

Effect of Electrical Stimulation on Chronic Leg Ulcer Size and Appearance

Background and Purpose. Electrical current has been recommended for use on chronic pressure ulcers; however, the ability of this modality to improve healing of other types of chronic ulcers is less well established. The purpose of this study was to examine the effect of high-voltage pulsed current (HVPC) on healing of chronic leg ulcers. **Subjects.** Twenty-seven people with 42 chronic leg ulcers participated in the study. **Methods.** The subjects were separated into subgroups according to primary etiology of the wound (diabetes, arterial insufficiency, venous insufficiency) and then randomly assigned to receive either HVPC (100 microseconds, 150 V, 100 Hz) or a sham treatment for 45 minutes, 3 times weekly, for 4 weeks. Wound surface area and wound appearance were assessed during an initial examination, following a 1- to 2-week period during which subjects received only conventional wound therapy, after 4 weeks of sham or HVPC treatment, and at 1 month following treatments. **Results.** The results indicated that HVPC applied to chronic leg ulcers reduced the wound surface area over the 4-week treatment period to approximately one half the initial wound size (mean decrease=44.3%, SD=8.8%, range=2.8%-100%), which was over 2 times greater than that observed in wounds treated with sham units (mean decrease=16.0%, SD=8.9%, range=-30.3%-83.7%). **Discussion and Conclusion.** The results of the study indicate that HVPC administered 3 times a week should be considered to accelerate wound closure of chronic leg ulcers. [Houghton PE, Kincaid CB, Lovell M, et al. Effect of electrical stimulation on chronic leg ulcer size and appearance. *Phys Ther.* 2003;83;17-28.]

Key Words: *Acetate tracings, Chronic ulcers, Diabetic foot ulcers, Electrical stimulation, Photographic Wound Assessment Tool (PWAT), Venous leg ulcers, Wound size and appearance.*

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Chronic vascular leg ulcers due to venous insufficiency, atherosclerosis, diabetes mellitus, or small vessel disease affect approximately 1% of the general population and up to 10% of individuals who are in health care facilities.¹ Slow-healing vascular ulcers have serious human consequences, including pain, lost workdays, and marked reduction in quality of life.² Furthermore, 70% to 90% of leg amputations are due to vascular ulcers, and foot ulceration and infection are leading causes of hospitalization among people with peripheral vascular disease due to diabetes mellitus.³ Chronic ulcers due to venous insufficiency represent approximately 70% to 90% of chronic lower-extremity ulcers. Costs associated with the management of these ulcers on an outpatient basis in the United States have been as high as \$2,500 per ulcer for a 4-month period.⁴ Given that many of the factors that predispose individuals to develop chronic wounds are more prevalent with advancing age, the human and financial costs of assessing and managing this problem

are likely to rise significantly as the average age of the North American population increases.

Researchers have begun to examine the efficacy of various therapeutic approaches designed to accelerate wound healing.^{5,6} A therapeutic approach that accelerates wound closure could reduce health care costs. Several putative therapeutic approaches have been proposed, including the use of antiseptics, antibiotics, growth factors, pressurized oxygen, biologically engineered skin substitutes, and physical therapy modalities such as electrical stimulation.

Numerous reports⁷⁻²¹ support the use of electrical stimulation for managing chronic wounds. In randomized controlled clinical trials,^{7,8,15,17,19,21} electrical stimulation has been shown to improve the healing rates of chronic pressure ulcers occurring with limited mobility or limited cognitive ability because of conditions such as spinal cord injury, stroke, or brain trauma.

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Dr Houghton and Ms Kincaid provided concept/idea/research design. Dr Houghton provided writing and project management, and Dr Houghton and Ms Lovell provided data collection. Dr Woodbury provided data analysis and consultation (including review of manuscript before submission). Ms Campbell, Dr Harris, and Dr Keast provided fund procurement, subjects, facilities/equipment, and institutional liaisons. The authors acknowledge the following students enrolled in the undergraduate program in physical therapy at the University of Western Ontario for their invaluable contributions to this research project: Leya DeBryn, Michelle Allin, Anna Banks, Jeannie Tschirart, Megan Close, Jada Close, and George Paradalis were involved in administering weekly treatment sessions; Lisa Morrison played a key role in establishing documentation skills and reliable outcome measures; and Beth Desveaux, Donovan Stewart, and Linh Nyugen performed the data analysis of wound surface areas and the calculation of wound appearance scores.

Study approval was obtained from the Review Board for Health Sciences Research Involving Human Subjects at the University of Western Ontario and from the Research Committee at Parkwood Hospital of St Joseph's Health Care London and the Clinical Research Investigation Committee at Victoria Campus of London Health Sciences Centre.

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Using this research, the US Department of Health and Human Services' Agency for Healthcare Research and Quality (AHRQ) (formerly the Agency for Health Care Policy and Research [AHCPR]) developed and published clinical practice guidelines for the management of pressure ulcers.²² The guidelines state that "electrical stimulation is the only adjunctive therapy with sufficient supporting evidence to warrant recommendation by the panel,"^{22(p55)} to be used for enhancing the healing rate of stage II or III pressure ulcers that have been unresponsive to conventional therapy. The evidence for the use of electrical stimulation for chronic pressure ulcers was revisited in a 1998 review of the research literature performed by Dr Liza Ovington.²³ Based on this more recent review of the research literature, she suggested that the strength of evidence rating should be upgraded to the highest rating possible (rating of A = positive results exists from 2 or more randomized controlled clinical trials).

Despite the strong evidence supporting the use of electrical stimulation for chronic wounds, most research has examined the effect of this modality on either pressure ulcers⁷⁻¹⁶ or ulcers due to mixed etiologies.¹⁷⁻²¹ Few researchers have examined the effectiveness of electrical stimulation for chronic wounds due to other etiologies such as venous and arterial insufficiency.²⁴⁻²⁹ Therefore, the purpose of our study was to examine the effect of HVPC on wound healing of chronic lower-extremity ulcers due to diabetes or to arterial or venous insufficiency.

Method

Subject Recruitment

Individuals with at least one lower-extremity chronic wound lasting longer than 3 months were recruited into the study via advertisements in local media and through collaboration with physicians and wound care specialists serving either outpatient clinics or an inpatient population. Individuals who agreed to participate in the study signed an informed consent statement and then were screened using inclusion and exclusion criteria as approved by local institutional review boards. The inclusion criteria were: (1) the individual had one or more full-thickness skin ulcers located below the knee of greater than 3 months' duration; (2) the primary etiology of the wound was either venous or arterial insufficiency, or the wound was due to diabetes mellitus; and (3) the individual had received medical attention for the medical condition believed to be the primary cause of the wound that included appropriate standardized wound care and nutritional information.

Subjects were excluded from the study if they were undergoing corticosteroid therapy, radiation therapy, or

chemotherapy for cancer, all of which would interfere with the ability to heal. Other exclusion criteria included any of the following medical conditions for which electrical stimulation is contraindicated⁵: (1) ventricular arrhythmia, (2) atrial fibrillation, (3) use of a cardiac pacemaker, (4) history of deep radiation therapy within the local region, (5) known deep venous thrombosis or thrombophlebitis, (6) superficial metal ions or metal implants near the area, (7) pregnancy, or (8) active osteomyelitis.

Subject Demographics

A total of 33 individuals volunteered to participate in the study. Four subjects did not meet the inclusion and exclusion criteria, and 2 subjects did not complete the 4-week treatment program. Both of these subjects had been assigned to a group who received a sham treatment. They elected to withdraw from the study for reasons unrelated to the treatment. A total of 27 people with 42 ulcers completed the study protocol.

Demographic information on the subjects enrolled in the study was obtained from a standardized subject interview, physical examination, vascular flow laboratory session, or medical chart review (Tab. 1). Subjects were randomly assigned to either a group who received HVPC (n=14) or a group who received sham HVPC (n=13) (see "Study Design" section). A similar number of female subjects were present in each treatment group. The average ages of the subjects were 66.3 years (SD=4.8, range=25-91) for the subjects who received HVPC and 62.4 years (SD=5.6, range=31-81) for the subjects who received the sham treatment. The mean duration of time the subjects had their ulcers prior to entry into the program was 2.96 years (SD=1.4, range=0.8-15) for the subjects who received HVPC and 5.47 years (SD=2.4, range=0.25-25) for the subjects who received the sham treatment. The relatively high value for the mean duration of ulcer in the sham treatment group was due to one subject in this group who had an ulcer that had been present for 25 years. Nineteen out of 27 ulcers were located in the ankle or malleolar region of the leg, with all ulcers under study located below the level of the knee. Approximately half of the ulcers in the study were venous ulcers. Arterial ulcers represented the type of ulcer present in fewest number of subjects in the study (n=2). Three subjects in each treatment group had diabetes and venous insufficiency or arterial disease.

Initial Examination

Relevant information about the history and severity of any medical conditions known to influence wound healing were determined using a questionnaire and were verified by use of a medical chart review. After obtaining the relevant medical history, both limbs were observed and any signs of vascular insufficiency were noted. These

Table 1.

Patient Demographics and Coexisting Medical Conditions Determined in Initial Evaluation

Factor Affecting Healing	Subjects Who Received HVPC ^a (n=14)	Subjects Who Received Sham Treatment (n=13)
Sex	5 female/9 male	5 female/8 male
Age (y)		
\bar{X}	66.3	62.4
SD	4.8	5.6
Range	25-91	31-81
Duration (y)		
\bar{X}	2.96	4.57
SD	1.4	2.4
Range	0.8-15	0.25-25
Initial wound size (cm ²)		
\bar{X}	6.39	5.53
SD	1.85	1.96
Range	0.24-38.1	0.24-29.8
Ankle brachial index		
\bar{X}	0.85	0.89
SD	0.1	0.1
Blood glucose concentration (mmol)		
\bar{X}	6.53	8.81
SD	0.9 (4 subjects >10 mmol)	1.8 (5 subjects >10 mmol)
Visual analog scale pain score (mm)		
\bar{X}	1.48	1.16
SD	0.6	0.6
Sensory impairment (no. of subjects in group)	6	7
Infected wounds (n)	8	4
Wound location		
Toe	2	1
Foot	2	2
Ankle/malleolus	6	7
Leg	4	2
Type of ulcer		
Diabetic	2	3
Arterial	2	0
Venous	7	6
Mixed	3	3
No. of factors affecting wound healing per subject		
\bar{X}	4.85	4.91
SD	0.5	0.9

^a HVPC=high-voltage pulsed current.

observations included the presence of pale, shiny, skin, thickened nails, little hair growth, cool skin temperature, weak or absent foot pulses, and the presence of varicosities or visual identification of skin stained with dark brown hemosiderin pigment, or bilateral limb swelling or lymphedema.³⁰ A small blood sample was obtained and analyzed using a glucose monitor (One Touch Blood Glucose Monitoring System*) to identify subjects with hyperglycemia. A calibrated nylon 5.07 Semmes-Weinstein monofilament was applied with suffi-

cient pressure to produce filament bending to 10 predetermined locations of the plantar aspect of the subjects' feet in a random cadence and order. Results obtained using these monofilaments vary little and that filaments produce a controlled reproducible force of 10 g.³¹ People who are unable to detect this monofilament have a higher risk of foot ulceration and are considered to lack the protective sensation necessary to detect and respond to excessive external pressure.³²

The relative amount pain associated with the wound was assessed prior to manipulating the wound in any way using a well-established visual analog scale. The reliabil-

* Lifescan Canada Ltd, 300-4170 Creek Dr, Burnaby, British Columbia, Canada V5C 6C6.

ity of results obtained on initial and repeated assessments of an individual's pain is considered excellent ($r=.95$).³³ This pain assessment involved asking the subjects to indicate their level of pain on a 100-mm line marked at one end with the descriptor "worst pain" and at the other end with the descriptor "no pain." We also noted the presence of signs of infection, including a positive swab culture, marked redness extending beyond wound margins, increased pain, and foul-smelling purulent wound exudate.

Information gained during this interview was used to document the number and type of medical conditions known to affect wound healing that were present in the subjects such as chronic obstructive pulmonary disease, congestive heart failure, or coronary artery disease. The observations from this initial examination together with results from Doppler ultrasound studies performed in a vascular flow laboratory also were used to determine the primary etiology of the wound (diabetic, arterial, or venous). Subjects were considered to have diabetes if they had a blood glucose concentration within the last 24 hours that was greater than 10 mmol (180 mg/dL). We considered arterial insufficiency to be present if the Doppler ultrasound recorded an ankle brachial pressure index of less than 0.8, a value commonly used to designate the presence of moderate arterial insufficiency.³⁴ We considered venous insufficiency to be present if a subject had varicosities, gravity-dependent leg edema or lipodermatosclerosis, or hemosiderin staining of the lower extremity.³⁵

Eight subjects who received HVPC and 4 subjects who received the sham treatment had signs of infection at the time of the initial examination and were prescribed appropriate antimicrobial therapy. A similar number of subjects in each group were unable to accurately detect a 10-g Semmes-Weinstein monofilament and thus were considered to have lack a protective sensory response.³² Based on the initial evaluation, we counted the number of factors known to affect wound healing for each subject. On average, the subjects in each group had 5 of these factors known to affect wound healing. On the basis of these descriptive data, we believe that our subjects represented a relatively broad heterogeneous subject population of individuals who typically have chronic leg wounds.

Comparing the frequency of each of these factors known to affect healing between treatment groups using a Mann-Whitney rank sum test revealed that none of these descriptive variables were different between treatment groups. Mean values for age, duration of the ulcer, initial wound size, ankle brachial index, mean pain score, and blood glucose concentration were compared for subjects in each treatment group using the Student *t* test. We

found that the mean values for each of these factors known to affect wound healing were not different between the 2 treatment groups.

Pearson product moment correlation coefficients were calculated to examine the correlation between subject demographics, coexisting medical conditions, and concurrent therapies with the change in wound size that occurred over the study period. Wound healing, considered as a reduction in wound size, that occurred over the study period in the subjects in either treatment group was negatively correlated with duration of ulcer ($r=.547$), blood glucose concentration greater than 10 mmol ($r=.345$), and the number of factors affecting wound healing ($r=.409$). These correlations were not statistically significant.

Study Design

We designed the study to be a randomized, double-blind, prospective clinical trial. Subjects satisfying the inclusion and exclusion criteria were divided into 3 subgroups based on predetermined criteria according to the primary etiology of the wound (diabetes, arterial insufficiency, venous insufficiency). The subjects then were randomly assigned to either group A or group B. Both groups of subjects were treated identically using electrical stimulators (EGS Model 300 electrical stimulators[†]) that were marked "A" or "B." The equipment used on the subjects who received the sham treatment had been deactivated by the manufacturer in an inconspicuous manner so that neither the subjects nor the researcher were aware of which group of subjects were receiving real or sham treatment. Some of the subjects ($n=11$) were admitted to the study with more than one wound. Two of these subjects developed a new ulcer that did not resolve with standard wound care over a 3-month period and were readmitted to the study. Nine of these subjects had bilateral ulcers seven of which were venous leg ulcers. In all these cases one ulcer was randomly selected to be treated with a electrical stimulator marked "A," and the other ulcer was treated with an electrical stimulator marked "B." At the completion of the study, when all the data had been collected and analyzed, it was revealed that electrical stimulators marked "A" were active and those marked "B" had been deactivated.

Subjects enrolled in the study were told during the initial treatment session that although they could expect some discomfort during procedures involved in removing the dressing, cleansing the wound, and placing the active electrode in the wound, they should not experience pain during the course of the 45-minute treatment period. Subjects were told that if they were to feel any discomfort

[†] Electro-Med Health Industries, 11601 Biscayne Blvd, Ste 200A, North Miami, FL 33181.

Table 2.
Concurrent Wound Interventions

	Subjects Who Received HVPC ^a (n=14)	Subjects Who Received Sham Treatments (n=13)
Optimal wound dressing (maintains good wound moisture)	10	9
Debridement	5	4
Pressure relief	3	4
Compression	7	4
Patient nonadherence	3	3
Primary etiology not adequately addressed	3	4

^a HVPC=high-voltage pulsed current. Numbers represent the number of subjects in each group.

during the treatment, they should inform the therapist, who would adjust the stimulator. No subject in either treatment group reported any discomfort during a treatment session, and no adverse reactions following treatment sessions were recorded during the course of the study.

Standard Wound Care

Table 2 presents information on concurrent interventions also administered during the study. These interventions included pressure relief and protection for individuals with sensory impairment and compression therapy for persistent leg edema. Wound dressings used in the study included nonadherent gauze pads, hydrogels, hydrocolloids, and absorbent foam dressings. Dressings suspected of adversely interacting with electrical stimulation, such as topical agents with metal ions and petrolatum-based products, were not prescribed. A standardized dressing protocol was not used in this study; rather, dressings were tailored to meet the needs of each subject and to promote moist interactive healing. Wound dressings were changed if the wound was either macerated or desiccated. In most cases, the wound dressing used by the patient before enrolling in the study was continued throughout the treatment period.

Sharp debridement procedures were performed, as needed, by qualified personnel in a relatively small number of subjects in each treatment group (n=4 and n=5). These procedures were done most often on a single occasion during the 1- to 2-week period during which subjects received only conventional wound therapy and involved primarily the removal of excess callus formed around foot ulcers. When we believed infection might be present, the subject's attending physician was contacted and oral antibiotic therapy was initiated where indicated. These concurrent interventions were used consistently throughout the treatment program and were applied similarly for subjects in both treatment groups. In addition, subjects were asked to rate their

ability to adhere to the standard wound care program during the 4-week treatment period. Very few individuals enrolled in the study did not carry out all of the necessary interventions, and the number of subjects who were unable to adhere to the wound care program was similar in both treatment groups (n=3).

Treatment Session

Following the 1- to 2-week period during which subjects received only conventional wound therapy, all subjects were treated for 45 minutes with either real or sham electrical stimulation 3 times a week for 4 weeks. The active electrode made of Metalline gauze[†] was secured directly over the wound, which previously had been loosely packed with sterile gauze soaked in isotonic saline. A second dispersive electrode was placed approximately 20 cm proximal to the wound. A portable high-voltage pulsed galvanic stimulator[†] supplied by Electro-Med Health Industries was used to deliver the electrical stimulus. Because this stimulator is a battery-operated unit, the batteries were recharged regularly at the beginning of each week of treatment. The following settings were used: pulse duration = 100 microseconds, peak intensity = 150 V, and pulse frequency = 100 Hz. The polarity of the active electrode was negative, and this polarity was maintained throughout the 4-week treatment period. These settings were selected based on the results of previous studies.^{15,19-21,23} Following treatment, the wound was redressed in a manner consistent with the condition of the wound and the standard wound care protocol we described earlier. All materials applied to the wounds of the subjects had been sterilized previously, and the active electrodes were discarded after each use. Universal precautions were observed at all times, including hand washing, use of clean latex-free gloves, posttreatment decontamination of treatment areas and equipment, and appropriate disposal of wound care supplies.

Evaluation

Wound healing was assessed by a licensed physical therapist, nurse, or trained research assistant using previously validated outcome measures³⁶⁻³⁹ during the initial evaluation, following the 1- to 2-week period during which subjects received only conventional wound therapy, after the 4-week treatment period, and at the 1-month follow-up assessment. In addition, any changes in leg girth, pain, or treatment (eg, wound dressings, medications, subject adherence) during the study were recorded. Any reports of adverse responses or of pain or

[†] Lohmann Medical, 3000 Earhart Ct, Hebron, KY 41048.

discomfort from subjects during the treatment sessions also were noted.

Outcome Measures

Wound size. The wound surface area was measured at scheduled intervals by the use of acetate tracing and subsequent planimetric determination. This measure has been used extensively for wounds and has established validity and reliability.^{36,37} Wound tracings were accomplished by outlining the wound circumference onto a transparent film (EZ Graph[§]) applied directly over the wound. In order to improve the accuracy of these tracings, each wound was traced 3 times and the same individual performed all wound tracings. This individual had previously demonstrated on over 50 wounds of mixed etiology what we consider excellent intrarater reliability, with this wound measurement technique (intraclass correlation coefficient >.98).⁴⁰ The wound surface area was determined from wound tracing using a planimeter (PLANIX 7^{||}) by a single assessor who also was blinded as to the identity of the subject and to the treatment group assignment. The percentage of decrease in wound surface area from the wound size (% ↓ WSA) measured during the initial evaluation was calculated for each subject. The mean and standard error of the mean (SEM) for the % ↓ WSA was determined for the and for the subjects who received the sham treatment. Values for % ↓ WSA were calculated for measurements obtained during the initial evaluation, after the 1- to 2-week period during which subjects received only conventional wound therapy (prior to treatment), following the 4-week treatment period, and during the 1-month follow-up assessment.

Wound appearance. The appearance of each wound was assessed through direct observation of the wound at the subjects' bedside using the Pressure Sore Status Tool (PSST). The PSST is supposed to yield valid and reliable measurements that characterize changes in the appearance of chronic ulcers.^{38,39} The PSST is a pen-and-paper tool with 13 domains that measure, on a scale between 1 and 5, characteristics of wound size and depth, wound bed composition, wound exudate, and viability of wound edge and periulcer skin. A total PSST score between 13 and 65 is derived by summing the scores given to each of the domains, with lower total PSST scores indicating better wound appearances.

Wounds were photographed at the time of the assessment using a Nikon FM-2 (N-50) camera* that was equipped to adjust automatically to variations in lighting

and with a macro lens to permit close-up images of the wound. All images included a 15.24-cm (6-in) disposable ruler that had a subject identification number and date written on it. Care was taken to ensure that the camera was placed perpendicular to the wound bed. The distance between the camera and the wound was varied in order to capture in the picture frame the entire wound, the ruler, and a sample of the surrounding skin (0.9–1.8 m [3–6 ft] away). These photographs were then used to evaluate changes in wound appearance using a semi-quantitative analysis of wound appearance by the Photographic Wound Assessment Tool (PWAT). The PWAT is a pen-and-paper tool consisting of 6 domains that assess the composition of the wound bed and viability of the wound edge and periulcer skin that are capable of being viewed using a wound photograph. Scores assigned on a scale of 0 to 4 to each of the domains of the PWAT are summed to derive a total PWAT score between 0 and 24, with 0 representing a healed wound. The PWAT has previously been shown to produce reliable measurements of chronic leg ulcers and is responsive to changes in wound status.⁴¹

The total PSST score of wound appearance assigned by examining the wound directly at the bedside was calculated for each wound. In addition, the total PWAT score was determined by viewing wound photographs taken at the same time of assessment. The mean (±SEM) of the total PSST scores and total PWAT scores for wounds in both treatment groups were determined for measurements obtained during the initial examination, after the 1- to 2-week period during which subjects received only conventional wound therapy, following the 4-week treatment period, and during the 1-month follow-up assessment.

Data Analysis

Factors affecting wound healing. The demographics of the subjects and coexisting medical conditions known to affect wound healing were obtained from the subject interview and observation, vascular flow laboratory session, and medical chart review and are outlined in Table 1. Differences in these values between treatment groups were compared using the Student *t* test for parametric data and the Mann-Whitney rank sum test for nonparametric data.

A secondary analysis was conducted to determine the association between the amount of wound healing that occurred during the study and subject demographics, coexisting medical conditions, and concurrent interventions. Pearson product moment correlation coefficients were calculated for correlations between each of these factors known to affect wound healing and the amount of wound healing (% ↓ WSA) that occurred over the

§ EZ Graph of Victoria Inc, 1606 E Brazos, Ste B, Victoria, TX 77901.

|| Sokkia Corp Canada, 1050 Stacey St, Mississauga, Ontario, Canada L4W 2X8.

* Nikon, 1300 Walt Whitman Rd, Melvin, NY 11747-3064.

4-week treatment period in wounds treated with either real or sham HVPC.

Wound healing in combined vascular ulcers. The mean (\pm SEM) of the % \downarrow WSA and the total PWAT and PSST scores representing changes in wound size and wound appearance, respectively, were calculated and compared between the treatment groups. To account for the fact that multiple ulcers were treated on the same individual, a single wound was randomly selected from each subject in both treatment groups. These values were compared between the 2 groups using the Student *t* test. In addition, the change in wound size (% \downarrow WSA) and wound appearance (PWAT scores) that occurred in the HVPC- and sham-treated wounds over the time period of the study were analyzed statistically using a one-way repeated-measures analysis of variance (ANOVA). Probability values less than .05 were considered statistically significant.

Wound healing in bilateral venous leg ulcers. The % \downarrow WSA also was calculated for 7 subjects who had bilateral venous leg ulcers. In these subjects, one of the ulcers was randomly selected for treatment with HVPC, and the other ulcer was treated with sham HVPC. Comparison of the % \downarrow WSA between HVPC- and sham-treated wounds was done using a paired *t* test, and the change in WSA that occurred over the 4 measurement periods was analyzed statistically using a one-way repeated-measures ANOVA. Statistical significance was accepted at the 95% confidence interval.

Results

Wound Healing of Combined Vascular Ulcers

Following the 4 weeks of treatment, the % \downarrow WSA was greater for chronic vascular ulcers treated with HVPC than for the sham-treated wounds (Fig. 1). There was no difference in % \downarrow WSA between groups at the 1-month follow-up assessment. The % \downarrow WSA measured prior to the start of either HVPC or sham treatments (after the 1- to 2-week period during which subjects received only conventional wound therapy) was minimal compared with % \downarrow WSA measured during the 4-week treatment period and during the follow-up assessment. There was no difference in the % \downarrow WSA that occurred over the 1- to 2-week period during which subjects received only conventional wound therapy between the subjects treated with HVPC and those who received the sham treatment, and the mean wound surface area was similar between groups at the time of the initial evaluation. Examination of the change in wound size that occurred over the study period revealed that there was a decrease in wound surface area over the 4-week treatment period in the HVPC-treated wounds but not in the sham-treated wounds.

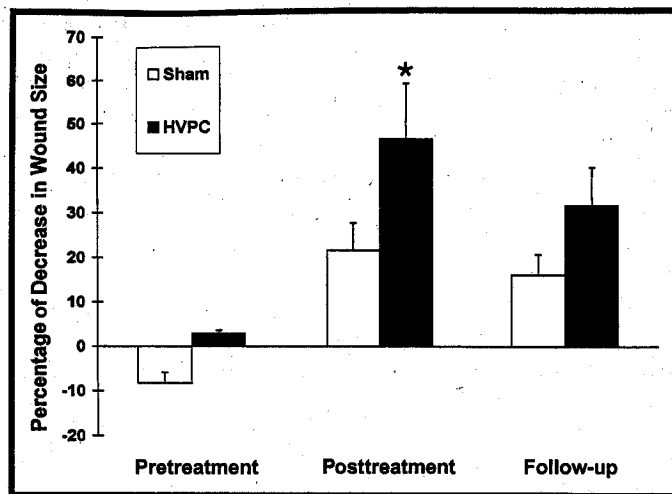


Figure 1. Mean (\pm SEM) of the percentage of decrease in wound surface area from the wound size measured during the initial evaluation calculated for subjects randomly selected to receive high-voltage pulsed current (HVPC) (closed bars) and subjects randomly selected to receive sham treatment (open bars). Values were calculated from measurements taken after the 1- to 2-week period during which subjects received only conventional wound therapy (pretreatment), following the 4-week treatment period (posttreatment), and at the 1-month follow-up assessment. Asterisk denotes statistically significant difference between treatment groups ($P < .05$, one-way analysis of variance for repeated measures).

Prior to the start of treatment, the mean PWAT scores assigned from examining wound photographs were similar between treatment groups (Fig. 2). However, there was a decrease in PWAT scores following the 4-week treatment period in wounds treated with HVPC ($P < .05$). This improvement in wound appearance was reflective of the loss of necrotic tissue and the relative increase in healthy granulation tissue present in the wound bed of HVPC-treated wounds. A similar decrease in total PWAT scores did not occur in wounds treated with sham HVPC. The improved wound appearance observed in HVPC-treated wounds was not apparent at the 1-month follow-up assessment when the PWAT scores were similar in HVPC- and sham-treated wounds. The total PSST score obtained from a bedside assessment of the wound produced variable results and did not yield any detectable change in wound appearance over time. Furthermore, total PSST scores calculated for HVPC-treated wounds (31.7 ± 1.55) and for sham-treated wounds (28.8 ± 2.1) also were found to be similar for the 2 treatment groups.

Wound Healing of Bilateral Venous Ulcers

In the subjects who had bilateral venous leg ulcers ($n=7$), the ulcers that received HVPC treatment were $57\% \pm 15\%$ of original size versus $20\% \pm 18.6\%$ for sham-treated ulcers located on the contralateral leg ($P < .05$, Fig. 3). The difference in the mean % \downarrow WSA after the 4-week treatment period was not present at the 1-month follow-up assessment. There was no difference in mean

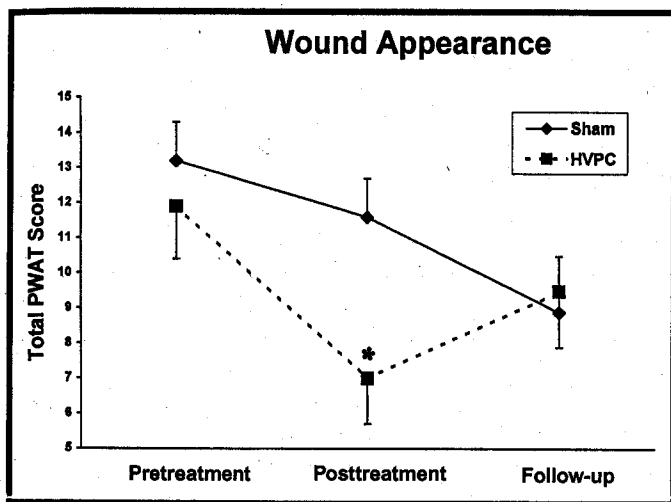


Figure 2. Mean (\pm SEM) of the total Photographic Wound Assessment Tool (PWAT) score assigned by a single observer from an assessment of wound appearance using a wound photograph. Total scores were calculated for subjects randomly selected to receive high-voltage pulsed current (HVPC) (square symbols) and subjects randomly selected to receive sham treatment (diamond-shaped symbols). Values were calculated from measurements obtained from photographs taken after the 1- to 2-week period during which subjects received only conventional wound therapy (pretreatment), following the 4-week treatment period (posttreatment), and at the 1-month follow-up assessment. Asterisk denotes statistically significant difference between treatment groups ($P < .05$, Mann-Whitney rank sum test).

% \downarrow WSA between the HVPC- and sham-treated wounds at the time of the initial assessment or over the 1- to 2-week period during which subjects received only conventional wound therapy.

Discussion

This placebo-controlled, double-blind, randomized controlled clinical trial demonstrated that HVPC applied to chronic leg ulcers (diabetic, arterial, or venous ulcers) 3 times per week reduced the wound surface area over the 4-week treatment period to approximately one half of the original size. This rate of wound closure was appropriately twice that observed in wounds treated identically with sham HVPC. The ability of HVPC to stimulate wound healing of chronic leg ulcers was particularly evident in 7 subjects with bilateral venous ulcers where the HVPC-treated wounds had consistently faster wound closure rates than did sham-treated wounds located on the contralateral limbs of the same individuals. We reviewed notes taken after each treatment session and found that no adverse reactions occurred during the course of any of the treatments. Therefore, we believe that therapy involving the use of electrical current can be applied in comfortable manner that is relatively painless to the patient with minimal safety concerns.

Our study was performed within a single research center that involved a relatively small sample size (27 subjects

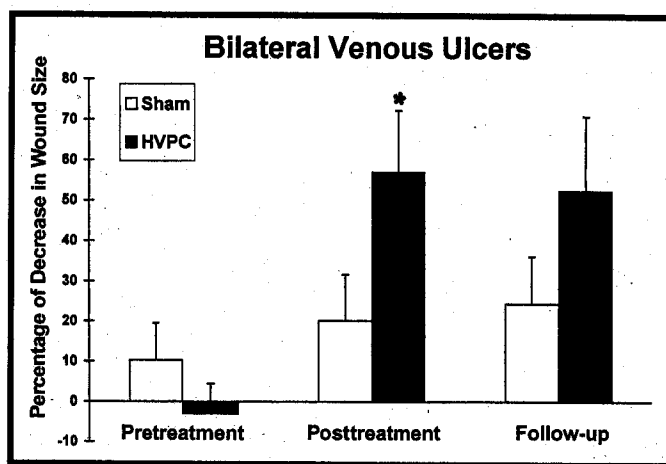


Figure 3. Mean (\pm SEM) of the percentage of decrease in wound surface area from the wound size measured during the initial evaluation calculated for 7 subjects who had bilateral venous leg ulcers. In these subjects, one of the ulcers was randomly selected to be treated with high-voltage pulsed current (HVPC) (closed bars) and the other ulcer was treated with sham HVPC (open bars). Values were calculated from measurements taken after the 1- to 2-week period during which subjects received only conventional wound therapy (pretreatment), following the 4-week treatment period (posttreatment), and at the 1-month follow-up assessment. Asterisk denotes statistically significant difference between treatment groups ($P < .05$, one-way analysis of variance for repeated measures).

with 42 ulcers). However, our sample size was sufficient to detect differences that we believe are clinically meaningful. Prior to the study, we determined that a sample size of 12 subjects per group would be required to detect differences between treatment groups with a statistical power of 80%. Additionally, based on calculations of effect size using data collected from the 27 subjects enrolled in this study, we determined that we had 80% power to detect at least a 10% difference in % \downarrow WSA between treatment groups. That is, differences of less than 10% between treatment groups would not be detected in this study (Type II statistical error), which is reasonable because we would not consider differences less than this to be clinically meaningful.

In this study, we monitored and recorded all factors we believed could affect wound healing such as subject demographics, coexisting medical conditions, and concurrent standard wound care interventions. No difference in these factors was detected between the subjects who received HVPC and the subjects who received the sham treatment. We believe, therefore, it is likely that the observed acceleration in healing was attributable to the exogenous application of electrical current to the wound bed rather than being due to other factors.

The beneficial effects of HVPC that we observed were in a sample who were, on average, over the age of 60 years and had an average wound history of 3 to 5 years with several coexisting medical conditions known to interfere

with their ability to heal. Healing rates in both HVPC- and sham-treated wounds were inversely related to the number of factors affecting wound healing and to the inability to manage the primary wound etiology such as poorly controlled blood glucose concentrations. Therefore, we believe the benefits of this therapeutic approach are best obtained in conjunction with an optimal wound management program that addresses the underlying cause of the wound and reduces the factors working against wound healing.

The changes in wound healing that occurred over the study period were evaluated using measurements of wound size and wound appearance. These measurements were taken by a single observer who was blinded to the treatment groups, thus, we contend, reducing rater bias. Measurements of wound surface area using acetate tracings with subsequent planimetry have been shown to be sensitive to change over time.^{36,37} This technique of determining wound size has been recommended by researchers⁴² who have systematically compared numerous wound measurement tools that are currently available. Although a more accurate description of wound extent should include measurements of wound depth or volume, we did not measure these variables in our study because measurement tools that produce reproducible and accurate measurements of wound depth or volume are not readily available.

We expressed wound healing as a percentage of change in order to normalize large variations in initial wound size that existed in each treatment group. The use of percentage of decrease in wound size as an index of rate of healing has been used in previous reports.^{13,18} We also determined the change in surface area from the initial evaluation and the percentage of initial wound size and found that regardless of how wound healing was expressed, HVPC treatment consistently produced better outcomes than the sham treatment.

Wound appearance was assessed using the well-established PSST^{38,39} and by using a recently developed tool that has been modified for use on wound photographs (PWAT).⁴¹ Changes in wound appearance over the 4-week treatment period occurring in wounds treated with HVPC were detected when the change in total PWAT scores was examined. Examination of the change in total PSST scores did not show a difference over time in either treatment group, nor was a difference detected in PSST scores between the subjects who received HVPC and the subjects who received the sham treatment. These findings were not surprising because although the PSST has been validated and used extensively to assess the appearance of chronic pressure ulcers,^{38,39} no published reports exist to demonstrate the validity and reliability of PSST measurements for assess-

ing leg ulcers due to vascular insufficiency. Recently, the validity and reliability of PWAT scores were tested in study in which 56 pressure ulcers and 81 chronic leg ulcers were rated by 5 independent observers, and the PWAT was found to have excellent reliability, concurrent validity, and sensitivity to change.⁴¹

These measurements of wound size and appearance were taken after 4 weeks of treatment. This duration of treatment is consistent with that used in other clinical trials of other wound care treatments. Previous studies^{9,13,28,43} have demonstrated that 4 weeks of treatment is sufficient to evaluate the efficacy of wound treatment. Although 4 weeks of treatment was sufficient to assess the effectiveness of the HVPC treatment, it was not long enough to produce complete wound closure. Initial improvements in wound closure rate were no longer obvious 1 month following completion of the 4-week treatment program. Therefore, continued HVPC treatments of greater than 4 weeks or until wound closure need to be studied to determine whether improvements in the healing of these chronic leg ulcers would occur.

A standardized wound care program was provided in our study to both subjects who received HVPC and subjects who received the sham treatment. A variety of dressing materials were used in an effort to promote moist interactive healing and to optimize the wound environment. This approach to dressing selection is consistent with most published recommendations that the "best dressing" is one that meets the functions and characteristics of the wound and considers the needs of the patient.^{44,45} Research examining the influence of various dressing types on the rate of wound closure has yielded inconclusive results and has not identified any particular superior dressing.²³ Therefore, it is unlikely that different dressings utilized by subjects enrolled in the study contributed to accelerated wound closure rates observed following HVPC treatments. There is research evidence to suggest that appropriate and timely debridement procedures can accelerate wound closure⁴⁶; however, an equal number of subjects in each treatment group in our study received relatively minor wound debridement procedures.

Electrically induced acceleration of wound closure in subjects with leg ulcers due vascular compromise caused by diabetes mellitus has been demonstrated in 4 studies, including 2 randomized controlled clinical trials.²⁴⁻²⁷ Thurman and Christian²⁴ reported on a subject with juvenile diabetes who had a nonhealing ulcer located on the toes. In this case, HVPC was used to heal the wound and as a result avoided a previously scheduled foot amputation. Lundeborg et al,²⁶ in a well-controlled clinical trial, found differences in the percentage of healed ulcer area and the number of healed ulcers

treated with electrotherapy compared with those receiving sham treatment.

Baker et al²⁷ conducted a prospective randomized clinical trial involving 80 subjects with diabetes and 114 open wounds. They demonstrated that the application of electrical stimulation using an asymmetrical biphasic waveform accelerated the healing of wounds in people with diabetes. The healing rates they observed, however, in patients with diabetes were lower than those found for pressure ulcers by the same investigators in a different study.⁹ Slower healing rates induced by electrical stimulation observed in people with diabetic ulcers versus pressure ulcers are presumably due to the numerous negative effects that diabetes has on wound healing.⁴⁷ Therefore, although electrical stimulation is effective in accelerating wound closure of diabetic ulcers, we expect the expected rate of healing to be lower than for other types of ulcers.

There is little research that has examined the effect of electrical stimulation on chronic venous ulcers. In 1968, Assimacopoulos²⁸ presented 3 case reports describing the use of low-intensity direct current to stimulate wound closure in subjects with chronic venous insufficiency. The wounds had not responded to previous treatments. Although the case reports suggest that electrotherapy may be beneficial in managing chronic venous ulcers, no subsequent controlled clinical trial has confirmed these findings. In 1987, Katelaris et al²⁹ reported on the effects of electrical stimulation on chronic venous ulcers. The electrical current, however, was administered in combination with povidone-iodine solution. This negative result is not surprising given what is now known about the cytotoxic effects of povidone-iodine solution.⁴⁸ Therefore, we believe that our study represents the first properly designed clinical trial to demonstrate that direct application of HVPC to the wound bed produces faster closure of chronic venous ulcers compared with sham-treated wounds.

The electrical stimulus settings used in our study were selected based on results of previous studies.^{13,19-21,25} Electrical stimulation in our study was delivered using a monopolar setup with the active electrode placed directly in to the wound bed using specialized electrodes composed of sterile conductive material and a larger dispersive electrode placed on intact skin close to the wound. Placement of the active electrode directly in the wound bed is the electrode placement used most often when administering HVPC waveforms.^{13,19-21,25} However, successful outcomes also have been reported when using other waveforms of electrical current such as asymmetrical biphasic pulsed current delivered through electrodes placed on periwound skin.²⁷

The frequency and duration of treatments reported in the literature vary greatly. Most authors suggest that the optimal treatment schedule necessary to produce maximal tissue healing response is not known, but, in general, it is recommended that treatments should be given for 1 hour a day, 5 times a week, in order to stimulate wound closure.^{49,50} We found that electrical current delivered for only 45 minutes 3 times a week was beneficial. Although it is probable that more frequent treatments would optimize wound healing, this is not always feasible for people living in the community. Our treatment protocol was selected to accommodate individuals being treated in an outpatient setting.

Conclusion

Our results demonstrated that HVPC administered 3 times per week for 4 weeks to chronic vascular leg ulcers produced a reduction in wound size and an improvement in wound appearance as compared with sham-treated wounds. Therefore, it appears that electrotherapy treatments of the type we used are not only effective in managing chronic pressure ulcers but also should be used to accelerate wound healing of chronic vascular leg ulcers. Further work is needed to determine the exact mechanism(s) underlying the electrically induced wound repair and to elucidate electrical stimulation settings, electrode setups, and treatment schedules. Most importantly, future research is needed to determine whether the type of electrical stimulation we used can be conducted in a manner that not only decreases wound size but also leads to wound closure.

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