ORIGINAL ARTICLE

Electrical Stimulation Therapy Increases Rate of Healing of Pressure Ulcers in Community-Dwelling People With Spinal Cord Injury

Pamela E. Houghton, PT, PhD, Karen E. Campbell, RN, PhD, Christine H. Fraser, RD, HBSc, Connie Harris, RN, ET, MSc, David H. Keast, MD, MSc, Patrick J. Potter, MD, Keith C. Hayes, PhD, M. Gail Woodbury, PhD

ABSTRACT. Houghton PE, Campbell KE, Fraser CH, Harris C, Keast DH, Potter PJ, Hayes KC, Woodbury MG. Electrical stimulation therapy increases rate of healing of pressure ulcers in community-dwelling people with spinal cord injury. Arch Phys Med Rehabil 2010;91:669-78.

Objective: To investigate whether electric stimulation therapy (EST) administered as part of a community-based, interdisciplinary wound care program accelerates healing of pressure ulcers in people with spinal cord injury (SCI).

Design: Single-blind, parallel-group, randomized, controlled, clinical trial.

Setting: Community-based home care setting, Ontario, Canada.

Participants: Adults (N=34; mean age ± SD, 51±14y) with SCI and stage II to IV pressure ulcers.

Interventions: Subjects were stratified based on wound severity and duration and randomly assigned to receive either a customized, community-based standard wound care (SWC) program that included pressure management or the wound care program plus high-voltage pulsed current applied to the wound bed (EST+SWC).

Main Outcome Measures: Wound healing measured by reduction in wound size and improvement in wound appearance at 3 months of treatment with EST+SWC or SWC.

Results: The percentage decrease in wound surface area (WSA) at the end of the intervention period was significantly greater in the EST+SWC group (mean ± SD, 70±25%) than in the SWC group (36±61%; $P=.048$). The proportion of stage III, IV, or X pressure ulcers improving by at least 50% WSA was significantly greater in the EST+SWC group than in the SWC group ($P=.02$). Wound appearance assessed using the photographic wound assessment tool was improved in wounds treated with EST+SWC but not SWC alone.

Conclusions: These results demonstrate that EST can stimulate healing of pressure ulcers of people with SCI. EST can be incorporated successfully into an interdisciplinary wound care program in the community.

Key Words: Electric stimulation; Pressure ulcer; Rehabilitation; Spinal cord injuries.

PEOPLE WITH SPINAL CORD injury are at increased risk for developing pressure ulcers. They are particularly susceptible to pressure ulcers occurring in the skin overlaying the ischial tuberosity because of their extensive wheelchair use. The annual prevalence of pressure ulcers in SCI has been reported to be 31% to 52%[1] with 31% to 79%[2] of the population troubled with recurrent pressure ulcers. It also has been estimated that as many as 79% of people with SCI will experience a pressure ulcer at some time during their lives.[3] Pressure ulcers can limit mobility, interfere with activities of daily living, and impair quality of life.[4] Delayed healing of a pressure ulcer causes deconditioning that is difficult to restore and can lead to serious, and even life-threatening, medical conditions.[5]

EST involves delivering low levels of electric current directly to or surrounding the wound bed using specialized surface electrodes and equipment. It has been shown to induce cellular actions in virtually all phases of the wound healing cascade, including stimulation of several activities of fibroblasts, such as enhanced collagen and deoxyribonucleic acid synthesis, adenosine triphosphate production, and calcium influx,[6] and an increased number of growth factor receptor sites.[7,8] Results from in vitro studies on macrophages,[9] epithelial cells,[10] and fibroblasts[6] have demonstrated that electric stimulation promotes the migration and activation of key cells in the wound site. In vivo studies involving animal models have revealed that electric stimulation of these important wound healing processes results in more collagen deposition,[11] enhanced angiogenesis,[11-13] greater wound tensile strength,[14] and a faster wound contraction rate.[15]

In addition to these direct cellular actions, electric stimulation has been shown to improve tissue perfusion[15] and reduce

List of Abbreviations

CCAC	community care access center
EST	electrical stimulation therapy
PSST	pressure sore status tool
PWAT	photographic wound assessment tool
SCI	spinal cord injury
SWC	standard wound care
WSA	wound surface area
% ↓ WSA	percentage wound surface area reduction from baseline

From the School of Physical Therapy, Faculty of Health Sciences, University of Western Ontario (Campbell, Woodbury), Parkwood Hospital, St Joseph's Health Care London (Fraser, Keast, Potter, Hayes), Rehabilitation and Geriatric Care Center, Lawson Health Research Institute (Houghton, Keast, Campbell, Hayes), London, Ontario; Care Partners Inc, Waterloo, Ontario (Harris), Canada.

Supported by the Ontario Neurotrauma Foundation (grant no. 2004-SCI-SC-01), which required matching in kind support from industrial partners. Equipment and supplies industrial partners are Prizm Medical Inc, The Roho Group, Argentum Medical Inc, and Dermasciences Canada Inc.

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit on the authors or on any organization with which the authors are associated.

Correspondence to Pamela E. Houghton, PT, PhD, School of Physical Therapy, Rm 1588, Elborn College, University of Western Ontario, London, Ontario, Canada N6G 2A9, e-mail: *phoughto@uwo.ca*. Reprints are not available from the author.

0003-9993/10/9105-00969$36.00/0
doi:10.1016/j.apmr.2009.12.026

edema formation.[16] Electrically induced enhancement of tissue perfusion has been shown to produce significant increases in transcutaneous oxygen pressures in the sacral region of people with SCI.[15] Negatively charged direct current applied directly to the wound bed has been shown to reduce the number of *Pseudomonas aeruginosa* bacteria present in infected human wounds[17] and *Staphylococcus aureus*–inoculated rabbit incisional wounds.[18] For a comprehensive review of the biological effects of EST, see the recent article by Kloth.[19]

The most common application technique for electric stimulation involves using a monopolar setup with specialized electrodes composed of sterile conductive material. In this technique, the active electrode is placed directly into the wound, and a larger dispersive electrode is placed on intact skin proximal to the wound. Accelerated wound closure also has been demonstrated after electric stimulation of distant acupuncture points[20] and extremities.[21] Protocols with bipolar placement of electrodes on the periulcer skin on either side of the wound have demonstrated significant benefits for wound healing.[22] Numerous different stimulus parameters have been shown to be effective in accelerating wound closure. High-voltage pulsed current is a type of pulsed current with a characteristic twin-peaked monophasic waveform that is commonly associated with the successful treatment of chronic wounds.[22-24] Other types of current including asymmetric biphasic pulsed current also have been shown to be effective.[22] In the literature, treatment schedules vary from 1-hour treatments given 3 times weekly to overnight treatments involving successive treatments administered over 8 hours.[21]

Application of EST in previous clinical trials has been consistently shown to accelerate healing and stimulate closure of chronic pressure ulcers[25,26] as well as other types of chronic, nonhealing wounds.[20,21,24] Several of these randomized clinical trials specifically examined the effects of EST on wounds occurring in people with SCI.[22,23,27-31] Clinical practice guidelines in Canada[32,33] and the United States[34,35] have recommended EST as a treatment for this patient population. However, the use of EST for pressure ulcer treatment in rehabilitation settings and community-based care in Canada remains limited. Recent technologic advances have facilitated the ease with which EST may be incorporated into existing wound care regimens and have added safety features to allow patients or their caregivers to provide EST treatments over extended treatment times. Peters et al[21] found this technology could be used safely and effectively with people who had diabetic foot ulcers. We therefore set out to evaluate the effectiveness of a self-guided EST program within a community care setting. The specific purpose of this study was to test the hypothesis that EST administered as part of a community-based, interdisciplinary wound care program improves healing of pressure ulcers in people with SCI. Implementation of this program involved providing education and training to personnel in several nursing agencies and CCACs located in southwestern Ontario, Canada.

METHODS

This study was a single-blind, parallel-group, randomized, controlled, clinical trial that compared group differences in wound size and appearance after 3 months of intervention with SWC with or without EST (fig 1). The protocol was approved by the university ethics review board for research involving human subjects. People with SCI living in the community were recruited into the study using referrals from health care professionals working in the field and by way of advertisements posted to the general public. Eligible subjects included those with either paraplegia or quadriplegia caused by congenital, medical, or traumatic SCI who were over the age of 18 years and living in the community. Participants were recruited into the study provided they also had a stage II to IV pressure ulcer between 1 and 20cm^2 present for at least 3 months. An extensive screening process confirmed that these individuals (1) were able to participate actively for at least 3 months in an SWC program that included appropriate pressure redistribution, (2) did not have serious or multiple medical conditions that would limit healing, and (3) did not have any condition that was contraindicated for EST (cardiac pacemaker, osteomyelitis, pregnancy, cancer).

Subjects who met study inclusion criteria and enrolled in the study were stratified into 4 groups according to ulcer duration and severity of the ulcer at initial assessment. Severity of ulcer at the time of inclusion in the study was classified using the National Pressure Ulcer Advisory Panel definitions for stages of pressure ulcers (2007).[36] The 4 groups included those with stage II or III ulcers present for more than 2 years, stage II or III ulcers present for less than 2 years, stage IV or unstageable (stage X) ulcers present for more than 2 years, and stage IV or X ulcers present for less than 2 years. Eligible subjects were then assigned to receive either SWC or EST+SWC using a concealed, random process that involved opening an opaque envelope prepared by an independent person with random number generation. All subjects were evaluated on a monthly basis for at least 3 months. Thereafter study subjects were followed whenever possible for an average of 4 months to see whether ulcers went on to heal completely, ulcers reoccurred, or new ulcers formed. For ethical reasons, subjects randomly assigned to receive only standard care initially were offered EST and those who had wound size reduction with EST treatments were offered continued EST treatment after the 3-month intervention period.

Group 1: SWC Program

Study subjects were evaluated in their homes and in a clinic setting by an interdisciplinary team of professionals (nurse, occupational therapist, physical therapist, dietitian) with experience treating SCI and/or pressure ulcers. Medical and wound histories were collected in order to identify medical factors, socioeconomic conditions, and personal preferences that might interfere with healing. A patient activity schedule was completed that identified all surfaces encountered and the type of transfers performed daily. In cases in which wheelchair seating was a concern, a complete seating assessment that included pressure mapping was conducted. A comprehensive review of nutritional issues was also conducted that included an assessment of factors that might influence dietary intake and the routes and extent of nutrient and fluid losses. Considerations included gastrointestinal disorders, drug/nutrient interactions, wound exudates, dentition, dysphagia, food allergies, barriers to obtaining and preparing food, and other factors that might affect nutrition/hydration status. A 3-day food/fluid intake record; food habits survey; and questionnaire that obtained anthropometric data, information about current supplement use, and family health history were submitted by study subjects for assessment prior to the individual consultation with a registered dietitian. In addition, blood analysis was performed to screen for markers of nutrition/hydration status and metabolic disorders such as anemia (iron deficiency anemia or anemia of chronic disease), impaired glycemic control, thyroid dysfunction, dehydration, hypoalbuminemia, and hypoprealbuminemia. A wound assessment was performed to assess the appropriateness of the wound dressing protocol with respect to moisture control, bacterial burden, and debridement needs. Based on this comprehensive, interdisciplinary assessment, an

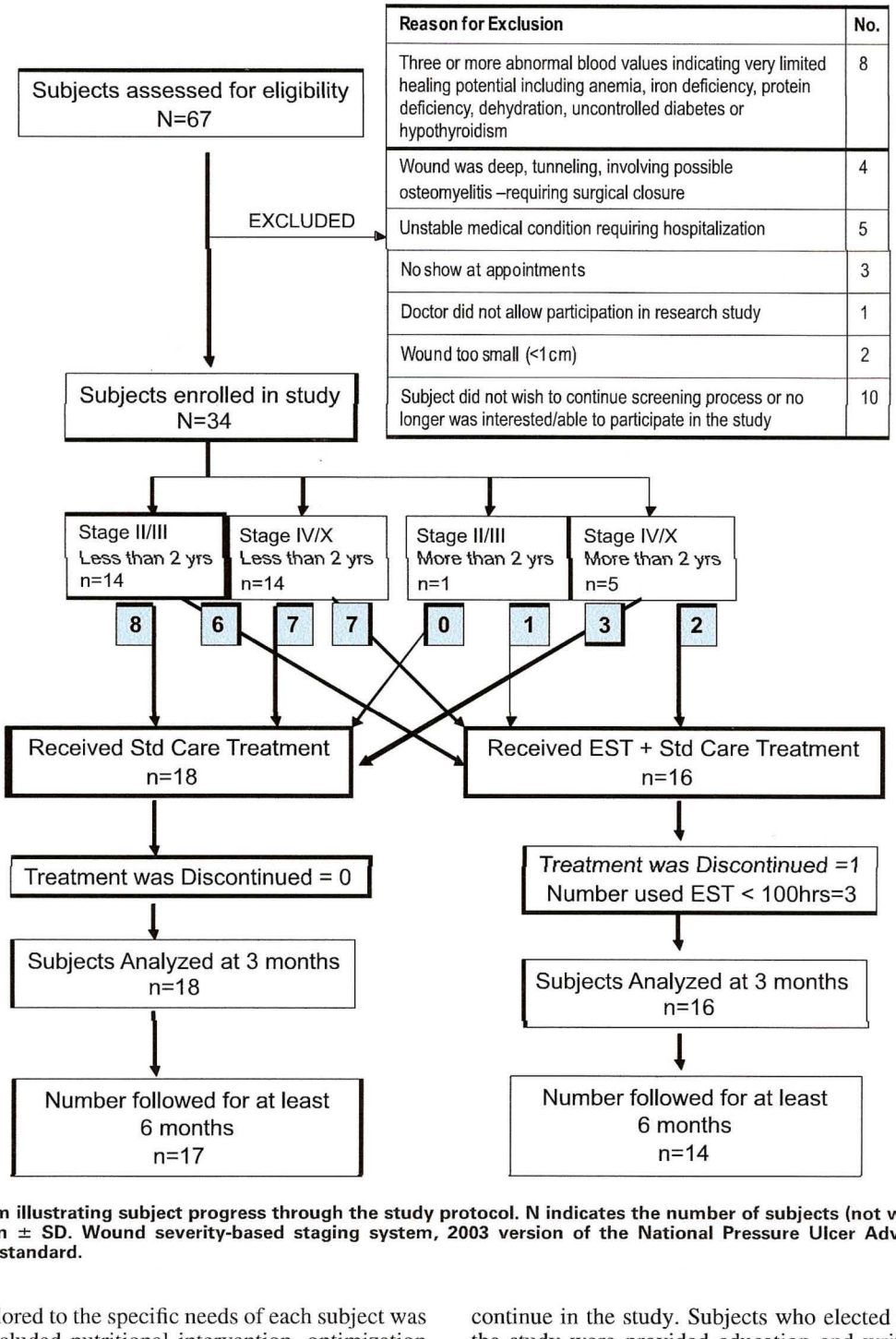

Fig 1. Flow diagram illustrating subject progress through the study protocol. N indicates the number of subjects (not wounds). Values are expressed as mean ± SD. Wound severity-based staging system, 2003 version of the National Pressure Ulcer Advisory Panel (2007). Abbreviation: Std, standard.

SWC program tailored to the specific needs of each subject was developed that included nutritional intervention, optimization of wound dressing protocol, and continence management. Subjects did not receive the same wound dressing protocol; rather, each subject had a customized program that employed a variety of wound care products, was consistent with best practices,[32] and followed wound bed preparation principles.[37] In addition, all participants received a comprehensive pressure management program that involved modification to their activity schedule and, in most cases, provision of a new high-profile air-filled cushion[a] for use in their primary wheelchairs. This SWC program was described to all potential study subjects prior to randomization so that they could decide whether to continue in the study. Subjects who elected not to continue in the study were provided education and written recommendations with suggested changes to their standard wound program.

Group 2: EST+SWC

Subjects randomly assigned to the EST+SWC group had a similar SWC program that addressed nutritional, pressure, continence, and wound care needs. In addition, they were provided EST using a community-based delivery model of care in which patients, family, and/or community nurses were trained to apply daily treatments of EST. These training sessions included a 1-hour general inservice followed by 2 to 3 half-hour sessions in which specific instructions were provided by experienced

study personnel to 2 to 3 caregivers at the bedside. Wounds were loosely packed with silver nylon dressing premoistened in sterile water or coated in hydrogel.[b] This silver dressing was selected to facilitate conduction of electric current throughout the wound bed and to the base of deep wounds in particular. Additional inactive packing materials (eg, gauze, hydrofiber) and cover dressings (foam, nonadherent pads, hydrocolloids) that were free of ionic materials (silver, zinc, hypertonic saline) or petrolatum-based products were added as needed in order to manage the wound moisture properly for each subject. In most cases (11/16 subjects), a single electrode (4.8×10.2cm) was placed directly over the wound and a larger (12.7×20.3cm) dispersive electrode was placed on intact skin at least 20cm from the wound (monopolar method). In 2 patients for whom access to the wound was not safe or practical, 2 equally sized (4.8×10.2cm) self-adhesive electrodes were placed on periulcer skin on either side of the wound (bipolar method). Three subjects with wounds on their feet or ankles applied the EST to the lower limb using an electroconductive sock. In all cases, a small portable, programmable device (Micro Z[c]) was used to deliver a twin-peaked monophasic pulsed current (high-voltage pulsed current) with 50μs pulse duration. Intensity of the machine was set between 50 and 150V at a level that was below the level of muscle contraction and based on sensory level on intact skin. The machine was programmed to provide 20 minutes at a pulse frequency of 100Hz followed by 20 minutes at 10Hz and then 20 minutes off cycle each hour for 8 hours each day for a period of at least 3 months. The polarity of the active electrode used in a monopolar set-up was initially negative (cathode) and alternated each week. This protocol was selected based on positive results obtained when using this device in a previously published clinical trial involving patients with diabetic foot ulcers.[21] Subjects or their primary caregivers were trained to self-administer the treatment and instructed to apply the treatment daily when it fit into their daily schedules. Typically these treatments were applied overnight.

A monitor on the machine allowed the researchers to record the total treatment time the EST machine was used by each subject. The EST protocol was incorporated into regular wound dressing changes scheduled every 1 to 3 days and performed by home care nurses, nonskilled caregivers, or themselves. Because this EST program was provided within an existing home care program, implementation required coordinating care with hundreds of community nurses and several agencies contracted to provide health care by 6 different CCACs. CCACs are government-funded organizations responsible for coordinating home care services in a specific region of Ontario, Canada.

The EST treatment and regular wound dressing changes were continued during the 3-month intervention or until the ulcer healed. Once the ulcer healed, the subject was discharged from wound care services; however, monthly evaluations by research personnel continued for at least 6 months when possible, and maintenance of the pressure management program, nutritional changes, and other preventative strategies was recommended.

Outcome Measures

Primary outcome. The primary outcome was the percentage decrease in wound surface area at the end of 3 months of intervention with either EST+SWC or SWC. Wound surface area was determined using the Visitrak system,[d] which was validated previously[38,39] and has been used in several previous clinical trials.[24] This involves tracing the wound perimeter onto single-use transparent acetate film and digitizing it using a calibrated tablet.

Secondary outcomes. The secondary outcomes were as follows:

1. The proportion of wounds was calculated that improved significantly (at least 50% smaller), completely healed, and worsened (wound size increase) at the end of 3 months of intervention with either EST+SWC or SWC.
2. Changes in wound appearance at the end of 3 months of treatment were evaluated using the PWAT and PSST. The PWAT is a pen-and-paper tool with 6 items that describe the appearance of the wound bed, periulcer skin, and wound edges. Each item is ranked on a scale of 0 to 4 to yield a total score of between 0 and 24, with 0 equaling a well healed wound. It has been established previously that the PWAT is very reliable[40] and can detect changes in wound appearance over time.[24] In the present study, PWAT was applied to digital images taken of the wound and periulcer skin using a digital camera (Canon Rebel 300D EOS, 8 megapixel resolution, 60mm macro lens with ring flash[e]) and including a self-adhesive ruler with a millimeter scale to indicate relative wound size. We also assessed wound appearance at the bedside using the recently updated version of the PSST, also called the Bates-Jensen wound assessment tool.[41] Both the acetate tracings and digital images were analyzed by a single assessor who was not involved in either EST or standard wound treatment and was blind to group assignment.
3. EST compliance: A meter tracked the total number of hours the machine was used to determine the actual amount of time EST treatments were applied for each study subject.
4. Adverse reactions: A record of adverse reactions was kept.

Data Analysis and Statistics

WSA (cm^2) was determined for each study subject during the initial assessment, immediately before commencement of treatment (pretreatment), and at monthly intervals for 3 months of treatment with standard care with or without EST. The % ↓ WSA was calculated at 3 months as follows:

$$\%\downarrow \text{WSA} = \frac{\text{initial WSA } (cm^2) - \text{WSA } (cm^2) \text{ at 3 mo}}{\text{initial WSA } (cm^2)} \times 100$$

Wounds that closed during the 3-month intervention were assigned a value of 100%↓WSA and, provided the wound remained closed, they were assigned this value for successive assessments. When subjects in the study had more than 1 wound, the most severe wound (highest stage) that was free of underlying osteomyelitis was selected as the index ulcer and was included in data analysis.

The proportion of stage III, stage IV, or unstageable (stage X) wounds with WSA at the end of intervention (at 3mo) that were significantly better (at least 50% smaller) or worsened (became larger than initial WSA) was determined for each group. The changes in the total PWAT and PSST score before and at the end of 3 months of treatment with EST+SWC or SWC were determined for each subject. The number of subjects whose PWAT and PSST scores improved (lower total scores) after 3 months of EST+SWC or SWC was also computed. Differences between groups were determined at baseline and at the end of the 3-month intervention using Student *t* tests for continuous variables and chi-square analysis for categorical data. *P* values less than .05 were considered statistically significant.

Table 1: Characteristics of Subjects With SCI and Their Pressure Ulcers

Subject and Wound Characteristics	SWC Group (n=18)	EST+SWC Group (n=16)	*P*
Age (y)	50.8±11.6 (32–79)	50.3±17.3 (23–74)	.91
Sex (male:female)	12:6	8:8	
SCI level (no. of subjects)			.68
Quadriplegia	8	7	
Paraplegia	8	6	
Spina bifida	2	3	
SCI duration (years since traumatic injury; excluding spina bifida)	23±11 (5–41)	18±16 (1–51)	.28
Wound location (no. of subjects)			.43
Buttock region			
- Ischial tuberosity	11	8	
- Sacrum, coccyx, hip	4	4	
Leg: foot, ankle, knee	3	4	
Wound duration (y)	3.0±5.6 (0.3–15,20)	1.2±1.0 (0.3–4.1)	.52
No. of subjects with duration of ulcer >2y	4	3	
Wound severity (no. of subjects) NPUAP stage (II, III, or IV, unstageable)	Stage II=4 Stage III=4 Stage IV=10 Stage X=0	Stage II=1 Stage III=6 Stage IV=7 Stage X=2	.19
Initial wound surface area (cm^2)	2.73±2.89 (1.1–10.9)	3.38±3.44 (1.2±12.0)	.21
No. of subjects with multiple wounds	5	8	.19
No. of subjects with previous or recurrent problems with pressure ulcers	11	10	.93

NOTE. Subjects with SCI and their pressure ulcers (wounds) were randomly assigned to either the control group, which received a customized wound care program (SWC group), or the same wound care program with electrical stimulation therapy (EST+SWC group). Values are expressed as frequency distribution or mean ± SD with maximum and minimum values per group in brackets. Wound severity is indicated by using NPUAP definitions, 2007. n values denote the number of subjects per group. *P* values derived from either the Student *t* test or χ^2 analysis detected no statistically significant difference between treatment groups in any of the measures illustrated in table 1.
Abbreviation: NPUAP, National Pressure Ulcer Advisory Panel.

RESULTS

Subject Inclusion/Exclusion

Sixty-seven people with SCI were screened for inclusion in this study, and a total of 34 people with SCI enrolled in the 3-month trial of EST+SWC or SWC. Reasons subjects were not randomized to receive either treatment are outlined in figure 1. Several potential subjects elected not to enroll in the study because they were unwilling or unable to follow an SWC program that included appropriate pressure redistribution. An additional 3 subjects failed to show for scheduled screening visits. Five subjects who asked to be considered for entry in this trial had unresolved medical problems and/or recent emergency department visits and/or hospitalization. A further 8 subjects were identified via a standard blood test to have evidence of multiple (2 or more) nutritional deficiencies or underlying metabolic disorders that can impair wound healing including anemia, hyperglycemia, iron deficiency, protein malnutrition, dehydration, or hypothyroidism.

All subjects who enrolled in the study and were randomized to a treatment group completed the 3-month trial of either standard care or standard care plus EST. Seventeen of 18 subjects in the SWC group were followed for at least 3 months after the intervention period (total of 6 months), and 8 of 13 subjects with unhealed ulcers used EST as part of SWC provided by their local home care agency. Fourteen of 16 subjects in the EST+SWC were followed for at least 6 months, and 6 of 10 subjects with unhealed wounds after 3 months of intervention elected to continue EST treatment.

Sample Characteristics

Demographic and wound characteristics of the 34 subjects enrolled in this study are provided in table 1. The sample population consisted of 20 men and 14 women who had quadriplegia, paraplegia caused by a traumatic spinal injury, or spina bifida. The average age of both the SWC and EST+SWC groups was 50 years. Subjects all lived in communities that were located within a 4-hour drive (approximately 400km) from the university-based study center and a Regional SCI Rehabilitation Center. Most subjects had an ulcer over the ischial tuberosity, which is expected given that all participants were heavily dependent on wheelchairs (>8h/d). This group of people with SCI had longstanding pressure ulcers: 2 of the subjects who received EST had very chronic ulcers (16 and 20y). Many subjects in each treatment group currently had multiple pressure ulcers and a long history of recurrent skin breakdown. Even distribution based on duration of the ulcer and National Pressure Ulcer Advisory Panel definitions for stages of pressure ulcers was achieved by stratification prior to randomization to SWC or EST+SWC groups. Measures of initial wound surface area and maximum wound depth indicated that most wounds were relatively small and superficial pressure ulcers. There was no statistically significant difference between groups in any of these variables measured at baseline prior to commencement of the intervention phase of the study.

Wound Healing

The % ↓ WSA at 3 months posttreatment was significantly greater in the EST+SWC group (mean ± SD, 70±25%) than the SWC group (36±61%; *P*=.048) (fig 2). Four of the wounds in the SWC group increased in size, whereas none of the wounds in the EST+SWC group worsened over the 3-month treatment period (odds ratio=.09; 95% confidence interval, .02–.45; *P*=.003). All of the partial thickness stage II pressure ulcers healed regardless of treatment group (1 in the EST+SWC group and 4 in the SWC group). The proportion of

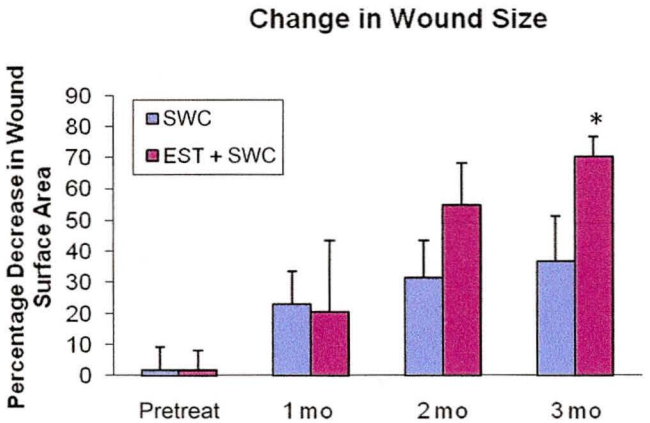

Fig 2. Values are mean ± SEM of the % ↓ WSA measured after 1, 2, and 3 months of treatment. Results are divided into a control group of subjects treated with either a customized wound care program (SWC) or an active treatment group that received SWC plus EST. Pretreat values are taken just prior to commencement of treatment, which was approximately 1 month after baseline values were recorded during the initial assessment. *Percentage decrease in wound surface area from baseline was significantly different between treatment groups after 3 months of treatment (P=.048).

stage III, IV, or X pressure ulcers that were more than 50% smaller at 3 months was 12 (80%) of 15 for wounds treated with EST+SWC and 5 (36%) of 14 for wounds receiving only SWC, a difference that was statistically significant (odds ratio=7.2; 95% confidence interval, 1.4–38.3; P=.02).

Mean PWAT scores ± SD after 3 months of intervention with EST+SWC were 9±5.1, which was significantly lower than PWAT score measured in this group prior to EST+SWC intervention (13.38±3.0; P=.031). Twelve (75%) of 16 wounds had improved PWAT scores over the 3-month EST treatment period, whereas only 8 (44%) of 18 subjects in the SWC group had lower PWAT scores (P=.07). Fifty percent of subjects in both the EST+SWC and the SWC groups had lower (improved) PSST scores after 3 months of treatment (P=.56) (table 2).

Adverse Reactions

Adverse reactions reported in this study were minor and rare. The most common reaction reported by subjects using EST was red, raised, itchy skin beneath the large dispersive electrode. This was attributed to contact dermatitis because the area resolved within 24 hours of discontinuing the use of the self-adhesive electrode. A nonadhesive carbon electrode was substituted in these cases. One patient had a persistent (>24h) red area or burn under the active electrode after EST treatment. The area resolved within 48 hours and was remedied by turning down the intensity of subsequent EST treatments. One subject complained of dizziness and delusions while he was receiving EST treatments. EST treatments were discontinued; however, his symptoms persisted, and he was transported to the hospital for evaluation. After careful evaluation by emergency department staff, his symptoms were attributed to withdrawal from narcotics caused by a lapse in his prescription. He refused to continue EST treatments but remained in the study for evaluation.

EST Compliance

Subjects in the study used EST for a mean ± SD of 3.0±1.5h/d, which was lower than the recommended treatment time (8h/d). Only 4 of the 16 individuals in the EST group used the treatment within the recommended time. Those individuals who healed during EST treatment used the EST machine for more time (539 total hours; 3.54h/d) than those who did not heal with EST (331 total hours; 2.24h/d). The average number of days that EST was used in subjects who achieved complete wound closure was 136.4 days (4.5mo).

DISCUSSION

The results of this study have demonstrated that chronic and recurrent pressure ulcers present in people with SCI had a greater reduction in wound size when EST was added to an SWC program than a similar group of subjects who were treated with only standard care. A greater proportion of severe pressure ulcers (stage III, IV, X) were more than 50% smaller after 3 months of treatment with EST than those treated with standard care alone. People were also less likely to have wounds that increased in size (worsened) when their wound treatment included EST.

The number of healed ulcers within 3 months was similar in the EST+SWC (n=6) and SWC (n=5) groups. However, this result is likely because of the greater proportion of stage II ulcers in the SWC group (4 in the SWC group and 1 in the EST+SWC group), and all stage II pressure ulcers healed regardless of group allocation. The unexpected result with stage II pressure ulcers suggests that optimization of the SWC protocol including pressure management may be sufficient to heal stage II pressure ulcers in this patient population.

Given the population of patients with SCI who had predominantly longstanding (1–3y), severe (stage III or higher), and recurrent ulcers, we did not expect complete wound healing to occur within the 3-month intervention period. We therefore selected the primary outcome for wound healing as percentage

Table 2: Wound Healing Outcomes

Outcomes	SWC Group (n=18)	EST+SWC Group (n=16)	P
Intervention period (3mo)			
% ↓ WSA over 3-mo intervention	36±61%	70±25%	.048
Proportion with improved PWAT scores	8/18=44%	12/16=75%	.070
Proportion with improved PSST scores	9/18=50%	8/16=50%	.560
Proportion of wounds that increased in size (worsened)	4/18=22%	0/16=0%	.001
Proportion of stage II ulcers healed	4/4=100%	1/1=100%	.620
Proportion of stage III, IV, X ulcers healed	1/14=7.1%	5/15=33.3%	.550
Proportion of ulcers stage III, IV, X ulcers at least 50% smaller	5/14=36%	12/15=80%	.020

NOTE. Values are expressed as frequency distribution or mean ± SD for subjects in the control group that received standard wound care (SWC group) or SWC plus EST (EST+SWC group). P values less than .05 were considered statistically different between treatment groups.
Abbreviation: BWAT, Bates-Jensen wound assessment tool.

decrease in wound surface from baseline (also termed percentage area reduction from baseline). This calculation has been used extensively to detect wound size changes in previous clinical trials evaluating the effectiveness of advanced wound treatments.[42,43] Previous epidemiologic reports have compared various methods of expressing wound size changes, and %↓WSA has consistently been recommended for use as the surrogate endpoint in clinical trials. It accounts for large variances in actual wound size, normalizes the data based on initial wound size, and is known strongly to predict ultimate wound closure. The ability of this outcome measure (%↓WSA) to predict complete healing was confirmed in our study. We found that 78% of subjects who had greater than 50%↓WSA after 3 months of receiving either EST+SWC or SWC completely closed (healed) with continued treatment.

All of the subjects enrolled in the study completed the 3-month study period. Fourteen (88%) of 16 subjects originally assigned to the EST+SWC group were followed until wound closure or for at least 6 months. Six of 10 people whose wounds remained unhealed after 3 months of EST+SWC treatment elected to continue EST treatments. All but 1 of these individuals eventually healed. Thus treatment with EST+SWC produced wound closure in a total of 11 (69%) of 16 subjects. Six subjects closed after 3 months of EST+SWC treatment, and subsequently, 3 closed within 6 months and 2 within 1 year of EST treatment. The average time for EST+SWC treatment to produce complete healing was 4.5 months. By comparison, only 7 (39%) of 18 of subjects who received SWC achieved complete wound closure by 6 months. This was despite the fact that some of these individuals received EST treatment as part of SWC available in this region. We feel a key reason EST did not produce complete wound closure in study subjects was that they elected to stop using the EST machine prematurely, before the wound was healed. Four of 5 subjects in the EST+SWC group and 5 of 8 subjects in SWC group who remained unhealed after 6 months did not use the EST machine for more than 3 months. These posttreatment observations suggest that EST treatment longer than 3 months is required to produce complete healing in this patient population with very chronic and recurrent pressure ulcers.

In addition to changes in wound size, we also detected a greater proportion of subjects treated with EST who had improvements in wound appearance. We used the PWAT to assess wound appearance. The PWAT has been validated previously[40] and shown to be able to detect change in wound status when used in clinical trials.[24] This assessment tool has many practical advantages for use in clinical trials that evaluate the effectiveness of wound healing therapies because PWAT scores can be derived from digital images of wounds. In this way, results from several centers can be sent to a single assessor who is blind to treatment allocation. Interestingly, we failed to detect a difference over time or between treatment groups when wound appearance was assessed at the bedside using the PSST. The inability of this popular tool to detect changes between groups of wounds with obvious differences in wound healing outcomes has been reported previously[24] and by other groups.[44,45]

Our results are consistent with other controlled clinical studies that have reported a benefit of EST treatment of pressure ulcers in group of subjects with SCI.[22,23,27-31] Two studies showed that monophasic pulsed current applied for 45 to 60 minutes daily directly to the wound bed can produce significant reductions in wound size within 3 to 4 weeks of commencing EST treatment.[23,27] Baker et al[22] applied biphasic asymmetric current at a similar intensity (sensory level) to the periulcer skin of people with SCI and also reported significantly more healing than control wounds receiving only SWC. This indirect approach, while more practical, did require longer exposure times (1.5h/d for 6wk) to produce notable differences between groups. A group of researchers in Slovenia[28-31] have applied EST to over 230 subjects with SCI. They reported in several articles that EST doubled the relative rate of healing within 4 weeks of commencing treatment. Their approach most often involves EST applied to the periulcer skin using relatively higher intensities sufficient to produce muscle contraction. While the type and intensity of electric current, location of electrodes, and EST treatment time varied greatly between these previous studies, they consistently report an added benefit of EST compared with a similar group of control wounds. Whether the amount of wound healing induced by EST is dependent on intensity or exposure time cannot be determined because all these studies expressed wound healing using different outcome measures.

We applied EST to wounds in this study using a variety of approaches, each of which has been shown to be successful in previous clinical reports. The advantage of varying the EST protocol is that we were able to tailor the treatment regimen based on client preferences and caregiver skill. This allowed the EST to be delivered in a home care setting by the subjects or by the chosen caregivers. Considering that all subjects with SCI treated in this study lacked sensation in the wound area and were not able to provide feedback during EST treatments, we were pleased with the relatively few and minor side effects attributed to this treatment. The dermatitis or burn produced in the skin under the electrodes quickly resolved and was easily remedied with slight modifications to the EST protocol without patient or caregiver concern. Given the relatively few and minor adverse reactions that were attributable to the EST treatment, we feel this patient-centered approach is relatively safe.

We hoped this patient-centered approach would increase the subjects' ability to comply with recommended treatment times. However, we were surprised that even though the device was to be applied while subjects were sleeping, very few subjects were able to use the device for the recommended 8h/d. Previous researchers have had similar difficulties achieving such extended treatment times.[21] Because this study was conducted within an existing health care system, we feel that 3h/d represents an accurate estimation of the length of time daily EST treatments can be expected to be applied. Individuals whose wounds healed used the EST device for a longer time than did individuals whose wounds did not heal. This suggests that longer EST exposure time is associated with better healing rates; however, because of the large variation in time that the EST device was used, this difference was not statistically significant.

The rate of healing produced by this EST protocol average of 70% reduction in 3 months is relatively slow compared with other reports,[22,24-26] especially considering the extended daily treatment times used in the present study (average=3h/d). The percentage area reduction after 4 weeks of EST treatment calculated for subjects in this report (37%) is slightly lower than the average percentage area reduction after 4 weeks achieved with EST treatment in other studies on an SCI population (43%)[22,23,27-31] and markedly lower than healing rates for diabetic foot ulcers and venous ulcers. The slower healing rates reported herein is likely a result of the fact that subjects with SCI recruited into this study had very chronic ulcers (average ulcer duration was over 1y). Furthermore, most subjects included in this study had a history of skin breakdown, more than 1 pressure ulcer, and current pressure ulcers that were predominantly severe (stage IV or X).

Examination of baseline characteristics revealed that key determinants of wound healing (age, wound duration, initial wound size) were not different between groups. Similarities between treatment and control groups were facilitated by our robust study design, which involved stratification based on ulcer severity (National Pressure Ulcer Advisory Panel definitions for stages of pressure ulcers) and ulcer duration and also by the randomization process. The ulcers included in this study were relatively small and superficial and did not involve any underlying bone or osteomyelitis. We also did not include subjects who were considered medically unstable (requiring emergency department visits or hospitalization) or had multiple underlying conditions that interfere with healing (anemia, uncontrolled blood glucose, iron deficiency, protein malnutrition). Therefore, the promising effects of EST on pressure ulcers observed in this study cannot be extended to people with severe, deep pressure ulcers complicated by unresolved medical conditions that are associated with poor healing. EST treatment provided in this study was given in conjunction with an interdisciplinary wound management program. This is consistent with best practice recommendations for the treatment of pressure ulcers.[32,33,35] Although the specific program was not identical for all subjects, a similar approach was applied across all subjects, and this program was designed prior to random allocation to the study groups. Some subjects elected not to enter the study because they were unable or unwilling to follow the pressure management program that involved changing a wheelchair surface or altering their daily activity schedule. We feel this inclusion criterion was justified because clinical practice guidelines recommend that advanced wound therapies like EST should not be applied if the underlying wound etiology has not been addressed.

Study Limitations

This study involved a relatively small number of subjects. The small sample size is reflective of the relatively small population of people who have SCIs and pressure ulcers living in this region. Our exclusion/inclusion criteria, while important to ensure a relatively homogenous study population, further constrained subject recruitment.

This single-blind study was not set up in a manner that blinded subjects receiving EST. We elected to use only active EST machines in this study for safety reasons because patients or unskilled care givers were involved in delivering EST treatments and subjects were living in communities remote from the regional treatment center. We contend that the objective nature of wound healing outcomes used in this study (WSA and proportion of completely healed ulcers) are not affected by this lack of blinding.

EST treatments were applied in the present study in combination with silver dressings. Silver-containing dressings have been shown to reduce bacteria colonization in wounds,[46] and the restoration of bacterial balance in chronic wounds has been associated with improved healing rates.[47] Recent studies suggest combination of EST with silver dressings may have a synergistic effect on killing bacteria present in infected wounds.[48-50] Therefore, positive wound healing outcomes observed in the EST+SWC group may be a result of the combination of silver dressing and EST. We attribute accelerated healing rates observed in the EST+SWC group primarily to the EST rather than the silver dressing because all but 4 subjects in the SWC group used a silver dressing as part of SWC protocol.

All of the subjects randomized to 1 of the 2 treatment groups completed the intervention period. Three of the 5 individuals who were included in the EST treatment group used the EST machine for an average of 67 total hours over 3 months, which was far less than the average time of EST use of subjects enrolled in the study (443h). None of these individuals who failed to comply with the recommended EST protocol had wounds that healed. Because it was our intention to treat these subjects, we still included their data in the analysis of primary outcomes and main results reported in this study. If results of the 3 subjects who did not use the EST as recommended were excluded from analysis, the mean percentage decrease in wound surface area $\pm$ SD was $76\pm24\%$ in the EST+SWC group, and the difference between treatment groups remained statistically significant ($P=.03$).

We found that 8 subjects in each treatment group had recurrent or new pressure ulcers develop within 4 months of closure. These results are similar to other pressure ulcer recurrence rates.[2] They suggest that low levels of EST administered in or around the wound bed can accelerate wound closure but do not prevent recurrent pressure ulcers from returning or new ulcers from appearing elsewhere on the body. Some reports suggest EST can help prevent pressure ulcers; however, the EST used prophylactically involves stimulation of active muscle contraction, which requires much higher intensity of electric current than that employed here. Other researchers have proposed that there is a distinct set of risk factors and different underlying etiology of recurrent pressure ulcers in the SCI population. The effect of advanced wound treatments including EST on the complex pathophysiological processes associated with chronic, recurrent pressure ulcers that occur more frequently in this patient population needs to be investigated further.

CONCLUSIONS

This study represents the first demonstration that EST can be successfully integrated into an existing community-based wound care program. When EST was added to an interdisciplinary wound care program, faster reduction in wound size, improved wound appearance occurred over 3 months. The average time EST was used by subjects who had complete wound closure in these participants with SCI with chronic, recurrent pressure ulcers was 136.4 days (4.5mo). Subjects were able to use the EST machine a mean $\pm$ SD of 3.0 ± 1.5h/d, which was lower than recommended (8h/d). Advanced technology allowed patients or their caregivers to administer the EST in their home setting in a safe and effective manner.

Acknowledgments: We appreciate the collaboration with CCACs in the London Middlesex and Kitchener Waterloo Regions of Ontario and the work of Sherry Green, RN, the research nurse; Anneke Salman, MSc, the study coordinator; and Michelle Akragi, BHSc, who collated and analyzed study outcomes.

References

1. Vogel LC, Krajci KA, Anderson CJ. Adults with pediatric-onset spinal cord injury, part 1: prevalence of medical complications. J Spinal Cord Med 2002;25:106-16.
2. Krause JS, Broderick L. Patterns of recurrent pressure ulcers after spinal cord injury: identification of risk and protective factors 5 or more years after onset. Arch Phys Med Rehabil 2004;85:1257-64.
3. Chen Y, DeVivo MJ, Jackson AB. Pressure ulcer prevalence in people with spinal cord injury: age-period-duration effects. Arch Phys Med Rehabil 2005;86:1208-13.
4. New PW, Rawicki HB, Bailey MJ. Nontraumatic spinal cord injury rehabilitation: pressure ulcer patients, prediction, and impact. Arch Phys Med Rehabil 2004;85:87-93.
5. Garber SL, Rintala DH. Pressure ulcers in veterans with spinal cord injury: a retrospective study. J Rehabil Res Dev 2003;40:433-42.

6. Bourguignon G, Bourguignon L. Electric stimulation of protein and DNA synthesis in human fibroblasts in cell culture. FASEB 1987;1(5):398-402.
7. Bourguignon G, Wenche J, Bourguignon L. Electric stimulation of human fibroblasts causes and increase in Ca2+ influx and the exposure of additional insulin receptors. J Cell Physiol 1989;140:385-97.
8. Falanga V, Bourguignon C, Bourguignon L. Electrical stimulation increases the expression of fibroblast receptors for transforming growth factor beta. J Invest Dermatol 1987;88:488-92.
9. Orida N, Feldman J. Directional protrusive pseudopodial activity and motility in macrophages induced by extra-cellular electric fields. Cell Motil 1982;2:243-55.
10. Sheridan D, Isseroff R, Nuccitelli R. Imposition of a physiologic DC electric field alters the migratory response of human keratinocytes on extracellular matrix molecules. J Invest Dermatol 1996; 106:642-6.
11. Thawer HA, PE Houghton. Effects of electrical stimulation on the histological properties of wounds in diabetic mice. Wound Repair Regen 2001;9:107-15.
12. Junger M, Zuder D, Steins A, Hahn M, Klyscz T. Treatment of venous ulcers with low frequency pulsed current (Dermapulse) effects on cutaneous microcirculation. Der Hautartz 1997;18:879-903.
13. Smith J, Romansky N, Vomero J, Davis RH. The effect of electrical stimulation on wound healing in diabetic mice. J Am Podiatr Assoc 1984;74:71-5.
14. Stromberg B. Effects of electrical currents on wound contraction. Ann Plast Surg 1988;21:121-3.
15. Mawson A, Siddiqui F, Connolly B, Sharp C, Summer W, Binndo J Jr. Effect of high voltage pulsed galvanic stimulation on sacral transcutaneous oxygen tension levels in the spinal cord injured. Paraplegia 1993;31:311-9.
16. Taylor K, Fish MR, Mendel FC, Burton HW. Effect of a single 30 minute treatment of high voltage pulsed current on edema formation in frog limbs. Phys Ther 1992;72:63-8.
17. Rowley B, McKenna J, Chase GR, Wolcott LE. The influence of electrical current on infecting organisms in wounds. Ann N Y Acad Sci 1974:238:543-51.
18. Barranco SD, Spadero JA, Berger TJ, Becker RO. In vitro effect of weak direct current on Staphylococcus aureus. Clin Orthop 1874;100:250-5.
19. Kloth LC. Electrical stimulation for wound healing: a review of evidence from in vitro studies, animal experiments, and clinical trials. Lower Extremity Wounds 2005;4:23-44.
20. Kaada B. Promoted healing of chronic ulceration by transcutaneous nerve stimulation (TNS). Vasa 1983;12:262-9.
21. Peters EJ, Armstrong DG, Wunderlich RP, Bosma J, Stacpoole-Shea S, Lavery LA. The benefit of electrical stimulation to enhance perfusion in persons with diabetes mellitus. J Foot Ankle Surg 2001;37:396-400.
22. Baker LL, Rubayi S, Villar F, Demuth SK. Effect of electrical stimulation waveform on healing of ulcers in human beings with spinal cord injury. Wound Repair Regen 1996;4:21-8.
23. Griffins JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, El-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991;71:433-44.
24. 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.
25. Adunsky A, Ohry A. Decubitus direct current treatment (DCCT) of pressure ulcers: results of a randomized double-blinded placebo controlled study. Arch Gerontol Geriatr 2005;41:261-69.
26. Wood J, Evans P, Schallreuter KU, et al. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993;129: 999-1009.
27. Adegoke BO, Badmos KA. Acceleration of pressure ulcer healing in spinal cord injured patients using interrupted direct current. Afr J Med Sci 2001;30:195-7.
28. Jercinovic A, Karba R, Vodovnik L, et al. Low frequency pulsed current and pressure ulcer healing. IEEE Trans Rehabil Eng 1994;2:225-33.
29. Karba R, Semrov D, Vodovnik L, Benko H, Savrin R. DC electrical stimulation for chronic wound healing enhancement, part 1: clinical study and determination of electric field distribution in the numerical wound model. Bioelectrochem Bioenergetics 1997;43: 265-70.
30. Trontelj K, Karba R, Vodovnik L, Savrin R, Strukelj MP. Treatment of chronic wounds by lower frequency pulsed electrical current. J Tissue Viability 1994;4:105-9.
31. Stefanoska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields, part 2: value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993;31:213-20.
32. Registered Nurses of Ontario (RNAO) Best Practice Guidelines for treatment of pressure ulcers. 2003. Available at: http://www.rnao.org. Accessed July 20, 2009.
33. Keast DH, Parslow N, Houghton PE, Norton L, Fraser C. Best practice recommendations for the prevention and treatment of pressure ulcers: update 2006. Wound Care Can 2006;4:31-43.
34. Bergstrom N, Bennett MA, Carlson CE, et al. Clinical practice guideline, number 15: treatment of pressure ulcers. Rockville: U.S. Department of Health and Human Services, Agency for Health Care Policy and Research; 1994.
35. Consortium of Spinal Cord Medicine. Pressure ulcer prevention and treatment following spinal cord injury: a clinical practice guideline for health care professionals. Sponsored by Paralyzed Veterans of America. 2000.
36. National Pressure Ulcer Advisory Panel (NPUAP) updated staging system 2007. Available at: http://www.npuap.org/pr2.htm. Accessed July 20, 2009.
37. Sibbald RG, Williamson D, Orsted HL, et al. Preparing the wound bed. Ostomy Wound Manage 2000;46:14-35.
38. Majeske C. Reliability of wound surface area measurements. Phys Ther 1992;72:138-41.
39. Haghpanah S, Bogie K, Wang X, Banks PG, Ho CH. Reliability of electronic versus manual wound measurement techniques. Arch Phys Med Rehabil 2006;87:1396-402.
40. Houghton PE, Kincaid CB, Campbell KE, Woodbury MG. Photographic assessment of the appearance of chronic pressure and leg ulcers. Ostomy Wound Manage 2000;46:20-30.
41. Bates Jensen BM, Vredevoe PL, Brecht ML. Pressure ulcer status tool. Decubitus 1992;5:20-8.
42. Cardinal M, Eisenbud DE, Phillips T, Harding K. Early healing rates and wound area measurements are reliable predictors of later complete wound closure. Wound Repair Regen 2008;16:19-22.
43. Kantor J, Margolis DJ. Efficacy and prognostic value of simple wound measurements. Arch Dermatol 1998;134:1571-4.
44. Taly AB, Sivaraman Nair KP, Murali T, John A. Efficacy of multiwavelength light therapy in the treatment of pressure ulcers in subjects with disorders of the spinal cord: a randomized double-blind controlled trial. Arch Phys Med Rehabil 2004;85:1657-61.
45. Gardner SE, Frantz RA, Berqquist S, Shin CD. A prospective study of the pressure ulcer scale for healing (PUSH). J Gerontol A Biol Sci Med Sci 2005;60:93-7.
46. Sibbald RG, Contreras-Ruiz J, Coutts P, Fierheller M, Rothman A, Woo K. Bacteriology, inflammation, and healing: a study of nanocrystalline silver dressings in chronic venous leg ulcers. Adv Skin Wound Care 2007;20:549-58.
47. Lo SF, Chang CJ, Hu WY, Hayter M, Chang YT. The effectiveness of silver-releasing dressings in the management of non-

healing chronic wounds: a meta-analysis. J Clin Nurs 2009;18:716-28.
48. Deitch E, Marino A, Gillispie T, et al. Silver nylon: a new antimicrobial agent. Antimicrobial Agents Chemother 1983;23:356-9.
49. Marino A, Deitch E, Albright J. Electric silver antisepsis. IEEE Trans Biomed Eng 1985;32(5):336-7.
50. Thibodeau E, Handelmann S, Marquis R. Inhibition and killing of oral bacteria by silver ions generated with low intensity direct current. J Dent Res 1978;57:922-6.

Suppliers

a. The Roho Group, 100N Florida Ave, Belleville, IL 62221-5429.
b. Argentum Medical Inc, Lake Rabun Rd, Lakemont, GA 30552.
c. Prizm Medical Inc, 3400 Corporate Way, Ste 1, Duluth, GA 30096.
d. Visitrak system; Smith & Nephew Inc, 2250 boul. Alfred-Nobel, Suite 300, St Laurent, Quebec, Canada H4S 2C9.
e. Canon Canada Inc, 6390 Dixie Rd, Mississauga, Ontario, Canada L5T 1P7.