# 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 epithelialization

Ahl T., Andersson G., Herberts P., and Kalen R. (1984) Electrical treatment of non-united fractures. *Acta Orthop. Scand.* 55, 585-588.
Abstract: The semi-invasive technique for electrical stimulation of bone healing developed by Brighton et al. (1977) was used in 23 patients with nonunited fractures of the tibia (14 cases), humerus (4 cases), scaphoid, femur and fibula as well as one failed arthrodesis of the ankle. The fractures were clinically not healed and not operated on within a minimum of 6 months. The mean period from fracture to treatment was 18 months. Electrical stimulation led to solid bone healing in 10 cases. Two deep infections occurred during the treatment. Of 13 cases that did not unite, a great range of motion in the nonunion area was an obvious cause of failure in seven cases. The results in this series cannot compete with those of bone graft surgery for nonunions

Ahmed A.N., Islam K.M., Rahman M.F., Islam M.S., and Rabbani K.S. (1987) Effect of electrical stimulation on the early phase of healing in induced fracture in rat tibiae. *Bangladesh Med. Res. Counc. Bull.* 13, 69-79.

Akai M., Oda H., Shirasaki Y., and Tateishi T. (1988) Electrical stimulation of ligament healing. An experimental study of the patellar ligament of rabbits. *Clin. Orthop.* 296-301.
Abstract: To examine the effects of direct electric current on ligament healing in rabbits, a full-thickness defect of the patellar ligament was electrically stimulated for time periods of up to seven weeks. The rabbits were randomly assigned to biomechanical and biochemical studies, and healing was evaluated by these parameters. Electrical stimulation was shown to restore tensile stiffness in a short period of time and to decrease the relative proportion of Type III collagen more rapidly than in the control group. However, electrical stimulation did not change the collagen content of newly formed tissue. Electricity enhances the repair process of the ligament by changing the ratio of collagen types

Akai M., Wadano Y., Yabuki T., Oda H., Sirasaki Y., and Tateishi T. (1991) [Effect of a direct electric current on modification of bone and ligament repair processes--

experimental investigation of a rabbit model]. *Nippon Seikeigeka Gakkai Zasshi* 65, 196-206.
Abstract: Investigations of the effect of direct current on 1) fracture healing, and 2) ligament healing was conducted by applying 10 microA to 1) the defect of the fibula, and 2) that of the patellar ligament of adult rabbits. After time periods for stimulation all specimens were tested with combinations of roentgenological, histological, biomechanical and biochemical methods. The results were analyzed and compared with the non-stimulated, opposite side and with the normal tissue. The electricity produced 1) a more massive callus with normal histological features in an early stages at the fracture site, and 2) higher tensile stiffness and earlier change of the collagen types in the newly-formed tissue, though no significant differences were observed as to 1) the mechanical parameters of callus and bone material, and 2) histological findings of repairing tissue. Electrical stimulation was indicated not only on bone tissue but also on non-osseous tissues and their components

al Holou N., Benghuzzi H., and Forbes K. (1997) Development of a microcomputer-based system to monitor healing from injury. *Biomed. Sci. Instrum.* 34, 181-185.
Abstract: It is well documented that induction of electric current in bone not only prevents the bone loss of functional disuse, but also induces new bone formation. Moreover, the literature suggests that the skeletal response is optimal at a distinct frequency range 10-30 Hz. Indeed, even at peak strains, well below those typical of habitual physiological loading, applications of 30 Hz were shown to be osteogenic. This evidence supports the concept that inducing even very low strains may generate an effective osteogenic stimulus, provided that they are induced at optimal frequency (10 to 30 Hz). Bone appears to respond with greater selectivity and sensitivity to this frequency range of electrical stimulation. Inducing insulin-like growth factors, which are negatively charged, will provide the required electrical stimulus. Traditionally, the progression of the cellular events during trauma is normally followed by x-ray to determine a healing rate. Frequent use of this method can result in serious side effects to the vital and reproductive organs. The objective of this study is to develop a microcomputer-based system to monitor the cellular events associated with healing. The system is capable of transmitting an electrical signal directly to the site of injury to improve the healing process and to monitor the progress of osteogenesis. The system consists of a base unit and implanted units. One implanted unit will be inserted in the femur with induced trauma and the other implant will be in the control femur. The base unit will transmit low frequency electromagnetic waves to the implanted units as well as receive periodic information about the ion movement in both femurs

Albert S.F. and Wong E. (1991) Electrical stimulation of bone repair. *Clin. Podiatr. Med. Surg.* 8, 923-935.
Abstract: Interest in methods of accelerating bone healing persists. Electrical stimulation has demonstrated consistently high success rates in recalcitrant, complicated nonunions. The promise of successful noninvasive alternatives for treating nonunions continues to be realized. Given the rapidity of advances in this field, it appears likely that acceleration of fracture repair by electrical stimulation will become more widespread in the future

Alexander L.G. (1997) HCFA's decision to not cover electrical stimulation for the treatment of wounds is delayed 60 days. *Ostomy. Wound. Manage.* 43, 62.

Ammer K. (1994) [Electrotherapy]. *Wien. Med. Wochenschr.* 144, 60-65.
Abstract: Electrotherapy is defined as the sum of therapeutic modalities of physical medicine capable to change the threshold of elicitation of nerve or muscle. Classification due to applied pulse frequencies, way of action of transcutaneous nerve stimulation (= TENS) and of iontophoresis is described. Pain syndromes, muscle atrophy by loss of activity and support of wound healing are named as accepted indications for electrotherapy. The difficulties of electrical stimulation of paretic muscles and the problem, whether different indications for certain forms of electrotherapy exist or not, is discussed

Aro H., Aho A.J., Vaahtoranta K., and Ekfors T. (1980) Asymmetric biphasic voltage stimulation of the osteotomized rabbit bone. *Acta Orthop. Scand.* 51, 711-718.
Abstract: An experimental study was performed to determine the effect of electric current on the healing of osteotomies in the antebrachium of the rabbit. Starting with the assumption that the waveform of biphasic asymmetric voltage simulates the asymmetric pattern of stress-induced physiological electrical potentials in normal bone, biphasic asymmetric voltage was applied to the osteotomized radius or ulna. The effects of the electrical stimulation were evaluated by means of X-rays and histological studies. The voltage supplied induced periosteal proliferation whether implanted, insulated electrodes were employed or uninsulated external transfixation pins were used as electrodes. The stimulation had not only osteogenic but also chondrogenic effect. The external callus formation at the osteotomy sites and around the transfixation pins proved to be greater in the stimulated animals than in the controls

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.

Becker M.H., Lassner F., Dagtekin F.Z., Walter G.F., and Berger A. (1995) Morphometric changes in free neurovascular latissimus dorsi flaps: an experimental study. *Microsurgery* 16, 786-792.
Abstract: This study was designed to investigate regeneration of reinnervated, free transplanted muscles. We used a rat model, consisting of eight rats per group, in which the latissimus dorsi muscle was transplanted orthotopically and then harvested and evaluated after 2 and 12 weeks. Age-matched control animals were used to oppose non-operated muscles. At date of removal the patency of the vascular anastomoses was checked clinically and histologically. Electrophysiological measurements were also performed and conventional and enzyme histochemical histological slides manufactured. Two weeks after the free neurovascular flap transfer the muscle was not yet innervated, and histologically a dissolved pattern of type 1 and type IIA muscle fibres was found. The muscle fibres demonstrated a decrease of more than 50% cross-sectional area. After 12 weeks the muscles were reinnervated again; muscle contraction was positive with electrical stimulation and the cross- sectional area had regained 80% of the activity of normal muscle fibres. With enzyme histochemical staining the typical type grouping of reinnervated muscles could be demonstrated

Beer L., Hintner J., Kleditzsch J., and Lorenz T. (1990) [Behavior of alkaline serum phosphatase (AP) and its bone isoenzyme in healing of the osteotomized tibia in rabbits--an animal experimental study]. *Z. Exp. Chir Transplant. Kunstliche. Organe.* 23, 230-232.
Abstract: The effectiveness of the electrical stimulation on the healing of an osteotomy was proved by determining the total alkaline phosphatase (AP) in the serum and its bone isoenzyme in rabbits. A non-stimulated animal group served as control. The changes appeared more distinctly by interference stimulation than by stimulation with bipolar rectangle impulses

Bertsch V. (1980) [The treatment of Dupuytren's contracture from the medical gymnastic standpoint]. *Handchirurgie.* 12, 119-123.
Abstract: A special treatment program has been developed for each individual patient. Each day the patient receives three different treatment modalities--active exercises, passive exercises and electrical stimulation. On days when X-ray therapy is administered, the patient performs only active exercises and receives no electrical stimulation. The patient is also directed to perform certain exercises at home. Patients are advised strongly against the use of hot baths. Dynamic splints are adjusted regularly. In winter and during cold weather, patients are instructed to wear gloves. This therapy, combined with meticulous surgical technique, permits the rehabilitation of most hands affected by Dupuytren's contracture. The goal of rehabilitation is tailored to the needs of the patient and should include a sufficiently strong grasp, chuck pinch and possibly a good pulp pinch. When necessary, the therapy should be continued for long periods of time because a small gain in mobility may represent a significant improvement in overall function of the hand

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

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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.

Branham G.B., Triplett R.G., Yeandle S., and Vieras F. (1985) The effect of electrical current on the healing of mandibular freeze- dried bone allografts in dogs. *J. Oral Maxillofac. Surg.* 43, 403-407.
Abstract: Low levels of electrical current have been shown to affect the process of osseous repair. This study experimentally evaluated the effect of electrical stimulation on the healing of freeze-dried mandibular allogeneic bone grafts in dogs. Healing of the grafts was monitored by sequential submento-occlusal radiographs and radionuclide bone imaging at two, four, six, and eight weeks after grafting. Results indicated no significant difference in the osseous repair of stimulated and nonstimulated freeze-dried allogeneic bone grafts

Brighton C.T., Hozack W.J., Brager M.D., Windsor R.E., Pollack S.R., Vreslovic E.J., and Kotwick J.E. (1985) Fracture healing in the rabbit fibula when subjected to various capacitively coupled electrical fields. *J. Orthop. Res.* 3, 331-340.
Abstract: The effect of capacitively coupled electrical stimulation on the healing of midshaft transverse osteotomies of the rabbit fibula is assessed roentgenographically, mechanically, and histologically. The results show that a dose-response curve for capacitive coupling and fracture healing exists and that a 220 mV, 250 microA, 60 kHz applied electrical signal (0.33 V/cm internal electric field) is the most effective signal for fracture stimulation in this model

Brondbo K., Jacobsen E., Gjellan M., and Refsum H. (1992) Recurrent nerve/ansa cervicalis nerve anastomosis: a treatment alternative in unilateral recurrent nerve paralysis. *Acta Otolaryngol.* 112, 353-357.
Abstract: Sectioning of the right recurrent nerve was done in 5 mongrel dogs under general anaesthesia. The distal stump was anastomosed with the ansa cervicalis nerve branch to the sternothyroid muscle. Three to 5 months later the vocal cord movements during light and very light anaesthesia were videorecorded. Under light anaesthesia contraction and medial bulging of the reinnervated right vocal cord

occurred in 4 of the dogs. Under very light anaesthesia there was also some adduction of the right vocal cord in these 4 dogs. The right recurrent nerve was then sectioned proximally to the anastomosis and stimulated electrically. In all 5 dogs we observed that electrical stimulation produced a strong adduction of the right vocal cord. Histochemistry of the right vocal and posterior cricoarytenoid muscles showed that reinnervation had taken place. The study indicates that in cases of unilateral vocal cord paralysis an anastomosis between the ansa cervalalis and the recurrent nerve will result in improved phonatory function of the affected vocal cord

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

Buntine J.A. and Johnstone B.R. (1988) The contributions of plastic surgery to care of the spinal cord injured patient. *Paraplegia* 26, 87-93.
Abstract: Plastic surgeons have contributed to the understanding of pressure sore pathophysiology and prophylaxis. Increasingly sophisticated surgical techniques such as myocutaneous or innervated flaps add to the reliability and durability of repairs. The majority of quadriplegics may benefit from surgical restoration of active elbow extension, lateral pinch and grasp. Prolonged postoperative care in bed or immobilisation of the upper limb demands that patients should understand fully all that the reconstructive procedure involves. The nature and importance of subsequent rehabilitation must be appreciated by the patient so that he will be motivated to achieve the best possible result. Functional electrical stimulation may find an increasing role in the years to come

Caliskan M.K. (1993) Success of pulpotomy in the management of hyperplastic pulpitis. *Int. Endod. J.* 26, 142-148.
Abstract: Hyperplastic pulpitis is a variety of chronic open pulpitis which is regarded as irreversible. This condition is usually treated by root canal treatment, unless coronal damage does not permit restoration, in which case extraction is indicated. In the present study, 24 permanent teeth of individuals, aged 10-22 years and diagnosed as hyperplastic pulpitis were treated by pulpotomy using an atraumatic surgical technique with calcium hydroxide alone. The treatment was successful in 22 teeth, according to the following criteria: absence of clinical symptoms, absence of any intraradicular or periradicular radiographic pathological changes, presence of dentine bridge detected by clinical examination and sometimes observed

radiographically, and sensitivity to electrical stimulation. The follow-up examination ranged from 12 to 48 months. The high frequency of clinical healing in this study appears to justify recommending pulpotomy as the treatment regime in selected cases of chronic hyperplastic pulpitis

Carr R.W., Delaney C.A., Westerman R.A., and Roberts R.G. (1993) Denervation impairs cutaneous microvascular function and blister healing in the rat hindlimb. *Neuroreport* 4, 467-470.
Abstract: Skin sensory nerve nocifensor functions were investigated non- invasively in rats by measuring neurogenic inflammation and blister healing-rate after unilateral hindlimb denervation. Axon reflexes were evoked by transdermal iontophoresis of acetylcholine (ACh) or noxious electrical stimulation (TNS). Sodium nitroprusside (SNP) evoked direct dilator responses. Resultant changes in skin microvascular blood flux were measured by laser Doppler flowmetry. Compared with their sham-operated control limbs, denervation reduced inflammatory responses (ACh or TNS) by more than 85% and SNP responses by 28% ($p < 0.05$). Healing of dry-ice blisters raised on the hindpaw 14d post-denervation was significantly slower to complete healing (42d) than controls (26d) and initial inflammation was attenuated, confirming that innervation is important for inflammation and blister-healing

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

Chakkalakal D.A., Lippiello L., Shindell R.L., and Connolly J.F. (1990) Electrophysiology of direct current stimulation of fracture healing in canine radius. *IEEE Trans. Biomed. Eng* 37, 1048-1058.
Abstract: Electrophysiological mechanisms involved in the electrical stimulation of fracture healing remain largely unknown. The purpose of the present study was to establish relationships between osteogenetic response and intraosseous measures of electrical dose in experimental fractures (osteotomies) of canine radii stimulated by direct currents. The response was determined postmortem at seven weeks after osteotomy by measuring the bending rigidity and four physicochemical properties: tissue density, mineral density, matrix density, and mineral-to-matrix ratio. The currents measured in bone ranged from 0.1 to 17 microA. Three regions of enhanced osteogenetic response were observed at approximately 1, 7, and 13 microA, separated by regions of unstimulated response. Evidence presented in this paper suggests that enhanced response resulted mainly from electrical modulation of early events in the fracture repair sequence

Chakkalakal D.A., Lippiello L., Wilson R.F., Shindell R., and Connolly J.F. (1990) Mineral and matrix contributions to rigidity in fracture healing. *J. Biomech.* 23, 425-434.

Abstract: The purpose of this study was to investigate the relationships among selected properties of fracture callus: bending rigidity, tissue density, mineral density, matrix density and mineral-to-matrix ratio. The experimental model was an osteotomized canine radius in which the development of the fracture callus was modified by electrical stimulation with various levels of direct current. This resulted in a range of values for the selected properties of the callus, determined post mortem at 7 weeks after osteotomy. We found that the rigidity (R) of the bone-callus combination obeyed relationships of the form R = axb, where x is the tissue density, mineral density, matrix density or the mineral-to-matrix ratio of the repair tissue. These are analogous to power-law relationships found in studies of compact and cancellous bone. The results suggest that fracture callus at 7 weeks after osteotomy in canine radius behaves more like immature compact bone than cancellous bone in its mechanical and physicochemical properties. The present study demonstrates the feasibility of developing non-invasive in vivo densitometric methods to monitor fracture healing, since models may be developed that can predict mechanical properties from densitometric data. Further studies are needed to develop a refined model based on experimental data on the mechanical and physicochemical properties and microstructure of fracture callus at different stages of healing

Chang W.H., Hwang I.M., and Liu H.C. (1991) Enhancement of fracture healing by specific pulsed capacitively-coupled electric field stimulation. *Front Med. Biol. Eng* 3, 57-64.
Abstract: The histologic procedure technique was used to evaluate the bone fracture healing rate of manually fractured fibulae after they were submitted to several different types of capacitively-coupled electric field stimulation, classified depending on the parameters of peak-to- peak voltage, frequency and duration. Using a completely randomized design, 30 New Zealand male rabbits were divided into six different groups: a control group, a 60 kHz and 220 mVp-p sine wave group as proposed by Brighton in 1985, and four special parameters of pulse wave groups. After comparing these different types of electrical stimulation, the group with the parameters of a pulse train repetition frequency of 15 Hz, a pulse frequency of 10 kHz and 5 V peak-to-peak intensity experienced the same enhancement of bone fracture healing as the group with the parameters suggested by Brighton in 1985

Cheng K., Tarjan P.P., and Mertz P.M. (1993) Theoretical study of rectangular pulse electrical stimulation (RPES) onskin 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 electroporation 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

Cochran G.V., Johnson M.W., Kadaba M.P., Palmieri V.R., and Mahaffey G. (1987) Design considerations in development of a prototype, piezoelectric internal fixation plate: a preliminary report. *J. Rehabil. Res. Dev.* 24, 39-50.
Abstract: The piezoelectric internal fixation plate represents a new concept in orthopaedic implants. The purpose of this device is to provide stable bone fixation while delivering internally generated, microampere direct currents to prevent or treat nonunion of a fracture or osteotomy. Clinically, currents of this type have been effective in treatment of nonunion, but application has required separate, implanted, or external battery or radiofrequency powered circuits. The "piezoplate" being developed contains an integral piezoelectric element that generates current in response to either physiological loading such as weightbearing or to externally applied ultrasound. Currents are processed by a rectifying circuit for delivery to bone by electrodes. Specially designed series/parallel piezoelectric elements and dual processing circuits are required to generate optimum rectified currents from the low-frequency, high-voltage signals generated by weightbearing, as well as the high-frequency, low-voltage signals produced by ultrasound. This paper reports on the current status of development and describes design parameters of this device which combines the modalities of mechanical fixation and electrical stimulation in a single implant

Collier J.H., Camp J.P., Hudson T.W., and Schmidt C.E. (2000) Synthesis and characterization of polypyrrole-hyaluronic acid composite biomaterials for tissue engineering applications. *J. Biomed. Mater. Res.* 50, 574-584.
Abstract: New tissue engineering technologies will rely on biomaterials that physically support tissue growth and stimulate specific cell functions. The goal of this study was to create a biomaterial that combines inherent biological properties which

can specifically trigger desired cellular responses (e.g., angiogenesis) with electrical properties which have been shown to improve the regeneration of several tissues including bone and nerve. To this end, composites of the biologically active polysaccharide hyaluronic acid (HA) and the electrically conducting polymer polypyrrole (PP) were synthesized and characterized. Electrical conductivity of the composite biomaterial (PP/HA) was measured by a four-point probe technique, scanning electron microscopy was used to characterize surface topography, X-ray photoelectron spectroscopy and reflectance infrared spectroscopy were used to evaluate surface and bulk chemistry, and an assay with biotinylated hyaluronic acid binding protein was used to determine surface HA content. PP/HA materials were also evaluated for in vitro cell compatibility and tissue response in rats. Smooth, conductive, HA- containing PP films were produced; these films retained HA on their surfaces for several days in vitro and promoted vascularization in vivo. PP/HA composite biomaterials are promising candidates for tissue engineering and wound-healing applications that may benefit from both electrical stimulation and enhanced vascularization

Collier M.A., Kallfelz F.A., Rendano V.T., Krook L.P., and Schryver H.F. (1985) Capacitively coupled electrical stimulation of bone healing in the horse: in vivo study with a Salter type IV osteotomy model with stainless steel surface electrodes. *Am. J. Vet. Res.* 46, 622-631.

Abstract: The use of capacitively coupled low-voltage signals for stimulation of osteogenesis has been reported in a variety of animal models. Electrically induced osteogenesis was investigated with a capacitively coupled electric field on a radius (distal-lateral orientation) osteotomy model, in conjunction with internal fixation and postoperative loading. Twelve adult horses of either sex were allotted to 2 groups of 6; 1 group was given electrical stimulation and the other served as controls. A low-voltage high-frequency capacitively coupled electrical signal was locally and continuously applied to the electrically stimulated group for 60 days through external, bare stainless steel surface electrodes which were placed on the skin in circuit with a small, portable power source. Harness compatibility and stimulator and battery durability were excellent. However, stainless steel electrodes required a rigid maintenance schedule to maintain consistent current levels. Synovial fluid evaluation demonstrated intra- articular inflammation (decreased viscosity, hyaluronic acid, and increased protein concentration) 1 week postoperatively that generally improved during subsequent weeks and no distinction between groups was observed at 60 days. Radiographically, there was no difference in the appearance of the healing process of control and that of stimulated horses during the 60 days. Angiography showed bridging blood vessels in both groups. Uptake of a bone seeking radiopharmaceutical peaked at 3 weeks in both groups and was 1.92 +/- 0.6 cps/pixel/mCi and 1.26 +/- 0.40 csp/pixel/mCi for control and stimulated horses, respectively. At any given observation period, uptake in the lesion area was greater in the control group. Ultimate strengths of trabecular bone in 60-day control radii and stimulated radii were 12.64 +/- 3.013 and 9.60 +/- 3.95 MN/m2, and the flexural moduli of elasticity were 698.0 +/- 423 and 402.0 +/- 523 MN/m2, respectively. Porosity index was similar for all specimens. Gross, histologic, and microradiographic evaluations indicated that controls healed more efficiently than stimulated horses. A capacitively coupled applied voltage of 2.2 V RMS (mean) producing a current of 17.32 mA (mean) did not stimulate sufficient bone production in a metaphyseal osteotomy model to affect the mechanical properties of the bone or accelerate the healing process

Collier M.A., Brighton C.T., Norrdin R., Twardock A.R., and Rendano V.T. (1985) Direct current stimulation of bone production in the horse: preliminary study with a "gap healing" model. *Am. J. Vet. Res.* 46, 610-621.
Abstract: The effect of a 20-microA direct-current implantable bone growth stimulator (BGS) on bone production with a "gap healing" model in the horse was evaluated. The right and left 4th metatarsal bones (Mt-4) were used in 7 adult horses to create the "gap healing" model. A 4-mm section of the Mt-4 bone was resected bilaterally in each horse. The BGS was surgically placed into the 7 left Mt-4 defects. The 7 right Mt- 4 defects served as controls. Six horses survived the 16-week experimental period. Signs of pain, decreased range of limb motion, or lameness was not observed in any animal during the 16 weeks. None of the animals showed complete healing radiographically. Four stimulated sites showed less periosteal reaction and 2 showed greater reaction than the 6 controls. The greatest amount of periosteal reaction or bone resorption was seen around the screws and plates in both groups. Uptakes of 99mTc-MDP in counts/pixel for control sites and stimulated sites were 7.90 and 8.25 in the "gap defect" and 5.19 and 5.06 in the areas adjacent to the gap defect. The ratio of uptake between the gap defect and adjacent area was 1.5 and 1.58 respectively. Biocompatability of the BGS was excellent; however, 1 horse had a broken cathode wire 5 cm from the generator capsule at 6 weeks. All polyethylene cathode sheaths were fluid filled at 16 weeks. The average mineralization rates were 1.57 +/- 0.34, 1.71 +/- 0.28 mm/day and bone formation activity was 0.0182 +/- 0.171, and 0.0168 +/- 0.0149 mm2/day for control limbs and stimulated limbs, respectively. There was no significant difference between groups in any of the histomorphometric values measured. Direct current (20 microA) did not increase bone production in this experiment. Methods to objectively evaluate electrically induced osteogenesis and a "gap defect" model for BGS research on the horse are discussed. The results provide a basis for additional research on electrical stimulation of fractures in the horse and for dose-response studies

Connolly J.F. (1981) Selection, evaluation and indications for electrical stimulation of ununited fractures. *Clin. Orthop.* 39-53.
Abstract: Management of nonunions requires careful and critical assessment of the true biologic status of the fracture. The mere radiographic persistence of a fracture line does not invariably indicate nonunion. Ten percent of fractures considered initially to be ununited in this series healed spontaneously without further treatment. The patient who has no pain with weight-bearing and no demonstrable motion on careful stress studies does not usually require further treatment, except for protection against reinjury. Intraosseous venography may be useful to distinguish the delayed from the nonunion in order to institute appropriate and early treatment. Percutaneous direct-current electrostimulation is proving to be a reliable and effective method of managing the most common nonunion of the tibia or distal femur. It appears less satisfactory for the more proximal femoral fractures and for fractures of the humerus. Electrical stimulation does not eliminate the need to stabilize the nonunion of either the femur or the upper limb. Electrical stimulation also does not eliminate the need for bone grafting in approximately 15% to 20% of nonunions. The fractures' biologic inability to respond may be identifiable by 99MTc diphosphonate bone scan. The implantable direct-current electrical stimulatory device proved ineffective in this series. Hopefully, further development of this technology may produce more consistent results in the future. The electromagnetic noninvasive stimulator appears to be a useful alternative method to the semi-invasive system. This, of course, should depend on the individual needs of the patient and the nature and location of

the fracture. Continued technologic improvement in all electrical stimulatory methods should broaden their usefulness and applicability. However, the healing status of the fracture and the processes by which each fracture responds must be carefully assessed to appreciate what is being effected by electrical stimulation. Critical evaluation and clarification of indications are essential if the patient is to be offered the most effective therapy available

Davis R., Houdayer T., Andrews B., and Barriskill A. (1999) Paraplegia: prolonged standing using closed-loop functional electrical stimulation and Andrews ankle-foot orthosis. *Artif. Organs* 23, 418-420.
Abstract: One T10 paraplegic male (CS) implanted in 1991 with a Nucleus FES-22 stimulator has been able to achieve closed-loop standing for 1 h. The knee angles are monitored by electrogoniometers, resulting in the quadriceps stimulation time being less than 10%. Stance stability is achieved by the Andrews anterior ankle-foot orthosis (AFO). The use of accelerometers for trunk inclination and vertical acceleration during controlled stand-to-sit, diminishes slamming onto the seat. CS does one- handed tasks with objects of 2.2 kg. In another T10 paraplegic male (FR), surface stimulation was applied over 1.5 years to both femoral nerves at the groin for conditioning and prolonged standing. With quadricep conditioning, 55 Nm at 45 degrees of knee flexion is produced. With the AFO and knee monitoring, FR can stand uninterrupted for up to 70 min and perform one-handed tasks. In August 1998, he was implanted with the multifunctional Praxis FES 24-A stimulator for restoration of limb movements, bladder and bowel function, and pressure sore prevention

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

de Haas W.G., Lazarovici M.A., and Morrison D.M. (1979) The effect of low frequency magnetic fields on the healing of the osteotomized rabbit radius. *Clin. Orthop.* 245-251.
Abstract: The object of this experimental work was to evaluate the effect of a noninvasive method of electrical stimulation on the healing of freshly- created

osteotomies of the rabbit radius. The apparatus consisted of a solid core electromagnet energized by a square wave unidirectional current. The magnetic field was pulsed transversely across the osteotomy site of the radius while the animal was confined to a restraining device 6 hours daily for 5 days per week. In one group of animals the influence of different pulse frequencies, using 0.1 Hz, 1 Hz, and 4 Hz, was evaluated, while the period of stimulation was kept constant at 2 weeks. In another group of animals, exposure was continued for 3 and 4 weeks while the pulse frequency was kept constant at 1 Hz. Histologic and radiologic comparison with control animals revealed that the initiation of the healing process can be accelerated in magnetic fields pulsed at 1 Hz, but that this effect is not maintained, and that the total period of time required for union is not significantly shortened. In view of these findings, this form of treatment is not recommended for clinical use in the treatment of recent fractures of long bones

de Haas W.G., Watson J., and Morrison D.M. (1980) Non-invasive treatment of ununited fractures of the tibia using electrical stimulation. *J. Bone Joint Surg. Br.* 62-B, 465-470.
Abstract: A non-invasive method of electrical stimulation of healing in ununited fractures of the tibia by pulsed magnetic fileds has been evaluated. In a series of 17 patients all but two of the fractures united within 4 to 10 months, with an average time of just under six months. The method is sufficiently promising to merit further clinical investigation

de Haas W.G., Beaupre A., Cameron H., and English E. (1986) The Canadian experience with pulsed magnetic fields in the treatment of ununited tibial fractures. *Clin. Orthop.* 55-58.
Abstract: A clinical survey of 56 patients was conducted at four different centers in Canada to evaluate the effect of extremely low frequency pulsed magnetic fields (PMF) on ununited fractures of the tibia. All ten patients with delayed union and 84% of the 44 patients with nonunion healed. One case with a traumatic pseudarthrosis and one with a congenital pseudarthrosis failed to respond to treatment. These results compare favorably to those reported by others using a system with different pulse characteristics. Prolonged immobilization is necessary and poses problems of rehabilitation. Nonunions with a gap between the tibial fragments and pseudarthroses are better treated with bone grafting and internal fixation prior to electrical stimulation

Dunn A.W. and Rush G.A., III (1984) Electrical stimulation in treatment of delayed union and nonunion of fractures and osteotomies. *South. Med. J.* 77, 1530-1534.
Abstract: This study reviews the cases of 52 patients with 52 ununited fractures and osteotomies who were treated with two methods of electrical stimulation, one surgical, the other nonsurgical. Seventeen patients, 14 of whom had concomitant bone grafting, had implantation of a bone growth stimulator. There were three synovial pseudarthroses but no active infection in this group. The overall success rate in healing of the fractures was 82%. Thirty-five patients, of whom four had initial concomitant bone grafting, were treated with pulsing electromagnetic fields (PEMF). There were six draining infections but no pseudarthrosis in this group. Two nonunions healed after bone grafting was combined with PEMF treatment, when the latter alone had failed. Eighty-one percent of the fractures united, and drainage ceased in five of the six infections

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

Enneking W.F., Eady J.L., and Burchardt H. (1980) Autogenous cortical bone grafts in the reconstruction of segmental skeletal defects. *J. Bone Joint Surg. Am.* 62, 1039-1058.
Abstract: The results of using segmental cortical autogenous bone grafts to reconstruct defects created by resection of tumors were analyzed in forty patients. Thirty-three patients had dual grafts while seven had a single fibular graft. Dual grafts were used for major bones (humerus, femur, and tibia without fibula) while single grafts were used for the radius and for the tibia when the ipsilateral fibula was intact. Thirty patients had good or excellent results; seven, fair; and three, poor results. In twenty-five patients primary union was achieved within tweleve months and in two, in twenty months, while twelve patients required a second, supplementary cancellous graft at the site of non- union to obtain stability. One patient required removal of an infected graft and had a poor result. Stress fractures of the grafts occurred in eighteen of the forty patients after union had occurred. The stress fractures healed in fifteen of these patients: in six with no treatment (the fracture was identified retrospectively), in seven with external immobilization, and in two after bone-grafting of the ununited fracture. There were three persistent non-unions of stress fractures despite bone-grafting, internal fixation, and electrical stimulation, and these account for two of the three poor results. The length of the defect did not affect the incidence of non-union but it did affect the number of fatigue fractures. The shorter grafts (7.5 to twelve centimeters) were associated with a 33 per cent incidence of non-union (four non-unions of twelve grafts) while the longer grafts (twelve to twenty-five centimeters) had a 32 per cent rate of non-union (nine non- unions of twenty-eight grafts). The incidence of fatigue fractures in the longer grafts (58 per cent) was much greater than that in the shorter grafts (17 per cent). The grafts decreased in density during the first six months but gradually regained their mass and were generally comparable to normal cortical bone at two years. As the patients became functiona, most (55 per cent) of the the grafts became more dense than normal, some (34 per cent) remained the same, and a few (11 per cent) became less dense. Similarly, some (32 per cent) hypertrophied, most (58 per cent) remained the same size, and a few (9 per cent) atrophied. There was little morbidity (three of forty patients) associated with graft procurement. In twelve patients an additional graft was implanted experimentally, labeled with tetracycline, and subsequently removed at the time of a secondary procedure. These grafts were analyzed to determine if human grafts were repaired in the same fashion as grafts in experimental animals. The studies showed that human grafts are repaired in the same fashion, but that the sequence takes approximately twice as long as it does in the dog

Enwemeka C.S. (1989) Inflammation, cellularity, and fibrillogenesis in regenerating tendon: implications for tendon rehabilitation. *Phys. Ther.* 69, 816-825.
Abstract: The initial three weeks of tendon healing were followed via electron microscopy to elucidate the process of inflammation, fibrillogenesis, and the cellular and subcellular events in tenotomized Achilles tendons, a model that is commonly used to determine the biomechanical effects of electrical stimulation, physical activity, ultrasound, and other forms of physical therapy. The right Achilles tendons of 18 rabbits were tenotomized, sutured, and immobilized. On each of postoperative days 5, 7, 12, 15, 18, and 21, the right Achilles tendons of three experimental rabbits were excised and processed for electron microscopy. To compare these tendons to normal tendons, the Achilles tendons of three control rabbits were excised bilaterally without prior tenotomy and processed for electron microscopy. Electron micrographs thus obtained revealed 1) an initial period of inflammation lasting at least five days, 2) a subsequent period of fibroplasia and fibrillogenesis, and 3) a third period of progressive alignment and organization of the collagen fibrils into bundles that were oriented in the longitudinal axis of the tendon. Although healing in rabbits may not translate directly to healing in humans, the findings of this study indicate that healing begins soon after tenotomy and that the regenerating Achilles tendon undergoes different stages of healing. Because each stage entails a different set of ultrastructural events, therapeutic interventions should be modified to address the specific events of each stage

Esterhai J.L., Jr., Brighton C.T., Heppenstall R.B., and Thrower A. (1986) Nonunion of the humerus. Clinical, roentgenographic, scintigraphic, and response characteristics to treatment with constant direct current stimulation of osteogenesis. *Clin. Orthop.* 228-234.
Abstract: Forty-six trauma patients who had developed non-union of the humerus were evaluated from 1972 through 1981 as part of a large prospective study on nonunion. The average age of the 46 patients was 55 years. Women outnumbered men (29 women and 17 men). Seventy-one percent of the fractures occurred below the midpoint of the humerus. Inadequate immobilization and/or distraction and failure of internal fixation devices to obtain and maintain fracture fragment contiguity and stability was noted. Of the 46 patients referred, 39 were treated with constant direct current, using percutaneously inserted electrodes. Senile and disuse osteoporosis (62%), synovial pseudarthrosis (42%), obesity (20%), and osteomyelitis (5%) in this older patient population made this a difficult treatment problem. Seventeen patients' nonunions healed (46%). Electrical stimulation of nonunion of the humerus is not a panacea. Patient selection is critical

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

Farkas L.G., Herbert M.A., and James J.S. (1980) Peritendinous healing after early movement of repaired flexor tendon: anatomical study. *Ann. Plast. Surg.* 5, 298-304.
Abstract: In 64 chickens the deep flexor tendon of the third toe was divided and resutured, preserving the sheath and flexor sublimis tendon. The leg was placed in a cast for 35 days postoperatively; in some birds minimal flexion of the toes was induced by electrical stimulation of the deep flexor muscle in the last 17 days of cast immobilization. At day 35 the cast was removed, and the return of flexion carried out in the third toe was measured up to day 60. Assessment of the tendon repair site was at 18, 35, and 60 days. Restored peritendinous connections in specific areas were similar to those in controls. Early movement resulted in fewer adhesions, a significantly higher incidence of free intertendinous spaces (standard error of difference = 6.3, difference = 14.5%), and significant lengthening of bridges between the flexor profundus and phalanx (p = 0.01). The effect of early movement gradually decreased from the dorsal to the ventral structures

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

Ferguson A.C., Keating J.F., Delargy M.A., and Andrews B.J. (1992) Reduction of seating pressure using FES in patients with spinal cord injury. A preliminary report. *Paraplegia* 30, 474-478.
Abstract: The aim of this study was to investigate the use of functional electrical stimulation (FES) as a means of pressure sore prevention in seated spinal cord injured (SCI) subjects. Nine SCI subjects took part in tests in which electrical stimulation was applied to the quadriceps with the lower legs restrained. Ischial pressures were measured during periods of quiet sitting and FES application. A strain gauged lever arm was used to measure the knee moment during quadriceps stimulation. The average pressure drop at the right and left buttocks was 44 mmHg and 27 mmHg respectively. In general the greatest reductions occurred in subjects with larger knee moments; however, there was no direct relationship between the

pressure reduction obtained and the quadriceps strength. This form of FES may be useful as a prophylactic aid in the management of pressure sores in SCI subjects

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

Fontanesi G., Traina G.C., Giancecchi F., Tartaglia I., Rotini R., Virgili B., Cadossi R., Ceccherelli G., and Marino A.A. (1986) Slow healing fractures: can they be prevented? (Results of electrical stimulation in fibular osteotomies in rats and in diaphyseal fractures of the tibia in humans). *Ital. J. Orthop. Traumatol.* 12, 371-385.
Abstract: The purpose of the study was to evaluate the possibility of preventing delayed union in fractures by the use of low-frequency pulsing electromagnetic fields (PEMFs). The study was conducted in two parts, both with control groups. Fibular osteotomies in rats and diaphyseal fractures of the tibia in humans were treated with and without electrical stimulation (PEMF). The rats were sacrificed on the 8th and 23rd days respectively in order to evaluate the histological picture of the repair callus and its mechanical resistance. In the human subjects, the clinical and radiological follow-up took into account various factors known to affect the rate of union in the various fracture groups. The results obtained suggest that PEMF stimulation is capable of accelerating and modulating the physiological process of union by its favourable effect on osteogenesis

Forsted D.L., Dalinka M.K., Mitchell E., Brighton C.T., and Alavi A. (1978) Radiologic evaluation of the treatment of nonunion of fractures by electrical stimulation. *Radiology* 128, 629-634.
Abstract: A procedure is described in which nonunion of fractures is treated by implantation of electrodes with direct electric current at the site of fracture. Of 107 patients treated with electrode stimulation, 71 (66%) healed. If one eliminates 9 cases of congenital pseudoarthrosis and 11 patients treated with only 10

microamperes of current, 70 of 87 patients (8095%) healed. Severe osteoporosis and sclerosis were common radiologic findings, but had no value in predicting which patients would respond to therapy

Frank C., Schachar N., Dittrich D., Shrive N., deHaas W., and Edwards G. (1983) Electromagnetic stimulation of ligament healing in rabbits. *Clin. Orthop.* 263-272.
Abstract: To evaluate the effect of a specific noninvasive method of electrical stimulation on ligament healing in rabbits, a solid core electromagnet energized by a square wave unidirectional current was applied to injured and repaired medial collateral ligaments seven hours per day, five days per week for intervals of up to six weeks. Healing was evaluated by gross, histologic, biochemical, and biomechanical parameters. Stimulation was shown to increase histologic maturity relatively, restore stiffness and failure strength earlier, and return collagen content toward normal unoperated values sooner in these healing ligaments. It is uncertain whether the end point of healing is affected by this technique, but at six weeks both histologic and biochemical evidence of acceleration remains. Further investigation into the effect of electromagnetic stimulation by this and other fields on non-osseous tissues and their components is indicated

Frenzel P., Kleditzsch J., and Kienemund A. (1990) [A procedure for quantitative roentgen image analysis for follow-up of Harrington scoliosis surgery]. *Beitr. Orthop. Traumatol.* 37, 117-122.
Abstract: A photometric procedure for evaluating non-standardized X-ray films is described. The X-ray series of a total of 23 patients operated on because of idiopathic scoliosis have been measured out. In 16 patients Harrington's method with dorsal spondylodesis was applied and in 7 patients an electrical stimulation with an implanted stimulator was additionally employed. A time-saving effect of about 30 per cent for the osseous consolidation is obtained by this method. The fundamental suitability of the photometric procedure can be demonstrated

Fujita M., Hukuda S., and Doida Y. (1992) The effect of constant direct electrical current on intrinsic healing in the flexor tendon in vitro. An ultrastructural study of differing attitudes in epitenon cells and tenocytes. *J. Hand Surg. [Br. ]* 17, 94-98.
Abstract: Light and electron microscopy were performed in a study of the effects of electrical stimulation upon the reparative processes in flexor tendons cultured in vitro. After one or two weeks of incubation, the unstimulated control tendons were covered with fibroblastic surface cells, thought to have originated from the epitenon. In contrast, the tendons subjected to electrical stimulation had no proliferation of the epitenon cells in the surface layer. The results indicate that electrical currents of low amperage suppress adhesion-causing synovial proliferation in the epitenon and promote active collagen synthesis in the tenocytes. This suggests the potential value of electrical stimulation in the control of adhesion formation after flexor tendon repair

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

Goh J.C., Bose K., Kang Y.K., and Nugroho B. (1988) Effects of electrical stimulation on the biomechanical properties of fracture healing in rabbits. *Clin. Orthop.* 268-273.
Abstract: One hundred fifteen white rabbits with an average weight of 2.0 kg were used to study the influence of electrical stimulation on osteogenesis. They were divided into three groups: Group I was electrically stimulated with a constant direct current of 20 microamperes delivered to the fracture site; Group II was the control group having the same protocol as Group I except that the stimulator was not switched on; and Group III was the normal fracture healing group (no introduction of electrodes to the fracture site). Roentgenologic and histologic assessment showed that new bone formation in the electrical stimulation group was more exuberant than those in the other two groups in observation periods from three to eight weeks. However, at 12 weeks no difference was observed among the three groups. Biomechanical analysis showed definite increases in the breaking strength and bending stiffness of the fracture healing tibia in Group I, especially at six weeks after surgery. However, at 12 weeks no significant difference was observed among the three groups. Therefore, electrical stimulation of fracture healing has a positive effect

only at the midphase of the healing process, and it does not lead to faster fracture healing

Gum S.L., Reddy G.K., Stehno-Bittel L., and Enwemeka C.S. (1997) Combined ultrasound, electrical stimulation, and laser promote collagen synthesis with moderate changes in tendon biomechanics. *Am. J. Phys. Med. Rehabil.* 76, 288-296. Abstract: The biomechanical, biochemical, and ultrastructural effects of a multitherapeutic protocol were studied using regenerating rabbit Achilles tendons. The multitherapeutic protocol was composed of low- intensity Ga:As laser photostimulation, low intensity ultrasound, and electrical stimulation. Achilles tendons of 63 male New Zealand rabbits were tenotomized, sutured, immobilized, and subjected to the multitherapeutic protocol for five days, after which casts were removed and the therapy was continued for nine more days without electrical stimulation. The tendons were excised and compared with control tendons. Multitherapy treatment produced a 14% increase in maximal strength, a 42% increase in load-at-break, a 20% increase in maximal stress, a 45% increase in stress-at-break, a 21% increase in maximal strain, and a 14% increase in strain-at-break. Similarly, multitherapy treatment was associated with an increase in Young's modulus of elasticity of 31%, an increase in energy absorption at maximum load of 9%, and an increase in energy absorption at load-at-break of 11%. Biochemical analysis of the tendons showed an increase of 23% in the total amount of collagen in the multitherapy-treated tendons, with fewer mature crosslinks (decrease of 6%). Electron micrographs revealed no ultrastructural or morphologic changes in the tendon fibroblasts or in the extracellular matrix. The improvements measured in tendons receiving multitherapy were consistent but less remarkable compared with our earlier works with single modality protocols. The results warrant the hypothesis that the beneficial effects of ultrasound and laser photostimulation on tendon healing may counteract one another when applied simultaneously

Gupta T.D., Jain V.K., and Tandon P.N. (1991) Comparative study of bone growth by pulsed electromagnetic fields. *Med. Biol. Eng Comput.* 29, 113-120. Abstract: Pulsed electromagnetic fields have been widely used for treatment of non-united fractures and congenital pseudarthrosis. Several electrical stimulation systems such as air-cored and iron-cored coils and solenoids have been used the world over and claimed to be effective. Electrical parameters such as pulse shape, magnitude and frequency differ widely, and the exact bone-healing mechanism is still not clearly understood. The study attempts to analytically investigate the effectiveness of various parameters and suggests an optimal stimulation waveform. Mathematical analysis of electric fields inside the bone together with Fourier analysis of induced voltage waveforms produced by commonly used electrical stimulation wave-forms has been performed. A hypothesis based on assigning different weightings to different frequencies for osteogenic response has been proposed. Using this hypothesis astonishingly similar effective values of electric fields have been found in different systems. It is shown that effective electric field rather than peak electric field is the main parameter responsible for osteogenesis. The results are in agreement with experimental findings made on human beings by different investigators

Guttler P., Kleditzsch J., and Schieche A. (1980) [The control of the effect of the electrical stimulation for the callus formation by means of conductance measurement in the rabbit tibia after osteotomy]. *Z. Exp. Chir* 13, 290-296.

Abstract: The measurement of the resistance between the electrodes for stimulation during the operation shows the electrical field strength in the osteotomie. This one will recommend for the comparison of the results of stimulation experiments. The measurement in the course of healing shows faults at the electrodes and the contacts, whereas as the assertions about the process of healing are slightly

Han Z.F. and Zhang Y.C. (1985) [Electrical stimulation in promoting healing of mandibular defects in the rabbit]. *Zhonghua Kou Qiang. Ke. Za Zhi.* 20, 32-4, 64.

Hanaoka T. (1983) [The effects of pulsed micro-electrical currents on internal remodeling in long tubular bone and bone healing]. *Nippon Seikeigeka Gakkai Zasshi* 57, 151-166.
Abstract: The effects of pulsed micro-electrical currents on internal remodeling in the cortex of long tubular bone were evaluated by the following three experiments. 1. Electrodes were inserted in both femora of 14 adult mongrel dogs, 15 mm apart, and pulsed micro-electrical current was applied in the right femoral cortex for 4 weeks, but not in the left femur, which was left as a control. Dogs were divided into 4 groups; in each of these groups current with 1Hz-10 microA, 0.1 Hz-10 microA, 50 Hz-10 microA and 1Hz-20 microA was applied. The effects were evaluated by histometric parameters, i.e. number of resorption cavities (Ar), osteons with osteoid seam (osAf), mineralization rate of osteoid seam (Mo), and perimeter of osteoid seam (Sf). Number of Ar and osAf increased. Bone formation rate (Vf) which is the product of osAf, Mo and Sf increased, especially in the group in which current with 1Hz-10 microA was applied. The main reason for increase of Vf was considered due to that the activation frequency in internal remodeling increased by electrical stimulation. 2. A metal plate was placed on the right humerus, not on the left humerus, both femora of 5 dogs, and electrical current of 1Hz-10 microA was applied in the right femur for either 12 or 16 weeks. Decrease of internal remodeling tended to take place in the mid-portion of the plated area of femur, whereas Vf increased by pulsed micro-electrical currents. Decrease of internal remodeling thus caused by placing a plate and screws increased by pulsed micro- electrical current. 3. Number of osteons in the newly formed bone in the osteotomized gap and in the cortex adjacent to the gap of femora of 7 dogs, which were plated for either 4 or 6 weeks, was measured in longitudinal sections labelled by tetracycline. The number of osteons increased more in the right femur in which current of 1Hz-10 microA was applied than in the left femur. Based on the results above described, it was concluded that bone healing was enhanced by pulsed micro- electrical currents

Harris W.H., Moyen B.J., Thrasher E.L., Davis L.A., Cobden R.H., MacKenzie D.A., and Cywinski J.K. (1977) Differential response to electrical stimulation: a distinction between induced osteogenesis in intact tibiae and the effect on fresh fracture defects in radii. *Clin. Orthop.* 31-40.

Haupt H.A. (1984) Electrical stimulation of osteogenesis. *South. Med. J.* 77, 56-64.
Abstract: The three electrical stimulation systems available for treating nonunion of long bones are successful in approximately 85% of cases. The percutaneous direct current bone growth stimulator is partially invasive, allows patient mobility, can be used with magnetic fixation devices, and can be monitored for proper function, but it requires an operation, cannot be used where infection exists, and is subject to breakage. The implantable direct current bone growth stimulator is similar, but is totally invasive. The external pulsing electromagnetic field bone growth stimulator is

noninvasive and can be used where infection exists, but it requires long, exact patient compliance and cannot be used with magnetic fixation devices or at certain sites. None of the systems can be used where synovial pseudarthrosis or a sizeable gap between bone ends exists, nor are they more effective than bone grafting. Whether their use might evoke malignant transformation or might accelerate or retard epiphyseal growth patterns is not known. Many controlled studies are needed before it is clear how commonly electrical stimulation should be used to treat bony ununion

Hellinger J. and Kleditzsch J. (1980) Electrical stimulation of the callus formation by means of bipolar rectangular pulse sequences. *Arch. Orthop. Trauma Surg.* 96, 241-246.
Abstract: The clinical application of the electrical stimulation, lasting several weeks, for the callus formation is reported in 11 patients. Bipolar rectangular pulse sequences were used for the stimulation at a frequency of 1 Hz and a current intensity of +/-20mu amp. The electrical stimulation was successfully employed after distraction osteotomies with a KDA-apparatus in shortening of the leg provoked by different causes or in the treatment of pseudarthroses. The realignment of the newly formed callus and the osseous consolidation are stimulated and speeded up by the bipolar rectangular pulse sequences as it is also shown in the light of the roentgenograms of a case

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

Il'inskii O.B., Lebedev V.P., Savchenko A.B., Solov'eva A.I., and Spevak S.E. (1987) [Effect of transcranial non-invasive stimulation of the antinociceptive structures of the brain on processes of repair]. *Fiziol. Zh. SSSR Im I. M. Sechenova* 73, 223-229.
Abstract: Transcranial electrical stimulation (AC + DC) of antinociceptive brain structures causing the maximal analgetic effect accelerated skin-wound healing in rats. The effect being completely blocked with naloxone. Participation of opioidergic, antinociceptive brain structures in wound healing and maintenance of structural homeostasis, is discussed

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

Johnson E.E., Urist M.R., and Finerman G.A. (1992) Resistant nonunions and partial or complete segmental defects of long bones. Treatment with implants of a composite of human bone morphogenetic protein (BMP) and autolyzed, antigen-extracted, allogeneic (AAA) bone. *Clin. Orthop.* 229-237.
Abstract: Twenty-five patients with resistant nonunions including partial or complete segmental defects were treated with a composite alloimplant of human bone morphogenetic protein (h-BMP) and autolyzed, antigen-free, allogeneic bone (AAA). The series consisted of 16 females and nine males; average age was 45 years. Preoperative symptoms averaged 30 months (range, five to 83 months); 22 of 25 patients had failed multiple attempts at electrical stimulation. Twenty-three of 25 patients had an average of three prior failed surgical attempts at union (range, one to ten). There were ten segmental defects with an average length of 4 cm (range, 2-9 cm). The composite implant was incorporated as an onlay in 15 extremities and as an inlay graft supported by internal fixation in ten extremities. Seven patients received supplementary autogeneic cancellous bone grafting. Average healing time was six months (range, three to 14 months). Average follow- up time was 21 months (range, five to 82 months). Functional results were rated as excellent, 14; good, five; and fair, five. One failed to unite because of a recurrent infection. Union was obtained in 24 of 25 patients. There were five failures of the original operation that required reoperations; union eventually occurred in four of five extremities by repeat composite grafting and replacement of the failed internal fixation. Bony union between host bone and the composite implant began at an average of eight weeks postoperatively. Present results indicate that h-BMP/AAA composite implants represent adjunctive treatment of difficult nonunions. The h-BMP/AAA composite implants may be implanted in either partial or complete segmental defects of long bones.(ABSTRACT TRUNCATED AT 250 WORDS)

Jorgensen T.E. (1977) Electrical stimulation of human fracture healing by means of a slow pulsating, asymmetrical direct current. *Clin. Orthop.* 124-127.
Abstract: Twenty-eight tibial fractures were treated with external fixation by means of a Hoffmann apparatus. Through two electrode-screws in the Hoffmann apparatus a slowly pulsating, asymmetrical direct current was applied to the fracture site in each patient. The stimulated patients experienced a 30 per cent acceleration in healing as determined by mechanically stressing the Hoffmann apparatus used for immobilization of the fracture

Kahanovitz N. and Arnoczky S.P. (1990) The efficacy of direct current electrical stimulation to enhance canine spinal fusions. *Clin. Orthop.* 295-299.
Abstract: A prospective experimental study was devised to examine the effect of direct current electrical stimulation on the healing of lumbar spinal fusions. Twelve mongrel dogs had posterior facet fusion bilaterally at L1-L2 and L4-L5. A direct current electrical stimulator was placed through each facet fusion. One-half of the electrodes were functional, while the remainder served as controls. Two animals were killed at two and four weeks, and four animals were killed at six and 12 weeks, postoperatively. Each facet fusion was evaluated using high-resolution roentgenograms and routine histology. In the two-, four-, and six-week specimens, there was little difference in the roentgenographic or histologic appearance of the control and stimulated fusions. However, by 12 weeks, all eight stimulated facet joints showed roentgenographic and histologic evidence of solid bony fusion, but none of the eight control facet joints demonstrated osseous bridging of the fusion site. The results of this study suggest that direct current electrical stimulation appears to enhance the bony union of facet fusions in the canine lumbar spine

Kahanovitz N. (1996) Spine update. The use of adjunctive electrical stimulation to enhance the healing of spine fusions. *Spine* 21, 2523-2525.
Abstract: The use of electrical stimulation as an adjunct to enhance lumbar spinal fusion continues to gain popularity. The different types of electrical stimulation and their varying effects on posterior and anterior spinal fusion are discussed. The selection of an electrical stimulation device should be based on the clinical and experimental evidence of efficacy

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)

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)

Kernahan D.A. (1978) Muscle repair in unilateral cleft lip, based on findings on electrical stimulation. *Ann. Plast. Surg.* 1, 48-53.
Abstract: The appearances, distribution, and direction of muscle in the unilateral cleft lip as indicated by electrical stimulation are described. The findings differ from those reported by Fara and associates in their dissections in that functionally the fibers do not appear to parallel the margin of the cleft. Based on these findings, a method of layer-by-layer, step-by-step closure of the unilateral cleft lip is described that attempts to split the orbicularis bulge and advance the lateral muscle into the philtrum to a position more nearly imitating the direction and extent of the muscle in a normal lip

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

Kloth L.C. (1999) The APTA electrical stimulation lawsuit and its aftermath. American Physical Therapy Association. *Adv. Wound. Care* 12, 472-475.

Kondo J. (1985) [Experimental histopathological studies of electrical callus formation and mechanism of bone healing by direct micro-electrical current]. *Nippon Seikeigeka Gakkai Zasshi* 59, 803-817.
Abstract: In order to get better understanding of the effects of electrical stimulation on bone healing processes, the author compared the healing processes of the femur in dogs between two groups: a stimulation group and a control group (non-stimulation group) which were experimentally prepared. These bone specimens were periodically extirpated and used for pathological examinations and X-ray micro-analysis. In the stimulation group, strong proliferation of osteoblasts and new trabecular formation in the bone marrow were observed at the 3rd day, and transition from fibrous to bony callus were noted at the 9th day; after the 3rd week bone remodeling was sparsely seen and bone healing period was shortened. In electromicroscopic observation, calcification of bone matrix and bone remodeling also seemed to be facilitated in this group. However, no marked differences in histological process of bone healing were observed between the stimulation group and the control group

Lavine L.S. and Grodzinsky A.J. (1987) Electrical stimulation of repair of bone. *J. Bone Joint Surg. Am.* 69, 626-630.

Litke D.S. and Dahners L.E. (1994) Effects of different levels of direct current on early ligament healing in a rat model. *J. Orthop. Res.* 12, 683-688.
Abstract: Electrical stimulation has been shown to enhance the repair of biological tissues such as bone and tendon. The objective of this study was to determine whether low level direct current enhances the early healing of injured medial collateral ligaments. Eighty-seven rats were divided into three groups on the basis of

the level of current delivered. All underwent transection of the medial collateral ligament bilaterally. The experimental medial collateral ligaments received current (which varied by group), while the contralateral medial collateral ligaments (the controls), with identical electrodes, received no current. After 12 days, each ligament was tested biomechanically with use of a hydraulic materials testing machine. Group 1 (8.6 +/- 5.9 microA) showed statistically significant improvements in maximum rupture force, energy absorbed, stiffness, and laxity. The groups that had received lower levels of current did not show significant improvements. In this study, stimulation of 1-20 microA was the most effective level of direct current for the enhancement of early healing of the medial collateral ligament

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

Mammi G.I., Rocchi R., Cadossi R., Massari L., and Traina G.C. (1993) The electrical stimulation of tibial osteotomies. Double-blind study. *Clin. Orthop.* 246-253.
Abstract: The effect of electromagnetic field stimulation was investigated in a group of 40 consecutive patients treated with valgus tibial osteotomy for degenerative arthrosis of the knee. All patients were operated on by the same author and followed the same postoperative program. After surgery, patients were randomly assigned to a control group (dummy stimulators) or to a stimulated one (active stimulators). Four orthopedic surgeons, unaware of the experimental conditions, were asked to evaluate the roentgenograms taken 60 days postoperatively and to rate the osteotomy healing according to four categories (the fourth category being the most advanced stage of healing). In the control group, 73.6% of the patients were included in the first and second category. In the stimulated group, 72.2% of the patients were included in the third and fourth category. On a homogeneous group of patients, electromagnetic field stimulation had positive effects on the healing of tibial osteotomies

Marino A.A., Gross B.D., and Specian R.D. (1986) Electrical stimulation of mandibular osteotomies in rabbits. *Oral Surg. Oral Med. Oral Pathol.* 62, 20-24.
Abstract: The use of electrical stimulation to accelerate mandibular healing was studied in rabbits that had undergone bilateral mandibular slot osteotomies. Stimulation on the day of surgery and for 3 successive days thereafter (2 hours per

day) produced accelerated healing as evaluated histologically 8 days after surgery. Stimulation during the entire postoperative period did not result in accelerated healing. Intermittent stimulation in the early postoperative period may be clinically useful for accelerating the healing of mandibular fractures

Masureik C. and Eriksson C. (1977) Preliminary clinical evaluation of the effect of small electrical currents on the healing of jaw fractures. *Clin. Orthop.* 84-91.
Abstract: A clinical investigation has been carried out into the effect of small electrical currents on the healing of mandibular fractures. Electrical stimulation of fracture healing was carried out in 40 patients with a direct current of 10 or 20 microamperes delivered through a platinum electrode. An equal number of patients with similar fractures were selected as controls. Rate of repair was assessed by measuring the mobility of the fracture. Serum phosphatase and calcium were regularly measured at intervals in both groups after reduction and suggested that alkaline phosphatase activity increased in the stimulated group. The repair process was enhanced in the electrically stimulated fractures compared to the controls in the first 10-14 days after reduction

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

McCulloch J.M. (1998) The role of physiotherapy in managing patients with wounds. *J. Wound. Care* 7, 241-244.
Abstract: The physiotherapist is a highly respected member of the wound-care team in the USA. While assisting in all aspects of wound care, including debridement and dressing selection and application, the physiotherapist also provides a unique function. The numerous physical agents, such as electrical stimulation, ultrasound, hydrotherapy and heat all have benefits to offer the patient in contributing to healing. The background knowledge of biomechanics possessed by members of this discipline likewise enhances the services of the wound-care team. Physiotherapists

recommend strategies to relieve or redistribute pressure for those confined to bed or wheelchair or for the ambulatory individual with an insensate foot. It is perceived that physiotherapists who remain uninvolved in wound care are a major untapped resource with great potential for promoting wound healing

McElhannon F.M., Jr. (1975) Congenital pseudarthrosis of the tibia. *South. Med. J.* 68, 824-827.
Abstract: Congenital pseudarthrosis of the tibia is a rare and difficult problem. The cause is unknown, the treatment is nonstandardized, and the results are generally poor. One or two good attempts at union should be made, followed by amputation if union is not obtained or if deformity is worse than that produced by a prosthesis. Electrical stimulation of bone healing is not yet technically advanced enough for use in stimulating fractures to heal in humans, but it has been proven to promote healing in animals and holds considerable promise for the future

McLachlan C.S., Jelinek H.F., Kummerfeld S.K., Rummery N.M., Jusuf P.R., Hambly B., and McGuire M.A. (2000) Cross-sectional infarct edge jaggedness does not influence ventricular electrical stability in a rabbit model of late myocardial infarct healing. *Redox. Rep.* 5, 122-123.
Abstract: Previous studies have suggested that the jaggedness of the healed or healing infarct edge influences cardiac electrical stability. However, these findings have been based on histological observations rather than quantitative measurements. The aim of this study was to assess infarct jaggedness by calculating its fractal dimension and to examine how this influences cardiac electrical stability during late infarct healing in the rabbit. Using programmed electrical stimulation, it was found that the fractal dimension did not differ significantly in 19 rabbits that had inducible ventricular tachycardia and 16 that did not. We conclude from these studies in the mature rabbit that infarct edge jaggedness does not influence the ease with which ventricular tachycardia is induced during late myocardial infarct healing

Miller G.J. (1983) Experience with electrical stimulation of nonunions. *Bull. Hosp. Jt. Dis. Orthop. Inst.* 43, 178-186.
Abstract: The use of electrical stimulation modalities for the treatment of nonunions in the orthopaedic patient population is receiving increasing attention. The following report briefly describes the early results obtained from using three commercially available devices in 33 patients

Moriya M. and Tanaka H. (1990) [Experimental study on the application of direct current to the intra- osseous implant]. *Nippon Hotetsu. Shika. Gakkai Zasshi* 34, 309-317.
Abstract: The purpose of this study is to investigate the effect of the direct current electrical stimulation on surrounding tissue of the intra- osseous implant. The implant was composed of a peripheral hydroxyapatite layer and a central metal which was used as electrodes, and applied 10 microA constant direct current. They were implanted in femurs of four guinea pigs. These results were as follows: 1. When the bone marrow is stimulated electrically with 10 microA direct current for 28 days, large amount of bone formation around the implant was seen in wide area. 2. There was a different reaction surrounding tissue between cathode and anode. Around the cathode, bone formation on the surface of the implant was recognized remarkably. Around the anode, little amount of bone formation on the surface of the implant was

recognized. 3. The electrical stimulation, with newly developed power unit and electrode, accelerated new bone formation

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

Nessler J.P. and Mass D.P. (1987) Direct-current electrical stimulation of tendon healing in vitro. *Clin. Orthop.* 303-312.
Abstract: The intrinsic capacity of tendons to heal in response to injury has recently been demonstrated by many investigators. Electrical stimulation is often assumed to augment regeneration of various tissues. Using newly developed methods of whole-tendon culture, the authors examined the effect of direct-current electricity on healing in vitro. Deep flexor tendons of rabbits were excised, transected, repaired, and grown in an acellular culture medium for seven, 14, 21, or 42 days. Tendons through which a continuous 7-microAmp current was passed at the repair site were compared with nonstimulated controls. The incorporation of (14C)proline and its conversion to (14C)hydroxyproline was measured at seven days. The mean (14C)proline and (14C)hydroxyproline activities were 91% and 255% greater, respectively, in the stimulated group. The activity was also higher in the stimulated group, by 42 days. Histologic sections showed that intrinsic tenoblastic repair may be enhanced with electrical stimulation in vitro

Ni R.X. (1982) [Augmentation of bone repair by electrical stimulation: experiment and clinical observation (author's transl)]. *Zhonghua Wai Ke. Za Zhi.* 20, 103-105.

O'Malley T.J. (1992) A review of the functional electrical stimulation equipment market. *Assist. Technol.* 4, 40-45.
Abstract: The market for functional electrical stimulation (FES) equipment for use in rehabilitation is growing as increasingly sophisticated products enter the market each year. Factors that impact the availability of FES equipment include technological limitations, government regulation, reimbursement status, and clinician training. New products have become available in the last decade with many innovative applications available under investigational status. The current availability of FES equipment for selected applications such as therapeutic muscle stimulation, cardiovascular exercise, restoration of function in the lower and upper extremities, respiratory assist, restoration of bladder function, electroejaculation, and scoliosis correction is reviewed. A review of FES equipment for nonneuromuscular applications such as control of epilepsy, cochlear implants, electrotactile stimulation, and systems to enhance wound healing and bone growth is also included. Key manufacturers are identified

Okada Y. and Shiba R. (1984) [The relationship between electrical callus formation and the amount of electricity]. *Nippon Seikeigeka Gakkai Zasshi* 58, 1013-1023.
Abstract: Electrical stimulation to enhance callus formation has been in use for some time now. This experiment was undertaken to find the relationship between electrical callus formation and the amount of electricity. In this experiment, the long bones of canines were stimulated by direct current and observed microscopically for callus formation. Moreover, distribution patterns of electric potential and current density were calculated theoretically by finite element method. The results are summarized as follows: Electrical callus formation was observed in the medullary canal with 8.7-20 microA direct current. Electrical callus is fibrous ossification and the peak of callus formation is from fourteen to twenty one days. There is no difference in volume and/or speed of callus formation between the simple and the constant direct current. Using platinum electrodes, the amount of callus formed around the cathode and anode is the same. To prevent electrolysis of the tissues, distance between electrodes must be kept at a minimum. On the other hand, the surface area of the electrodes must be widen to keep the electric potential at the minimum level. The area of callus formation is related to 5-10 microA/cm2 of electric current density

Osterman A.L. and Bora F.W., Jr. (1986) Electrical stimulation applied to bone and nerve injuries in the upper extremity. *Orthop. Clin. North Am.* 17, 353-364.
Abstract: In conclusion, electrical stimulation of bone has advanced from the laboratory to clinical reality. Despite the lack of good double-blind clinical studies, it is impossible to ignore the excellent results reported from numerous multicenter trials. Doubts and controversies will and should continue. Electrical stimulation has a definite place in the treatment of scaphoid nonunion as well as other failures of osteogenic biology in the upper extremity. The future may realize the enormous potential of electrical stimulation in areas of nerve repair, wound healings, or osteoporosis. The hand surgeon may soon be operating in the age of biophysics where he or she can charge by the kilowatt hour. Yet one should not become a mere technician, but understand the basic science of what one is doing and, above all, maintain a balanced and critical approach

Paterson D.C., Carter R.F., Maxwell G.M., Hillier T.M., Ludbrook J., and Savage J.P. (1977) Electrical bone-growth stimulation in an experimental model of delayed union. *Lancet* 1, 1278-1281.

Abstract: An experimental model has been devised for the consistent production of delayed bone healing of the tibia in adult dogs. A double-blind trial, with bias eliminated, was used to evaluate the use of a commercially available direct-current bone-growth stimulator with this model. The stimulator produced a statistically significant acceleration of bone healing at four weeks in the experimental model. Osteogenesis was normal, and no dysplastic, inflammatory, or neoplastic changes were found. This research has shown that electrical stimulation of bone is safe and augments bone formation. The bone-growth stimulator unit remains on trial, but in future it may alter the management of many difficult orthopaedic problems

Paterson D.C., Hillier T.M., Carter R.F., Ludbrook J., Maxwell G.M., and Savage J.P. (1977) Experiemtnal delayed union of the dog tibia and its use in assessing the effect of an electrical bone growth stimulator. *Clin. Orthop.* 340-350.
Abstract: A technique has been described for the consistent production of delayed bone healing of the tibia in an animal model. A controlled double blind trial, where independent observors did not know the coding of the stimulators and did not collaborate with each other, has evaluated the use of a direct current bone growth stimulator in such an animal model. The conclusion of the experiment is that this commercially available direct current stimulator does produce a significant acceleration of bone healing at 4 weeks in the experimental model used. There is no evidence of inflammatory or neoplastic changes. The eventual clinical role of electrical bone stimulation remains uncertain and many questions remain unanswered, but are promising enough to encourage a controlled clinical trial in situations of disturbed bone healing. Electrical stimulation is apparently safe and appears to significantly augment bone formation. A controlled clinical trial is now being carried out in major medical centers in Australia

Paterson D.C., Carter R.F., Tilbury R.F., Ludbrook J., and Savage J.P. (1982) The effects of varying current levels of electrical stimulation. *Clin. Orthop.* 303-312.
Abstract: An effort has been made to find an experimental delayed union of a long bone that could be used to evaluate the osteogenic effect of different current strengths. It is important that the optimum current strength be determined. Any such model should be able to produce a difference in new bone formation with an active and an inactive stimulator, particularly one using a 20 microA direct current. Attempts to produce a nonunion model in dogs were unsatisfactory, possibly because the defect was too small and surrounded by normal bone, and excessive movement occurred at the cathode plate. The optimum range of electrical stimulation using a titanium cathode has not been established by this work. The changes in serum alkaline phosphatase, serum calcium and serum phosphorus concentrations in response to trauma have been shown to be the same in the bone formation induced by electrical current

Petersson C.J. and Johnell O. (1983) Electrical stimulation of osteogenesis in delayed union of the rabbit fibula. *Arch. Orthop. Trauma Surg.* 101, 247-250.
Abstract: The present paper describes an experimental model where union was delayed in an osteotomy gap of the rabbit fibula by means of a silicone rubber spacer during 48 days. After the silicone spacer had been removed, electrical transistor regulated direct current of 20 microamperes delivered through stainless steel electrodes was used to stimulate osteogenesis on the right side during 62 days. On the left side a sham operation inserting stainless steel electrodes without current was performed. In one out of six animals overbridging callus was received on the

stimulated side. In the rest of the animals a high frequency of synostoses between the fibular ends and the tibia was found. There was no significant difference in synostosis formation between the right and the left side. No adverse effect of the current could be detected histologically

Piekarski K., Demetriades D., and Mackenzie A. (1978) Osteogenetic stimulation by externally applied dc current. *Acta Orthop. Scand.* 49, 113-120.
Abstract: A new, simple, safe and noninvasive technique for the electrical stimulation of fracture healing is introduced. The safety and the simplicity of the technique makes it possible to apply it almost immediately to clinical experimentation. Electrodes were applied externally to the fractured site producing current across the limb. It was observed that the current density changes the volume of callus and affects the direction of the trabecular orientation. When the trabecular orientation is completely changed from longitudinal to transverse, the larger volume of callus does not compensate for the loss of strength as compared with the callus on the control bone

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

Reswick J.B. and Simoes N. (1975) Application of engineering principles in management of spinal cord injured patients. *Clin. Orthop.* 124-129.
Abstract: Engineering services currently being used for spine stabilization, respiratory assist, and pressure sore prevention are discussed as well as devices under development for bowel and bladder control, reduction of contractural deformities and spasticity, and electrical stimulation of paralyzed muscles. Concepts and devices for improved function are divided into categories of: orthotic devices; environmental control systems; mobility systems; page-turning devices. A wide range of engineering devices are available but strict attention must be given to medical rationale for their use

Rinaldi R., Shamos M., and Lavine L. (1974) Uptake of tritiated thymidine during electrical stimulation of induced cortical bone defects. *Ann. N. Y. Acad. Sci.* 238, 307-313.

Rogerson A.R., Clark K.F., Bandi S.R., and Bane B. (1996) Voice and healing after vocal fold epithelium removal by CO2 laser vs. microlaryngeal stripping. *Otolaryngol. Head Neck Surg.* 115, 352-359.
Abstract: Controversy exists regarding voice recovery after the use of laser vs. microforceps techniques in the removal of benign vocal fold lesions. The purpose of this study is to compare recovery of voice and healing between groups of cats undergoing vocal fold epithelium removal by CO2 laser and those having vocal fold stripping. Fourteen adult female cats underwent standardized unilateral vocal fold injuries by CO2 laser ablation or stripping. After a 6-week recovery period, phonations were evoked by electrical stimulation of the midbrain periaqueductal gray area. Phonations were recorded for acoustic analysis. The larynges were harvested, fixed, and sectioned for histologic correlation. Acoustic analysis showed the mean

signal-to-noise ratios in the laser group (19.72) to be significantly higher than those in the stripped group (13.51) ($p = 0.04$). The stripped group showed significantly greater amplitude perturbation (8.68% vs. 2.43%, $p = 0.02$). No between-group difference was found for period perturbation. Histologically, the laser group showed minimal Reinke's space scarring and near-normal epithelial regeneration, and the stripped group showed marked subepithelial scarring, often involving the vocalis muscle. These results demonstrate superior recovery of voice and healing in animals undergoing vocal fold epithelium removal with the CO2 laser. Inferior outcomes seen in the stripped group may be related to difficulty in preserving Reinke's space during epithelium removal

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

Sanders-Shamis M., Bramlage L.R., Weisbrode S.E., and Gabel A.A. (1989) A preliminary investigation of the effect of selected electromagnetic field devices on healing of cannon bone osteotomies in horses. *Equine Vet. J.* 21, 201-205.
Abstract: The effect of electrical stimulation by means of selected electromagnetic field devices on healing of cannon bone osteotomies in horses was examined. The defects were created as 3 cm x 1 mm longitudinal osteotomies through the dorsal cortices of the mid- metacarpi/metatarsi of adult horses. This type of defect would asses bone healing in a situation similar to an acute, stable fracture of the cortex. Three electromagnetic devices of different design were tested in three different groups of horses. Healing was evaluated radiographically and histologically. Results showed that osteotomies treated with the electromagnetic devices healed similarly to untreated controls. Our conclusion is that the electromagnetic devices studied did not have a local effect on the repair process of an acute, stable, osseous defect

Sanderson K., Nyberg F., and Khalil Z. (1998) Modulation of peripheral inflammation by locally administered hemorphin- 7. *Inflamm. Res.* 47, 49-55.
Abstract: OBJECTIVE: Sensory nerves mediate peripheral inflammation via the release of sensory peptides at the site of tissue injury. Using a blister model of inflammation, we have previously documented that endogenous opioids modulate chronic but not acute inflammation. Hemorphins are nonclassical opioid peptides found in the region of the beta-chain of hemoglobin (Hb). The heptapeptide hemorphin-7 is identical with residues 35-41 of the beta-chain of the human Hb. The aim of this study was to examine the effect of hemorphin-7 on the inflammatory response in acute and chronic injury models. METHODS: We have used a vacuum-induced blister model in the footpad of anaesthetized rats to induce an inflammatory response in naive skin by (a) electrical stimulation (ES) of the distal end of the cut sciatic nerve at 20 V, 5 Hz, 2 ms for 1 min or (b) superfusion of sensory peptides; substance P (SP) or calcitonin gene related peptide (CGRP) over the blister base. In addition, we examined the effect of hemorphin- 7 on the inflammatory response to

SP induced in a previously injured but healed skin site (recurrent injury model) and in denervated skin site due to chronic nerve lesion (chronic injury model). RESULTS: The results showed that prior and concomitant perfusion of hemorphin-7 over the blister base inhibited the acute inflammatory response to ES of the sciatic nerve at C-fibre strength in a dose-dependent manner. Significant inhibition was achieved at 20 and 200 microM concentration of hemorphin-7. When hemorphin-7 (20 microM) was perfused prior to and together with SP or CGRP (both at 1 microM), over the base of acutely induced blister in naive skin, it significantly reduced the inflammatory response to SP (both plasma extravasation and vasodilatation), but was without effect on the vasodilatation response to CGRP. Naloxone, the general opioid antagonist at (1 mg/kg i.v.) reversed the inhibitory effect of hemorphin-7 on the inflammatory response to SP. On the other hand, hemorphin-7 had no effect on the inflammatory response to SP in the recurrent injury or the chronic injury models. CONCLUSIONS: The results of this study suggest that hemorphins might play a role in inhibiting the inflammatory response in acute, but not in recurrent or chronic injury conditions. Evidence is also provided that the modulatory inhibitory effect of hemorphin-7 is mediated via activation of opioid receptor(s). The significance of this study in conjunction with our previous work, is that it raises the possibility that different endogenous inhibitory mechanisms may operate under different injury conditi

Schubert T., Kleditzsch J., and Wolf E. (1986) [Results of fluorescence microscopy studies of bone healing by direct stimulation with bipolar impulse currents and with the interference current procedure in the animal experiment]. *Z. Orthop. Ihre Grenzgeb.* 124, 6-12.
Abstract: 42 cross-breed rabbit bastards of either sex were osteotomized on the left proximal third of the tibia. A teflonisolated stable plating was made by means of the polychromatically KF-AO-instrumentarium. The animals were fluorescentlabelled in weekly intervals. Tetraverinex, alizarin complexon, fluorexon, xylenol orange and calceine were used as colours. The animals were stimulated in the bipolar squaretopped pulse current procedure (1 Hz and 10 Hz, resp., +/- 25 and +/- 50 microA, resp., intensity, permanent stimulation) or in the interference current procedure (oscillation frequency 100 Hz, intensity 1 mA, 4 hours daily). An osteotomized group served as a control. The undecalcified bone sections were quantitatively measured in the area of the periosteal and endoosteal accummulation seams as well as in the area of the Haversians canals and compared by means of multiple variance analyses. A delay in the Haversian remodelling within the first 2 weeks was found in the animals only osteotomized. This delay could not be detected in all electrically stimulated groups. The electrical stimulation leads to a shortening of the fracture healing period by skipping the physiologically occurring delay of the Haversian remodelling in fractures and osteotomies. Further on there was derived a growth function of the osteones as a regression function r (t) = a + beta X e gamma t. For the rabbit the concrete formula expression r (t) = 50.9 X e-0.094 X t + 17.4 for the animals not treated and r (t) = 42.9 X e-0.067 X t + 8.5 for the electrical stimulated animals has been found.(ABSTRACT TRUNCATED AT 250 WORDS)

Shandler H.S., Weinstein S., and Nathan L.E., Jr. (1979) Facilitated healing of osseous lesions in the canine mandible after electrical stimulation. *J. Oral Surg.* 37, 787-792.
Abstract: A study was performed to investigate the effect of electrical stimulation on the repair of osseous lesions in the canine mandible. Results showed considerably more osteoblastic activity on the electrically stimulated side, with maximal growth

nearest the negative electrode. Histologic examination showed healing consisted of the production of intramembranous bone, with no evidence of neoplastic changes. The practical uses of electrical stimulation in the practice of oral and maxillofacial surgery are discussed

Sharp I.K. and Lightwood R. (1983) Stimulation of bone union by externally applied radio-frequency energy. *Injury* 14, 523-530.
Abstract: Pulsed radio-frequency electrical energy has been used for many years in the treatment of various soft tissue lesions, and this paper describes its use in stimulating repair in delayed and non-union, with a success rate in 16 cases equal to that of the other electrical stimulation techniques. The equipment is described and a theory proposed that the cell membrane has a diode effect in allowing the absorption of electrical charge, which, by its influence on the calcium ion, stimulates the cell into activity

Simonis R.B., Shirali H.R., and Mayou B. (1991) Free vascularised fibular grafts for congenital pseudarthrosis of the tibia. *J. Bone Joint Surg. Br.* 73, 211-215.
Abstract: We describe 11 patients with congenital pseudarthrosis of the tibia treated by a free vascularised fibular graft (FVFG) and followed up from 10 to 64 months (mean 38). Bony union was achieved in nine of the 11 cases: two failures required amputation. The mean time for union in the successful cases was five months. Nine of the 11 patients had had an average of four surgical procedures before the FVFG, so the graft was a salvage procedure for which the only alternative was amputation. FVFG is recommended as a primary procedure for the treatment of congenital pseudarthrosis of the tibia if there is a large tibial defect (over 3 cm) or shortening of more than 5 cm. The primary use of this operation is not advised for cases in which standard orthopaedic procedures are expected to succeed. For a small defect with a favourable prognosis (Boyd and Sage 1958), we recommend conventional bone grafting, intramedullary nailing and electrical stimulation

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.

Spadaro J.A. (1977) Electrically stimulated bone growth in animals and man. Review of the literature. *Clin. Orthop.* 325-332.
Abstract: The literature on the electrical stimulation of bone growth and fracture healing has been increasing exponentially in recent years. About 95 per cent are positive reports despite an extraordinarily wide selection of experimental techniques and models. Fourteen research groups report that electrical currents stimulated fracture healing with few if any complications in a total of 595 patients. The mechanisms of action and ideal technique for applying stimulation has yet to be determined

Spielholz N.I. and Kloth L.C. (2000) Electrical stimulation and pulsed electromagnetic energy: differences in opinion. *Ostomy. Wound. Manage.* 46, 8, 10, 12.

Srivastava K.P. and Saxena A.K. (1977) Electrical stimulation in delayed union of long bones. *Acta Orthop. Scand.* 48, 561-565.
Abstract: The role of electricity in the promotion of fracture union of long bones in human beings requires further investigation. An electric stimulator was devised through which 15 microamperemeter current was applied to the fractured long bones

of 20 patients with delayed union. The best results were obtained in cases where the negative electrode was introduced at the fracture site and the positive electrode was placed proximal to the fracture area. In 90 per cent of cases treated by different methods in this series, union occurred within an average period of 9 1/4 weeks. The rate of infection following introduction of electrodes for electrical stimulation was 20 per cent

Srivastava K.P. and Saxena A.K. (1977) Fracture healing in a case of nonunion of the tibia by electrical stimulation. *Int. Surg.* 62, 35-36.

Srivastava K.P., Lahiri V., Khare A., and Chandra H. (1982) Histomorphologic evidence of fracture healing after direct electrical stimulation in dogs. *J. Trauma* 22, 785-786.
Abstract: A histomorphologic study was done at intervals up to 10 days after causing a fracture in both hindleg tibiae in dogs and giving direct electrical stimulation in one tibia, the other being used as control (20 microns ampere of direct current were passed in 28 limbs and the current was maintained with the help of a simple regulator developed by the authors). The radiologic and histomorphologic study showed definite evidence of early start and completion of healing processes in the electrically stimulated hindlegs. Negative potentials induced at the fracture sites appeared to be the cause of improved healing. The incidence of infection and focal necrosis at the anode was minimal in this experiment

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

Steiner M. and Ramp W.K. (1990) Electrical stimulation of bone and its implications for endosseous dental implantation. *J. Oral Implantol.* 16, 20-27.
Abstract: Applied electrical potentials can alter cellular movement, stimulate production or destruction of cells, and change the chemical concentration and composition of both soft tissue and bone. These actions vary depending on the microamperage and duration of the applied current and whether it is continuous or pulsed, the type of metallic electrode, and the types of cells or tissues involved. Relative to skeletal effects, researchers have accumulated data from bone cell cultures, embryonic and adult animal bone, and human clinical studies. This article reviews the historical use of electric current for fracture healing, the piezoelectric effect found in tissues, and the possible deleterious effects of electrical stimulation. The types of electric current presently used for treating extremity fractures and reports where electric current has been used on tissues in the oral cavity are

discussed. Alternate sources of energy to stimulate bone and possible implications for use of electrical stimulation to augment attachment of endosseous dental implants are also included

Stewart K.M. (1991) Review and comparison of current trends in the postoperative management of tendon repair. *Hand Clin.* 7, 447-460.
Abstract: The precision of the Evans/Burkhalter protocol and the work by Silverman and associates exemplify one of the most valuable of all current trends in rehabilitation of the healing tendon. Knowledge of tendon excursion at each level and throughout the range of motion in each joint gives us safe parameters for tendon mobilization. Hand rehabilitation is becoming more of a science while remaining an art. Research into tendon healing, nutrition, anatomy, biomechanics, and physiology gives us a solid basis for our treatment techniques. We now need to replicate studies already performed and quantify more precisely the data we have. Many questions remain unanswered. There is a wide variety in the position of splinting for flexor tendon mobilization under current protocols: What joint positions are optimal and why? The number and frequency of repetitions in early mobilization protocols varies greatly: What number and frequency is more appropriate for which patients? How much tendon excursion will control adhesions, promote healing, and avoid gap formation or elongation of the repair? How much force should we apply passively to maintain or increase joint motion? How soon should we start active motion, and how can we control the strength of those early muscle contractions? Do "place-hold" exercises truly place less tension on the repair site? How soon should we begin resisted exercise, and how much resistance are we applying with each type of exercise? Should blocking exercises be considered resistive? How should tendon management protocols be adapted in the presence of associated injuries? Lack of space has prevented discussion here of recent and needed research in a number of areas, such as the effectiveness and appropriate precautions for the use of ultrasound, iontophoresis, and neuromuscular electrical stimulation in tendon management. The evidence is growing, but we have a long way to go. To improve our clinical results, the trend toward precision must continue and grow

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

Uhl R.L. (1989) The use of electricity in bone healing. *Orthop. Rev.* 18, 1045-1050.
Abstract: The history of electrical bone healing and the vast amount of laboratory and clinical data that support its efficacy are reviewed. The paper presents guidelines for the proper use of electrical stimulation and a description of the various systems available. The use of electrical stimulation to treat scaphoid fractures is covered in detail. Contraindications to the use of electrical stimulation are also addressed

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

Walter T.H. (1985) Bioelectrical osteogenesis: acceleration of fracture repair and bone growth. An alternative to bone grafting in nonunions. *Clin. Podiatry.* 2, 41-57.
Abstract: Electrical stimulation of fracture nonunions has become a viable alternative to bone grafting. The success rate is comparable but the morbidity rate is significantly lower. Individual fracture healing problems must be thoroughly assessed and the treatment designed for the individual patient

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

Westerman R.A., Carr R.W., Delaney C.A., Morris M.J., and Roberts R.G. (1993) The role of skin nociceptive afferent nerves in blister healing. *Clin. Exp. Neurol.* 30, 39-60.
Abstract: Because sensory neuropeptides improve survival of critical skin and muscle flaps in rats, skin nociceptive sensory nerve function in blister healing was examined. Sensory nerve ablation by unilateral hindlimb denervation or cutaneous axon reflex enhancement by 14 days systemic nicotine treatment (5 mg kg-1 day-1) decreased and increased, respectively, peripheral motor functions of nociceptive (peptidergic) skin nerves. Effects on nociception were measured by a radiant heat

tail-flick test. Axon reflex flares were evoked by transdermal iontophoresis of acetylcholine or noxious electrical stimulation under pentobarbitone 40 mg kg-1 anaesthesia. Resultant changes in cutaneous microvascular blood flux were measured non-invasively by laser Doppler flowmetry. In nicotine-treated rats compared with placebo-treated controls, acetylcholine-evoked axon reflex flare was enhanced by 240% ($p < 0.01$) without enhancement of electrically evoked flare. Thus, nicotine-sensitized nociceptors show stimulus specificity in their enhancement of neurogenic flare responses. No significant changes were seen in other endothelial-dependent or smooth muscle-dependent microvascular dilator responses. Nicotine-treated rats had prolonged tail-flick withdrawal latencies to noxious radiant heat stimuli compared with placebo-treated controls ($p < 0.05$), suggesting an antinociceptive or analgesic effect of nicotine-treatment. Neurogenic effects on wound healing rate were assessed by measuring the dimensions of standardized blisters twice daily. The blisters were raised on hindpaw glabrous skin using a constant weight and diameter of compressed dry ice pellet applied for 30 secs at constant force. Dry- ice blisters raised on the hindpaw 14 days post-denervation were significantly slower to heal completely (42 days) than controls (30 days: $P < 0.05$) and the surrounding inflammation was reduced. By contrast, nicotine-treated rats showed more rapid blister healing (25 days) than controls (30 days), seen only in the later phase after day 15. Finally, resting substance P release from blisters, after direct cutaneous nerve stimulation, appears to be enhanced in nicotine-treated rats. Thus nociceptive innervation appears critical for inflammation and rapid healing of blisters in rat skin. The data signal a possible important role for neuropeptides in these processes and question the function of nicotinic receptors on sensory nerves

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