how electrical fields will interact with an adult skeleton — specifically, one that normally undergoes haversian remodeling. Published work also has not

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**Table I**

<table>
<thead>
<tr>
<th>Group</th>
<th>Average Power (×T²/s)</th>
<th>Change in Area*</th>
<th>Change in Least Square Mean of Area†</th>
<th>No. of Animals</th>
<th>Signif. Different Groups‡</th>
</tr>
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<tbody>
<tr>
<td>1 Disuse</td>
<td>13.0 ± 3.4</td>
<td>-11.59 ± 5.21</td>
<td>3</td>
<td>3, 4, 5</td>
<td></td>
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<tr>
<td>2 0.0</td>
<td>-10.8 ± 4.8</td>
<td>-9.67 ± 5.21</td>
<td>4</td>
<td>4, 5</td>
<td></td>
</tr>
<tr>
<td>3 0.002</td>
<td>-0.4 ± 3.0</td>
<td>+0.79 ± 3.84</td>
<td>7</td>
<td>1, 5</td>
<td></td>
</tr>
<tr>
<td>4 0.01</td>
<td>+12.3 ± 3.3</td>
<td>+13.41 ± 5.21</td>
<td>4</td>
<td>1, 2, 3, 6, 7</td>
<td></td>
</tr>
<tr>
<td>5 0.04</td>
<td>+9.7 ± 3.4</td>
<td>+9.69 ± 2.95</td>
<td>10</td>
<td>1, 2, 6, 7</td>
<td></td>
</tr>
<tr>
<td>6 0.10</td>
<td>-7.2 ± 2.5</td>
<td>-6.74 ± 3.26</td>
<td>9</td>
<td>4, 5</td>
<td></td>
</tr>
<tr>
<td>7 0.15</td>
<td>-8.2 ± 9.4</td>
<td>-6.21 ± 5.21</td>
<td>4</td>
<td>4, 5</td>
<td></td>
</tr>
</tbody>
</table>

* Mean and standard error.
† Least square means of percentage area changes are estimates based on fit to a linear model. The analysis indicates that: (1) inactive coil treatment is not significantly different from functional isolation alone, (2) coil treatment can produce a significant change in bone-remodeling activity, and (3) there are significant differences between different coil powers.
‡ p < 0.01; with section sign (§), p < 0.05.

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**Figure 4**

Change in cross-sectional area of the bone versus relative power of the individual electromagnetic fields. The average induced power is proportional to the square of the rate of change of the magnetic flux time and to the total rise time of the magnetic flux pulse. The data are shown as actual arithmetical means, with bars representing the standard error of the mean.
delineated whether electricity induced at frequencies and intensities closer to a physiological character also can have a beneficial effect; that is, while electrical fields may influence skeletal homeostasis, is this the normal mechanism for the interaction of physical activity and adaptation?

The objective of this study was to begin to identify specific aspects of the electrical signal that have the potential to regulate bone-cell activity. We attempted to correlate cortical osteogenesis and the intensity of the induced electrical power, the level of which could potentially be generated during normal physiological activity.

The pulse burst pattern of the pulsed electromagnetic field that was used in this study was similar to those used clinically. However, while the general characteristics of the waveform were not altered throughout the protocols, it was necessary to control the level of pulse power through simultaneous regulation of both the time rate of change of the magnetic flux and the duration of the magnetic flux pulse. Therefore, while a large variation in the effectiveness of the pulsed electromagnetic field was found, it is not conclusive evidence that the most effective signal of this study is an optimum signal for bone regulation, or that any power is the ideal parameter to optimize. Rigorous optimization can be obtained only through systematic investigation of the influence of the separate parameters of the pulse (width, amplitude, intrapulse interval, and so on). However, these results do identify a specific dose-response regulation of adult bone mass by electrical fields in the absence of mechanical stimulation. The most osteogenic effect was obtained with field intensities of 0.01 and 0.04 tesla's, with inhibition of the osteoporotic process being achieved by the combined effect of a decrease in the level of intracortical remodeling, inhibition of endosteal resorption, and stimulation of both periosteal and endosteal new-bone formation. Induced electrical power of more or less than these levels was less effective.

We concluded that there is an effective window of pulsed electromagnetic fields in which bone mass can be controlled in the absence of function. This is achieved by comparatively short daily periods of exposure (one hour), generated within a physiological intensity and frequency. Because of the physiological characteristics of the signal, we believe that electricity influences the behavior of cell populations that are responsible for bone-remodeling in a manner similar to what occurs in the normal milieu. Finally, we have shown that these electrical fields can slow, inhibit, or even reverse the osteoporotic processes that normally accompany disuse in our animal model.

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References