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Low Energy Pulsing Electromagnetic Fields Modify Biomedical Processes

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Summary

Low-energy, pulsed electromagnetic fields (PEMFs) have reversed therapeutically resistant pathologic processes in the musculo-skeletal system. Their development as a non-thermal therapeutic agent is based on 30 years of study of the electro-biological properties of connective tissues. Specific energy characteristics in applied PEMFs produce selected biological effects by modifying synthetic and other behavioral patterns of target cells; some mechanisms of action are defined. The technology appears safe and effective in clinical treatment of un-united fractures, avascular necrosis of bone, and chronic, refractory tendinitis. An expanding, rational use in biomedical science is predicted.

Introduction

Low-energy, pulsed electromagnetic fields (PEMFs) were first applied therapeutically 13 years ago at Columbia. A child with a fractured tibia, un-united after 12 operations over a 10-year interval, was facing amputation. The underlying problem, congenital pseudarthrosis (a 'false joint') of the tibia, typically is resistant to surgical and non-surgical intervention. For the six months prior to starting PEMFs she was in a cast, on crutches, without X-ray evidence of healing. The only modification of management was to add a pair of energized wire coils opposite the break. Within 4 months healing occurred,[1] and since then her united tibia has allowed participation in young adult activities.

In the intervening 13 years, this surgically non-invasive approach has proven riskless in more than 100 children with this rare condition. Dr Clinton Compere, in an editorial entitled Electromagnetic Fields and Bones' wrote '... from my own observations one of the most dramatic effects of these [i.e. electrical] procedures has been on congenital pseudarthrosis.'[2] Dr Harold Boyd stated: 'One would not applaud a 40% failure rate; however, this is superior to the results which follow the first operation – and may surpass the results of repeated operations.'[3] These views are shared by others, all of whom have cited the biological effectiveness of PEMFs in producing bony union in congenital pseudarthrosis.[4, 5]

Chronically un-united fractures in adults, also, are therapeutic challenges, albeit less than congenital lesions. More than 60,000 have been treated safely, as outpatients, with an overall success rate of 80% or more and with a significant economic advantage over surgical approaches.[6] Many unhealed patients were > 2 years after injury actively infected and had had > 3 unsuccessful surgical repairs. Amputation had been recommended frequently for these patients, in whom spontaneous healing is exceedingly rare.[7] As a control for this remote possibility, casts were applied to long-standing non-unions of the tibia, the patient placed on crutches, and serial X-rays taken for 3–4 months. No evidence of healing began *until* 1 to 2 months after PEMFs were started as the sole change in management. Similar findings recently were reported in a series of 147 patients who had failed to heal with external skeletal fixation.[8]

Concomitant with extensive clinical use of PEMFs, in which more than 10,000 American orthopaedic surgeons have participated, a number of laboratories studied biological effects in animal and culture models. These confirmed that PEMFs affected cellular processes pertinent to bone repair. Before considering these results, it is appropriate to review well-established features of fracture healing.[9, 10]

Cell Responses to Fracture

Initially, an 'explosion' of DNA synthesis and cell proliferation occurs between the dense bony cortex, flanking the break, and the ensheathing periosteum. Sleeves of new bone, the anchoring callus, are deposited proximally and distally. Opposite the break, an influx of young connective tissue cells form fibrocartilage, linking the sleeves of newly formed bone with a rubbery bridging callus. Progressive calcification of the bridge permits penetration of new vessels, removal of calcified fibrocartilage and its centripetal replacement by young fiber bone. This sequence, endochondral ossification, is closely akin to events occurring in growth centers. After the bone ends are mechanically joined by hard tissue, 'stress-working' (remodelling and maturation) proceeds in 95% of fractures. Early phases of repair occur in the presence of electrical currents of injury which have been postulated to trigger healing.[11, 12, 13]

In chronically un-united fractures (non-unions), injury currents have subsided, unless re-injury occurs. The provisional bridge of soft tissue, opposite the fracture, is not calcified. Failure to complete this critically important step blocks later stages of repair, since vascular penetration of uncalcified fibrocartilage does not occur.

Mechanism of Action; PEMF Effects on Calcium

The pathologic features of non-union suggest that initiation of calcification will 'restart' the stalled, final phases of fracture repair. In fact, surgical methods to treat non-unions by plates or with bridging bone grafts achieve this end.[14] PEMFs produce similar effects. Changes in cellular calcium content and calcification have been confirmed in a number of experimental systems and in patients. These responses appear in canine models of non-unions and in chick chondrocytes in tissue culture.[15] Effects on calcification were confirmed in the U.K. by Fitton Jackson, at the Strangeways Research Laboratory in Cambridge.[16] Several other reports indicate that PEMFs affect local mineralization processes[17, 18] but not total body calcium metabolism.[19] Modifications in cellular calcium, also, have been implicated in several biological effects of PEMFs. These include rapid alterations in adenylcyclase and phosphodiesterase,[20] depression of DNA synthesis in phytohemagglutinin-stimulated lymphocytes,[21] altered division rates in Paramecium,[22] increased collagen production and reduced lactate in fibroblasts,[23, 24, 25] modified proteoglycan synthesis[26, 27, 28, 29]

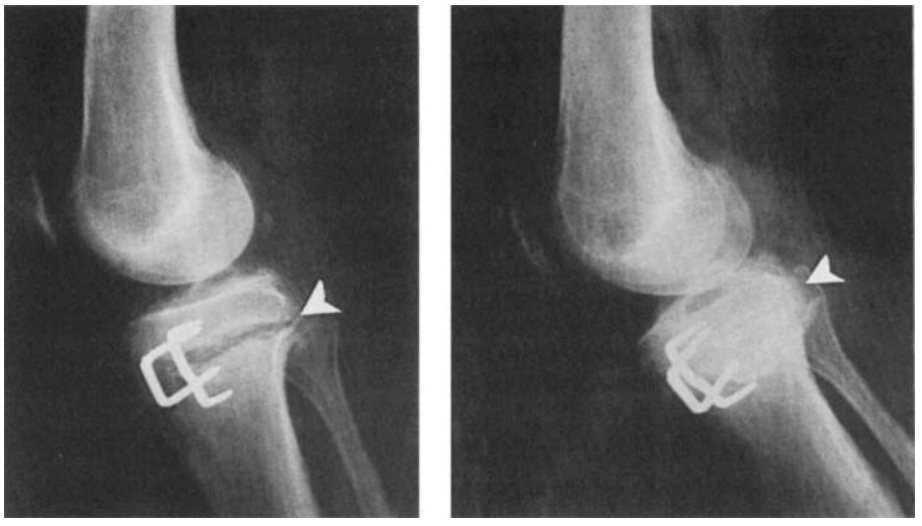

Fig. 1. *X-rays of a non-union of the knee region (upper tibia) of two years' duration before PEMF treatment (left) and six months after their use was started. Note changed density of radio-lucent line below the joint (arrows). This patient was healed, clinically, by X-ray, and by biopsy, which disclosed bony bridging with only a few remnants of old calcified fibrocartilage.*

and decreased insulin secretion by pancreatic cells,[30] among others. Investigators have noted similarities in PEMF effects and the calcium-blocker action of Verapamil.[22, 30]

In PEMF-treated non-unions, a progressive increase in radiographic density of the gap region characteristically appears within 1–2 months.[6] This increase coincides with the calcium deposition noted in tissue (biopsy) specimens.[10] Later, endochondral ossification and bony bridging are confirmed, both radiographically and microscopically (Fig. 1). These clinical data are entirely consistent with experimental findings. Together, they support a primary mechanism of PEMF action in un-united fractures, namely triggering calcification of soft tissues in the gap so that final phases of bony bridging and maturation can begin in normal fashion. The exact mechanisms by which calcium kinetics are modified in the cell remain to be determined. Certainly, changes in Ca^{2+} in cell membranes and mitochondria are prime targets for study. Furthermore, PEMF effects on enzymes which may play a role in mineralization (e.g. pyrophosphatase and lysozyme) deserve attention. Finally, field effects on collagen synthesis,[25, 26] proteoglycan production,[26, 29] and new blood vessel formation (angiogenesis),[31] could be beneficial, hypothetically, during endochondral ossification.

For those steeped in transmembrane potentials of 50 mV or more, the relatively weak potentials of 1–20 mV/cm induced by PEMFs might seem inconsequential. In all probability, their mechanism of action does not derive from modifications of these potentials, but rather by interactions with fixed charge on membrane components of the cell through alterations of calcium or through resonance phenomena. Details of some of these hypotheses have been set forth previously.[32, 33, 34]

PEMFs – Pro or Con? I

Rational treatment of disease requires appropriate therapeutic mechanisms of action to correct or modify the pathology. By this criterion, use of PEMFs for non-unions is rational. None the less, there are those who allege that therapeutic claims are ill founded.[35, 36, 37] Four main arguments have been advanced to support a negative stance. (1) The mechanism of action is unknown, so all results are suspect. (2) Several different types of pulses have been reported to be effective; claims for specific action, therefore, are open to question. (3) Negative bone-healing experiments with PEMFs contradict both positive *in vitro/in vivo* experiments and clinical results. (4) A 'double blind' study of patients with non-unions has concluded that immobilization, alone, produced effects equal to PEMFs.

The first of these arguments has been answered already, in the preceding section, and the remaining three will be rebutted in order. First, certain physical and biological details, central to the debate, should be considered since many biologists and physicians are more familiar with biochemical than with bioelectric phenomena. Even in physics and electrical engineering, subspecialists deal with specifics of field characteristics and design. Few of these experts have a working knowledge of biology or medicine. In an interdisciplinary vacuum, it is possible to think the world flat!

PEMF Characteristics

The acronym, PEMFs, is not meant to be generic for all electromagnetic fields. It is restricted to pulse types in common clinical usage to treat unhealed fractures and other pathologic processes. Each of these pulses simulates the shape and amplitude of asymmetric electrical waveforms detected when bone is dynamically deformed (Fig. 2).[32] These electromechanical phenomena in bone have been well characterized in the past 25 years.[31, 38, 39, 40] Electrical responses to mechanical deformation appear to result from piezoelectric and electrokinetic (streaming potentials) behavior and are postulated to provide feedback control of cell behavior during stress-related remodelling (Fig. 3).[31] The pulses used in PEMFs are quasi-rectangular or quasi-triangular when the voltage waveforms are recorded by a standardized coil-probe dosimeter (Fig. 4). Their repetition rates lie in the extremely low-frequency (ELF) range. When analysed by discrete Fourier transforms, these several waveforms share some frequency-content characteristics and

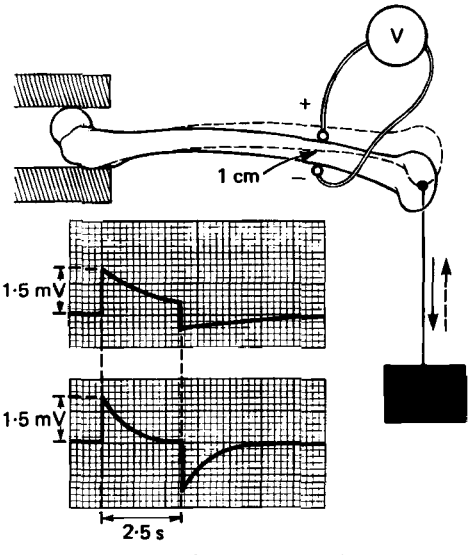

Fig. 2. *Diagram of symmetric and asymmetric waveforms recorded from rapidly loaded and unloaded whole bone (top trace) and bone strips (bottom trace). Ag/AgCl electrodes, 1 cm apart, are used to detect these electric potentials, which result from piezoelectric phenomena and from streaming potentials. Both quasi-rectangular and quasi-triangular features are present. The relatively long decay characteristics via-à-vis PEMF-induced pulses (see Fig. 4b) may be explained by a summation of asynchronous electric charge separation, produced by the viscoelastic properties of mechanically deformed bone. Differences in initial voltages, also, may be accounted for in this manner, as well as through quantitative differences in time and energy inputs by PEMFs and mechanical stress.*

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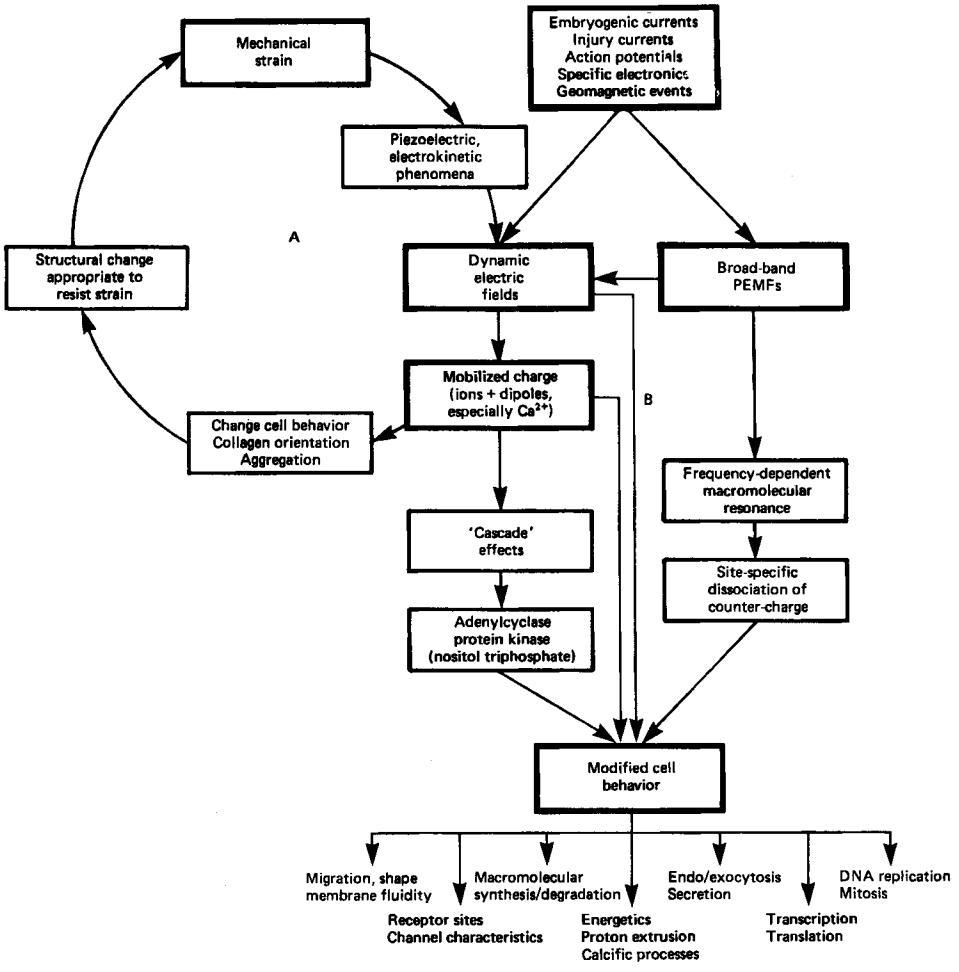

Fig. 3. *Diagram of hypothesized, unified pathways relating various electrical, magnetic and mechanical influences on cell function. Cycle A represents a feedback pathway for Wolff's law, which links bone form and function. This cycle may also apply to other tissues, such as connective tissues and plants in which the structural fabrics contain long-chain, charged biopolymers (e.g. collagen, proteoglycan, cellulose and chitin). 'B' pathways do not, necessarily, involve feedback. The left-hand vertical and the central pathways concern mainly ultra- and extremely low-frequency events and the right-hand pathways represent higher frequency events. The left-hand low-frequency pathways may be permissive for action of higher frequency content, through electrical biasing.*

all can be categorized as 'broad-band'. Depending upon the rise and fall times, the specific shape, the amplitude and the rate of repetition, single pulses or pulse burst quasi-rectangular waveforms contain frequencies ranging from ≈ D.C. to ≈ 10 MHz (Fig. 5).

Although each of the two quasi-rectangular pulse patterns has its own individual frequency-content profile, there are common ranges in both.[41] Other PEMFs, characterized by quasi-triangular waveforms, also contain frequencies which overlap. Gaussian white noise, centered on the frequency range found in quasi-rectangular and quasi-triangular pulses, applied to patients with fresh fractures, increases technetium polyphosphate incorporation significantly.[42]

Whilst effectiveness of different waveforms may derive from common physical features, rigorous assessment of relative efficacy has yet to be made in a non-union model. None the less, alterations in pulse specifications can selectively modify calcification during repair.[43] It is conceivable that the situation, ultimately, may prove analogous to the relationship between penicillin G and ampicillin. These somewhat similar members of the antibiotic family exert slightly different antibacterial actions. The argument which cites lack of pulse specificity as a rationale for questioning PEMF efficacy in non-unions fails to consider common energy characteristics, which place PEMFs in a family.

Windows

How specific are the actions of PEMFs? Do changes in energy patterns result in different effects? Several examples have been cited already. A burst elevates calcium content, whilst a single pulse lowers it.[15] Polytene chromosomes, exposed to two different PEMF patterns, respond quite differently. Single pulses trigger an 11-fold increase in mRNA within 15 minutes, but bursts produce control values.[44] Selected pulse modifications appear to activate gene-specific transcription and translation.[45] Embryonic development (e.g. DNA and dry weight of bones) of the chick is influenced in different ways by different pulse patterns.[46] Single pulses and bursts affect collagen and proteoglycan synthesis, selectively, depending on whether the target tissue is bone or cartilage.[17]

Dominant sine wave frequencies have been identified in Fourier-transformed broad-band pulses. By substituting one or more of these sine patterns for a PEMF, contributions of certain individual frequencies have been identified.[17] They are postulated to operate within normal control systems and may involve balances between synthesis and degradation.[23, 27] Within a broad-band pulse, selected frequencies could affect both activities, depending upon the functional state of cells during PEMF exposure. For example, cultures in growth and confluent phases respond differently.[27] Length of exposure to PEMFs, also, appears to be important in certain systems. PEMF-triggered transcription is significantly less after 45 minutes than after 15 minutes.[44]

Windows or thresholds for different biological effects of time-varying fields were suspected to exist over a decade ago.[31, 34, 47] PEMF windows appear to encompass more factors than dose response alone. Frequency, amplitude and timing, singly or in combination, appear to be involved in many of the experimental studies cited above. Windows appear, also, to determine calcium release by brain and other in ELF, sine-modulated 50 and 450 MHz carrier-wave fields.[48, 49]

Unfortunately, few publications contain sufficient details to permit window duplication in *non-sinusoidal* field experiments. Unless standardized PEMF equipment is used, pulse patterns should be specified *in air* or *in target tissues, using a universally acceptable dosimetric technique*. Dosimeters should have a good frequency response from D.C. to at least 10 MHz. Even detailed descriptions of circuits are insufficient; significant variations in fields can arise from different coil designs and circuit components (e.g. capacitors, resistors, solid-state devices). Current delivered to the coil(s) by different units constructed from the same circuit diagram can vary in subtle details of frequency content unless constructed with rigorous control and 'tuned' to desired

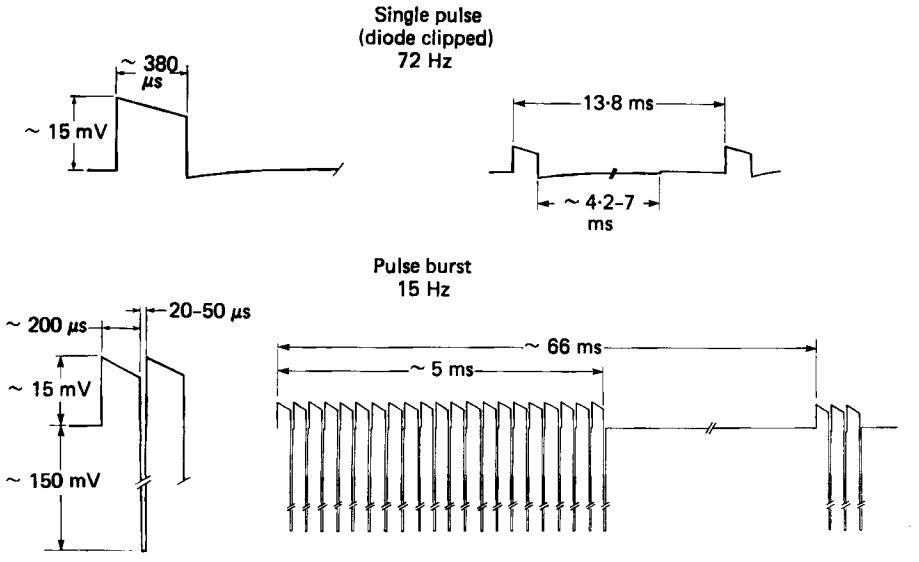

Fig. 4a. *Diagram of electric field patterns in clinical use,* as measured with a standardized coil probe dosimeter *placed in air at the same relative positive as the tissue to be treated. The rate of change in the magnetic field (see Fig. 4b, top) associated with the repetitive single pulse is ≈ 9·54 Teslas/second (T/s) during field expansion and ≈ 0·69 T/s during field collapse. For the repetitive pulse burst, the rates are ≈ 8·5 T/s and ≈ 43 T/s, respectively. Details of individual pulses are given at the left. Variations of single quasi-rectangular (top), generally, are used for avascular necrosis, osteoporosis, congenital pseudarthrosis, chronic refractory tendinitis and pathologic entities characterized by excess bone destruction. Pulse bursts have been used routinely, thus far, to treat adult non-unions in this country. Other investigators have used, successfully, PEMF waveforms with quasi-triangular shapes (similar in shape to the bottom trace in Fig. 2).*

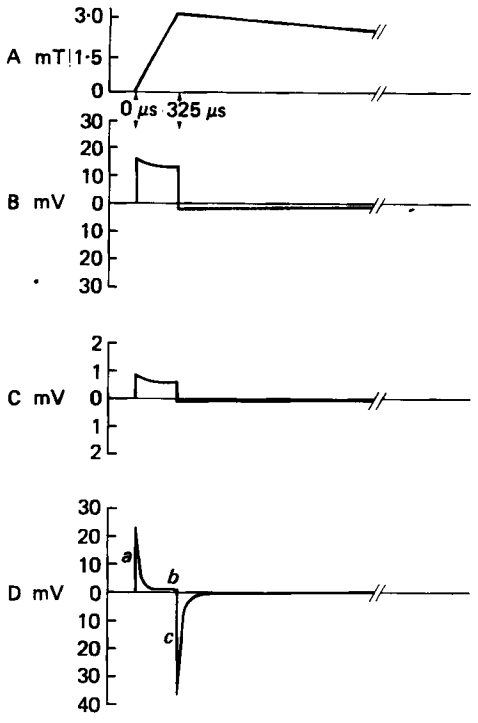

Fig. 4b. *Diagram of representative waveforms of the single-pulse type as detected by different measurement techniques.*

(A) *Depicts the magnetic field in air as measured with a Hall probe. The peak field strength is 31 gauss (3·1 mT), which is reached rapidly and then falls slowly (see Fig. 4a for details of rate of change).*

(B) *Electric field pattern in air, as detected with a standard coil probe dosimeter positioned at the target tissue level.*

(C) *Drawing of voltage recorded in the same magnetic field by a pair of matched, shorted Ag/AgCl electrodes, placed in the central axis of a Helmholtz coil pair.* **Note change of scale.**

(D) *Voltage waveform recorded from cortical bone in response to the time-varying magnetic field in* (A). *Two pairs of Ag/AgCl electrodes (one pair shorted as reference, the other recording in a* differential input mode) *are placed in the central axis of the magnetic field, with the tissue sample out of the central axis and contacted by the recording pair of electrodes. Note* $a+b \cong c$. *Waveforms would have different amplitudes and shapes, if samples of cartilage, tendon, nerve, muscle, or kidney, etc., were substituted for cortical bone.*

tolerances. Once in use, monitoring of signals is necessary because circuit components 'age' with use.

Athermal Nature of PEMF Action

Before pertinent physical principles are discussed, the issue of heating should be considered. The total energy input from PEMFs, with burst-type quasi-rectangular shapes, is 10^{-10} W/mm³ of tissue. At nominal impedances, the temperature change is < 0·001 °C. Indeed, tissue culture experiments, with temperature carefully monitored, detect negligible thermal changes from PEMF exposure.[23, 24, 25] If heating occurs, depending on pulse characteristics, it derives from easily measured and controlled ambient changes caused by coils, not from energy dissipation in cells or tissues. Additional evidence of athermal action stems from recent studies with *Sciara coprophila* chromosomes, in which heat-shock responses are well characterized. PEMFs produce quite different patterns of transcription of mRNA and of translation.[45] If fields, *other than PEMFs*, are sufficiently high in frequency and amplitude, thermal effects can occur. When they do, it is difficult to separate electrical and thermal contributions to results. For example, brief application of pulsed 27·8 MHz fields elevates body temperature by 2 °C during neural regeneration experiments.[50]

Characteristics of Inductively Coupled Fields

Physical parameters of a PEMF investigation must be controlled and matched to an appropriate biological model. Lack of reproducibility from study to study and laboratory to laboratory can be attributed, in the main, to lack of familiarity with critically important field characteristics. In any PEMF, both magnetic (B) and electric (E) field components exist. Inductive coupling of a time-varying $\bar{B}$ field with electrically conductive elements in biological systems (mainly ionic) results in E-driven pulsed currents within the organism. Although the B component may prove to affect certain cell functions, the E component appears to be a major factor in PEMF results, to date. In accord with Maxwell's equations $\nabla \times E = -\frac{1}{c}dB/dt$, both B magnitude and its rate of change (i.e. rise and fall times) determine the E value. This value, also, reflects position in the B field, being zero in the center axis of a Helmholtz field and increasing by $1/2r$, peripherally. Furthermore, E has a vectoral quality which imposes constraints on position *and* orientation of the target if reproducibility is to be achieved. Thus, when a biological system is exposed to a given pulse it may respond in one manner if parallel to B, another at right angles to B, another in the central axis of B and yet another if peripherically located. When non-uniform fields are employed, complexity is increased.

Any experiment designed to test a given PEMF, also, may be influenced by extraneous weak time-varying geomagnetic and man-made fields. Dubrov called attention to work demonstrating that organisms in *magnetically* shielded environments display altered metabolic patterns.[51] More recently, one rate of Ca^{2+} efflux from brain tissue occurred when the Earth's time-varying magnetic field (measured in gammas, i.e. 10^{-9} Teslas) was nulled and another when it was not.[48] Similarly, RNA synthesis

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was affected by PEMFs emanating from equipment several meters distant to an unshielded incubator in which 'control' studies were being conducted.[45] *In vitro* studies in which control dishes and active coils are in the same incubator should be carefully scrutinized. This is particularly true if controls are placed in inactive coils which function as an antenna.

Furthermore, when *unshielded* incubators house control cultures, stray fields should be monitored. A recent study of weak sinusoidal field effects on DNA synthesis (as judged by [^{3}H]thymidine incorporation) contained no detail on this point, nor on the cell counts which were necessary to judge the origin of the increased isotope uptake (e.g. nuclear or mitochondrial).[52] Stray fields, also, must be considered in animal and human investigations when contralateral anatomic sites serve as controls for regions being treated with active coils.[53]

PEMFs – Pro or Con? II

During this presentation, two of the four arguments advanced by PEMF antagonists were considered. First, at least one pertinent mechanism of action for non-unions is defined. Second, PEMF waveforms used for non-unions are broad-band and are members of a family, sharing frequencies. The third argument invokes three negative animal studies to refute PEMF validity in treating non-unions.[37, 54, 55] Each of the three reports is based on fresh bony injuries which have biologic features quite different from a non-union. Furthermore, each employed PEMFs with energies which do not conform to those used clinically and the contralateral (i.e. control) limb was exposed to a lower-amplitude signal which, none the less, may well have been biologically active. A recent tissue culture study involving PEMFs, also, was stated not to support their use in non-unions.[19] It addressed *total body calcium metabolism* – an issue not directly pertinent to local calcification processes in fibrocartilage. None the less, collagen synthesis, expressed as a function of DNA, was slightly elevated in experimental cultures, whilst details of control culture exposure were not given.

The fourth argument used to refute PEMF effectiveness in non-unions is based on one 'double-blind' study of very small groups[56] of unmatched patients.[57, 58] It may well have been a dose-response study in fact. Patients *in the control group* were exposed to weak

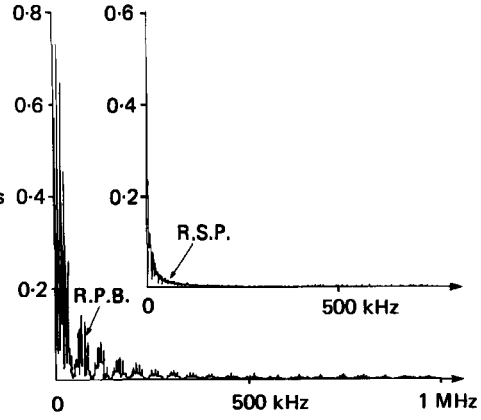

Fig. 5. *Diagram of a discrete Fourier transform of the single pulse (R.S.P.) and pulse burst (R.P.B.), as recorded with a coil probe dosimeter. Note different frequency, amplitude and harmonic distributions for the two pulses which extend out to 10 MHz.*

time-varying magnetic fields by virtue of connections to an internal load in the putative dummy machines. Placebos should not contain a small amount of the active factor! Hopefully, broader interdisciplinary grasp of physical and biological variables will foster greater care in design *and* interpretation of future experiments. Failure to increase precision will only retard progress of this new therapeutic tool, which has a broad potential to improve patient care in many, if not all, medical specialties.

Expanding Clinical Indications for PEMFs

Progress has been made already in expanding the use of PEMFs outside the non-union arena, using pertinent biologic responses to selected PEMFs, as demonstrated in the laboratory or clinic. Avascular necrosis (osteonecrosis) of the adult hip and Legg–Perthes disease in children have been treated successfully.[59, 60] The biological activity of PEMFs and their clinical usefulness in therapeutically recalcitrant tendinitis of the shoulder have been proven in a double-blind study with $P < 0{\cdot}005$.[61]

A pilot study of patients with postmenopausal and senile osteoporosis and laboratory observations appear to justify double-blind studies of PEMFs' ability to restore bone mass.[62, 63] Selected PEMFs improve the rate of peripheral nerve regeneration and function,[64, 65] promote growth of new small blood vessels (angiogenesis)[31] and modify the local action of certain hormones.[66] These laboratory observations await clinical evaluation in patients with severed nerves and neuropathies, and with marginal circulation in skin grafts and the myocardium.

Unlike investigations with new drugs, these clinical endeavors will not impose known risks. PEMFs have proven to be remarkably safe in broad human application over the past 10 years. No toxicologic or teratologic effects have been demonstrated in extensive *in vitro* and *in vivo* safety testing. This is not to say that *all* time-varying magnetic fields share the same record of safety. The energetics of other parts of the electromagnetic spectrum, for example radio frequency (R.F.), microwave and X-ray, can be harmful. Even at the lower end of this spectrum, certain frequency combinations may produce deleterious effects in some biological systems. Recent observations of possible human teratologic action of electric blankets and the impact of other types of time-varying fields on chick embryo development dictate the need for due diligence.[67, 68, 69] Certainly, a clearer definition of field parameters by all concerned will help dispel some of the 'hysteria' now developing in a near vacuum of precise knowledge.[70] With care and a bit of luck, the next decades can witness an era of electrobiological achievement which may rival that of molecular biology.

REFERENCES

The standard editorial policy of *BioEssays* is to limit the number of literature citations to 30. However, exceptions are occasionally made for articles that deal with controversial issues. The subject covered by Dr Bassett is in this category. For this reason, a significantly longer than usual list of references has been assembled, to permit readers to refer to the original publications rather than reviews, the better to form their own opinions about the state of the work.

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PLACES

Instituto de Investigaciones Bioquimicas 'Fundación Campomar': The new laboratories of Luis F. Leloir

Clara R. Krisman-Fischman and W. J. Whelan

Luis Federico Leloir, the 1970 Nobel Laureate in Chemistry, distinguished for his researches in carbohydrate metabolism, notably for the discovery of the nucleoside diphosphate sugars, celebrated his 80th birthday on 6 September 1986. Typical of his shyness and his wish to avoid the public eye, he was nowhere to be found when the day came. His career, its fortunes and vicissitudes, epitomizes the struggle of basic biological scientists to gain a secure footing in his native Argentina and demonstrates how a wealth of talent can emerge under the patronage of exemplary, steadfast, caring and unselfish leadership.

A pupil of Bernardo Houssay, himself a Nobel Laureate in Physiology or Medicine, sharing the Prize in 1947 with Carl and Gerty Cori, Leloir, working under conditions that would have dismayed and discouraged most others, has been the inspiration and benevolent 'Dire' to generations of Argentinian biochemists and the lifeline without which many careers would have foundered. His scientific achievements have been documented in numerous places, sometimes by himself, in his self-effacing way, when his shyness and humility come through. This account, in our 'Places' series, uses the occasion of his milestone birthday to describe the new laboratories where he is the President of the administrative Council.

Returning from sojourns in the laboratories of Frederick Gowland Hopkins in Cambridge and Carl Cori in St Louis, to an Argentina that in 1943 had experienced a revolution and in 1946 was to be ruled by General Peron, Leloir was confronted by a situation in which university professors were forced to resign and go into exile. Others, like Houssay and Leloir, decided, with help from the private sector, to remain, and in doing so created first-rate institutes which gained international renown.

Then in 1947, Don Jaime Campomar, a prominent textile manufacturer, provided funds for the creation of the 'Instituto de Investigaciones Bioquimicas' which, in memory of his parents, Juan and Maria Scasso de Campomar, was named the 'Fundación Campomar'. Its statutes define the