Electrical Stimulation and Wound Healing References

Agren M.S., Engel M.A., and Mertz P.M. (1994) Collagenase during burn wound healing: influence of a hydrogel dressing and pulsed electrical stimulation. Plast. Reconstr. Surg. 94, 518-524. Abstract: Epithelialization of second-degree burn wounds is known to be accelerated by topical treatment with hydrogel dressings and further enhanced by pulsed electrical stimulation compared with no treatment (air exposure). Tissue collagenase has been proposed to be involved during the process of epithelialization. In the present study collagenase levels were examined in partial-thickness burn wounds in the skin of four domestic pigs. Collagenase levels, assayed on postburn days 1 to 10, were substantially reduced in deblistered and air-exposed burn wounds compared with excisional partial-thickness wounds. Early application of hydrogel dressing to the burn wounds was accompanied by elevated collagenase activities and an increased inflammatory reaction in dermis. Addition of pulsed electrical stimulation increased ($p < 0.001$) collagenase levels twofold above those with hydrogel alone during initiation of epithelialization (postburn days 3 and 4). These results suggest that collagenase is closely linked to wound epithelialisation.

Baker L.L., Chambers R., DeMuth S.K., and Villar F. (1997) Effects of electrical stimulation on wound healing in patients with diabetic ulcers. Diabetes Care 20, 405-412. Abstract: OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

Bassett C.A., Becker R.O., Brighton C.T., Lavine L., and Rowley B.A. (1974) Panel discussion: To what extent can electrical stimulation be used in the treatment of human disorders? Ann. N. Y. Acad. Sci. 238, 586-593.

Bauerle J. and Neander K.D. (1996) [Use of pulsed electrical stimulation in the therapy of decubitus ulcers]. Krankenpfl. J. 34, 270-275.

Biedebach M.C. (1989) Accelerated healing of skin ulcers by electrical stimulation and the intracellular physiological mechanisms involved. Acupunct. Electrother. Res. 14, 43-60. Abstract: Evidence is reviewed (8 studies involving 215 clinical patients with ischemic skin ulcers and 7 animal tissue or tissue culture studies) that electrical stimulation of fibroblast cells accelerates the intracellular biosynthesis necessary to form new granulation tissue in a healing wound, and that both a direct local tissue effect and a circulatory improvement occur. A model is presented in which transmembrane currents open voltage-controlled calcium channels in fibroblast cells, causing ATP resynthesis, activation of protein kinase mechanisms to synthesize new cellular protein, and the DNA replication necessary for mitotic cell division. Stimulation efficacy appears to be determined by a number of basic electrical parameters, and judicious waveform control is desirable.

Black J. (1985) Electrical stimulation of hard and soft tissues in animal models. Clin. Plast. Surg. 12, 243-257. Abstract: Studies in animals have clearly established that various forms of electrical stimulation positively affect the growth, repair, and remodeling of hard and soft tissue. Although the various electrical stimulation modalities (faradic, capacitive, and inductive) are different in their physics and biochemistry, each produces a variety of biological responses in a wide range of animal models. The level of interest in animal studies of electrical stimulation is rising rapidly, and new understanding, in parallel with studies in vitro and in the clinic, will continue to be gained. The future holds the promise of a wide range of hard and soft tissue conditions being routinely treated by electrical stimulation, based in part on progress in studies in animals.

Bogie K.M., Reger S.I., Levine S.P., and Sahgal V. (2000) Electrical stimulation for pressure sore prevention and wound healing. Assist. Technol. 12, 50-66. Abstract: This paper reviews applications of therapeutic electrical stimulation (ES) specific to wound healing and pressure sore prevention. The application of ES for wound healing has been found to increase the rate of healing by more than 50%. Furthermore, the total number of wounds healed is also increased. However, optimal delivery techniques for ES therapy have not been established to date. A study of stimulation current effects on wound healing in a pig model has shown that direct current (DC) stimulation is most effective in wound area reduction and alternating current (AC) stimulation for wound volume reduction at current densities of 127 microA/cm2 and 1,125 microA/cm2, respectively. Preliminary studies have been carried out at two research centers to assess the role of ES in pressure sore prevention. Surface stimulation studies have shown that ES can produce positive short-term changes in tissue health variables such as regional blood flow and pressure distribution. The use of an implanted stimulation system consisting of intramuscular electrodes with percutaneous leads has been found to produce additional long-term changes. Specifically, gluteal muscle thickness increased by 50% with regular long-term ES application concurrent with a 20% decrease in regional interface pressures and increased tissue oxygen levels. These findings indicate that an implantable ES system may have great potential for pressure sore prevention, particularly for individuals who lack sensation or who are physically unable to perform regular independent pressure relief.

Braddock M., Campbell C.J., and Zuder D. (1999) Current therapies for wound healing: electrical stimulation, biological therapeutics, and the potential for gene therapy. Int. J. Dermatol. 38, 808-817.

Brown M., McDonnell M.K., and Menton D.N. (1988) Electrical stimulation effects on cutaneous wound healing in rabbits. A follow-up study. Phys. Ther. 68, 955-960. Abstract: The purpose of this study was to determine the effects of high voltage monophasic pulsed electrical stimulation on wound healing using positive polarity. Forty-four rabbits were assigned to experimental or control groups and followed for four or seven days. We classified the groups as Exp4, Con4, Exp7, and Con7, respectively. Each animal was anesthetized, and a full-thickness incision, 3.5-cm long, was made on its back. After 24 hours, the Exp4 and Exp7 rabbits received high voltage electrical stimulation for two hours twice daily. Wound closure for the Exp4 rabbits (50%) was significantly less than that of the Con4 rabbits (78%). After seven days, however, the Exp7 and Con7 rabbits had similar wound-closure values (80% and 82%, respectively). Tensile- strength values for the control and experimental animals were comparable at both time periods. Histologic examination of the wounds suggested a more rapid rate of

epithelization between the Exp4 and Exp7 rabbits compared with the Con4 and Con7 rabbits. The results of this study are inconclusive, but may indicate that positive-polarity stimulation enhanced wound closure between four and seven days of treatment.

Castillo E., Sumano H., Fortoul T.I., and Zepeda A. (1995) The influence of pulsed electrical stimulation on the wound healing of burned rat skin. Arch. Med. Res. 26, 185-189. Abstract: Electrostimulation of wounds caused healing to proceed in a thoroughly organized manner. A trial using rats subjected to second degree burns was conducted to evaluate, under scanning electron microscopy (SEM), the healing capabilities of skin to which an antiseptic (iodine) and referred electrical stimulation were applied. Untreated, unharmed skin was also studied as control. Images obtained using SEM revealed that only the repaired skin of the electrostimulated group had an appearance similar to that of the control skin (kappa = 1), and that the overall appearance of the repaired skin was compatible with a well organized healing process.

Cheng K., Tarjan P.P., and Mertz P.M. (1993) Theoretical study of rectangular pulse electrical stimulation (RPES) on skin cells (in vivo) under conforming electrodes. Biomed. Sci. Instrum. 29, 349-354. Abstract: Our previous in vivo experimental results have shown RPES can enhance skin wound healing by using conforming electrodes. Based on an equation of polarization transmembrane voltage [Cole, K. S. 1972], two equations were derived to describe the peak RPES intensity on skin cells in vivo: (1) U = 1.5 a J/sigma, (2) Jm = 1.5 a (J/sigma) (Cm/tau). Where U: polarization transmembrane voltage. a: radius (R) for spherical cells or semi-length (L) for long fibers parallel to the electrical field. J: external imposed pulse current density under the electrode. sigma: average conductivity of skin tissue. Jm: transmembrane displacement current density. Cm: membrane capacitance per unit area and tau: time constant. Calculations indicated that the sensory fibers (SF) would receive the strongest stimulation compared to other cells in skin since generally LSF > or = 100 R. The sensitivity of SF to the stimulation could enhance skin wound healing as well as protect normal skin cells from harmful electroporation. From these theoretical calculations. We proposed a theoretical range of the pulse current density as: U1 sigma/(1.5 L) < or = J z or = U2 sigma/(1.5 L), where U1 and U2 are the excitation threshold voltage (about 0.01 V) and polarization lectroporation voltage (about 0.1 V) for a SF respectively, for RPES to enhance skin wound healing.

Cho M.R., Thatte H.S., Lee R.C., and Golan D.E. (2000) Integrin-dependent human macrophage migration induced by oscillatory electrical stimulation. Ann. Biomed. Eng 28, 234-243. Abstract: Electrical stimulation has been used to promote wound healing. The mechanisms by which such stimulation could interact with biological systems to accelerate healing have not been elucidated. One potential mechanism could involve stimulation of macrophage migration to the site of a wound. Here we report that oscillatory electric fields induce human macrophage migration. Macrophages exposed to a 1 Hz, 2 V/cm field show an induced migration velocity of 5.2+/-0.4 x 10(-2) microm/min and a random motility coefficient of 4.8+/-1.4 x 10(-2) microm2/min on a glass substrate. Electric field exposure induces reorganization of microfilaments from ring-like structures at the cell periphery to podosomes that are confined to the contact sites between cell and substrate, suggesting that the cells are crawling on glass. Treatment of cells with monoclonal antibodies directed against beta2-integrins prior to field exposure prevents cell migration, indicating that integrin-dependent signaling pathways are involved. Electric fields cause macrophage migration on laminin or fibronectin coated substrates without inducing podosome formation or changes in cellular morphology. The migration velocity is not significantly altered but the random movement is suppressed, suggesting that cell movements on a lam.

Davis S.C. and Ovington L.G. (1993) Electrical stimulation and ultrasound in wound healing. Dermatol. Clin. 11, 775-781. Abstract: The events that lead to tissue repair are very

complex. Because our understanding of these processes is increasing in scope, the use of nontraditional treatment therapies should be considered. Evidence is reported in the literature that both electrical stimulation and ultrasound therapies may be beneficial in certain circumstances to heal various wound types. Owing to clinicians' unfamiliarity with the current research and general understanding of such therapies, many patients receive only traditional treatment and remain unexposed to the potential benefits of the nontraditional. With continued research to better define optimal treatment parameters, improved wound healing will result.

Dayton P.D. and Palladino S.J. (1989) Electrical stimulation of cutaneous ulcerations. A literature review. J. Am. Podiatr. Med. Assoc. 79, 318-321. Abstract: The effect of electrical currents on living cellular systems has been studied by many researchers and is becoming useful in clinical medicine. Alteration of cellular activity with externally applied currents can positively or negatively influence the status of a healing tissue, thereby directing the healing process to a desired outcome. A review of the literature pertaining to the effect of electrical currents on tissue healing is presented and the relevance of this modality to ulcer healing is discussed.

Dunn M.G., Doillon C.J., Berg R.A., Olson R.M., and Silver F.H. (1988) Wound healing using a collagen matrix: effect of DC electrical stimulation. J. Biomed. Mater. Res. 22, 191-206. Abstract: Rapid fibroblast ingrowth and collagen deposition occurs in a reconstituted type I collagen matrix that is implanted on full- thickness excised animal dermal wounds. The purpose of this study is to evaluate the effects of direct current stimulation on dermal fibroblast ingrowth using carbon fiber electrodes incorporated into a collagen sponge matrix. Preliminary results suggest that fibroblast ingrowth and collagen fiber alignment are increased in collagen sponges stimulated with direct currents between 20 and 100 microA. Maximum fibroblast ingrowth into the collagen sponge is observed near the cathode at a current of 100 microA. These results suggest that electrical stimulation combined with a collagen matrix may be a method to enhance the healing of chronic dermal wounds.

Evans R.D., Foltz D., and Foltz K. (2001) Electrical stimulation with bone and wound healing. Clin. Podiatr. Med. Surg. 18, 79-95, vi. Abstract: Electrical stimulation has been used to heal fractures and ulcers and reduce pain through modulation of local body processes. It has been recognized that mechanical forces and bioelectricity have an intimate relationship in influencing the production of bone. Science has developed techniques to affect change in the electrical charge of fractures to positively affect the healing process. Electrical stimulation, through invasive and noninvasive applications, has produced excellent results in the treatment of nonunions and ulcer care. A thorough review of the electrical properties of bone and soft tissue and the influence of electrical stimulation on healing is presented here.

Feedar J.A., Kloth L.C., and Gentzkow G.D. (1991) Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys. Ther. 71, 639-649. Abstract: The purposes of this randomized, double-blind, multicenter study were to compare healing of chronic dermal ulcers treated with pulsed electrical stimulation with healing of similar wounds treated with sham electrical stimulation and to evaluate patient tolerance to the therapeutic protocol. Forty-seven patients, aged 29 to 91 years, with 50 stage II, III, and IV ulcers were randomly assigned to either a treatment group (n = 26) or a control (sham treatment) group (n = 24). Treated wounds received 30 minutes of pulsed cathodal electrical stimulation twice daily at a pulse frequency of 128 pulses per second (pps) and a peak amplitude of 29.2 mA if the wound contained necrotic tissue or any drainage that was not serosanguinous. A saline-moistened nontreatment electrode was applied 30.5 cm (12 in) cephalad from the wound. This protocol was continued for 3 days after the wound was debrided or exhibited serosanguinous drainage. Thereafter, the polarity of the treatment electrode on the wound was changed every 3 days until the wound progressed to a stage II classification. The pulse frequency was then reduced to 64 pps, and the treatment electrode polarity was changed daily until the wound was healed. Patients in the control group were treated with the same protocol, except they received sham electrical stimulation. After 4 weeks, wounds in the treatment and control groups were 44% and 67% of their initial size, respectively. The healing rates per week for the treatment and control groups were 14% and 8.25%, respectively. The results of this study indicate that pulsed electrical stimulation has a beneficial effect on healing stage II, III, and IV chronic dermal ulcers.

Fitzgerald G.K. and Newsome D. (1993) Treatment of a large infected thoracic spine wound using high voltage pulsed monophasic current. Phys. Ther. 73, 355-360. Abstract: This case report describes the use of electrical stimulation with high voltage pulsed monophasic current for treatment of a large, infected wound of the thoracic spine, following a surgical debridement procedure. The patient was a 21-year-old man with spastic quadriplegic cerebral palsy who was dependent for all self-care and was severely mentally retarded. The initial wound size was as follows: length = 17 cm, top width = 7.5 cm, middle width = 5.5 cm, bottom width = 2 cm, and depth = 5 cm. The wound was infected with Staphylococcus aureus. The initial treatment consisted of 60 minutes of electrical stimulation (20 minutes of negative polarity followed by 40 minutes of positive polarity) once daily. The frequency of treatment was increased to twice daily after 2 weeks. Total treatment duration was 10 weeks. The patient received antibiotic treatment and daily nursing wound care in addition to electrical stimulation treatment. The wound was completely closed after 10 weeks of treatment. The possible role of high voltage pulsed monophasic current in accelerating the wound-healing process is discussed.

Fleischli J.G. and Laughlin T.J. (1997) Electrical stimulation in wound healing. J. Foot Ankle Surg. 36, 457-461. Abstract: The authors present a review of the current literature regarding electrical stimulation with special focus on the merits of its uses in wound healing. Literature from a basic science, animal studies and clinical investigations are reviewed. The literature seems to suggest that electrical stimulation can effect wound healing, but the method of delivery remains uncertain.

Gardner S.E., Frantz R.A., and Schmidt F.L. (1999) Effect of electrical stimulation on chronic wound healing: a meta- analysis. Wound. Repair Regen. 7, 495-503. Abstract: The purpose of this meta-analysis was to quantify the effect of electrical stimulation on chronic wound healing. Fifteen studies, which included 24 electrical stimulation samples and 15 control samples, were analyzed. The average rate of healing per week was calculated for the electrical stimulation and control samples. Ninety-five percentage confidence intervals were also calculated. The samples were then grouped by type of electrical stimulation device and chronic wound and reanalyzed. Rate of healing per week was 22% for electrical stimulation samples and 9% for control samples. The net effect of electrical stimulation was 13% per week, an increase of 144% over the control rate. The 95% confidence intervals of the electrical stimulation (18- 26%) and control samples (3.8-14%) did not overlap. Electrical stimulation was most effective on pressure ulcers (net effect = 13%). Findings regarding the relative effectiveness of different types of electrical stimulation device were inconclusive. Although electrical stimulation produces a substantial improvement in the healing of chronic wounds, further research is needed to identify which electrical stimulation devices are most effective and which wounds respond best to this treatment.

Gentzkow G.D. and Miller K.H. (1991) Electrical stimulation for dermal wound healing. Clin. Podiatr. Med. Surg. 8, 827-841. Abstract: The investigations of biologic actions (in vitro, animal, and human) demonstrated several effects that help explain why electrical stimulation works. Based on the latest scientific understanding of the wound healing process, one would expect that a therapy that decreases edema, debrides necrotic tissue, attracts neutrophils and macrophages, stimulates receptor sites for growth factors, stimulates growth of fibroblasts and granulation tissue, increases blood flow, stimulates neurite growth, induces epidermal cell migration, prevents postischemic oxygen radical-mediated damage, inhibits bacteria, and reduces numbers of mast cells ought to be beneficial for wound healing. Numerous human and animal efficacy studies confirm that electrical stimulation of the proper charge, density, and total energy causes dramatically improved healing of dermal wounds. As of this writing, no devices have yet been approved by the FDA for use in wound healing, although several devices approved for other indications are being used for this purpose. One device (the Staodyn Dermapulse) has undergone controlled animal and human testing, and an application requesting approval for treating dermal ulcers has been submitted to FDA. Taken together, the efficacy studies and the "mechanism of action" studies provide compelling, scientific evidence that electrical stimulation is safe and effective for promoting the healing of dermal wounds.

Gentzkow G.D. (1993) Electrical stimulation to heal dermal wounds. J. Dermatol. Surg. Oncol. 19, 753-758. Abstract: BACKGROUND. Numerous human and animal efficacy studies have demonstrated that electrical stimulation of the correct charge, density and total energy causes dramatically improved healing of dermal wounds. The investigations of biological actions (in vitro, animal, and human) demonstrate several effects that go a long way to explaining why electrical stimulation works. OBJECTIVE. To discuss recent research and advances in electrical stimulation of wound healing. RESULTS. Based on the latest scientific understanding of the wound healing process, one would expect a beneficial outcome from a therapy what decreases edema, debrides necrotic tissue, attracts neutrophils and macrophages, stimulates receptor sites for growth factors, stimulates growth of fibroblasts and granulation tissue, increases blood flow, stimulates neurite growth, induces epidermal cell migration, prevents post- ischemic oxygen radical-mediated damage, inhibits bacteria, and reduces numbers of mast cells. CONCLUSION. Taken together, the efficacy studies and the "mechanism of action" studies provide compelling, scientific evidence that electrical stimulation is safe and effective for promoting the healing of dermal wounds.

Gilcreast D.M., Stotts N.A., Froelicher E.S., Baker L.L., and Moss K.M. (1998) Effect of electrical stimulation on foot skin perfusion in persons with or at risk for diabetic foot ulcers. Wound. Repair Regen. 6, 434-441. Abstract: The failure of foot wounds to heal results in 54,000 people with diabetes having to undergo extremity amputations annually. Therefore, treatment is needed to speed healing in people with diabetes in order to reduce the need for amputation. This study tested the effect of high- voltage pulsed current on foot blood flow in human beings who are at risk for diabetic foot ulcers. Neuropathy, vascular disease, Wagner Class, glucose, gender, ethnicity, and age were measured. A sample of 132 subjects was tested using a repeated-measures design. A baseline transcutaneous oxygen level was obtained; stimulation was applied, and transcutaneous oxygen measurements were recorded at 30- and 60- minute time intervals. The grouped foot transcutaneous oxygen levels decreased ($F = 5.66$, $p =.0039$) following electrical stimulation. Analysis of variance (Scheffe, $p <.05$) showed that initial transcutaneous oxygen was significantly higher than subsequent readings. However, oxygen response was distributed bimodally: 35 (27%) subjects showed increased transcutaneous oxygen (mean 14.8 mm Hg), and 97 (73%) experienced a decreased transcutaneous oxygen reading (mean 12.2 mm Hg). Logistic regression analysis did not explain these differences. Although this treatment appears to increase blood flow in a subset of patients, further study is needed to identify probable mechanisms for this response.

Gogia P.P. (1996) Physical therapy modalities for wound management. Ostomy. Wound. Manage. 42, 46-2, 54. Abstract: As part of a multidisciplinary team approach to the management of chronic wounds, physical therapists can add certain physical modalities to the care plan. Whirlpool, electrical stimulation, ultrasound, low- energy laser and compression therapy are physical therapy modalities that have been used to enhance wound healing. All of these modalities are used as adjunct treatments that, when appropriate, may help shorten the length of treatment and reduce patient suffering. Because the efficacy of some of these modalities remains to be established in controlled clinical trials, conventional wound care continues to be an important part of the team approach.

Houghton P.E. and Campbell K.E. (1999) Choosing an adjunctive therapy for the treatment of chronic wounds. Ostomy. Wound. Manage. 45, 43-52. Abstract: Adjunctive therapies such as ultrasound, laser, ultraviolet light, superficial heating, pulsed electromagnetic fields, and electrical stimulation have all been indicated in the treatment of chronic wounds. The purpose of this article is to outline the issues a healthcare professional must consider when choosing the best adjunctive therapy for a chronic wound. It summarizes the effects of therapeutic modalities on the wound healing process, analyzes the clinical research evidence, discusses practical considerations, and reviews indications, contraindications, precautions, and safety considerations. Finally, an algorithm is presented to help guide the clinician in selecting a modality. In summary, research evidence exists in the literature that suggests these adjunctive therapies can directly stimulate new tissue growth, augment wound tissue strength, improve local circulation and oxygenation, reduce edema, and/or inhibit bacterial growth. Electrical stimulation and ultrasound are the only therapeutic modalities that currently have sufficient clinical research evidence to support their use in the treatment of chronic wounds. Practical issues such as cost, time and training required, and patient and therapist safety concerns, will ultimately influence the selection of these modalities.

Jivegard L., Augustinsson L.E., Carlsson C.A., and Holm J. (1987) Long-term results by epidural spinal electrical stimulation (ESES) in patients with inoperable severe lower limb ischaemia. Eur. J. Vasc. Surg. 1, 345-349. Abstract: Arterial reconstruction is the treatment of choice for patients with severe lower limb ischaemia, but may at times be technically impossible. Thirty-two consecutive patients with impending (n = 24) or already established (n = 8) distal arteriosclerotic or diabetic lower limb gangrene, in whom vascular surgery was either technically impossible or had failed, were treated with epidural spinal electrical stimulation (ESES) for 27 +/- 16 (S.D.) months. All patients had severe rest pain, which was reduced by ESES in 91% of the cases. Improved ulcer healing was noted in 58% of the patients who had skin ulceration. Eighty-three percent of those patients who did not have established gangrene when ESES was started, retained their leg after 1 year, and 54% after 3 years. These results suggest that ESES often provides pain relief and improves skin healing in patients with impending arteriosclerotic or diabetic gangrene in whom vascular surgery is impossible or has failed. Epidural spinal electrical stimulation (ESES) does not affect the progression of established gangrene but may provide pain relief. The observed outcome of severe limb ischaemia in this study could be used to compare with those after arterial reconstruction performed in patients with poor run-off vessels, and may allow us to examine the natural history of this disease when adequate pain relief is provided. The results reported here and the previously reported enhancement of cutaneous blood flow in severely ischaemic extremities by ESES may suggest, that ESES enhances limb salvage by improving skin blood flow.

Kambic H.E., Reyes E., Manning T., Waters K.C., and Reger S.I. (1993) Influence of AC and DC electrical stimulation on wound healing in pigs: a biomechanical analysis. J. Invest Surg. 6, 535-543. Abstract: To evaluate the effects of electrical stimulation on the mechanical properties of healing skin, 20 Hanford mini-pigs weighing 10-15 kg with trochanteric pressure ulcers were subjected to electrical stimulation. Examination of the biomechanical properties of the skin and changes in wound area and volume was done on previously wounded and healing pigskin subject to AC or DC electrical stimulation. The behavior of normal pigskin was compared to (1) denervated controls, (2) denervated AC-stimulated skin, and (3) denervated DC-stimulated skin. A denervated limb trochanteric pressure sore model developed in house permitted the use of a 6.5-mm percutaneous cancellous screw for wound formation and a 3-cm-diameter spring compression indentor to create reproducible and uniformly controlled grade 3 or higher tissue ulcers in the monoplegic hind limbs. Denervation was accomplished by right unilateral extradural rhizotomies from L2 to S1 nerve roots. Electrodes were placed 1 cm distal and proximal to the wound periphery, and wounds were stimulated 2 h/day, 5 days/week for 30 days. Dumbbell-shaped skin specimens with a length to width ratio of 3:1 were uniaxially loaded in tension until failure at an extension rate of 150 mm/min. The stiffness values for skin samples oriented parallel to the current flow were reduced by nearly half the values obtained for normal controls. Statistical differences ($P < .05$) were found for stress, Young modulus, and stiffness when compared to normal skin. Samples oriented in the perpendicular direction were comparable to normal skin (P = NS).(ABSTRACT TRUNCATED AT 250 WORDS)

Khalil Z. and Merhi M. (2000) Effects of aging on neurogenic vasodilator responses evoked by transcutaneous electrical nerve stimulation: relevance to wound healing. J. Gerontol. A Biol. Sci. Med. Sci. 55, B257-B263. Abstract: We have previously shown an age-related decline in the modulation of skin vascular reactivity by sensory nerves that correlates with a decline in wound repair efficacy. This study was designed to examine the possibility that improving the functional ability of aged sensory nerves using noninvasive transcutaneous electrical nerve stimulation (TENS) could also accelerate tissue repair. TENS of the sciatic nerve, combined with measuring blood flow responses in the rat hind-footpad using laser Doppler flowmetry, was used to establish the vascular effects. Following TENS (using parameters 20V, 5 Hz for 1 min), similar increases in vascular responses were obtained in both young (13.2+/-0.9 cm2) and old rats (11.6+/-2.3 cm2). In contrast, capsaicin-pretreated rats showed markedly diminished responses. Sympathetic fibers did not appear to modulate these sensory nerve responses. In the second part, a thermal wound was induced (using a CO2 laser) in the interscapular region of old rats (under anesthesia). In the active treatment group, TENS was applied twice daily for the initial 5 days, and the sham group received inactive TENS. Using the healing endpoint as the time when full wound contraction occurred, the active group required 14.7+/-0.2 days for complete healing, a significant improvement over the sham group (21.8+/-0.3 days). We contend that low-frequency TENS can improve the vascular response of old rats. In addition, wound healing in aged rats can be accelerated by peripheral activation of sensory nerves at low-frequency electrical stimulation parameters.

Kloth L.C. and Feedar J.A. (1988) Acceleration of wound healing with high voltage, monophasic, pulsed current. Phys. Ther. 68, 503-508. Abstract: The purpose of this study was to determine whether high voltage electrical stimulation accelerates the rate of healing of dermal ulcers. Sixteen patients with stage IV decubitis ulcers, ranging in age from 20 to 89 years, participated in the study. The patients were assigned randomly to either a Treatment Group (n = 9) or a Control Group (n = 7). Patients in the Treatment Group received daily electrical stimulation from a commercial high voltage generator. Patients in the Control Group had the electrodes applied daily but received no stimulation. The ulcers of patients in the Treatment Group healed at a mean rate of 44.8% a week and healed 100% over a mean period of 7.3 weeks. The ulcers of patients in the Control Group increased in area an average of 11.6% a week and increased 28.9% over a mean period of 7.4 weeks. The results of this study suggest that high voltage stimulation accelerates the healing rate of stage IV decubitis ulcers in human subjects.

Kloth L.C. (1995) Physical modalities in wound management: UVC, therapeutic heating and electrical stimulation. Ostomy. Wound. Manage. 41, 18-4, 26. Abstract: In spite of efforts to create an optimum wound environment for healing, there are times that a wound may not heal, may heal very slowly, or may worsen. In these cases, a series of treatments with an appropriate physical agent can be added to the patient's care plan to augment tissue reparative processes. Three modalities that have received support in the literature for use in wound healing are ultraviolet "C" radiation (UVC), therapeutic heating, and electrical stimulation. Treatment goals for UVC are hyperplasia and enhanced re-epithelialization or desquamation of the leading edge of periulcer epidermal cells, granulation tissue formation, sloughing of necrotic tissue, and bactericidal effects. Treatment goals for therapeutic heating are increased blood perfusion with subsequent increased delivery of oxygen to the tissues (avoiding the dessication of wound tissues). The treatment goal for electrical stimulation is to attract negatively or positively charged cells into the wound area, such as neutrophils, macrophages, epidermal cells and fibroblasts that in turn will contribute to wound healing processes by way of their individual cellular activities.

Kloth L.C. and McCulloch J.M. (1996) Promotion of wound healing with electrical stimulation. Adv. Wound. Care 9, 42-45. Abstract: Clinicians involved in the conservative care of chronic wounds have many treatment interventions from which to choose, including debridement/irrigation, dressings, pressure-relieving devices, hyperbaric or topically applied oxygen, whirlpool/pulsed lavage, ultrasound, topical antibiotics, and cytokine growth factors. All except the last two interventions are physical treatments that create a wound-tissue environment conducive to healing. Unfortunately, many chronic wounds heal very slowly, do not heal, or worsen despite the best efforts of caregivers to promote tissue repair. An intervention commonly used to treat chronic wounds, especially by physical therapists, is electrical stimulation (ES). The rationale for use of this method is based on the fact that the human body has an endogenous bioelectric system that enhances healing of bone fractures and soft- tissue wounds. When the body's endogenous bioelectric system fails and cannot contribute to wound repair processes, therapeutic levels of electrical current may be delivered into the wound tissue from an external source. The external current may serve to mimic the failed natural bioelectric currents so that wound healing can proceed. Certain chemotaxic factors found in wound substrates contribute to tissue repair processes by attracting cells into the wound environment. Neutrophil, macrophage, fibroblast, and epidermal cells involved in wound repair carry either a positive or negative charge. When these cells are needed to contribute to autolysis, granulation tissue formation, anti-inflammatory activities, or epidermal resurfacing, ES may facilitate galvanotaxic attraction of these cells into the wound tissue and thereby accelerate healing.

Lundeberg T.C., Eriksson S.V., and Malm M. (1992) Electrical nerve stimulation improves healing of diabetic ulcers. Ann. Plast. Surg. 29, 328-331. Abstract: A controlled study of the effects of electrical nerve stimulation (ENS) was performed in conjunction with a standard treatment for healing chronic diabetic ulcers on 64 patients divided randomly into two groups. All patients received standard treatment (paste-impregnated bandage and a self-adhesive elastic bandage) plus placebo ENS or ENS (alternating constant current; frequency, 80 Hz; pulse width, 1 msec; intensity-evoking strong paresthesias) for 20 minutes twice daily for 12 weeks. Comparison of percentages of healed ulcer area and the number of healed ulcers was made after 2, 4, 6, 8, and 12 weeks. There were significant differences ($p < 0.05$) in both ulcer area and healed ulcers in the ENS group compared with the placebo group after 12 weeks of treatment. The results of the present study support the use of ENS in diabetic ulcers. ENS is easy to apply and can be used by the patient at home following instructions from a medical doctor or a therapist experienced in electrical stimulation and the treatment of ulcers. Additional studies are needed to identify the mechanisms involved in the promotion of ulcer healing with electrical stimulation and to determine the stimulus variables that most efficaciously accelerate tissue repair.

Mawson A.R., Siddiqui F.H., and Biundo J.J., Jr. (1993) Enhancing host resistance to pressure ulcers: a new approach to prevention. Prev. Med. 22, 433-450. Abstract: Pressure ulcers are notoriously common in spinal-cord-injured patients, in patients with other neurological deficits, in malnourished and severely debilitated patients, and in the frail elderly. Prolonged localized external pressure, coupled with insensitivity to ischemia resulting from neurologic injury, has long been considered the major causal factor. Preventive efforts have focused on the relief of pressure via frequent repositioning and the use of pressure-relieving devices. However, consensus is growing that host factors also play a role in the development of pressure ulcers, the most important in spinal-cord-injured patients being the injury-induced loss of vasomotor control below the level of the lesion, resulting in hypoxemia. Accordingly, pressure ulcers may be prevented not only by reducing external pressure but also by increasing the patient's resistance to pressure, that is, by directly influencing tissue oxygenation. Review of the literature suggests that electrical stimulation increases cutaneous blood flow and promotes the healing of pressure ulcers. Moreover, high-voltage pulsed galvanic stimulation (75 V, 10 Hz) applied to the back at spinal level T6 in spinal-cord-injured persons lying supine on egg-crate mattresses can raise sacral transcutaneous oxygen tension levels into the normal ranges (A. R. Mawson, F. H. Siddiqui, B. J. Connolly, C. J. Sharp, W. R. Summer, and J. J. Biundo, Jr., Paraplegia in press). Randomized controlled trials are needed to determine the efficacy of high-voltage pulsed galvanic stimulation for preventing pressure ulcers in spinal-cord-injured persons and other groups at high risk.

Morykwas M.J. and Argenta L.C. (1997) Nonsurgical modalities to enhance healing and care of soft tissue wounds. J. South. Orthop. Assoc. 6, 279-288. Abstract: The rapidly aging population and patients with multiple concomitant pathologies present an increasing population of patients with nonhealing and problem wounds causing an unwelcome challenge for all health care providers. Many of these patients are not surgical candidates, or surgical procedures have failed to close their wounds. These wounds are particularly worrisome when an orthopaedic component is included, since bone and hardware must be covered as quickly as possible to prevent infection and even worse complications. We present a brief overview of several nonsurgical modalities that may be used to heal soft tissue wounds completely or to prepare the wound so a smaller surgical intervention may be done with greater chance for success. We include exogenous application of growth factors, cultured keratinocyte grafts, electrical stimulation, hyperbaric oxygen, and a vacuum- assisted closure system (V.A.C.).

Nath C. and Gulati S.C. (1998) Role of cytokines in healing chronic skin wounds. Acta Haematol. 99, 175-179. Abstract: In the chronic wound, the normal cascade of inflammation, granulation and reconstruction phases of healing is interrupted. Cytokines are now known to orchestrate different biochemical mediators resulting in the restoration of the healing phases. Growth factors may play a significant role in stimulating wound repair by stimulating growth and proliferation. Since growth factors stimulate a variety of functions depending on cell type and wound stage and since wound-healing defects may occur at any phase of healing, a mixed combination of growth factors would be predicted to be more effective than a single factor. Factors that may modulate the action of growth factors include electrical stimulation, weight bearing, debriding and ischemia.

Polak A., Franek A., Hunka-Zurawinska W., Bendkowski W., Kucharzewski M., and Swist D. (2000) [High voltage electrical stimulation in leg ulcer's treatment]. Wiad. Lek. 53, 417-426. Abstract: The results of leg ulcers treatment in two comparative groups, A and B, are presented in the article. In the group A 22 patients with leg ulcers were treated with the use of high voltage electrical stimulation. In the group B 20 patients with leg ulcers were treated actively with the use of traditional methods. The average time of treating patients subjected to electrical stimulation was 7 weeks and in the control group the average time of treatment was 6 weeks. The healing progress was estimated on the basis of rate of wounds surfaces and volumes changes per week and their proportional changes. In the group A the average rate of ulcer surface decreasing was 1.4 cm2 per week and the average volume diminishing in this group was 1.0 cm2 per week. These indicators in the group B were respectively 1.0 cm2 and 0.6 cm3. In the group A wound surface decreased by 73.4% during the treatment and wound volume by 91.3%. In the group B these indicators were respectively 46.9% and 67.6%. After the treatment all indicators estimating the progress of wound healing in the groups A and B proved the statistically significant increases. The proportional indicators of wounds surfaces and volumes were significantly higher in the group A than in the group B.

Reger S.I., Hyodo A., Negami S., Kambic H.E., and Sahgal V. (1999) Experimental wound healing with electrical stimulation. Artif. Organs 23, 460-462. Abstract: The effect of alternating current (AC) and direct current (DC) stimulation was studied on experimental pressure ulcer healing in a new monoplegic pig model. The study was conducted in 30 healthy young Hanford minipigs. The rate of wound healing, histology, vascularization, collagen formation, microbiology, perfusion, and the mechanical strength of the healed wounds were studied. Normal pigskin was compared to denervated control and denervated AC and DC stimulated healed skin. Hind limb denervation was by right unilateral extradural rhizotomies from the L2 to S1 nerve roots. Reproducible uniformly controlled Stage III or higher tissue ulcers were created. When compared to the control wounds, both the AC and DC stimulated wounds showed reduced healing time and increased perfusion in the early phases of healing. DC stimulation reduced the wound area more rapidly than AC, but AC stimulation reduced the wound volume more rapidly than DC. The electrical stimulation did not reduce the strength of the healing wounds below those of the nonstimulated controls. The applied current appears to orient new collagen formation even in the absence of neural influences.

Reich J.D., Cazzaniga A.L., Mertz P.M., Kerdel F.A., and Eaglstein W.H. (1991) The effect of electrical stimulation on the number of mast cells in healing wounds. J. Am. Acad. Dermatol. 25, 40-46. Abstract: Many cutaneous disorders are associated with activation or increased numbers of mast cells. Electrical stimulation has been shown to be effective in treating many of these disorders. This study is designed to examine the effect of electrical stimulation on mast cells in acute wounds. Four pathogen-free pigs received 20 wounds, each of which was subjected to biopsy at various times after wounding. Half of the wounds were treated with electrical stimulation and the other half were treated with a sham electrode. The biopsy specimens were fixed in Carnoy's medium and stained with alcian blue and Nuclear Fast Red. Mast cells from both sets of wounds were counted and analyzed. Highly significant reductions in the number of mast cells were seen with electrical stimulation on days 1 and 2 compared with nonstimulated control wounds. Electron microscopy was performed to compare the stimulated and control mast cells for characteristic features in morphology, location, and evidence of degranulation. Electrical stimulation did not appear to induce degranulation. The ability of electrical stimulation to decrease the number of mast cells may be related to a reduction of either proliferation or migration of these cells and may prove to be a valuable therapeutic technique.

Romanko K.P. (1991) Pressure ulcers. Clin. Podiatr. Med. Surg. 8, 857-867. Abstract: Progress in treatment of pressure ulcers over the past decade has contributed to our ability to more effectively treat problem ulcers. Through choice of the proper dressing, wound environment and cellular activity may be positively influenced and wound repair accelerated. Electrical stimulation, biologic implants, and growth factors are advanced forms of treatment that will become more accessible during the 1990s. Despite all the progress made, one must remember that these modalities are not substitutions for the care necessary to prevent the occurrence of pressure ulcers. Appropriate care and knowledge of available products are necessary to ensure the most effective treatment.

Smith J., Romansky N., Vomero J., and Davis R.H. (1984) The effect of electrical stimulation on wound healing in diabetic mice. J. Am. Podiatry. Assoc. 74, 71-75.

Steckel R.R., Page E.H., Geddes L.A., and Van Vleet J.F. (1984) Electrical stimulation on skin wound healing in the horse: preliminary studies. Am. J. Vet. Res. 45, 800-803. Abstract: The effect of low-level direct-current stimulation on skin wound healing in the horse was assessed. Self-sustaining electrical circuits with electrodes were implanted subcutaneously in or near the wound. Stimulation by direct current (10 or 20 microA) was used to determine the effect on equine skin healing. The efficacy of electrotherapy was evaluated by sequentially comparing the clinical appearance of the wound and measuring the size of the granulating wound bed. The histologic appearance of the healing stimulated wounds was compared with that in nonstimulated control wounds created on 9 horses. Seemingly, electrical stimulation had no discernible effect on experimentally created skin wounds. Clinical observation and histologic examination of the wounds indicated that severe tissue reaction from the implanted electrodes and concurrent local infection produced local detrimental effects to wound healing.

Sumano H. and Mateos G. (1999) The use of acupuncture-like electrical stimulation for wound healing of lesions unresponsive to conventional treatment. Am. J. Acupunct. 27, 5-14. Abstract: Based on previous experimental evidence suggesting improved healing of wounds treated with electrical stimulation, we conducted a clinical trial with patients seeking alternative medicine after unsuccessful conventional medical treatment. Electricity was delivered in two forms: (1) For wounds with extensive loss of tissue and/or those that had failed to heal spontaneously, electrical stimulation was delivered via subcutaneously inserted needles surrounding the wound edges and applying a dose charge of 0.6 coulombs/cm2/day; (2) in second degree burn injuries, lesions were covered with gauze soaked in a 10% (w/v) sterile saline solution and the same dose of electricity was applied as for (1). Forty-four patients were treated with electrical stimulation of the skin; 34 in group (1) and 10 in group (2). Following electrostimulation in all patients in both groups healing proceeded in a thoroughly organized manner, almost regardless of the severity of the type of wound or burn treated. Advantages and limitations of this technique are discussed.

Taskan I., Ozyazgan I., Tercan M., Kardas H.Y., Balkanli S., Saraymen R., Zorlu U., and Ozugul Y. (1997) A comparative study of the effect of ultrasound and electrostimulation on wound healing in rats. Plast. Reconstr. Surg. 100, 966-972. Abstract: A comparative study has been carried out to investigate the effects of electrical stimulation and ultrasound on wound healing. Eighty-four female rats were divided into four groups depending on the treatment received. The first group was given electrical stimulation of 300 microA direct current, 30 minutes daily, starting with negative polarity and then changed after 3 days of treatment. Group 2 received sham electrostimulation treatment. The third group received 0.1 W/cm2 pulsed ultrasound using the moving applicator technique for 5 minutes a day. Group 4 received sham ultrasound treatment. A total of 7 days of treatment was given to all groups. Histopathologic and biochemical analyses on the fourth and seventh days and wound breaking strength on the twenty-fifth day were performed for all groups. By accelerating the inflammatory phase, electrical stimulation had progressed the proliferative phase of wound healing earlier than ultrasound had done. Both electrical stimulation and ultrasound have positive effects on proliferative phases, but electrical stimulation was superior to ultrasound at the maturation phase. There was no difference between the two experimental groups on the mast cell reduction effect. Although ultrasound treatment may seem to be efficient in terms of time, when the effects of electrical stimulation and ultrasound on wound healing with the methods employed in our study are considered, it is concluded that electrical stimulation is a means of treatment superior to ultrasound in wound healing.

Unger P.G. (1992) Wound healing currents: a brief review of recent research points to electrical stimulation as a viable treatment technique. Rehab. Manag. 5, 42-43.

Valdes A.M., Angderson C., and Giner J.J. (1999) A multidisciplinary, therapy-based, team approach for efficient and effective wound healing: a retrospective study. Ostomy. Wound. Manage. 45, 30-36. Abstract: This paper presents a 4-year retrospective study (1994 to 1998) of therapy-based treatment outcomes for chronic wounds of all stages and most common etiologies. Treatment in this study consists of outpatient wound treatments given by trained therapists and nurses who were supervised by the podiatrist or internist. Many patients were referred to the clinic for last-resort treatment (i.e., electrical stimulation, topical hyperbaric therapy, etc.) before major lower extremity amputations: hip disarticulation, above knee amputation (AKA), below- knee amputation (BKA). This study does not consider age, sex, chronicity, or ethnicity because the authors want to demonstrate the effectiveness of this treatment approach for healing chronic wounds notwithstanding these variables. Wound healing was achieved in 100% of patients who completed their treatment program (233 patients with 242 wounds). This study shows the total average healing time for wounds is 7 weeks for Stage II wounds, 10 weeks for Stage III wounds, and 19 weeks for Stage IV wounds. The average healing time for diabetic wounds is 14 weeks (wounds of neuropathic origin heal in 12 weeks and wounds of ischemic origin heal in 16 weeks). The average healing time for venous stasis wounds is 8 weeks. The study includes patients with ischemia who are not candidates for revascularization. The authors assert that the most effective treatment for wound healing is a therapy- based, multidisciplinary team approach. This retrospective study shows that the goal of complete healing is attainable.

Waldorf H. and Fewkes J. (1995) Wound healing. Adv. Dermatol. 10, 77-96. Abstract: Wound healing is a dynamic biologic process of repairing insults to the integumentary system. It is commonly divided into three phases: inflammatory, proliferative, and maturation. Each phase has unique cellular and substance constituents without which it cannot progress normally. A large variety of factors may influence any part of wound healing, including local factors such as bacteria, oxygen tension, and bleeding, and systemic factors such as the mental and physical health of the patient. There are also extrinsic factors that can be influenced by the caretakers of the wound to enhance wound healing. Areas of intervention include using antiseptic technique when one is dealing with the wound, using good surgical technique, choosing the appropriate wounding method and repair for the individual patient, and using antibiotics and special wound dressings. Modern science and technology are giving us new insights into wound healing and leading us to exciting new ways of influencing it, including the topical use of growth factors, artificial skins, cultured epithelium with and without dermal components, and electrical stimulation. The future of wound healing holds a better understanding of the complexities of the physiologic events that occur and a translation of that into a biologically active and interactive wound care.

Weiss D.S., Kirsner R., and Eaglstein W.H. (1990) Electrical stimulation and wound healing. Arch. Dermatol. 126, 222-225. Abstract: Living tissues possess direct current surface electropotentials that regulate, at least in part, the healing process. Following tissue damage, a current of injury is generated that is thought to trigger biological repair. In addition, exogenous electrical stimuli have been shown to enhance the healing of wounds in both human subjects and animal models. Intractable ulcers have demonstrated accelerated healing and skin wounds have resurfaced faster and with better tensile properties following exposure to electrical currents. This article examines the bioelectric properties of living systems and reviews the existing literature on electrical stimulation and wound healing.

Yarkony G.M. (1994) Pressure ulcers: a review. Arch. Phys. Med. Rehabil. 75, 908-917. Abstract: This article reviews the etiology, pathology, description, risk factors, prevention, medical and surgical management, and complications of pressure ulcers. Pressure ulcers, which develop primarily from pressure and shear, are also known as decubitus ulcers, bed sores, and pressure sores. They continue to occur in hospitals, nursing homes, and among disabled persons in the community. Estimates of the prevalence of pressure ulcers in hospitalized patients range from 3% to 14% and up to 25% in nursing homes. Persons with spinal cord injury and the elderly are two groups at high risk. The most common sites of development are the sacrum, ischium, trochanters, and about the ankles and heels. Areas of ongoing research such as electrical stimulation and growth factors are discussed.