Electromagnetic Biology and Medicine, 30(1): 21–45, 2011

ISSN: 1536-8378 print / 1536-8386 online
DOI: 10.3109/15368378.2011.566775

informa
healthcare

Pulsed radio frequency energy (PRFE) use in human medical applications

Lifei Guo[1], Nicole J. Kubat[2] & Richard A. Isenberg[2]

[1]Division of Plastic Surgery, Brigham and Women's Hospital, Boston, Massachusetts, USA, and [2]Regenesis Biomedical Inc., Scottsdale, Arizona, USA

A number of electromagnetic field-based technologies are available for therapeutic medical applications. These therapies can be broken down into different categories based on technical parameters employed and type of clinical application. Pulsed radio frequency energy (PRFE) therapy is a non invasive, electromagnetic field-based therapeutic that is based on delivery of pulsed, shortwave radio frequency energy in the 13–27.12 MHz carrier frequency range, and designed for local application to a target tissue without the intended generation of deep heat. It has been studied for use in a number of clinical applications, including as a palliative treatment for both postoperative and non postoperative pain and edema, as well as in wound healing applications. This review provides an introduction to the therapy, a summary of clinical efficacy studies using the therapy in specific applications, and an overview of treatment-related safety.

Keywords Postoperative pain and edema, Non postoperative pain and edema, Wound healing, Clinical efficacy studies, Safety, Electromagnetic field, Radio frequency

INTRODUCTION

In modern day society, the biological impact mediated by exposure to electromagnetic fields (EMF) is a topic of significant interest, both for reasons related to understanding potential effects of commonly encountered manmade sources of EMF (such as cell phones), as well as from a beneficial perspective of exploiting EMF for use in medical applications.

The electromagnetic spectrum spans from low-frequency radio waves to microwaves, to the mid-range frequencies of ultraviolet, visible light, and infrared, to the high frequency forms of radiation of x-rays and gamma rays. In the case of EMF-based medical applications, specific biological effects are dependent not only on the wavelength/frequency used within the electromagnetic spectrum, but also on numerous other parameters, both exogenous (technology-related) parameters (i.e., field strength, energy exposure, mode of delivery) as well as endogenous parameters related to the patient/target tissue (i.e., anatomical and pathological variables). Thus, both the efficacy and safety of a given EMF application depend on these and other such variables.

Address correspondence to Richard A. Isenberg, Regenesis Biomedical Inc., 1435 North Hayden Road, Scottsdale, AZ 85257-3773, USA; E-mail:isenberg@regenesisbio.com

SHORTWAVE RADIO FREQUENCY-BASED MEDICAL APPLICATIONS

Therapeutic medical application of radio frequency (RF) energy at a carrier frequency between 13–27.12 MHz is referred to as shortwave diathermy[1,2] and can be divided into two general categories based on mode of delivery: continuous RF energy delivery and pulsed RF energy delivery. Continuous delivery of shortwave energy to a tissue leads to an increase in tissue temperature, and is used for the therapeutic delivery of deep heat. Delivery of pulsed RF energy to a tissue can allow for the dissipation of heat between pulses, providing therapeutic effects in the absence of substantial tissue temperature elevation, a therapy first developed to diminish negative complications that can occur with tissue heating, while conserving other therapeutic benefits of this type of application. Pulsed RF energy has a wide range of therapeutic uses, is well tolerated due to the non-invasive nature of application, and serves as an effective adjunctive treatment for many conditions.

Nomenclature

Multiple terminologies exist to identify electromagnetic field-based modalities and treatments. For shortwave applications, there is a historical relevancy to the current use of multiple names for sometimes similar or near-identical therapies. The term *diathermy* (meaning *heating through*) was first used in the early 1900's to describe the application of certain types of electrical currents to the body for the delivery of deep heat (Sherman, 2007). Eventually, the term *shortwave diathermy* became used to describe the medical application of either continuous or pulsed shortwave energy, and *non thermal shortwave diathermy* used to further describe the therapeutic application of pulsed shortwave energy exclusively.

Additional terms also became used to describe pulsed shortwave applications. Some of these terms describe specific applications within this broader FDA-defined category[1]. In addition, they provide an alternative to the use of a term that implies heat (*diathermy*) for an application that was developed to circumvent problems that can arise with deep tissue heating. Table 1 provides a description of the overlapping terms commonly used for shortwave applications.

Pulsed electromagnetic energy (PRFE) therapy

In this review, *pulsed radio frequency energy* (PRFE) therapy is used to refer to the therapeutic application of pulsed RF energy therapy in the 13–27.12 MHz carrier frequency range to a target tissue without the intended generation of deep heat. PRFE therapy has been studied for use in a range medical applications, including postoperative and non postoperative pain and edema, as well as in wound healing applications. Use of the term PRFE differs from that of the term *pulsed electromagnetic field* (PEMF), which has been used to refer to technologies that employ a broad range of carrier frequencies, from as low as 1 Hz to as high as 27 MHz, with narrowly defined waveform and pulse pattern (see Table 1). PEMF devices with low (30–300 KHz) and extremely low (1 Hz–30 Hz) frequencies have been used to promote bone growth, cartilage stimulation, wound healing, and pain reduction. This review addresses only the literature for technologies that are in the shortwave range, and therefore does not address these PEMF devices. With that said,

[1] U.S. Food and Drug Administration, Code of Federal Regulations, Title 21, Part 890, Section 890.5290.

[2] Shortwave, in this context, refers to this specific carrier frequency range designated by the FDA for this medical device category. In other contexts, such as in engineering, shortwave refers to a much wider range of the radio spectrum.

TABLE 1 PRFE and other terms commonly used to describe electromagnetic field applications using 27.12 MHz carrier frequency

Acronym	Term	Carrier Frequency	Nonthermal or Thermal[1]	Description, other[2]
		Pulsed		
PRFE	Pulsed Radio Frequency Energy	13–27.12 MHz; 27.12 MHz for clinical use	Nonthermal[3]	
PRF	Pulsed Radio Frequency Field	15–40 MHz[4]; 27.12 MHz for clinical use[4,5,6]	Nonthermal[6]	Pulse duration (typical): 65 μsec[5,6] and 42 μsec[5]; pulse repetition rate: 80–600 pps; induced electric field strength: V/cm[5,6]
PRFS	Pulsed Radio Frequency Shortwave			Another term for PRF[6]
PEMET	Pulsed Electromagnetic Therapy	27.12 MHz[7]		Pulse duration (typical): 20–400 μsec; pulse repetition rate: 100–600 pps[7]
PSWD	Pulsed Shortwave Diathermy	27.12 MHz[5,6]	Tissue heating that allows for heat dissipation[6]	Pulse duration (typical): 95 μsec; duty cycle 3.9%; induced electric field strength: V/cm[6]
Low-Level Thermal PRF	Low-Level Thermal Pulsed Radio Frequency			Another term for PSWD[5]
PSWT	Pulsed Shortwave Therapy	13.57 MHz, 27.12 MHz, and 40.68 MHz; 27.12 MHz for clinical use[8]	Nonthermal or thermal (mean power the main determinant)[8]	
PEMF	Pulsed Electromagnetic Field	27.12 MHz[5,9]	Nonthermal[5,6]	Pulse duration: 1–100 ms; pulse repetition rate: 1–100 pps; induced electric field strength: mV/cm[5,6]; asymmetric pulse shape[5]
		Continuous		
CSWT	Continuous Shortwave Therapy	13.57 MHz, 27.12 MHz, and 40.68 MHz; 27.12 MHz for clinical use[8]	Thermal[8]	
CSWD	Continuous Shortwave Diathermy	13.57 MHz, 27.12 MHz, and 40.68 MHz; 27.12 MHz for clinical use[6]	Thermal[6]	Induced electric field strength: V/cm[6]

Table 1 (*Continued*)

Acronym	Term	Carrier Frequency	Nonthermal or Thermal[1]	Description, other[2]
			Pulsed or Continuous	
	Shortwave Diathermy	13–27.12 MHz[10]	Nonthermal or thermal[10]	An FDA therapeutic device category. Devices in this category include: (a) those used to apply therapeutic deep heat for select medical conditions, and (b) those used to treat medical conditions by means other than deep heat. (does not include devices used for the treatment of malignancies)[10]

[1] In regards to pulsed applications: relatively speaking, thermal effects increase with longer pulse duration coupled with greater pulse frequency.
[2] Definitions, descriptions, and values provided in this table are based on descriptions provided in the references cited. Some terms may describe overlapping (or identical) applications as others listed, and descriptions may not be all encompassing.
[3] Nonthermal is defined here as a treatment that does not result in an appreciable increase in tissue temperature (i.e. pulsed delivery of energy that allows heat generated to dissipate during the relatively long signal-off period in between pulses).
[4] Pilla (2007).
[5] Kloth and Pilla (2010).
[6] Sussman and Bates-Jensen (2007).
[7] Goats (1989).
[8] Al-Mandeel and Watson (2008).
[9] In the literature, this term is also used to describe applications outside the shortwave frequency range.
[10] U.S. Food and Drug Administration, Code of Federal Regulations, Title 21, Part 890, Section 890.5290.

TABLE 2 Devices used for PRFE therapy

Devices used in clinical studies described in this review[1]
Bentall (proprietary)
Curapuls (Enraf Nonius, The Netherlands)
Diapulse (Diapulse Corporation, USA)
Megapulse (Electro-Medical Supplies, United Kingdom)
Magnatherm (International Medical Electronics, USA)
Provant (Regenesis Biomedical, USA)
SofPulse (Ivivi Technologies, USA)
Therafield Beta (United Kingdom)

[1]All cited devices, except Curapuls, deliver the electrical and magnetic field components of the shortwave energy via a single applicator antenna. The Curapuls device uses an antenna to deliver the magnetic field and paired contact electrodes to deliver the electrical field.

this review does address the subset of PEMF devices that have carrier frequency in the 13–27.12 MHz carrier frequency range.

Treatment modality

PRFE treatment involves the use of a treatment device to apply shortwave energy to a target tissue at a frequency of 13–27.12 MHz without the intended generation of deep heat. In general, such devices described in the literature use a carrier frequency of 27.12 MHz. Devices are available that are easy to use and portable. In addition, the therapy serves as a relatively inexpensive treatment option. Table 2 provides a list of devices used in clinical studies described later in this review.

Intended uses

PRFE treatment has been studied as a palliative treatment for postoperative pain and edema, for non-postoperative pain and edema, and as an adjunctive wound healing therapeutic in superficial soft tissue. Numerous studies have also been performed related to other uses, such as for bone healing, cerebral edema, nerve regeneration, and migraines, although are outside the scope of this review.

Mode of delivery

PRFE treatment involves a non-invasive mode of delivery in which pulsed RF energy is delivered from the treatment device to the target tissue of the patient without direct electrode contact to the body.

Technical parameters

A summary of technical parameters and therapeutic outputs related to PRFE treatment and treatment devices can be found in Fig. 1. Table 3 summarizes actual parameters used in clinical reports described later in this review.

Mechanisms of action

While there is a substantial body of efficacy data related to PRFE treatment, the underlying biophysical mechanisms are less understood. An in-depth review of the subject is outside the scope of this review, however a brief summary of current findings related to the topic is provided here.

In general, the biophysical effects of PRFE are thought to be largely mediated by the electric field that is induced in the target tissue by the time-varying magnetic field of the application device (Kloth and Pilla, 2010). The specific effect mediated is likely dependent on several variables, including parameters of the electromagnetic field

Carrier frequency is the frequency of the wave delivered by the shortwave radio source. The carrier frequency used in PRFE field treatment is in the band of 13-27.12 MHz.

Pulse duration is the time duration of a single pulse.

Duty cycle is the ratio of the pulse duration versus the total time of one cycle. A cycle is the time sequence of signal on (pulse) and signal off (interpulse).

Pulse repetition rate is the number of pulses per second. It is measured in hertz (Hz).

Time period of exposure is the number of cycles multiplied by pulse duration.

Field strengths are measured in volts/meter (V/m) for the electric field, and ampere/meter (A/m) for the magnetic field. Field strength decreases with distance from the shortwave radio source.

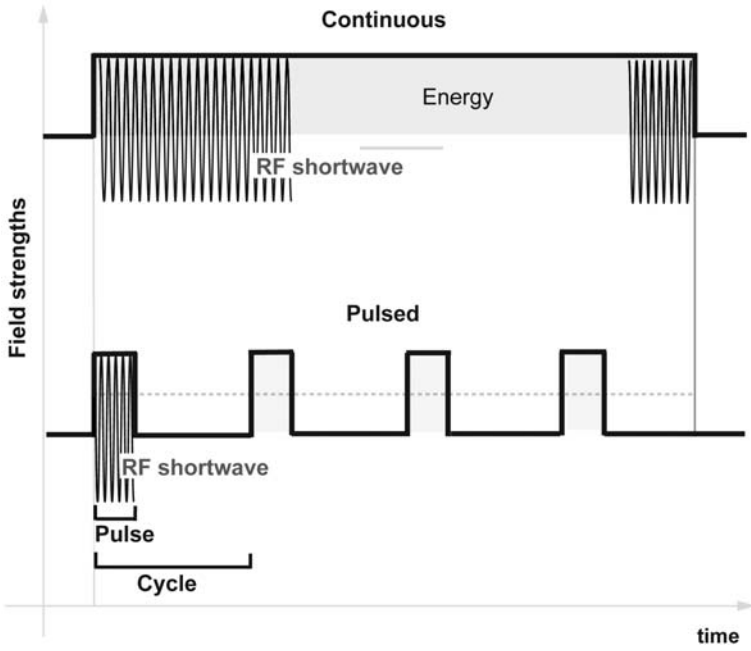

FIGURE 1 Technical parameters and therapeutic outputs of PRFE therapy. Technical parameters and therapeutic outputs related to PRFE treatment and treatment devices.

used, physiological state of the target tissue, and biological target of the induced electric field itself (Kloth and Pilla, 2010; Sussman and Bates-Jensen, 2007).

The cell membrane is thought to be a site of interaction between the induced electric field and it's biological target(s), where it may influence events such as receptor-ligand binding and changes in ion flow across the membrane (for a review, see Al-Mandeel and Watson, 2008; Kloth and Pilla, 2010; Pilla, 2007; Sussman and Bates-Jensen, 2007)). Such changes have the potential to trigger large-scale downstream effects through the activation of signal transduction cascades, which function to regulate a wide range of cellular processes through their ability to modulate gene expression, protein modification, and other molecular events within the cell.

PRFE has been shown to modulate a number of such biochemical and cellular processes. For example, PRFE can promote Ca^{2+} binding to its ligand calmodulin *in vitro* (Markov, 2007), as well as enhance the phosphorylation of myosin (Pilla, 2007), a process dependent on a bound Ca^{2+}/calmodulin complex. PRFE has also been shown to mediate phosphorylation of p44/42 MAP kinase (Gilbert et al.,

TABLE 3 PRFE treatment parameters used in clinical reports

Characteristic/Output	Range Reported in Literature (n articles)[1]
Pulse Width	All studies: 42–2,000 μsec (n = 34)
	PO[2]: 65–2,000 μsec (n = 8)
	NPO: 60–400 μsec (n = 14)
	WH: 42–500 μsec (n = 12)
Pulse Frequency	All studies: 2 Hz–46 MHz (n = 29)
	PO: 2–1,000 Hz (n = 7)
	NPO: 26 Hz–46 MHz (n = 12)
	WH: 20–1,000 Hz (n = 10)
Duty Cycle[3]	All studies: 0.4–16% (n = 25)
	PO: 0.4–10% (n = 7)
	NPO: 0.5–16% (n = 8)
	WH: 0.1–5.5% (n = 10)
Duration of Therapy per Patient[4]	All studies: 0.5–672 h (n = 33)
	PO: 0.5–24 h (n = 8)
	NPO: 0.5–672 h (n = 14)
	WH: 1.93–242.6 h (n = 10)
Energy Exposure[5]	All studies: 0.2–1088.6 min (n = 23)
	PO: 0.2–144 min (n = 6)
	NPO: 0.2–1088.6 min (n = 7)
	WH: 4.2–611.4 min (n = 10)

[1] Articles used for the table are those described later in this review.
[2] **PO:** postoperative studies; **NPO**: non postoperative studies; **WH:** wound healing studies;
[3] Calculation utilized: reported pulse width (μsec) × pulse frequency (Hz)/10,000.
[4] Calculation utilized: reported duration of treatment session (hours) × number of treatment sessions.
[5] Calculation utilized: reported minutes of therapy (min) × calculated duty cycle (%)/100.

2002), a calcium-activated enzyme involved in cell proliferation, as well as promote the process of cell proliferation in a Ca^{2+}-dependent manner (George et al., 2002). At the level of gene expression, microarray analysis results have shown widespread increases in transcript levels of genes involved in wound repair within minutes to hours following PRFE treatment of cells in culture (Moffett et al., in press; Moffett et al., 2010). PRFE-mediated effects on molecular processes have been observed in clinical studies as well. In a recent clinical report, significantly lower concentrations of IL-1β, a cytokine involved in the inflammation process, were found in wound exudates of patients receiving PRFE treatment following breast reduction surgery compared to patients receiving sham treatment (Rohde et al., 2010). Thus, the overall impact of PRFE can be observed at multiple levels, a combination of which, on a larger scale, likely contributes to PRFE-mediated therapeutic effects observed in clinical use.

CLINICAL EFFICACY

Early development

Diathermy was first described for medicinal use by D'Arsonval in 1889 (Geddes, 1999). It was soon recognized that application of shortwave energy in a continuous, non pulsate fashion led to a focal increase in tissue temperature that was potentially therapeutic. The first data on the medicinal merit of "deep heat" diathermy was presented in 1907 by Nagelschnidt at the Congress in Dresden (Sherman, 2007).

During the 1930's, as thermal complications with deep heat diathermy came to the attention of the medical community, attempts were made to modify the technology to obviate the thermal risks. Ginsberg experimented with pulsed shortwave energy and found he could attain the same beneficial effects as with

TABLE 4 Summary of study parameters

Non Postoperative Pain and Edema		
Author	Injury Type or Anatomical Location of Pain	Study Groups[1]
Aronofsky	oral surgery	**T1(30):** a 15-min treatment 24 h prior to surgery, and 10-min treatments immediately before surgery, immediately following surgery, and at 24, 48, and 72 h post surgery (600 pps/65 μsec pulse width). **T2(30):** Postsurgical treatment only as described for T1. **C(30):** No PRFE therapy.
Rhodes	oral surgery	**T(247)**: In conjunction with standard dental chemotherapy, three 10-min treatments around the face, a 10-min treatment over the liver area, and a 10-min treatment over the adrenal area, beginning three to five days pre-operatively, and continuing daily post-operatively until the patient was discharged (600 pps/65 μsec pulse width). **C(254):** standard dental chemotherapy only.
Hutchinson et al.	oral surgery	**T(37):** 10-min treatments immediately before surgery, immediately after surgery, and once a day for three days following surgery over the surgical site (500 pps/penetration setting of 5). **C(37):** sham treatment with an inactivated device over surgical site.
Kaplan and Weinstock	foot surgery	**T(50):** a 10-min treatment prior to surgery and 15 min treatments twice a day after surgery, both at the site of surgery as well as at the epigastrium (600 pps/65 μsec pulse width). **C(50):** sham treatment with an inactivated device.
Santiesteban and Grant	foot surgery	**T(23):** 30-min treatments immediately after surgery and 4 h post surgery (700 pps/75 μsec pulse width/120 W power setting). **C(24):** no PRFE therapy.
Rohde et al.	breast reduction	**T1(12):** 20-min bilateral treatments immediately after surgery, then every 4 h for the first three days, every 8 h for the next three days, and then twice daily (2 pps/2,000 μsec pulse width/0.05 G magnetic field/32 ± 6 mV average induced electric field). **C(12):** bilateral sham treatment.
Heden and Pilla	breast augmentation	**T1(14):** 30-min bilateral treatments immediately after surgery, then every 4 h for the first three days, every 8 h for the next three days, and then every 12 h until the follow-up visit, which normally occurred seven days post-operatively (2 pps/2,000 μsec pulse width). **T2(14):** 30-min contralateral treatments (one breast received active treatment, and the other received sham treatment) as described for T1. **C(12):** bilateral sham treatment.
Silver	breast augmentation	**SSG(41*)**: PRFE therapy along with massage and closed capsulotomy treatment (*number of breasts in study group)
Mayrovitz et al.	Mastectomy	**SSG(7):** four to six 60-min treatments over a two week period (700 pps/95 μsec pulse width).
Frank	gynecological	**SSG:** two five-min treatments the first day of treatment, followed by five-min treatments once a day for three days (25 pps/65 μsec pulse width).
Nicolle and Bentall	blepharoplasty	**T(19):** a 24-h treatment immediately following surgery (1,000 pps/100 μsec pulse width). **C(19):** no PRFE treatment.
Bentall and Eckstein	orchidopexy	**T(31):** a 20-min treatment over the surgical site and a 10-min treatment over the epigastrium (500 pps/penetration setting of 5 at surgical site and of 4 at epigastrum). **C(31):** sham treatment (inactive device).

Table 4 (*Continued*)

Non Postoperative Pain and Edema		
Author	Injury Type or Anatomical Location of Pain	Study Groups[1]
Barclay et al.	hand injury	**T(114):** 30-min treatments twice daily until discharged (approximately seven days post-procedure). **C(116):** no PRFE therapy.
Wilson	acute ankle inversion injury	**T(20):** one h of treatment per day for three days around the foot and ankle (65 μsec pulse width/975 W (peak emission) with a resting interval of 1.6 μsec). **OT(20):** Two 15-min thermal diathermy treatments, given within a one-h time interval, were given each day for three days around the foot and ankle with the dosage adjusted according to the patient's tolerance to tissue heating.
Pennington et al.	grade I and II acute ankle sprains	**T(25):** a 30-min treatment on the medial side of the ankle, a 30-min treatment on the lateral side of the ankle, and a 10-min treatment over the epigastrum. **C(25):** no PRFE therapy.
Shandles et al.	recalcitrant heel pain due to heel neuromas	**T(101):** basic standard care (including injection therapy) plus adjunctive PRFE therapy. Each injection was immediately followed by a single PRFE treatment session, consisting of PRFE treatment of the affected heel(s) and epigastrum (1–11 injections per patient), consisting of 10–15-min treatments over the affected area and the epigastrium 2–3 times per week (600 pps (affected area) and 400 pps (epigastrum)/65 μsec pulse width). **C(216):** basic standard care only (including injection therapy).
Pasila et al.	ligamentous injuries (ankle and foot)	**T1(100):** 20-min treatments on three consecutive days (average power setting of 38 W/sec). **T2(100):** Same as T1 except with a different PRFE device (average power setting of 40 W/sec). **C(100):** no PRFE treatment.
Barker et al.	lateral ligament sprain (ankle)	**T(34):** a 45-min treatment within 36 h of the injury, followed by 45-min treatments on the following two consecutive days (640 pps/65 μsec pulse width). **C(39):** equivalent regimen with a sham treatment device (inactive device).
Buzzard et al.	acute calcaneal fractures	**T(9):** two 15-min treatment per day (26 pps/200 μsec pulse width) **OT(11):** six 20-min ice therapy sessions per day for five days.
Foley-Nolan et al.	long-term neck pain	**T(10):** wore active therapy collar 8 h per day for 6 weeks (450 pps/60 μsec pulse width). **C(10):** wore sham collar (inactivate device) 8 h per day for 3 weeks, followed by active therapy collars 8 h per day for 3 weeks.
Foley-Nolan et al.	acute whiplash injury	**T(20):** wore active therapy collar 8 h per day for 12 weeks (450 pps/60 μsec pulse width). **C(20):** wore sham collar (inactivate device) 8 h per day for 12 weeks.
Wagstaff et al.	chronic lower back pain	**T1(8):** 15-min treatments twice a week for three weeks (82 pps/700 W (maximum power) and 23.2 W (mean power)). **T2(7):** same regimen as T1, except using different PRFE dose (200 pps/300 W (maximum power) and 23.2 W (mean power)). **OT(8):** same regimen as T1 and T2, except using thermal shortwave diathermy. For all groups: most patients were also taking analgesics and were instructed on various exercises to maintain during the study.

Table 4 (*Continued*)

Non Postoperative Pain and Edema		
Author	Injury Type or Anatomical Location of Pain	Study Groups[1]
Jan et al.	osteoarthritis (knee)	**T1(14*):** Thirty 20-min treatments over a span of eight weeks. **T2(14*):** same regimen as T1, but in addition, also received nonsteroidal anti-inflammatory drugs (NSAIDS). **C(16*):** no treatment. (*number of knees in study group)
Laufer et al.	osteoarthritis (knee)	**T(38):** Three 20-min treatments per week for three weeks (110 pps/82 μsec pulse width). **OT(32):** Same regimen as T1, except with thermal shortwave diathermy. **C(33):** equivalent regimen with a sham treatment device (inactive device).
Callaghan et al.	osteoarthritis (knee)	**T1(10):** one 20-min treatment to the affected knee joint (400 pps/200 μsec pulse width). **T2(10):** same regimen as T1, except using different PRFE dose (400 pps/400 μsec pulse width). **C(10):** equivalent regimen with a sham treatment device (inactive device).
Svarcova et al.	osteoarthritis (weight-bearing joint)	**T(60):** Ten 2-min treatments from the anterior and posterior fields, in two-day intervals over three weeks (26 MHz pulse frequency/700 W (maximum peak intensity)). **OT1(60):** Same regimen as (T) but using ultrasound treatment. **OT2(60):** Same regimen as (T) but using galvanic current treatment. All groups: within each group, half of the patients (n = 30) received ibuprofen 400 mg twice daily while the other half received placebo tablets.
Cameron	orthopedic	**SSG(465):** Treatments were given twice per day three times per week for two weeks, then twice per day two times per week for one week, then twice per day once a week (400 pps/65 μsec pulse width), with the duration of treatment varying from one day to over six months.
Comorosan et al.	posttraumatic algoneurodystrophies	**T1(10):** a 10-min treatment at the algoneurodystrophy site and also at either the homolateral lumbar or cervical paravertebral ganglia of sympathetic trunk on day one, followed by 10-min treatments at the algoneurodystrophy site and sympathetic ganglia on days two through nine. On days 10–15, patients underwent a local treatment followed by treatment of the sympathetic ganglia (60–600 pps/65 μsec pulse width). **C(20):** standard (classical) treatment only (no PRFE treatment).
Grant et al.	perineal trauma post child birth	**T(135):** Three 10-min PRFE treatments within 36 h after childbirth (100 pps/65 μsec pulse width). **OT(140):** Three 2-min ultrasound treatments at each area affected within 36 h after childbirth. **C(139):** sham PRFE or ultrasound treatment (non active devices used).
Wound Healing		
Author	Wound Type	Study Groups
Cameron	surgical	**T(50):** 20-min treatments over the surgical site and over the liver twice per day for four days (400 pps/65 μsec pulse width). **C(50):** sham treatment.

Table 4 (*Continued*)

Non Postoperative Pain and Edema		
Author	Injury Type or Anatomical Location of Pain	Study Groups[1]
Cameron	surgical	**SSG(81):** 20-min treatments over the affected area and over the liver twice per day for four days (400 pps/65 μsec pulse width).
Goldin et al.	skin grafts	**T(29):** 30-min treatments at the graft site immediately before the procedure and post-operatively every six h for seven days (400 pps/65 μsec pulse width/975 W (peak output) and 23.3 W (mean output)). **C(38):** equivalent regimen with a sham treatment device (inactive device).
Salzberg et al.	pressure ulcers	**T(10, stage II ulcers; 5, stage III ulcers):** 30-min treatments twice daily for 12 weeks or until the ulcer healed (80–600 pps/65 μsec pulse width). **C(10, stage II ulcers; 5, stage III ulcers):** sham treatment (inactive device).
Kloth et al.	pressure ulcers	**T(5):** 30-min treatments five days a week for four weeks (600 pps/65 μsec pulse width). **C(5):** sham treatment (inactive device).
Seaborne et al.	pressure ulcers	**T1(5):** 20-min treatments, twice daily, during the second and fourth weeks of the study for a total of 20 treatments (electromagnetic field applied) (20 pps / 0.036 W/cm^2). **T2(5):** same regimen as T1, except using a different dose (110 pps / 0.199 W/cm^2). **OT1(5):** 20-min treatments, twice daily, during the second and fourth weeks of the study for a total of 20 treatments (electrostatic field applied) (20 pps / 0.042 W/cm^2). **OT2(5):** same regimen as OT1, except using a different dose (110 pps / 0230 W/cm^2).
Itoh et al.	stage II and III pressure ulcers	**T1(7, stage II ulcers) and T2(13, stage III ulcers):** 30-min treatments twice daily (600 pps/65 μsec pulse width/975 W (peak output)) until healed.
Wilson	chronic stage III pressure ulcers	**CS (3):** In conjunction with saline wet/dry dressing, twice daily treatments until one week beyond wound healing.
Tung et al.	stage II, III, and IV decubitus ulcers	**CS (4):** 30-min treatments three times daily (stage III and IV ulcers) and 30-min treatments twice daily (stage II ulcers) until healed. All patients were treated with conventional modes of supportive therapy (wound dressing, debridement as required, antibiotics when appropriate and tube feedings as necessary).
Larsen and Overstreet	complex diabetic foot wounds	**CS(2):** 30-min treatments twice daily (1,000 pps/42 μsec pulse width).
Porreca and Giordano-Jablon	stage III and IV pressure ulcers	**CS(1; 3 stage III and IV ulcers):** 30-min treatments twice daily (1,000 pps/42 μsec pulse width).
Frykberg et al.	chronic lower extremity wounds	**CS(5):**30 min treatments twice daily until wounds fully closed (1,000 pps/ 42 μsec pulse width).
Muirhead et al.	pre-tibial lacerations	**T(48):** In conjunction with standard care therapy, 10-min treatments three times per week until lacerations healed (20–26 pps/400 μsec pulse width). **C(48):** standard care therapy only (no PRFE treatment).

[1] **T:** PRFE treatment group (adjunctive PRFE treatment); **OT:** other treatment group (study group that received an adjunctive treatment other than PRFE); **C:** control (non treated or sham-treated); **SSG:** single study group (adjunctive PRFE treatment); **CS:** case study (adjunctive PRFE treatment); **(n):** number of patients in study group.

continuous shortwave energy without the heating effects. The design of a pulsed, non thermal shortwave diathermy device was completed in 1936, and animal trials were conducted in 1940–1941. World War II prevented further experimentation and delayed product introduction to the medical community until the 1950's (Hayne, 1984). The first commercially available pulsed shortwave therapy device was introduced in the early 1950's; other devices followed in subsequent decades. Since that time, a large number of clinical efficacy studies have been performed.

Clinical efficacy reports

There is a growing list of clinical efficacy reports on the use of PRFE therapy. Below provides a summary of clinical studies related to PRFE use in postoperative patient care, non postoperative patient care (injury and non-injury related), and in wound healing applications. Table 4 summarizes study groups and PRFE parameters reported for each study.

Postoperative pain and edema

Oral surgery

Aronofsky et al. (1971) reported on the effective use of PRFE therapy for the reduction of postsurgical pain and inflammation in oral surgery patients. 72 h following surgery, a greater percentage of PRFE-treated patients reported an absence of pain (treated: 63% (T1)[3] and 40% (T2), vs. control: 7% (C); $p \leq 0.0057$*)[4] and an absence of inflammation (treated: 76.7% (T1) and 53.3% (T2), vs. control: 6.7% (C); $p < 0.0001$*) than control group patients who received no PRFE treatment. In addition, while over half of control group patients were reported with considerable inflammation at the same time point, the same was true for less than 5% of PRFE-treated patients (treated: 3.3% (T1) and 3.4% (T2), vs. control: 56.6%(C)). In 1981, Rhodes reported results of a 501-patient study, which reported shorter average duration of hemorrhaging (0.95 days (T) vs. 2.77 days (C)), edema (2.51 days (T) vs. 10.29 days (C)), and pain (0.90 days (T) vs. 9.51 days (C)) following oral surgery in patients receiving PRFE treatment compared to control group patients (Rhodes, 1981). The average total number of days to heal was also reduced for patients in the PRFE treatment group (26.06 days (T) vs. 50.43 days (C)), who were reported to return to their normal routine an average of 12 days earlier than control group patients as well. Results from a 1978 study by Hutchinson et al. involving PRFE treatment of patients who underwent removal of a mandibular third molar were more neutral, showing no significant differences between PRFE-treated patients and control group patients (Hutchinson et al., 1978). The authors concluded that their results do not disprove the effectiveness of PRFE therapy, although the PRFE dosage used did not provide a worthwhile reduction in the symptoms assessed[5].

Podiatric surgery

Kaplan and Weinstock (1968) reported on results of a 100-patient study designed to assess the impact of PRFE therapy on pain, edema, and erythema following foot surgery. PRFE-treated patients were reported with lower occurrence of moderate or

[3] Table 4 provides a description of abbreviations used in the text.

[4] Asterisk (*) indicates that the p-value was calculated based on data provided in the article.

[5] There is statistical evidence that neutral outcomes in some PRFE efficacy studies may be a consequence of insufficient energy dosing (Guo, L., Kubat, N.J., Nelson, T.R., and Isenberg, R.A. Meta-Analysis of Clinical Efficacy of Pulsed Radio Frequency Energy Treatment. Submitted.).

severe edema compared to patients in the sham-treated control group as early as two days postoperatively, and by the day of suture removal, the rate of occurrence remained less for the PRFE treatment group (19% (T) vs. 54% (C); $p = 0.0008$*). Reported moderate and severe pain was also less for patients in the PRFE-treatment group on the day of suture removal (30% (T) vs. 60% (C); $p = 0.0046$*), as was erythema (15% (T) vs. 50% (C)). In 1985, Santiesteban and Grant also reported postoperative benefits using PRFE treatment for foot surgery patients (Santiesteban and Grant, 1985). In a 47-patient, randomized study, the mean length of hospital stay was less for patients in the PRFE treatment group compared to control group patients (42.09 days (T) vs. 50.04 days (C), $p < 0.01$), with a significant difference noted in Type I (mild) analgesic consumption between the groups.

Female-related surgeries

Rohde et al. (2010) reported on findings from a double-blind, placebo-controlled study of PRFE treatment use for postoperative pain in breast reduction patients. Pain was assessed using a visual analog scale (VAS) and by narcotic pill consumption. Based on mean VAS scores, PRFE-treated patients showed a 57% decrease in pain at 1 h following surgery ($p < 0.01$), and a 300% decrease in pain at 5 h following surgery ($p < 0.001$), which persisted 24 and 48 h postoperatively. Conversely, no significant pain reduction was reported for the sham-treatment group at the same postoperative time points. Mean pill count was also significantly lower in the PRFE treatment group (5 pills $\pm$ 0.9 (T) vs. 11 pills $\pm$ 1.2 (C); $p = 0.002$). In addition, a significantly lower mean concentration of IL-1β was measured in wound exudates from active treatment group patients compared to exudates from sham-treated patients starting at 1 h postoperatively (350% lower mean concentration of IL-1β (T) vs. (C); $p < 0.001$), a trend that continued for the duration of the sampling period. In 2008, Heden and Pilla reported on the efficacy of PRFE treatment at reducing pain following elective breast augmentation (Heden and Pilla, 2008). By postoperative day (POD) three, patients receiving bilateral PRFE treatment were reported with a statistically significant reduction in pain compared to control patients (2.57 times greater reduction in pain than patients in the bilateral sham treatment group), and consumed on average 2.9 times fewer pain pills, a trend which continued through POD seven. Another study, published by Silver (1982), evaluated the use of PRFE therapy for the treatment of capsular contracture following breast augmentation. PRFE therapy, along with massage and closed capsulotomy treatment, was applied to 41 breasts that developed capsular contracture (representing 9% of 462 total implants in the study), with successful elimination of capsular contracture reported for all study patients over a period of 3 months to 2.5 years. In 2002, Mayrovitz et al. reported positive results using PRFE therapy to treat post-mastectomy arm lymphedema (Mayrovitz et al., 2002). Seven post-mastectomy patients with long-standing, grade two lymphedema that failed complete decongestive therapy were included in the study. A significant decrease in arm volume was reported after just one PRFE treatment (24.5 $\pm$ 7.3% to 18.5 $\pm$ 6.3%; $p < 0.01$) with an average reduction in edema of 56.2 $\pm$ 8.4% following the fourth treatment. Significant increases in skin blood perfusion levels during and immediately following PRFE treatment were reported as well. In 1985, Frank reported on the successful use of PRFE treatment for pain reduction and wound healing in gynecological patients (Frank, 1985). Patients included those with extensive bruising and inflammation following caesarean sections or post-hysterectomies, as well as large distended hemorrhoids or extensively sutured vaginas post-child delivery.

Other surgeries

The therapeutic effect of PRFE on postoperative outcomes has been studied in patients undergoing other types of surgeries as well. Outcomes of ecchymosis and swelling were reported by Nicolle et al. (1982) for 19 patients treated with PRFE following blepharoplasty surgery. Improvement was apparent in over half of PRFE-treated eyes, which was most obvious at 24 hours when treatment was ended. At this point edema, and to a lesser extent ecchymosis, were distinctly less for PRFE-treated eyes as well, with continued improvement through POD six when the follow-up period ended. In 1975, Bentall and Eckstein studied 62 patients in a randomized, blinded study of postoperative PRFE therapy use for palliative care of pediatric patients (ages 1.5–12.5 years of age) following orchidopexy (Bentall and Eckstein, 1975). Results of the study reported a significant reduction in discoloration by the 6^{th} and 8^{th} day follow-up evaluations for patients in the treatment group compared to control group patients ($p < 0.05$).

Non postoperative pain and edema

Hand injuries

Barclay et al. (1983) reported results from a 230-patient study that assessed the efficacy of PRFE treatment in decreasing pain and swelling and improving disability in patients presenting with a variety of hand injuries, including contused lacerations, incised lacerations, and severed fingertips. Patients were assigned to either a PRFE treatment group or a control group, with 30 matched patient pairs, matched for age, sex, and degree of trauma, included in the comparison. In each category measured, average improvement reported for treated patients was greater than three times that of matched control group patients.

Ankle and foot injuries

Wilson (1974) reported on the outcomes of a 40-patient, matched-case, controlled study comparing PRFE therapy to thermal shortwave diathermy for treatment of acute ankle inversion injuries. Patients were paired for age, weight, sex, and degree of trauma. PRFE treatment was more effective than thermal shortwave diathermy in all categories assessed, including improvement in pain (86.4% improvement (T) vs. 43.2% improvement (OT)), swelling (67.5% improvement (T) vs. 35.1% improvement (OT)), and disability (93.2% improvement (T) vs. 53.8% improvement (OT)). The effectiveness of PRFE treatment at reducing pain and swelling following ankle injury was also reported by Pennington et al. (1993). In a 50-patient, randomized, double-arm study of patients with grade I and II acute ankle sprains, PRFE-treated patients reported a greater reduction in pain (64% (T) vs. 33% (C), $p = 0.0465$*), as well as a significantly greater decrease in both average ankle volume (44 cc reduction (T) vs. 11 cc reduction (C), $p < 0.01$), and average percent decrease in ankle volume (4.7% reduction (T) vs. 0.95% reduction (C), $p < 0.01$). PRFE therapy use for the reduction of heel pain was the subject of a 267-patient study published by Shandles et al. (2002). The study, which included a ten-year period of data collection, included patients with recalcitrant heel pain due to heel neuromas, who were provided with either standard care (including injection therapy) alone, or the equivalent care in conjunction with PRFE treatment. 20% fewer surgeries were required for patients who received adjunctive PRFE therapy as compared to patients receiving the standard of care treatment alone (95% of PRFE-treated patients did not require further surgery, compared to 75% of patients in the control group; $p < 0.001$*). Results of a study to examine PRFE therapy use for patients with recent ligamentous injuries of the ankle and foot were reported by Pasila et al. (1978). A statistically significant reduction in swelling was found for patients in one of the PRFE treatment groups (T2) compared with the control group as measured

circumferentially ($p < 0.01$); however, there were no statistical differences found in volume ($p = 1.0^*$). It was also noted that patients in one of the PRFE treatment groups recovered from limp at a faster rate than the control group ($p < 0.01$). The authors concluded that the effect of PRFE was not as favorable as other reported studies, which may be explained by differences in dosage used. A study examining the use of PRFE treatment for lateral ligament sprains of the ankle was reported by Barker et al. (1985). Each patient was either PRFE- or sham-treated for 45 min within 36 h of the injury as well as on the next 2 consecutive days. Patients were assessed for pain, swelling, gait, and range of motion, although no reported differences were found between the PRFE-treatment and sham-treatment groups. Finally, outcomes of a randomized study comparing PRFE treatment with ice therapy for the treatment of acute calcaneal fractures were reported by Buzzard et al. (2003). However, results of the study showed no reported differences in either swelling or range-of-motion between the PRFE treatment group and the ice therapy group ($p = 0.22$).

Neck and back pain

The effects of PRFE therapy on long-term neck pain was reported by Foley-Nolan et al. (1990). Half of the patients in the six-week study received daily PRFE therapy, while control group patients received sham therapy for three weeks, followed by PRFE therapy for three weeks. At three weeks, a statistically significant improvement in PRFE-treated patients relative to control group patients was reported both for pain and range of motion. In addition, 80% of patients in the PRFE treatment group were reported as feeling either "moderately better" or "much better," compared to only 20% of control group patients. At six weeks, following three weeks of PRFE treatment, 70% of the control group reported feeling either "moderately better" or "much better," with no reported difference in pain between study groups. In addition, 100% of the patients who received the full six weeks of PRFE therapy reported feeling either "moderately better" or "much better" at the conclusion of the study. Therapeutic use of PRFE for acute whiplash injury was the topic of another study by Foley-Nolan et al. (1992). Half of the patients in the 12-week study received daily PRFE therapy, while control group patients received sham therapy from an inactive device. At two and four weeks, there was a statistically significant difference in reported pain between study groups, with less pain reported for patients who received PRFE treatment. At four weeks, PRFE treatment group patients also consumed, on average, less analgesics than control group patients, with 85% of patients in the treatment group reported to feel either "moderately better" or "much better," compared to only 35% of patients in the control group. In addition, while range of motion scores for the treatment group were significantly worse than those for the control group at entry to the trial ($p < 0.05$), they were significantly better than reported for the control group at the end of the trial ($p < 0.05$). Finally, Wagstaff et al. (1986) reported the therapeutic benefit of PRFE for patients with chronic lower back pain. The study design involved two groups of patients who received PRFE treatment (treatment parameters differed between the two groups), and one group of patients who received thermal shortwave diathermy. While all groups demonstrated a significant improvement in pain over the course of the study, there was a significantly greater reduction in pain reported for patients in the PRFE therapy groups compared to patients who received continuous thermal therapy (pain reduction of 4.23 cm (T1) and 4.57 cm (T2) vs. 1.79 cm reduction (OT), as measured using a VAS scale of 0–15 cm; $p < 0.05$).

Knee and hip-related (osteoarthritis)

Jan et al. (2006) described a reduction in pain and synovial sac thickness in patients receiving PRFE treatment in a report that evaluated PRFE therapy use in patients

with degenerative osteoarthritic knees (grade 3 or less). After 10 treatment sessions, reduction in synovial sac thickness was already apparent in PRFE-treated patients (T1 and T2: 16–19% reduction, C: no change, $p < 0.0001$), with a statistically significant difference in reported pain between PRFE-treated and control group patients as well ($p < 0.005$). Improvement in both parameters continued throughout the course of the study for PRFE-treated patients, with a final average reduction in synovial sac thickness of 28–33% compared to no change in the control group ($p < 0.0001$). In addition, non steroidal anti-inflammatory drug (NSAIDS) use in conjunction with PRFE treatment provided similar results to PRFE treatment alone (study group T1 vs. T2). The effects of PRFE on osteoarthritis of the knee was studied in a 30-patient, randomized, blinded trial with outcomes reported by Callaghan et al. (2005). There was no reported difference in outcome measures between PRFE-treated patients and sham-treated control group patients, with the exception of knee range of motion, in that the control group range of motion had statistically significant improvement in comparison to the treatment groups ($p < 0.05$). Outcomes of a 180 patient randomized, three-arm study of PRFE, galvanic current, and ultrasound in patients with osteoarthritis of a weight-bearing joint (knee or hip) were reported by Svarcova et al. (1988). Within each group, half of the patients also received ibuprofen (400 mg) twice daily while the other half received placebo tablets. The analgesic effect of the various therapies was noted as early as after the 5^{th} treatment, but there was no reported statistical difference between the groups. After the 10^{th} treatment, the combined effect of physical and drug therapy appeared better than that of physical therapy alone. There was no statistical difference between the three types of physical therapy. Results of PRFE therapy use in patients with degenerative osteoarthritic knees was reported by Laufer et al. (2005). All patients were assessed using the WOMAC Osteoarthritis Index, which assessed pain, stiffness, and functional ability, and four measures of mobility (timed "get up and go test," stair climbing, stair descending and a 3-min walk). No differences were reported between the groups in any measures at the follow-ups, however, there was a noted reduction in pain and stiffness across time for all three groups ($p = -0.033$ and $p = 0.008$).

Additional orthopedic studies

Cameron (1964) reported on a 465-patient, non controlled study that assessed the use of PRFE therapy for treatment of non operative orthopedic patients. Following a three-week PRFE treatment regimen, 61.3% of patients were reported in "excellent" condition, 22.6% in "good" condition, 10.5% in "fair" condition, and 5.6% "poor" condition. The author concluded that PRFE treatment did not cure arthritis in his patients, but was useful as an aid in therapy to achieve excellent to good results as noted.

Additional trauma-related studies

Comorosan et al. (1991) reported on the effectiveness of PRFE for the treatment of posttraumatic algoneurodystrophies. In a two-arm matched case study, a considerable decline in pain and edema was reported for PRFE-treated patients after two weeks of treatment (pain reported as "none" or "mild," 82% (T) vs. 15% (C), $p < 0.0001$)[6]. Similar improvement was reported for edema at the same time point (edema reported as "none" or "mild," 86% (T) vs. 30% (C), $p < 0.0001$). Improvements were also reported for the degree of osteoporosis as measured by

[6] Percentage and p-values were calculated based on the information available in the literature.

photodensitometry. By the conclusion of the study, 19 patients in the PRFE treatment group were reported with no osteoporosis, compared to none of the patients in the control group. Grant et al. (1989) reported on the outcome of PRFE use for the treatment of post-delivery perineal trauma. Reported pain, rates of dyspareunia, urinary incontinence, fecal incontinence, and general feeling of well-being did not differ between any of the study groups at 36 h post delivery.

Wound healing

Postoperative

Cameron (1964) reported on the use of PRFE in the promotion of wound healing following surgery. Patients undergoing a variety of surgeries, including neck, chest, extremity, abdominal, back, and kidney surgery, were included in the 100-patient, double blind study. Best results were obtained for patients who had undergone extremity and back surgeries, with the least notable differences found for abdominal surgery patients. 48% of patients in the PRFE treatment group reported sutures removed by POD five, compared to 18% of control group patients ($p = 0.026$)[7]. In addition, the length of hospitalization was moderately reduced for PRFE-treated patients as well. Another study by Cameron investigated the effects of PRFE on postoperative wound healing in orthopedic surgical patients (Cameron, 1964). The results demonstrated 7.4% of patients remained the "same", 85.2% of patients were "better", and 7.4% of patients were "worse" at the end of treatment. Sutures were removed by POD five in 86.4% of patients and the average hospital stay was 9.7 days per patient (which the author concluded as relatively short). Goldin et al. (1981) reported accelerated wound repair in skin graft patients receiving pre- and postoperative PRFE treatment. Patients included in the 67-patient, randomized study had medium-thickness split-skin grafts taken from the thigh with a mean thickness of 0.22 mm. Healing (greater than 90% of original wound size healed) was assessed on the seventh postoperative day, with healing rates reported as 59% for the treatment group compared to 29% for the control group ($p = 0.0239$)[8].

Pressure ulcers, diabetic wounds, and chronic wounds

Salzberg et al. (1995) reported on a 30-patient study that involved PRFE treatment of stage II and III pressure ulcers in spinal cord-injured patients. After one week of treatment, PRFE-treated stage II ulcers were on average smaller in size (ulcer size: 2.7 cm (T) vs. 16.5 cm (C), $p = 0.015$), and a greater percent were completely healed (84% (T) vs. 40% (C), $p = 0.010$) compared to those in the sham treatment group. In addition, the total average number of days to heal was also less for PRFE-treated stage II ulcers (13.0 days (T) vs. 31.5 days (C), $p < 0.001$). For stage III ulcers, 3/5 PRFE-treated stage III ulcers healed completely by the end of the study, with complete healing achieved after an average of 43 treatment days. None of the stage III ulcers in the sham-treatment group healed completely during the study. Overall,

[7] Conservatively used p-value associated with overall comparison. This action is conservative because the publication reported an 81 patient single arm study that validated the results seen in the all but abdominal surgery subgroup. The analysis for the all but abdominal surgeries subgroup in the double-blind study reported the following proportion of treated patients with suture removal as compared to control (Treatment: 89%, Control: 13%, $p < 0.0001$). Within the subgroup with abdominal surgery, the proportion with their sutures removed by 5 days was not found to differ between groups (Treatment: 28%, Control: 21%, $p = 0.5704$). The lack of a significant effect in the abdominal surgery subgroup as reported in the publication is due to conservative behavior on the part of the surgeon to avoid possible wound dehiscence. The 81 patient single arm study results reported 86% of patients with sutures removed by day 5.

[8] p-value reported in publication is in error and is reported to be between 0.05 and 0.25.

PRFE-treated stage III ulcers also showed a greater reduction in size (70.6% (T) vs. 20.7% (C)) by the end of the study, than those receiving sham (control) treatment. Kloth et al. (1999) also reported a positive outcome using PRFE therapy for treatment of pressure ulcers in spinal cord-injured patients. All patients in the study had pressure ulcers of duration greater than 30 days that measured greater than 4 cm^2 and less than 100 cm^2 in area. Following four weeks of treatment, 64 ± 15% of PRFE-treated wounds had healed compared to no change reported for the control group ($p = 0.016$). There was no statistical difference between the treatment and control groups wound area measurements prior to the start of treatments. Seaborne et al. (1996) also reported effective treatment of pressure sores using PRFE therapy. Patients included in the study were non ambulatory with prolonged bed rest with pressure sores of mean duration of 13.5 weeks. After 20 treatments, wounds in both PRFE treatment groups (T1 and T2) showed a statistically significant decrease in mean surface area relative to measurements taken at the onset of the study ($p = 0.001$), with the mean size of wounds in one PRFE treatment group (T1) decreasing to less than 5% of their original mean surface area. Using PRFE therapy, Itoh et al. (1991) also reported successful healing of stage II and III pressure ulcers that had not healed following conventional therapy alone. Patients included in the study presented either with stage II ulcers that remained unhealed following 3–12 weeks of conventional treatment, or stage III ulcers that remained unhealed following 8–168 weeks of conventional treatment. Successful wound healing was reported for all 22 patients included in the study, with a reported mean time to healing of stage II ulcers of 2.3 weeks (range: 1–6 weeks) and of stage III ulcers of 8.85 weeks (range: 1–22 weeks). An ease of use study by Wilson (1995) reported on a three-patient case study using PRFE therapy for the treatment of chronic stage III pressure ulcers. Healing was noted within the first week, when edema and inflammation had been eliminated. All three ulcers were completely healed at the end of three weeks. A four patient case study using PRFE therapy for the treatment of decubitus ulcers was reported by Tung et al. (1995). PRFE therapy was used to treat all four patients in the study, and healing was reported for all ulcers treated, in several cases avoiding potential amputation. One patient presented with three black necrotic ulcers involving the entire lateral aspect of the right foot and the right fourth web space. The three ulcers healed after 6, 15, and 32 weeks of PRFE treatment. A second patient presented with necrotic black bilateral heel decubitus ulcers measuring 1.5 × 1 × 0.4 cm and 9 × 3 cm, which healed within nine and 30 weeks, respectively, following the start of PRFE therapy. Healing of a 12 × 7 cm heel ulcer in a third patient was achieved following 43 weeks of treatment, and healing of a 3.5 × 2.3 × 6 cm heel ulcer in a fourth patient was achieved after 25 weeks of PRFE treatment. Larsen and Overstreet (2008) reported on a two patient case study using PRFE for the treatment of complex diabetic foot wounds. One patient presented with a 24-month history of an unremitting wound overlying his left Achilles tendon. The second patient presented 3 days post-operatively with wide deshiscence of an amputation site. The reported results were complete wound closure within 16 and 16.7 weeks, respectively, for the 2 patients. A single case study using PRFE for the treatment of stage III and stage IV pressure ulcers in a quadriplegic patient was reported by Porreca and Giordano-Jablon (2008). The 59-year-old patient presented with three large, chronic (>6 years) stage III and IV pressure ulcers that were unresponsive to conventional therapy. Following twice daily PRFE therapy, the 5 cm^2 right lateral foot ulcer (stage III) healed to closure in 4 weeks (wound healing rate of 16.7 mm^2/day), the left heel ulcer (stage III) decreased in size from 60 to 2 cm^2 in 7 months (95% reduction 28. 5 mm^2/day), and the a sacral ulcer (stage IV) decreased from 295 to 20 cm^2 in 7 months (88% reduction; 13.1 mm^2/day) reaching full closure

in 11 months. Finally, Frykberg et al. (2009) reported on five case studies using PRFE for the treatment of chronic lower extremity wounds. In all five cases, PRFE therapy was successful in the treatment of patients that had not responded to the standard therapy offered at their center. Wounds included a failed fillet flap closure of the great toe, a chronic venous insufficiency wound of several years' duration, a recurrent venous ulcer on the lateral leg, an open transmetatarsal amputation of the foot, and chronic bilateral full-thickness decubitus heel and Achilles tendon ulcerations. Progression to full wound closure occurred after 2–4 months of PRFE therapy for 4 of the 5 patients. For the fifth patient, wounds remained unhealed following 18 months of standard therapy, and a cell-based construct in addition the PRFE therapy was then used, after which the right decubitus ulceration progressed to full closure in 3 months, and the left ulceration with exposed Achilles tendon healed completely in 8 months.

Additional reports

Wound healing outcomes of a randomized study using PRFE for the treatment of pre-tibial lacerations were reported by Muirhead et al. (1991). The reported healing rate for the treatment group was 27.21 days compared to 31.25 days for the control group patients ($p = 0.43$), with an associated healing rate of 0.187 cm^2/day and 0.194 cm^2/day, respectively ($p > 0.80$). A sub-group analysis of females under the age of 60 demonstrated a statistically significant reduction in healing time (19.5 days (T), 29.2 days (C), $p = 0.04$). While modestly beneficial outcomes were reported, results were less dramatic than other wound healing reports described above.

SAFETY AND CONTRAINDICATIONS

The safety of radio frequency (RF) radiation, including the shortwave frequency range, has been the focus of extensive study by governmental agencies and independent societies over the past 20 years. Based on the results of hundreds of human, animal, and basic science studies, U.S. federal and international authorities have concluded that there are no adverse health effects with RF exposure that are not thermally related (i.e., adverse health effects that are not associated with the heating of tissue).

In its report, *Questions and Answers about Biological Effects and Potential Hazards of Radiofrequency Electromagnetic Fields* (Cleveland and Ulcek, 1999), the U.S. Federal Communications Commission (FCC) states that "at relatively low levels of exposure to RF radiation, i.e., field intensities lower than those that would produce significant and measurable heating, the evidence for production of harmful biological effects is ambiguous and unproven." The ANSI/IEEE Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields (3 kHz–300 GHz) (ANSI/IEEE C95.1-2005) (Zundert et al., 2005) cites an extensive review of RF biological effects comprising over 1,300 primary peer reviewed publications published since 1950 within the ANSI/IEEE/WHO RF literature database[9]. The IEEE evaluated teratogenicity, reproduction, development, immune function, ocular and auditory effects, and cancer promotion and epidemiology, among other effects, and concluded in the Standard that "there are no adverse health

[9] The ANSI/IEEE Standard references a larger literature database shared between the American National Standards Institute, The Institute of Electrical and Electronic Engineers, and the World Health Organization. While this database includes articles relevant to the discussion of the risks of shortwave diathermy, it also includes extensive literature pertaining to other RF frequency bands (extending from 3 kHz–300 GHz). The findings of the literature review and conclusions pertain directly to shortwave diathermy as well as the larger defined RF frequency spectrum.

TABLE 5 Warnings and contraindications

Warnings and Contraindications
PRFE should not be used on patients who have any implanted metallic lead, or any implanted system that may contain a lead.
Use of PRFE is contraindicated in patients with implanted cardiac rhythm devices.
Use of PRFE is contraindicated in patients with metallic implants in the area of application.
Use of PRFE is contraindicated in pregnancy.
The effect of PRFE on preexisting malignancy at the site of treatment has not been fully evaluated.
PRFE should not be used over the joints of patients with immature bone development.

effects that are not thermally related." The Standard cites 16 other scientific expert groups and government agencies which have reached consistent conclusions, including the International Commission on Non-Ionizing Radiation Protection (ICNIRP), and the Australian, French, Dutch, Hong Kong, Japanese, Singapore, Swedish, and UK ministries of health, radiation protection and/or telecommunications. The ICNIRP (Ahlbom et al., 2004) reviewed the world epidemiologic literature in 2004 with a specific focus on occupational RF exposure[10] (including shortwave diathermy) and the risk of cancer, adverse reproductive outcome, cardiovascular disease, and cataracts, and concluded that there is "no consistent or convincing evidence of a causal relation between RF exposure and any adverse health effect." Finally, in 2007, the European Commission performed a global review of literature related to 27 MHz electromagnetic energy applied without direct electrode contact to the body[11] (i.e., shortwave diathermy) when used for soft tissue healing and identified no side effects (CNRS, 2007). The findings specifically address the risk of nonthermal shortwave diathermy (i.e., PRFE) as applied to wound healing.

Specific safety concerns and contraindications

While in general, no adverse health effects are associated with PRFE therapy, there are certain circumstances in which, due to specific safety concerns, PRFE should not be used. Specific concerns and contraindications are summarized here and in Table 5.

Patients with implanted wire leads and other metal implants (thermal injury risk)

Shortwave diathermy (including PRFE) should not be used on patients who have any implanted metallic lead, or any implanted system that may contain a lead. There is serious risk of thermal injury when PRFE is used in patients with implanted metallic leads. The FDA issued a public health notification in its Patient Safety News warning that the danger of thermal injury can occur even when the shortwave diathermy device is in non heating mode, when the implanted device is not turned on, and when the implant has been removed from the patient's body and the metal leads are left behind (FDA, 2003). The implanted devices that were the subject of FDA's public health notification included cardiac pacemakers and defibrillators, cochlear implants, bone growth stimulators, and deep brain, spinal cord, and other nerve stimulators.

[10] The risk to technicians and clinicians operating the medical devices.

[11] PRFE therapy typically delivers RF by means of an electromagnetic field that does not involve direct contact with the body, unlike other technologies that deliver energy by use of electrodes in direct contact with the body (e.g., surgical instruments for RF ablation and cutting, certain bone growth stimulators).

Patients with implanted cardiac rhythm devices (electromagnetic interference risk)

In addition to posing a risk of thermal injury in patients with implanted cardiac rhythm devices, use of PRFE in such patients also poses a risk of electromagnetic interference. Shortwave diathermy-associated pacemaker interference has been associated with clinically significant pacemaker dysfunction, such as increased and decreased pacemaker rate and rhythm, cessation of impulses, and ventricular fibrillation. Such reports of adverse interactions associated with shortwave diathermy and multiple other medical, industrial and household devices prompted the pacemaker industry to develop filters and shields intended to protect the devices from electromagnetic interference (Digby et al., 2009; Irnich et al., 1978; Reis, 1979). However, recommendations from international physiotherapy societies and labeling by manufacturers of cardiac rhythm devices uniformly have warned against use of shortwave diathermy (including PRFE) in patients with such implanted devices (Digby et al., 2009).

Patients with metal implants (not involving wire leads)

Current practice recommendations indicate that shortwave diathermy should not be applied to body regions with metal implants because of the possibility of thermal tissue damage. Seiger attributes this widely accepted rule to "common sense and consensus" rather than evidence-based decision making, and considers it an extrapolation of concerns arising from the effect on the metal of implanted pacemakers and neurostimulators (Seiger and Draper, 2006).

Pregnancy

Adverse effects associated with shortwave diathermy related to pregnancy, including congenital anomalies and low birth weight (Lerman et al., 2001; Ouellet-Hellstrom and Stewart, 1993; Taskinen et al., 1990), appear to be consequent to a detrimental elevation of maternal and/or fetal temperature, and are limited to devices which cause tissue heating, specifically thermal shortwave diathermy (Heynick et al., 2003). None-the-less, in the absence of definitive evidence for the safety of PRFE with respect to pregnancy, a conservative approach assumes that this risk, to some degree, could be applicable to PRFE devices, extrapolated from reports with thermal diathermy modalities, and thus the use of PRFE is contraindicated in pregnancy.

Patients with a preexisting malignancy

Exposure of preexisting tumors to elevated temperatures (i.e., between 40°C and 41.5°C) has been associated with accelerated tumor growth rate (Burr, 1974). In addition, multiple reports have demonstrated selective tumor heating and tumor cell proliferation with exposure to thermal shortwave diathermy (Auda et al., 1980; Kim and Hahn, 1979; LeVeen et al., 1976; Storm et al., 1979). Such reports have enhanced concerns in the physiotherapy community about the risk of thermal diathermy in patients with evidence of cancer, and serve as the basis for the precaution against thermal diathermy in patients with cancer. While animal and epidemiological studies have not demonstrated a carcinogenic effect of nonthermal RF (Heynick et al., 2003), *in vitro* studies have demonstrated induction of cellular proliferation with PRFE in human and rat cell lines (George et al., 2002), suggesting a possible risk of such therapy to patients with an established malignancy. A single adverse event involving malignancy and PRFE was reported to the FDA's MDR/MAUDE database[12] in a paraplegic patient with an ulcer of very long

[12] A search of the FDA's MDR and MAUDE databases was performed by searching for reports under the FDA assigned product code ILX through June 30, 2009.

(51-year) duration, though whether PRFE was a contributing factor is unknown[13] (Asuquo et al., 2007; Chraibi et al., 2004; Dumurgier et al., 1991; Mustoe et al., 1986).

Patients with immature bone development

Review of the literature identifies a potential detrimental effect of shortwave diathermy on the growth plates in children (Shields, 2004). Experimental studies are inconclusive regarding whether treatment accelerates or decelerates bone development (Shields, 2004). Shortwave diathermy has been used in the treatment of children undergoing orchidopexy (Bentall and Eckstein, 1975) and gluteal muscle contracture (Zhao et al., 2009) without adverse events.[14] In addition, there were no adverse events reported to FDA's MDR/MAUDE database pertaining to the treatment of children.

CONCLUSION

PRFE is an effective, easy-to-administer treatment modality used in the adjunctive care of patients in numerous clinical areas. It has been used in soft tissue as a palliative treatment for pain and edema (both postoperative and non-postoperative), and as an adjunctive wound healing therapeutic. When used as directed, adverse side effects are rare. The treatment is non invasive, and can be applied locally to the target tissue. In efficacy studies related to postoperative and non postoperative pain and edema, PRFE treatment has been reported to not only relieve pain and edema, but to facilitate faster recovery time and to reduce length of hospital stay, a notable benefit in an era of ever-increasing health care costs. Its effectiveness at promoting the healing of difficult-to-heal wounds, such as diabetic and chronic wounds, makes it an important adjunctive wound healing treatment option, particularly for wounds non responsive to standard of care treatment. With the number of patients presenting with diabetes on the rise, as well as a growing geriatric population, this is particularly noteworthy. With its demonstrated efficacy in numerous clinical areas, limited risks, ease-of-use and relative low-cost, the clinical application of PRFE therapy is likely to become increasingly widespread in the years to come.

ACKNOWLEDGEMENTS

We would like to thank Jill Munsinger for analysis, writing, and editing contributions, Teresa Nelson for analysis contributions, and John Moffett for editing contributions as well as insightful discussions during manuscript preparation.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

REFERENCES

Ahlbom, A., Green, A., Kheifets, L., et al. (2004). Epidemiology of health effects of radiofrequency exposure. *Environ. Health Perspect.* 112:1741–1754.

[13] Development of squamous cell carcinoma (SCC) in the wound bed (a chronic ulcer of 51-year duration), likely as a complication known as Marjolin's Ulcer, a rare, spontaneous complication arising in chronic cutaneous ulcers of long duration, occurred 10 months after a $1\frac{1}{2}$ year PRFE treatment regimen. Whether PRFE was a contributing factor is unknown.

[14] The former article (Bentall and Eckstein) involved use of PRFE. The thermal character of the diathermy device in the latter article (Zhao) is not discussed.

Al-Mandeel, M. M., Watson, T. (2008). Pulsed and continuous shortwave therapy. In: Watson, T. *Electrotherapy: Evidence-Based Practice* (pp. 137–160). Edinburgh, New York: Churchill Livingstone.

Aronofsky, D. H. (1971). Reduction of dental postsurgical symptoms using nonthermal pulsed high-peak-power electromagnetic energy. *Oral Surg. Oral Med. Oral Pathol.* 32:688–696.

Asuquo, M., Ugare, G., Ebughe, G., et al. (2007). Marjolin's ulcer: the importance of surgical management of chronic cutaneous ulcers. *Int. J. Dermatol.* 46(Suppl. 2):29–32.

Auda, S. P., Steinert, H. R., Elias, E. G., et al. (1980). Selective tumor heating by shortwave radiofrequency (RF). *Cancer* 46:1962–1968.

Barclay, V., Collier, R. J., Jones, A. (1983). Treatment of various hand injuries by pulsed electromagnetic energy (Diapulse). *Physiotherapy* 69:186–188.

Barker, A. T., et al. (1985). A double-blind clinical trial of low power shortwave therapy in the treatment of soft tisssue injury. *Physiotherapy* 71:500–504.

Bentall, R. H. C., Eckstein, H. B. (1975). A trial involving the use of pulsed electro-magnetic therapy on children undergoing orchidopexy. *Zeitschrift für Kinderchirurgie* 17(4):380–389.

Burr, B. (1974). Heat as a therapeutic modality against cancer. *Report NO16*, U.S. National Cancer Institute, Bethesda, MD.

Buzzard, B. M., Pratt, R. K., Briggs, P. J., et al. (2003). Is pulsed shortwave diathermy better than ice therapy for the reduction of oedema following calcaneal fractures?: Preliminary trial. *Physiotherapy* 89: 734–742.

Callaghan, M. J., Whittaker, P. E., Grimes, S., et al. (2005). An evaluation of pulsed shortwave on knee osteoarthritis using radioleucoscintigraphy: a randomised, double blind, controlled trial. *Joint Bone Spine* 72:150–155.

Cameron, B. M. (1964). A three phase evaluation of pulsed, high frequency, radio short waves (Diapulse): 646 patients. *Amer. J. Orthop.* 6:72–78.

Chraibi, H., Dereure, O., Teot, T., et al. (2004). The diagnosis and treatment of carcinomas occurring at the sites of chronic pressure ulcers. *J. Wound Care* 13:447.

Cleveland R. F. and Ulcek, J. L. (1999). Questions and answers about biological effects and potential hazards of radiofrequency electromagnetic fields. Office of Engineering and Technology (OET) Bulletin. Federal Communications Commission. Washington, D.C. 56 (4): 10. Retrieved from http://www.fcc.gov/oet/info/documents/bulletins/

CNRS (2007). European Commission Joint Research Center/CNRS. (2007). Effects of exposure to electromagnetic fields: from science to public health and safer workplace. Reports on the level of evidence of the results present in the literature and research projects describing clinical applications (Deliverable 14). p. 13. European Union 6th Framework Programme. Retrieved from http://web.jrc.ec.europa.eu/emf-net/doc/reports/D14_level_of_evidence.pdf

Comorosan, S., Pana, I., Pop, L., et al. (1991). The influence of pulsed high peak power electromagnetic energy (Diapulse) treatment on posttraumatic algoneurodystrophies. *Rev. Roum. Physiol.* 28:77–81.

Digby, G. C., Daubney, M. E., Baggs, J., et al. (2009). Physiotherapy and cardiac rhythm devices: a review of the current scope of practice. *Europace* 11:850–859.

Dumurgier, C., Pujol, G., Chevalley, J., et al. (1991). Pressure sore carcinoma: a late but fulminant complication of pressure sores in spinal cord injury patients: case reports. *Paraplegia* 29: 390–395.

FDA (2003). Warning on diathermy and implanted leads. FDA Patient Safety News. U.S. Food and Drug Administration. Silver Spring, MD. Show 13, March 2003. Retrieved from transcript of video webcast at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/psn/transcript.cfm?show=13#5

Foley-Nolan, D., Barry, C., Coughlan, R. J., et al. (1990). Pulsed high frequency (27 MHz) electromagnetic therapy for persistent neck pain. A double blind, placebo-controlled study of 20 patients. *Orthopedics* 13:445–451.

Foley-Nolan, D., Moore, K., Codd, M., et al. (1992). Low energy high frequency pulsed electromagnetic therapy for acute whiplash injuries. A double blind randomized controlled study. *Scand J Rehabil Med* 24:51–59.

Frank, R. (1985). Treatment of the perineum by pulsed electro magnetic therapy. *Midwives Chron.* 98(1174):297–298.

Frykberg, R., Tierney, E., Tallis, A., et al. (2009). Cell proliferation induction: healing chronic wounds through low-energy pulsed radiofrequency. *Int. J. Low Extrem. Wounds* 8:45–51.

Geddes, L. A. (1999). Retrospectroscope. d'Arsonval, Physician and Inventor. *IEEE Eng. Med. Biol.* July/August:118–122.

George, F. R., Lukas, R. J., Moffett, J., et al. (2002). In-vitro mechanisms of cell proliferation induction: a novel bioactive treatment for accelerating wound healing. *Wounds* 14:107–115.

Gilbert, T. L., Griffin, N., Moffett, J., et al. (2002). The Provant Wound Closure System induces activation of p44/42 MAP kinase in normal cultured human fibroblasts. *Ann. N Y Acad. Sci.* 961:168–171.

Goats, G. C. (1989). Pulsed electromagnetic (short-wave) energy therapy. *Br. J. Sports Med.* 23:213–216.

Goldin, J. H., Broadbent, N. R., Nancarrow, J. D., et al. (1981). The effects of Diapulse on the healing of wounds: a double-blind randomised controlled trial in man. *Br. J. Plast. Surg.* 34:267–270.

Grant, A., Sleep, J., McIntosh, J., et al. (1989). Ultrasound and pulsed electromagnetic energy treatment for perineal trauma. A randomized placebo-controlled trial. *Br. J. Obstet. Gynaecol.* 96:434–439.

Guo, L., Kubat, N.J., Nelson, T.R., and Isenberg, R.A. Meta-Analysis of Clinical Efficacy of Pulsed Radio Frequency Energy Treatment. Submitted.

Hayne, C. R. (1984). Pulsed high frequency energy - its place in physiotherapy. *Physiotherapy* 70(12): 459–466.

Heden, P., Pilla, A. A. (2008). Effects of pulsed electromagnetic fields on postoperative pain: a double-blind randomized pilot study in breast augmentation patients. *Aesthetic Plast. Surg.* 32:660–666.

Heynick, L. N., Johnston, S. A., Mason, P. A. (2003). Radio frequency electromagnetic fields: cancer, mutagenesis, and genotoxicity. *Bioelectromagn. Suppl.* 6:S74–100.

Hutchinson, D., Witt, S., Fairpo, C. G. (1978). Pulsed electromagnetic energy therapy in third molar surgery. *Oral Surg. Oral Med. Oral Pathol.* 46:748–754.

Irnich, W., de Bakker, J. M., Bisping, H. J. (1978). Electromagnetic interference in implantable pacemakers. *Pacing Clin. Electrophysiol.* 1:52–61.

Itoh, M., Montemayor, Jr, J. S., Matsumoto, E., et al. (1991). Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). *Decubitus* 4:24–25, 29–34.

Jan, M. H., Chai, H. M., Wang, C. L., et al. (2006). Effects of repetitive shortwave diathermy for reducing synovitis in patients with knee osteoarthritis: an ultrasonographic study. *Phys. Ther.* 86: 236–244.

Kaplan, E. G., Weinstock, R. E. (1968). Clinical evaluation of diapulse as adjunctive therapy following foot surgery. *J. Amer. Podiat. Assoc.* 58:218–221.

Kim, J. H., Hahn, E. W. (1979). Clinical and biological studies of localized hyperthermia. *Cancer Res.* 39: 2258–2261.

Kloth, L. C., Berman, J. E., Sutton, C. H., et al. (1999). Effect of pulsed radio frequency stimulation on wound healing: a double-blind pilot study. In: Bersani, F. *Electricity and Magnetism in Biology and Medicine* (pp. 875–878). New York: Academic/Plenum.

Kloth, L. C., Pilla, A. A. (2010). Electromagnetic stimulation for wound repair. In: McCulloch, J., M.Kloth, L. C. *Wound Healing: Evidence-Based Management* (pp. 514–544). Philadelphia: F. A. Davis Company.

Larsen, J. A., Overstreet, J. (2008). Pulsed radio frequency energy in the treatment of complex diabetic foot wounds. *J. WOCN* 35(5): 523–527.

Laufer, Y., Zilberman, R., Porat, R., et al. (2005). Effect of pulsed short-wave diathermy on pain and function of subjects with osteoarthritis of the knee: a placebo-controlled double-blind clinical trial. *Clin. Rehab.* 19:255–263.

Lerman, Y., Jacubovich, R., Green, M. S. (2001). Pregnancy outcome following exposure to shortwaves among female physiotherapists in Israel. *Amer. J. Ind. Med.* 39:499–504.

LeVeen, H. H., Wapnick, S., Piccone, V., et al. (1976). Tumor eradication by radiofrequency therapy. Responses in 21 patients. *JAMA* 235:2198–2200.

Markov, M. S. (2007). Pulsed electromagnetic field therapy history, state of the art and future. *The Environmentalist* 27(4):465–475.

Mayrovitz, H. N., Sims, N., Macdonaki, J. (2002). Effects of pulsed radio frequency diathermy on postmastectomy arm lymphedema and skin blood flow: a pilot investigation. *Lymphology* 35:353–356.

Moffett, J., Kubat, N. J., Griffin, N. E., et al. Pulsed radio frequency energy field treatment of cells in culture results in increased expression of genes involved in angiogenesis and tissue remodeling during wound healing. *J. Diabetic Foot Complic*. In press.

Moffett, J., Griffin, N. E., Ritz, M. C., et al. (2010) Pulsed radio frequency energy field treatment of cells in culture results in increased expression of genes involved in the inflammation phase of lower extremity diabetic wound healing. *J. Diabetic Foot Complic.* 2(3):57–64.

Muirhead, R. J., Place, D., Buswell, W. A., et al. (1991). Pulse electromagnetic energy and pre-tibial lacerations: a randomized clinical trial. *Arch. Emerg. Med.* 8:152–154.

Mustoe, T., Upton, J., Marcellino, V., et al. (1986). Carcinoma in chronic pressure sores: a fulminant disease process. *Plast. Reconstr. Surg.* 77:116–121.

Nicolle, F. V., Bentall, R. M. (1982). Use of radio-frequency pulsed energy in the control of postoperative reaction in blepharoplasty. *Aesthetic Plast. Surg.* 6:169–171.

Ouellet-Hellstrom, R., Stewart, W. F. (1993). Miscarriages among female physical therapists who report using radio- and microwave-frequency electromagnetic radiation. *Amer. J. Epidemiol.* 138:775–786.

Pasila, M., Visuri, T., Sundholm, A. (1978). Pulsating shortwave diathermy: value in treatment of recent ankle and foot sprains. *Arch. Phys. Med. Rehab.* 59:383–386.

Pennington, G. M., Danley, D. L., Sumko, M. H., et al. (1993). Pulsed, non-thermal, high-frequency electromagnetic energy (DIAPULSE) in the treatment of grade I and grade II ankle sprains. *Mil. Med.* 158:101–104.

Pilla, A. A. (2007). Mechanisms of therapeutic applications of time-varying and static magnetic fields. In: Greenebaum, F. S. B. A. B., *Handbook of Biological Effects of Electromagnetic Fields Biological and Medical Aspects of Electromagnetic Fields* (pp. 351–411). Boca Raton, FL: CRC Press.

Porreca, E. G., Giordano-Jablon, G. M. (2008). Treatment of severe (stage III and IV) chronic pressure ulcers using pulsed radio frequency energy in a quadriplegic patient. *Eplasty* 8:e49.

Reis, R. (1979). Potential interference with medical electronic devices. *Bull. NY Acad. Med.* 55:1216–1221.

Rhodes, L. C. (1981). The adjuctive utilization of Diapulse therapy (pulse high peak power electromagnetic energy) in accelerating tissue healing in oral surgery. *Quart. NDA* 39:166–175.

Rohde, C., Chiang, A., Adipoju, O., et al. (2010). Effects of pulsed electromagnetic fields on interleukin-1beta and postoperative pain: a double-blind, placebo-controlled, pilot study in breast reduction patients. *PRS* 125:1620–1627.

Salzberg, C. A., Cooper-Vastola, S. A., Perez, F. J., et al. (1995). The effects of non-thermal pulsed electromagnetic energy (Diapulse) on wound healing of pressure ulcers in spinal cord-injured patients: a randomized double-blind study. *Wounds* 7(1):11–16.

Santiesteban, A. J., Grant, C. (1985). Post-surgical effect of pulsed shortwave therapy. *J. Amer. Podiatr. Med. Assoc.* 75:306–309.

Seaborne, D., Quirion-DeGirardi, C., Rousseau, M., et al. (1996). The treatment of pressure sores using pulsed electromagetic energy (PEME). *Physiother. Cancer* 48:131–137.

Seiger, C., Draper, D. O. (2006). Use of pulsed shortwave diathermy and joint mobilization to increase ankle range of motion in the presence of surgical implanted metal: A case series. *J. Orthop. Sports Phys. Ther.* 36:669–677.

Shandles, I. D. P., J., Reynolds, K. L. (2002). Heel Neurooma: the egigma of recalcitrant heel pain and an innovative approach highlighting sixty surgical cases and areview of two hundred and fifty seven symptomatic but non-surgical cases. *Foot* 12:10–20.

Sherman, G. A quick review of pulsed radiofrequency stimulation (PRFS). *Podiat. Manage.* 2007 (June/July): p. 187.

Silver, H. (1982). Reduction of capsular contracture with two-stage augmentation mammaplasty and pulsed electromagnetic energy (Diapulse therapy). *Plast. Reconstr. Surg.* 69(5):802–808.

Storm, F. K., Harrison, W. H., Elliott, R. S., et al. (1979). Normal tissue and solid tumor effects of hyperthermia in animal models and clinical trials. *Cancer Res.* 39:2245–2251.

Sussman, C., Bates-Jensen, B. M. (2007). Induced electrical stimulation: pulsed radio frequency and pulsed electromagnetic fields. In: Sussman, C., Bates-Jensen, B. M. *Wound Care: a Collaborative Practice Manual for Health Professionals* (pp. 555–590). Philadelphia: Lippincott Williams & Wilkins.

Svarcova, J., Trnavsky, K., Zvarova, J. (1988). The influence of ultrasound, galvanic currents and shortwave diathermy on pain intensity in patients with osteoarthritis. *Scand. J. Rheumatol.* 67:83–85.

Taskinen, H., Kyyronen, P., Hemminki, K. (1990). Effects of ultrasound, shortwaves, and physical exertion on pregnancy outcome in physiotherapists. *J. Epidemiol. Commun. Health* 44:196–201.

Tung, S., Khaski, A., Milano, E., et al. (1995). The application of diapulse in the treatment of decubitus ulcers: case reports. *Contemp. Surg.* 47:27–33.

Wagstaff, P., Wagstaff, S., Downey, M. (1986). A pilot study to compare the efficacy of continuous and pulsed magnetic energy [short-wave diathermy] on the relief of low back pain. *Physiotherapy* 72: 563–566.

Wilson, C. M. (1995). Learning to use a medical technology. *Geriatr. Nur. (London)* 16:20–21.

Wilson, D. H. (1974). Comparison of short wave diathermy and pulsed electromagnetic energy in treatment of soft tissue injuries. *Physiotherapy* 60:309–310.

Zhao, C. G., He, X. J., Lu, B., et al. (2009). Classification of gluteal muscle contracture in children and outcome of different treatments. *BMC Musculoskelet Disord* 10:34.

Zundert, J. V., de Louw, A. J. A., Joosten, E. A. J., et al. (2005). Pulsed and continous radiofrequency current adjacent to the cervical dorsal root ganglion of the rat induces late cellular activity in the dorsal horn. *Anesthesiology* 102:125–131.