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Designed Electromagnetic Pulsed Therapy: Clinical Applications

GLEN A. GORDON*

Electromagnetic Research and Education Foundation (EMREF), Port Gamble, Washington

First reduced to science by Maxwell in 1865, electromagnetic technology as therapy received little interest from basic scientists or clinicians until the 1980s. It now promises applications that include mitigation of inflammation (electrochemistry) and stimulation of classes of genes following onset of illness and injury (electrogenomics). The use of electromagnetism to stop inflammation and restore tissue seems a logical phenomenology, that is, stop the inflammation, then upregulate classes of restorative gene loci to initiate healing. Studies in the fields of MRI and NMR have aided the understanding of cell response to low energy EMF inputs via electromagnetically responsive elements. Understanding protein iterations, that is, how they process information to direct energy, we can maximize technology to aid restorative intervention, a promising step forward over current paradigms of therapy.

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As our solar system formed, including earth, the Schumann resonances and elements responsive to electromagnetic perturbation also evolved. Such elements included metals, sulfur, oxygen, and nitrogen; this included all elements except noble gases. Self-assembled proteins incorporated these simpler compounds and elements as living systems evolved. The key to electromagnetic field (EMF) -driven biologic rhythms and responsiveness was thus designed at the formative stages of life on the planet.

Acronyms (see addendum) abound from DC, pulsed electromagnetic field (PEMF), time varying electromagnetic field (TVEMF) to pulsed electric stimulation (PES) and pulsed electromagnetic therapy (PEMT). Designed electromagnetic pulsed therapy (DEPTH) is chosen to reflect the penetration we see clinically, the need to specifically design the pulse for maximal bio-efficacy, and the general understanding that pulsed fields demonstrate increased efficacy over static designs. This review hopes to address how these extremely weak fields exert such prominent effects at depth, based upon treating 20,000 acute and chronic trauma cases. The basic science literature (Gordon, 2007) supports a direct EMF interaction in cell function via protein iteration of phonon acoustical signals. Phonons are produced by electromagnetically responsive elements, located within the protein matrix, acting as oscillators in response to this universal force.

The similar responses to extrinsic electromagnetic fields in living systems from Planaria through man strongly suggests an electromagnetic universe (Ikehara et al., 2005) in which mechanisms involving EMF perturbations evolved to stop inflammation first, and then to initiate healing. It has been this investigator's experience that, given a proper pre-set of oxidative stress, and an appropriately designed electromagnetic pulse, both can occur very rapidly in comparison to traditional therapies and slower electric or electromagnetic technologies, a conclusion corroborated in the NASA study by Dennis and Goodwin (2003), our own studies (submitted), and noted by Eichwald and Walleczek (1996b).

Electromagnetic fields are studied extensively as electro-pollutants, for example, cell phones, as well as a therapy, under the general heading of PEMF technology. Electro-pollutants are manifestly different in field strength and frequency in comparison to therapeutic applications, yet the USFDA (2002) considers them the same and lists therapeutic devices as "potentially dangerous" by association. World Health Organization convened scientists from around the world that found field strengths less than 20,000 gauss, that is low field MRI, free of adverse side effects (Repacholi and Greenbaum, 1999). Pulsed therapeutic fields are usually more effective if less than 30 gauss (see Curie's Law and dipole saturation), and frequencies are commonly less than 100 Hz, below which they are referred to as extremely low frequency (ELF). Cell phones are several magnitudes of order larger in both considerations.

DEPTH employs up to the microwave sector of the electromagnetic spectrum for maximum tissue penetration in therapeutic field strengths as small as 50 milligauss. MRI, a diagnostic EM technology, employs static fields from 15,000 to 50,000 gauss coupled to radiowaves for much the same reason, that is, tissue penetration. In terms of molecular effects, concern might be expressed for repetitive Transcranial Magnetic Stimulation (rTMS), an EM treatment for mental illness employing extremely low frequencies (ELF) combined with field strengths of several thousand gauss.

Abbreviations: DC, a static electromagnetic field; EMF, electromagnetic field; PEMF, pulsed electromagnetic field; TVEMF, time varying electromagnetic field; PES, pulsed electric stimulation; PEMT, pulsed electromagnetic therapy; DEPTH, designed electromagnetic pulsed therapy; MRI, magnetic resonance imaging; NMR, nuclear magnetic resonance; TVE, time varying equilibrium (chemical only).

Rise Time: The speed with which a pulse goes from zero to peak power (dB/dt), shown to include the scope of harmonics possible within the pulse by the Fourier analysis.

Conformational Adaptive Response: Pre-programmed changes in protein structure that allow activation or completion of homeostatic reactions. Phonon energy processed by proteins that is developed by the interaction of EM fields and paramagnetic species are increasingly proposed to control this activity.

Iteration: A computational process in which a series of operations are repeated until a condition is met

Tesla/Gauss measure: 1 Tesla equals 10,000 gauss

Time Varying Equilibrium: Chemical- the state in which the concentrations of the reactants and products have no net change over time.

*Correspondence to: Glen A. Gordon, MD, FACSM, P.O. Box 124, Port Gamble, WA 98364. E-mail: drgordon@em-probe.com

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In terms of quenching inflammation, the appreciation for constitutive versus transcriptive injury intervention is markedly heightened by the healing rates one sees with treatment immediately after injury. Local trauma is appreciated for its insignificance when one quickly restores the time varying equilibrium (TVE) between free radicals and native antioxidants to stop inflammatory cascade progression, chemical degradation, and growing disability.

History

Described as an "irregular science" and purged from US medical curricula following publication of the Flexner Report in 1910, the medical science community here lagged behind other nations in attempting to understand and utilize this vital, universal force through the 1960s. Upon entering the field to study nanosecond pulsed electromagnetic field (nPEMF) interaction in 1980, the literature was heavily weighted by USSR and Central European investigators who reported widespread use of sine wave and millisecond pulsed technology in injury and illness, but generally lacked scientific rigor by Western standards.

US track coaches reported impressive injury restoration among Eastern bloc athletes at international competitions, allegedly due to "some device" used, and 20 US cardiologists witnessed the use of PEMF technology in a 1972 State Department hosted trip to the USSR's Myasnikov Institute. One attendee noted (personal communication) their cases demonstrated "impressive" results in the treatment of ischemic heart disease, myocarditis, and congestive heart failure that was not pursued here "because it wasn't a priority."

Maxwell's concepts of electromagnetism were expanded into a century of Nobel prize work centered around a realization that electromagnetism controlled "all chemical reactions, including life itself" (Hawkings, 1996). Insisting "there is no scientific evidence to support any of the claims made for these devices" (Basford, 2001; American Cancer Society, 2005) is a matter of what is chosen for review or designed into the study method. Two Danish engineers published a paper several years ago, since lost to this author's archives, which compared successful studies to non-successful outcomes across three bell distributions of field strength, frequency, and exposure time. They reported none of the latter fit within S2 for all three distributions of the former. To cite all uses as, "of no scientific evidence for any claims" disserves reports of established investigators (Aarons, 1998; Johnson et al., 2004; Liboff, 2004), and ignores what one of our century's most brilliant minds, and a Nobel laureate, already accepts (Hawkings, 1996).

Aarons (1998) speaking at a peer reviewed symposium on Tissue Healing for NIEHS (NIH) noted, "there is robust and credible evidence that pulsed electromagnetic field technology is effective in healing wounds, nerve injury, fractures . . ." That symposium gathered, and critiqued, an exhaustive group of protocols involving sine wave and millisecond technology to 1998. Upwards of 2000 abstracts on DEPTH are cited in the National Library of Medicine's PubMed website under pulsed electromagnetic, PEMF, or other acronyms. These articles report on older technology of sine wave and millisecond designs, yet report efficacy at a statistically significant level. Beginning in the late 1990s, many began to report enzyme and gene upregulation, of late referred to as "electrogenomics."

Standardization

This technology is plagued by a lack of standardization, especially in clinical applications. Dennis and Goodwin (2003) in the NASA study were the first to differentiate pulse design characteristics as to efficacy in upregulating classes of genes associated with tissue restoration. We are in preparation on a comparison between nanosecond (EMpulse, EM-PROBE Technologies) and millisecond technologies that corroborate the NASA findings in an *in vivo* model with HSP 70 as the end point. Both studies indicate rise time (dB/dt) as a critical determinant of efficacy, a characteristic not previously cited in a literature dominated by field strength, frequency, and duration. We had long suspected rise time was critical due to the harmonic content the Fourier analysis predicts for vertical rise times.

As DEPTH literature grew from almost exclusively Soviet and Eastern Europe to largely English, and now a vigorously growing Chinese mainland output, little movement toward standardization has evolved; that continued oversight will justify criticism of the entire technology so long as it continues.

Electromolecular medicine

Electromolecular medicine is the growing use of DEPTH in living tissues to induce electrical currents that:

1. stabilize cytosolic [Ca++]
2. restore equilibrium in ROS (free radical)/antioxidant chemistry
3. upregulate classes of protective and restorative gene loci
4. downregulate dysregulatory and apoptotic gene loci.

Calcium—cytosolic & calcium channel influence. The cellular response to homeostatic challenge is the release of calcium from intracellular stores that prompts mitochondria to produce free radicals and heightens DNA response (Schild and Reiser, 2005), a function reported to be substantially controlled with DEPTH (Ikehara et al., 2005), a first order effect of this technology in preventing the onset of inflammatory dynamics.

The impact of EMF on calcium channel protein conformational adaptive response is repeatedly cited (Lieb et al., 1980; McLeod et al., 1992; Baureus Koch et al., 2003; Rosen, 2003) since the mid-late 1980s.

Stabilized free radical chemistry. Paramagnetic species increase their reactive state with compatible compounds in an electromagnetic field by being drawn to the field and oriented in it (Zumdahl, 1992). Although weaker than ferromagnetic attraction, the contribution of molecular alignment is suggested in the Arrhenius equation (Zumdahl, 1992).

Svante Arrhenius became the father of modern rate reaction chemistry in 1885 when he demonstrated concentration, temperature, and molecular alignment contributed to rate reactions (Zumdahl, 1992). Since oxygen-based free radicals and antioxidants containing transitional metals are both paramagnetic species they are attracted to, and undergo dipole alignment in a magnetic field (Zumdahl, 1992) to reflect their positive and negative charge states. In addition to enhancing the conformational adaptive response in protein antioxidants, these fields also enhance molecular alignment, proposed here to be a next generation evolution of the Arrhenius equation. When taken together, they may enhance antioxidant efficacy up to a hundredfold (Eichwald and Walleczek, 1996a).

The importance of being able to upregulate antioxidant efficacy immediately as opposed to waiting for natural transcription to restore that equilibrium can be a matter of life and death. The time delay needed to establish a time varying equilibrium between free radicals and antioxidants in the secretory or constitutive phase of injury, that is, the first seconds to minutes, determines whether there is activation of the entire inflammatory cascade including cytokine release (18). Applied immediately, the ability to enhance antioxidant efficacy can restore the imbalance that eventually leads to stunning and

cell death (Guzik et al., 2003), and the death of the entire organism if unabated. Awaiting DNA/RNA transcriptive activity to restore this balance is several hours, and may be an eternity away. Timing is critical to prevent chemical degradation that immeasurably contributes to disability and pain, for example, ankle sprains that degrade from active ambulation the night of injury to being incapable of supporting weight the next morning. Late application after 12–24 h is helpful in our experience, but not nearly as effective in reducing pain and restoring function in local motion segment or soft tissue injury.

Pennington's double blind study (Pennington et al., 1993) among active duty military personnel treated 50 grade 1 and grade 2 ankle sprains with one 30 min post-injury DEPTH intervention and reported a statistically significant difference in outcome causing him to conclude, "this technology could significantly reduce time loss in active duty military personnel" experiencing this common injury. The result was clear, but the device unwieldy and expensive. This is no longer an issue with lightweight contemporary nanosecond technology, which is also more bio-effective.

Once inflammation is held in abeyance, gene upregulation and healing can begin, up to four times more efficiently than any other electric or electromagnetic technology (Dennis and Goodwin, 2003). In this NASA study, but unreported, were 300–400% increases in mitochondrial densities after 10–12 days treatment (personal communication, Goodwin, 2005) in appropriate oxidative stress pre-sets in nearly all tissues reviewed.

If DEPTH intervention in a timely manner can quench escalating concentrations of free radicals that degrade organs and tissues to levels of stunning and death, it may find application in intermediate and massive trauma. In Iraq, the number two cause of death among injured warfighters in the first hours is "the lethal triad." Symptoms of acidosis, vascular instability, hypothermia, and coagulopathy are natural outcomes of free radical chemistry, and call for prioritizing the mitigation of that imbalance versus treating symptoms. DEPTH's prominent pain relief, cytoprotective ability, and free radical/antioxidant equilibrium restoration may become a credible scientific treatment for this "triad," a non-invasive, immediately available, safe intervention.

Enthusiastic cardiopulmonary resuscitation that results in, "he coded just when we thought we had him," reflects impossible concentrations of free radicals being returned to systemic circulation without adequate restoration of antioxidant capacity—perhaps another next generation intervention in appropriate situations.

Upregulate classes of growth and restoration genes. Her group recognized as established EMF investigators in gene upregulation modeling (Lin et al., 2001; Blank and Goodman, 2004), George et al. (submitted), in collaboration with cardiologists and cardiovascular surgeons at Columbia University reported the upregulation of HSP 70, and dramatically enhanced survival in a lethal challenge protocol calling for PEMF application before occlusion of the left anterior descending coronary artery. The mortality was 80% in the sham group and 20% in the treated group after one 30-min pre-treatment. Goodman cites the cytoprotective role of HSP 70 in ischemia–reperfusion injury, and suggests (personal communication) similar cytoprotection might be expected in stabilizing warfighters against lethal challenge if applied before going into battle and re-utilized if injured, all highly possible with modern technology. It is this author's belief HSP 70 is just a part of a cluster of cytoprotective and restorative dynamics EMFs set into play when tissue is oxidatively compromised.

Recently, Goodman and this author verified that faster rise time (dB/dt) resulted in more rapid onset and several fold increase in a standard HSP 70 model, over technology she had studied for 30 years (Goodman and Gordon, submitted). In seeing the difference in efficacy for the first time, she, an established sine wave investigator, noted, "I wouldn't have believed it if I hadn't seen it."

Other studies demonstrate efficacy in focal cerebral ischemia (Grant et al., 1994) and spinal cord injury (Crowe et al., 2003), which is not the first to demonstrate efficacy in that injury. Johnston of Paralyzed Veterans of America reported on Polish use in humans with good results (PVA newsletter, 2005). Gene upregulation to statistically significant degrees is widely reported in peer reviewed rigorous studies including nerve injury (Longo et al., 1999), bone osteotomies (Ibiwoye et al., 2004), graft survival (Tepper et al., 2004; Weber et al., 2004), and osteoporosis (Chang and Chang, 2003).

Downregulate dysregulatory genes. In the NASA study (Dennis and Goodwin, 2003) some 13,000 gene loci responses to square wave with rapid dB/dt pulse characteristics were studied with two software programs at an $n = 96$. It found that 3,000 loci were upregulated that represented classes of restorative genes, 2,000 were downregulated representing dysregulatory loci, and 8,000 loci were unaffected. The latter were reported as "house-keeping" loci and "other closely conserved sites." This also seems a logical phenomenology among living systems to achieve homeostasis; this knowledge may pose interesting possibilities when cancer mitigation becomes part of this technology.

Discussion

Blank and Goodman's work (2004), Aarons (1998) NIEHS symposium, and the Dennis and Goodwin (2003) NASA study are primers for interested reviewers. The NASA study is an in vitro study of metabolic effects and gene upregulation in human neuronal tissue, while the former considers tissue restoration in preclinical or clinical protocols.

It remains, and was clearly demonstrated in the 2003 NASA study, and our own (Gordon and Goodman, in preparation), that effect and efficacy are two very different end points, which is difficult to introduce into the established PEMF community, whether investigative or entrepreneurial.

Following Maxwell's description of electromagnetism in 1865, scientists expanded it to usher in "The New Era of Science" as the 20th century dawned. Pauling's Nobel work identified atoms and molecules from their EM profiles (see NobelPrize.org), and Stephen Hawkings clearly states electromagnetism is, "the basis for life itself" (Hawkings, 1996). It behooves us to expand upon such assessments, as has the mainland Chinese research community, which recently noted "EMF interaction in tissue restoration is a matter of national priority in biophysics" (Guan et al., 2000).

If Schumann resonances generate energy from atoms and small molecules via dipole forces, which as a part of Pierre Curie's law has been experimentally verified (Halliday et al., 1993), it seems we can improve that interaction with this side effect free technology (Repacholi and Greenbaum, 1999) to provide safe, new interventions superceding current paradigms as others have predicted (Johnson et al., 2004; Liboff 2004). Technologically driven as we are, it is inexplicable that we remain with such deadly paradigms as drugs and surgery, when a safe, non-invasive technology that may replace them awaits our serious interest.

The demonstration that EM forces control Ca++ channel activity, gene upregulation, and free radical activation cycles is critical to evolving the next level of therapeutic intervention. We cannot continue to ignore a universal force, particularly one that controls all chemical reactions, all cellular events. It is suggested here, DEPTH technology can be an integral part of a safer, more bio-effective future; as Milton noted, "they also serve who only stand and wait."

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