Effects of Pulsed Electromagnetic Fields on Interleukin-1β and Postoperative Pain: A Double-Blind, Placebo-Controlled, Pilot Study in Breast Reduction Patients

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Background: Surgeons seek new methods of pain control to reduce side effects and speed postoperative recovery. Pulsed electromagnetic fields are effective for bone and wound repair and pain and edema reduction. This study examined whether the effect of pulsed electromagnetic fields on postoperative pain was associated with differences in levels of cytokines and angiogenic factors in the wound bed.

Methods: In this double-blind, placebo-controlled, randomized study, 24 patients, undergoing breast reduction for symptomatic macromastia received pulsed electromagnetic field therapy configured to modulate the calmodulin-dependent nitric oxide signaling pathway. Pain levels were measured by a visual analogue scale, and narcotic use was recorded. Wound exudates were analyzed for interleukin (IL)-1β, tumor necrosis factor-α, vascular endothelial growth factor, and fibroblast growth factor-2.

Results: Pulsed electromagnetic fields produced a 57 percent decrease in mean pain scores at 1 hour ($p < 0.01$) and a 300 percent decrease at 5 hours ($p < 0.001$), persisting to 48 hours postoperatively in the active versus the control group, along with a concomitant 2.2-fold reduction in narcotic use in active patients ($p = 0.002$). Mean IL-1β concentration in the wound exudates of treated patients was 275 percent lower ($p < 0.001$). There were no significant differences found for tumor necrosis factor-α, vascular endothelial growth factor, or fibroblast growth factor-2 concentrations.

Conclusions: Pulsed electromagnetic field therapy significantly reduced postoperative pain and narcotic use in the immediate postoperative period. The reduction of IL-1β in the wound exudate supports a mechanism that may involve manipulation of the dynamics of endogenous IL-1β in the wound bed by means of a pulsed electromagnetic field effect on nitric oxide signaling, which could impact the speed and quality of wound repair. (*Plast. Reconstr. Surg.* 125: 1620, 2010.)

Postsurgical pain increases patient morbidity and slows healing, particularly if narcotics, even by means of pain pumps, are used for pain management.[1–3] Therefore, surgeons are continually looking for other means of delivering postoperative analgesia. There is a growing body of clinical evidence that noninvasive, nonpharmacologic pulsed electromagnetic field therapy can have physiologically significant effects on inflammation and tissue repair.[4–6] Outpatient pulsed electromagnetic field therapy has been used extensively for the treatment of recalcitrant bone fractures for more than 30 years, and is reported to be as successful as an initial bone graft.[7] Recent advances in knowledge of the mechanism of the effects of pulsed electromagnetic field on tissue repair have led to the development of signals that can target the antiinflammatory cascade involving the calmodulin-dependent nitric oxide pathway. A pulsed electromagnetic field signal based on this model[8] has been shown to accelerate wound repair in a rat cutaneous wound model by 60 percent

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at 21 days[9] and Achilles tendon repair in a rat model by 70 percent at 21 days.[10] The same pulsed electromagnetic field signal has been reported to accelerate postsurgical pain relief in breast augmentation patients by 2.7-fold, with a concomitant decrease in the use of pain medication.[11]

Soft-tissue healing is a complex process involving the interactions of multiple cell types and a variety of molecules.[12] Cytokines, the humoral mediators of inflammation, are induced within minutes to hours after tissue damage, and serve as signals to engulf damaged tissue, destroy infectious agents, and clear the wound bed for healing.[13] Angiogenesis provides new vascular conduits for oxygen, nutrients, and hormones, and numerous studies indicate that pulsed electromagnetic fields can have a significant impact on angiogenesis both in vitro and in vivo.[14–18] Two of these studies showed, using specific antagonists, that modulation of fibroblast growth factor (FGF)-2 production was involved.[17,18] Indeed, many studies have demonstrated that pulsed electromagnetic fields modulate both cytokine and growth factor synthesis,[19–21] but to date there have been no examinations of the effects of pulsed electromagnetic fields on the molecular indices of pain, inflammation, and angiogenesis in postsurgical patients.

This pilot study was designed to determine whether pulsed electromagnetic field therapy, provided as a supplement to the current standard of care, could reduce postoperative pain, and to examine the content of wound exudates for levels of inflammatory cytokines and angiogenic factors as indices to better understand how pulsed electromagnetic field therapy may act on these processes.

Disclosures: *The pulsed electromagnetic field devices used in this study are cleared by the U.S. Food and Drug Administration for relief of postoperative pain and edema in superficial soft tissues and were donated by Ivivi Technologies, Inc. (Montvale, N.J.); Christine Rohde, M.D., Austin Chiang, and Omotinuwe Adipojou, M.D., have no financial interest or connections with Ivivi Technologies, Inc. They have no financial interests or sources of support to disclose. Diana Casper, Ph.D., receives research support from Ivivi Technologies, Inc., for unrelated cellular studies at Montefiore Medical Center and had no contact with patients in this study. Arthur A. Pilla, Ph.D., is a paid scientific consultant to Ivivi Technologies, Inc., and had no contact with patients in this study.*

MATERIALS AND METHODS

This study was approved by the Institutional Review Board at Columbia University Medical Center. Before the start of this study, a sample size analysis, assuming a clinically meaningful 50 ± 40 percent decrease in pain scores from pulsed electromagnetic field treatment,[22] suggested that 11 patients per group were needed. Thus, 24 healthy women, aged 27 to 59 years, who were candidates for breast reduction for symptomatic macromastia, were admitted to this double-blind, placebo-controlled, randomized study. All patients undergoing breast reduction surgery were asked to participate and all enrolled patients gave informed consent. Randomization was performed by the blinded assignment of devices from a list of their serial numbers. Breast reductions were performed by the same surgeon (C.R.) using standard breast reduction techniques with superomedial pedicles. Use of pulsed electromagnetic field coils was the only addition to the current standard of care. As is the routine practice for this surgeon, 10-mm Jackson-Pratt drains were placed into each breast and brought out through the incision. These drains were left in place until the first postoperative morning, when they were removed at the bedside before the patient was discharged from the hospital. This permitted the collection of wound exudates in the immediate postoperative stages of healing. Exudates were collected into 15-ml polypropylene tubes and stored at −80°C for subsequent analysis.

Patients were randomly assigned a disposable dual-coil pulsed electromagnetic field device (SofPulse Duo; Ivivi Technologies, Inc., Montvale, N.J.), placed within the postsurgical support bra normally used for all patients, as shown in Figure 1. Devices were activated on transfer to the recovery stretcher. The pulsed electromagnetic field signal, configured a priori to modulate Ca^{2+} binding to calmodulin, consisted of a 2-msec burst of 27.12-MHz sinusoidal waves repeating at two bursts per second. Peak magnetic field was 0.05 G, which induced an average electric field of 32 ± 6 mV/cm in each breast.[8,23,24] An active pulsed electromagnetic field device automatically provides a 20-minute treatment every 4 hours for the first 3 days of treatment, then once every 8 hours for the next 3 days, then twice daily thereafter. The availability of this automatic regimen ensures patient compliance and allows these devices to be used throughout the various stages of wound repair.[25] Sham devices were used in exactly the same manner as active devices but produced no electromagnetic field in tissue. These pulsed electromag-

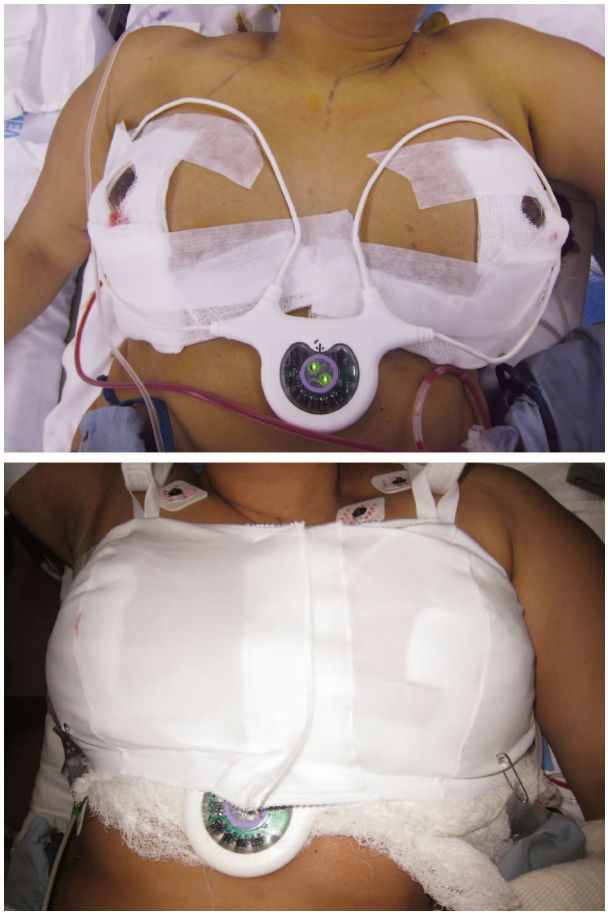

Fig. 1. The pulsed electromagnetic field device used in this study. (*Above*) Pulsed electromagnetic field device in place with each coil surrounding one breast. The battery-powered signal generator is at the bottom between the coils. Once activated, indicator lights flash approximately once per second for both active and sham devices. Note the surgical drains leading from each breast. (*Below*) Postsurgical support bra, normally used with this procedure, in place holding pulsed electromagnetic field device in position.

netic field devices do not produce heat or cause any sensation in tissue. The average in situ magnetic field induced by the pulsed electromagnetic field signal used in this study is at least 1000-fold below the earth's magnetic field and not detectable using standard gaussmeters. Therefore, only measurements with specialized laboratory equipment, not normally available in the recovery or hospital room or in the patient's home, could determine whether a device was active. Neither physicians nor patients knew whether a device was active throughout the study. General unblinding occurred after all data were collected.

Pulsed electromagnetic field signal amplitude and configuration was verified for each device by a third party, who had no contact with patients, at the beginning and end of pulsed electromagnetic field treatment with a calibrated field probe (model FCC-301-1-MR1; Fischer Custom Communications, Torrance, Calif.) connected to a calibrated 100-MHz oscilloscope (model 2358; Tektronix, Beaverton, Ore.). Measurement of the pulsed electromagnetic field signal distribution in a tissue phantom and in air provides an accurate map of the signal in tissue.[26] Such plots revealed that the amplitude dose of the electromagnetic field in the treated breast from active devices was uniform to within ±20 percent.

The two primary outcome measures in this study were (1) postsurgical pain and (2) cytokine and growth factor concentrations in wound exudates. Pain levels were assessed by self-evaluation with a visual analogue scale previously validated for postsurgical pain.[27,28] Visual analogue scale data were obtained at intervals starting at hour 1 postoperatively and at specified intervals thereafter for 48 hours. Use of narcotic pain medication (oxycodone/acetaminophen) over the first 48 hours was assessed by comparing pill counts for each group. All patients received oxycodone/acetaminophen (Percocet; Endo Pharmaceuticals, Newark, Del.) as soon as they were able to tolerate oral intake, usually within several hours after surgery, and discharged with a prescription. Because oxycodone/acetaminophen was the most common narcotic pain medication taken postoperatively, an equianalgesic table was used to convert other narcotics (e.g., morphine, hydromorphone, fentanyl, codeine, hydrocodone) given in the immediate postoperative period into Percocet equivalents.[29] This conversion enabled a comparison of pain medication use between the two groups.

Wound exudate was collected hourly starting at 1 hour postoperatively for the first 6 hours, and on the first postoperative morning before drain removal (at 15 to 24 hours postoperatively). All exudate fluid at each time point was removed completely, so that samples contained fluid drained only since the prior fluid collection. These samples were coded in a manner such that subsequent analyses were performed in a blinded fashion. For determination of cytokine and growth factor levels, exudates were thawed, cellular debris was pelleted by centrifugation, and resulting supernatants were divided into smaller aliquots and frozen at −80°C until analysis. Interleukin (IL)-1β, tumor necrosis factor (TNF)-α, vascular endothelial growth factor (VEGF), and FGF-2 were quantified using the appropriate enzyme-linked immunosorbent assay kit (R&D Systems, Minneapolis, Minn.). Pilot assays were performed initially with at least two samples to determine appropriate dilutions of exudates that fell within the linear range of quan-

tification for each assay. The Mann-Whitney rank sum test, analysis of variance, or repeated measures analysis of variance was used, as appropriate, to compare mean visual analogue scale scores and cytokine and growth factor levels. Significance was accepted at $p \leq 0.05$.

RESULTS

The portable and disposable pulsed electromagnetic field devices were well tolerated. No adverse events were reported. Data from 24 patients (12 active and 12 sham) were available for analysis. There was no significant difference between the two patient groups in terms of age, body mass index, or amount of tissue resected. Mean visual analogue scale scores over the 48-hour postsurgical period were compared. The results show a 57 percent decrease in mean pain at 1 hour ($p < 0.01$) and a 300 percent decrease at 5 hours, persisting to 48 hours postoperatively, in the active group compared with the untreated control group ($p < 0.001$). There was no significant change in mean visual analogue scale scores over the same postoperative time in the sham group. These results are summarized in Figure 2.

The mean pill count over the first 48 postoperative hours (using oxycodone/acetaminophen equivalents) in the active group was 5 ± 0.9 compared with 11 ± 1.2 in the sham group, demonstrating a significant 2.2-fold reduction in narcotic use in patients treated with pulsed electromagnetic field therapy ($p = 0.002$). Importantly, the magnitude of this effect correlates well with the decrease in mean visual analogue scale score over the same postoperative period in these patients. These results are summarized in Figure 3.

Wound exudates, collected from 22 patients at 1 to 24 hours postoperatively, were analyzed to quantify levels of IL-1β, a master cytokine induced at early times after tissue injury[30]; TGF-α, a cytotoxic factor[31]; VEGF, a central mediator of angio-

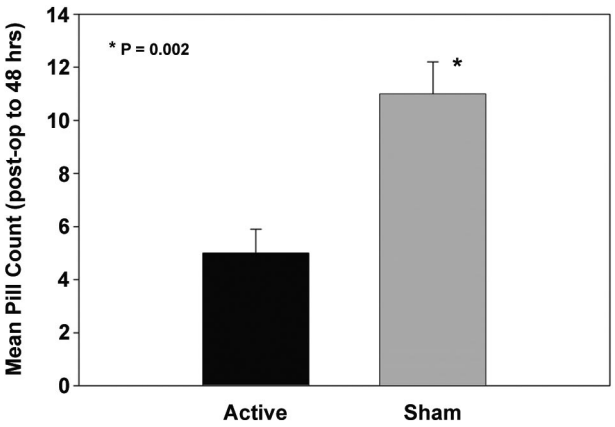

Fig. 3. Effect of pulsed electromagnetic field therapy on narcotic use (Percocet) following breast reduction surgery. The results show approximately 2.2-fold fewer pills were taken over the first 48 postoperative hours, correlating with the decrease in mean visual analogue scale score over the same period (Fig. 1).

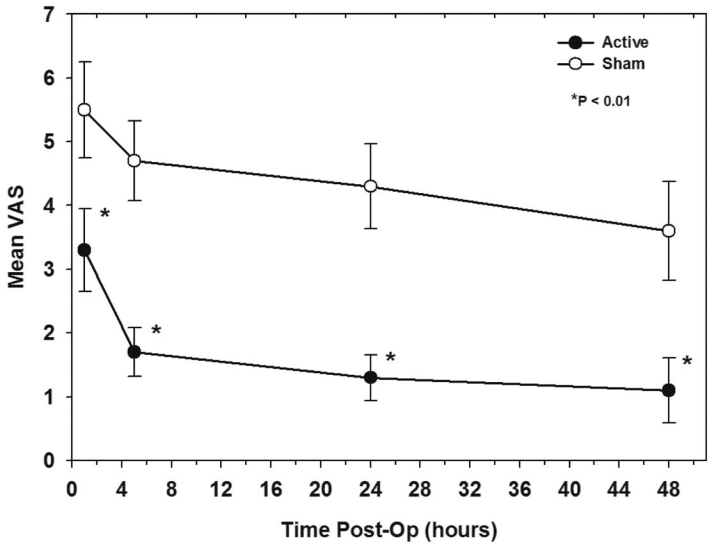

Fig. 2. Effect of pulsed electromagnetic field therapy on pain following breast reduction surgery. Mean visual analogue scale (*VAS*) score was significantly reduced starting at 1 hour postoperatively and approximately 3-fold lower at 5 hours postoperatively in the active group. There was no significant difference in mean visual analogue scale score in the sham group over the first 48 hours postoperatively.

genesis[32]; and FGF-2, an important factor in wound healing that can induce both fibroblast proliferation and angiogenesis.[33] The concentrations of these factors in the wound exudates collected in this study are consistent with levels reported in other studies.[34–37] No differences between active and sham groups were found for TNF-α, VEGF, or FGF-2 concentrations over the entire postoperative sampling period. In addition, the concentrations of these factors did not significantly increase over the same sampling period, as reported for the same early postoperative period in other studies.[38] In contrast, the overall mean IL-1β levels in the active cohort were approximately 275 ± 36 percent lower than in the sham cohort over the same postoperative sampling period ($p < 0.001$). A summary of the wound exudate data for the 6-hour sample is shown in Table 1.

Table 1. Mean Concentration, at the 6-Hour Postoperative Sample Time, of the Cytokines and Growth Factors in the Wound Exudates Evaluated in This Study*

Factor	Active (pg/ml)	Sham (pg/ml)	Active vs. Sham (%)	*p*
IL-1β	100 ± 11	208 ± 32	–200	0.001*
TNF-α	13 ± 3	15 ± 3	–14	0.572
FGF-2	577 ± 49	468 ± 59	+22	0.176
VEGF	970 ± 89	1026 ± 96	–5	0.671

*There is no significant difference for TNF-α, FGF-2, or VEGF. Only IL-1β was significantly lower in the active cohort ($p = 0.001$).

It is also of interest to compare the postoperative time course of the increase of IL-1β in the sham and active cohorts. This is shown in Figure 4, in which the concentration of IL-1β at each time point shown represents its accumulation in the wound exudate since the previous sample. IL-1β varied from 350 percent lower in exudates collected at 1 hour ($p < 0.001$), to 300 percent lower at 3 hours ($p < 0.001$), to 200 percent lower at 6 hours ($p < 0.001$), remaining at 200 percent lower at 15 to 24 hours (average, 18 hours) postoperatively ($p < 0.01$), than the sham group at the equivalent postoperatively time. These results correlate well with the temporal reduction in mean visual analogue scale pain scores and in the use of pain medication by patients in the active cohort. The mean volume of wound exudate collected between 6 and 15 to 24 hours was not significantly different from that collected between 5 and 6 hours, indicating that the rate of exudate accumulation in the wound bed had slowed significantly.

DISCUSSION

Results from this randomized, double-blind, placebo-controlled study demonstrate that pulsed

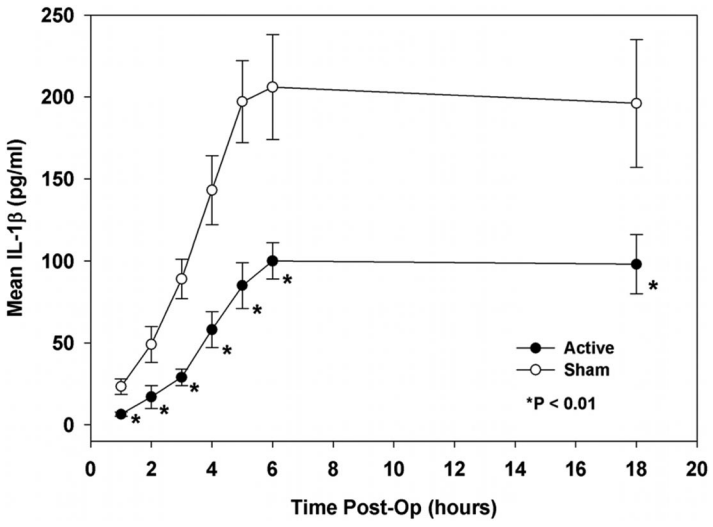

Fig. 4. Effect of pulsed electromagnetic field therapy on IL-1β concentrations in wound exudates following breast reduction surgery. Mean IL-1β concentration varied from approximately 350 percent lower at 1 hour postoperatively ($p < 0.001$), to approximately 300 percent lower at 3 hours, to approximately 200 percent lower at 6 hours ($p < 0.001$), and remaining approximately 200 percent lower at an average of 18 hours ($p < 0.01$) in the active group compared with the sham group. These results correlate well with the variation of mean visual analogue scale score over the same postoperative period (Fig. 2).

electromagnetic field therapy has a significant impact on postoperative pain. We believe that these findings could have major implications in developing new strategies for pain management. The effects of pulsed electromagnetic fields on pain reported here are of higher magnitude than those reported for pain pumps.[3] The effects on analgesia are also similar to those reported using the same pulsed electromagnetic field signal in an independent study on postoperative pain in breast augmentation patients performed in Sweden by different clinical investigators under different conditions,[11] supporting the consistency and validity of this type of therapeutic modality. The Swedish study did not include cytokine and/or growth factor analyses, but did include a third contralateral cohort in which one breast received pulsed electromagnetic field therapy and the contralateral breast received sham treatment. That study reported that the pulsed electromagnetic field effects on postoperative pain reduction for both active and sham breasts were not significantly different from each other or from that for the active cohort in which both breasts received pulsed electromagnetic field therapy. Analysis of the distribution of the pulsed electromagnetic field signal in both breasts in the contralateral cohort showed that the sham breast received approximately 60 percent of the signal amplitude present in the active breast. In other words, because of the spatial distribution of pulsed electromagnetic field signal propagation from the coil applicator, it was technically impossible to ensure zero signal amplitude in the sham breast. In view of the above, no attempt was made to include a contralateral cohort in the present study. It is also important to note that the effect of pulsed electromagnetic fields on pain was highly significant; mixed effect analyses[39] were not required.

No significant differences were found for TNF-α, VEGF, and FGF-2, which may be attributable to the slower kinetics of their appearance in the wound bed, as reported by other groups.[12,37] In contrast, quantitative data demonstrate that IL-1β levels in the wound exudates of patients treated with active pulsed electromagnetic field coils were concomitantly and significantly reduced. Interestingly, the postoperative time course of both pain and IL-1β reduction were similar, suggesting that a common mechanism produced both effects. The importance of this finding may be related to reports that the dynamics of IL-1β delivery in the wound bed affects the rate and quality of wound repair.[40] This is also supported by results from another study in which genetic disruption of IL-1 signaling reduced wound fibrosis and collagen deposition (scar), improved skin architecture, and increased tensile strength.[41] Although inflammation is essential for healing, it is the most painful stage of wound repair and, if not resolved quickly, can delay healing and lead to complications such as fibrosis, scarring, and keloid formation. Indeed, manipulation of the dynamics of IL-1β using pharmacologic antagonists to minimize or even eliminate scar formation is currently a highly discussed topic in wound repair research.[42,43] Our results suggest that pulsed electromagnetic field signals can produce endogenous changes in the dynamics of IL-1β availability, which should impact the many known subsequent inflammatory events that are mediated by this cytokine.[29] Importantly, pulsed electromagnetic field therapy is not systemic and not governed by pharmacokinetics. Indeed, the pulsed electromagnetic field signal appears instantaneously in all compartments of the target tissue where endogenous antiinflammatory and subsequent tissue repair processes can be modulated.

The mechanism of action of pulsed electromagnetic field signals in this study is not completely elucidated. However, it is intriguing to consider that the known effects of pulsed electromagnetic fields on the modulation of Ca^{2+} binding to calmodulin, with subsequent enzyme activation,[6,23,24] may be applicable here. Calmodulin-dependent activation of nitric oxide synthase to produce nitric oxide and its subsequent stimulation of cyclic guanosine monophosphate formation, which plays an orchestrating role in tissue repair,[44] has recently been reported to be sensitive to pulsed electromagnetic fields. DNA synthesis in cultured articular chondrocytes can be stimulated by pulsed electromagnetic fields through the calmodulin/nitric oxide/cyclic guanosine monophosphate pathway, where inhibition of calmodulin, nitric oxide synthase, and guanylate cyclase, individually, eliminated the effect.[45] Pulsed electromagnetic field effects on osteoblast proliferation and differentiation were also shown to be mediated by nitric oxide.[46] Direct evidence of the effect of a pulsed electromagnetic field signal configured for the Ca^{2+}/calmodulin pathway on real-time nitric oxide production in a neuronal cell line, which could be eliminated by calmodulin and nitric oxide synthase inhibitors, has also recently been reported.[47,48] Other effects of pulsed electromagnetic fields involving nitric oxide include the following: increased vasodilatation,[49] inhibition of the vasoconstrictor endothelin-1,[50] increased neuronal regeneration,[51] and increased nitric oxide in nasal and sinus mucosa.[52]

Neutrophils, the first cellular responder in the inflammatory phase of wound repair, produce IL-1β which, in turn, can up-regulate inducible nitric ox-

ide synthase activity, resulting in proinflammatory amounts of nitric oxide to be released into the wound bed.[53] Protracted exposure to nitric oxide leads to the induction of cyclooxygenase-2, increasing levels of prostaglandins and unnecessarily extending the inflammatory phase of healing, which can lead to pain, fibrosis, and other complications.[12] Pulsed electromagnetic fields have been reported to down-regulate inducible nitric oxide synthase at the mRNA and protein levels in monocytes,[54] supporting the notion that the actions of pulsed electromagnetic fields on tissue repair include an early antiinflammatory component. Furthermore, it has been reported that the calmodulin/endothelial nitric oxide synthase/nitric oxide signaling pathway down-regulates both IL-1β and inducible nitric oxide synthase.[55,56] It follows that the pulsed electromagnetic field signal used in this study, configured to target this calmodulin-dependent nitric oxide signaling pathway, could down-regulate both IL-1β and inducible nitric oxide synthase by means of its effect on nitric oxide signaling. In addition, inducible nitric oxide synthase activity would be indirectly attenuated because of its known dependence on IL-1β.[53] Together with the known effects of pulsed electromagnetic fields on vasodilatation,[16] these events could account for the accelerated pain relief experienced by patients in this study who received pulsed electromagnetic field therapy. This leads to the proposed mechanism depicted in Figure 5 for pulsed electromagnetic field attenuation of the inflammatory phase of wound repair, based on a general pulsed electromagnetic field mechanism for tissue repair reported elsewhere.[57] Additional basic and clinical studies will be necessary to further test the validity of this proposed mechanism.

It is also of importance that increased nitric oxide production by means of pulsed electromagnetic

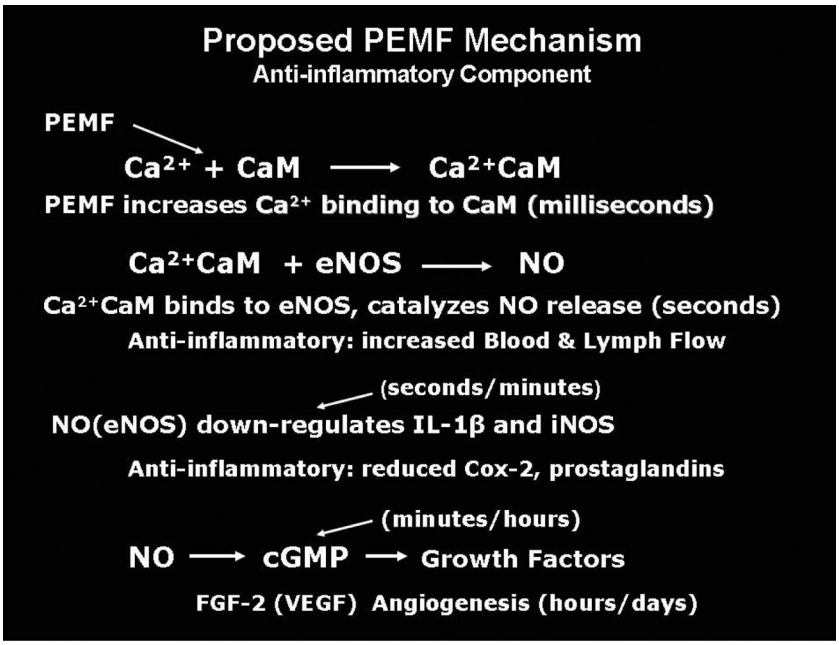

Fig. 5. Summary of proposed mechanism for the pulsed electromagnetic field (*PEMF*) effects on postoperative IL-1β and pain. The pulsed electromagnetic field signal was configured to modulate the kinetics of Ca^{2+} binding to calmodulin. This, in turn, modulates endothelial nitric oxide synthase activation and manipulates the concentration of IL-1β and inducible nitric oxide synthase activity in the wound bed. The result is accelerated postoperative pain relief. Also shown is the proposed pulsed electromagnetic field pathway for increased angiogenesis that has been reported in other studies (Tepper OM, Callaghan MJ, Chang EI, et al. Electromagnetic fields increase in vitro and in vivo angiogenesis through endothelial release of FGF-2. *FASEB J.* 2004;18:1231–1233; and Callaghan MJ, Chang EI, Seiser N, et al. Pulsed electromagnetic fields accelerate normal and diabetic wound healing by increasing endogenous FGF-2 release. *Plast Reconstr Surg.* 2008;121:130–141). *CaM*, calmodulin; *eNOS*, endothelial nitric oxide synthase; *NO*, nitric oxide; *iNOS*, inducible nitric oxide synthase; *cGMP*, cyclic guanosine monophosphate.

fields also leads to increased cyclic guanosine monophosphate production that may act to stimulate the synthesis and/or release of specific growth factors appropriate for each particular stage of healing if used during later postoperative periods as the inflammatory stage dissipates. Although no significant differences in levels of FGF-2 were detected in wound exudates within 24 hours postoperatively, it is still possible that a pulsed electromagnetic field effect on the production of this factor could be observed at a later time. Indeed, other studies have demonstrated increases in FGF-2 levels in response to pulsed electromagnetic field signals in vitro and in vivo,[17,18] and it is known that this factor, which has pleiotropic effects on fibroblasts and endothelial cells, can be induced by nitric oxide/cyclic guanosine monophosphate signaling.[58–60]

The clinical implications of our findings are significant. The pulsed electromagnetic field devices do not increase the normal effort or time required to place a postoperative dressing. The device weighs only 2.4 ounces, fits easily in a surgical bra and, once positioned and activated, requires no further intervention. Patients are instructed to remove the device only for bathing and to replace the device in its original position under the bra. The cost of the pulsed electromagnetic field device used in this study is approximately $100. As a comparison, implantable local anesthetic pain pump catheters cost from $200 to $280 per patient, and require more, and invasive, intervention.[61] It is also important to note that there are no known side effects associated with the use of pulsed electromagnetic field devices, whereas narcotic pain medications can cause side effects of nausea, vomiting, or constipation, and have addictive potential. With this in mind, the cost of the pulsed electromagnetic field device is a fraction of the potential cost of treating side effects from narcotics. The benefits of reducing the severity and duration of the inflammatory phase of wound repair with noninvasive, nonpharmacologic pulsed electromagnetic field therapy, which can manipulate the body's endogenous orchestration of wound repair with no known side effects, could thus have a major impact on the reduction of patient morbidity. This, in turn, may lead to a reduction in length of hospital stay with consequent reductions in the cost of health care. We are embarking on additional prospective studies that will compare pain levels, cytokine and growth factor analyses in exudate, and length of stay as outcome measures of pulsed electromagnetic field therapy in more complex reconstructive operations.

It is intriguing to speculate that the use of pulsed electromagnetic fields to manage postsurgical pain through its effect on inflammatory cytokines, followed by its anticipated modulation of endogenous growth factors,[6,19] may also lead to an overall acceleration of wound healing in humans.[25] Pulsed electromagnetic field therapy may also be accompanied by a concomitant reduction in scar formation, thus enhancing the quality of healing.

CONCLUSIONS

This study provides further evidence that pulsed electromagnetic field therapy can reduce pain levels and pain medication requirements in the immediate postoperative period. The concomitant reduction of IL-1β in the wound bed, possibly by means of nitric oxide/cyclic guanosine monophosphate signaling, suggests that pulsed electromagnetic field therapy could have a profound effect on wound repair outcomes. Larger clinical studies that include more extensive cytokine and growth factor analysis are clearly warranted. If these results are confirmed, the current availability of both economical and disposable pulsed electromagnetic field devices could easily translate to many, if not most, postsurgical situations, leading to lower morbidity, shorter hospital stays, increased productivity, and a reduction in the cost of health care.

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