chapter 27

Electromagnetic Stimulation for Wound Repair

Luther Kloth PT, MS, FAPTA, CWS, FACCWS
Arthur Pilla, PhD

Principles of Electromagnetic Radiation

In this chapter we will cover the use of exogenously applied, time-varying electromagnetic (EM) fields from the nonionizing radio frequency (RF) part of the EM spectrum, which, when placed near open or closed wounded soft tissues, will induce a healing electric field inside those tissues that is proportional to the rate of change of the magnetic field. In this context we will present the evidence for the use of nonthermal pulsed electromagnetic fields (PEMF), pulsed radio frequency energy (PRF), and low-level thermal PRF, which may also be referred to as pulsed shortwave diathermy (PSWD), as adjunctive treatments for patients with chronic wounds. Please note that continuous shortwave diathermy (CSWD) is also derived from the 27.12-MHz frequency, but because it generates vigorous tissue heating if tissues are well vascularized, it is generally not used for wound healing applications. Table 27.1 lists devices and their acronyms.

PEARL 27•1 It is important to emphasize here that all of these alternative wound healing interventions are derived from a primary continuous RF sinusoidal wave (27.12 MHz) called a "carrier," which can be modulated to produce nonthermal PEMF and PRF and mild thermal PSWD, each of which will be described later.

What Is Electromagnetic Radiation?

EM radiation is a type of energy that is created when electric charges are accelerated. When electric charges move, they produce waves of electric and magnetic energy in space. A familiar example is electric charges that move back and forth as alternating current emitted from a radio station tower (antenna) and that travel (broadcast) at the speed of light through space as RF radiation. These waves have a distinctive frequency and wavelength and can be reflected, refracted, and absorbed when they interact with matter.

What Is Frequency and How Does It Affect Tissues?

The frequency of EM radiation corresponds to the number of waves per second that cross a fixed point in space. EM waves are typically sine waves that cover a vast range of frequencies and corresponding wavelengths. Lower energy levels represented by the spectrum are produced by lower-frequency sine waves (eg, 60 Hz for electric power), whereas very high frequencies (10^{19} Hz) produce high-energy level gamma rays. RF radiation is the area or band of the EM spectrum in which most radio communication takes place and consists of propagating sine waves typically between 10 kilohertz (kHz) and 300 gigahertz (GHz) (1 kHz = 1×10^3 Hz; 1 GHz = 1×10^9 Hz.)[1] (Fig. 27.1) The electromagnetic spectrum also includes the familiar waves of visible light, infrared, and ultraviolet. Unlike the lower pulsed current frequencies used to excite nerve and muscle cell membranes,

Table 27•1 List of Devices and Their Acronyms

Acronym	Device/EM Energy
PEMF	Pulsed electromagnetic field
PRF	Pulsed radio frequency
PSWD	Pulsed shortwave diathermy
CSWD	Continuous shortwave diathermy

the higher RFs are not capable of depolarizing motor nerves or eliciting contractions from skeletal muscle because the duration of each cycle of alternating current in this frequency range is too short to cause migration of ions through cell membranes of nerve or muscle.[2] Another advantage of EM energy in the RF range is that, unlike photons produced by x-rays and sufficiently high frequencies (ionizing radiation) that have enough energy to eject electrons (ionize) from atoms or molecules, RF signals do not. When a cell's contents are ionized, very reactive compounds called *free radicals* are formed that can damage vital parts of the cell. Cells are equipped to deal with some free radicals, which can be produced by normal metabolism, but excessive ionizing radiation can overpower a cell's ability to control and repair the free radical damage and thus disrupt normal function. The damage from ionizing radiation that cannot be repaired accumulates over time in the cell, hindering or preventing mitosis and causing permanent tissue damage. Ionizing radiation may also directly damage DNA and RNA.[3] The ultraviolet wavelength of 100 nm and frequency 3×10^{15} Hz, is conventionally taken as the dividing line between ionizing and nonionizing radiation.[3] Energy from the RF part of the spectrum may or may not penetrate the skin. Regardless, RF energy is only a fraction of that required to produce ionization in tissue. Therefore, with RF energy, no mutations are induced nor does DNA single-strand uncoupling occur, such as that which results from ionizing x-ray radiation therapy used in cancer treatment.[3] However, as shown in Figure 27.1, RF waves that have appropriate dosage parameters are capable of producing thermal energy that may be used to therapeutically heat body tissues such as occurs with mild thermal level PSWD. Recall that all frequencies in the EM spectrum travel through a vacuum at the speed of light and that they consist of two components, an electric field and a magnetic field that transmit electric and magnetic energy (electromagnetic waves) through space. The magnetic component of the EM signal has a negligible physiological effect on the tissue target. The induced electric field can interact with electric charges, for example, ions, to produce the desired effect. It is fundamental that, for EM waves to have an effect on target tissues within the body, they must be absorbed by those tissues that contain cells and molecules. This fact is upheld by the law of Grotthus-Draper, which states that only radiation that is absorbed can produce chemical change. However, absorbed radiation does not necessarily cause a chemical reaction. Absorbed radiation may simply be converted into heat, or it may be reemitted as light of a different wavelength, which is the phenomenon called *fluorescence*. Thus, while waves from one part of the spectrum may be absorbed when they encounter an object, waves from other parts of the spectrum may either be reflected or pass through the object. Nonionizing RF waves delivered to the body for therapeutic purposes cause atoms and molecules to vibrate and rotate without ionization.

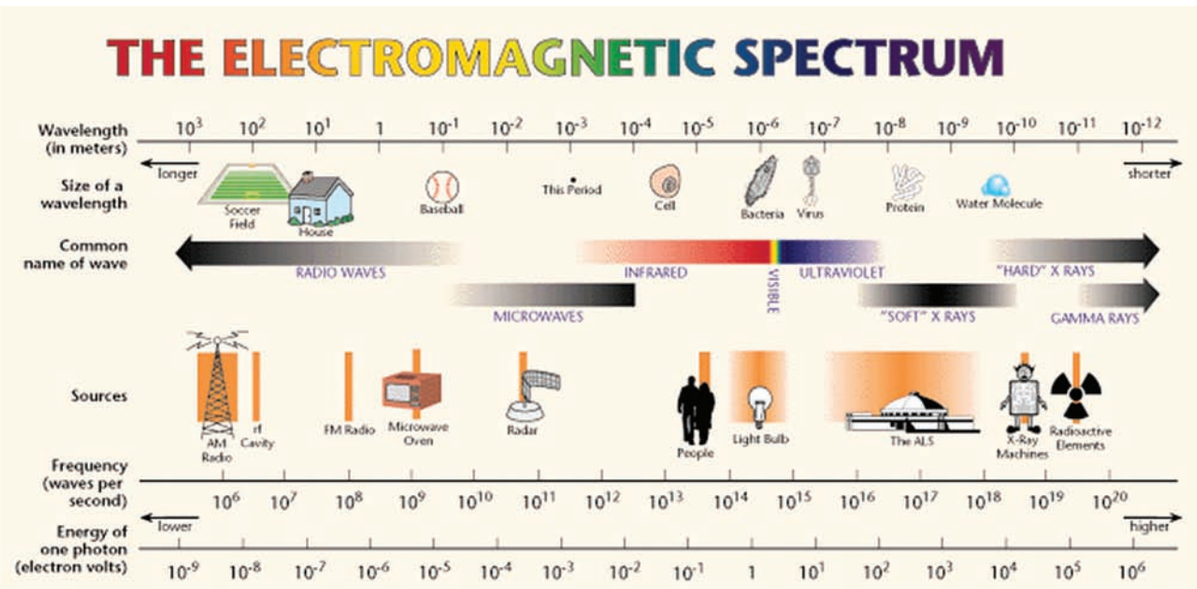


Figure 27•1 *Electromagnetic radiations showing the radio frequency part of the spectrum.* www.lbl.gov/MicroWorlds/ALSTool/EMSpec/EMSpec2.html

Energy from the RF field is transferred to tissue by increasing the vibrational and rotational energy of dipoles (primarily water) in the tissue.

PEARL 27•2 At the carrier frequency of interest (27.12 MHz), and in the near field, that is, with the tissue target placed next to the transmitting antenna (patient treatment coil applicator), the primary component of the EM signal is the electric field that produces the desired physiological thermal effect of heat or nonthermal cellular signaling.

PEARL 27•3 Thus, RF effects on cells and molecules are generally limited to nonthermal (PEMF and PRF) and low-level thermal (PSWD) through changes that occur secondary to increased kinetic activity rather than the direct breaking of chemical bonds.[3]

Because of the high demands for the use of various frequencies for communication, the Federal Communications Commission (FCC) has very carefully regulated what frequencies can be used in television and radio transmission, radar, and medical applications. In the past the FCC allowed the use of three different RF frequencies in the medical applications of PEMF, PRF, and PSWD. However, for practical electronic reasons, only the 27.12-MHz frequency is used in these devices in the United States.

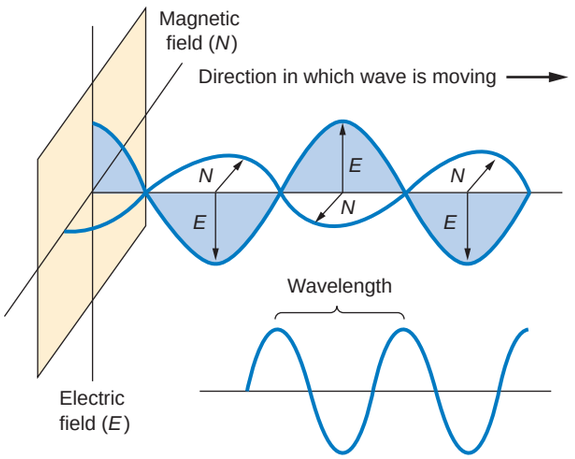
What Is Wavelength?

The time that elapses between successive peaks of a propagating RF sine wave is called the *period* of the wave. The distance traveled by EM waves in one period is the wavelength. (Fig. 27.2) EM wavelengths are inversely related to frequency and can range from one-billionth of a meter up to miles. All of these wavelengths do not pass through the body with equal ease, however; there is no simple relationship between wavelength and the ability of these EM waves to travel through the body almost unimpeded. This explains why you can listen to a radio when a person or a wall is between you and a broadcasting radio. Wavelengths of RF described above used for tissue healing and therapy lie between 3×10^5 and 3×10^{-3} meters. It is within this range that the wavelengths are found for devices used to deliver the PEMF, PRF, and PSWD signals previously mentioned.

PEARL 27•4 The wavelength that corresponds to the FCC-approved frequency of 27.12 MHz is 11 meters. This wavelength readily penetrates human skin and produces electric fields at a depth that is sufficient for most therapeutic uses.

Modulation of the Radio Frequency Carrier Wave

As previously mentioned, the RF carrier wave (27.12 MHz) is used to produce PEMF, PRF, and PSWD treatment signals. RF waves may be deli vered to the body either as continuous oscillations or by periodically interrupting the



Field and wavelength relationships in an electromagnetic wave.

Figure 27•2 *Magnetic and electric field components at right angles to each other and wavelength of an electromagnetic wave. (From: Yost MG: Nonionizing radiation questions and answers. In: Clemmensen J: Nonionizing Radiation: A Case for Federal Standards? San Francisco, San Francisco Press, 1993, p.2, with permission)*

continuous waves at regular intervals to produce pulses or bursts of RF energy. Continuous waves of RF are associated with increasing tissue temperature, first observed by Nagelschmidt in 1906.[4] RF devices that deliver continuous waves used for therapeutic heating are called continuous shortwave diathermy (CSWD) machines, and they are capable of producing high to moderate tissue heating effects (*diathermy* means to heat through) for adjunctive treatment of a variety of musculoskeletal conditions. (Table 27.2) RF devices that deliver pulses of RF waves are referred to as pulsed radio-frequency (PRF) and pulsed shortwave diathermy (PSWD) devices. PRF devices that have low average power output produce nonthermal effects on absorbing tissues, whereas PRF devices with high average power produce pulsed shortwave diathermy (PSWD), which has low heating effects. The pulsed version created from RF was originally reported to elicit a nonthermal biological effect by Ginsberg.[5] In contrast to PRF and PSWD devices, PEMF devices operate with a different modulated waveform frequency. Figure 27.3 shows waveforms for PRF and PSWD (bottom) and PEMF (top). Several differences in the characteristics of the two signals are evident. The most visible difference is pulse shape. The PRF signal is characterized by sequences of sine waves contained within rectanguar burst envelopes that typically have a duration of 65 µsec. Each pulse or burst envelope contains 1760 sine waves of the 27.12 MHz carrier RF. The frequency of this pulsed signal varies between 80 and 600 pulses per second, and the duty cycle is less than 4%. The PEMF pulse duration and the pulse frequency may vary between 1 and 100 msec and 1 and 100 pulses per second, respectively. Each of the three signals that have been briefly described will be addressed in greater detail below, in the order of PEMF, PRF, and PSWD.

Table 27•2 Characteristics and Effects of Radio Frequency Devices

Device	Signal/Frequency	Pulse Duration	Induced Voltage	Effects on Tissues/Cells
PEMF	Sinusoidal; 27.12 MHz; 1–00 pps	1–100 msec	mV/cm	Nonthermal and cellular; no nerve/muscle excitation
PRF	Sinusoidal; 27.12 MHz, 42 and 65 μsec	65 μsec	V/cm	Nonthermal, cellular, and circulatory; no nerve/muscle excitation
PSWD	Sinusoidal; 27.12 MHz; 3.9% duty cycle	95 μsec	V/cm	Mild heating, circulatory; no nerve/muscle excitation
CSWD	Sinusoidal; 27.12 MHz	Continuous	V/cm	Moderate to high heating; enhances collagen extensibility; no nerve/muscle excitation

PEMF, pulsed electromagnetic field; PRF, pulsed radio frequency; PSWD, pulsed shortwave diathermy; CSWD, continuous shortwave diathermy.
Modified with permission from Sussman, C: Induced electrical stimulation: Pulsed radio frequency and pulsed electromagnetic fields. In: Sussman C, Bates-Jensen B (eds): Wound Care: A Collaborative Practice Manual for Health Professionals, ed. 3. Philadelphia, Lippincott Williams & Wilkins, 2007, p 557.

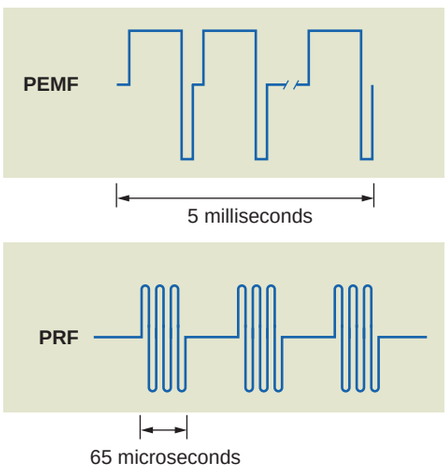


Figure 27•3 *Pulsed electromagnetic field (PEMF) signal was designed for bone growth stimulation, while the pulsed radiofrequency (PRF) signal is used primarily for treatment of soft tissue closed and open wounds. Note that the PEMF signal is asymmetrical with a 5-ms duration, while the PRF signal consists of 65-μsec rectangular pulse bursts. (From Markov MS, Pilla AA: Electromagnetic field stimulation of soft tissues: Pulsed radio frequency treatment of post-operative pain and edema. Wounds 1995; 7:144, with permission)*

PEARL 27•5 Depending on the average power delivered to the body by these pulses of RF energy, tissue temperature may or may not increase. Thus, PRF may have either thermal or nonthermal effects on tissues.

PEARL 27•6 Another main difference between the two signals is the magnitude of the induced voltage, which is in the V/cm range for PRF and mV/cm for PEMF.[6]

Pulsed Electromagnetic Fields for Bone Tissue Repair

The number of people who have received substantial clinical benefit from the exogenous application of pulsed electromagnetic fields (PEMF) is likely in the millions worldwide and increasing rapidly as new clinical indications emerge. PEMF and PRF therapies present as alternatives to many pharmacological treatments with no pharmacokinetic limitations and no known toxicity or side effects. This chapter reviews the scientific and clinical evidence that shows that PEMF and PRF can modulate molecular, cellular, and tissue function in a physiologically significant manner. In Chapter 26, enhanced soft tissue healing was reported to be augmented by the use of capacitively (conductively) coupled electric stimulators that have electrodes in direct contact with wound and periwound skin. Such technologies deliver waveforms similar to those produced by pulsed current devices currently cleared by the FDA for relief of acute and chronic pain.[6,7] Unlike the direct contact (conductive coupling) method described in Chapter 26, here emphasis will be on PEMF and PRF technologies that inductively couple the signal to the tissue target and have been reported to be clinically effective for healing bone fractures and soft tissue repair, respectively.

PEARL 27•7 PEMF devices produce physiologically effective voltage and current in tissue without the necessity of skin or wound tissue contact.[6,8] In addition, the Center for Medicare Services (CMS) determined in 2004 that PRF had produced sufficient positive clinical outcomes to permit reimbursement for its off-label use in the treatment of chronic wounds, such as pressure ulcers, diabetic leg and foot ulcers, as well as chronic wounds caused by arterial and venous insufficiency.[9]

Background—Pulsed Electromagnetic Field–Induced Osteogenesis

The development of modern PEMF therapeutics was stimulated by the clinical problems associated with nonunion and delayed union bone fractures. It started with an attempt to answer the fundamental orthopedic question of how bone adaptively and structurally responds to mechanical stresses by suggesting that an electric signal may be involved in the transduction of the mechanical (weight loading) signal to cellular activity. This led to the suggestion that superimposing an exogenous PEMF upon the endogenous bioelectric fields that occur following bone fracture may help in the treatment of difficult-to-heal fractures. The first animal studies employed microampere level direct currents (DC) delivered via implanted electrodes. Remarkably, this resulted in new bone formation, particularly around the cathode.[10] As these studies progressed, it became clear that the new bone growth resulted from the chemical changes around the electrodes caused by electrolysis.[11] The first therapeutic devices were based on these early animal studies and used implanted and semiinvasive electrodes that delivered DC to the fracture site.[12,13] This was followed by the development of clinically preferable, externally applied electromagnetic field technologies.[14-17] Subsequent studies concentrated on the direct effects of electromagnetic fields, leading to devices that provided a noninvasive, noncontact means of applying an electric signal to a cell or tissue target. Therapeutic uses of these technologies in orthopedic practice have led to clinical applications, approved by regulatory bodies worldwide, for treatment of recalcitrant fractures and spine fusion and recently for osteoarthritis of the knee.[18-27] Additional clinical indications for PEMF have been reported in double-blind studies for the treatment of avascular necrosis and tendinitis.[28-30]

At present, the clinical PEMF technologies in use for bone repair consist of DC electrodes implanted directly into the repair site or noninvasive capacitive or inductive coupling. *Direct current* is applied via one electrode (cathode) placed in the tissue target at the fracture site and the anode placed in soft tissue. DC currents of 5 to 100 μA are sufficient to stimulate osteogenesis.[18] The *capacitive* or *conductive coupling* (CC) technique uses external skin contact electrodes placed over a cast on opposite sides of the fracture site.[31] (Fig. 27.4) This requires openings in the cast or orthosis to allow skin access. Sinusoidal waves of 20 to 200 kHz are typically employed to induce 1 to 100 mV/cm electric fields in the repair site.[32] The *inductive coupling* (PEMF) technique induces a time-varying electric field at the recalcitrant fracture site by applying a time-varying magnetic field via one or two non-skin contact electric coils. The induced electric field parameters are determined by frequency characteristics of the applied magnetic field and the electrical properties of the tissue target.[15,16,33,34] Several waveform configurations have been shown to be physiologically effective. Peak time-varying magnetic fields of 0.1 to 20 gauss (G) that induce 1 to 150 mV/cm peak electric fields in a 3-cm diameter tissue target have been used.[15,35] The relationship between inductively coupled waveform characteristics and their ability to produce physiologically significant bioeffects will be considered below.

Figure 27•4 *PEMF induction of an electric field into a fracture site to promote healing. A non-surgical option for long bone and small bone nonunion and delayed union fractures, the device may be worn over a cast, orthopedic device, of clothing without lessening its effectiveness. (Physiostim™ Model 3202, permission of Orthofix Inc., McKinney, TX)*

Cellular Studies/Bone Repair

Cellular studies have addressed effects of PEMF on signal transduction pathways and growth factor synthesis. The clinical benefit to bone repair is enhanced production of growth factors upregulated as a result of the fracture trauma. The induced electric field thus acts as a triggering mechanism that modulates the normal process of molecular regulation of bone and soft tissue repair mediated by growth factors.

PEARL 27•8 The important overall result from these studies is that PEMF signals can stimulate the secretion of growth factors (eg, insulin-like growth factor II) following a short-duration trigger stimulus.

Studies underlying this working model have shown effects on calcium ion transport,[36] a 28% increase in cell proliferation,[37] a fivefold increase in IGF-II release,[38] and increased IGF-II receptor expression in osteoblasts.[39] Increases of 53% and 93% on IGF-I and II, respectively, have also been demonstrated in rat fracture callus.[40] Additionally, PEMF stimulation of TGF-β and mRNA by threefold in a bone induction model in the rat has been reported.[41] The latter study also suggests that the increase in growth factor production by PEMF may be related to the induction of cartilage differentiation.[42] Moreover, it also suggests that the responsive cell population is most likely mesenchymal cells,[43] which are recruited early during PEMF treatment to enhance cartilage formation. Upregulation of TGF-β mRNA by 100%, as well as collagen and osteocalcin synthesis by PEMF has been reported in the human osteoblast-like cell line MG-63.[44,45] PEMF stimulated a 130% increase in TGF-β1 in bone nonunion cells.[46] That the upregulation of growth factor production in bone may be a common denominator in the soft tissue level mechanisms underlying electromagnetic stimulation is supported by several key studies.[47-50]

Use of specific inhibitors suggests PEMF acts through a calmodulin-dependent (CaM-dependent) pathway.[48] This follows reports that specific PEMF and PRF signals, as well as weak static magnetic fields, modulate Ca^{2+} binding to CaM by a twofold acceleration in Ca^{+2} binding kinetics in a cell-free enzyme preparation.[51-57] (Fig. 27.5)

PEARL 27•9 PEMF has been reported to increase angiogenesis by threefold in an endothelial cell culture.[58] A recent study confirms this and suggests PEMF increases in vitro and in vivo angiogenesis through a sevenfold increase in endothelial release of FGF-2.[59]

PRF signals configured on the basis of a transduction mechanism that involves Ca^{2+} binding to CaM are discussed below, along with several basic and clinical examples. It is useful to consider that PRF signals are configured to act as a first messenger for a second messenger, which in turn modulates biochemical cascades related to tissue growth and repair. The likely second messenger is Ca^{2+} binding to CaM, which activates epithelial or neuronal nitric oxide synthase (eNOS or nNOS) to produce nitric oxide (NO). The result is that PRF can act to reduce the inflammatory phase of tissue repair and then accelerate the remaining phases of repair by directly modulating the appropriate growth factor release at the appropriate time and with the correct kinetics. A scheme for PEMF/PRF acceleration of tissue healing based upon this model is shown in Figure 27.4.

Animal Studies—Bone Repair

PEMF signals have been reported to accelerate bone repair in a wide variety of conditions, including osteotomies,[60,61] osseus defects,[62,63] osteopenia,[64-67] and a bone disuse model.[68] Experimental models of bone repair show enhanced cell activity, proliferation, calcification, and increased mechanical strength with DC currents in spinal arthrodeses,[69-73] fusion,[74] and other experimental bone repair conditions.[75-79] The mechanical strength of late-phase osteotomy gap healing in the dog was 35% stronger in PEMF-treated limbs,[75] and PEMF increased bone ingrowth into hydroxyapatite implants in cancellous bone by 50%.[76]

PEMF/PRF Mechanism for Tissue Repair

PEMF →

Ca^{2+} + CaM ⟶ Ca^{2+}CaM

PEMF increases Ca^{2+} binding to CaM (milliseconds)

Ca^{2+}CaM + eNOS ⟶ NO

Ca^{2+}CaM binds to eNOS, catalyzes NO release (seconds)
Anti-inflammatory: increased Blood & Lymph Flow
Pain/Edema Decrease (seconds)

NO ⟶ cGMP ⟶ Growth Factors (hours/days)

VEGF	Angiogenesis (hours/days)
FGF	Collagen/Granulation (days)
TGF-β	Remodeling (days/weeks)

Figure 27•5 *A schematic showing a proposed mechanism for PEMF/PRF-modulated tissue repair. The RF signal induces sufficient voltage and current to accelerate Ca^{2+} binding to CaM. This accelerates the production of NO from endothelial NOS, which acts rapidly as an anti-inflammatory. There follows accelerated production of cGMP, which starts the growth factor cascades. (From A. Pilla with permission)*

Clinical Studies—Bone Healing

PEMF technologies have been used clinically to treat fresh fractures, osteotomies, spine fusions, and delayed and nonunion fractures. The efficacy of PEMF stimulation on bone repair has been studied in a formal meta-analysis.[8] Twenty RCTs were identified. Fifteen trials supported electromagnetic field (EMF) effectiveness, and five failed to show effectiveness. Most studies used PEMF. In all cases, the primary outcome measure was bone healing assessed by radiographs and clinical stability test. Results from pooled trials of 765 cases supported the effectiveness of PEMF stimulation of bone repair. However, because of the inability to pool data from all studies, conclusions regarding PEMF efficacy in bone repair were only suggestive. PEMF significantly accelerated union of femoral and tibial osteotomies in randomized, placebo-controlled studies by approximately 50%.[80-82]

Bone Healing–Spinal Fusions

PEMF has been used to promote healing of spinal fusions for the treatment of chronic back pain from worn or damaged intervertebral discs. This is measured by the increase in successful fusions from 50% to approximately 80% using PEMF as adjunctive treatment. This application has also been subjected to meta-analysis.[83] Five RCTs and five nonrandomized case controlled studies showed positive results for the enhancement (by 60%) of spine fusion by electrical and electromagnetic stimulation. There are many studies and reviews that show electrical and electromagnetic stimulation is effective in promoting spinal arthrodesis.[84-88]

Bone Healing—Recalcitrant Extremity Fractures

The effectiveness of PEMF in promoting healing of recalcitrant fractures has been reviewed.[89] Twenty-eight studies of nonunited tibial fractures treated with PEMF were compared with 14 studies of similar fractures treated with bone graft with or without internal fixation. The overall success rate for the surgical treatment of 569 nonunited tibial fractures was 82%, while that for PEMF treatment of 1718 nonunited tibial fractures was 81%, suggesting it is significantly more advantageous for the patient to use PEMF than to submit to invasive surgery for the first bone graft. There are several observational studies suggesting the efficacy of PEMF techniques in stimulating healing of delayed unions and nonunions.[90-98] Studies comparing PEMF with bone graft show their equivalence in promoting union of delayed union or nonunion fractures.[89,99-101] Finally, there is a promising study on the effects of PEMF on distraction osteogenesis for the correction of bone length discrepancies.[102]

PEARL 27•10 PEMF technologies now constitute the standard armamentarium of orthopedic clinical practice. Since the success rate for these interventions has been reported to be equivalent to that for the first bone graft, a huge advantage to the patient ensues because PEMF therapy is noninvasive and is performed on an out-patient basis.

PEMF therapy also provides significant reductions in the cost of health care since no operative procedures or hospital stays are involved. This also applies for the increased success rate of spinal fusions with PEMF. Thus, the clinical effects of PEMF on hard tissue repair are physiologically significant and often constitute the method of choice when standard of care has failed to produce adequate clinical results. It is interesting to note that PEMF may be the best modulator of the release of the growth factors specific to each stage of bone repair, certainly more so than the exogenous application of the same growth factors.

Biophysical Considerations of Pulsed Electromagnetic Field Therapeutics

The biophysical mechanism(s) of interaction of weak electric and magnetic fields on biological tissues as well as the biological transductive mechanism(s) have been vigorously studied. At present, the most generally accepted biophysical transduction step is ion/ligand binding at cell surfaces and junctions that modulate a cascade of biochemical processes resulting in the observed physiological effect.[103-106] A unifying biophysical mechanism that could explain the vast range of reported results and allow predictions of which EMF signals and exposures are likely to induce a clinically meaningful physiological effect has been proposed.[107-109]

Electromagnetic bioeffects from relatively weak signals (below heating and excitation thresholds) can be produced with a time-varying electric field, $E(t)$, induced from an applied time-varying magnetic field, $B(t)$. The PEMF clinical devices in present use for bone repair and PRF devices for wound repair induce 1 to 100 mV/cm peak E at the treatment site.[8,35,83] Determination of the amplitude and spatial dosimetry of the induced EMF within the tissue target site has been rigorously studied for the laboratory dish with coils oriented vertically or horizontally.[110-112] Models have been created for the distribution of induced voltage and current in human limbs and joints.[113,114] Three-dimensional visualizations of clinical PEMF signals have been reported.[115] Thus, the distribution of current in a given tissue target from a coil placed in proximity to that target is relatively well understood, and adequate dosage should present no problem in clinical applications of PRF for wound repair.

Inductively Coupled Clinical Pulsed Electromagnetic Field Waveforms

The electric field induced via a time-varying magnetic field waveform is directly related to the electrical characteristics of the coil employed and the current waveform applied to the coil. Induced electromotive force (emf) is proportional to the rate of change of current in the coil (dI_{coil}/dt), which produces the shape of the induced electric field. A pulse-type induced electric field waveform in common clinical use for bone repair is shown in Figure 27.6. Note that this is the in situ waveform, that is, the PEMF stimulus at the cell/tissue level. The rationale behind the configuration of this waveform was based on the assumption that the induced electric field (and associated induced current density) is the primary stimulus. In other words, the magnetic component was considered to be the carrier or coupler, not significantly contributing to the biological effect.

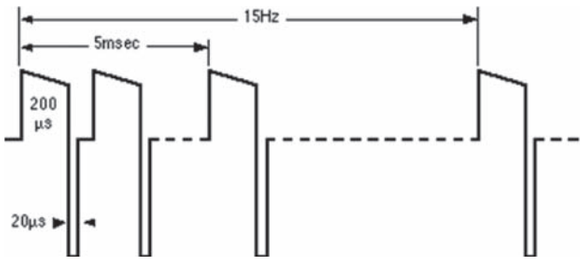


Figure 27•6 *Induced electrical field in tissue from the time-varying magnetic fields used in PEMF devices for clinical applications to bone repair. The waveform consists of bursts of asymmetrical pulses. Peak E is 1–10 mV/cm in a 2-cm cell/tissue target. Positive clinical and biological effects have been reported for this signal. (From A. Pilla with permission.)*

The waveform shown in Figure 27.6 represents the time variation of the electric field signal induced in a cell/tissue target (eg, fracture site). The distribution of current flow depends upon the geometry of coil and target. The basic rule is that the voltage induced will be defined by the distribution of magnetic flux within the tissue and the electrical properties of the target. The induced E field will be greater when the magnetic field intercepts a greater cross-sectional area of the sample, that is, maximum E field in the target depends upon target size. Peak E field and associated current density, J, at a radius of 2 cm is often used for dosimetry comparisons. It is also convenient to use dB/dt (rate of change of the magnetic field with time) as a measure of the peak induced electric field, assuming identical target size, for a given PEMF signal. For example, a common clinical bone repair signal produces a 20-G peak magnetic field in 20 µsec. Thus, $dB/dt = 10^6$ G/sec for which peak $E_\phi(t) = 1$ V/m = 10 mV/cm at a radius of 2 cm in the target, a typical dose metric for PEMF bone-growth stimulators.

The Pulsed Electromagnetic Field Transduction Mechanism

For a living cell or tissue to respond functionally to an exogenous electric field, it is necessary that it reach and be detected at the appropriate molecular, cellular, or tissue site. An important step, therefore, is the characterization of the electrical properties of cells and tissues. It has been proposed that a complete description of the electrical properties of cells and tissues should include the electrical equivalents of the electrochemical processes that could be involved in the signal transduction pathway.[15] The electrical equivalents

of electrochemical processes at cell surfaces and junctions and their relevance to EMF therapeutics have been described.[15,33,108,116,117] Thus, induced current can affect cell surfaces and junctions via a complex, but readily discernible set of electrochemical steps that are representative of the cell's real-time response to perturbations in its charged environment for any given functional state.

The electrochemical pathways involved in the transduction of an exogenous EMF signal into a physiologically significant endpoint appear to be operationally similar to the initial gating process involved in the production of the action potential via membrane depolarization.[118] It is therefore appropriate to consider the configuration of EMF waveforms in terms of an informational approach, or signaling in contrast to one designed to supply energy to drive the biochemical cascade. Examples of the latter would be the use of direct currents large enough to cause cells to move along the electric field in wound repair applications and electroporation, wherein short voltage pulses are applied with sufficient electric field to temporarily cause the cell membrane to become permeable to macromolecules such as DNA or chemotherapeutic agents.

The Electrochemical Information Transfer Model

It was proposed by Pilla in 1972 that nonthermal, subthreshold electromagnetic fields may directly affect ion binding and/or transport and possibly alter the cascade of biological processes related to tissue growth and repair.[116] This electrochemical information transfer (EIT) hypothesis postulated the cell membrane as the site of interaction of low-level electromagnetic fields through modulation of the rate of binding of, for example, calcium ion to receptor sites as a first step in a biochemical cascade relevant to the desired clinical outcome.

Equivalent electrical circuit models representing electrochemical processes at cell surfaces and junctions have been derived.[15,33,109,117] Typically, most calculations consider a membrane model that consists of a capacitance, C_d, in parallel with an ionic leak pathway, R_M (see Fig. 27.3). While all membranes exhibit these properties, this simple model does not completely describe the dielectric properties of a functioning membrane, particularly with respect to the EMF transduction pathway. Impedance measurements on isolated cells have revealed the existence of relaxation processes that appear to reflect the kinetics of ion or ligand binding, as well as follow-up biochemical reactions.[118-122] Thus, a more general description of membrane dielectric properties, which takes into account electrochemical processes relevant to EMF sensitivity, considers an ion-binding step that precedes and possibly triggers a subsequent chemical reaction at the membrane surface.

The EIT model strongly guided the creation of the first clinically effective PEMF signal for recalcitrant fracture repair.[16,17] According to the EIT model, the requirements for an effective waveform could be met if it contained frequency components of sufficient amplitude within the time constant of the proposed target pathway.[15] Transmembrane ion transport, for which kinetics is in the millisecond range, was chosen as the target pathway for bone repair.[118] This, coupled with practical restrictions on the size of the coil for patient use, led to the pulse burst waveform shown in Figure 27.3 (top). It was supposed that the cell would ignore the short opposite polarity pulse and respond only to the envelope of the burst that had a duration of 5 msec, enough to induce sufficient amplitude in the kilohertz frequency range. Although the reasoning behind the asymmetric pulse in this waveform was erroneous because the EIT model was not yet complete and required further knowledge of the transduction mechanism, this signal is nonetheless effective for bone repair. It continues to be part of the standard armamentarium of the orthopedist for the nonsurgical noninvasive treatment of recalcitrant bone fractures.

Dosimetry for Pulsed Electromagnetic Field Signals

Classical biophysical lore suggests that, unless the amplitude and frequencies of an applied electric field are sufficient to trigger an excitable membrane (eg, heart pacemaker), to produce tissue heating, or to move an ion along a field gradient, there could be no effect. This was a formidable obstacle in the quest for therapeutic applications of weak EMF signals. However, the classical biophysics position had to be changed as the evidence for weak (nonthermal) EMF bioeffects became overwhelming. The clinical evidence offered by many double-blind clinical studies, coupled with the database of hundreds of thousands of successful treatments of delayed and nonunion bone fractures registered with the FDA, simply could no longer be ignored. Noninvasive PEMF treatment is actually as successful as the first bone graft, to the huge benefit of the patient. The task was to provide solid testable models for the biophysical mechanism of weak electric field bioeffects.

PEARL 27•11 The underlying problem for any model that claims to describe the biophysical mechanism of weak EMF bioeffects relates to whether the induced signal can be detected at the molecular/cellular/tissue target in the presence of thermal noise, that is, signal-to-thermal noise ratio (SNR). SNR compares the amplitude of a desired signal (eg, the noise produced by an induced electric field) to the amount of undesirable background noise (eg, thermal or cell membrane noise) that has mixed with it. The higher the ratio, the less obtrusive is the background noise.

Considering the cell membrane as the target, the burden of proof is to show that the induced voltage is not buried in thermal and other voltage noise, that is, that the applied signal is detectable. Without resorting to signal processing or metabolic amplification, it is still necessary to attempt to understand the remarkable sensitivity of biological systems to weak electric fields. In terms of target geometry, certainly the spherical cell model is oversimplified and cannot represent the geometric complexity of cellular and tissue EMF targets. For example, the successful outcome of a healing fracture, wherein bone tissue differentiates both functionally and spatially, is a clinically relevant illustration of cell-cell communication.[123] This suggests the target for the PEMF signals used to affect

nonunions and delayed unions of bone is a highly organized ensemble of cells. In fact, all organized tissue is developed and maintained by an ensemble of complex geometry cells that have coordinated activity.[124] The most prevalent cell shape in living system tissue is elliptical and flattened, with processes extending in at least two directions. Gap junctions provide pathways for ionic and molecular intercellular communication.[125] They are present in all tissues, including bone.

The presence of gap junctions in the cells of an organized or organizing (repairing) tissue cause the induced transmembrane voltage (V_M) to be substantially higher than that for the same cell in isolation for the same applied EMF. The frequency range in which increased V_M occurs versus that for a single isolated cell is shifted toward a substantially lower range. This places different frequency requirements on the induced electric field waveform dependent upon whether the target is a macromolecule, single cell, or tissue. As array length increases beyond 1 mm, the rate of increase in V_M diminishes because of the dissipation of intracellular current via transmembrane resistance (R_M). In the case of myelinated nerve axons, R_M is substantially higher, and array lengths above 1 cm can provide further significant increases in V_M.[126]

Assuming Ca^{2+} binding to CaM, signal-to-thermal noise ratio (SNR) may be evaluated for molecular, cellular, or tissue targets. An interesting example is wound repair. A common model is the full-thickness linear incision performed through the skin down to the fascia on the dorsum of adult Sprague-Dawley rats.[127] Acceleration of wound repair is assessed by tensile strength measurements at 21 postoperative days. At this time point, untreated (control) strength is approximately one third that of the fully healed wound. One study used the PEMF signal commonly employed for bone repair and reported no effect.[128] (Fig. 27.7) A second, more recent study used a PRF signal, having a carrier frequency of 27.12 MHz specifically configured to enhance Ca^{2+} binding to CaM with the specific goal of enhancing growth factor release. A 59% increase in tensile strength versus controls at 21 days ($P < 0.001$) was reported.[129] SNR analysis for the signals used in these studies is shown in Figure 27.8. It is clear that the induced electric field produced by the PEMF bone repair signal consisting of a 5-msec burst of bipolar pulses (200/20 μsec asymmetrical duration), repeating at 15/sec and inducing a gross peak electric field of 1 mV/cm ($dB/dt = 10^6$ G/sec), produced very low induced voltage across the Ca/CaM pathway. (Fig. 27.5) The resultant SNR was below the detection threshold. In contrast, the PRF signal that consisted of a 2-msec burst of 27.12-MHz sinusoidal waves repeating at 1/sec, $dB/dt = 10^7$ G/sec, produced a significantly larger induced voltage with a larger effect on Ca^{2+} binding.

A recent study compared the effects of the PEMF bone repair signal used in the example above ($dB/dt = 10^6$ G/sec) with a 65-μsec burst of rectangular pulses of 4-μsec and 12-μsec duration per polarity repeating at 1.5 bursts/sec ($dB/dt = 10^4$ G/sec) on bone repair in a rat osteotomy model.[79] In this study the standard clinical bone repair PEMF signal produced a twofold increase in new woven bone and callus stiffness, whereas the 4/12-μsec signal was ineffective. SNR, assuming a Ca/CaM target pathway, reveals peak SNR greater than 1 for the clinical PEMF signal and peak SNR less than 1 for the 4/12-μsec signal. Note that modulation of the Ca/CaM pathway for bone repair requires frequency components of sufficient amplitude in the 10^2 to 10^4 Hz range, and neither of these signals was configured accordingly.

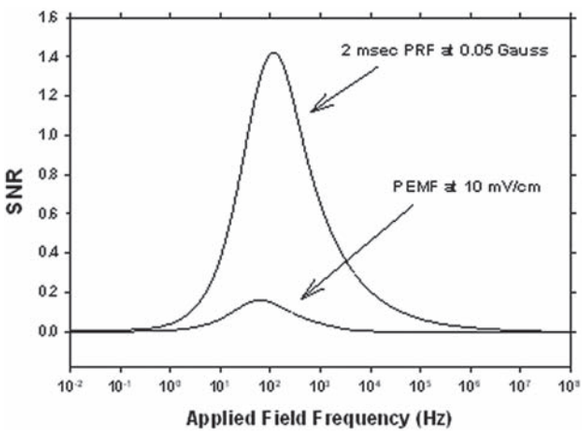


Figure 27•7 *SNR in a Ca/CaM pathway for PEMF and PRF waveforms used in a rat cutaneous wound model. The PEMF asymmetrical repetitive pulse bone repair signal produced low (below detection threshold) SNR and had no effect on wound repair. The 27.12-MHz PRF repetitive sinusoidal burst produced sufficient SNR for detection in the Ca/CaM pathway and enhanced tensile strength by 59% at 21 days. (From: Strauch, B, et al (129) with permission.)*

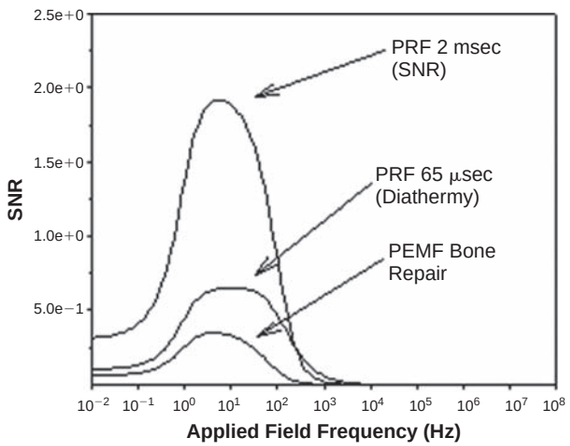


Figure 27•8 *SNR for PRF signals consisting of a 2000-μsec burst of 27.12-MHz sinusoidal waves repeating at 5/sec (configured a priori for the Ca/CaM pathway), a 65-μsec burst at 600/sec (a diathermy-based signal in clinical use for soft tissue repair), and the original PEMF bone healing signal consisting of a 5-msec burst of 200/20-μsec pulses repeating at 5/sec. Both PRF signals were predicted effective, the 65-μsec signal significantly less so since it was not matched to the bandpass of Ca^{2+} binding. The PEMF bone repair signal was predicted ineffective. (From Zborowski M, et al (139) with permission.)*

Pulsed Electromagnetic Field Stimulation for Chronic Wound Healing (Lower Extremity Venous and Arterial Insufficiency Leg Ulcers)

In a double-blind trial to determine the effect of nonthermal PEMF on venous leg ulcers, Ieran and colleagues randomly assigned 44 patients to a treatment group ($N = 22$, active PEMF device) and to a control group ($N = 22$, inactive PEMF device).[130] Patients in both groups were treated 4 hours a day for 90 days. The active device delivered PEMF from a noncontact coil at 75 Hz and 2.8 mT intensity for the amount of time just stated. Because of patient noncompliance with the protocol or other reasons for patient exclusion, the data analysis was done on 18 patients in the treatment group and on 19 patients in the control group. At day 90, 6 patients (31.5%) were healed in the control group compared with 12 patients (66.6%) in the treatment group ($P < 0.02$). Within 1 year from the start of the study, 8 patients (42.1%) had healed among the control group, and 16 patients (88.8%) had healed among the treatment group ($P < 0.005$). No ulcers worsened in the treatment group, while four ulcers worsened in the control group. After healing, the rate of recurrence of ulcers was greater in the control group (50%) than in the treatment group (25%). In a befo re-and-after study, Duran et al reportedly used PEMF to treat 18 venous leg ulcers 10 times for 15 minutes each session.[131] They reported that reepithelialization resulted in a significant decrease in mean surface area of 33% after 10 treatment days. In another study labeled a double-blind randomized, controlled trial, Todd et al treated 19 patients with venous leg ulcers twice weekly with PEMF over a 5-week period.[132] Their device reportedly delivered a field strength of 60 units (not identified) at 5 Hz for 15 minutes by placing noncontact coils on opposite sides of the wound over the dressings. Outcome measures included ulcer size, pain level, lower leg girth, and presence of infections. After removing data from one patient from the active treatment group who had a very large ulcer that slanted the mean pretreatment and posttreatment wound areas, they reported a trend toward a positive healing effect but no statistical difference between the active and inactive treatment groups.

In a prospective, randomized, double-blind, placebo-controlled, multicenter study, Stiller et al assessed the efficiency of PEMF treatment on the healing of intractable venous leg ulcers.[133] Patients were instructed to treat themselves 3 hours daily at home for 8 weeks with a portable PEMF device. PEMF parameters derived from bone healing research were 3.5-msec pulse duration, a biphasic delta B waveform, and an intensity of about 22 G. At week 8 the active group had a 47.7% reduction in wound surface area, compared to a 43.3% increase for the placebo group ($P < 0.0002$). Additional evaluations by the investigators revealed that 50% of the wounds in the active group closed or distinctly improved versus 0% in the placebo group, and 0% of the active group worsened compared with 54% of the placebo group ($P < 0.001$). Significant reductions in wound depth and pain (both $P < 0.04$) occurred for the active group. From in vitro research, Canedo-Dorantes et al found that extremely low-frequency (ELF) PEMF interacts with peripheral blood mononuclear cells (PBMCs) via Ca^2 channels, activating signal transduction cascades, which in turn promote cytokine synthesis, changing cell-proliferation patterns.[134] They then configured ELF frequencies to interact in vitro with the proliferation patterns of PBMC obtained from normal human subjects. Since, as mentioned above, ELF interacts with peripheral blood mononuclear cells, they applied the ELF peripherally (to the arms rather than directly to the wounds) as the sole treatment to 26 patients with 42 chronic venous or arterial leg ulcers that had not responded to previous medical and/or surgical treatments in a before-and-after design. The purpose of PEMF application approach was to ascertain whether the ELF could alter systemic effects by interaction with action potentials at the peripheral (lower extremity) wound site. They theorized that ELF frequencies previously tested on normal human volunteers could increase proliferation of PBMCs in the bodies of patients with chronic leg ulcers. The treatment involved placing an arm into a chamber containing a magnetic field for 2 to 3 hours, three times a week, for a 4-month period. The strength of the ELF inside the chamber was 36.36 G. Based on before-and-after wound surface area measurements and photographs, the investigators divided patient's data into "responders" (closed wounds or wounds reduced greater than 50%) and "nonresponders," who had at least one wound that decreased in size less than 50% or increased in size. Twenty-nine wounds that earlier were unresponsive to medical-surgical treatment responded to ELF and began to heal by week 2. By the end of study, 15 arterial and 14 venous wounds were in the responder groups while 2 arterial and 11 venous ulcers were in the nonresponder groups. After ELF treatment over the 4-month study period, 69% of all wounds were either closed or had healed more than 50%. Defective wound healing was observed in ulcers associated with arterial occlusion, hypertension, severe lipodermatosclerosis, nonpitting edema and obesity.

PEARL 27•12 The positive outcomes seen in this study could be attributed to the greater overall electrical energy dosage accumulated over the 8-week study period compared with the previously cited studies that introduced considerably less electrical energy into the wounds.[131,132]

Although the five small studies described above and summarized in Box 27.1 have reported positive chronic wound healing effects with PEMF signals that are configured for treatment of nonunion and delayed union fractures, more research is needed to establish the efficacy of these signals in being able to significantly enhance healing of chronic wounds.

Summaries Regarding PEMF

As shown in Figure 27.6, PEMF signals may be very specifically configured to modulate Ca^{2+} binding to calmodulin, which in turn can affect a variety of biochemical cascades,

Box 27•1 Venous Leg Ulcer Clinical Trials With Pulsed Electromagnetic Field and Nonthermal Pulsed Radio Frequency

- PSWD and PRF provide comparative dosimetry and uniformity of the induced magnetic field in wound and periwound tissues.
- PSWD and PRF provide postoperative reduction of pain and edema.
- PSWD and PRF enhance tissue perfusion, either directly or consensually, and secondarily increase tissue oxygen saturation.
- PSWD and PRF can be applied without making contact with wound or periwound tissues, thus obviating pain and avoiding wound contamination.
- PSWD elevates tissue temperatures.
- PSWD can mildly increase temperature within deep wounds, tunnels, and abscessed areas.
- PRF excites cellular activity and cell membrane transduction mechanisms.
- PRF can be transmitted through clothing, wound dressings, compression bandages, casting materials, and splints.

Modified with permission from Sussman, C: Induced electrical stimulation: Pulsed radio frequency and pulsed electromagnetic fields. In: Sussman, C, Bates-Jensen, B (eds): Wound Care: A Collaborative Practice Manual for Health Professionals, ed. 3. Philadelphia, Lippincott Williams & Wilkins, 2007, p 573.

starting with a very rapid anti-inflammatory component and ending with the modulation of growth factors important to tissue repair

Nonthermal Pulsed Radio Frequency for Soft Tissue Wound Repair

Animal Studies (Induced Wounds)

A recent study showed the PEMF signal used for bone repair accelerated wound closure in diabetic and normal mice.[135] Cell proliferation and CD31 density were significantly increased in the PEMF-treated groups. Cultured medium from human umbilical vein endothelial cells exposed to PEMF exhibited a threefold increase in FGF-2, which facilitated healing when applied to wounds.[136] Skin on diabetic mice exposed to nonthermal PRF did not exhibit tissue necrosis and demonstrated oxygen tensions and vascularity comparable to those in normal animals.[135] PRF signals produced a statistically significant several-fold increase in neovascularization in an arterial loop model, suggesting an important clinical application for the angiogenesis that is so critical to wound repair.[137,138] PRF signals, configured a priori assuming a Ca/CaM transduction pathway, accelerated wound repair in a rat cutaneous wound model by approximately 60% as measured by tensile strength.[129] A similar 70% increase in tensile strength in an Achilles tendon model in the rat has been reported.[139] In another study investigators reported that acute wounds induced in rabbits treated with nonthermal PRF had lower contraction but higher epithelialization rates than control wounds.[140]

Design of Pulsed Radio Frequency Signals for Clinical Wound Repair

Having established the rationale for the a priori configuration of PEMF and PRF signals to obtain a predicted bioeffect, the following cases demonstrate specific applications to clinical wound repair.

PEARL 27•13 For all of the clinical results presented in Figures 27.14 through 27.17, the a priori SNR analysis was applied to a nonthermal PRF signal. This signal had the standard 27.12 MHz sinusoidal carrier, for which pulse modulation (burst duration and repetition rate) was configured according to an assumed Ca/CaM transduction pathway.

Signal configuration is proceeded by evaluation of SNR in a two-step pathway involving Ca^{2+} binding to CaM, followed by Ca^{2+}/CaM binding to epithelial or neuronal nitric oxide synthase (eNOS and nNOS, respectively), which mediates nitric oxide (NO) release. Assuming this pathway, Figure 27.8 shows SNR for PRF signals consisting of a 2000-µsec burst of 27.12-MHz sinusoidal waves repeating at 5/sec (configured a priori for the Ca/CaM pathway), or a 65-µsec burst at 600/sec (a diathermy-based signal in clinical use for soft tissue repair), and the original PEMF bone healing signal consisting of a 5-msec burst of 200/20-µsec pulses repeating at 5/sec. Both PRF signals were predicted to be effective, the 65-µsec signal significantly less so since it was not matched to the bandpass of Ca^{2+} binding. The PEMF bone repair signal was predicted to be ineffective. The validity of this approach was reported on Achilles tendon repair in the rat.[139] The significance of results such as these was to permit the design of cost-effective clinical PRF units that are simple, portable, and even disposable. The PRF signal configured a priori for the Ca/CaM transduction pathway was employed in all of the devices for which the clinical results are reported below.

Pulsed Radio Frequency Nonthermal Devices

Nonthermal PRF is created by modulating the primary 27.12-MHz RF carrier by using a timing mechanism in the device to interrupt the carrier frequency waves so the output is turned on and off at preset intervals, allowing bursts of pulse trains to be emitted from the treatment coil. Hence, within each burst or pulse train is a series of high-frequency sine wave oscillations. The pulse train duration, or "on time," is usually separated by a longer lasting "off time." (Fig. 27.8 bottom)

PEARL 27•14 The biophysics community defines a nonthermal PRF device as one that raises the temperature of the target tissue less than 1°C after exposure for 1 hour.[174]

Some nonthermal PRF devices allow the clinician a few choices of pulse burst durations, while others provide a fixed burst duration, which typically is 65 µsec. The pulse train frequency within bursts can be varied and determines the duration of the off time between bursts. At 27.12 MHz, there are 27.12×10^6 cycles in 1 sec and 27.12 cycles in 1 µsec. Therefore, for FDA class III nonthermal PRF devices with fixed 65-µsec pulse durations, such as the Diapulse® (Diapulse Corporation of America, Great Neck, NY) and the former solid-state MRT 911® (Electropharmacology Inc., Pompano Beach, FL), each burst contains 1762.8 oscillations. (Fig. 27.9) At a maximum frequency choice of 600 pulses per second (pps), each complete period lasts 1666.66 µsec (1.7 ms), and the interval between successive pulses is 1601.66 µsec. At a frequency choice of 400 pps, each period lasts 2500 µsec (2.5 ms) and the interval between successive pulses is 2435 µsec.[141] At 600 pps, the duty cycle is 65/1666 = 0.039, or less than 4%, while at 400 pps, the duty cycle is 65/2500 = 0.026, or less than 2.6%. Thus, with nonthermal PRF devices such as the Diapulse and the former MRT 911 that have fixed 65-µsec pulse durations, when the peak pulse power is preset by a clinician, a manual increase in the pulse frequency from a minimum of 80 pps toward the maximum of 600 pps will increase the mean power accordingly. With nonthermal PRF devices, as with thermal PRF devices, the power driving the patient treatment coil does not represent the level of absorbed power in the tissues. The power driving the treatment coil can be measured either as peak pulse power, which, for Diapulse and the former MRT 911, ranges from 185 to 975 W, or as mean power, which (for both devices) is much lower, ranging from 7.5 to 38 W.

These values are determined by the settings of peak power and pulse frequency. Another nonthermal PRF device, the Provant CPI® (Regenesis Biomedical, Scottsdale, AZ), has a fixed 42-µsec burst duration. (Fig. 27.10) Since the MRT 911, the Diapulse, and Provant CPI® devices are described and categorized by the FDA as class III, none of the three devices (according to the FDA class III definition) are supposed to induce any significant tissue-heating effect, even at the highest peak power and pulse frequency settings.[141] Of the three devices, the MRT 911 is no longer on the market; however, a newer version, the MRT SofPulse® (Ivivi Technologies, Northvale, NJ), has a burst duration that varies from 2 to 5 msec, with frequencies between 1 and 5 pps and maximum power < 1 watt. (Fig 27.11) The most recent version of this

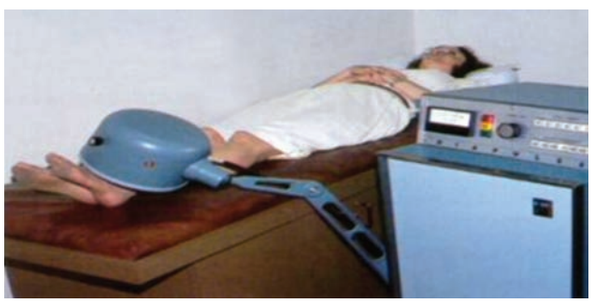


Figure 27•9 *Diapulse™ nonthermal PRF device. (Courtesy of Diapulse Corp., Great Neck, NY.)*

Figure 27•10 *Provant CPI™ nonthermal PRF device. (Courtesy of Regenesis Biomedical Inc., Scottsdale, AZ.)*

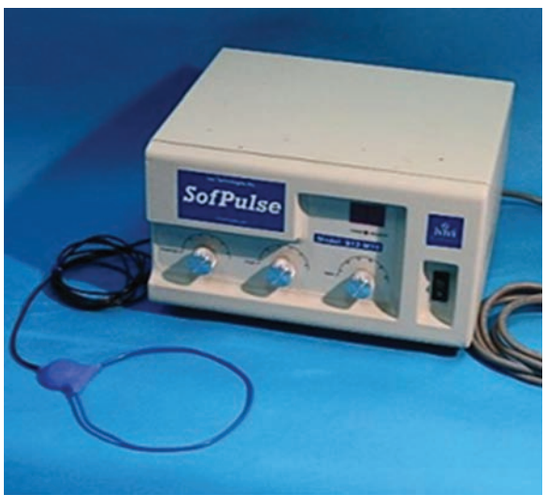


Figure 27•11 *MRT 912™ nonthermal PRF device. (Courtesy of Ivivi Technologies, Northvale, NJ.)*

SofPulse technology requires less than 10 watts of peak input power to induce a magnetic field in tissue that is 50-fold less intensity (0.05 G) compared to the 2 G intensity delivered by the other three nonthermal PRF devices using >400 W peak input power. (Fig. 27.12) Nonthermal PRF signals were originally used for the treatment of infections in the preantibiotic era and are now widely employed for the reduction of posttraumatic and postoperative pain and edema.[142]

PEARL 27•15 Since 38 W or more of mean power is used as a measure of the heating effect for thermal PRFD, less than 38 W mean power driving the treatment coil is used as an indicator of minimal or no heating effect for nonthermal PRF.

PEARL 27•16 If transient, imperceptible tissue heating with these devices does occur with each burst, there should be no accumulative heating effect as long as perfusing blood dissipates the thermal energy.

Nonthermal Pulse Radio Frequency in Postsurgical Wound Pain Suppression

A PRF signal configured a priori for the Ca/CaM pathway was tested clinically in a randomized double-blind pilot study on 30 patients for its effect on pain reduction immediately after breast augmentation.[143] The PRF signal used in this study was configured a priori, assuming a Ca/CaM transduction pathway, and consisted of a 2-msec burst of 27.12-MHz sinusoidal waves repeating at 2 bursts/sec and at 0.05-G peak amplitude (SofPulse; Alletgan, Irvine, CA). (Fig. 27.12) The PRF signal is inductively coupled and can thus be applied through clothing or dressings, requiring no contact with the skin. PRF was delivered from a small (2.5-cm diameter, 1-cm thick) battery-powered generator to a single-turn 15-cm diameter electrical coil. A portable and disposable PRF device (Torino II, Ivivi Technologies Inc., Northvale, NJ) was placed on the patient as part of normal postsurgical procedure, and the signal was activated before the patient left the operating room. (Fig. 27.13) Once active, the PRF device automatically provided a 30-minute treatment according to a regimen as follows: every 4 hours for the first 3 postoperative days; then every 8 hours for the next 3 days; and every 12 hours until the follow-up visit, normally at postoperative day (POD) 7. Pain was assessed twice daily using a validated Visual Analogue Scale (VAS).

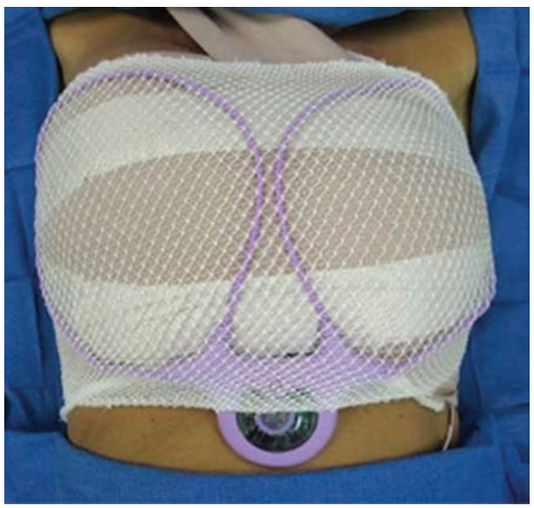


Figure 27•12 *PRF (SofPulse Duo™, nonthermal PRF device (Courtesy of Allergan, Irvine, CA) in use to control postoperative pain following breast augmentation surgery. (From Heden P, Pilla A (143) with permission.)*

The results are shown in Figure 27.14. Bars represent the mean postoperative VAS pain score for all breasts and at POD 7 for both the active and sham groups. Mean (± SD) VAS score was 54 plus or minus 9 mm for all groups postoperatively. Mean VAS decreased to 17 plus or minus 4.4 mm in the treated group (218%, $P < 0.001$ vs postoperative mean VAS) and to 31 plus or minus 5.6 mm in the sham group (74%, $P < 0.001$- vs postoperative mean VAS). The difference in mean pain between the active and sham cohorts was also statistically significant ($P < 0.001$), suggesting postsurgical use of PRF therapy could produce a clinically meaningful reduction in pain by nearly a factor of 3. A 2-fold increased reduction in pain by PEMF was already observed by POD 2. Active patients also had a concomitant decrease in pain medication by a factor of 2.9 by POD 7.[143]

A second randomized double-blind clinical study using the same PRF signal configured to target the anti-inflammatory cascade involving the CaM/NO/cGMP signaling pathway reported postoperative pain decreased by 300% by 5 hrs postsurgery, accompanied by a 275% decrease in IL-1β in the wound bed at the same postoperative time.[143A] Twenty four

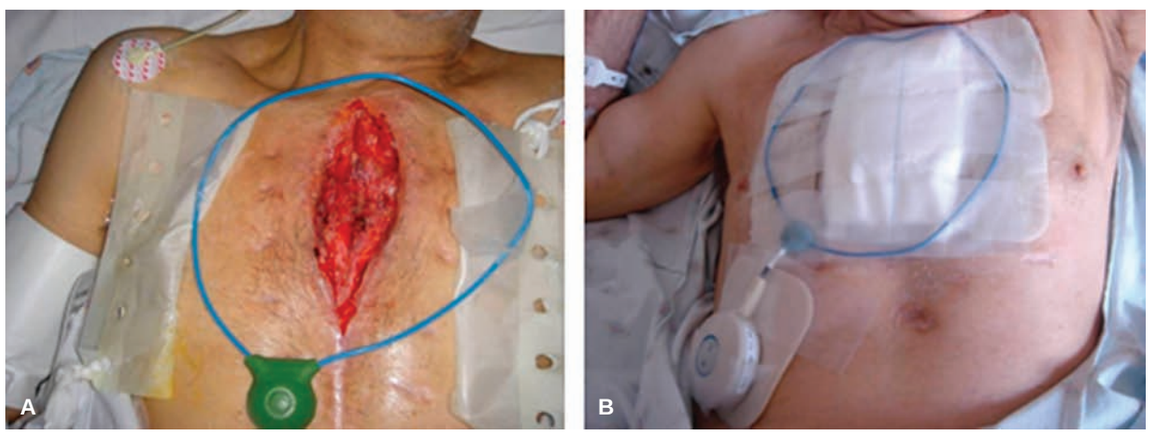


Figure 27•13 *Case 1: (A) PRF treatment started in hospital with Ivivi Roma clinic device. Note coil is positioned above wound that is within coil perimeter. (B) Patient is discharged after 1 week with disposable PRF device. Coil is incorporated in dressing. (Courtesy B. Strauch, MD, Mount Sinai School of Medicine, New York, NY.)*

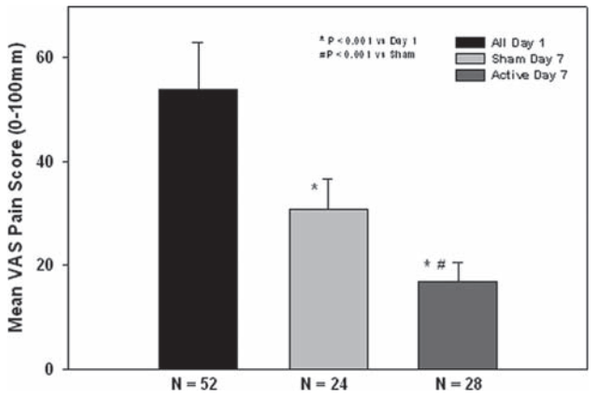


Figure 27•14 *Effect of PRF therapy on postsurgical pain from breast augmentation. Bars represent the mean VAS pain score at POD 7 vs initial postsurgical VAS score. Mean VAS score was 54 ± 9 mm for all groups postoperatively. Mean VAS decreased to 17 ± 4.4 mm in the treated group (218%, P < 0.001 vs postoperative) and to 31 ± 5.6 mm in the sham group (74%, P < 0.001 vs postoperative), representing a clinically meaningful reduction in pain by approximately 2.7-fold. (From Heden P, Pilla A (126) with permission.)*

healthy women, who were candidates for breast reduction for medical reasons, were admitted to this double-blind, placebo-controlled randomized study. Breast reduction was performed by the same surgeon using the standard Wise or vertical incision techniques with superomedial pedicles. Patients were equally divided into active and sham groups. A disposable dual coil radio frequency PEMF device (Ivivi Technologies, Inc., Northvale, NJ), placed in the post surgical support bra normally used for all patients, was activated on transfer of the patient to the recovery stretcher. The PEMF signal, con figured, *a priori*, to modulate Ca^{2+} binding to CaM, consisted of a 2 msec burst of 27.12 MHz sinusoidal waves repeating at 2 bursts/sec. Peak magnetic field was 0.05G which induced an average electric field of 32 ± 6 mV/cm in a 9 cm^3 target in each breast. An active PEMF device automatically provided a 20 minute treatment every 4 hours for the observation period of 24–48 hours post-surgery. Sham devices were activated in exactly the same manner as the active devices, but produced no RF signal in tissue. The primary outcome measure was the effect of non-thermal RF on the rate of post surgical pain reduction, using a Visual Analog Scale (VAS) which patients self-recorded throughout the overnight hospital stay. Post-operative pain medication was monitored for each patient. Wound exudates were analyzed for IL-1β, TNF-α, VEGF, and FGF-2.

Mean VAS scores showed this RF signal produced a 57% decrease in mean pain scores at 1 hour ($P < 0.01$), and a 300% decrease at 5 hours post-op ($P < 0.001$), persisting to 48 hours post-surgery in the active, versus no significant change in the control group. There was a concomitant 2.2-fold reduction in narcotic use in active patients over the first 24 hours postsurgery ($P = 0.002$). Mean IL-1β concentration in the wound exudates of treated patients was 275% lower at 5 hours postsurgery ($P < 0.001$) vs the sham group. There were no significant differences found for TNF-α, VEGF, and FGF-2 concentrations in the first 18 hours post-op.

These randomized placebo-controlled double-blind pilot studies confirm that non-thermal radio frequency PEMF therapy significantly reduced post-operative pain and narcotic use in the immediate post-operative period. It was also shown that PRF produced a significant reduction of IL-1β in the wound bed within the same post-op time frame. This non-thermal RF signal can provide its effect independent of pharmacokinetic limitations since the time-varying magnetic field appears instantaneously in all compartments of the target tissue. This could explain the rapidity of the PRF effect. It is intriguing to consider that the known effects of PEMF on NO release via effects on Ca^{2+} binding to CaM which, in turn, activates the constitutive nitric oxide synthases (cNOS) may be applicable here. NO from cNOS is known to downregulate inducible NO synthase (iNOS, not CaM-dependent) and IL-1β.

These studies provides further evidence that pulsed electromagnetic field therapy (PEMF) can rapidly reduce pain levels and pain medication requirements in the immediate post-operative period. The concomitant reduction of IL-1β in the wound bed, possibly via NO/cGMP signaling, suggests that PEMF could have a profound effect upon wound repair outcomes. The current availability of both economical and disposable PEMF devices could easily translate to many, if not most, post-surgical situations, leading to lower morbidity, shorter hospital stays, increased productivity, and a reduction in the cost of health care.

PEARL 27•17 The postoperative use of PRF using disposable economical devices could help decrease post-surgical patient morbidity in many surgical procedures. The technique is clinically simple to use and may also contribute to reduced costs for health care, particularly for more complex surgical procedures.

Nonthermal Pulsed Radio Frequency Clinical Studies—Effects on Pain, Edema, and Function Associated with Acute Soft Tissue Trauma (Closed Wounds)

In the soft tissue closed-wound area, nonthermal PRF signals are now employed for the reduction of acute posttraumatic and postoperative pain and edema. In a study designed to evaluate the effects of nonthermal PRF (Diapulse) on pain, edema, and disability associated with inversion ankle sprains, Wilson demonstrated that PRF reduced pain and disability in several acute ankle sprains significantly better than did thermal shortwave diathermy (SWD) treatment.[144,145] In one study, Wilson compared the nonthermal effects of PRF with the placebo effects of PRF.[144] He assigned patients with recent inversion ankle sprains to two match-paired groups of 20. The treatment

group received a 1-hour treatment of PRF daily for 3 days. For these treatments, a PRF device with a frequency of 27.12 MHz was set to provide a peak pulse power of 975 W for each 65-msec pulse. The off time interval between successive pulses was approximately 1600 msec. The control group received a 1-hour PRF placebo treatment daily for 3 days. Wilson reported that, statistically, symptoms of pain and disability were relieved more rapidly in the treatment than in the control group; however, there was no significant difference between the two groups regarding improvement in swelling. To assess the possibility that the beneficial effects observed in the treatment group might have resulted from an increase in blood flow owing to some small, transient degree of heating (which is the mode of action attributed to thermal SWD), a second clinical study was conducted to compare the effects of nonthermal PRF with thermal SWD.[145] The same number of patients with recent inversion ankle injuries were assigned in matched pairs to two groups and, depending on the group, received either a 1-hour treatment of PRF or two 15-minute treatments within 1 hour of inductive thermal SWD daily for 3 days. Analysis of the data revealed statistically significant differences—at the 1.0% level of confidence in reduction of swelling and at the 0.1% level in reduction of pain and disability—by PRF compared with SWD. In comparing total energy delivered to patients in the two groups, it was found that those treated with SWD received approximately 22.5 watt-hours compared to 15 watt-hours received by patients treated with PRF. The fact that better clinical responses were produced with less energy was interpreted by Wilson as support for the idea that beneficial results occurred because of specific nonthermal effects.[144] It is widely accepted, however, that heat applied in the early stages following soft-tissue trauma may exacerbate the inflammatory response to injury. Thus, it is possible that patients in this study who were treated with heat either did not improve or got worse, whereas those who received PRF would have improved spontaneously without any treatment. This question could have been resolved if the design of the study had included a control group.

In a prospective, randomized, double-blind study, Pennington et al also evaluated the effects of nonthermal PRF (Diapulse) on pain and edema in 50 military personnel with grade I and II ankle sprains when PRF was applied between 1 and 24 hours, 25 and 48 hours, and 49 to 72 hours after the injury.[146] They found a statistically significant ($P < 0.01$) decrease in edema in ankles treated with an active PRF signal (4.7%) versus control ankles treated with an inactive PRF signal (0.95%). They also reported that pain was reduced by 64% and 33% in ankles treated with active and inactive PRF signals, respectively, and that the favorable outcomes resulted in a significant decrease in time loss from military training.

Additionally, double-blind clinical studies have been reported for acute ankle sprains, wherein PRF edema reduction was sevenfold versus the control group, and acute whiplash injuries, in which pain decreased by 50% and range of motion increased by 75% in the treated versus control patients.[147-149] In contrast to outcomes reported in the above-mentioned studies, Barker et al reported no significant differences between two groups of patients following nonthermal PRF treatment or placebo applications to acute ankle sprains with respect to range of motion, gait, pain, or swelling.[150]

Nonthermal PRF has also produced positive outcomes in the treatment of hand injuries and the accompanying inflammatory symptoms of pain, edema, and compromised function. Barclay et al evaluated 60 matched pairs of patients with hand injuries that had occurred within 36 hours of enrollment into his research study.[151] In the PRF-treated group, by the third day all but two of the patients had complete resolution of edema compared with the control group, whose swelling increased compared to baseline measurements. By the third day, 17 patients in the treatment group were symptom free, and by the seventh day only1 patient in the treatment group had slight loss of function while the other 30 patients had been discharged. In comparison, of the 30 patients in the control group, 3 had been discharged, while the other 27 were still symptomatic with pain, edema, and loss of function.

In a study on burn wounds treated with PRF, Ionescu et al observed that pain and edema formation were prevented and related local symptoms were reduced.[152] When the investigators compared samples of some proteins and enzymes found in normal and burned tissues before and after PRF therapy, they found that the enzymatic activities of skin decrease when the skin is traumatized or burned. Interestingly, they found that the enzymatic activity of the burned skin significantly improved after PRF treatment and that the sooner the treatment is administered after being burned, the sooner the normal enzyme activity is restored.

PEARL 27•18 With respect to the pain and swelling that accompanies trauma and burns and the associated loss of function, the three studies mentioned—Pennington,[146] Barclay,[155] and Ionescu[152]—have shown that early intervention with PRF during the inflammatory phase resulted in successful outcomes in terms of reduced pain, swelling, and earlier return to functional activities.

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A meta-analysis was performed on randomized clinical trials that used PEMF and PRF signals on injuries involving soft tissues and joints.[8] The results showed that both PEMF and PRF were effective in accelerating repair of soft tissue (closed wound) injuries,[146-149,153] as well as providing symptomatic relief in patients with osteoarthritis and other joint conditions.[25-27]

Nonthermal Pulsed Radio Frequency Chronic Open Wound Case Studies

The PRF signal configured a priori for the Ca/CaM pathway has been used with success for hundreds of chronic wounds, typically in long-term acute care facilities. The following series of case studies is typical of the results obtained with either clinic-only (Roma, Ivivi Technologies, Northvale, NJ) or portable/disposable (Torino, Ivivi Technologies, Northvale, NJ) devices. The hospital treatment regimen was typically two times daily manually and after discharge in a home setting automatically every 4 hours for the first 3 days, every 8 hours the next 3 days, and two times daily thereafter for the life of the

disposable unit (7–10 days), which is usually replaced at 6 to 7 days.

Nonthermal Pulsed Radio Frequency for Chronic Wound Healing—Clinical Research Reports

(Pressure Ulcers)

Duma-Drzewinska and Buczyski used a nonthermal PRF device at a mean power of 38 W for 20 minutes to treat 27 pressure ulcers, followed by a 15-minute application at a mean power of 15.2 W to the suprarenal and liver areas once or twice daily until complete wound healing was documented by photography.[154] Eleven of 12 superficial ulcers healed 100% in 4 weeks and 4 of 15 deep ulcers healed 100%. However, a much longer period of time was required to close the deep ulcers, but this time was not reported.

Studies have been reported in which PRF-treated pressure ulcers closed by 84% versus 40% closure in untreated wounds in one study and 60% closure versus no closure in the control group in another study.[155-156] In a double-blind study, Salzberg et al randomized 30 male spinal cord–injured patients with stage II and III pressure ulcers to receive two 30-minute treatments from either an active or a placebo nonthermal PRF device (Diapulse) for 12 weeks or until healed.[155] Ten patients with stage II ulcers were randomized to an active device and 10 others to a placebo device. The 10 patients with stage III ulcers were also evenly distributed to active and placebo devices. The 10 patients with stage II ulcers who were treated with the active device had a significantly shorter median time to complete healing of the ulcer (13.0 days) compared to that of the placebo group (31.5 days; $P = 0.002$). The stage III ulcers treated with an active device also healed faster than ulcers treated with the placebo device, but the small sample size precluded statistical analysis. Itoh et al reported the results from a case series study in which nonthermal PRF with Diapulse was used at 600 pps, a peak pulse power setting of 6 (38 W mean power) for 30 minutes two times daily, plus standard wound care to treat 9 stage II and 13 stage III pressure ulcers over a period of 9 months.[157] They reported that all 9 stage II ulcers healed in a mean of 2.3 weeks, after standard wound care had failed to heal them over a mean of 8 weeks. The 13 stage III ulcers that failed to heal over a mean of 35 weeks with standard wound care closed over a mean of almost 9 weeks.

Wilson reported on the results of an uncontrolled study in which 32 patients, ages 77 to 88 years, with 25 stage II, 11 stage III, and 14 stage IV refractory pressure ulcers were treated with PRF (Diapulse) for which no treatment parameters were mentioned.[158] Patients served as their own controls since all received standard wound care for several weeks up to 2 years prior to inclusion in the study. Clinically significant healing was observed for most wounds between 3 and 7 days. Although wound exudation increased in most wounds during the first 2 days of PRF treatment, it was minimal in all wounds by the third day of treatment. All except one wound closed, but that ulcer improved considerably before the patient died from other causes.

In a study involving 20 nonambulatory patients with pressure ulcers of the trochanter and sacrum, Seaborne et al randomized them into four groups of five for treatment with what they referred to as PSWD.[159] Each group was treated over a period of 7 days with one of four interventions, which included an electrostatic field at either 20 or 110 pps and PEMF (likely PRF) nonthermal at 20 and 119 pps. The number and duration of patient treatments was not reported. Using an ABAB multifactorial analysis, the investigators reported a highly significant decrease in wound surface area for each treatment group, without significant differences between the groups.

In a randomized, double-blind, placebo-controlled study, Ritz et al evaluated the wound healing effects of a PRF device (Provant® Wound-Closure System, Regenesis Biomedical Inc., Scottsdale, AZ) on 34 patients with chronic pressure ulcers, of which 60% were more than 6 months old.[160] Inclusion criteria were stage II and III pressure ulcers in patients who were 18 years of age or older. Exclusion criteria were change in Norton Risk Assessment score greater than or equal to 7 within 30 days; osteomyelitis; immune dysfunction or repeated systemic infection; cancer; concurrent treatment with other wound healing devices (eg, hyperbaric oxygen (HBO), electrical stimulation). Patients with stage II and stage III wounds were separately randomized to groups that received 30-minute twice-daily active PRF plus SWC or placebo PRF plus SWC. Patients and caregivers were blinded to group assignments. Patients were followed for 12 weeks, until wound closure, or until they were discharged. ANOVA, chi-square, and *t* tests were used as appropriate to determine alpha levels, set a priori at 0.05. PRF induced significantly more wound closures than did placebo. At 6 weeks, 100% of stage II active PRF wounds were closed compared to 36% of placebo-treated wounds, ($P \leq 0.005$). By 12 weeks, 64% of placebo wounds had closed. Stage II active PRF wounds healed 60% faster (26 days) than stage II placebo wounds (66 days, $P \leq 0.005$). At 12 weeks, 59% of stage III active PRF wounds were closed, compared to 14% for placebo wounds ($P \leq 0.01$). Active PRF wounds had an average 87% decrease in surface area compared to a 56% reduction for placebo wounds ($P \leq 0.05$). The results from this study suggest that PRF delivered by the Provant Wound Closure System accelerates closure of stage II and III pressure ulcers. (See Fig. 27.10) (The pressure ulcer studies described above are summarized in Table 27.3.)

Venous Leg Ulcers

Kenkre et al described the device they used on venous leg ulcers (VLU) as an "electromagnetic therapy" machine (Elmedistrall, United Kingdom) that generated perpendicular electric and magnetic fields delivered via a pulse generator capable of creating frequencies of 100, 600, or 800 Hz.[161] The pulsed current generated a magnetic field strength of 25 microteslas (μT), which was delivered to the patient through a pair of electrodes positioned on the patients' involved lower extremities by means of an elastic bandage. The parameters mentioned seem to classify this device as a PRF apparatus. The aim was to establish the potential efficacy, tolerability, and side effect profile of electromagnetic therapy as an adjunct to conventional dressings in the

Table 27•3 Pressure Ulcer Clinical Trials with Nonthermal Pulsed Radio Frequency

Condition Treated	Heat Dosage Level	Duration of Treatment	Frequency of Treatment	Heat Sensation Reported by Patient	Output of Energyfrom Device (%)	Rate of Tissue Temperature Rise (°C/min)	Tissue Temperature Increase Goal (°C)
Acute inflammation	1. Lowest	1–3 min	Daily 1–2 wks	None; dose is just below sensation of heat.	1/4 maximum output	0.4–0.8	37.5–38.5
Subacute inflammation	2. Low	3–5 min	Daily 1–2 wks	Barely felt	1/2 maximum output	0.8–1.2	38.5–40.0
Repair phase	3. Medium	5–7 min	Daily 1–2 wks	Distinct but pleasant heat sensation	3/4 maximum output	1.2–2.0	40.0–42.0
Chronic conditions	4. High	5–7 min	Daily or 2/wk for 1 wk to 1 mo	Definite heat sensation, well within tolerance	3/4 maximum output	2.0–2.7	42.0–44.0

treatment of VLUs. Nineteen patients who demonstrated unsatisfactory healing for at least the previous 4 weeks were randomized to active or placebo PRF treatment. All patients received a 30-minute treatment on weekdays for a total of 30 days, after which patients were followed during a 4-week observation period, with dressing changes only, and final assessment on day 50. Of the 19 patients recruited, 9 were treated with the placebo device, one group of 5 was treated with active 600 Hz, and a second group of 5 received active 800 Hz. Sixty-eight percent of patients treated with active PRF devices achieved improvements in ulcer size, and 21% closed completely. At day 50 patients treated with electromagnetic therapy at 800 Hz were found to have significantly greater healing ($P < 0.05$) and pain control ($P < 0.05$) than placebo therapy or treatment with 600 Hz. All patients reported improved mobility at the end of the study. The electromagnetic therapy was well tolerated by patients, with no differences between groups in reporting adverse events. This study is summarized in Box 27.1.

Diabetic Foot Ulcers

A recent case study by Larsen and Overstreet was found in which two patients with complex diabetic ankle and/or foot ulcers were treated with electromagnetic energy from a PRF device (Provant Wound Therapy System).[162] (Fig. 27-9) One case, a 59-year-old male with a 24-month history of a refractory wound over his left Achilles tendon had a 14-year history of poorly controlled type I diabetes mellitus, anemia, and hypertension. Over the previous 2 years of treatment, consisting of débridement, serial custom orthotics, silver-impregnated dressings, and platelet-derived growth factor (Regranex, Ortho McNeil Pharmaceuticals, Sommerville, NJ), the wound size increased with the development of a second adjacent wound. Adjunctive PRF treatment of 30 minutes twice a day was initiated when the patient's glycosylated hemoglobin levels (HbA_{1c}) was 12.9% and the combined surface area of his two Achilles tendon wounds was 1.75 cm^2. Other interventions included off-loading, sharp débridement, and silver-based and petrolatum gauze dressings. After the first 10 weeks of therapy, the wound decreased in surface area by 54.3%. In spite of poor glucose control (HbA_{1c} varied from 8.0% to 10.3%), the wound closed in 16 weeks at a healing rate of 1.56 mm^2/day and remained closed at a 9-month follow-up.

A second case involved a 79-year-old male with a right transmetatarsal (2-5) amputation that was performed for a draining, conspicuously infected, second toe, with underlying osteomyelitis. The patient presented 3 days postoperatively with a wide dehiscence of the surgical site that measured 7 cm^2 in surface area and was noticeably inflamed. Collectively, he had several other conditions that could be considered impediments to healing, including obesity, hypertension, type II diabetes mellitus, a history of peripheral neuropathy, posttraumatic stress disorder, chronic obstructive pulmonary disease, and colon cancer. His HbA_{1c} was within normal limits at 6.2%. Treatment of his wound consisted of débridement, off-loading, silver-based dressings, and PRF 30 minutes twice a day. The wound closed within 16.7 weeks at a healing rate of 6.0 mm^2/day and remained closed at a 7-month follow-up. In these two cases, patients received comprehensive standard wound care without alteration, other than the addition of PRF therapy. Although these reports are anecdotal, the results suggest that PRF treatment may have prevented amputation, possibly by enhancing blood perfusion.

Nonthermal Pulsed Radio Frequency—Blood Perfusion Studies

Regarding PRF and blood perfusion, Mayrovitz and Larsen conducted a study on the effects of nonthermal PRF (MRT SofPulse) on microvascular perfusion in healthy individuals

by exposing the right forearms of nine men and women to PRF having a pulse duration of 65 μsec, a pulse frequency of 600 pps, and a duty cycle of 0.039 for 45 minutes.[163] After 40 minutes with laser Doppler instrumentation, they recorded a 29% increase in cutaneous blood perfusion compared with no change in perfusion in the left (control) forearms. In a second study, the same investigators evaluated the effects of PRF (MRT SofPulse) on perfusion in periwound skin of 15 subjects who had had diabetes for at least 5 years and each of whom had an ulcer on the foot or toe of one lower extremity for a minimum of 8 weeks.[164] The intact contralateral lower limb served as the control. Noninvasive vascular testing revealed that 9 subjects had peripheral arterial disease in the ulcer-bearing limb; however, these limbs had pretreatment perfusion and volume much greater than the control limb. With PRF parameters of 65 μsec, 600 pps at peak power, and the induction coil 1.5 cm above the ulcer surface, and a single 45-minute treatment at the periulcer site, an increase in laser Doppler perfusion occurred due mainly to an increase in blood volume. There was no change in any laser Doppler parameter at the contralateral control site nor was there an increase in skin temperature at either site. These findings suggest that if resting perfusion is marginally insufficient to allow timely ulcer healing, an increase in perfusion secondary to PRF stimulation may enhance perfusion enough to allow ulcer healing.

Unlike the previous study by Mayrovitz and Larsen who applied PRF directly over periwound skin,[164] Erdman used the consensual or indirect approach by applying nonthermal PRF from the inductive coil of Diapulse over the epigastrium to see if blood flow changes occurred to the feet of 20 healthy young adults.[165] Using cutaneous thermometry he measured an increase in foot temperature of 2.0°C and an average blood volume increase of 1.75-fold at the maximum power output settings. There were no changes in rectal temperatures or pulse rates. The foot-warming effect continued for a short time after the treatment was terminated. These findings suggest that PRF may be applied remotely over the epigastrium to elicit enhanced perfusion to the distal lower extremities.

Nonthermal Pulsed Radio Frequency—Postsurgical Wounds

Goldin et al conducted a controlled, double-blind clinical study that compared donor sites of medium-thickness split-skin grafts treated with an active nonthermal PRF device ($N = 29$) with control donor sites treated with a placebo PRF device ($N = 38$).[166] Patients in both groups received a 30-minute treatment before receiving medication prior to surgery and then received a 1-hour treatment daily for 7 days after surgery. The active PRF treatment group received a peak output of 975 W at a frequency of 400 pps and a pulse duration of 65 μsec. The mean power output was 25.3 W. Wounds were evaluated daily by medical staff unaware of the patients' grouping. On the seventh postoperative day, dressings were removed and the percentage of wound area healed was determined. In the active treatment group, 17 of 29 patients had wounds that were healed 90% or more, compared with only 11 of 38 patients in the placebo group. Data analysis revealed that this difference was statistically significant.

Cameron reported favorable results in postsurgical wound healing from a "double-blind" study using Diapulse in which 100 patients were assigned to an active PRF group or a placebo PRF group.[167] The credibility of the reported findings from this study is uncertain because many results were based on observational subjectivity, and other interventions were used along with PRF, making it difficult to evaluate the effects of PRF.

In a study of 100 patients who received a variety of podiatric surgical procedures (fewer than five), Kaplan and Weinstock randomly applied placebo or active nonthermal PRF postsurgically with Diapulse.[168] They delivered PRF to the epigastrium with the signal frequency set at 400 pps and to the surgical site with the frequency set at 600 pps. The power levels and treatment durations for the two treatment sites were 4 for 15 minutes and 6 for 15 minutes, respectively. A modified Likert scale was used to grade the tissues for pain, edema, and erythema. A drawback to this study is that they descriptively reported significant reductions in severe to moderate edema for the active PRF group on the third postoperative day (80%) versus the placebo group (58%), but reported nothing regarding the effects of PRF on pain or erythema.

The use of nonthermal PRF (Diapulse) to reduce pain and edema and improve the rate of soft-tissue healing has also been reported following dental surgical procedures. In a nonrandomized controlled trial, Aronofsky divided 90 patients who had had dental surgery into three groups of 30.[169] One group was treated with active PRF for 72 hours, both preoperatively and postoperatively; a second group was treated with active PRF 72 hours only postoperatively, and a third group that served as controls received placebo PRF. PRF pulse frequency was set at 600 pps and peak power output. Patients in both active PRF groups reportedly exhibited substantially less time for their wounds to heal compared to wounds of patients in the control group, and inflammation and pain were absent at 72 hours for the preoperative/postoperative and postoperative treatment groups.

In a double-blind clinical trial, Bentall and Eckstein used both the indirect and direct application methods of transmitting PRF (Diapulse) to the epigastrium and scrotum of 50 pairs of boys who had undergone orchidopexy.[153] One boy in each pair served as the control. The objective was to assess the effects of PRF on postsurgical bruising and edema. Repeated circumferential measurements and pictures of the scrotum were recorded before and after surgery. PRF pulse frequency was set at 500 pps with the intensity at level 5 for 20 minutes over the scrotum and at 500 pps and intensity at 4 over the epigastrium for 10 minutes. The treatment protocol was performed three times daily for the first 4 postoperative days. The investigators reported a trend toward reduced edema buildup and significantly enhanced reduction of posttraumatic bruising.

One other noncontrolled study by Comorosan et al also used the indirect and direct methods of transmitting nonthermal PRF (Diapulse) over the epigastrium and the postsurgical trauma site.[170] They selected 15 patients to be treated with

PRF and 10 others who served as controls. They initiated treatment on the second postoperative day and continued for 5 successive days. PRF was transmitted to the postsurgical site at 600 pps and maximum power output for 20 minutes, followed by epigastric application at 400 pps at a power level of 4 for 10 minutes. The criteria used to evaluate the effects of PRF included disappearance of edema, hematoma, and parietal seroma; lack of inflammation and infection; presence or absence of keloid scaring; and the level of postoperative site sensitivity. Subjectively, the investigators reported that after 5 days, all of these characteristics were noticeably improved. The credibility of the reported findings from this study is uncertain because results were based on observational subjectivity. A summary of these studies is presented in Table 27.4.

Case Study 27•1

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Sixty-year-old male; episternal after post cardiac surgery. (see Figs. 27.14 and 27.15)

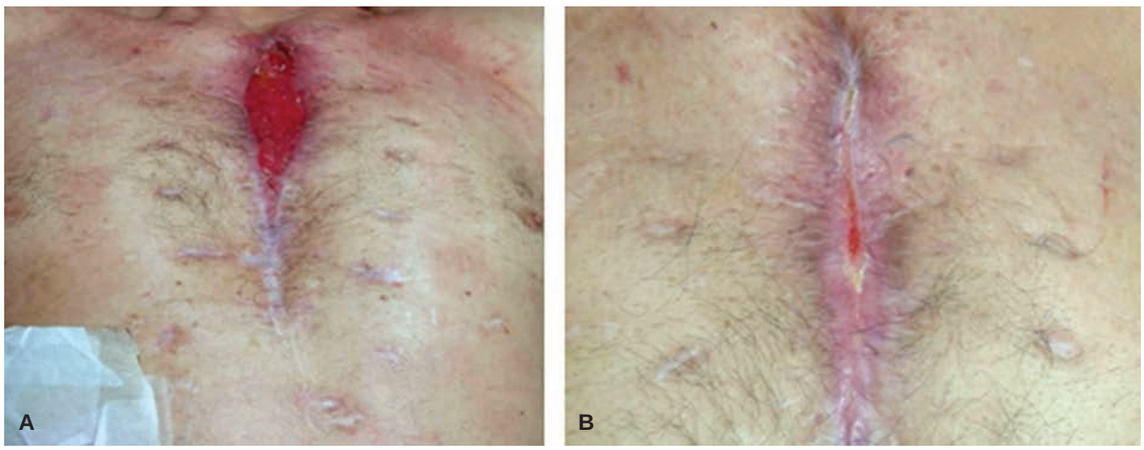

Figure 27•15 *Case 1: (A) Progress at 4 weeks after discharge using disposable PRF unit. (B) Wound resolved at 8 weeks. Therapy regimen was as described in Figure 27.14.*

Case Study 27•2

Seventy-nine-year-old female; large open wound secondary to right mastectomy for papillary carcinoma; NPWT in place at admission; discontinued due to pain. (Fig 27.16)

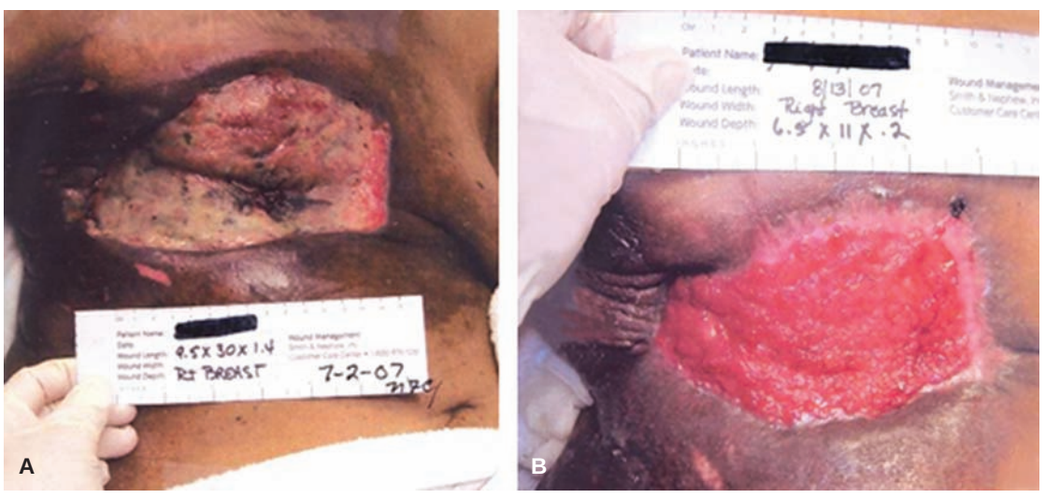

Figure 27•16 *Case 2: (A) Wound at admission; treated 30 minutes every 4 hours with disposable PRF device (see Figure 27.14B). (B) Wound after 41 days of treatment; wound volume had decreased by 96%; patient deferred graft and was discharged. (Courtesy NF Cher, RN, MSA, CWOCN, Regency Hospital, Macon, GA.)*

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Table 27•4 Postsurgical Clinical Trials with Nonthermal Pulsed Radio Frequency

Investigator	Ieran, Zaffuto, Bagnacani[130]	Duran et al[131]	Todd et al[132]	Stiller et al[133]	Canedo-Dorantes et al[134]	Kenkre et al[161]
Study design	DB-CT	Observational	DB-RCT	DB-RCT	Before-after	DB-RCT
Type of device	PEMF	PEMF	PEMF	PEMF	PEMF (ELF)	PRF
Frequency	75 Hz	Not reported	5 Hz	25% duty cycle	Not reported	600 Hz 800 Hz
Amplitude	2.8 mT	Not reported	Field strength 60 (units not reported)	0.06 mV/cm 22 G	Field strength 36.36 G	25 μT
Treatment duration	4 hr/day for 90 consecutive days	15 min for 10 treatments	15 min 2/wk for 5 wks	3 hrs/day for 8 weeks	2–3 hrs, 3/wk for 4 mo	30 min 5/wk for 30 days
Treatment effect	Wounds closed: 66% exp 31% control	33% decrease in mean surface area	Mean decrease of ulcer size was 7% for both exp and controls. Girth of ulcerated leg: Exp: decrease 2.8% Control: increase 1.2%	*Wound surface area:* Exp 47.1% decrease Control 48.7 decrease *Wound depth decrease:* Exp 46% Control 3.8% *Granulation quality and quantity:* Exp 14.1% decrease in unhealthy granulation Control 0% decrease *Clinical assessment based on 8-point scale:* Exp 50% closed Control 54% worse	After 4 mo, 69% of all wounds either closed or had decreased in size >50%.	*Wound surface area:* Placebo Group: ↓14.2% 20 days ↓21.8% 30 days 600-Hz Group: ↑28.2% 20 days ↑76% 30 days 800-Hz group: ↓24.7% 20 days ↓38% 30 days
Posttreatment effect	Wounds closed: 89% exp 42% controls					Day 50 800-Hz group had significantly greater healing (63%) than placebo group (34%).
Method of measurement	Wound closure	Decrease in wound surface area	Decrease in wound surface area	Wound characteristics	Decrease in wound surface area	Decrease in wound surface area
Wound etiology and number	Venous ulcers *N* = 44	Venous ulcers *N* = 18	Venous ulcers *N* = 19	Venous ulcers *N* = 31	Venous and arterial ulcers *N* = 42	Venous leg ulcers *N* = 19

Modified with permission from Sussman, C: Induced electrical stimulation: Pulsed radio frequency and pulsed electromagnetic fields. In: Sussman, C, Bates-Jensen, B (eds): Wound Care: A Collaborative Practice Manual for Health Professionals, ed. 3. Philadelphia, Lippincott Williams & Wilkins, 2007, p 570. .
DB-CT = double blind controlled trial; DB-RCT = double blind randomized controlled trial

Case Study 27•3

A patient admitted with open venous insufficiency wounds; standard treatment started 11/06; wounds nonhealing despite conservative therapy. (Fig. 27.17)

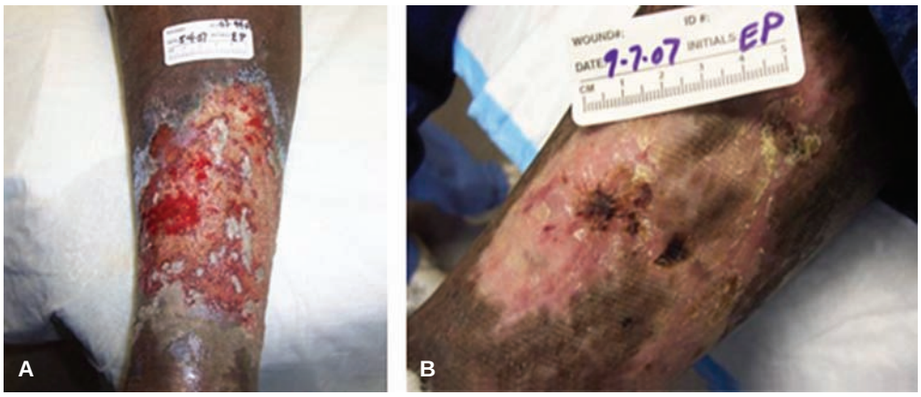

Figure 27•17 *Case 3: (A) Wound after 10 months conservative treatment; PRF with disposable unit is started (B) Healed at 12 weeks with no recurrence as of spring 2008. (Courtesy P. Justice RN, CWS, FACCWS, Indian Health Service, Skiatook, OK.)*

Summary Regarding Pulsed Radio Frequencies

The technology of pulsed radio frequencies has certainly advanced due to a greater understanding of the mechanism of action of EMF therapeutic signals. The clinician has at hand a powerful armamentarium of PRF tools that allow greater treatment flexibility and use with a wider array of patients, at the same time reducing the cost of health care. The clinical wound healing results presented here strongly suggest that PRF therapy has considerably advanced. Portable, even disposable, economical devices are now available for all aspects of wound repair. Although FDA regulatory clearance restricts PRF indications to postoperative pain and edema reduction, it is clear that all stages of wound repair appear to be modulated by specifically configured PRF signals.

Pulsed Shortwave Diathermy—Mild Thermal Effects on Wound Healing

At the beginning of the chapter, we addressed modulation of the RF carrier wave (27.12 MHz) that is used to produce nonthermal PEMF, PRF, and pulsed shortwave diathermy (PSWD) treatment signals. We said that depending on the average power delivered to the body by these pulses of RF energy, tissue temperature may or may not increase. Some of the effects of PRF and PSWD on wound healing are shown in Table 27.5.

PEARL 27•19 As we have seen prior to this section, both PEMF and PRF devices produce mean power outputs less than 38 watts that classify them as being nonthermal and therefore capable of having nonthermal effects on tissues. On the other hand, RF devices that have higher average power outputs between 38 and 80 watts (PSWD) are capable of elevating tissue temperature to produce mild thermal effects (38°–40°C) in superficial to deep absorbing wound tissues that are vascularized sufficiently to dissipate the mild heat.[171]

Continuous Shortwave Diathermy Versus Pulsed Shortwave Diathermy

Both continuous shortwave diathermy (CSWD) and pulsed shortwave diathermy (PSWD) use the 27.12-MHz RF carrier frequency. CSWD may be used safely on individuals who are sensate and can respond to painful stimuli and who have blood perfusion that is sufficient to dissipate local and regional heating through blood flow. In patients with arterial insufficiency of the extremities (peripheral arterial disease), heating is contraindicated because of poor heat dissipation, which places them at higher risk for burns.[174] PSWD has frequency rates between 1 and 7000 pps, and the pulse duration varies between 65 and 400 μsec. The combination of longer pulse durations and higher frequencies provide more energy to the tissues, which results in a greater thermal effect. The clinical use of the thermal effects of CSWD and thermal/nonthermal effects of PRF may be

Table 27•5 Effects of Pulsed Shortwave Diathermy and Pulsed Radio Frequency on Wound Healing

Investigator	Goldin et al[166]	Cameron[167]	Kaplan and Weinstock[168]	Aronofsky[169]	Comorosan, Paslaru, and Popovici[170]
Study design	DB-RCT	Study 1: DB controlled Study 2: Uncontrolled	DB-RCT	CT (nonrandomized, unblinded)	CT
Type of device	PRF (Diapulse)	PRF (Diapulse)	PRF (Diapulse)	PRF (Diapulse)	PRF (Diapulse)
Frequency	400 pps/600 pps 65 μsec	400 pps 65 μsec	400 pps/600 pps 65 μsec	600 pps 65 μsec	400 pps/600 pps 65 μsec
Amplitude	25.3 W/38 W	Med power (4)	Peak power (6) Med power (4)	Peak power	Peak power (6) Med power (4)
Treatment duration	10 min hepatic 20 min wound every 6 hrs for 7 days	Study 1: 20 min hepatic 20 min wound Twice a day for 4 days Study 2: Same as in study 1	30 min postsurgery and 4 hrs later	Gr 1: 15 min 24 hrs preoperative and 10 min preoperative Postoperative: 24, 48, 72 hrs Gr 2: 10 min postoperative Postoperative: 24, 48, 72 hrs Gr 3: no PRF	10 min hepatic 15 min wound
Treatment effect	90% or more healing for 59 % of treatment group 29% healing for placebo group (NS)	Study 1: Treatment group little improvement for abdominal incision re suture removal; all others had sutures removed on fifth postoperative day. Study 2: Shorter hospital stay for treatment group	Postoperative day 3: Severe/moderate edema Exp: 80% ↓ edema Placebo: 58% ↓ edema	Inflammation 72 hrs post operative: Gr 1: None 75% Mod 20% High 30% Gr 3: None 2% Mod 57% High: 37% Pain 72 hrs post operative: Gr 1: None 63% Mod 30% High 6.7% Gr 3: None 7% Mod 57% High 37% Healing group 1: 3–5 days post operative Group 2: 5–7 days post operative Group 3: 10–12 days post operative	Plasma: fibronectin concentration ↑ on postoperative day 7 in treatment group; lower than baseline in control group
Method of measurement	Degree of pain	Retrospective review of medical records Subjective measurements	Likert-like scale grading for edema, erythema, pain	Not reported	Observation of inflammation/infection processes, scar formation, and laboratory measurements
Wound etiology and number	Split-thickness skin graft donor sites *N* = 29 Exp *N* = 38 placebo	Heterogeneous surgical wounds *N* study 1 = 100 *N* study 2 = 81	Postsurgical podiatric patients	Oral surgery *N* = 90 (30/group)	Heterogeneous surgical wounds *N* = 15 Exp *N* = 10 Control

Modified with permission from Sussman, C: Induced electrical stimulation: Pulsed radio frequency and pulsed electromagnetic fields. In: Sussman, C, Bates-Jensen, B (eds): Wound Care: A Collaborative Practice Manual for Health Professionals, ed. 3. Philadelphia, Lippincott Williams & Wilkins, 2007, p 561.
DB-RCT = double blind randomized controlled trial; CT = controlled trial

divided into two categories: (1) functional restoration and analgesia and (2) facilitation of healing of acutely injured soft tissue and chronic dermal ulcerations.

PEARL 27•20 When the RF carrier is not interrupted into pulses or bursts of energy, it is called CSWD, which generally has a power output range between 55 and 500 watts,[172] and is capable of raising the temperature of deep, well-vascularized soft tissues to between 38°C and 45°C for enhancing the resiliency of structures that have a high collagen content.[173]

Rationale for Treating Wounds with Mild Thermal Energy (Pulsed Shortwave Diathermy)

The beneficial effects of heat on tissue healing have been recognized for centuries. The literature on the history of medicine has long made reference to the use of a variety of heat methods to treat wounds. Early civilizations used various heat applications to promote drainage and healing of boils, provide analgesia, and limit the spread of infection. Hippocrates himself once said, "Wounds love warmth; naturally, because they exist under shelter; and naturally they suffer from the opposite."[175]

PEARL 27•21 Increasing wound and periwound tissue temperature increases oxygen delivery, and oxygen uptake increases subsequent to an increase in blood perfusion.[176-180]

These findings are especially important with respect to tissue healing because, in addition to subcutaneous oxygen tension being correlated with tissue perfusion, it is also correlated with an increased resistance to infection and acceleration of wound healing.[176-188] Moreover, through its effect on fibroblasts, tissue oxygen tension impacts collagen deposition and scar tensile strength and, through oxidative killing, is an important defense against pathogens that colonize wounds.[189-192] In an experimental study on rats, Ninnikoski et al found that when the temperature of the wound area in ischemic wounds was intermittently elevated by infrared heat,[193] a statistically significant increase in healing rate was observed. They proposed that the increased rate of healing in response to heat was due to increased blood perfusion and oxygen delivery to the wound tissues.

Bello et al measured the temperature of wound tissue and periwound skin and found that compared to body core temperature, average wound and periwound skin temperatures were 5.6°F and 4.5°F cooler, respectively, than core temperature.[194] They proposed that because of the relatively low temperature of wound and periwound tissues, a controlled level of heat applied to these tissues could be beneficial to wound healing. In fact, Kloth et al and others have reported positive wound healing outcomes from mild thermal effects produced by an infrared device that maintained the wound temperature at 38°C.[195-197]

Suggested Protocols for Pulsed Shortwave Diathermy Treatment of Wounds

Based on the earlier definitions of mild and vigorous tissue heating by Lehman and deLateur,[173] Kloth and Ziskin proposed a protocol for the adjunctive use of PSWD for wound healing in the acute, subacute, and chronic inflammatory phases of healing.[198] They divided PSWD power output into four dosage levels that corresponded to percentages of maximum output: level 1 (lowest, subthermal); level 2 (low, mild heat sensation); level 3 (medium, moderate, comfortable heat sensation); and level 4 (high, vigorous heating, well tolerated, decrease to just below maximum tolerance). Table 27.6 shows the lowest- and low-thermal dosage levels of PSWD that may be use at the discretion of the clinician to enhance healing of well-vascularized wounds.

Pulsed Shortwave Diathermy Blood Flow Studies on Healthy Subjects

Some PSWD devices allow selection of parameters that provide mild heating of tissues. Examples of such devices are the Magnatherm SSP® (International Medical Electronics, Kansas City, MO) and the Megapulse® II (Accelerated Care Plus, Reno, NV). (Figs. 27.18 and 27.19) The Magnatherm SSP device has two treatment applicators designed to allow each to be set at the same or different thermal dosages. Heating effects are produced at high pulse frequencies and long pulse durations, whereas nonthermal effects are produced at low pulse frequencies and short

Figure 27•18 *Magnatherm SSP diathermy device that has the capability for mild tissue heating (PSWD) and vigorous tissue heating (CSWD). (Courtesy of International Medical Electronics Ltd., Kansas City, MO.)*

Table 27•6 Dosage Guide for Diathermy Treatments.

Investigator	Salzberg et al [155]	Iltoh et al[157]	Wilson[158]	Seaborne, Quirion-DeGirardi, and Rousseau[159]	Ritz et al[160]
Study design	DB-RCT	Uncontrolled Unblinded	Uncontrolled	Blinded RCT	Prospective, DB, RCT, placebo controlled
Type of device	PRF (Diapulse)	PRF (Diapulse)	PRF (Diapulse)	ES vs PRF	PRF (Provant)
Frequency	600 pps 65 μsec	600 pps 65 μsec	Not reported	20 pps ES 110 pps ES 20 Hz PRF 110 Hz PRF	Not reported
Amplitude	Peak power	Peak power	Not reported	Not reported	Not reported
Treatment duration	30 min twice daily for 12 wks	30 min twice daily	Not reported	Not reported	30 min twice daily for 12 wks
Treatment effect	Stage II Exp group: 84% closed at 1 wk Median no. days to complete closure = 13 Placebo group: 40% closed at 1 wk Median no. days to closure = 31.5 Stage III ulcer area Exp group: Wounds decreased in size mean of 70.6% Placebo group: Wounds decreased in size 20.7%	All wounds closed. Stage II mean size = 5.56 cm^2. Closed mean of 2.33 wks Stage III mean size = 8.78 cm^2 Mean healing/wk: Stage II 57% Stage III 8.9%	Initial increase in wound exudates 1–2 days. All wounds closed except 1.	All groups demonstrated highly significant decrease in wound surface area. No statistical difference between groups.	Stage II Exp group: At 6 wks 100% closed vs 36% for placebo. Stage III Exp group: At 12 wks 50% closed vs 14% for placebo.
Method of measurement	Wound area	Wound area	Observational	Wound area	Wound area
Wound etiology and number	Pressure ulcers/SCI *N* = 10 stage II *N* = 10 stage III	Pressure ulcers *N* = 9 stage II *N* = 13 stage III	Pressure ulcers *N* = 25 stage II, *N* = 11 stage III, *N* = 14 stage IV	Pressure ulcers *N* = 20 (4 groups of 5)	Pressure ulcers *N* = 19 stage II 15 stage III

Modified with permission from Kloth, L, Ziskin, M: Diathermy and pulsed radiofrequency radiation. In: Michlovitz, S (ed): Thermal Agents in Rehabilitation, ed. 3. Philadelphia, F.A. Davis, 1996, p 188.
DB-RCT = double blind randomized controlled trial; RCT = randomized controlled trial

Figure 27•19 *Magnapulse II diathermy device that has the capability for nonthermal PRF, mild thermal PSWD, and vigorous heating (CSWD). (Courtesy of Accelerated Care Plus, Reno, NV.)*

pulse durations. The Megapulse II device also provides several pulse-frequency and pulse-duration options for producing thermal and nonthermal effects in soft tissues.

In reviewing the literature related to the use of PSWD to enhance blood flow, only three studies were found. Silverman and Pendleton compared the effects of CSWD and PSWD on lower-extremity perfusion in healthy young adults.[199] They used plethysmography to measure blood flow changes to the calf and foot and also measured skin temperature before and after indirect applications of PSWD or CSWD to the abdominal area. Following 20 minutes of both CSWD and PSWD independently set at a high mean power setting of 65W and 2400 pps or low mean power of 15 W and 600 pps, they recorded mean increases in foot circulation of 165% with PSWD and 195% with CSWD, both at the high mean power settings. No circulatory changes occurred with either device at the low power setting. The mean skin temperature increase was 5.3°C with CSWD and 5.8°C with PSWD. The foot temperature increased 1.9°C and 2.2°C, respectively. The skin of the abdomen of subjects who received low power increased 3.1°C and 3.4°C, respectively, for CSWD and PSWD. These changes in temperature and blood flow are statistically significant, which verifies the thermal capability of PSWD. However, the differences between the CSWD and PSWD devices were not statistically significant,

In another study that evaluated the effects of diathermy on lower-extremity perfusion, Santoro et al applied thermal PSWD to the legs of 10 patients diagnosed with moderate to severe peripheral arterial disease.[200] They delivered PSWD via two coil applicators to the plantar surface of the foot and the ipsilateral midanterior thigh simultaneously for 30 minutes, 5 days a week, for 20 days over 1 month. For patients with both limbs affected, both coil applicators were placed over the plantar surfaces of both feet. During the first 20 minutes of the protocol, the PSWD device was set at 100% of its maximum power output (95 µsec pulse duration and 7000 pps). During the remaining 10 minutes, the power output was reduced to 10% of maximum (95 µsec pulse duration and 700 pps), which was described as a "cooling phase." In five patients they measured skin temperature, $TcPO_2$, and segmental Doppler blood pressure and superficial blood flow with a laser Doppler flowmeter. In these five patients, the percentage of change between the pre-$TcPO_2$ and post-$TcPO_2$ measurements was insignificant in the treated limb, but significant in the untreated limb ($P < 0.0001$). They suggested that the untreated limb could have experienced reflex vasodilation owing to circulation of warmed blood and sympathetic nerve activity. Subjectively, 60% of the patients felt the treatments helped them to walk farther, especially following treatment. However, no long-term vasodilation effects were detected over the 1-month of treatment.

In a randomized study, Santiesteban and Grant used PSWD at a dosage of 700 pps and a power setting of 12 (approximately 120 W) to treat 25 patients, either immediately after or 4 hours after foot surgery.[201] Two coil applicators were used, with one placed over the plantar surface of the postoperative foot and the other over the ipsilateral inguinal area. If foot surgery was bilateral, the coil applicators were placed over the plantar surfaces of both feet. They reported that patients who received the treatment had hospital stays that averaged 8 hours shorter and required lower dosages of analgesic medications than did 25 patients in the control group. Although these investigators did not measure blood flow, it is possible that enhanced perfusion secondary to heating led to improvement of patients who were discharged earlier.

Safety Concerns

Pulsed Radio Frequency

Because PRF signals can interfere with electronic devices, for example, hearing aids and watches, ask patients to remove such devices before treating them with PRF. Also, avoid applying PRF over metal objects on the patients or in their clothing, because the signal will reflect the energy away from the intended tissue target.

Pulsed Shortwave Diathermy

In addition to the safety concerns mentioned for PRF, the presence of metal in the patient (eg, orthopedic hardware, shrapnel) or in contact with the patient (jewelry, zippers, bra fasteners and underwires, metal bed parts) should not be in the PSWD field because they can be selectively heated and cause burns. PSWD can also melt or ignite synthetic materials such as some types of patient clothing. Because of the potential for excessively heating a moist dressing in the wound, which could cause wound tissue burning, prior to performing the PSWD treatment of a wound the clinician should replace any moist dressings with a dry sterile gauze dressing. If the wound is likely to produce significant

exudates that will moisten the dry gauze during the PSWD treatment, stop the treatment as often as needed and replace the moist dressing with a dry one.

Clinician Safety

Some older PRF and PSWD devices may not have adequate shielding around device applicators and cables, allowing some energy to be dissipated into the immediate area close to the equipment. Normally, clinicians in close proximity to the equipment will absorb a small amount of EMF energy when they are within 0.5 m from the cables and 0.2 m from the inductive coil treatment applicators. When clinicians are at least 1.0 m from the applicator and 0.5 m from the cables during operation of the device, there is little danger of absorbing harmful energy.[202] Table 27.7 lists FDA contraindications, warnings, and cautions for PRF and PSWD.

Summary

Both nonthermal PEMF and thermal / nonthermal PRF technologies have important clinical applications to pain suppression and facilitation of tissue healing. The biophysical effects of these electromagnetic energies is a function of the time varying parameters of the signals that are transmitted to the target tissues. Various conditions for which PEMF and continuous and pulsed PRF are beneficial have been discussed.

Table 27•7 FDA Contraindications, Warnings, and Cautions for Pulsed Radio Frequency and Pulsed Shortwave Diathermy

PSWD	PRF
Do not treat over ischemic tissue with inadequate blood flow.	Do not use as a substitute for treatment of internal organs.
Do not treat over metallic implants.	Do not use on patients who have any implanted metallic lead or wire, or any implanted system that may contain a metallic lead including devices such as pacemakers. This device and related diathermy devices may have adverse effects on electronic pacemakers or implanted defibrillators in cardiac patients, and on nerve stimulators.
Do not use over metal implants.	Do not use on patients who are pregnant.
Do not use on patients with cardiac pacemakers.	Do not treat over immature bone.
Do not treat in any region where the presence of primary or metastatic growth is known or suspected.	
Do not treat over immature bone.	
Do not treat over acute osteomyelitis without adequate drainage or before adequate drainage has been established.	
Do not treat patients who have a tendency to hemorrhage (including menses).	
Do not treat over pelvic or abdominal region or lower back during pregnancy.	
Do not treat transcerebrally.	
Do not use over anesthetized areas.	
Avoid situations that could concentrate the field, including moist dressings, perspiration, adhesives.	
Use caution when treating patients with heat sensitivity.	
Use caution when treating patients with inflammatory processes.	

Data from International Medical Electronics, Magnatherm® Model 1000 Instruction Manual (International Medical Electronics, Kansas City, MO) and Electropharmacology, MRT® sofPulse™ User's Manual (MRT, Boca Raton, FL).

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