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Improved Healing of Pressure Ulcers Using Dermapulse, A New Electrical Stimulation Device

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ABSTRACT: A double-blind, clinical study of pulsed electrical stimulation using the Dermapulse® device was carried out on 40 pressure ulcers, randomized to receive either active (stim) or sham treatment.

Electrodes were placed over saline-moistened gauze on the ulcers. An electrical current of 35mA was delivered to the wound tissues at a frequency of 128 pulses per second. Polarity was negative until the wound debrided, then alternated from positive to negative every three days. Ulcers were treated for 30 minutes twice daily for four weeks, after which sham patients could cross over to active treatment, and stim patients could continue active treatment. Ulcer healing was determined by measuring the length and width of the ulcer and calculating the L x W product. The same clinicians measured the ulcers each week, were kept blinded to treatment group, and were not the same persons who applied the treatment.

Nine centers treated 40 ulcers (19 sham and 21 stim). Analysis of the characteristics of the patients, the ulcers, and concomitant wound care by both univariate and multivariate analyses showed comparability of the groups. After four weeks, the stim ulcers healed more than twice as much as the sham ulcers (49.8% vs. 23.4%; ($p = 0.042$). The stim ulcers healed 12.5% per week compared to 5.8% for the sham group. In the 15 crossover patients, four weeks of active stimulation caused nearly four times as much healing as their four weeks of sham treatment (47.9% vs. 13.4%; $p = 0.012$). By the last week of active stimulation they had healed an average of 64%, and complete healing occurred in 40% of these ulcers after an average of nine weeks. Seventeen of the active treatment ulcers had extended therapy, and by their last week of treatment had healed an average of 75%. Forty-one percent of these ulcers healed completely after an average of 11.8 weeks. There were no significant safety problems identified.

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Pressure ulcers are a major healthcare problem in the United States. The National Pressure Ulcer Advisory Panel, based on the available literature, estimated the prevalence of pressure ulcers among hospitalized patients to be between 3% and 14%, among patients in long term care settings between 15% and 25%, and between 7% and 12% in home care settings.[1] This translates to more than one million cases, and possibly two million cases of pressure

ulcers in the U.S.[1] Various studies estimate the cost to heal one ulcer to be from $5,000 to more than $25,000, and the total financial burden runs well over five billion dollars annually.[2] These wounds often heal slowly, and are associated with increased morbidity and mortality.[3]

Since the middle of the twentieth century, electrical stimulation has been shown to improve the healing of wounds in humans[4–12] and experimental wounds in animal models.[13–19] Cell culture studies have shown that electrical fields can influence the migratory, proliferative, and functional capacity of cells involved in the healing process.[20–29] Other studies have reported measurements of injury potentials, skin battery voltages, and wound lateral voltage gradients which have been theorized to trigger bioelectric repair and enhancement of wound healing.[30–38] If electrical signals play a role in the stimulation of wound repair, then exogenous application of electric current to chronic wounds could be expected to mimic the body's bioelectric currents and enhance tissue healing processes. Reports from numerous clinical and experimental studies provide evidence in support of this idea.[4–29]

Because of different ways of reporting electrical output parameters, the literature at first appears chaotic with respect to what kinds of stimulation are effective. Reich and Tarjan reviewed the literature on the electrical stimulation of wounds in order to determine the range of efficacious treatment parameters.[39] When they converted reported outputs to certain common parameters (current density, total charge delivered, and average charge delivered/cm^2), they found that "successful" treatments were within certain ranges. "Effective" treatments delivered a total charge per day between 0.1 and 2 coulombs. It was also noted that changing polarity during treatment was a common procedure.

The importance of polarity was demonstrated by Davis, et al in a study of partial thickness wounds in pigs, in which a regimen that utilized negative followed by positive polarity was found to be more effective than other regimens.[16] Other animal studies showed that cathodal (negative polarity) electrical current solubilizes clotted blood,[30–33] confirming clinical observations that cathodal direct current stimulation facilitates debridement of necrotic wound tissue, which consists primarily of coalesced blood elements in a protein mesh. Current of negative polarity has also been shown to be most effective at increasing local blood flow.[38,39] It has also been demonstrated that white blood cells involved in the inflammatory phase of wound healing are attracted to the negative pole[23,25] and that isolated epidermal cells, cell clusters and cell sheets migrate toward the negative pole.[20] Those interested in a more complete review of the literature on the effects of electrical stimulation on wound healing are referred to an upcoming article by Gentzkow and Miller.[42]

Recognizing the need for new, effective treatments for pressure ulcers and benefiting from previous experimental work, the Dermapulse device was developed. It was extensively tested in animal models to optimize treatment parameters before a program of human testing was undertaken.

Pressure ulcers are difficult to study for several reasons. There is great heterogeneity in the size, character, location and chronicity of the ulcers, in the basic physical state of the patients, and in the "standard" treatments utilized. In order to obtain sufficient numbers of ulcers to study, multicenter efforts are necessary. Furthermore, most of the patients are elderly and ill, so that controlled trials are frequently interrupted by death, or acute illness requiring transfer to another facility. No doubt this is why most of the studies published on pressure ulcer treatments are anecdotal or lack controls, or else report on a small number of patients.

Our randomized, controlled study was designed to satisfy current scientific standards, to be convincing both to federal regulators and to clinicians, and to have enough subjects for sound statistical analysis. At the same time, it needed to be practical, and easy to carry out in multiple investigational sites without unduly complicating routines of care.

The purpose of this study was to investigate the safety and effectiveness of electrical stimulation using the Dermapulse device for the treatment of pressure ulcers, as an adjunct to standard care.

Materials and Methods

Study design. The study was carried out, according to a common protocol, at nine investigational sites with centralized monitoring and data analysis. After signing the informed consent, patients who met the selection criteria were randomly assigned to receive treatment with either an active (stim) or a sham device. Devices were identical in appearance and were assigned by number. Investigators and patients were unaware of whether the device was active or sham, and all study procedures were identical for both groups.

Patients were treated for 30 minutes twice daily for four weeks. Four weeks was chosen as the time for efficacy evaluation because investigators were reluctant to keep patients on devices that might be sham for longer than that. At the end of the four weeks, at the investigator's discretion, sham patients were allowed to cross over to non–blinded active treatment, and stim patients could continue to be actively treated.

The primary measure of ulcer healing was the relative change in size of the ulcers, determined by measuring the length and width of the ulcer and calculating the L x W product. It was recognized that the length x width product only estimates the true area of an ulcer. Nonetheless, it is quite reproducible and simple to use clinically, and it is quite useful for monitoring changes in ulcer size (change in size, not absolute size, was the parameter of interest).

Subject selection. Patients were included if they had pressure ulcers that were open and Stage II, III or IV. Stages were defined as follows: Stage II, full thickness skin defect extending into subcutaneous tissue; Stage III, defect extending into muscle; Stage IV, defect extending to bone or joint structure. (Note: In the now widely used IAET staging system, our Stage II would be Stage III, and our Stages III and IV would both be Stage IV.) To be included, the ulcers were to be between 4 cm^2 and 100 cm^2 in area as determined by the L x W product.

Patients could have more than one ulcer entered into the study (the ulcers had to be on opposite sides of the body) in which case each ulcer was randomized separately, giving the possibility that two ulcers would both be sham treated, both actively treated, or one of each. Patients also had to be cooperative and available for the duration of the study, and willing to sign an informed consent (or have a legal representative sign for them).

Ulcers were excluded from entry into the study if they were totally occluded by eschar, had bleeding or involving major blood vessels; were located in presternal, periorbital, or laryngeal/pharyngeal regions; occurred in subjects who were pregnant, wore a cardiac pacemaker, had osteomyelitis or peripheral vascular problems predisposing them to thrombosis; were cancerous; or occurred in patients who were on long–term steroid therapy, chemotherapy, radiation therapy, or who were very obese.

Study procedures. Information on each patient was obtained concerning age, sex, mobility status, systemic medications, systemic conditions, and whether they were inpatients or outpatients.

Information on each study ulcer was obtained regarding etiology, location, stage, duration, past treatment, type of concomitant wound treatment used during the study, and presence or absence of tunnels or eschar. The ulcers were measured for length, width, and depth, were charted as to location, and were diagrammed on a chart.

Conventional care was prescribed by the physician according to the needs of the individual patient, and was recorded. In all patients, wounds were kept hydrated with saline–moistened gauze between treatments.

The treatment regimen was chosen based on: unpublished animal studies performed at the

University of Miami, Johns Hopkins School of Medicine, Duke University Medical Center, and the Medical University of South Carolina; and previous clinical experiences and published animal and clinical studies.[4–19]

The study utilized a Dermapulse stimulator as the device to deliver the pulsed electrical current. Powered by a six-volt battery, this device delivers current at pulse rate/pulse duration settings between 2 pps/350 microsec. to 128 pps/150 microsec., at intensity settings between 0 and 150 mA., and in either positive or negative polarity. It has an automatic timer that shuts off the current at the end of the 30–minute treatment.

Treatments were given twice per day for 30 minutes each, with a minimum of four and a maximum of eight hours between treatments. Identical procedures were followed for sham and stim treated ulcers.

The ulcer bed was flushed with saline solution before each treatment and kept moist with saline solution between treatments. To enhance conduction of electricity to the wound, clean 4 x 4 gauze pads moistened with saline solution were placed directly over or into the ulcer. The electrode pads were composed of a carbon silicone rubber, covered with a cellulose sponge with an active contact area of 58 cm^2. The electrode pad was saturated with saline, placed on top of the gauze pads and secured into place. For large ulcers, two electrode pads were used.

A large nontreatment or return electrode was wetted and placed on a large muscle group at a minimum distance of 12 inches from the ulcer and secured with velcro belts.

The Dermapulse stimulator controls were set to provide pulsed electrical stimulation at a rate of 128 pps and an intensity of 35 mA. Using a 58 cm^2 electrode, these stimulus parameters delivered a charge of 0.89 coulombs per 30 minute treatment, or 1.78 coulombs per day, which is consistent with the delivered energy found to be effective in other studies.[39]

The treatment electrode polarity was initially set as negative and remained that way until the ulcer was debrided and a serosanguinous drainage appeared. Thereafter, the polarity was switched back and forth from positive to negative every three days. When the ulcer progressed to a Stage II classification, the pulse rate was changed to 64 pps and the pad polarity was changed each day until the ulcer was healed.

Inpatients were treated by healthcare practitioners. For those at home, either the patient or a family member was trained to apply the stimulator and to document the treatment times each day and the machine settings on the daily treatment log.

Only trained healthcare practitioners performed the ulcer measurements, and they were kept blinded during the four week study as to whether the unit was sham or active. The same clinicians measured the ulcers each week, and they were not the same persons who applied the treatment.

Safety was assessed daily (by inspection of the ulcer and by recording of patient complaints) and a daily log of treatments was kept.

At baseline and weekly during treatment, the clinicians diagrammed the ulcer and measured its length, width and depth, and determined if any tunnels were present. Detailed instructions for measuring the ulcers and for diagraming the ulcers on the data reporting forms were provided in the protocol. The length was measured across the longest distance of the ulcer, the width at the widest distance across the ulcer. Depth was measured at the estimated deepest location of the ulcer, but was used only to compare the treatment groups at baseline.

Color photographs were taken biweekly to provide a visual record. These were not standardized nor did they always include a scale in the field, and they were not intended for planimetric analysis.

Patients who crossed over or had extended therapy continued to have daily safety and weekly efficacy assessments as long as they were treated. Post–study follow–up was carried out weekly for four weeks for safety and to determine if there were any problems and if healed ulcers continued to be healed.

Table 1. Patient and ulcer characteristics by treatment group.

	SHAM	STIM	TOTAL
Age			
Mean	62.2	63.3	62.8
SD	18.4	17.8	17.6
Range	31–90	29–91	29-91
Sex			
Male %	47.4	61.9	55.0
Female %	52.6	38.1	45.0
Initial Ulcer Area (cm^2)			
Mean	12.5	19.2	16.0
(SD)	(11.9)	(23.2)	(18.79)
Initial Ulcer Depth (cm)			
Mean	1.4	1.1	1.2
(SD)	(2.3)	(2.1)	(2.2)
Stage			
II	1	0	1
III	14	16	30
IV	4	5	9
Total	19	21	40
Location			
Hip/Ischium	6	9	15
Sacrum/Coccyx	8	4	12
Leg	1	2	3
Foot	4	6	10
Total	19	21	40
Duration	%	%	%
<1 month	11.1	20.0	15.8
1 to 3	16.7	5.0	10.5
3 to 6	22.2	25.0	23.7
6 to 12	16.7	35.0	26.3
>12	33.3	15.0	23.7
Tunnels/Undermining	%	%	%
Yes	26.3	38.1	32.5
No	73.7	61.9	67.5
Eschar	%	%	%
Yes	21.1	28.6	25.0
No	78.9	71.4	75.0

Statistical methods. It was calculated that approximately 23 patients per group would be needed to detect differences of 15% or more in percent healed at four weeks, with an alpha error of 0.05 and a power of 80%, and an estimated variance of 18%.

For continuous variables such as age, duration of ulcer, and percent healed, statistical comparisons of the stim and sham groups were performed using the two sample Student's t–test. This test was used with the pooled variance estimate if there was no evidence of differences in the variances at the 5% level by Cochran's test. Where there was evidence of significantly different variances, the test was employed using the separate variance estimates for the two groups with the degrees of freedom adjusted accordingly.

For categorical variables, e.g. sex, or tunnels/undermining, the stim and sham groups were compared using the chi square test. Yate's correction for continuity was used for dichotomous variables.

Stepwise multiple discriminant analysis was employed to ascertain factors or combinations of baseline characteristics that might distinguish the stim and sham groups.

Stepwise multiple regression analysis was performed to explore and model the possible effects of various factors and treatment group on treatment outcome as indicated by percent healed.

Three–way analysis of variance was performed to evaluate the separate effects on percent healed of investigational center or ulcer location when considered with treatment group and tunnels/undermining.

For crossover ulcers, the paired t–test was used to compare the percent healed during the four–week sham and active stimulation periods.

For this report, all references to statistical significance are based on the 0.05 significance level for two–tailed tests, unless otherwise specified.

Results

Enrollment and exclusion from analysis. Forty–nine ulcers (24 sham, 25 stim) were enrolled into the study at nine investigational sites. Six ulcers (4 sham, 2 stim) were excluded from analysis because they received less than four weeks of treatment and thus did not have enough data for analysis. Three ulcers (1 sham,

Table 2. Part 1

Summary of results of the statistical tests used to compare the SHAM and STIM groups of comparability of patients and ulcer characteristics.

[1] All chi-square values for fourfold tables include Yate's correction for continuity.

[2] With adjustment for heterogeneity of variances.

Characteristics	Statistical Test	Test Statistic	Degree of Freedom	Significance Value (p-value)
Sex	chi-square[1]	0.37	1	0.55
Age	t-test	-0.18	38	0.86
Wound stage	chi-square	1.15	2	0.56
Duration	t-test[2]	1.34	20.94	0.20
	chi-square	4.28	4	0.37
Tunnels/Undermining	chi-square	0.21	1	0.65
Initial Wound:				
size (L x W)	t-test[2]	-1.18	30.46	0.25
depth	t-test	0.44	38	0.66
Previous Treatment:				
conservative	chi-square	0.81	1	0.37
debridement	chi-square	0.45	1	0.50
antibiotics	chi-square	0.02	1	0.88
medication	chi-square	0.09	1	0.76
Sytemic conditions:				
cardiovascular	chi-square	0.17	1	0.68
central nervous	chi-square	0.00	1	1.00
metabolic	chi-square	0.04	1	0.85
musculoskeletal	chi-square	0.82	1	0.37
Degree of mobility	chi-square	0.29	2	0.86
In/out patient	chi-square	0.00	1	1.00
Eschar	chi-square	0.03	1	0.86
Receiving Treatment for other conditions:				
antibiotics	chi-square	0.03	1	0.86
diabetics	chi-square	0.02	1	0.88
cardiovacular	chi-square	0.00	1	1.00
psychotropic	chi-square	0.32	1	0.57
Concomitant Therapy:				
surgical or whirlpool therapy	chi-square	0.00	1	1.00
bedrest & elevation of extremity	chi-square	0.00	1	1.00

Part 2.

A stepwise discriminate analysis of factors potentially differentiating the treatment groups was done using the characteristics listed in Part 1. None of these characteristics alone or in combination was found to be statistically different between treatment groups at the 0.10 significance level.

2 stim) were excluded from analysis because of serious protocol violations which made it impossible to analyze critical data. Patients were not excluded for minor protocol violations, and every effort was made to include as many patients in the analysis as possible.

Overall, 40/49 ulcers (19 sham, 21 stim) or 81.6% were included in the analysis. These 40 ulcers were on 37 patients; three patients each had two ulcers included in the analysis. The randomization resulted in approximately equal numbers of pressure ulcers being enrolled in the sham and stim groups overall and at each center. Nearly equal numbers in each group are included in the analysis as well.

Patient, ulcer, and care characteristics. Table 1 lists the key characteristics of the patients and the ulcers for the sham and stim groups. Patient ages ranged from 29 to 91 years. The mean ages of the patients in the sham and stim groups were nearly identical, 62.2 and 63.3 years respectively. Overall, there were 55% males and 45% females, but there was a higher proportion of females in the sham group than the stim group (52.6% vs. 38.1%).

The mean initial ulcer area was somewhat larger in the stim group (19.2 vs. 12.5 cm^2), while the sham group had slightly deeper ulcers (1.4 vs. 1.1 cm). Nine of the wounds were Stage IV, 30 were Stage III, and the only Stage II wound was in the sham group. Location of ulcers were: hip/ischium 15, sacrum/coccyx 12, leg 3, and foot 10. The ulcers were distributed similarly between the groups. Duration of the ulcers prior to the study was also similar in both groups, with 15.8% less than one month, 10.5% 1 to 3 months, 23.7% 3 to 6 months, 26.3% 6 to 12 months, and 23.7 greater than a year. Tunnels/undermining of the ulcer were present somewhat more often in the stim group, 38.1% vs. 26.3%. About one–fourth of the ulcers in each group had eschar on them at the beginning of the study.

Not shown in Table 1 are additional baseline data. Approximately 80% of each group were treated as inpatients. Nearly equal percentages of each group were bedbound (50%), wheelchair bound (42%) or ambulatory (8%). There were no meaningful differences in the type of care the ulcers had received prior to the study, the systemic conditions of the patients, or the drugs they were taking.

The type of concomitant ulcer care (in addition to the electrical stimulation procedures) provided during the study was recorded, and virtually identical percentages of sham and stim ulcers received normal saline and dressings (100%), surgical or whirlpool debridement (10%) turning to relieve pressure (100%), or bed rest and elevation of an extremity (55%).

Comparability of sham and stim groups. It is of critical importance to determine if the active treatment (stim) and control (sham) groups were comparable at the time of enrollment, as a check that randomization produced comparable groups and to see if any factors that are correlated with the healing of the ulcers existed. Univariate and multivariate comparisons of the groups for characteristics for which data were gathered were performed and are listed in Table 2. None of the variables was significantly different between the groups, nor did any variable even approach statistical significance at the 0.05 or 0.10 significance level.

It can be concluded that there was no statistical evidence of differences between the two treatment groups at baseline and the significant differences in treatment outcome are not likely to be attributable to any differences in group characteristics.

Efficacy: Four week double–blind results. As shown in Table 3, at four weeks the stim group had healed more than twice as much as the sham group (49.8% vs. 23.4%), a rate of 12.5% per week versus 5.8% per week. This difference was statistically significant ($p = 0.042$). Inspection of the standard deviations also shows that the variability in healing response was less with active treatment. Figure 1 graphically displays the rate of healing for the two groups over the four weeks of the blinded study.

Table 3

Treatment Group	Week 1 %	Week 2 %	Week 3 %	Week 4 %
SHAM (N=19)	3.7	10.2	23.1	23.4
(SD)	(25.7)	(38.1)	(40.3)	(47.4)
STIM (N= 21)	18.0	33.2	35.1	49.8
(SD)	(19.6)	(29.0)	(36.1)	(30.9)
P Value	0.053	0.037	0.325	0.042

SD = Standard Deviation
P values are calculated by T–Test, 38 degrees of freedom, two–tailed

Table 3. Percentage of ulcer healed at weeks 1,2,3, and 4 for the SHAM and STIM groups. Each patient's wound area at each week was compared to the area at baseline, and the percentage healed was calculated. The data reported are the mean of these individual percentages.

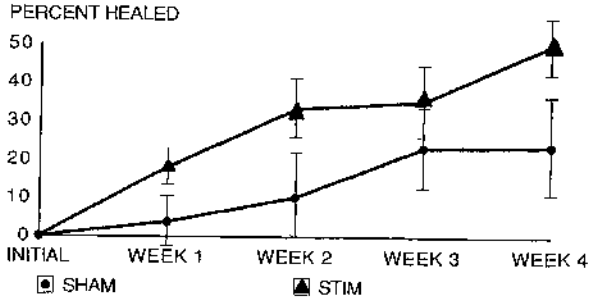

Figure 1. The percentage of the ulcer healed (Mean +/– SEM) at weeks 1,2,3, and 4 for the SHAM control group (lower line) versus the percentage healed for the actively treated STIM group (upper line). Each patient's wound area at each week was compared to the area at baseline, and the percentage healed was calculated. The data reported are the mean of these individual percentages.

The foregoing univariate analysis does not adjust for any factors other than treatment group which might be associated with treatment outcome. Consequently, a stepwise multiple regression analysis was performed to assess the possible simultaneous effects of various potential co–factors on the four week mean percentage of ulcer healed. The same characteristics of the patients, their ulcers, and concomitant wound therapy listed on Table 2 were employed in this analysis as potential predictors of treatment outcome.

Table 4 lists the five variables that were found to meet the 0.05 significance criterion. The multiple regression coefficient for these data (R = 0.751) is quite high. Not surprisingly, treatment group was significantly associated with outcome. Metabolic condition, having tunnels/undermining in the ulcer, sex, and stage of the ulcer are also associated with outcome. The fitted model derived from this analysis can be expressed as follows: The expected percentage healed after four weeks: +41.41% if actively stimulated, +27.17% if the patient has a metabolic condition, +26.32% if the patient is female, –37.40% if tunnels/undermining are present, –22.28% if Stage IV vs. III (or III vs. II).

Although none of these variables was significantly different between the treatment groups, if there were any bias in the results due to imbalances in the treatment groups, this would be expected to work against finding an effect of the active treatment because the stim group had fewer patients with metabolic conditions (mainly diabetes), fewer females, more tunnels, and slightly higher stages than the sham group.

Since treatment by electrical stimulation (treatment group) and presence of tunnels/undermining were already determined by the stepwise multiple regression analysis to have major effects on healing rates, it was possible to look at the individual effects of other categorical factors when combined with those two factors in a three–way ANOVA. Whereas treatment group and tunnels/undermining were still found to be significantly associated with outcome ($p < 0.05$), this analysis provided no evidence of an effect on outcome due to either anatomic location ($p = 0.71$) or investigational center ($p = 0.28$).

Patients who crossed over from sham to active stimulation. At the end of the four week study period the investigators could cross over

Table 4.

Stepwise multiple regression analysis of mean percentage of wound healed as a possible function of various factors including treatment group.

Step	Variable	Multiple R	R^2	Partial R^2	Coefficient*	p–value*
1	Metabolic Condition	0.391	0.153	0.153	27.17	0.0227
2	Treatment group	0.539	0.291	0.138	41.41	0.0003
3	Tunnels	0.632	0.400	0.109	–37.40	0.0027
4	Sex	0.709	0.502	0.102	26.32	0.0141
5	Stage	0.751	0.563	0.061	–22.28	0.0419
	(constant)				52.72	0.1763

No other variables met the 0.05 significance level.
* as of final equation

Table 4. *Results of the multiple regression analysis undertaken to determine factors associated with wound healing.*

the sham ulcers to unblinded active therapy. Of the 19 sham ulcers with analyzable four–week data, 15 were crossed over, completed at least four weeks of active therapy, and continued for a mean total of 9.8 weeks (range 5 to 16 weeks) of active stimulation. At the end of the sham treatment period these ulcers had healed only an average of 13.4 percent. After four weeks of active stimulation they had healed an average of 47.9 percent of their size at the time of crossover. This fourfold greater healing during four weeks of stim versus four weeks of sham in the same ulcers is statistically significant ($p = 0.012$; t–test, two–tailed).

The average healing after four weeks of active stimulation in these ulcers (47.9%) was almost identical to the healing after the first four weeks (49.8%) in the active treatment group, indicating a consistent treatment effect.

By their last week of active treatment the crossover ulcers had healed an average of 63.9 percent. Forty percent of the ulcers healed completely, after an average of nine weeks.

Extended therapy in active treatment patients. Of the 21 patients in the active treatment group, 17 received additional stimulation beyond the first four weeks of therapy. The total duration of stimulation (including the first four weeks) averaged 10.7 weeks, with a range of 5 to 26 weeks. After their initial four weeks of therapy, these patients had healed an average of 45.0%; by their last week of therapy they had healed an average of 74.6%. Forty–one percent of the ulcers healed completely, after an average of 11.8 weeks therapy.

Post–study follow–up. Four–week post–study follow–up did not reveal any adverse effects of treatment in any of the ulcers. All of the ulcers that were completely healed during the initial study, after crossover, or during extended therapy were still healed at follow–up. Three ulcers had not quite healed during active treatment but were fully healed upon follow–up.

Safety. There were no significant safety problems during the study and no patient was withdrawn because of an adverse event. The only complaints that could be attributed to the active treatment were uncomfortable sensations in the ulcer when the current was turned on, which occurred in 13.6% of ulcers during active treatment versus 4.2% of ulcers during sham treatment.

Discussion

This double–blind, randomized, placebo–controlled, multicenter study demonstrated the safety and effectiveness of pulsed electrical stimulation, utilizing the Dermapulse device, for the promotion of healing of pressure ulcers. During the four weeks of double–blinded treatment, the stimulated ulcers healed more than twice as much as the sham ulcers and this difference was statistically significant. Multiple regression analysis confirmed a highly significant positive association of active stimulation with amount of ulcer healing. These healing rates are consistent with those reported in other studies of electrical stimulation.[4–10] In comparing these rates of healing, it should also be noted that these were all severe pressure ulcers, with all but one meeting the IAET criteria of Stage IV.

Some degree of healing in the sham group was not surprising because of the increased care given to the ulcers as part of the study procedures, and the maintenance of a moist wound environment. But active treatment significantly added to this "non–specific" treatment effect. The sham group did not show any further healing between weeks three and four, suggesting that the "non–specific" healing effects may have reached their maximum at three weeks.

Controlled clinical studies of pressure ulcers are inherently difficult. Nonetheless, this study fulfills the generally accepted criteria for a well–controlled trial. It was carried out in compliance with the Institutional Review Board and Informed Consent regulations. Blinding and randomization were done carefully and systematically. Investigators were trained in study procedures and agreed to conduct the study in compliance with FDA regulations. The study sites were closely monitored to insure compliance with protocol procedures and record–keeping requirements. Problems that arose in study conduct were identified and corrected. Analysis of data was carried out using accepted statistical techniques and included multiple analyses to characterize baseline and outcome parameters.

Multivariate analysis also indicated that metabolic condition and female sex were associated with better healing, and that presence of tunnels/undermining and a more severe stage of ulcer were associated with poorer healing. To the extent that the treatment groups were unbalanced with regard to these characteristics, the difference favored the sham group in every case. Based on these results, if there was any bias in the results due to these factors it would have been expected to work against finding an effect of the active treatment.

One potential weakness in the study design is the use of the length x width product to estimate wound size. In designing this study, other techniques such as photography with planimetry and tracings were considered. In order to be reproducible and accurate, photography requires expensive and extensive controls. Each center must be provided with standardized cameras and flash units and a means of controlling exposure, lighting, and focal distance. The angle of the photograph is critical and variations in angle may give false data on planimetric analysis. Wounds that curve around a body part are especially difficult to photograph accurately. Small changes in the position of the patient when photographing mobile tissue, such as the gluteal areas, can greatly distort the wound outline. Tracing is subject to many of these same problems, and still requires expensive planimetric analysis. For these reasons, we did not choose to use these techniques in this study.

It was recognized that the length x width product only estimates the true area of a wound. Nonetheless, it is quite reproducible

and simple to use clinically, and it is quite useful for monitoring changes in wound size (change in size, not absolute size, was the parameter of interest). If one were trying to distinguish quite small changes between treatments it would be more problematical, but the magnitude of changes observed in this study are quite readily measurable by this technique. Furthermore, the photographic record, though not adequate for planimetric analysis, at least provided visual confirmation of the large changes in wound size.

The results also point out that four weeks was a long enough study period to demonstrate significantly different healing results between the sham and stim groups, but was not long enough in most patients to produce complete healing. Complete healing required nine to twelve weeks treatment on the average.

Not all ulcers were continued long enough to determine if complete healing would occur. The usual reason for incomplete healing in the study was that therapy was stopped before complete healing took place. Of necessity, the experimental therapy, following a detailed protocol, and demanding extensive documentation, can only be carried out at specially designated investigational sites. Thus, for example, when a nursing home patient experiences an intercurrent illness and must go to the acute care hospital for a few days, the study is terminated for that patient.

The treatment proved to be extremely safe. There were no significant safety problems identified and no patient was withdrawn from the study because of an adverse event or skin irritation. The only treatment–related adverse events were the occurrence of uncomfortable sensations in the ulcers at the time of treatment, which happened in 13.6% of the stim ulcers versus 4.2% of the sham ulcers. All of these happened only once or twice during weeks of treatment and only at the beginning of therapy. Since sensations were perceived by only a minority of patients, some in each group, and only once or twice during all of the treatments, we do not believe this compromised the blinding.

We conclude that in this study pulsed electrical stimulation using the Dermapulse device was safe and effective for the promotion of healing of pressure ulcers as an adjunct to standard ulcer care, and suggest that it may prove to be an important addition to the care of this important health problem.

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