Electrical stimulation in wound care

Editorial and opinion
Electrical stimulation for wound healing needs serious consideration
Keith Harding

Technology update
Electrical stimulation and wound healing
Michael Clark
Expert commentary
Eike Sebastian Debus

Case report
Clinical experience: Electrostimulation with the woundEL® device
Jean Paul Lembelembe

Wound digest
A selection of the most important articles on electrical stimulation for wound healing

This eSupplement to Wounds International was sponsored by
Editorial and opinion
Keith Harding Page 3
Electrical stimulation for wound healing needs serious consideration

Technology update
Electrical stimulation and wound healing Page 4
Michael Clark provides a thorough review of this technology

Expert commentary Page 7
Eike Sebastian Debus comments on the use of electrical stimulation for wound healing

Case report
Clinical experience: Electrostimulation with the woundEL® device Page 8
Jean Paul Lembelembe reports three chronic, complex wounds treated with electrical stimulation

Research
Wound digest Page 11
A selection of the most important articles on electrical stimulation for wound healing

- A review of endogenous electrical field control of cell behaviour.
- PI3Kγ and PTEN genes essential for electric-signal-induced wound healing.
- Treatment guidelines for pressure ulcers: NPUAP–EPUAP recommendations.
- Using a new electrical stimulation device for pressure ulcer wound healing.
- Enhanced healing of chronic dermal ulcers using pulsed electrical stimulation.

Citing this publication:
Electrical stimulation therapy has sound foundations and is increasingly part of the therapeutic armamentarium. Clinicians need to ensure that the therapy is selected for the correct patient with an appropriate outcome measure.

For those of us who have been involved in wound healing over recent years, we have witnessed many exciting developments in this area.

Following the discovery in the 1960s that moist wound healing was the optimum environment for healing, an explosion of new dressing materials and technologies emerged. More recently, there has been great interest in the development of devices to either manage the environment in or around the wound or to directly stimulate a wound healing response.

Electrical stimulation therapy in wounds involves the use of an externally applied current to create an electrical flow through the tissues. In recent years, there has been a renewed interest in using this as a treatment where wound healing is delayed and a range of sophisticated products have been developed to provide electrical flow through the tissues, although the exact mechanism for some of these effects is not known.

The literature supporting electrical stimulation as a useful therapy for wound healing is being strengthened rapidly following the 2009 guidelines on pressure injury from the European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel[1] that suggests it is an effective intervention. Not only does electrical stimulation appear to convey patient benefits, but it also has data to support multiple modes of action.

Although electrical stimulation may appear to many of us as the “new kid on the block”, it is a technology that has significant research underpinning it that we should all be aware of [2–5]. We should also be prepared to keep our minds open and review our current practice, while considering using this technology in managing patients with hard-to-heal complex wounds.

**AUTHOR DETAILS**

Keith Harding is Professor of Rehabilitation Medicine and Wound Healing, Director of the Wound Healing Research Unit, Cardiff University, Cardiff, UK.

**References**


The application of electrical currents for therapeutic ends is almost as old as the use of electricity itself. Electrostatically charged gold leaf is reported to have been used in the treatment of skin wounds ranging from smallpox lesions to ischaemic and venous leg ulcers, and to accelerate bone fracture healing. In physiotherapy, electrical stimulation (ES) has been used in the prevention of muscle atrophy, and for rehabilitation and pain relief.

For the purposes of wound care, ES is defined as the application of an electrical current through electrodes placed either within the wound itself or on the periwound skin. ES may be delivered via a number of modalities, a clear and comprehensive review of which is provided by Kloth.

The two main approaches to delivering ES are by using direct current or a pulsed current. To date, there have been no reports of using alternating current in wound care. ES using direct current is the application of a one-way flow of electrons between the positively and negatively charged electrodes placed in or adjacent to the wound, with the current applied being in the microamperage range and maintained for 1 second or longer with no pulses in the flow.

ES using a pulsed current comprises a cyclic flow and no flow of electrons during treatment; a low-intensity pulsed current provides ES at approximately 10 µA, repeated 100 times per second. High-intensity pulsed current typically provides two short pulses (2–20 microseconds) at 100–500 V.

The complexities of the mode of application is further compounded by decisions regarding the frequency and duration of pulses, the size of the current applied, and the selection of appropriate electrodes.

The European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel published their joint guidance on pressure ulcer prevention and treatment in 2009. Of the 399 recommendations on pressure ulcer treatment, only one was considered to be supported by direct evidence from appropriately designed and conducted controlled trials in humans with pressure ulcers. The recommendation was that clinicians should “consider the use of direct contact (capacitative) electrical stimulation in the management of recalcitrant category II, III, and IV pressure ulcers to facilitate wound healing.”

Given the variety of interventions used in pressure ulcer treatment – including advanced wound dressings, sophisticated support surfaces, and other physical modalities (i.e. negative pressure wound therapy) – it may be surprising that only electrical stimulation was found to be supported by high-level clinical evidence. The justification for the recommendation that electrical stimulation should be strongly considered in wound healing will be considered in this review.
ES: HOW DOES IT WORK?
The human body can be viewed as a complex electrical system and medicine has used this system for many years both for diagnosis (electrocardiogram, encephalograms, etc) or to mimic endogenous electrical signals in therapy (heart pace makers, defibrillators, transcutaneous electrical nerve stimulation for pain management, etc).

At the core of all endogenous electric signals are measurable electric potentials that exist at cellular level (cell membrane), interstitial (between cell layers) and, most importantly for wound healing, at the epidermis. The potential at the epidermis is known as “transepithelial potential” (TEP) and varies between 10 mV and 60 mV (average, 23 mV). The TEP is caused by the concentration of negative chloride ions at the surface and positive sodium and potassium ions in the tissues, separated by the insulating levels of tight junctions of superficial cells.

During wounding, this epithelial seal is broken. The TEP collapses to 0 mV at the wound edge and ions immediately begin to leak out, establishing an “injury current” (ca. 10–100 µA) accompanied by its electric field (EF) of ca. 140 mV/mm, which rapidly falls to 0 mV/mm only 2–3 mm away from the wound edge. Depending on EF direction (i.e. polarity), neighbouring healthy cells – which are also electrically polarised – will be attracted or repelled and the speed and direction of their motility (electrotaxis) will be influenced by this.

Physiological EF also regulates the proliferation and the axis of cell division for all types of cells, thus contributing to filling the “wounded gap” – not only with regular tissue cells, but also with endothelial or nerve cells.

As wounds require different types of cells at different healing stages, and these cells have different polarisation, it is known that the DC impulses applied may vary at the different stages of wound healing. Monophasic DC impulses have been shown to give the most effective treatment as the response time of cells on application of an EF can vary between minutes and several hours.

Kloth provides a summary of the main biological effects of electrical stimulation in animal and human skin and soft tissues that is summarised in Box 1.

CLINICAL EFFECTS
In 2009, Koel reported the preliminary stages of a Cochrane review of the effects of ES on wound healing. Twenty randomised controlled trials (RCTs) published between 1985 and 2008 were included in the analysis. The included studies covered a range of wound types, including pressure ulcers, diabetic foot ulcers, venous leg ulcers, arterial leg ulcers, surgical wounds, and unspecified open, dermal or mixed aetiology wounds. ES in these studies was delivered via a number of modalities including direct current, pulsed current (in a variety of formats including monophasic and asymmetric biphasic), and high-voltage pulsed current.

The variety of wound types and treatment modalities makes synthesis of these trials challenging. Regardless of this, Koel presented two summary plots from 13 of the 20 RCTs comparing the effects of ES: one on all applied ES types, the other on monophasic ES. In 13 studies where all ES modes or sham ES were delivered; 44.4% (187/421) of those who received active ES healed, while only 25.9% (87/335) of wounds in the sham ES group healed, with an odds ratio of 2.12 (95% confidence interval [CI], 1.55–2.90) suggesting a higher rate of healing in the subjects who received ES. Koel also presented a summary
Electrical stimulation (ES) increases fibroblast production, promotes cell migration, increased wound angiogenesis and tissue oxygenation, and decreases bacterial burden. Some key questions remain to be answered before ES becomes a common clinical intervention in wound care, including whether specific wound types respond better to ES than others.

Key questions that remain to be answered before ES becomes a common clinical intervention in wound care are:

1. What are the best solutions to achieve the optimum wound healing response?
2. Do some wound types respond better to ES than others?
3. What is the best way to deliver ES to achieve maximum healing (frequency and duration of ES application for each wound type and anatomical location)?

**CONTRAINDICATIONS**

The contraindications for ES in wound care can be summarised as follows:

- ES might result in mitogenic activity in cancer cells, so it should not be used where there is a carcinoma or melanoma in the wound or adjacent skin.
- ES should not be used where there is untreated osteomyelitis in the base of a wound because ES might cause early closure of the soft tissue prior to resolution of the osteomyelitis, leading to potential abscess formation.
- ES should not be applied to the neck or thorax to prevent current flow through tissues such as the carotid sinus, the muscles of the larynx, or the pericardial area.
- ES should not be used where the electrodes are positioned in such a way that current flows through tissues where a pacemaker device is in place.

**FUTURE DEVELOPMENTS**

While the recommendations made by the European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel highlight the role of ES in the management of pressure ulcers, there is a need to optimise the delivery of ES, and this can only be achieved through research that compares the effects of different ES modalities, and treatment durations and frequencies on healing in like-wounds.

Key questions that remain to be answered before ES becomes a widely-used intervention in wound care are:

- What is the best way to deliver ES to achieve the optimum wound healing response?
- Do some wound types respond better to ES than others?
- What are the best solutions to achieve maximum healing (frequency and duration of ES application for each wound type and anatomical location)?

**CONCLUSION**

Although questions remain, reports from basic research in bioelectrochemistry, and the first analysis of clinical effects of ES in wound healing, show that ES has the potential to become a mainstream intervention in the treatment of chronic wounds.

**References**

Electrical stimulation means the stimulation of the human body using externally applied electrical charges and electrical fields. However, it is also a procedure that has been used for years in wound healing.

Over the past 15 years, scientists involved in basic bioelectric-chemical research have obtained important new information that has substantially improved our current understanding of the process of wound healing and electrical stimulation.

Uninjured skin forms a barrier between the negative charge on the surface of the skin and the positive charge below the skin. A wound breaks down this electrical insulation and creates a “short circuit current”. This “wound current” is accompanied by an electrical field (EF) that can last for 3–5 days. Current flows at the edge of a wound current (10–100 µA/cm²), but no current can be measured 2–3 mm away from the wound, and the transepithelial potential (TEP) has normal values.

These are physiological processes in a healthy organism. The EF at the edge of the wound is approximately 140 mV/mm and plays an important role in the control of different aspects of cell biology during wound healing. Conversely, in a chronic wound the ion flow necessary for healing is reduced or completely halted.

To reactivate healing in the chronic wound, the current (or rather the ion flow) must be recreated. At time-separated intervals (2 × 30 minutes per day) a pulsed direct current with a certain amplitude is applied to the wounds. The cells necessary for wound healing are attracted depending on the polarity setting. The activity of cells in wound healing (i.e. DNA synthesis, cell division, cell movement) is increased, growth factors are produced at an increased rate, the pH value of the wound changes, and nerve/vessel cells grow inwards. The charges also have an antibacterial effect, and pain from the wound is diminished. Therapy-resistant wounds can be stimulated to heal, and normal healing is accelerated by a factor of 2.8, compared to conventional therapies.

In his article, Michael Clark points out the recommendation made by the European Pressure Ulcer Advisory Panel and the National Pressure Ulcer Advisory Panel in their 2009 guidelines. It is strongly recommended that clinicians should consider the use of direct contact electrical stimulation in the management of recalcitrant pressure ulcers to facilitate wound healing. Interestingly, only electrical stimulation was reported to be supported by high-level clinical evidence.

The argument given in his article for the use of electrical stimulation is fully supported – and additionally, this recommendation not only should be applied to pressure ulcers, but on chronic wounds in general. The use of this technology is based on numerous conclusive experimental and clinical studies, strongly demonstrating the positive effects for accelerated wound healing on a cellular basis. The clinical setting of a large comprehensive wound healing unit shows that electrical stimulation has a positive impact on various chronic and hard-to-heal wounds.

References
The woundEL® device (Mölnlycke Health Care) has been successfully used for treating recalcitrant, hard-to-heal wounds in Germany for more than 3 years. This innovative technology comprises a device that delivers pulsed direct current through electrodes embedded within a dressing. This technology was trialled on patients at the author’s clinic. Over a 2-month period, patients with wounds of long duration that had shown no improvement with standard wound care received woundEL therapy. The therapy was evaluated on the basis of its ability to speed up debridement and induce granulation in these hard-to-heal wounds. Three cases are presented here.

Clinical experience: Electrostimulation with the woundEL® device

The woundEL® device (Mölnlycke Health Care) consists of a therapy device with dressing electrodes and a dispersing electrode. The device generates adjustable, low frequency direct current impulses that are applied through a sterile dressing electrode to the wound. The sterile dressing electrode is a medical-grade hydrogel layer, which not only provides a moist environment for healing, but also absorbs excess wound exudate.[1]

CLINICAL CASE 1: VENOUS ULCER OF LONG DURATION
A 79-year-old woman presented with a venous ulcer on the left internal malleolus [Fig 1]. This highly sloughy wound had been present for more than 5 years. The wound measured 25 cm², 10 cm at its longest point and 3.5 cm at its widest.

Treatment
The patient was treated for 4 months with the clinic’s standard protocol: hydrogel, alginates, and hydrocellular dressings. She was also treated with class 2 compression. The dressing was changed on average every 2 days.

After 4 months, treatment with woundEL was initiated twice a day for 30 minutes per session, and compression continued.

The dressing electrodes were changed at saturation (on average every 3 days).

Results
During the 4 months of hospital treatment prior to the start of electrotherapy, the wound was not progressing. Following the initiation of woundEL treatment, the wound started granulating and epithelialisation progressed until full healing was achieved within 2 months.

CLINICAL CASE 2: VENOUS ULCER OF LONG DURATION
A 46-year-old woman developed osteomyelitis following tibia and fibula fractures. While the osteomyelitis was treated successfully, a wound developed as a consequence of post-thrombotic venous disease and had persisted for the past 14 years. She was referred to the author’s clinic in mid-2008. The wound was very painful and the patient required high morphine doses.

Treatment
A decision was made not to treat the wound surgically and the patient was treated for 4 months with multilayer compression, soft
silicone wound contact layer dressings, and absorbent foam dressings with soft silicone wound contact surface. Although the wound healed with this regimen, healing was not sustained and the ulcer broke down. Over the following 10 months, treatment with standard methods was ineffective and the wound worsened.

The patient was commenced on woundEL therapy as an inpatient, then treated in the community when she was able to mobilise. The dressing electrode was changed every 3 days.

**Results**

In under 2 months, the wound progressed towards healing [Fig 1], and the patient reported that it was no longer painful.

**CLINICAL CASE 3: MARTORELL HYPERTENSIVE ISCHEMIC ULCER**

The patient, a 63-year-old man, was treated for a wound originating from a Martorell hypertensive ischemic ulcer on the middle third of the back of the right calf.

Martorell hypertensive ischemic ulcers are rare and result in severe skin necrosis of the lower extremities. They occur in people with long-term, poorly-controlled hypertension and are defined by pain disproportionate to the size of the ulcer. These ulcers are more common in women than men and may be misdiagnosed as pyoderma gangrenosum or necrotic vasculitis.

The patient had multiple comorbidities (chronic obstructive pulmonary disease, obesity, type 1 diabetes, hypertensive cardiopathy, allergies) which created a number of treatment challenges. Wound dimensions at the start of therapy were 35 cm², with a length of 7 cm and width of 6.5 cm [Fig 3].

**Treatment**

Following hospitalisation, the patient was put on a hygiene and diet plan. He was treated with advanced dressings (hydrogels, alginates, hydrocellular), which were changed every 2 days, and underwent surgical debridement to remove necrosis. The wound did not progress following debridement and necrosis reformed within 3 days of surgical debridement. The patient was treated with woundEL twice a day, with each treatment lasting 30 minutes and the electrode dressing changed every 3 days.

**Results**

Following the start of woundEL treatment, the wound was free of necrosis within 8 days.
Case report

and granulation was observed. Islands of epithelialisation appeared in the wound. Within 3 weeks of initiation of wound EL treatment, the wound bed was healthy and skin grafting was undertaken. Following the graft, woundEL was used until complete epithelialisation.

OVERALL RESULTS

The three cases described here show impressive results with the use of electrostimulation. Treatment resulted in improvements in the quality of the wound bed and rapid granulation. In each case presented, the wound granulated within 8 days of the initiation of woundEL treatment. These results – in wounds that had been recalcitrant for several months and even years – is clinically significant. At the time of writing, case two and three presented here remain healed. Case one relapsed, 14 months after healing, and died before treatment of the wound could be resumed.

Following this testing phase at the author’s clinic, woundEL therapy was adopted for wider use. Based on the literature[6–9], and the author’s clinic’s own audit, the primary criterion for electrostimulation therapy initiation is wound-healing stagnation following 4-weeks’ treatment with a traditional wound care protocol.

CONCLUSION

The experience of using woundEL in these cases indicates that electrotherapy is a promising treatment. It is well-tolerated and offers an alternative option for the treatment of hard-to-heal wounds.

Acknowledgement

This report was sponsored by Mölnlycke Health Care.

References

The authors review endogenous electrical fields (within tissues), how cells respond to these electrical gradients and their contribution to tissue development and repair. In chick embryos, endogenous currents and voltage gradients have been shown to be present during development, and therefore disruption of these gradients leads to impaired development. In vivo studies in rat cornea have demonstrated that natural electric fields regulate epithelial cell proliferation, cell division, nerve growth and ultimately wound healing. Physiological electric fields are important in directed cell migration; cells from the same tissue are able to migrate to different locations in response to the electric fields they encounter in development and regeneration. In vivo corneal studies in models in which chemical gradients and freed wound edge are thought to regulate wound healing have shown enhanced healing with addition of electric fields, with the polarity of the electric field determining whether a wound closed or opened up. This indicates a dominate healing effect of the electric fields. In addition to interacting with chemical gradients, electric fields also stimulate the secretion of growth factors and upregulation of growth factor receptors. The authors conclude that endogenous electric fields are present for many hours or days in wounds and during cell development with potential involvement across the broad spectrum of cell biology. Their physiological roles need to be explored further.


The National Pressure Ulcer Advisory Panel (NPUAP) and the European Pressure Ulcer Advisory Panel (EPUAP) collaborated to produce treatment recommendations as a guide for evidence-based care for individuals with pressure ulcers. The NPUAP–EPUAP definition of a pressure ulcer is a localised injury to the skin and/or underlying tissue as a result of pressure or pressure combined with shear. There are four pressure ulcer categories: non-blanchable erythema (I), partial thickness (II), full-thickness skin loss (III), and full-thickness tissue loss (IV).
Healthcare professionals are instructed to complete an initial assessment (including physical examination, complete medical history, nutritional analysis) of the individual with a pressure ulcer and conduct pressure ulcer assessments at least weekly, documenting all observations.

Assessments for pain related to pressure ulcers or its treatment using validated scales (different for adults and children), and measures to prevent (minimising or avoiding pressure) pain are recommended.

Wound dressings are vital for pressure ulcer care. Dressing selection is based on the tissue in the ulcer bed, condition of the surrounding skin and the goals of the individual. Different types of dressings and their maintenance are outlined.

The importance of educating the individual, caregivers, and healthcare providers about the causes, assessment, and management of pressure ulcer pain is highlighted.

These pressure ulcer treatment guidelines include strength of evidence ratings for each recommendation based on current research, offering healthcare professionals a quick and informed guide to the treatment of pressure ulcers.

The use of electrical stimulation for pressure ulcers was given the highest strength of evidence rating.


Using a new electrical stimulation device for pressure ulcer wound healing

Electrical stimulation has been shown to improve healing of pressure ulcers.

The aim of this prospective study was to examine the effect of pulsed electrical stimulation on indolent, persistent pressure ulcers.

Wounds that showed signs of healing in response to standard care (including maintenance of moist wound environment, infection control, turning to relieve pressure) were not included in this study, in an attempt to rule out the contribution of spontaneous healing.

The study cohort consisted of 61 stage III or IV pressure ulcers. The majority (54.1%) of ulcers were located in the sacral, buttock, or hip regions.

The study consisted of a 4-week pretreatment phase in which standard care was administered, and a treatment phase with evaluations at weeks 2, 4, and study end. During the treatment phase, all ancillary care was kept the same as in the pretreatment phase.

Treatment involved twice-daily 30-minute sessions of pulsed electrical stimulation using the Dermapulse® device (Staodyn; this device is no longer commercially available but has been succeeded by woundEL® [Mölnlycke] with the identical signal) at an initial rate of 128 pps at a peak amplitude of 29.2 mA. The stimulation rate was reduced to 64 pps on progression to stage II.

After 4 weeks, treatment-group and control-group wounds succeeded by woundEL® [Mölnlycke] with the identical signal) at an initial rate of 128 pps at a peak amplitude of 35 mA.

The primary efficacy measurement was important in wound stage or character after 2 weeks of treatment. Wound character improvement (by two or more levels) was achieved in 60.7% of ulcers, and wound stage improvement (by one or more stages) was achieved in 27.9%.

After 4 weeks of treatment, wound character was improved in 80.4% and wound stage in 58.8%. At the last week of treatment (mean, 7.3 weeks), improvements were seen in 82.0% and 73.8%, respectively.

With no safety problems reported, the authors concluded that the Dermapulse electrical stimulation device was safe and effective in promoting healing in indolent pressure ulcers.


Enhanced healing of chronic dermal ulcers using pulsed electrical stimulation

Clinical and experimental studies have shown that electric fields have a role to play in wound healing; the exogenous application of electric current to chronic wounds may mimic the body’s bioelectrical currents and enhance tissue healing processes.

The aims of this randomised, double-blind, multicentre study were to compare wound healing with pulsed electrical stimulation versus sham electrical stimulation of chronic dermal ulcers, and to assess patient tolerance to the therapeutic protocol.

The study population consisted of 47 participants who had 50 stage II, III, or IV chronic dermal ulcers between them. The age range was 29–91 years; 52% of participants were men.

Participants were randomly allocated to the treatment group (n=26) or control group (n=24). The trial lasted 4 weeks with treatment (according to the protocol) consisting of twice-daily 30-minute active or sham electrical stimulation.

Electrical stimulation was via the Vara/Pulse® device (Staodynamics; this device is no longer commercially available but has been succeeded by woundEL® [Mölnlycke] with the identical signal]) at an initial rate of 128 pps at a peak amplitude of 29.2 mA. The stimulation rate was reduced to 64 pps on progression to stage II.

After 4 weeks, treatment-group and control-group wounds were on average 44% and 67%, respectively, of their original size (P<0.02). The healing rates were 14.0% and 8.2% per week, respectively.

Only one type of treatment-related adverse event (tingling sensations in the wound) was reported, occurring in 10% of the control group and 20% of the treatment group.

The authors concluded that the pulsed electrical stimulation used in this study was safe and effective in wound healing of stage II, III, and IV chronic dermal ulcers.