Effect of low-intensity direct current on the healing of chronic wounds: a literature review

Few studies have assessed the effectiveness of electrical stimulation on chronic wounds. Nevertheless, the evidence suggests it is a potentially useful, accessible and cheap therapy, which might play a valuable role in everyday practice.

**Low-intensity direct current; wound healing; electrical stimulation**

Recent studies have shown that physical therapies (the term used in the US for the prevention, treatment and management of disease through non-surgical and/or non-pharmacological methods) such as compression therapy, electrical stimulation, ultrasound, laser therapy and ultraviolet exposure (electromagnetic radiation, invisible light) can play a role in the treatment of chronic wounds. This paper focuses on electrical stimulation, focusing on low-intensity direct current (LIDC).

**Electrical stimulation**

The effects of using electrical stimulation to promote healing chronic wounds have been studied since the 1960s. Electrical stimulation:
- Stimulates DNA and collagen synthesis
- Guides the movement of epithelial, fibroblast and endothelial cells into the wound
- Slows the growth of some wound pathogens
- Increases the tensile strength of the wound scar.

Four types of electrical stimulation are used to treat chronic wounds:
- Low-intensity direct current
- Low-voltage pulsed current (LVPC)
- Alternating current (AC)
- Transcutaneous electrical nerve stimulation (TENS).

Differences between the currents of these four types of electrical stimulation are illustrated in Fig 1.

We undertook a literature review to determine whether or not LIDC is an effective treatment for wound care. We focused on LIDC because it was the first current used in wound management and has been tested in animal and human studies. We plan to review studies on other types of electrical stimulation in the near future.

**Direct current**

Direct current (also known as continuous current or galvanic current) is an electrical current that flows in one direction (Fig 1), and is produced by batteries, thermo couplings and solar cells. In wound care, a low intensity (20–1000µA) direct current is used to avoid damaging healthy tissue.

Low-intensity direct current promotes chronic wound healing via two mechanisms:
- Galvanotaxis
- Its antibacterial effect.

Galvanotaxis is the mechanism by which an electrical field promotes wound healing by stimulating the migration of fibroblasts and keratinocytes. This occurs because wounds and injured skin carry electrical charges which move when an external electrical current is applied.

A surgical wound is initially electropositive, but gradually becomes negative during the healing process. Wood et al., who measured this in abdominal surgical wounds, stated that ‘the normal healthy human epidermis has polarity with the outer surface (ie, the stratum corneum and stratum granulorum), being electronegative, while the base layer is electropositive.’

Animal and human studies have shown that a direct current has an antibacterial effect. Rowley stated that a current of 1–140mA inhibits the growth of *Escherichia coli B*, with the effect being attributed mainly to the negative electrode. Other studies also found that direct current (like other types of electrical stimulation) slows the growth of *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa*.

**The literature search**

A search of Pubmed, Cinahl, Web of Science and the Cochrane Collaboration Database, using the key words ‘electrical stimulation’, ‘wound healing’ and ‘low intensity direct current’, identified 314 clinical trials, randomised controlled trials (RCTs) and meta-analyses. Of these, only seven met the inclusion criteria:
- Studies on humans with chronic wounds
Studies involving LIDC
Studies whose subjects were aged 20 years and above.

Of those seven studies, four used constant LIDC (CLIDC) and three intermittent LIDC (ILIDC). The excluded literature mostly comprised case reports and animal studies, or involved the use of other types of electrical-stimulation waves, such as low-voltage pulsed current and TENS.

Constant low-intensity direct current
The four CLIDC studies measured the wound size, changes in wound characteristics and the healing rate (ie, the percentage reduction in wound surface area). Study durations varied from four to eight weeks.

In an eight-week clinical trial, Gault et al. used CLIDC to treat 76 patients with 106 ischaemic skin ulcers. They applied a negative electrode directly onto the wound for the first three days in the expectation that this would have an antibacterial effect and debride the necrotic tissue. They intended to replace the negative electrode with a positive one when the wound was debrided. They placed a saline-soaked gauze pad between the wound and the electrode. The current used was 200–800µA for two hours, three times daily.

Six of the 76 patients had bilateral ulcers, which were almost symmetrical. In each of these six patients, one ulcer was treated with CLIDC and the other conventionally (cleansing and debridement). The latter six ulcers were classified as the ‘controls’.

The mean healing rate per week for the 100 ulcers was 28.4%. The mean healing time was 4.7 weeks (range three days to 24 weeks). Forty-eight of the 100 ulcers healed completely. Furthermore, the negative electrode debrided the necrotic tissue.

In the six patients with bilateral ulcers, the mean healing rate for the CLIDC ulcers was 30% per week, compared with 14.7% for the six ‘controls’. Three CLIDC ulcers healed completely during the study. In contrast, none of the control ulcers healed and two increased in size.

However, bilateral symmetrical ulcers very rarely occur in practice, so the number of ‘controls’ was very small. A larger control group would be needed to give more meaningful results. Nevertheless, the application of both CLIDC and conservative treatment to the same patient provides an interesting clinical insight into the potential benefits of the former therapy, while the study as a whole had a large sample size of 100 patients, and so could make a good case for more rigorous research.

In a controlled clinical trial, Carely and Wainapel treated 15 (unspecified) wounds with CLIDC and 15 with conservative treatment (debridement and wet to dry gauze) for five weeks. The CLIDC was applied at an intensity of 300–700µA for two hours in two sessions per day, five days per week. For the first three days, the negative electrode was placed directly on the wound and the positive electrode was positioned 15–25cm away on the healthy surrounding tissue. On the fourth day, the polarity was switched.

At the end of the five weeks, the mean healing rate for the treatment group was 89%, compared with 45% for the control group. P values for the differences in healing rates between the two groups were <0.05 at weeks 3 and 4 and <0.01 at week 5; these were statistically significant. The researchers did not report the healing times and number of healed ulcers.

The researchers followed up the patients after they had completed the CLIDC therapy, although they did not provide detailed information on this. They reported that the CLIDC had a positive effect on ‘scar formation’: there were no signs of clinical infection, and no further debridement was needed. In contrast, in the control group healed skin reopened, infection occurred and debridement was needed every two weeks, although the number of patients affected was not specified.

A study limitation was that the randomisation
Fig 2. Placement of the electrodes in DC positive and DC positive and negative group

The process was not rigorous: participants were paired on the basis of age, diagnosis, wound aetiology, location and approximate wound size, and each member of the pair was then randomly assigned to one of the two groups. Furthermore, it was not possible to blind the researchers to the treatments.

Karba et al. conducted a double-blind clinical trial in which 50 spinal injured patients with pressure ulcers were allocated to one of three groups:
- DC positive group — where a positive electrode was applied onto the wound and a negative electrode (in the form of four self-adhesives) to the healthy surrounding skin (n=16 patients)
- DC positive and negative group — where a positive electrode was applied to the healthy surrounding skin on one side of the wound and a negative electrode to that on the other (n=18 patients). An earlier study had found this improved healing rates
- Control group (sham) — with a ‘positive’ and a ‘negative’ electrode on either side of the wound, as above (n=16 patients).

The positioning of the electrodes is illustrated in Fig 2. The current used was 0.06mA; the CLIDC was delivered for two hours per day on a daily basis. In addition, all groups received daily conventional treatment, which included cleansing and dry dressings.

The results showed a remarkable mean healing rate of 7.4% per day in the DC positive group, compared with 4.8% in the DC positive and negative group and 4.2% in the sham group. This difference between the DC positive and other groups was statistically significant (p=0.028). Healing times and the study duration were not reported.

These results indicate that the positioning of the electrode plays an important role in the healing outcome. However, there are study limitations that should be taken into account when interpreting the results: the inclusion criteria were not clearly stated, while the allocation method to the three groups was not specified. Furthermore, not all patients can tolerate a direct current for two hours on a daily basis, which will affect the generalisability of the results.

Adunsky et al. used direct current in a different way. They designed a device, which they termed ‘decubitus direct current treatment’ (DDCT), that delivers a direct current into the wound, but is also connected to a computer that can record patient data and photographs of the wound.

In their multicentred double-blind RCT, Adunsky et al. used this device to treat 63 patients with 35 stage III pressure ulcers for 45 days; patients were then followed up for 90 days. Thirty-five patients were randomised to receive DDCT and 28 to a placebo (sham). The electrodes were placed on intact skin surrounding the wound. The current used and frequency of the treatment sessions were not reported. Both groups received surgical debridement as required, followed by a hydrocolloid or collagen dressing. Pressure relief was also provided.

The mean healing rate reported in the DDCT group on day 45 was 44%, compared with 14% in the control group. However, the healing rate in the treatment group slowed down from day 56, and on day 135 was slightly higher in the control group.

Twenty-five patients dropped out of the study during the treatment phase for unspecified reasons. As a result, only 38 patients entered the follow-up phase. While this was a double-blind RCT with a large sample size, it did have limitations, including the large drop-out rate and use of an unvalidated LIDC device.

**Intermittent low-density direct current**

Intermittent low intensity direct current (ILIDC) delivers a current that goes up to 29.2 milliams (mA) and then back down to zero. The researchers who used ILIDC in their studies believed that the higher current would be more effective, while the intermittent application would avoid damaging the newly healed tissues.

In a double-blind multicentred controlled trial, Wood et al. allocated 43 patients with stage II and III pressure ulcers that had not responded to standard nursing practice to ILIDC and 31 to a placebo (sham ILIDC). The electrodes were placed 2cm from the edge of the wound on the healthy surrounding skin. The current used was 300–600μA. Both groups received standard treatment comprising wound cleansing, use of a simple dressing that promotes moist wound healing and whirlpool baths.

Twenty-five ulcers in the ILIDC group healed completely within eight weeks, and the remaining 18 had a mean healing rate of 80%. In the control group, only four ulcers had healed by up to 80% at eight weeks, while the rest had increased in size. The difference in healing rates between the two groups was statistically significant (p<0.001). Wood et al. also found that PLIDC facilitated calcium transportation in the skin.

While this double-blind study had a reasonably large sample size and appropriate statistical analysis,
the randomisation process was not described, and the difference in size between the two groups was not explained.

In a double-blind multicentred RCT, Feedar et al. allocated 47 patients with a total of 50 ulcers (17 pressure ulcers, six surgical wounds and three traumatic wounds) or a control (sham) (n=24 ulcers: 18 pressure ulcers, three surgical wounds, one vascular wound and two traumatic wounds). For the first three days, the investigators placed a negative electrode onto the wound and a positive electrode 15cm away on the healthy surrounding tissue. On the fourth day, the polarity was switched. The polarity was changed in this way every three days until the wound healed. Dosage was 35mA, applied for 30 minutes twice a day on a daily basis. Other than ILIDC, patients in both groups received debridement as needed.

The mean healing rate in the ILIDC group at the end of four weeks was 56%, compared with 33% for the control group. This difference was statistically significant (p<0.02).

A clear study limitation is the sample size of only seven participants, so the results are not generalisable. Nevertheless, it was double-blinded, and the inclusion of stage IV ulcers might have made it easier to compare healing rates.

Adegoke et al. treated four stage IV pressure ulcers in spinal injured patients with ILIDC and three with a placebo (sham). A negative electrode was placed on the wound and the dispersive electrode (a positive electrode, also known as an inactive electrode) on the healthy surrounding skin for 45 minutes daily. All patients received unspecified routine nursing care.

One participant from the treatment group dropped out. The mean healing rate at the end of four weeks was 22.2% for the four ulcers treated with ILIDC, compared with only 2.6% for the placebo group. Adegoke et al. recommended that the treatment duration should not be longer than one hour. Clearly, the study’s very small sample size limits the generalisability of the results.

The main results of all seven studies are summarised in Table 1.

### Table 1. Summary of the main results

<table>
<thead>
<tr>
<th>Reference</th>
<th>Type of trial</th>
<th>No. of patients</th>
<th>Mean healing rate</th>
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<tbody>
<tr>
<td><strong>Constant low-intensity direct current</strong></td>
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<tr>
<td>Gault and Gatens&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Clinical trial</td>
<td>CLIDC: 100</td>
<td>28.4% per week</td>
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<tr>
<td></td>
<td></td>
<td>CLIDC: 6</td>
<td>30% per week</td>
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<tr>
<td></td>
<td></td>
<td>Control: 6</td>
<td>14.7% per week</td>
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<tr>
<td>Carely and Wainapel&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Controlled clinical trial</td>
<td>CLIDC: 15</td>
<td>18% per week</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control: 15</td>
<td>9% per week</td>
</tr>
<tr>
<td>Karba et al.&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Double-blind clinical trial</td>
<td>DC positive: 16</td>
<td>7.4% per day</td>
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<tr>
<td></td>
<td></td>
<td>DC positive and negative: 18</td>
<td>4.8% per day</td>
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<td></td>
<td></td>
<td>Sham: 16</td>
<td>4.2% per day</td>
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<tr>
<td>Adunsky et al.&lt;sup&gt;17&lt;/sup&gt;</td>
<td>Multicentred double-blind RCT</td>
<td>CLIDC: 35</td>
<td>44% on day 45</td>
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<tr>
<td></td>
<td></td>
<td>Sham: 28</td>
<td>14% on day 45</td>
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<tr>
<td><strong>Intermittent low-intensity direct current</strong></td>
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<tr>
<td>Adegoke et al.&lt;sup&gt;18&lt;/sup&gt;</td>
<td>Small controlled trial</td>
<td>ILIDC: 4</td>
<td>Mean surface area of the ILIDC group had decreased by 22.2% at end of week 4 versus 2.6% for placebo group</td>
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<tr>
<td></td>
<td></td>
<td>Placebo: 3</td>
<td></td>
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<tr>
<td>Wood et al.&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Double-blind multicentred controlled trial</td>
<td>ILIDC: 43</td>
<td>Decrease in wound size of &gt;80%: 73% for ILIDC group versus 13% for placebo group</td>
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<tr>
<td></td>
<td></td>
<td>Placebo: 31</td>
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<tr>
<td>Feedar et al.&lt;sup&gt;8&lt;/sup&gt;</td>
<td>Double-blind multicentred RCT</td>
<td>ILIDC: 26</td>
<td>14% per week</td>
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<tr>
<td></td>
<td></td>
<td>Placebo: 24</td>
<td>8.5% per week</td>
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**Discussion**

In normal human skin, a difference in ionic concentration is dynamically maintained between the upper and lower epidermal layer (10–60mV). When
the skin layer is interrupted, the ionic current (injured current) flows through the subdermal region out of the wound and then returns, flowing between the stratum corneum and dermis. This endogenous current plays an active role in healing. This review demonstrates that application of LIDC can improve the endogenous current within the wound.

Four studies used CLIDC, although they applied the electrodes differently, with some of the researchers placing a negative electrode onto the wound for the first three days in the expectation that its antibacterial effect would stimulate granulation tissue formation. Indeed, the results do suggest that placing an electrode directly onto a wound increases the healing rate, compared with when it is placed on the surrounding skin.

The studies that used CLIDC reported higher healing rates than those that applied ILIDC. Unfortunately, there is as yet no explanation for this.

Low-intensity direct current therapy is accessible, easy to use and cheaper than many other complex wound therapies. However, practitioners will need training on the following:

- Preparing the patient for the therapy
- Dosage selection and frequency
- Application
- Indications, contraindications and precautions.

In our experience, use of CLIDC for at least one hour per day, five times a week, promotes wound healing. Fig 3 illustrate healing achieved after five weeks of LIDC. Fig 4 shows the electrodes on the wound. We reassure patients that the current will be reduced on request, although its use has not been associated with pain or discomfort. This therapy appears to be a potentially beneficial treatment option, but further, more rigorous studies are needed to generate further evidence.

**Conclusion**

Low-intensity direct current not only has an antibacterial effect, but also promotes healing of chronic wounds, thus benefiting both patients and practitioners. It appears that higher healing rates will be achieved if a negative electrode is placed directly onto the wound for the first three days or until the wound has been debrided. However, this therapy does appear to merit a place in clinical practice.

**References**