Effectiveness, Tolerability, and Safety of Electrical Stimulation of Wounds With an Electrical Stimulation Device: Results of a Retrospective Register Study

Katharina Herberger, MD;1 Eike Debus, MD;2 Axel Larena-Avellaneda, MD;2 Christine Blome, MD;1 Matthias Augustin, MD1

Abstract: The purpose of this study was to determine effectiveness, tolerability, and safety of electrical stimulation therapy (EST) using an electrical stimulation device to treat wounds under hospitalized and routine ambulatory conditions. Methods. This registered study was conducted as a multicenter, retrospective, noncontrolled study of EST for treating complex acute and chronic wounds. Data were collected and entered in a standardized manner in accordance to defined criteria. Results. Ninety-five (n = 95) patients with median wound duration of 13.7 months were treated with EST for an average of 48.1 days. Wound size decreased by 44.7%, complete granulation occurred in 30.4%, and epithelialization (full or partial) increased in 80.4%. Exudate, fibrin, necrosis, and wound odor decreased. Patients described the global effectiveness and treatment tolerability as good (77.2%) or very good (78.5%). A few adverse events occurred, including maceration (4 patients) and pain (1 patient) at the wound edge, where the wound was exposed to the dispersive electrode. Wound status deteriorated in 4 patients. Surgery, mainly second amputations or debridement, were required in 7 cases and were found to be related to a seriously ill patient cohort. Conclusion. Electrical stimulation therapy is a safe and effective treatment for chronic and complicated wounds, and is well tolerated by patients.

Electrostimulation therapy (EST) of refractory wounds has become an important treatment option in recent years.1 Several national and international guidelines recommend the use of EST for chronic wounds, including lower leg ulcers and pressure ulcers.1,2

The rationale for this decades old wound intervention lies in the pathophysiology of the electrochemical processes in the wound: a transepithelial potential (TEP) exists in human skin that is created and maintained by chloride ions on the skin surface, and the flow of sodium ions into the extracellular space of the dermis.3 Intact skin forms a barrier between the negative charges on the surface and the positive charges in the dermis. This barrier is lost when skin continuity is disrupted, resulting in a “short-circuit current.” This “wound current” is accompanied by an electrical field (EF), which can
last for up to 3–5 days, and has been shown to be essential for wound healing. Furthermore, there is evidence that electrical fields promote the migration of neutrophils and macrophages, stimulate fibroblasts, and improve blood flow.

Electrical fields that occur during normal wound healing vary depending on the stage of wound healing, and then disappear after the healing process. These fields are disturbed or absent in chronic wounds, and result in ulcers that will not heal. In the United States, Medicare has reimbursed EST since 2002 for the treatment of refractory leg ulcers and pressure ulcers.

The electrical stimulation device used in this study (woundEL®, Gerromed, Hamburg, Germany) stimulates the wound by means of low-voltage, low-frequency, monophasic, pulsed current of negative or positive polarity. Depending on the stage of the wound, negative impulses are applied initially, which are later followed with negative/positive stimulation. The stimulation results in wound cleansing, pain reduction, granulation or epithelialization, angiogenesis, and an antibacterial effect, depending upon the polarity. Despite extensive clinical research, there is still a need for systematic studies of EST for the treatment of refractory wounds.

The aim of the present study was to determine the tolerability, safety, and clinical effectiveness of EST as a primary wound treatment.

**Keypoints**
- There is evidence that electrical fields promote the migration of neutrophils and macrophages, stimulate fibroblasts, and improve blood flow.
- Depending on the stage of the wound, negative impulses are applied initially, which are later followed with negative/positive stimulation. The stimulation results in wound cleansing, pain reduction, granulation or epithelialization, angiogenesis, and an antibacterial effect, depending upon the polarity. Despite extensive clinical research, there is still a need for systematic studies of EST for the treatment of refractory wounds.

**Methods**

**Study design.** This multicenter, retrospective study of EST with an electrical stimulation device in refractory acute and chronic wounds was conducted in specialized German wound treatment centers. The criterion for patient recruitment was that the centers had treated at least 5 patients with wounds. The qualifying centers were the Evangelisch Lutherische Diakonissenanstalt, Flensburg; the Asklepiosklinikum Harburg, Hamburg; the St. Joseph Krankenhaus, Berlin; the Knappschaftskrankenhaus, Bottrop; the Universitätsklinik, Würzburg; and the Universitätsklinik, Regensburg.

An evaluator, independent of the treatment centers, gathered consecutive patient data from medical records (Figure 1). Approval from the hospitals’ ethics committees was not requested since data were collected for the primary purpose of quality assurance, and were recorded anonymously.

**Target criteria.** The primary target criteria for EST effectiveness were wound size reduction, change of wound status, and global therapeutic result (Patient Global Assessment) of efficacy and tolerability using a 5-point Likert Scale (0 = none, 4 = maximum effect).

Wound size was measured by using a scaled foil on the wound, drawing the wound margins, and determining the area inside in centimeters squared. Wound status was determined by improvement of granulation tissue, readiness to skin graft, and detection of wound odor. The written Likert scale was used to determine the aforementioned treatment outcomes. Photographs were taken in a standardized manner by taking a photo of the entire wound with a ruler placed beneath it for scale.

The target criteria for patient tolerability of EST were the patients’ assessment and determination of pain at rest, during treatment, and during exercise using a visual analogue scale (VAS, 0 = no pain, 10 = maximum pain). The frequency and nature of adverse events were documented and analyzed for association with the therapy.

**Patients.** Ninety-five adult patients with refractory wounds, in whom the standard wound care with modern wound dressings had failed to bring about improvement, were admitted to the study. The wounds consisted of vascular lower leg ulcers, particularly associated with severe arterial occlusive disease—diabetic foot ulcers, postoperative wounds, and pressure ulcers. Exclusion criteria were wound infection requiring treatment, osteomyelitis, malignant neoplasia in the wound region, or other serious underlying disease, such as a neoplasm currently requiring treatment, coronary heart disease, heart failure, and hepatic or renal disease. Relative contraindications were defined for patients with an allergy to components of the wound dressings, or patients with a cardiac pacemaker or metallic implant in the immediate vicinity of the wound, and for those undergoing therapy with a high-frequency surgical device.

**Electrical stimulation therapy.** The woundEL® sys-
A dressing system (Gerromed, Hamburg, Germany) consists of a dressing electrode, a dispersive electrode, and the stimulation device. The dressing electrode consists of a hydrogel, which keeps the wound moist, conducts the electrical current into the wound, and absorbs exudate. The electrode remained on the wound continuously and was changed every 3–4 days. The current was applied twice daily, 7 days a week, for 30 minutes by attaching the reusable dispersive electrode and connecting it to the EST impulse generator. The polarity was chosen according to the recommendations in the device instructions; initially, negative polarity was used to stimulate granulation tissue formation. The polarity was reversed after epithelialization was evident. Intensity was adapted to the patient's sensitivity by increasing the strength of current until the patient reported a slight stinging sensation.

**Study procedure.** Three visits were scheduled for each patient (PV). The first visit at the start of therapy included determination of wound size, wound status and odor, pain measurement at rest and during exercise, use of a VAS, and photographic documentation. Visit 2, follow-up after 2–6 weeks, and visit 3, before discontinuation of treatment.

**Figure 1.** Flow chart: Treated patients, dropouts, and reasons for dropout.

<table>
<thead>
<tr>
<th>T1: n=95 under EST with woundEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=91: wound data available</td>
</tr>
<tr>
<td>Drop-out at T1 (n=1)</td>
</tr>
<tr>
<td>-Patient failed to return after first treatment (n=1)</td>
</tr>
<tr>
<td>Drop-outs after T1 (n=29*)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T2: n=65 under EST with woundEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=63: wound data available</td>
</tr>
<tr>
<td>Drop-out at T2 (n=3)</td>
</tr>
<tr>
<td>-Pat. discharged, lost to follow-up (n=1)</td>
</tr>
<tr>
<td>-Allergy to the electrode (n=2)</td>
</tr>
<tr>
<td>Drop-outs after T2 (n=2)</td>
</tr>
<tr>
<td>-Flap graft, wound closure (n=1)</td>
</tr>
<tr>
<td>-Mesh graft (n=1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T3: n=60 under EST with woundEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=46: wound data available</td>
</tr>
<tr>
<td>Drop-outs at T3 (n=7)</td>
</tr>
<tr>
<td>-Pt. refuses mesh graft, then goes on holiday (n=1)</td>
</tr>
<tr>
<td>-Increasing necrotisation and infection of the wound (n=1)</td>
</tr>
<tr>
<td>-Mesh graft (n=3)</td>
</tr>
<tr>
<td>-Hospitalization for 2nd amputation and wound sealing (n=1)</td>
</tr>
<tr>
<td>Drop-outs after T3 (n=3)</td>
</tr>
<tr>
<td>-Intolerance of disperser electrode (n=1)</td>
</tr>
<tr>
<td>-rapid necrotisation of toes 3 and 4 (n=1)</td>
</tr>
<tr>
<td>-Mesh graft (n=1)</td>
</tr>
</tbody>
</table>

**Wound data available:**
- n=4: none
- n=7: only T1
- n=18: only T1 and T2
- n=1: only T1 and T3
- n=45: all 3 time points
Figure 2. Distribution of the wound sites under EST (n = 95).

Figure 3. Granulation and epithelialization, comparison of all registered patients (n = 95) with patients with a complete data set (n = 45), (ITT vs. PP analysis), scaling 0 = none, 1 = 25%, 2 = 50%, 3 = 75%, 4 = 100%.
T1 = Before treatment
T2 = Follow-up after 2–6 weeks
T3 = Follow-up after 8–12 weeks or treatment discontinuation

Figure 4. Mean wound area in cm² (all registered patients, n = 95).
T1 = Before treatment
T2 = Follow-up after 2–6 weeks
T3 = Follow-up after 8–12 weeks or treatment discontinuation

Figure 5. Proportion of patients with/without wound odor over the course of therapy (all registered patients, n = 95).
T1 = Before treatment
T2 = Follow-up after 2–6 weeks
T3 = Follow-up after 8–12 weeks or treatment discontinuation

Figure 6. Assessment of the wound margins (all registered patients, n = 95). The chart shows the percentage of patients with the respective variable.
T1 = Before treatment
T2 = Follow-up after 2–6 weeks
T3 = Follow-up after 8–12 weeks or treatment discontinuation
ES (weeks 8–12), included determination of these same parameters, plus the wound readiness for grafting, the Patient Global Assessment (PaGA), and the tolerability of the therapy (Table 1).

Table 1. Incidence of side effects at all study time points.

<table>
<thead>
<tr>
<th>Nature of the event/reason for termination of therapy</th>
<th>n</th>
<th>Association with electrotherapy as per retrospective expert assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesh graft transplant/flap graft/wound healed</td>
<td>14</td>
<td>No</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>3</td>
<td>No</td>
</tr>
<tr>
<td>Skin reaction to dispersive electrode</td>
<td>4</td>
<td>Yes</td>
</tr>
<tr>
<td>Maceration</td>
<td>1</td>
<td>Yes</td>
</tr>
<tr>
<td>Deterioration of wound status</td>
<td>3</td>
<td>No</td>
</tr>
<tr>
<td>Superinfection</td>
<td>1</td>
<td>No</td>
</tr>
<tr>
<td>Pain</td>
<td>1</td>
<td>Unclear</td>
</tr>
<tr>
<td>Operation (amputation/debridement)</td>
<td>7</td>
<td>No</td>
</tr>
<tr>
<td>Irritations of periwound skin</td>
<td>4</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>38</strong></td>
<td><strong>of these: 10 yes, 27 no, 1 unclear</strong></td>
</tr>
</tbody>
</table>

**Figure 7.** Wound pain at rest, during exercise, and during dressing changes (all registered patients, n = 95).
T1 = Before treatment
T2 = Follow-up after 2–6 weeks
T3 = Follow-up after 8–12 weeks or treatment discontinuation

**Figure 8.** Global assessment of the effectiveness and tolerability of electrical stimulation using an ESD (all registered patients, n = 95).

**Statistical Analysis**
A descriptive, exploratory analysis was performed for all 3 study time points (Figure 1). Both the values of the patients documented at the respective time point (intent-
Results

Patients. Ninety-five patients (68% men) were evaluated by ITT and 45 patients by PV, with a mean age in the ITT population of 69.1 ± 12.6 years. All cases were considered to be refractory to standard wound treatment and had been treated previously for an average of 13.7 months. A majority were vascular wounds (n = 62, 65.3%), followed by diabetic foot ulcers (n = 14, 14.7%), and pressure ulcers (n = 2, 2.1%). The remaining comprised various wounds (n = 14, 17.9%) that were mainly postoperative. The wounds were located overwhelmingly on the lower leg or foot (Figure 2). The mean duration of EST was 48.1 days.

Wound status. Granulation and epithelialization increased markedly under EST, which was determined by evaluating the scaled wound photos (Figure 3). The proportion of wounds without granulation decreased from 17% to 0% in the ITT evaluation, and complete granulation was achieved in 30.4% of the wounds. The proportion of wounds with epithelialization increased in the total group from 15.4% to 80.4%. The effects were more apparent in the patients observed throughout the entire study (PV analysis); the number of wounds that re-epithelialized increased in this group from 8.9% to 80% (Figure 3). The mean wound area was 44.7 cm², which decreased over the course of EST to 24.5 cm² (Figure 4).

Wound odor. The proportion of patients with wound odor decreased in the total group from 44.0% at T1 to 26.1% at T3 (Figure 5).

Wound margins. The condition of the wound margins improved under EST and was described as unirritated, reddened, edematous, macerated, reddened and edematous, reddened and macerated, reddened and necrotic, edematous and macerated, or macerated and livid. The proportion of unirritated wound margins increased markedly by a half (48.8%), while that of reddened margins fell by about half (51.9%). Macerations were relatively common with EST therapy, remaining constant at about one-third (T1 27.5%, T2 33.3%, T3 28.5%; Figure 6).

Periwound skin condition. Periwound condition was assessed on a 10-point scale (unirritated, reddened, edematous, macerated, dry, scaly, reddened and edematous, reddened and macerated, edematous and macerated, and livid). The proportion of unirritated wounds increased markedly by a half (48.8%), while that of reddened margins fell by about half (51.9%). Macerations were relatively common with EST therapy, remaining constant at about one-third (T1 27.5%, T2 33.3%, T3 28.5%; Figure 6).

Secretion. Overall, the number of secreting wounds declined from 88% to 70.6%. Above all, however, the amount of exudate decreased, and the proportion of wounds with moderate to profuse exudation decreased from 47.1% to 17.4% (Table 2).

Wound surface tissue. The proportion of patients with wound surface fibrin or necrosis decreased mark-
edly from T1 to T3: 85% of the wounds exhibited fibrin or necrosis at T1 compared to 25% at T3. Additionally, the proportion of wounds with no fibrin or necrosis increased from 5.5% to 41.3.

**Wound pain.** Wound-related pain was measured at rest, during exercise (normal daily activities), and during dressing changes. It was greatest during exercise at the start of the observation (T1) with a mean of 4.3; it was 2.4 at rest, and 2.6 during dressing change. Pain intensity decreased markedly on the VAS during EST by an average of 0.9 point at rest, by 2.0 during exercise, and by 0.9 during dressing change (Figure 7).

**Effectiveness and tolerability.** The global effectiveness of EST was described as “good” or “very good” by 74% of the patients, while the treatment was described as “good” by 48.1% and as “very good” by 29.1% (Figure 8). A majority of patients were also satisfied with the tolerability of EST, with 78.5% describing it as “good” or “very good” (54.4% and 24.1%, respectively; Figure 8).

**Adverse events and side effects.** Adverse events occurred in a total of 38 patients by the end of the study; they included 13 cases of mesh graft or flap graft, which automatically led to their exclusion from the study, although these were not adverse events per se. One or more adverse events were recorded in 37.3% of patients at T2 and in 14.6% at T3. There were 12 patients for whom it was not documented whether adverse events had occurred.

Side effects (ie, adverse events that were directly associated with EST) included skin reactions to the dispersive electrode (n = 4), irritation of the periwound skin (n = 4), and maceration (n = 1). An expert performed a retrospective assessment of whether an association existed between EST and the side effects.

Deterioration of the wound status occurred in 3, a superinfection developed in 1, and surgical treatment was required in 7 cases—mainly secondary amputation or debridement (Table 1). These side effects were not direct consequences of EST, but are typical complications in this patient population.

Serious adverse events occurred in 5 cases (2 deaths, 1 amputation, 1 hospitalization, 1 allergic reaction), none of which was causally related to the EST.

**Discussion**

The aim of this study was to determine the effectiveness and safety of EST to treat chronic wounds, an increasingly used intervention. The study was designed as a retrospective patient register to investigate the effectiveness and safety of EST with an electrical stimulation device (woundEL) as a primary wound care treatment.

These data show that EST is an effective, well tolerated, and safe intervention that promotes the healing of refractory wounds. An improvement was found in all clinical wound parameters, including a reduction of wound surface fibrin and necrosis, and an increase in granulation and epithelialization.

Thus, the authors’ data support earlier publications from the international literature. A study of 80 patients with diabetic foot syndrome showed significantly better wound healing of more than 60% for EST compared to the control group.17 Another study of 61 pressure ulcers showed significant improvement of wound status within 2 weeks in 60.7% of the cases, and complete healing in 23% of the wounds after the use of monophasic pulsed current therapy with an earlier model of the EST device used in this study.18 Conclusions about the benefits of EST could not be drawn from a 2001 metaanalysis because of a stated lack of valid data.19 However, data from a metaanalysis of 591 patients by Gardner et al,20 which were not taken into account, demonstrated a 2.7-fold acceleration of wound healing under the application of monophasic pulsed current compared to controls. In 2006, Houghton et al21 performed a metaanalysis of 19 studies with a total of 888 patients and found that EST accelerated wound healing. Preliminary data from a Cochrane meta analysis that included 13 randomized clinical trials showed that electrical stimulation accelerates wound healing, and furthermore, that monophasic current is the most effective in stimulating wound healing.22

Apart from the clinical evidence, there is also a physiological rationale for the use of EST. Chronic wounds stagnate in the inflammatory phase, unlike wounds that heal normally. This is distinguished by large amounts of fibrin, necrotic tissue, exudate, and reddening of the wound margins.

In the present study, woundEL EST led to an improvement of these parameters, which suggests that the
wounds had progressed from the inflammatory phase to the repair phase. This patient cohort displayed serious relevant disease and had a mean wound size of 44.7 cm². By way of comparison, the mean wound size was 9 cm² in the EST studies of 591 patients included in the Gardner et al metanalysis.

In the present study, a healing rate of 45.2% was found over the mean treatment period of 48.1 days. Although no conclusions can be drawn about the healing rate compared to standard wound care due to the lack of a control group, promotion of healing was quite distinct. The mean healing rate per week in Gardner's review was much higher (22.5%) compared to 6.6% in the present study. A possible limitation of the present study is that 13 (13.7%, n = 95) wounds underwent fibrin buildup early on that was regarded, conservatively, as an adverse event.

The open-label, noncontrolled design must also be considered a limitation of this study. The requirements of the CONSORT criteria are only partly met and, consequently, are of only limited use for the generation of data to form an evidence base for EST. Furthermore, this open-label design allowed a high proportion of severely ill patients to be included. Thus, the serious adverse events that were observed were not associated with the EST, but reflect the poor condition of the patients (e.g., amputations in stage IV peripheral arterial occlusive disease and 2 deaths). Such a clientele would not satisfy the criteria for a randomized, controlled study, and consequently, would most likely not be admitted to such a study. Nevertheless, it is precisely these patients for whom guideline-based treatments have so far failed to show any success, and in whom EST can be of great benefit. Moreover, data on the safety and tolerability of this therapy are of high value, particularly in a multimorbid patient population, since the latter represents a negative selection with an expected high incidence of undesirable events.

The primary target variables of the present study included the tolerability and effectiveness of EST from the patient's perspective, parameters for which a high degree of satisfaction was achieved.

woundEL therapy is a safe treatment technology with low side effects. As mentioned adverse events directly associated with the EST included reactions to the dispersive electrode, irritations of the periwound skin, maceration, and pain. Apart from the maceration documented as an adverse event, there were a number of wounds with periwound skin maceration, which remained constant in one-third of the patients. These are attributable to the fact that the conducting layer of gel, which contains a high liquid content needed for current conduction, can lead to maceration, particularly in the periwound skin. This relatively high number, nevertheless, reflects the great need for consistent protection of the wound margins under this treatment dressing/electrode (e.g., with a moisture barrier film). More frequent changing of the treatment electrode (dressing) may also be an option.

It cannot be said that a causal association with EST exists in the 3 wounds that deteriorated. Although, other adverse events (e.g., superinfection, necessary second amputations or debridement, and more serious adverse events) are not causally associated with the therapy, they do show that a closely monitored medical regime is essential for the early detection and prevention of serious events in these severely ill patients.

New therapeutic procedures are measured against tried and tested, evidence-based alternatives. Further randomized, controlled, comparative studies of the healing rate are required before conclusions can be drawn regarding the superiority of EST. An economic analysis under standard conditions would also be desirable to determine cost-effectiveness.

**Conclusion**

The present clinical data suggest that EST with woundEL is a promising and well-tolerated treatment option for refractory wounds. Thus, electrical stimulation is a promising alternative in the management of chronic wounds. Planned randomized, clinical studies and long-term data from an ongoing trial will provide further information about its effectiveness and benefits.

**Acknowledgement**

_Funding:_ This study was supported by an unrestricted research grant from Gerromed. _Disclosure:_ Dr. Larena-Avellaneda received speaker honoraria from Gerromed.

**Key Points**

- It cannot be said that a causal association with EST exists in the 3 wounds that deteriorated. Although, other adverse events (e.g., superinfection, necessary second amputations or debridement, and more serious adverse events) are not causally associated with the therapy, they do show that a closely monitored medical regime is essential for the early detection and prevention of serious events in these severely ill patients.
References


