

Low Frequency Pulsed Current and Pressure Ulcer Healing

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Abstract—In spite of the extensive clinical work reported in the area of electrical wound healing, electrical stimulation to augment chronic wound repair is still far from being widely accepted in clinical practice. Problems in designing clinical studies (size of the sample observed, control group, ethics of the procedure), evaluating treatment efficacy, rationales for use of the treatment, and unknown underlying mechanisms contribute to the aforementioned fact. In the present study, we evaluated low frequency electrical current for its beneficial effects in pressure ulcer management. Seventy-three spinal cord injured patients with 109 pressure ulcers participated in the study. Patients were randomly assigned to a control group receiving conventional treatment of their ulcers, or to a stimulation group, in which the ulcers were additionally treated with low frequency pulsed current. A comparison of the two groups showed significantly higher average healing rate for the stimulated group. Patients from the control group had the opportunity of crossing over to the stimulation group after the required control period of four weeks. This group (the crossover group) was analyzed separately. In all but one ulcer out of 20, an improvement in the healing process was observed after electrical stimulation was initiated.

Index Terms—Electric stimulation, electrotherapy, wound healing, pressure ulcer.

I. INTRODUCTION

FOR SPINAL cord injured (SCI) patients, pressure ulcers are a troublesome problem in rehabilitation. Patients are subject to the discomfort, stress, and high costs of long-term conventional treatment required for the healing of such ulcerations [1], [2]. The development of a pressure ulcer involves intrinsic and extrinsic factors [3]. Important intrinsic contributors to the development of pressure ulcers in SCI patients are sensory loss and loss of vasomotor control resulting in the lowering of tissue resistance to pressure, especially in the early stages following the spinal cord lesion [3], [4]. The most decisive extrinsic factor contributing to the formation of these typical chronic wounds is repetitive and prolonged pressure on particular parts of the body (most commonly over bony prominences: sacrum, trochanters, heels,

etc.). The combination of these intrinsic and extrinsic factors causes a complex chain of processes resulting in pressure-induced ischemia, which is considered to be the primary cause of pressure ulcer formation [4]. Even the most attentive conventional medical care, the use of a special pressure relieving device, and a carefully chosen diet often prove ineffective in prevention of pressure ulcer formation and/or initiation of the healing process. Very often, pressure ulcers prove to be resistant to standard therapy for several months or even years, developing into a chronic state and requiring plastic surgery. These wounds are also common among other immobile patients and the elderly [5]. A variety of nonstandard treatments for chronic wounds, such as electrical [6]–[17] and electromagnetic [18], [19] stimulation, hyperbaric oxygen treatment [20], use of ultrasound [21], and recently, the use of growth factors [22], [23] have been recommended. In spite of the favorable results reported, these methods are frequently considered curiosities, not potential remedies. Some arguments against wider application of the aforementioned treatments have arisen from critics of the studies and merit careful consideration. The major objections relate to:

- lack of controlled studies,
- inadequate quantification of the healing process, and
- ignorance regarding the mechanisms through which treatment might influence healing.

A survey of the existing literature on chronic wound-management reveals that, since the 1960's, numerous clinical studies have been performed on the application of various types of electrical and electromagnetic stimulation [24]. Besides the aforementioned objections, scepticism and confusion has been further increased by the variety of electrical stimulation patterns proposed for chronic wound management. In five of the studies, constant direct current (DC) stimulation was used [6]–[10]. A controlled study using DC stimulation was performed by Carley and Wainapel, and their results showed a 1.5 to 2.5 times faster healing rate for the treated group as compared to the control group [10]. Pulsed low intensity direct current (300–600 μA) has been shown to accelerate healing of indolent pressure ulcers in the study by Wood *et al.* [11]. Pulsed direct current of somewhat higher amplitude (29.2 mA) has been employed for the treatment of chronic dermal ulcers (pressure ulcers, ulcers caused by vascular insufficiency, trauma or surgery) by Feedar *et al.* [12]. The polarity of the stimulation electrode on the wound, as well as the pulse frequency, have been changed during the course of the study. This led to quite a complicated stimulation protocol for which

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no convincing explanation is given. However, a significant beneficial effect on healing of treated chronic dermal ulcers was observed. Two studies dealing with a homogeneous population of patients with pressure ulcers demonstrated accelerated healing due to stimulation with high voltage pulsed direct current (twin-peaked pulses of 100–200 V, 100 pps) [13], [14]. The polarity of the treatment electrode on the wound was kept negative in the study by Griffin *et al.* [13], while it was alternated in the study by Kloth and Feedar [14]. Biphasic pulsed current (pulse duration of 0.4 ms, frequency of 80 pps) has been employed for preventing and reversing established ischemia in skin flaps of patients who underwent reconstructive surgery for mammary carcinoma [15]. The same type of biphasic pulsed electrical stimulation as used in the present study has been shown to have a beneficial effect on healing of vascular wounds, pressure ulcers in geriatric patients, and posttraumatic wounds [16]. Kaada reported that low frequency transcutaneous electrical stimulation applied at remote sites (acupuncture points on the hand) promoted healing of chronic ischemic ulcerations [17]. In a double blind study on the effects of low-frequency pulsed electromagnetic fields on skin ulcers of venous origin, an improvement in the healing process of stimulated ulcers was reported by Ieran *et al.* [19].

Our rationale for using electrical stimulation (ES) to enhance wound healing was based on observations of some positive side effects of functional electrical stimulation (FES) which is being routinely used in paretic and paralyzed patients. Besides eliciting functional movement, the therapeutic effects of ES were also noted [25], [26]. The aforementioned patient population is at high risk of developing pressure ulcers. However, patients included in the FES rehabilitation program developed markedly fewer pressure ulcers, and surprisingly, existing chronic ulcers healed at a faster rate.

In order to verify this observation, we used the same ES parameters as in our FES program, except current amplitudes, and performed a study on the effects of electrotherapy on chronic wound healing. In this paper, the quantitative data obtained from a six-year controlled study will be presented. Pressure ulcer etiology is not yet totally understood and the healing mechanisms involve complex processes in a nonhomogeneous population. In view of the numerous stratification variables to be considered—such as age, duration of disability, ulcer area, depth, location, duration of ulcer prior to inclusion in the study, etc.—it is difficult to conduct an adequately controlled study. This is why a protocol comprising random parallel group-study and crossover study elements was carried out.

We present a comparison of the results obtained from the control and ES groups, both of which were treated with conventional wound care methods, but in addition, ulcers in the stimulated group also received pulsed current electrical stimulation. This paper emphasizes the data obtained from the group which crossed over from the control group to the stimulated group. A characteristic of the crossover group is that each ulcer served as its own control, thus assuring that most of the aforementioned variables were constant. The possible physiological mechanisms through which ES might have affected wound healing are discussed.

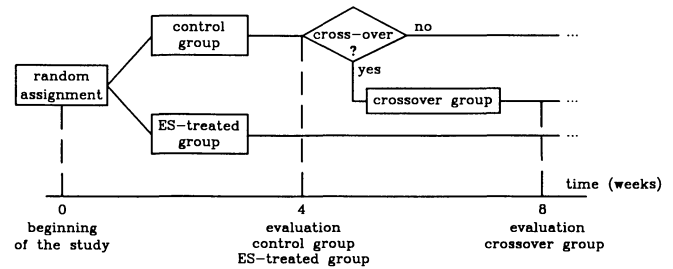


Fig. 1. Study design.

II. EXPERIMENTAL METHOD

A. Subjects

Seventy-three subjects with 109 pressure ulcers altogether participated in this study. The patients ranged in age from 18 to 68 years (36 ± 15 years, mean \pm standard deviation). All subjects were volunteers from the spinal cord injured inpatient population. They had no known additional diagnosis for diabetes, vascular disease, or cancer. When included in the study, the patients had been disabled from one month to several years (32 ± 60 months, mean \pm standard deviation). The pressure ulcers had developed in the decentralized skin below the spinal cord lesion level and, prior to patients entering the study, they were treated only with standard wound care. Twenty-four patients had more than one pressure ulcer at a time. The duration of the pressure ulcers before they were included in this study varied from one month to several years. Out of 109 ulcers, 34 were located on the sacral area, 28 on critical areas of the legs (heel, foot, knee), 27 on the trochanter areas, 9 on the gluteal area, and 11 on other locations.

B. Study Design

The patients were examined by a physician for an initial assessment of their wound status and related factors. The experimental procedure was explained to them and all patients agreed to participate in the study by signing an informed consent form. The format of our study design is shown in Fig. 1. Patients were randomly assigned either to a control group, where they received standard wound care treatment, or to a stimulation group (ES-treated group) in which ulcers were additionally treated with ES. After four weeks, i.e., at the end of the required control period, patients from the control group were offered the opportunity of crossing over to the ES-treated group. This was also done for obvious ethical reasons.

C. Control Group

The 31 patients assigned to the control group received standard treatment of their ulcers [27]. The standard treatment included initial selective debridement, the application of a new standard dressing to the ulcer two or more times per day, as needed, and a broad spectrum antibiotic in cases of infection, which were rather rare. The SCI patients included in the study were lying on dry-floatation mattresses and were turned to a new position every four hours during the night. The patients were included in the standard rehabilitation program

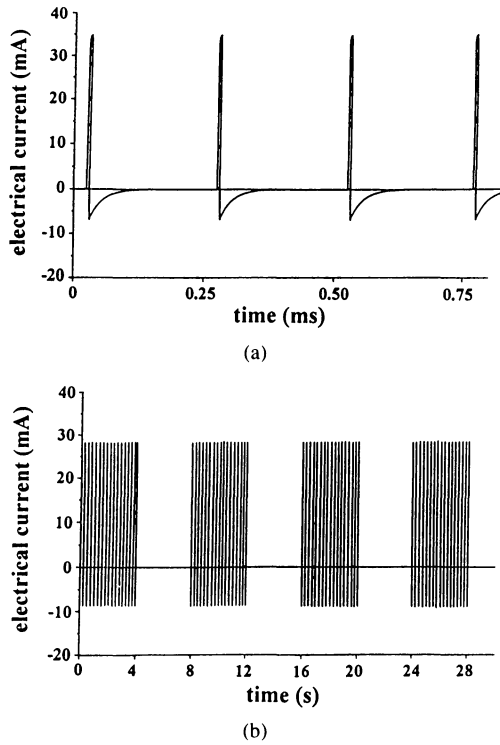


Fig. 2. (a) Biphasic, asymmetric pulsed current stimuli. (b) Electrical stimulation duty cycle (redrawn from [16]).

(FES excluded), one to two hours per day, depending on their conditions.

D. ES-Treated Group

In addition to the conventional treatment, the 42 patients in this group received two hours of ES daily, five days a week. The ES was delivered through the ulcer tissues via two flexible self-adhering electrodes measuring 75 or 50 mm in diameter (Pals plus, Axelgaard Manufacturing) which were placed on healthy skin approximately 3 cm from the edge of the ulcer. Biphasic, asymmetric, charge-balanced pulses having a repetition frequency of 40 pps and a pulse duration of 250 μ s were used. Pulses were delivered repeatedly in trains lasting 4 s, followed by a 4-s pause (Fig. 2). The amplitude was adjusted (up to 35 mA) for each patient individually to achieve minimal muscle contraction, when feasible. Because of visible muscle contractions, it was not possible to conduct a double-blind clinical trial.

E. Crossover Group

This group included patients who, after four weeks of conventional treatment, experienced ES treatment, as described above.

F. Evaluation of the Healing Process

To evaluate the healing process, weekly measurements of the wound area were performed. Changes in other very important ulcer measurements, such as the wound depth and the appearance of granulation, were recorded as well. Data

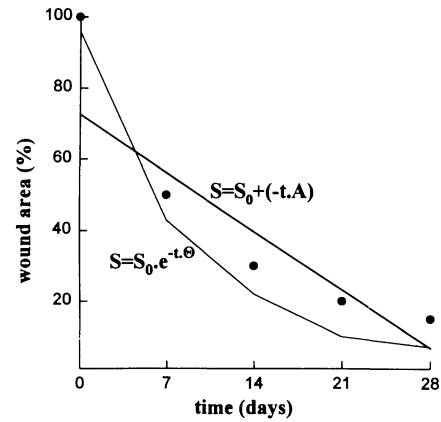


Fig. 3. Illustration of the linear and exponential fitting method and corresponding healing rates.

obtained during the first four weeks of treatment were included in the data analysis for evaluation of treatment outcomes.

An attempt to describe and assess the healing process or the rate of healing raised the question regarding the criteria which optimally govern the time-courses of the measured wound areas. Most researchers assume the healing process is linear. Others claim that for the majority of chronic wounds the fitting errors are reduced when exponential fitting is applied, i.e., the healing process exhibits an exponential behavior [3], [28], [29]. In order to avoid any of the mentioned assumptions, we will evaluate obtained wound area values using both quantification methods (Fig. 3), which could be described by the following equations:

exponential fitting $S_{exp} = S_0 * e^{-t\Theta}$,

linear fitting $S_{lin} = S_0 + (-A * t)$,

where S_0 represents the fitted initial wound area, S_{exp} and S_{lin} are the wound area at time t , and Θ and A are the healing rates for the best exponential and linear fitting, respectively. The parameters Θ and A , as a measure of the rate of wound healing expressed in % per day, are illustrated in the following manner: if healing rate = 0, the wound area remains unchanged, if healing rate < 0, the wound area is increasing, and if healing rate > 0, the wound area is decreasing. The capability of each model (exponential and linear) to describe the healing process can be evaluated by fitting errors. They are defined as

exp. fitting error $\epsilon_{exp} = \frac{\sum_{i=0..4} (S_{mi} - S_{exp i})^2}{\sum_{i=0..4} S_{mi}^2} * 100(\%)$

linear fitting error $\epsilon_{lin} = \frac{\sum_{i=0..4} (S_{mi} - S_{lin i})^2}{\sum_{i=0..4} S_{mi}^2} * 100(\%)$

where S_{mi} represents the measured value of the ulcer area after the i -th week of treatment, $S_{exp i}$ is the exponentially fitted ulcer area for the i -th week, and $S_{lin i}$ is the linearly fitted ulcer area for the i -th week.

The main purpose of our study was to test for the beneficial effects of pulsed ES treatment. In accordance with the study design involving two parallel groups and the crossover group, the statistical tests were as follows:

- 1) for the parallel groups (control and ES-treated group), the hypothesis that ulcers in the control group heal at

the same rate as those treated with low frequency pulsed current was tested using the two-sample *t*-test (separate variance estimate),

- 2) for the crossover group, the healing rate was statistically established by comparing the healing rate for the control period with that of the ES-treatment period, by means of the paired *t*-test, and
- 3) the equality of the exponential and linear fitting error was tested using the paired *t*-test. For each test, the difference was regarded as statistically significant if the probability of an error of the first kind was less than 0.05.

III. RESULTS

A. Control Versus ES-Treated Group

Table I summarizes the data concerning ulcers included in the study. An imbalance in the average initial values of ulcer size and duration between the control and ES-treated group was introduced by random assignment of patients to these groups. Ulcers in the control group were more complex regarding their initial size, and those in the ES-treated group regarding their tissue characteristics (appearance of granulation or necrotic tissue) and their duration prior to inclusion in the study. In comparing healing rates, the results (Fig. 4) show that the mean healing rate for the ES-treated group during the first four weeks was 2.2% for linear and 5.7% per day for the exponential fitting method, which is higher than the mean healing rate for the control group during the same period (1.5 for linear and 2.7% per day for exponential fitting method). The distribution of the healing rates A and Θ for the parallel groups is shown in Fig. 4. The hypothesis that conventionally treated ulcers heal at the same healing rate as those treated with ES could be rejected at a significance level of $p = 0.006$ in the case of the exponential method, but cannot be rejected with a chosen significance level of 0.05 in the case of the linear evaluation method ($p = 0.07$).

Demonstration of the statistically significant difference between mean healing rates of control and ES-treated wounds with exponential and not linear evaluation methods demands an analysis of respective fitting errors. The results on accuracy of the exponential and linear model for our sample of 109 ulcers (Table II) showed that the hypothesis about equality of their fitting errors could be rejected with a significance level of 0.005. For 48% of ulcers, the difference between the exponential and linear fitting error was less than or equal to 1%. However, the mean fitting error values indicate that the exponential fitting method is preferable for our sample of 109 wounds.

The data stratified on the basis of the ulcer location is presented in Table III. The results and comparison are meaningful only for the locations for which the control and ES-treated groups had at least 10 ulcers each. These are sacral area, trochanters, and legs. It can be seen that, for the sacral area, the initial complexity of the ulcers in the control and ES-treated group was similar. Mean healing rates, both linear and exponential, are significantly higher for the electrically

TABLE I
INITIAL CHARACTERISTICS OF PRESSURE ULCERS INCLUDED IN THE CONTROL (CO) AND ES-TREATED GROUP. ABBREVIATIONS ARE AS FOLLOWS: SD- STANDARD DEVIATION, SAC- SACRAL AREA, TROCH- TROCHANTER, GLUT- GLUTEAL MUSCLE, OT- OTHER LOCATIONS

	CO group	ES-treated group
Number of ulcers (n)	48	61
Mean initial area ± SD (cm ²)	17.2 ± 20	10.6 ± 13.3
Mean initial depth ± SD (mm)	4.0 ± 8.2	3.0 ± 8.5
Number of ulcers with initial depth < 5 mm	36 (75%)	51 (83%)
Number of ulcers with granulation	25 (52%)	27 (44%)
Mean ulcer duration ± SD (days)	125 ± 129 (n = 41)	158 ± 284 (n = 60)
Number of ulcers on sac. / troch. / legs / glut. / ot.	20 / 11 / 10 / 4 / 3	14 / 16 / 18 / 5 / 8

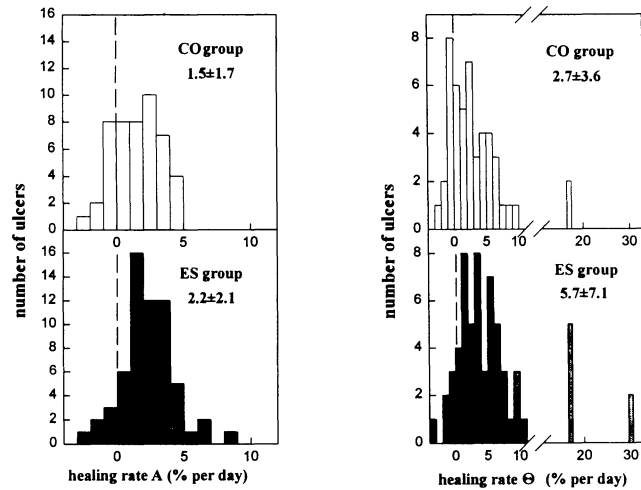


Fig. 4. The distribution of ulcer cases with regard to their healing rates for the control (CO) and ES-treated group. The mean healing rate values ± standard deviation for each group are presented.

treated sacral pressure ulcers ($p < 0.02$). Ulcers located on the trochanters and included in the ES-treated group were, on the average, deeper than conventionally treated ulcers in the same location. However, mean values of the healing rates imply a shorter healing period for the ES-treated group. Similar results were obtained for the ulcers located on the legs. Table III shows that the initial complexity of the leg ulcers between the control and ES-treated groups is not similar. Control leg ulcers had larger initial areas, while ES-treated ulcers on the same location were initially deeper with less granulation.

An increase in ulcer depth was observed in five cases in the control and four cases in the ES-treated group. In two of these latter four ulcers, this cannot be regarded as a negative trend in healing as it was a consequence of debridement, i.e., removal of the remaining necrotic tissue and subsequent appearance

TABLE II
EXPONENTIAL (ϵ_{exp}) AND LINEAR (ϵ_{lin}) FITTING
ERRORS FOR ULCERS INCLUDED IN THE STUDY

	CO group	ES-treated group	All
Number of ulcers (n)	48	61	109
Mean $\epsilon_{exp} \pm SD(\%)$	3.7 \pm 6.0	4.7 \pm 10.0	4.3 \pm 8.5
Mean $\epsilon_{lin} \pm SD(\%)$	3.5 \pm 5.6	9.7 \pm 14.0	7.1 \pm 11.7
Number of ulcers $ \epsilon_{exp} - \epsilon_{lin} \leq 1\%$	29 (60%)	23 (38%)	52 (48%)
Number of ulcers better exp. fit	6 (13%)	27 (44%)	33 (30%)
Number of ulcers better lin. fit	13 (27%)	11 (18%)	24 (22%)

TABLE III

DATA PRESENTED IN TABLE I STRATIFIED ON THE BASIS OF ULCER LOCATION. FOR THE SUPERFICIAL ULCERS, DEPTH = 1 MM WAS ADOPTED. ABBREVIATIONS ARE AS FOLLOWS: CO- CONVENTIONAL TREATMENT, ES-TREAT- ELECTRICAL STIMULATION WITH PULSED CURRENT, SD- STANDARD DEVIATION, Θ - EXPONENTIAL HEALING RATE, A- LINEAR HEALING RATE

Ulcer location	sacrum		trochanters		legs	
	CO	ES-treat.	CO	ES-treat.	CO	ES-treat.
Number of ulcers	20	14	11	16	10	18
Mean initial area \pm SD (cm ²)	18.6 \pm 16.6	16.2 \pm 17.4	17.3 \pm 18	18.3 \pm 15.3	8.1 \pm 5.2	4.5 \pm 3.0
Mean initial depth \pm SD (mm)	8.6 \pm 9.3	7.1 \pm 9.5	2.4 \pm 3.2	6.7 \pm 13.8	1.0 \pm 0.0	3.1 \pm 4.2
Number of ulcers initial depth < 5 mm	10 (50%)	7 (50%)	9 (82%)	11 (68%)	10 (100%)	13 (72%)
Number of ulcers with granulation	10 (50%)	7 (50%)	5 (45%)	9 (56%)	7 (70%)	6 (33%)
Mean $\Theta \pm$ SD (% per day)	1.8 \pm 2.8	6.2 \pm 5.1	3.4 \pm 4.2	3.6 \pm 3.2	3.2 \pm 2.3	5.9 \pm 6.5
Mean A \pm SD (% per day)	1.2 \pm 1.5	2.6 \pm 1.8	1.5 \pm 1.9	1.8 \pm 1.5	2.0 \pm 1.3	2.2 \pm 1.5

of granulation tissue. A marked decrease (more than 5 mm) of the ulcer depth was achieved in six out of 10 deep ulcers treated with ES, and in four out of 12 deep wounds in the control group.

B. Crossover Group

Out of 48 pressure ulcers in the control group, 20 crossed over into the ES-treated group (not included in the ES-treated group analysis described above). Table IV contains data concerning the pressure ulcers included in the crossover group and their healing rates during the four weeks of conventional treatment and the same period of ES treatment. During the

control period, when the ulcers were treated conventionally, the healing rates ranged between -2.9% and 3.2% per day for the linear, and between -2.2% and 6.2% per day for the exponential fitting method. After applying ES for four weeks, in all but one case (B_3), an improvement in ulcer healing rate was observed. It ranged between -0.3% and 5.4% per day for linear and between -0.3% and 14.7% per day for the exponential fitting method. The examples of the time-course of the ulcer area with the best fitted curve for cases A, B_1, D, E_1, E_2, K are presented in Fig. 5. The statistical analysis (paired t -test) indicates that the hypothesis regarding the equality of the healing rates during the conventional and ES treatments could be rejected at a significance level of $p = 0.001$ for both evaluation methods. A summary of obtained results, presenting the distribution of the healing rates for the crossover group, is shown in Fig. 6.

The positive trends in ulcer depth and/or appearance of granulation tissue were observed in four ulcers (B_3, K, E_3, J_3) after four weeks of the control period and in nine ulcers ($A, B_1, D, E_1, G, C_2, I, K, L$) after the same period of ES.

Ulcers in the patients involved in this study were observed for a maximum of one year. The final outcome of the treatment (complete ulcer closure) cannot be used as the quantification parameter because 20 patients from the control group crossed over to the ES-treated group after four weeks. However, closure as the main goal of all treatment modalities needs to be considered. Out of 81 pressure ulcers (61 from the ES-treated group and 20 from the crossover group) which received the ES treatment, 58 closed completely. Of these, 13 were deeper than 5 mm, while 45 were superficial wounds. The average initial area of ulcers that healed after introduction of ES was 7.9 ± 8.8 cm². Out of 28 wounds treated with conventional therapy only, 15 pressure ulcers healed. All were superficial ulcers with an average initial area of 6.1 ± 6.7 cm².

IV. DISCUSSION

The results presented demonstrate a very good therapeutic response of the pressure ulcers in SCI patients to treatment with pulsed electrical current.

Comparison of the control and ES-treated groups showed a higher average healing rate for ulcers treated with ES, indicating a 1.5 to 2 times shorter healing period. It is interesting to note that, in spite of there being 109 pressure ulcers included in the study, the size of the sample observed is still not large enough to exclude an imbalance in ulcer characteristics between groups introduced by the random assignment. Due to this nonhomogeneity of the groups, the comparison of control and ES-treated ulcers at particular anatomic locations might be more convincing (see Table III). However, we shall discuss more closely the results obtained in the crossover group, in which each wound served as its own control. In all but one ulcer out of 20 cases, an improvement in the healing rate was observed after the introduction of ES (see Table IV). In seven cases (A, C_1, D, F, H, E_2, I) which showed resistance to healing or responded poorly to conventional therapy, we can attribute the considerable improvement in the healing process and complete ulcer closure to the introduction of ES (see also

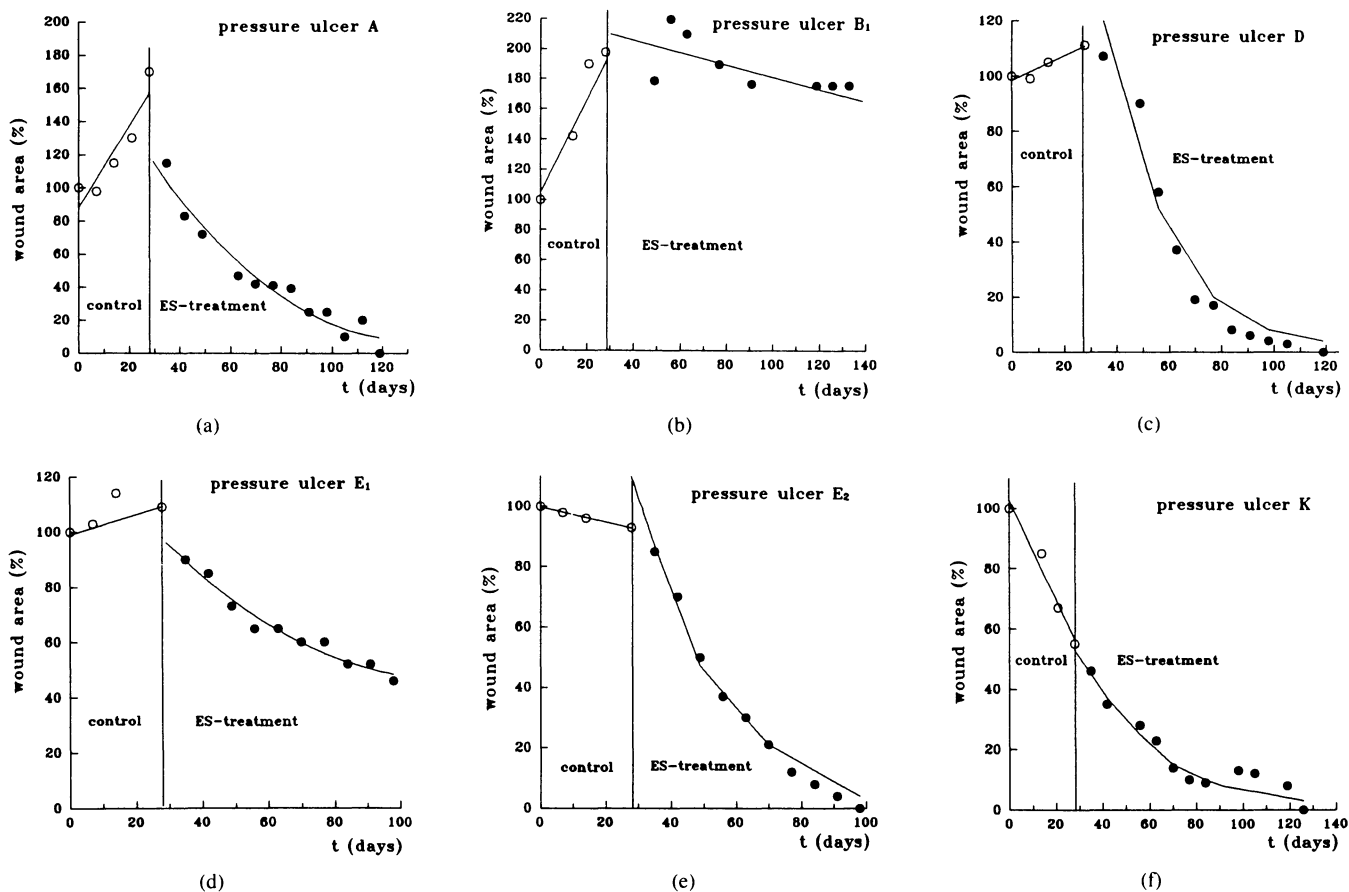


Fig. 5. Time-courses of the ulcer areas with the best fitted curve for wounds A, B₁, D, E₁, E₂, K.

examples in Fig. 5(a), (c), (e)). In seven cases which had already exhibited quite rapid healing when treated conventionally, further improved healing was obtained after applying ES treatment (see example in Fig. 5(f)). The successfulness of the healing of these wounds (J_1 , K, E_3 , J_2 , L, M, J_3) can not be attributed exclusively to ES, since the ulcer areas at the start of the application of ES were markedly smaller than the initial area values for the control period. In this case, much of the credit for complete closure can be attributed to conventional wound care. Three ulcers (E_1 , G, C_2) did not heal during the patients' stay at the Rehabilitation Institute, but the possibility of wound-closure was promising as the state of the wounds was improved, i.e., they decreased in depth and/or the granulation tissue appeared. In the remaining three ulcers (B_1 , B_2 , B_3) belonging to the same patient, the healing process was not successfully affected by ES (see example in Fig. 5(b)). The pressure ulcer is affected by many variables within the human organism. Therefore, the dynamics of pressure ulcer healing depend on the patient's general health. This can be well illustrated in patients having more than one wound (see Table IV). Comparison of healing rates for the parallel groups and the crossover group reveal lower healing rates for the control period of the crossover group than for the control group who were unsatisfied with the extent of their healing during four weeks of conventional wound treatment crossed over to the ES treatment. Healing rates obtained in the crossover group

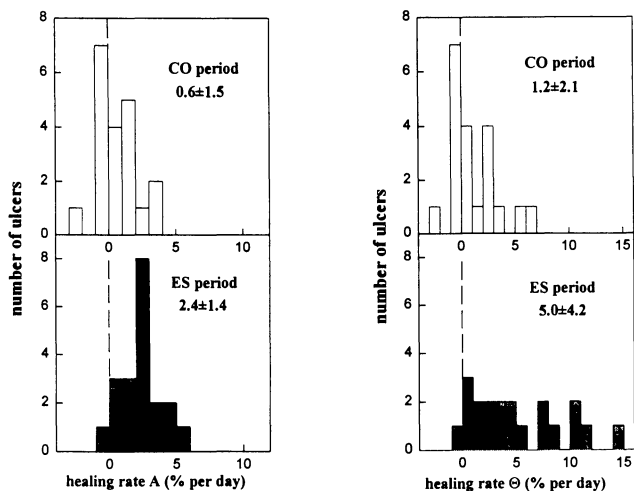


Fig. 6. The distribution of ulcer cases with regard to their healing rates for the crossover group. The mean healing rate values \pm standard deviations for each period are presented.

after four weeks of electrical stimulation are in agreement with the results obtained in the ES-treated group.

The results presented suggest that, in addition to conventional wound care, the simple and inexpensive ES treatment could initiate and/or accelerate pressure ulcer healing.

In searching for an explanation for the improved rate of healing caused by electrotherapy, several possible mechanisms have been proposed [9], [17], [19], [30]. Let us focus on the

TABLE IV

PRESSURE ULCERS INCLUDED IN THE CROSSOVER GROUP AND CHANGES IN THEIR AREA (HEALING RATES-LINEAR AND EXPONENTIAL FITTING METHOD), DEPTH AND GRANULATION APPEARANCE DURING THE CONVENTIONAL (CO PERIOD), AND ELECTRICAL STIMULATION TREATMENT (ES PERIOD). ULCERS BELONGING TO THE SAME PATIENT ARE MARKED WITH THE SAME LETTER. FOR THE SUPERFICIAL WOUNDS, DEPTH = 1 MM WAS ADOPTED. ABBREVIATIONS ARE AS FOLLOWS: LIN- LINEAR HEALING RATE, EXP- EXPONENTIAL HEALING RATE, GLUT- GLUTEAL MUSCLE, SAC- SACRAL AREA, TROCH- TROCHANTER, N- NO, Y- YES, M- MONTH, X- DATA NOT AVAILABLE, W- WEEK

Ulcer	Location	Initial area (cm ²)	Initial depth (mm) / granulation (Y/N)	Duration	Healing rate (% per day)		Depth (mm) / granulation (Y/N)		Healed (Y/N)
					lin. / exp.		CO period	ES period	
A	glut.	3.8	28 / N	4 M	-2.9 / -2.2	2.2 / 4.1	26 / N	15 / Y	Y / 12W
B ₁	troch.	21.6	5 / N	3 M	-1.4 / -1.0	-0.3 / -0.3	15 / N	20 / Y	N / 8W
C ₁	leg	7.7	1 / Y	4 M	-0.8 / -0.8	3.5 / 7.5	1 / Y	1 / Y	Y / 7W
D	glut.	13.0	10 / N	1 M	-0.4 / -0.4	2.1 / 3.0	39 / N	25 / Y	Y / 12W
B ₂	sac.	32.9	15 / Y	3 M	-0.3 / -0.3	0.4 / 0.4	20 / Y	20 / Y	N / 8W
E ₁	sac.	56.5	30 / N	X	-0.2 / -0.2	1.5 / 1.9	30 / N	20 / Y	N / 10W
F	troch.	2.2	1 / Y	20 M	0.0 / 0.0	2.4 / 3.6	1 / Y	0 / Y	Y / 3W
G	troch.	45.9	1 / N	X	0.0 / 0.0	0.8 / 0.9	1 / N	1 / Y	N / 12W
H	troch.	2.0	1 / Y	2 M	0.2 / 0.2	2.9 / 5.1	1 / Y	1 / Y	Y / 6W
E ₂	shin	62.8	1 / Y	X	0.2 / 0.2	2.3 / 3.2	1 / Y	1 / Y	Y / 10W
C ₂	sac.	35.5	16 / Y	4 M	0.5 / 0.6	1.4 / 1.8	16 / Y	1 / Y	N / 12W
B ₃	leg	8.3	3 / Y	3 M	0.6 / 0.7	0.2 / 0.2	1 / Y	1 / Y	N / 8W
I	sac.	21.9	5 / N	2 M	1.3 / 1.8	2.9 / 8.3	6 / N	1 / Y	Y / 5W
J ₁	leg	4.8	1 / Y	4 M	1.5 / 2.0	5.4 / 14.7	1 / Y	1 / Y	Y / 5W
K	sac.	15.7	30 / N	1 M	1.6 / 2.1	1.7 / 2.3	22 / Y	10 / Y	Y / 12W
E ₃	shin	94.3	3 / Y	X	1.8 / 2.6	2.6 / 4.0	1 / Y	1 / Y	Y / 10W
J ₂	leg	20.4	1 / Y	4 M	2.1 / 2.9	3.9 / 10.3	1 / Y	0 / Y	Y / 4W
L	sac.	23.5	16 / N	3 M	1.8 / 3.4	2.6 / 11.8	15 / N	12 / Y	Y / 12W
M	sac.	31.4	1 / Y	5 M	3.2 / 5.5	4.1 / 10.0	1 / Y	0 / Y	Y / 4W
J ₃	leg	8.6	3 / Y	4 M	3.1 / 6.2	4.4 / 7.9	1 / Y	0 / Y	Y / 4W

physiological effects of the ES used in this study. Electrical stimulation of skeletal muscle has been shown to be capable of increasing muscle blood flow with the most effective frequency range being between 16 and 50 pps [31], [32]. Tracy *et al.* have reported that a significant increase in blood flow to a muscle could be achieved using stimulation parameters similar to those we used (biphasic pulses, stimulation trains 4 s on/4 s off, a frequency range of 10 to 50 pps, stimulation intensity sufficient to produce torque equal to 15% of the predetermined maximal voluntary muscle contraction). The greatest effect was observed at 50 pps [31]. In our study, the frequency of 40 pps combined with the current amplitude adjusted to achieve minimal muscle contraction may have facilitated healing through improved blood flow [33].

The rhythmical exchanges of stimulation trains and pauses, as used in our study, perform a massage effect not only on the skeletal muscles in the ulcer area but also on the smooth muscles within the walls of blood vessels. Following smooth muscle contraction and relaxation increased blood flow likely occurred [34]. In our study, this relaxation could occur every 8 s during the 2 h of ES treatment.

Blood vessels supplying skeletal muscles possess a considerable vasodilator sympathetic nervous supply, which could also be activated by ES.

Chemical vasodilatation associated with increased metabolic activity is another mechanism that may enhance tissue healing [35], [36]. Minimal muscle contraction elicited by electrical stimulation in the vicinity of the ulcer may induce increased metabolic demands, thus initiating chemical processes resulting in improved blood flow.

All the listed mechanisms serve the same purpose, which is to improve the energy supply of the stimulated tissue through improved blood flow. The enhancement of blood flow by ES in the ulcer region could be a trigger and/or accelerator for the healing process by providing better conditions for the essential functions of some cells, such as the reparative capacity of macrophages, fibroblasts, keratinocytes, and endothelial cells [4], [37], [38].

An additional observation we made, and one which has been noted by others [18], concerns the improved quality of the newly developed tissues after the application of ES, a process which needs to be verified and objectified. The long-term benefits derived from the stronger and more elastic and aesthetic scar resulting from ES treatment could be of great interest for plastic surgery and skin/muscle flap surgery.

Insufficient blood supply and damaged microcirculation from pressure induced ischemia are often stated as the primary cause of pressure ulcer formation and the advantages of

employing ES for prevention of pressure ulcers have already been implemented [39]. But in preventive management, it is even more difficult to provide persuasive evidence of the efficacy of ES.

The further optimization of stimulation parameters and extensive studies on mechanisms by which ES augments wound repair could provide clinically applicable information about chronic wound healing and conditions for which ES treatment may be most effective.

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