Comparison of Ultrasound/Ultraviolet-C and Laser for Treatment of Pressure Ulcers in Patients With Spinal Cord Injury

Ethne L Nussbaum
Irene Biemann
Betsy Mustard

Background and Purpose. *The purpose of this study was to compare in patients with spinal cord injury the effect on wound healing of nursing care alone with the effect on wound healing of nursing care combined with either laser treatment or a regimen of ultrasound and ultraviolet-C (US/UVC).* ***Subjects.*** *Twenty patients (22 wounds) were randomly assigned to the treatment groups.* ***Methods.*** *All patients received standard wound care consisting of wound cleaning twice daily, application of moist dressings, and continuous relief of pressure until the wounds were healed. The laser protocol consisted of three treatments weekly using a cluster probe with an 820-nm laser diode and 30 superluminous diodes (10 each at 660, 880, and 950 nm), an energy density of 4 J/cm^2, and a pulse repetition rate of 5,000 pulses per second. The US/UVC regimen consisted of five treatments weekly, alternating the treatment modality daily. The pulsed US was applied at a frequency of 3 MHz and a spatial average-temporal average intensity of 0.2 W/cm^2 (1:4 pulse ratio) for 5 minutes per 5 cm^2 of wound area. The UVC dosage (95% emission at 250 nm) was calculated each session according to wound appearance. The dosage level was E_1 for clean/granulating areas, E_3 for purulent/slow-granulating areas, E_4 for heavily infected areas, and $2E_4$ for wound debridement. Wounds were traced every 14 days, and surface areas were calculated using the Sigma-Scan Measurement System. Weekly percentage changes in wound area were compared.* ***Results.*** *Results showed that US/UVC treatment had a greater effect on wound healing than did nursing care, either alone or combined with laser.* ***Conclusion and Discussion.*** *Ultrasound/ultraviolet-C may decrease healing time and may allow faster return to rehabilitation programs, work, and leisure activities for patients with spinal cord injury who have pressure ulcers. [Nussbaum EL, Biemann I, Mustard B. Comparison of ultrasound/ultraviolet-C and laser for treatment of pressure ulcers in patients with spinal cord injury. Phys Ther. 1994;74:812–825.]*

Key Words: *Laser, Pressure ulcers, Ultrasound, Ultraviolet, Wound healing.*

Development of pressure ulcers is a problem that threatens the activities of every person with spinal cord injury (SCI). There are many precipitating factors for ulcer formation. Intrinsic factors include sensory, autonomic, and motor impairment; obesity; malnourishment; and diabetes. Extrinsic factors include unrelieved pressure, friction, direct trauma, and inadequate skin hygiene. One estimate of the rate of ulcers in persons with SCI following rehabilitation is given as 44%.[1] Records of the Lyndhurst Spinal Cord Centre, a rehabilitation unit in Toronto, Ontario, Canada, exemplify the cost of ulcer formation. Forty patients per year occupy beds, for an average 133 days each, specifically for pressure ulcer management. In comparison, overall admission at this center for the period 1992 to 1993 was 259 patients; 127 were new patients who stayed on average 76 days, and 132 patients were readmitted and stayed on average 58 days. The cost to the center of caring for patients with pressure ulcers is approximately $3 million per year; the condition obviously has serious economic implications.

Healing of pressure ulcers has traditionally been claimed by nursing staff to be dependent on nursing expertise. Nursing treatment often consists of using topical solutions, applying wet or dry dressings, and keeping the patient off the affected area. This treatment may necessitate patients being restricted to a prone-lying position in bed or on a wheeled cart for periods ranging from 10 days to 9 months, which has considerable consequences for the patients' psychological and physical rehabilitation. Surgical closure of pressure ulcers is an alternative that may be appropriate for some patients. Disa et al[2] reported that among patients with traumatic SCI, surgical closure of wounds resulted in a 38% complication rate, a mean hospitalization period of 40 days, a 26% incidence of unhealed ulcers at discharge, and a 79% incidence of ulcer recurrence at the site of the healed flap within a mean of 10.9 months.

Numerous physical therapy approaches to wound healing are described, including ultrasound (US), ultraviolet radiation (UV), and laser. One author (ELN) has had 8 years of experience treating wounds using US and UVC on alternate treatment days and has noted an impressive healing response to this regimen (Ethne L Nussbaum, personal communication). There are no published studies that have combined US and UVC (US/UVC) for wound management, nor studies that have used laser for wound healing in patients with SCI.

Physical therapists currently use US to treat wounds at a spatial average-temporal average (SATA) intensity of 0.1 to 0.5 W/cm^2.[3–7] Ultrasound dosages that clinically enhance wound healing have also been shown to produce cellular ultrastructural changes that are critical to normal healing.[8–13] Some controlled human trials are reported.[4,6] We decided to use US applied at a frequency of 3 MHz and at an SATA intensity of 0.2 W/cm^2 (1:4 pulse ratio) based on our previous clinical experience treating chronic wounds. Our literature review indicated that with similar settings, all of the reported animal and cellular studies demonstrated positive results. Higher SATA dosages and continuous-mode US in human studies did not always show patient benefit.[14,15]

There is sparse reference in recent literature to physical therapists' use of UV for wound healing. Existing literature concentrates on broad-spectrum UV light sources, predominantly A (UVA) and B (UVB) wavelength.[16,17] Authors state their treatment goals are to clear wounds of bacteria,[16] to remove slough,[16] and to stimulate granulation tissue[17] and epidermal growth.[17] Wills et al[18] demonstrated significantly improved healing of pressure ulcers using a Kromayer lamp (predominantly UVA and UVB), but suggested that variations of the protocol should be explored to establish optimum use of UV. High and High[19] stated that the use of UVA to promote granulation tissue was "well established," and their study was limited to "proving" the effect of UVB on bacteria in vitro. They demonstrated that an E_1 dose partially destroyed bacteria, whereas an E_4 dose rendered all bacteria nonviable. El-Batouty et al[5] conducted a comparative study on the effects of US and UVC on animal tissue healing. They concluded that US was more beneficial than UVC, although both regimens showed significant improvement compared with controls.

The effectiveness of UV energy in producing biological changes differs at different wavelengths. Selecting the maximal effective wavelength for a desired effect, therefore, will allow patient benefit at the lowest irradiation level. The effects of UV that enhance wound healing include increased epithelial cell turnover,[20] followed by temporary epidermal hyperplasia; release of prostaglandin precursors, which play a role in UV-induced erythema and may mediate the cell proliferation[21]; histamine release, which adds to the increased skin blood flow[22]; increased vascular permeability, which leads to cellular elements of repair in the dermis as early as 30 minutes after UV exposure[23]; accelerated rate of DNA synthesis[24]; and bacterial cell inactivation.[19]

Erythemal effectiveness peaks at 250 nm (UVC), has a lower peak at 297 nm (UVB), and rapidly decays from 305 to 320 nm.[25] The most acute damage is caused by UVB, which produces intense erythema and blistering above E_2. With UVC, blistering or intense erythema seldom occur, even at high multiples of the minimal erythemal dose,[26] which increases safety margins using UVC versus UVB. Ultraviolet radiation has to be absorbed to have any effect. The absorption spectrum of nucleic acids (DNA) peaks at 250 nm.[25] Ultraviolet radiation of 254 to 300 nm is less effective in producing DNA changes, and approximately four times more radiant energy is required at 310 nm for the same effect.[27] Cell or viral inactivation action spectra peak at 250 nm.[25]

EL Nussbaum, MEd, BSc(PT), is Clinical Associate, Physical Therapy, Mount Sinai Hospital, and Assistant Professor, Department of Physical Therapy, University of Toronto, 256 McCaul St, Toronto, Ontario, Canada M5T 1W5. Address all correspondence to Ms Nussbaum.

I Biemann, BSc(PT), is Senior Physical Therapist, Lyndhurst Spinal Cord Centre, 520 Sutherland Dr, Toronto, Ontario, Canada M4G 3V9.

B Mustard, MSc, BSc(PT), was Clinical Specialist (Research), Lyndhurst Spinal Cord Centre, at the start of this study. She is currently a clinical and research consultant in private practice in Calgary, Alberta, Canada.

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The action spectra for erythema and melanogenesis are separated only for wavelengths of less than 296 nm.[25] This means that at 250 nm, the increase in skin blood flow is maximized, whereas tanning is minimized. Above 296 nm (ie, UVA and UVB) for *unexposed white skin*, the threshold dose for erythema *equals* that of tanning, but with repeated radiation (and naturally dark skin), melanogenesis occurs at lower radiation levels than erythema.[28] This finding means that if treatment is repeated using UVA or UVB, increasingly less UV is transmitted to the dermis because of the tanning, and doses must be incremented to achieve the initial effect. Pigmentation, however, has minimal influence on absorption of UVC, as less than 10% of the radiation is in any event transmitted to the dermis, where tanning occurs.[29] The epidermis absorbs 90% of incident UVC. An increase in epidermal thickness (ie, hyperplasia) will not decrease absorption of 250-nm UV.[30]

Histological changes in skin are complete sooner after exposure to UVC (within 8 to 24 hours) than to longer wavelengths.[31] This finding may explain why cumulative damage is greater for UVA and UVB than for UVC. Ultraviolet-C is the least effective wavelength for producing skin tumors. Sterenborg et al[32] suggest that abnormal differentiation of a layer of cells that is committed to being sloughed off anyway (UVC) is not harmful, whereas mutation of the basal cells (UVA or UVB) may result in skin cancer. Tumorigenesis is proportional to a power of the daily dose,[32] so it is advisable to provide effective treatment while keeping radiation levels as low as possible.

In summary, UV action spectra for cell deletion, hyperplasia, accelerated DNA synthesis, and viral inactivation parallel the erythema spectrum. The spectra for photocarcinogenesis, pigmentation, and chronic vessel injury differ from the erythema spectrum. Our use of UVC for this study was based on our understanding that wound debridement and tissue regeneration would occur with the lowest irradiance, with the least undesired effects, and in the most advantageous time frame using UVC compared with using UVA or UVB.

The use of lasers for healing wounds is becoming increasingly attractive to physical therapists. A number of animal and in vitro studies[33-36] have demonstrated that laser irradiation has a significant effect on components of tissue repair. The settings, however, that should be used to produce the same effects in patients are still uncertain.[34] Many existing studies provide incomplete details of treatment characteristics, making this research difficult to replicate.[37,38] A nonrandomized study of laser and Kromayer lamp UV treatment effects on chronic human ulcers[38] suggested that wounds that have failed to respond to topical treatments may benefit from either modality. Similar anecdotal reports of successful laser treatment of human wounds are plentiful, but controlled human studies scarcely appear in the literature. Previous work does not compare lasers with an alternative physical therapy modality.

Evaluation of different approaches to wound healing is complicated by the heterogeneous nature of the population of patients who have chronic wounds. These patients include those with diabetes, SCI, collagen diseases, dementia, multiple sclerosis, peripheral neuropathy, and arterial or vascular disease. Attempts to standardize medical, physical therapy, and nursing procedures within or between institutions are also difficult. A spinal cord center provides an opportunity to evaluate treatment responses in a fairly homogeneous group of patients with a high rate of chronic wounds. Due to the limited size of such a center, the treatment environment is also more easily standardized. This setting provides a useful starting point for comparing effects of different modalities on wound healing.

The purpose of this study was to compare, in hospitalized patients with SCI, the responses of acute and chronic wounds to standard wound care alone with their responses to standard wound care in combination with either low-power laser therapy or US/UVC. The null hypothesis was that there would be no difference in mean rate of healing among the three different treatment approaches.

Methods and Materials

Subjects

Hospitalized patients at Lyndhurst Spinal Cord Centre with a diagnosis of SCI and skin wounds were invited to participate in the study. Patients who gave informed consent were randomly assigned to one of three treatment groups: a control group (n=9), a US/UVC group (n=5), and a laser group (n=6). Twenty patients entered the study. Two subjects each had 2 wounds, giving a total of 22 wounds. The subject characteristics are shown in Table 1.

Procedures

Treatment was carried out by each patient's attending physical therapist and nurse, who had been trained in the procedures. All procedures were done with patients in bed, positioned so that wounds were accessible. All subjects received standard wound care as described for the control group.

Control Group

This group received standard wound care only, consisting of wound cleansing twice daily using Hygeol* (1:20),† Jelonet dressings‡ to keep the wound surface moist, and avoidance of lying

*Wampole Inc, Perth, Ontario, Canada K7H 3E6.

†One part 1% chlorine solution diluted in 19 parts water.

‡Smith & Nephew Medical Ltd, Hull, England HU3 2BN.

Table 1. *Group Characteristics at Day 0*

Characteristic	Group Control (n=6)	US/UVC[a] (n=6)	Laser (n=6)
Age (y)			
Range	15–46	26–59	30–61
$\bar{X}$	36	42.2	42
Male:female ratio	5:1	6:0	5:1
SCI[b] level			
Cervical	3	4	2
Thoracic/lumbar	2/1	2/0	4/0
Diabetes			1
UTI[c]	5	6	5
Tobacco use	3	3	0
Regular alcohol use	2	4	1
Obesity[d]	3	3	3
Malnourishment[d]	2	2	1

[a]US/UVC=ultrasound/ultraviolet-C.

[b]SCI=spinal cord injury.

[c]UTI=urinary tract infection at day 0.

[d]Estimated health risk zones according to body mass index.

or sitting positions that would cause pressure on existing ulcers.

Laser Group

Laser treatment was applied using an Intelect 800 cluster probe[§] purchased for the study and checked for accuracy of output by the manufacturer. The unit consists of an 820-nm laser diode (beam spot diameter of 4 mm, average power of 15 mW) and 30 superluminous diodes (10 each at 660, 880, and 950 nm). The unit's power density is 120 mW/cm^2. Pulse repetition rate was set at 5,000 pulses per second (pps) (pulse duration of 160 nanoseconds). Energy density was 4 J/cm^2 (treatment time of 35 seconds).

Treatment was applied three times weekly. The probe was covered with shrink-wrap plastic to prevent contamination of wounds, and treatment was given in contact, with the probe centered over the ulcer. For small wounds, the probe spanned the ulcer and surrounding skin, and one exposure comprised the whole treatment. For larger wounds, in addition to a central application, the probe was advanced around the wound perimeter until the entire perimeter had been exposed to laser irradiation at 4 J/cm^2 per spot.

Ultrasound/Ultraviolet-C Group

Ultrasound treatment was applied using an Omnisound 3000,[‖] which was calibrated by the manufacturer at the start of the study. The size of the treatment head was 5 cm^2, and treatment was delivered at a frequency of 3 MHz and at an SATA intensity of 0.2 W/cm^2 (1:4 pulse ratio). Ultrasound was applied to intact skin surrounding the wound, using coupling gel for contact, for 5 minutes per 5 cm^2 of wound area.

The UVC treatment was applied using a Birtcher cold-quartz lamp[#] (95% emission at 250 nm). A test dose was not performed for each subject. At the start of the study, the output of the lamp was calculated for an individual with average sensitive skin, and an E_1 dose was found to be 15 seconds at 2.5 cm distance. The "expected lamp dose" was used for treatment of all skin types because pigmentation has a negligible effect on absorption of UVC. The dosage was calculated for each session according to the wound appearance. If the appearance was not consistent across the surface, each different area was exposed to an appropriate dosage. Details of the dosage scheme are shown in Table 2. An area of skin surrounding the ulcer was treated with an E_1 dose at each session by holding the unscreened lamp centered over the ulcer. To screen skin or ulcer from undesired exposure to UV, a 2-mm-thick layer of vaseline was applied to the skin or ulcer surface with a spatula. Over this was placed a layer of heavy-duty paper towel (type supplied in sterile dressing trays) with a hole cut in it. Treatment time for the E_1 dose to skin remained at 15 seconds for repeat treatments.

The US and UVC treatments were alternated daily for 5 days per week. Ultrasound was usually applied three times weekly, but in the case of purulent wounds, UVC was applied three times weekly.

In all groups, subjects without pressure ulcers on or around the buttocks were allowed to sit and participate in their regular rehabilitation program. Subjects with ulcers that would be subjected to pressure in sitting were restricted to prone lying on a wheeled cart, and they participated in a rehabilitation program designed to accommodate their "grounded" status.

[§]Chattanooga Corp, PO Box 4287, Chattanooga, TN 37405.

[‖]Physio Technology Inc, 1925 W Sixth St, Topeka, KS 66606.

[#]Birtcher Corp, 4371 Valley Blvd, Los Angeles, CA 90032.

Table 2. *Dosage Scheme for Treating Ulcers With a Birtcher Cold-Quartz Ultraviolet-C Lamp*

Surface Appearance	Dosage Level	Exposure Time (s)	Lamp-Skin Distance (cm)
Clear exudate, red "bubbled" granulation, edges almost level with skin	E_1	15	2.5
Cloudy or purulent exudate, pale or grayish color, not granulating, edges vertical	E_3	90	2.5
Dense yellow surface, necrotic debris, ulcer base not visible, edges vertical or undetermined	E_4	120	Contact
Adherent black crust	$2E_4$	240	Contact

Measurement Procedures

Patient information was collected by questionnaire and from hospital records. For each subject, a baseline tracing of the ulcer perimeter was drawn on a transparency. Maximum depth of the ulcer was recorded by placing a disposable measuring tape directly into the deepest part of the wound. Follow-up measurements were taken on the same day for all subjects and were repeated every 14 days until wound closure (no scab remaining). All tracings were made by one investigator (ELN) who was not employed at the spinal cord center and was blind to the subjects' group assignments. At the end of the study, the same investigator analyzed the tracings using a digitizer tablet and stylus pen.**

Data Analysis

A computer graphics program was used to calculate the area of each ulcer. The mean weekly percentage of change in ulcer area was calculated for individual subjects, and this value was interpreted as the rate of healing. Subjects' group assignments were not disclosed until this procedure was complete.

Initial ulcer areas were subjected to tests of normality (SAS univariate procedure††). Because distribution was normal, parametric tests were used for comparisons. Groups were compared for difference in initial mean ulcer size and mean weekly healing rates using a one-way analysis of variance. A Student–Newman-Keuls Test was used for comparing differences in healing rates between pairs of groups. The level of significance was set at .05 for all statistical tests.

Results

Four subjects did not complete the study. Two subjects (1 laser group subject, 1 control group subject) were transferred to acute care hospitals with medical complications. Two other control group subjects elected to have their wounds surgically repaired and withdrew from the study. Results were analyzed for the remaining 16 subjects (18 wounds).

Some baseline characteristics are shown in Tables 1 and 3. The difference between groups in initial mean ulcer size was not significant.

Healing rate was not equal under all treatment conditions; therefore, the null hypothesis was rejected (P=.032). Paired comparisons showed the significant difference was between US/UVC and laser treatment. The difference between the control group subjects and the other two groups of subjects was not significant. Table 4 shows mean weekly healing rates for individuals. Mean weekly healing rates for groups of subjects are shown in Figure 1. The overall mean weekly rate of healing for all subjects who completed the study was 36.54%. The two control group subjects who withdrew from the study after 2 and 4 weeks, respectively, showed a 5.32% and 14.56% weekly rate of healing. The mean healing rates for the remaining control group subjects at equivalent periods were 14.91% and 19.67%, respectively.

Percentage of change in ulcer size from pretreatment to complete healing is shown for individual subjects by group in Figures 2 through 4. The laser group showed great within-subject variability of healing from one measurement to the next. Three subjects in the laser group showed deterioration during the study (ulcers increased in size between 62% and 167%). The laser group subject with diabetes (patient 13) showed deterioration at measurement intervals 1, 3, 5, and 8. Deterioration was recorded for one control group subject (58% increase in ulcer size) and for one US/UVC group subject (1% increase in ulcer size). The mean treatment time to wound closure was 4.1 weeks. The cumulative percentage of healed ulcers against time for each group is shown in Figure 5.

Table 4 shows individual subjects ranked by rate of healing and by initial ulcer size, and no trend is evident. In the laser group, the subject with the largest and deepest ulcer ($5.4\ cm^2 \times 1$ cm) had the second highest rate of healing in that group (41.02%).

**Sigma-Scan Measurement System, Jandel Scientific, 65 Koch Rd, Corte Madera, CA 94925.

††SAS Institute Inc, SAS Cir, Box 8000, Cary, NC 27512-8000.

Table 3. *Characteristics of Pressure Ulcers at Day 0*

Ulcer Characteristic	Group Control (n=6)	US/UVC[a] (n=6)	Laser (n=6)
Ulcer area (cm^2)			
Range	0.7–3.3	0.9–3.1	0.9–5.4
$\bar{X}$	2.1	1.9	2.8
Ulcer depth (mm)[b]			
1–5	6	6	4
6–10			2
Ulcer duration[b]			
Chronic ulcer (>6 wk)	4	6	6
Acute ulcer (<1 wk)	2		
Ulcer etiology[b]			
Unrelieved pressure	4	5	4
Friction	2		
Cast pressure			2
Surgical incision		1	

[a] US/UVC=ultrasound/ultraviolet-C.

[b] Expressed as frequencies of occurrence.

Table 4. *Subjects Ranked by Weekly Healing Rate (Percentage) Shown Against Ulcer Location and by Initial Ulcer Size*

Subject No.	Group	Rank by Weekly Healing (%)	Rank by Initial Ulcer Size	Ulcer Site
13	Laser	0.63	3	Ankle
5	Control	4.34	10	Ankle
16	Laser	10.64	13	Trochanter
12a	Laser	21.49	7	Calf
14	Laser	23.59	17	Chest
1	Control	28.70	1	Ankle
8b	US/UVC[a]	31.01	2	Heel
11	US/UVC	34.30	12	Ischium
4	Control	34.44	14	Trochanter
3	Control	35.91	11	Coccyx
2	Control	39.97	4	Ankle
15	Laser	41.02	18	Coccyx
12b	Laser	44.80	6	Thigh
8a	US/UVC	49.98	8	Trochanter
6	Control	51.10	16	Coccyx
9	US/UVC	55.23	15	Coccyx
10	US/UVC	61.74	5	Chest
7	US/UVC	88.48	9	Coccyx

[a] US/UVC=ultrasound/ultraviolet-C.

The relationship of wound site to healing rate is evident in Table 4. The trend was for ulcers to heal faster in sites in which healing could also occur by contraction, such as coccygeal ulcers. Although all coccygeal ulcers healed faster than the median healing rate, the overall trend was for coccygeal ulcers to heal fastest in association with US/UVC treatment. There was a greater tendency in laser-treated ulcers for wound surfaces to appear purulent and pale (recorded at time of measurement by the investigator).

Discussion

The results show that to heal wounds in patients with SCI, the US/UVC treatment combined with standard wound care had an advantage over standard wound care combined with laser treatment and an advantage over standard wound care alone.

We considered factors that may have influenced our results. Smoking, regular alcohol use, unrelieved pressure, obesity, poor nutrition, and concurrent medical problems are reported to deter healing; ulcer size, duration, and location may be factors.[39] Among our subjects, fewer subjects in the laser group smoked and more subjects in the US/UVC group used alcohol regularly. The proportion of obese and malnourished subjects was similar in all groups. The incidence of urinary tract infection was high in all groups. Urinary tract infection is a common problem for patients with SCI, and none of the subjects were treated with antibiotics for the condition. Our finding that initial wound size did not affect healing rate supports the work of previous authors.[4] These factors, therefore, do not explain why US/UVC was the more effective treatment.

We do not believe that the distribution of ulcer sites influenced group mean healing rates (Tab. 4). The interaction between US/UVC and coccygeal ulcers (healing rates of 55%–88%) produced greater benefit than the interaction between coc-

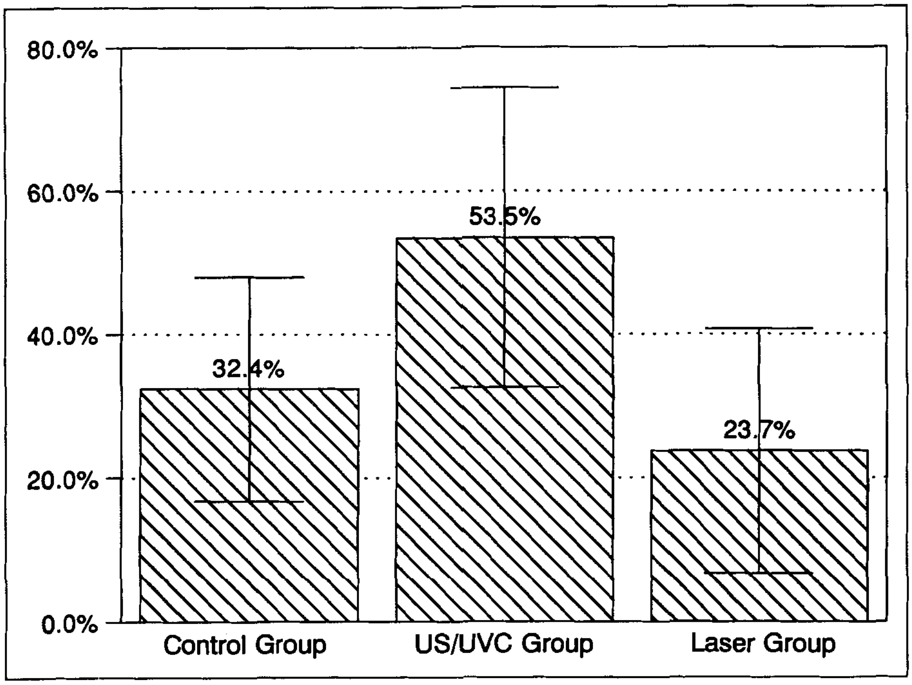

Figure 1. *Mean percentage of change per week in ulcer size (±1 standard deviation) from day 0 to complete healing for control, ultrasound/ultraviolet-C (US/UVC) treatment, and laser treatment groups. Results of analysis of variance significant at P=.032.*

cygeal ulcers and laser or control treatment (healing rates of 36%–51%).

Relative chronicity of wounds may be a factor in healing rate (Tab. 1). Subjects 2 and 6 in the control group had acute wounds that may have contributed to the relatively better results of these subjects in the group. Two control group subjects who were readmitted to the spinal cord center for management of chronic wounds may have elected surgery because they were dissatisfied with their progress. Their withdrawal may have improved the results for the control group, as their healing rates at 2 and 4 weeks were below the group means at equivalent periods. The inclusion of the only two subjects with acute ulcers and withdrawal of two subjects with slowly healing ulcers from the control group may explain why the control group averaged a better healing rate than the laser group, and why the difference between control group and US/UVC group healing rates was not significant.

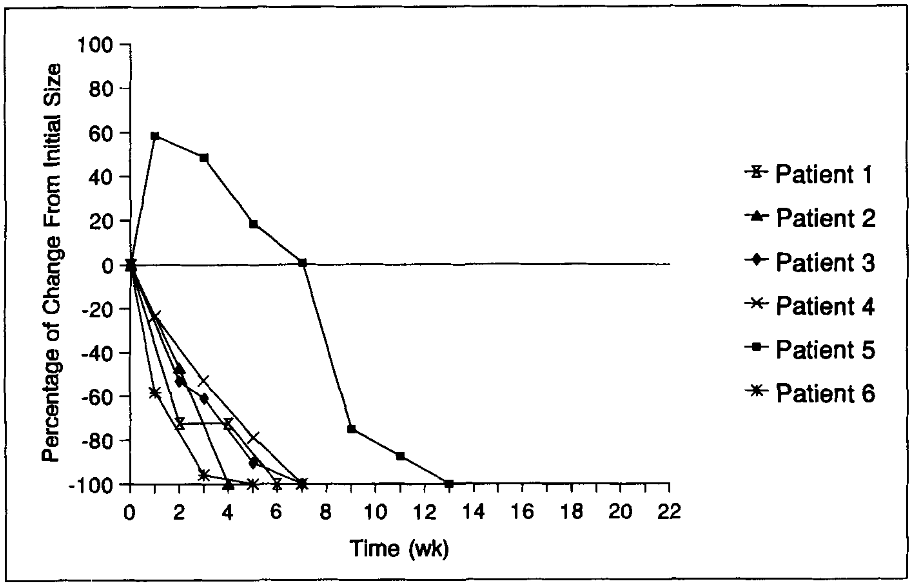

Figure 2. *Percentage of change in ulcer size from day 0 (0%) to complete healing (-100%) for subjects receiving standard wound care only.*

Subject 13, who had diabetes, showed the lowest healing rate (4.41%) (Fig. 4). Tissue ischemia due to diabetes could conceivably compound the problem of pressure ulcer healing that already exists for patients with SCI. Explaining this subject's healing rate on the basis of the diabetic condition, however, is pure conjecture. The investigator did not report any unusual pallor or coldness of the subject's lower-extremity skin during measurement.

Several personnel administered the three treatments. Because this method of administering the treatments reflects clinical practice, the results should be a valid indicator of the potential of the treatments to influence wound healing in this population.

We are satisfied that our method of collecting data was reliable. There is support in the literature for calculating ulcer area by the transparency tracing and digitizer method; intratester reliability of .99 is reported.[40] Measurements were performed by one researcher external to the institution and blinded to patients' group assignment.

Our failure to find a stimulating effect for laser therapy is surprising, because physical therapists' clinical impression is that it is effective for wound healing.[41] The problem of sorting out optimum treatment char-

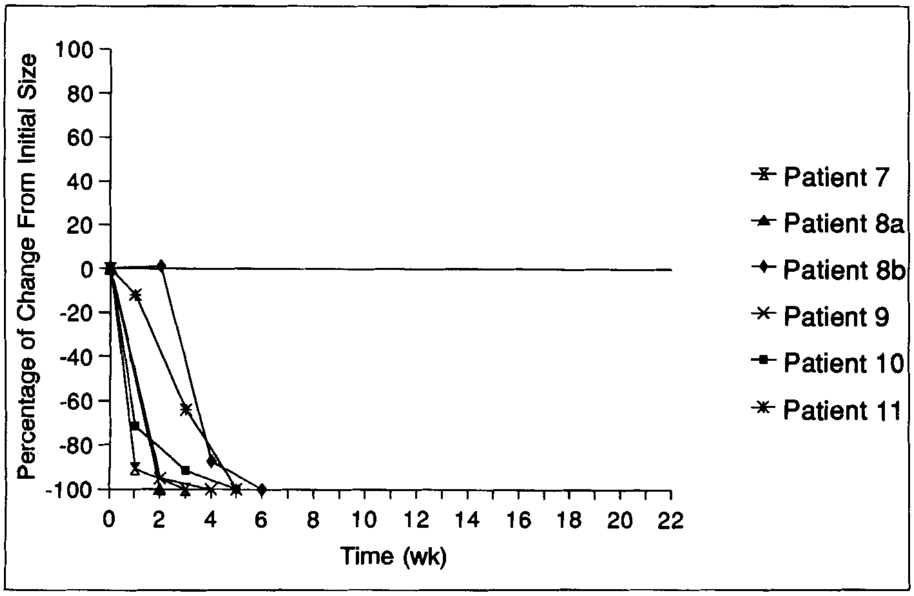

Figure 3. *Percentage of change in ulcer size from day 0 (0%) to complete healing (-100%) for subjects receiving ultrasound/ultraviolet-C treatment.*

acteristics for laser therapy may be complicated because of the large number of variables. Our results may be dependent on the wavelengths we used, pulse duration, energy density (ED), power density (PD), pulse repetition rate (PR), treatment repetition rate, or a combination of all of these factors.

In our study, we used 820-nm laser irradiation, in combination with noncoherent light, at an ED of 4 J/cm^2. Palmgren et al[42] used 820-nm laser irradiation (PD not given) at an ED of 1.6 J/cm^2 on infected postsurgical abdominal wounds and showed significantly better healing for the laser group. Results such as those reported by Palmgren et al accord with those of cellular studies that show laser irradiation at 820 nm has a positive effect on the immune system with the ED as low as 1.2 J/cm^2 at 5,000 pps.[43] We cannot propose that the differences between the results of our work and the results reported by Palmgren et al are due to our higher ED or multiple wavelength source because the PD and PR details of Palmgren and colleagues' work are not available. An additional factor may be that Palmgren and colleagues' subjects had wound dehiscence due to infection, but did not have vascular disturbances, inherent in SCI, that would additionally delay healing.

In our study, ulcer surfaces appeared purulent more often in association with laser treatment. Karu et al[44] observed laser effects on bacterial cultures using a wavelength (950 nm) and PD (120 mW/cm^2) we have used. They showed a relationship between PR and ED; at 5,000 pps, bacterial proliferation was inhibited only when the ED exceeded 30 J/cm^2. This finding suggests that ulcers may need to be treated with higher dosages periodically to control bacterial infection. Our use of laser treatment at 5,000 pps at a constant ED of 4 J/cm^2 may explain why ulcers appeared purulent in our study. Additional benefit to wound healing may be gained from periodic higher dosages if El Sayed and Dyson's findings in injured rat skin[36] have a parallel in human skin. Their laser protocol, using a cluster probe device similar to ours (it had an additional 940-nm diode) and an ED of 10.8 J/cm^2, increased the number and degranulation of mast cells. Mast cell degranulation releases an array of chemical factors that trigger repair events.

Young et al[35] tested the response of macrophage-like cells to laser irradiation and noncoherent light. They found that calcium uptake showed maximum enhancement at an ED of 4 to 8 J/cm^2, with wavelengths of 660, 820 (laser), and 870 nm and a PR of 5,000 or 16 pps. It has been noted that in clinical practice, ulcers that appear to plateau in their healing process respond favorably to a change of PR from 5,000 to 16 pps until heal-

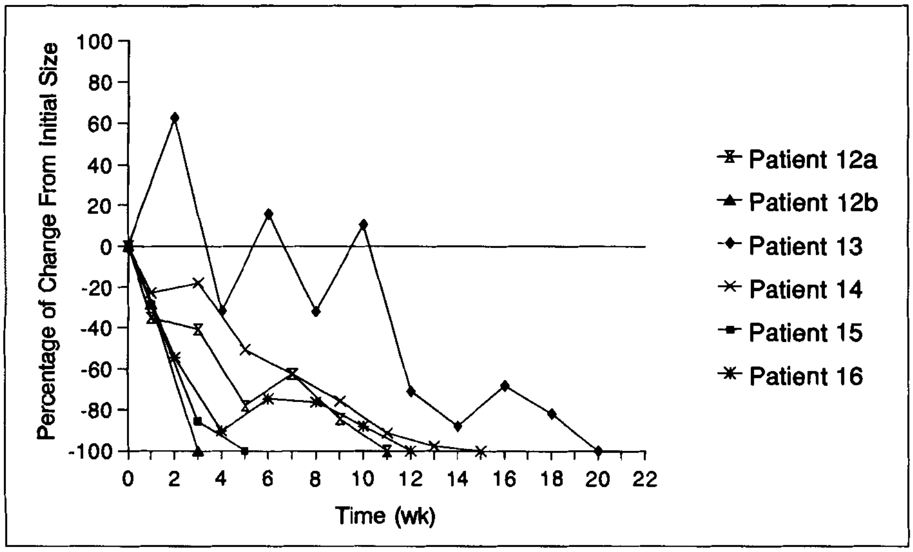

Figure 4. *Percentage of change in ulcer size from day 0 (0%) to complete healing (-100%) for subjects receiving laser treatment.*

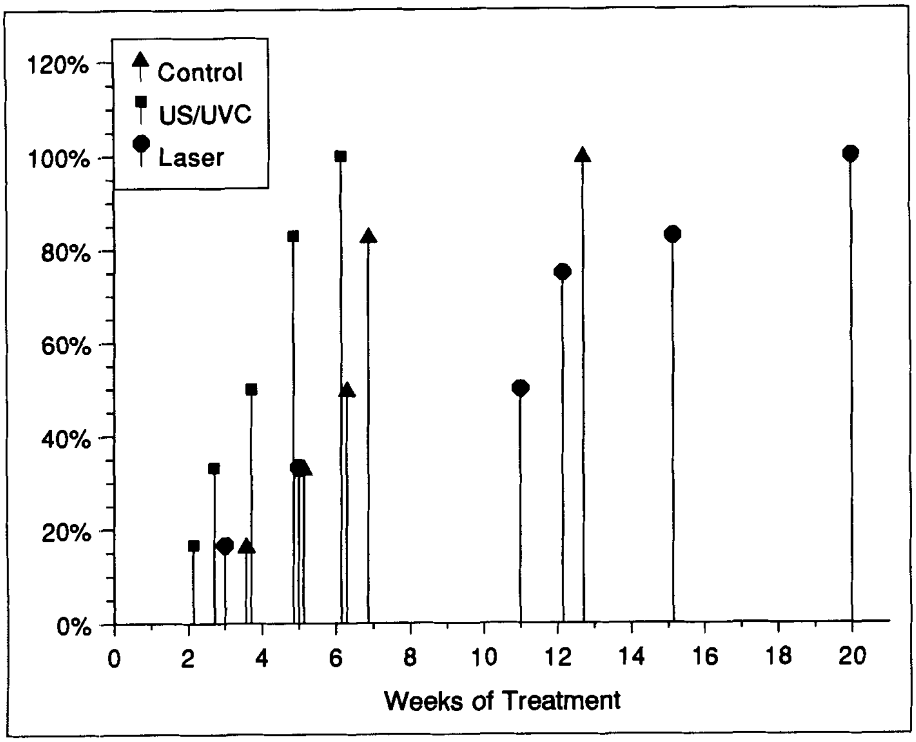

Figure 5. *Cumulative percentages of healed ulcers by treatment group against time. (US/UVC=ultrasound/ultraviolet-C treatment.)*

ing is complete or the next plateau occurs (Ethne L Nussbaum, personal communication).

Young and colleagues[45] also studied fibroblast proliferation using the 820-nm laser at 5,000 pps. Their results suggest that optimum relationships exist between PD and ED. The maximum enhancement of proliferation could be achieved at low ED (2.4 J/cm^2) using a high PD (800 mW/cm^2); alternatively, a higher ED (7.2 J/cm^2) using a lower PD (400 mW/cm^2) was equally effective. In further research,[46] they showed that maximum stimulation of macrophage release factors was effected by 660-nm noncoherent light. For this effect, at a PD of 120 mW/cm^2, the optimum ED was also 7.2 J/cm^2. With the low PD of our laser device (120 mW/cm^2), better results might have been achieved with an ED higher than 4 J/cm^2.

Other studies of laser effects on tissue repair[33,47–50] used alternative wavelengths (904 nm and HeNe 632.8 nm), PRs (73, 3,800, and 4,672 pps), and EDs (1.22–10 J/cm^2) to our study.

Because these authors report contradictory findings, it is difficult to compare our results with those of their studies. Comparison of the varying wound models and laser characteristics suggests that, in addition to the inverse relationship between PD and ED, the degree of benefit may be dependent on the extent of tissue damage. Significant acceleration of wound healing may occur only in the presence of a critical level of damage. Thus, animal wounds that consist of linear incisions without infection or ischemia may be inappropriate models for studying laser effects on chronic wounds.

The literature on US for wound healing deals mostly with chronic venous ulcers. We have not found any work specifically on ulcers in subjects with SCI. Although the development of ulcers differs in venous disease and SCI, the patients with these conditions have in common problems of tissue hypoxia, secondary bacterial contamination, and delayed wound healing. Therefore, analyzing use of US in treatment of venous ulcers may be helpful in explaining the results of our study.

The research we reviewed does not consistently demonstrate that US benefits patients with venous ulcers. Eriksson et al[14] showed no benefit treating ulcers with US twice weekly at 1 MHz with a continuous spatial average intensity of 1.0 W/cm^2, whereas Dyson et al[4] showed significant benefit treating ulcers three times weekly at 3 MHz with an SATA intensity of 0.2 W/cm^2 (1:4 pulse ratio). Callam et al[6] used a higher US intensity (continuous SATA intensity of 0.5 W/cm^2) than that of Dyson et al[4] once weekly at 1 MHz and found a significant benefit. When Lundeberg et al,[15] however, used the same SATA intensity dosage as Callam et al,[6] but in a pulsed mode with a pulse ratio of 1:9, the treatment showed only a "clear tendency" to benefit healing. It seems likely that Eriksson and colleagues' method[14] would have produced tissue heating, which would not be well dissipated by already hypoxic tissues, and could explain the lack of benefit found in their study.

There is also evidence from animal studies[51] that US applied continuously at 1 W/cm^2 can have an inhibitory effect on wound healing. Because Lundeberg and colleagues' SATA intensity dosage[15] was the same as that used by Callam et al,[6] some explanation is needed for the results obtained by Lundeberg et al. Two variables were different in the study by Lundeberg et al.[15] First, US was delivered with a higher temporal peak intensity (1:9) than either Dyson et al[4] or Callam et al[6] used, which might be damaging to hypoxic tissues. Second, there was a difference in treatment repetition rate. Lundeberg et al[15] treated subjects three times weekly for 4 weeks, then twice weekly for 4 weeks, then once weekly for 4 weeks. An initial trend for greater improvement in the US group diminished between 4 and 6 weeks, in parallel with the reduced treatment sessions. Treatment administered three times weekly may be the optimum plan when using low-dosage pulsed US.

Difference in technique of US application may underlie the lack of benefit found in some venous ulcer studies, even when low SATA intensity is used. Shamberger et al,[52] in an animal study on wound healing, were unable to show the benefit of using US at 5 MHz, applied continuously at 0.1 W/cm^2. However, they used a stationary transducer technique, and they reported that the temperature elevation at that intensity was approximately 5°C.

Our results agree with current research on experimental wounds in animals and surgical wounds in human subjects, which shows a significant advantage for healing with US at very low SATA intensity (0.1 W/cm^2 with a 1:4 pulse ratio).[8,53–55] As the subjects in previous studies did not have vascular disturbances and some wounds were sutured, however, it could not be assumed with certainty that the findings could be extended to patients with SCI.

There appears to be no previous study of UVC effects on wound healing in human subjects, which limits comparison of our UV regimen with other work. Basford et al[37] conducted a study comparing laser treatment (632.8 nm), UVC, occlusion, and exposure in wound healing in pigs. The UVC dosage was at the E_1 level, delivered twice daily (E_2 equivalent). Wounds in all treatment groups showed a tendency to heal faster than exposed wounds, but only in occluded wounds did the tendency reach clinical significance. The authors concluded that there was no advantage in using laser or UV treatment. It is unfortunate that Basford et al did not also assess the effect of each modality combined with occlusion. Different nursing regimens are known to influence rate of healing, and optimum clinical conditions appear to be dependent on a moist wound surface.[56] When wounds are allowed to dry out, viable tissue is subjected to secondary desiccation.

Basford and colleagues' work[37] is also interesting because it confirms that laser treatment, and to a lesser extent UVC treatment, has systemic effects. They found clinically reduced hypertrophic healing in treated and untreated wounds on the same animal. For laser treatment, the advantage was observed in 11/12 treated wounds and 21/24 untreated wounds on the laser-exposed pigs. For UVC treatment, the advantage was observed in 8/12 treated wounds and 12/24 untreated wounds on the UV-exposed pigs. In two pigs that had only occlusion or exposure, 1/12 and 2/24 wounds, respectively, were not hypertrophic. The reduced hypertrophy is of dubious advantage because the effect was lost 1 week after closure. What is important is the fact that control lesions were obviously affected by the treatments, which casts into doubt the validity of Basford and colleagues' results. Basford and colleagues' study appears to be the first indicator that UVC has a systemic effect.

Crous and Malherbe[38] compared laser and Kromayer-UV treatment of varicose ulcers that had failed to respond to medical management. Their UV regimen appeared similar to the UVC regimen of our study. An E_1 dosage was applied to surrounding skin and granulation tissue and an E_4 dosage (or greater) was applied to sloughing tissue, three times weekly. It was not stated whether each E_1 dosage to skin was increased over the previous dosage, which is expected using UVA and UVB.[57] Although both treatments appeared to be effective, the authors could not infer that either method was more advantageous, perhaps due to the very chronic state (up to 30 years) and large size of the ulcers and the short duration (4 weeks) of their study. No ulcers closed during the study period.

Wills et al[18] conducted a controlled study on superficial pressure ulcers (mean area=1.7cm^2) of 16 patients (mean age=84 years) in an extended care facility. They treated wounds initially with an E_4 dosage of UVA and UVB and continued twice weekly for 8 weeks using an E_2 dosage. All ulcers were healed at 10 weeks, but healing rate was significantly greater in the UV-treated ulcers, which averaged 6.25 weeks to heal. Patients were older and clinical diagnosis was different from our study, which complicates direct comparisons. Our US/UVC group's ulcers, however, healed in a mean time of 4.1 weeks. Wills et al stated that skin was screened to within 1 mm of the wound edge, which would seem to exclude a potential site for stimulating increased blood flow to the wound. The E_2 dosage was also increased by 50% at each treatment so that wounds requiring 16 treatments received a final exposure lasting 7.5 minutes. The factors that prevent transmission of UVA and UVB are skin thickening and pigmentation; therefore, it is surprising that Wills et al decided to increment the dosage when they were not exposing skin. Many factors were different in our study that might account for our better results—differences in irradiance levels, possible advantages of UVC versus UVA and UVB, our treatment of surrounding skin, and our additional US treatments.

Nordback et al[58] experimented with rat wounds and treated daily using UVA and UVB. They found a significant effect of UV on wound closure between 4 and 15 days, although the effect then diminished. They increased their treatment dosage daily from day 0 to day 8 but not from days 9 to 19. Regimens that start with low dosages followed by repeat exposures before histological changes of previous treatment are complete can cause severe cumulative phototoxic reactions in normal human skin.[59] It is difficult to know whether the initial wound healing effect shown by Nordback et al diminished because of overtreatment or undertreatment. Nordback et al also compared treatment outcome with control wounds on the same animal, which will have confounded their results.

Research on US and UV has depended mainly on animal wounds consisting of surgically excised skin.[5,12,52–54,57–59] The wound models excluded common problems associated with delayed healing, such as ischemia, infection, necrotic debris, loss of large amounts of subcutaneous tissue, sinus formation, and induration of surrounding tissue.[13] Our hypothesis is that US and UVC are complementary for wound healing, as each modality on its own does not address all the problems of delayed healing. Ultraviolet-C is specifically used for rapid wound debridement—its effect on surface slough and eschar is singularly dramatic—and against ongoing bacterial contamination. Necrotic debris blocks migration of fibroblasts, capillary budding, and epithelization,[13] and infection is a major deterrent to healing. Ultrasound has to be administered in contact, which precludes its application to central areas of large deep wounds. Ultraviolet treatment is ideal for these areas. The incident UV is absorbed directly by extracellular fluid components and capillaries.[60] This absorption promotes endothelial cell proliferation, giving the surface its typical red-bubbled appearance. Ultraviolet treatment markedly increases epithelial cell proliferation in superficial wounds. Cells migrate from intact skin and undestroyed portions of epidermal appendages (eg, hair follicles), which results in enhanced epithelial growth from within, as well as from edges of wounds. This growth complements the effect of US applied to peripheral skin only.

We hypothesized that US, alternating with UVC, would provide comprehensive wound management. One of the limitations of our study was that we did not compare the outcome of wound management combining wound care with placebo US or laser treatment. Because the US/UV regimen involves daily treatment, a placebo effect should be considered in further work, and the combined regimen should be compared with either US or UVC alone.

Conclusion

This study showed that our experimental conditions of laser treatment had no benefit for wound healing in patients with SCI. Although some clinical trials and animal and cellular studies suggest that laser treatment benefits wound healing, optimum laser characteristics for clinical treatment have still to be determined. Because laser treatment is time effective compared with US/UV, we consider it important to further investigate its use in wound healing. In future work, we would assess the advantage of using a higher ED with a 120-mW/cm^2 laser, varying the PR from 5,000 to 16 pps for wounds that heal more slowly than average and we would assess the effect of a bactericidal dosage (30 J/cm^2) on wound surfaces that appear purulent. Laser irradiation may still be beneficial for treating these wounds if used in a customized manner.

Our results show that US and UVC used separately on alternate days, five times weekly, have an advantage for wound healing in patients with SCI. The improved rate of healing in the US/UVC group in this study may be due to the combination of US and UVC rather than selection of the optimum characteristics for either modality. Previous clinical experience (Ethne L Nussbaum, personal correspondence) suggests that this treatment approach is effective for other types of wounds, such as diabetic ulcers, venous ulcers, and Grade IV pressure ulcers. This method needs to be tested on other patient populations, and this study should be extended to a larger number of patients in a placebo-controlled trial.

Chronic wounds are costly to patients. Their management interrupts work and leisure activities. Hospitalization is often required, and rehabilitation programs are delayed. Wounds are also costly to institutions because of increased nursing requirements, pharmacological products, and prolonged bed occupation. A surgical approach to the problem necessitates at least 6 weeks of hospitalization and may offer only a short-term solution for patients with SCI. A method of physical therapy that can reliably increase the healing rate of chronic wounds will be an advance in patient care.

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