14 Electrical Currents for Soft Tissue Healing

Michelle H. Cameron | Sara Shapiro | Michelle Ocelnik

CHAPTER OUTLINE

Mechanisms Underlying Electrical Currents for Tissue Healing
Galvanotaxis
Cell Activation
Antimicrobial Effects
Enhanced Circulation
Clinical Applications of Electrical Stimulation for Soft Tissue Healing
Chronic Wounds: Pressure Ulcers, Diabetic Ulcers, Venous Ulcers
Edema Control
Transdermal Drug Delivery: Iontophoresis
Contraindications and Precautions for Electrical Currents for Tissue Healing
Contraindications for Electrical Currents for Tissue Healing
Precautions for Electrical Currents for Tissue Healing
Adverse Effects of Electrical Currents for Tissue Healing
Application Techniques
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Electricity has been used to enhance wound healing for many centuries. About 300 years ago, electrostatically charged gold leaf was found to accelerate the healing of smallpox lesions. In the mid-1800s, Du Bois-Reymond was the first to measure the naturally occurring electrical current in a wound, and since the mid-1900s, exogenous electrical currents in the form of electrical stimulation have been used to treat wounds. More recently, through research in vitro, and in animals and in humans with several different types of wounds, we have come to better understand the mechanisms underlying the effects of electrical currents on tissue healing, including impact on cell migration, proliferation, and function.

Approximately 6 million Americans develop chronic, nonhealing wounds each year, with the costs of caring for these wounds exceeding $50 billion per year.[1] Wounds may impede rehabilitation, prevent the patient from participating in usual activities, and increase the overall cost of care. In people with diabetes and resulting peripheral vascular disease, foot ulcers and infection are the leading causes of hospitalization, and 70% to 90% of leg amputations are caused by vascular ulcers.[2] In people with spinal cord injury, untreated pressure ulcers can lead to hypoproteinemia, malnutrition, osteomyelitis, sepsis, and death.[3] Promoting wound healing is therefore essential, potentially improving quality of life, enabling patients to participate more fully in other components of rehabilitation, optimizing functional outcomes, and decreasing overall costs. Effective wound management requires an integrated multidisciplinary approach that includes collaboration among a team that may include nurses, physical and occupational therapists, dietitians, physicians, the patient, and the patient's family and their caregivers. This chapter focuses specifically on the role of electrical currents to promote soft tissue healing. This chapter does not cover the use of electrical currents to promote bone (fracture) healing. Although electricity, generally in the form of induced electrical fields, can promote fracture healing, electrical bone stimulators are almost always dispensed directly to the patient by a physician and are not used by physical therapists or occupational therapists, the primary readers of this book. This chapter also does not cover the other aspects of wound care including nutrition, debridement, positioning, dressings, and other interventions required to achieve wound healing. As with other physical agents, electrical stimulation serves as an adjunct to other aspects of care to help achieve optimal outcomes.

Clinical Pearl

Electrical stimulation is an adjunct to other aspects of wound care, which include nutrition, debridement, positioning, and dressings.

Mechanisms Underlying Electrical Currents for Tissue Healing

In rehabilitation, electrical stimulation is most commonly used to control pain or to produce muscle contractions, but it can also promote tissue healing. Tissue healing may be aided directly by applying current to a wound or indirectly by controlling edema or promoting transdermal delivery of medications.

In chronic wounds, the endogenous healing mechanism is disrupted. Electrical stimulation is thought to promote tissue healing by imitating endogenous electrical currents to attract appropriate cell types to the area **(galvanotaxis)**, activate these cells by altering cell membrane function, enhance antimicrobial activity, or promote circulation and thereby reduce edema and improve tissue oxygenation.

GALVANOTAXIS

Galvanotaxis, the directional movement of cells in response to an electrical field, is important for cells engaged in various

machine or external battery. Some research supports that with the equivalent mA-min dose, longer delivery with lower current delivers drug more effectively than shorter delivery at higher current.[107] Reducing the current amplitude also helps decrease the risk of local adverse effects including pain, skin irritation, and chemical burns.

TABLE 14.5 Current Amplitude and Treatment Duration for Iontophoresis Treatment

Current Amplitude, mA	Treatment Time, min	Dose, mA-min
1	40	40
2	20	40
3	13.3	40
4	10	40

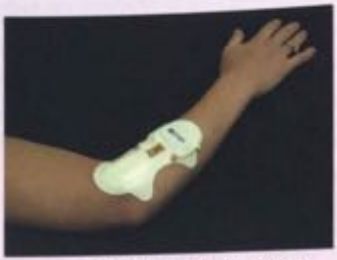

FIGURE 14.8 A 24-hour iontophoresis patch.

Documentation

Documentation is generally written in the form of a SOAP note. When using electrical stimulation to reduce edema or for tissue healing, document the following:

- The area of the body to be treated
- Patient positioning
- Specific stimulation parameters
- Electrode placement
- Treatment duration
- Patient's response and response of the wound to treatment, including the condition of the skin and surrounding areas.

The level of detail should be sufficient for another clinician to be able to reproduce the treatment using your notes.

EXAMPLES

When applying electrical stimulation (ES) to a full-thickness venous ulcer on the left lateral ankle, document the following:

S: Pt alert and oriented ×3. She states she has been keeping her L lower extremity elevated as much as possible because the edema in her L ankle increases with dependent positioning.

O: Intervention: Pt supine with 2 pillows under L leg for elevation. HVPC to L lower extremity ×1 h. Saline-soaked gauze treating electrode placed in wound, dispersive electrode placed on proximal posterior calf. Frequency 10(pps, negative polarity to treatment area, intensity to sensory level.

Posttreatment: Wound area decreased from 10 × 5 cm on first treatment 3 weeks ago to 8 × 3 cm today.

A: Pt tolerated treatment well. Wound size decreasing.

P: Continue HVPC to L lateral ankle area until wound closes. Change polarity if healing plateaus.

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CLINICAL CASE STUDIES

The following case studies demonstrate the concepts of the clinical application of electrical stimulation discussed in this chapter. Based on the scenario presented, an evaluation of the clinical findings and goals of treatment are proposed. These are followed by a discussion of the factors to be considered in the selection of electrical stimulation as an indicated intervention and in the selection of the ideal electrical stimulation parameters to promote progress toward the set goals of treatment.

CASE STUDY 14.1

Lateral Ankle Sprain

Examination

History

MC is a 23-year-old student. He injured his left ankle during a soccer game at school earlier today. He was seen by the attending physician on the field and diagnosed with a grade II lateral ankle sprain. MC's ankle was packed in ice, and he was sent to the locker room for immediate physical therapy follow-up. The physician instructed MC to use non-weight-bearing crutches to rest the injured ankle.

Systems Review

MC reports disappointment in his inability to finish the soccer season. Visual inspection shows MC is holding his ankle in a single position and expresses extreme hesitancy in allowing the therapist to move the joint. MC is otherwise healthy and denies a history of cancer, diabetes, or other significant health problems.

Tests and Measures

Gentle passive range of motion (PROM) reveals restrictions in all directions. Active range of motion (AROM) is minimal

stage III or stage IV pressure ulcers, arterial ulcers, diabetic ulcers, and venous stasis ulcers that have not previously responded to standard wound treatment in 30 days.[50] The cost of electrical stimulation for wound care is covered only when performed by a physician or a physical therapist or incident to a physician service.

Clinical Pearl

In 2002, the U.S. Centers for Medicare and Medicaid Services approved payment for electrical stimulation when performed by a physician or a physical therapist, or incident to a physician service, to treat chronic stage III or stage IV pressure ulcers, arterial ulcers, diabetic ulcers, and venous stasis ulcers that have not previously responded to standard wound treatment in 30 days.

Systematic reviews published in 2013 and 2014 of studies comparing electrical stimulation with standard care for healing any type of chronic wound both found 21 studies that met their inclusion criteria.[48,51] Overall, in these trials, electrical stimulation significantly accelerated the rate of wound healing. Systematic reviews with meta-analyses published in 2014 and 2015 focused specifically on studies evaluating the effects of electrical stimulation on pressure ulcers in individuals with spinal cord injury included 21 and 15 studies, respectively. More studies were included in the 2014 review than in the 2015 review because the 2014 review included studies on pressure ulcer prevention as well as treatment.[47,52] Overall, the 2014 meta-analysis came to no firm conclusion but the 2015 review concluded that electrical stimulation significantly decreased pressure ulcer size compared to standard wound care or sham stimulation and increased the likelihood of complete wound closure. Similarly, a 2014 systematic review of nine trials focused on the effects of electrical stimulation on healing pressure ulcers in any population found moderate evidence of efficacy with low risk of adverse effects and substantial savings in health care costs.[49] In evaluating all studies of treatments for pressure ulcers, a systematic review and a comparative effectiveness report from the Agency for Healthcare Research and Quality (AHRQ) concluded that electrical stimulation, as well as air-fluidized beds, protein supplementation, and radiant heat dressings, improved pressure ulcer healing but found no clear evidence to recommend one intervention, or any particular combination of interventions, over another.[53,54]

Intermittent electrical stimulation to produce muscle contractions has also been investigated as a means to prevent deep tissue injury.[55] In this context, electrical stimulation was found to significantly reduce pressure around the tuberosities, produce significant and long-lasting elevations in tissue oxygenation, and significantly reduce discomfort produced by prolonged sitting, performing as well as or better than both voluntary contractions and chair push-ups.

EDEMA CONTROL

Edema is a normal response after tissue trauma. Edema can have protective effects including splinting the injured area and being a component of the first stage of tissue healing, inflammation. However, edema is also associated with increased pain, decreased function, and prolonged recovery.[56] It is proposed that effective edema management can expedite return to activities from acute injuries such as joint sprains and strains and that electrical stimulation reduces inflammation-associated edema at least as well as medications such as ibuprofen, with fewer risks.[57]

Edema is an abnormal accumulation of fluid that produces swelling. Several potential causes of edema are known, including systemic disorders, inflammation, and lack of motion. Edema caused by systemic disorders such as heart failure, liver failure, or kidney failure generally causes symmetrical swelling in the dependent distal extremities, particularly the legs, and can cause fluid to accumulate in the lungs and abdomen. Electrical stimulation should not be used to treat edema suspected to have a systemic cause because this intervention may drive fluid from the extremities into the central circulation, further overwhelming the failing organ system and increasing the risk of pulmonary edema. Electrical stimulation may be used to treat edema caused by inflammation or by lack of motion.

Clinical Pearl

Electrical stimulation may be used to treat edema caused by inflammation or by lack of motion. Electrical stimulation should not be used to treat edema suspected to have a systemic cause because this intervention may drive fluid from the extremities into the central circulation, further overwhelming the failing organ system.

Edema Due to Inflammation

Edema can form directly after an acute injury as part of the inflammatory response. An area with this type of edema will appear red and feel warm. Applying electrical stimulation to control this type of edema has been studied extensively by Fish and Mendel and their coworkers.[58-64] A 2010 systematic review of the literature concluded that HVPC may curb edema formation after acute injury, although this conclusion is based primarily on studies of intentional injury in animals.[56] This review specifically supported the use of HVPC administered using negative polarity, with a pulse frequency of 120 pulses/s and an intensity of 90% of visible motor contraction, administered for four 30-minute sessions 4 hours apart or for one continuous 180-minute session. A 2011 review of treatments for acute edema associated with burns also supported the benefits of electrical stimulation to reduce edema formation.[64] Although studies show that applying electrical stimulation during the inflammatory response can retard the formation of edema, they have not clearly shown that this treatment reduces the amount of edema already present or accelerates return to play or activities.[63,64] Specifically, negative polarity HVPC below the threshold for motor contraction has been found to retard the formation of edema by approximately 50% compared with no treatment after acute injury in animal models.[63] In contrast, positive polarity HVPC[62] and **biphasic pulsed current**[67] have not been found to be effective for this application. The magnitude of the effect of negative polarity HVPC on the formation of acute edema is similar to that of ibuprofen[57] or cool-water immersion.[65]

The parameters used for electrical stimulation for iontophoresis are discussed in detail here and are summarized in Table 14.4.

Patient Positioning

When electrical stimulation is applied for iontophoresis, the patient should be positioned comfortably with the locations for both electrodes clearly visible by the clinician.

Electrode Type

Two distinct types of electrodes can be used for iontophoresis. Historically, iontophoresis has been delivered with a powered controller connected to two electrodes. With this setup, the dispersive electrode is a self-adhesive transmissive electrode, and the treatment electrode is a self-adhesive type that can be filled with the medication solution. At the present time, iontophoresis is more often delivered with a low-voltage, powered electrode patch. With this setup, a single, self-adhesive patch contains both electrodes and the power source. When the electrode surfaces are wetted and attached to the skin, the battery activates, initiating transmission of the drug.

Electrode Placement

For iontophoresis, the drug delivery electrode is placed over the area of pathology. When a low-voltage patch electrode is used, both negative and positive polarity electrodes are within the same patch. When an iontophoresis unit with wired electrodes is used, the dispersive or return electrode is placed a few inches away from the treatment electrode at a site of convenience over a large muscle or the belly (Fig. 14.7). The electrode should be large enough that the **current density** does not exceed 0.5 mA/cm^2 when the **cathode** (negative electrode) is used as the delivery electrode, and 1.0 mA/cm^2 when the **anode** (positive electrode) is used.[43]

Polarity

For iontophoresis, the drug delivery electrode should have the same polarity as the active ion of the drug to be delivered.

Current Amplitude and Treatment Time

As discussed earlier, for iontophoresis, the dose of electricity is determined by the current (amperage) multiplied by the time, such as 40 mA-min. A number of combinations of current and time can be used to achieve this dose: a 1-mA current for 40 minutes, 2-mA current for 20 minutes, and 4-mA current for 10 minutes all give treatment of 40 mA-min (Table 14.5). In practice, if a separate power source is used, the current amplitude should be set to patient comfort with a maximum of 4 mA, and then the device will adjust the treatment time to produce the intended dose. It is important to check the patient's skin during this treatment because the DC and the small electrodes used for iontophoresis produce a high current density, increasing the risk of burning the patient.

Alternatively, most iontophoresis applications in rehabilitation today use a powered electrode that generates a very low current amplitude

for many hours to achieve the dose (Fig. 14.8). The electrodes contain a battery that activates when the drug is applied to the electrode (also called a patch), and the patch is applied to the skin. The patch can be worn under clothing and requires no

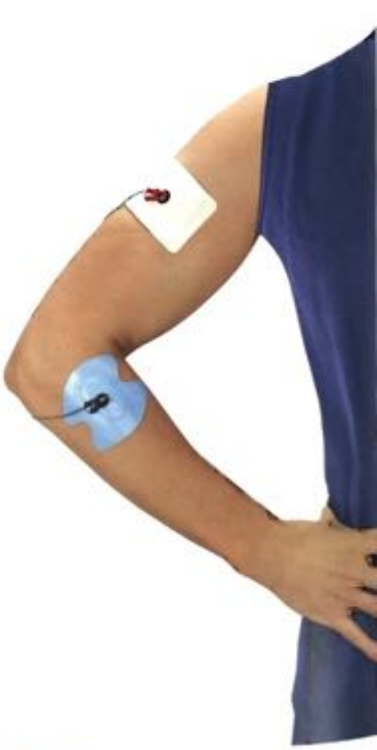

FIGURE 14.7 Electrode placement for iontophoresis with a wire unit.

TABLE 14.4 Recommended Parameter Settings for Electrical Stimulation for Iontophoresis

Parameter Settings/Goal of Treatment	Waveform	Pulse Frequency	Pulse Duration	Amplitude	Active Electrode Polarity	Treatment Time
Iontophoresis	DC	NA	NA	To patient tolerance, no greater than 4 mA	Same as drug ion (see Table 14.1)	Depends on amplitude, to produce a total of 40 mA-min

DC, Direct current; *NA*, not applicable.

CONTRAINDICATIONS FOR ELECTRICAL CURRENTS FOR TISSUE HEALING

CONTRAINDICATIONS

for Electrical Currents for Tissue Healing

Standard contraindications for all electrical stimulation (see Chapter 11 for details):

- Demand cardiac pacemaker, implantable cardiac defibrillator (ICD), or unstable arrhythmias
- Placement of electrodes over carotid sinus
- Areas where venous or arterial thrombosis or thrombophlebitis is present
- Pregnancy—over or around the abdomen or low back (electrical stimulation may be used for pain control during labor and delivery, as discussed in Chapter 13)

Additional contraindications for electrical currents for tissue healing:

- Malignant tumors
- Do not apply iontophoresis after any intervention that is likely to alter skin permeability.

Malignant Tumors

The presence of malignant tumors is generally a precaution for electrical stimulation. However, when monophasic currents such as those typically used for wound healing are applied, the presence of malignancy is of even greater concern. This is because the galvanotaxis (directional movement of cells in response to an electrical field or charge) may impact metastasis (i.e., movement of cells from the primary tumor to other sites.[99]

Ask the Patient

- "Have you ever had cancer? Do you have cancer now?"
- "Do you have fever, sweats, chills, or night pain?"
- "Do you have pain at rest?"
- "Have you had recent unexplained weight loss?"

Iontophoresis After Any Intervention That Is Likely to Alter Skin Permeability

Iontophoresis should not be administered after use of any physical agent that may alter skin permeability such as heat, ice, or ultrasound because this could alter the amount of drug that will penetrate the skin, potentially underdosing or overdosing. In addition, heat should be avoided before iontophoresis because it will cause vasodilation and increased blood flow, accelerating dispersion of the drug from the treatment area.

PRECAUTIONS FOR ELECTRICAL CURRENTS FOR TISSUE HEALING

PRECAUTIONS

for Electrical Currents for Tissue Healing

Standard precautions for all electrical stimulation (see Chapter 11 for details):

- Cardiac disease
- Impaired mentation
- Areas with impaired sensation
- Areas of skin irritation

Additional precautions for electrical currents for tissue healing:

- Infection control

Particular attention should be paid to the following when electrical current is used for tissue healing:

- Infection control
  - If electrodes are placed in wounds, a new electrode (typically gauze) should be used each time.
  - Self-adhesive electrodes should be single-patient use only.
  - Chronic open wounds should be kept clean but cannot be sterile.
  - Protective covers for electrical stimulation devices and leads are available to minimize the transmission of communicable diseases such as methicillin-resistant *Staphylococcus aureus* (MRSA). After these covers are used, they should be left in the patient's room.

Adverse Effects of Electrical Currents for Tissue Healing

Although electrical stimulation for wound healing is very safe in general, some adverse effects have been reported including excessive granulation formation, skin irritation, and burns when the stimulus intensity was set too high.[100,101]

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Application Techniques

APPLICATION TECHNIQUE 14.1 WOUND HEALING

General guidelines for the application of electrical stimulation are provided in Chapter 11. The following information builds on this foundation, providing specific recommendations, techniques, and parameters for applying electrical stimulation for wound healing.[10] These recommendations are summarized in Table 14.2.

Patient Positioning

When electrical stimulation is applied for wound healing, position the patient so that the wound is readily visible, and pressure on the wound is minimized.

Electrode Type

In general, when using electrical stimulation for wound healing, two or more electrodes are used: a treatment electrode or electrodes on or close to the wound and a dispersive electrode near the wound. The dispersive electrode completes the electrical current circuit and is not considered a "treating" electrode.

For the dispersive electrode, use a large, self-adhesive, disposable electrode. For the treatment electrode, use a purpose-made electrode form-fit to the shape of the wound. To do this, first place saline-soaked gauze directly in the wound and then cover it with a single-use

APPLICATION TECHNIQUE 14.1 WOUND HEALING—cont'd

Pulse Duration

When pulsed electrical current is used to promote wound healing, the recommended **pulse duration** is between 40 µs and 200 µs.[3] With HVPC, this parameter is generally preset in the device to approximately 70 to 100 µs by the manufacturer and cannot be changed by the clinician. However, with other monophasic pulsed currents, the pulse duration usually can be adjusted.

Frequency

Pulse **frequency** for promoting tissue healing should be 60 to 125 pps.

On:Off Time

Electrical stimulation is delivered continuously throughout treatment time when applied for tissue healing. This maximizes the amount of charge delivered and thus the attraction of charged particles.

Current Amplitude

The current **amplitude** should be sufficient to produce a comfortable sensation without a motor response. If the patient has decreased or altered sensation in the treatment area, the appropriate amplitude can be determined by first applying the electrode to another area of normal intact sensation.

Treatment Time

At the present time, most studies recommend treating for at least 5 days each week, with each treatment lasting 45 to 60 minutes.

APPLICATION TECHNIQUE 14.2 EDEMA CONTROL

When electrical stimulation is used to control edema, the therapist must determine whether edema is caused by acute inflammation, lack of muscle contraction, or by other systemic causes (e.g., heart, kidney, or liver failure). Electrical stimulation can be used to treat edema associated with acute inflammation or lack of muscle contraction, but different parameters must be used for these different types of edema. Electrical stimulation should not be used to treat edema from other causes. Patients with edema of other causes should be evaluated by a medical provider. The parameters used for electrical stimulation for edema control are detailed here and are summarized in Table 14.3.

Parameters for Edema Associated With Inflammation

Electrical currents can be used to control edema associated with inflammation. Note that the following recommendations apply only when edema is caused by inflammation and not when edema and circulatory compromise are caused by lack of muscle activity. The information presented here on application techniques to control edema caused by lack of muscle contraction is also presented in Chapter 12 for the reader's convenience.

Patient Positioning

When electrical stimulation is applied to inhibit the formation of edema associated with inflammation, the patient should be positioned with the involved area elevated to help promote flow of fluid out of the extremity to the central circulation. Ice and compression may also be applied to further control inflammation and edema.

Electrode Type

In general, when using electrical stimulation to control formation of edema associated with inflammation, self-adhesive disposable electrodes are recommended.

Electrode Placement

The negative polarity treatment electrodes should be placed directly over the area of edema, with the dispersive electrode placed over another large, flat area near the area of edema (Fig. 14.5).

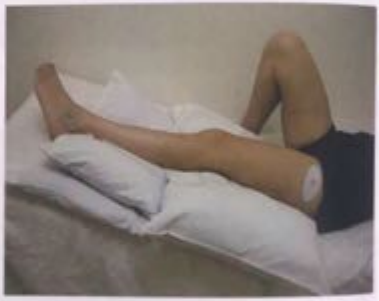

FIGURE 14.5 Electrode placement to retard acute edema formation at the ankle.

Waveform

HVPC is the recommended waveform.

Pulse Duration

The pulse duration for HVPC is usually fixed by the manufacturer in the range of 40 to 100 µs.

Polarity

The negative polarity electrode should be placed over the area of edema.

Frequency

The pulse frequency is set to 120 pps.[38]

APPLICATION TECHNIQUE 14.2 EDEMA CONTROL—cont'd

TABLE 14.3 Recommended Parameter Settings for Electrical Stimulation for Edema Control

Parameter Settings/ Goal of Treatment	Waveform	Polarity	Pulse Frequency	Pulse Duration	Amplitude	Treatment Time
Edema control: for edema associated with inflammation	HVPC	Negative	120 pps	Usually preset for HVPC at 40–100 µs	90% of visual motor threshold	30 min
Edema control: for edema associated with lack of motion	Biphasic (can use interferential if on:off time available)	NA	35–50 pps, 2–5 s equal on:off times	150–350 µs	To visible contraction	20–30 min

HVPC, High-voltage pulsed current; *NA*, not applicable; *pps*, pulse per second.

On:Off Time

Electrical stimulation is delivered continuously throughout the treatment time. This maximizes the amount of charge delivered and thus the attraction of negatively charged particles.

Current Amplitude

The current amplitude should be set to 90% of visual motor threshold.

Treatment Time

Electrical stimulation is generally applied for 30 minutes per session but may be used more than once a day, up to every 4 hours.

Parameters for Control of Edema Associated With Lack of Muscle Contraction

Electrically stimulated muscle contractions can also be used to help control edema and improve circulation when edema and poor circulation are caused by lack of muscle activity. Note that the following recommendations apply only when edema and circulatory compromise are caused by lack of muscle activity and *not* when edema is caused by inflammation. The information presented here concerning control of edema caused by lack of muscle contraction is also presented in Chapter 12 for the reader's convenience.

Patient Positioning

When electrically stimulated muscle contractions are used to control edema or promote circulation caused by lack of muscle activity, the patient should be positioned with the involved area elevated to help promote flow of fluid out of the extremity to the central circulation. In this circumstance, the electrically stimulated muscle contractions facilitate edema control and promote circulation by intermittently compressing the veins and lymphatics to promote venous and lymphatic return.

Electrode Type

In general, when using electrical stimulation for muscle contractions to facilitate edema control and promote circulation, self-adhesive disposable electrodes are recommended.

Electrode Placement

The electrodes should be placed on the muscles around the main veins draining the area (Fig. 14.6). For example, with edema in the foot, the electrodes should be placed on the calf of the same side.

Waveform

A pulsed biphasic waveform or **Russian protocol** is recommended.

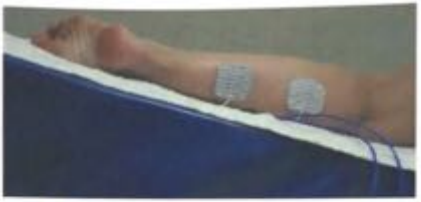

FIGURE 14.6 Electrode placement for neuromuscular electrical stimulation to control edema caused by lack of muscle activity.

Pulse Duration

When a pulsed biphasic waveform is used, the pulse duration should be between 150 and 350 µs—sufficient to produce a muscle contraction. When Russian protocol is used, the cycle duration cannot be adjusted.

Frequency and On:Off Time

When using electrically stimulated muscle contractions to control edema caused by disuse, the goal is to produce short, low-force, repetitive muscle contractions to pump fluid through the vessels. There are two different ways to achieve this.

1. If you have a device that allows you to set an **on:off time,** set the pulse frequency at 35 to 50 pps, as used to produce muscle contractions for other purposes, and set the on time and the off time at 1 to 2 seconds. This will produce tetanic contractions lasting 1 to 2 seconds with 1 to 2 seconds of relaxation between contractions.
2. If you have a device that does not allow you to set an on:off time, set the pulse frequency at 1 to 2 pps. This will produce one to two twitch contractions each second with relaxation between contractions.

Current Amplitude

The current amplitude should be sufficient to produce a small, visible muscle contraction.

Treatment Time

The stimulation is generally applied for 20 to 30 minutes per session but may be used more than once a day if needed to control edema.

TABLE 14.2 Recommended Parameter Settings for Electrical Stimulation for Tissue Healing[15,17]

Parameter Settings/ Goal of Treatment	Waveform	Polarity	Pulse Frequency	Pulse Duration	Amplitude	Treatment Time
Tissue healing: inflammatory phase/ infected	HVPC	Negative	100–105 pps	Usually preset for HVPC at ~100 µs	To produce comfortable tingling	45–60 min daily, 3–7 days/week
Tissue healing: proliferation phase/clean	HVPC	Positive	100–105 pps	Usually preset for HVPC at ~100 µs	To produce comfortable tingling	45–60 min daily, 3–7 days/week

HVPC, High-voltage pulsed current; pps, pulses per second.

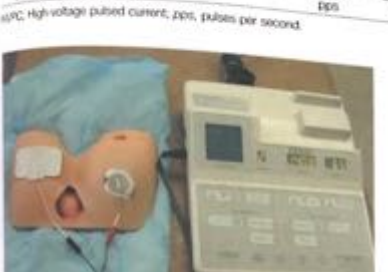

FIGURE 14.2 Electrode placement to promote tissue healing, with treatment electrode in the wound.

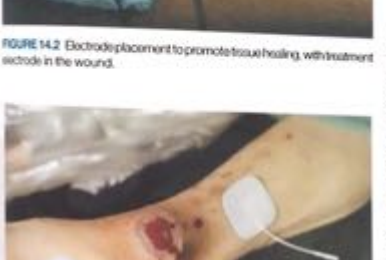

FIGURE 14.3 Electrode placement to promote tissue healing with treatment electrodes on either side of the wound.

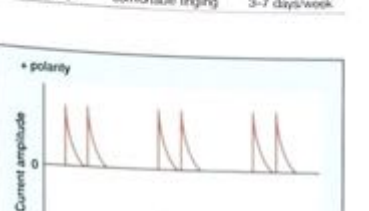

FIGURE 14.4 High-voltage pulsed current.

disposable electrode, a multiuse carbon rubber electrode, or a layer of heavy duty aluminum foil. Then attach the electrode to the lead wire (Fig. 14.2). Alternatively, commercially available self-adhesive electrodes may be placed on either side of the wound (Fig. 14.3), but this approach is probably less effective.[149]

Electrode Placement

Treatment electrodes may be placed in or around the wound. One treatment electrode is used when it is placed directly in the wound; it should be contoured to fit the wound. Two or more electrodes are used when applying stimulation to the area around the wound. Then place one large, dispersive electrode of opposite **polarity** to the treatment electrode on intact skin several inches away from the wound site. This electrode should be larger than the sum of the area of the treatment electrodes in or near the wounds. The large size allows the current to be dispersed over a greater area, providing greater comfort for the patient, while not limiting the intensity of the stimulation under the active electrode.

Waveform

When electrical stimulation is applied to promote tissue healing, a monophasic waveform—where the electrodes are of consistent opposite polarity—is generally recommended. HVPC, a **monophasic pulsed current** (Fig. 14.4), was used in most studies that showed benefit for this application and is likely to be most effective. Although a few studies have found low-intensity DC (LIDC), pulsed biphasic, and AC waveforms to be effective, they are generally less so,[150] have slightly higher risk of burns, and less closely mimic the endogenous current of injury.[43] Other parameter recommendations for the HVPC waveform are provided below.

Polarity

The polarity of the electrode on or nearest to the wound is selected according to the types of cells required to advance a particular stage of wound healing and the presence or absence of infection or inflammation in the wound.[7] Negative polarity is generally used during the early inflammatory stage of healing, whereas positive polarity is used later to facilitate epithelial cell migration across the wound bed. Kloth recommends using negative polarity for the first 3 to 7 days of treatment and changing to positive polarity thereafter; however, some researchers recommend using negative polarity for all treatments.[43,44,104] Another recommendation is to use negative polarity initially and for 3 days after the wound bed becomes free of necrotic tissue and the drainage becomes serosanguineous and thereafter to use positive polarity.[126,134] Consistent with many recommendations, most clinicians use negative polarity initially and, when the wound shows signs of inflammation, switch polarity when there are no signs of inflammation or when wound healing plateaus.

TABLE 14.1 Ions Used Clinically for Iontophoresis Including Ion Source, Polarity, Recommended Indications, and Concentration

Ion	Source	Polarity	Indications	Concentration (%)
Acetate	Acetic acid	Negative	Calcium deposits	2.5–5
Chloride	NaCl	Negative	Sclerotic	2
Copper	$CuSO_4$	Positive	Fungal infection	2
Dexamethasone phosphate	$DexNa_2PO_3$	Negative	Inflammation	0.4
Hyaluronidase	Wydase	Positive	Edema reduction	—
Iodine	—	Negative	Scar	5
Lidocaine	Lidocaine 1 :50,000 with epinephrine	Positive	Local anesthetic	5
Magnesium	$MgSO_4$	Positive	Muscle relaxant, vasodilator	—
Salicylate	NaSal	Negative	Inflammation, plantar warts	2
Tap water	—	Negative/positive	Hyperhidrosis	—
Zinc	ZnO_2	Positive	Dermal ulcers, wounds	—

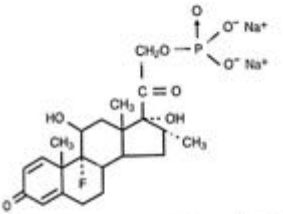

FIGURE 14.1 The molecular structure of dexamethasone sodium phosphate. The negatively charged dexamethasone phosphate ion is moved across the dermal barrier by iontophoresis using the negatively charged electrode.

time, the manufacturers of iontophoresis electrodes recommend using iontophoresis only to deliver dexamethasone. However, the use of other substances such as acetic acid for treatment of recalcitrant scarring, calcific tendinitis, or heel pain has been reported.[85–87] Dexamethasone is a corticosteroid with antiinflammatory effects. Dexamethasone iontophoresis has been found to be more effective than placebo or injection in the treatment of lateral epicondylitis and plantar fasciitis[79,80,83] and may be effective in other local inflammatory disorders.[88] Dexamethasone is delivered by iontophoresis using a 0.4% solution of dexamethasone sodium phosphate. The negative polarity electrode is used to promote penetration of the negatively charged dexamethasone phosphate ion through the skin (Fig. 14.1). The delivery of other medications by iontophoresis such as the nonsteroidals naproxen and ketoprofen to control inflammation and the synthetic opiate analgesic fentanyl to control pain has also been studied. Iontophoretic delivery of naproxen was shown to be effective in reducing pain in lateral epicondylitis, and an iontophoretic transdermal system is approved by the U.S. Food and Drug Administration to deliver fentanyl for control of postoperative pain.[81] Iontophoretic delivery of fentanyl has been shown to be more effective than placebo and to have comparable effects to intravenous morphine, supporting the approval of an iontophoretic fentanyl delivery system, by physician order only, for hospitalized patients.[82]

Much research has explored using iontophoresis to deliver a wide range of other medications, including insulin for diabetes, leuprolide for hormonal effects, calcitonin analogues for osteoporosis, cyclosporine for immunosuppression, beta blockers for hypertension, antihistamines for allergies, triptans for migraines, ondansetron for nausea and vomiting, prednisolone for bronchial asthma, zinc phthalocyanine tetrasulfonic acid for cancerous tumors, dexamethasone phosphate for dry eyes, and midazolam for pediatric sedation before surgery.[76,93–98] The primary challenges facing new applications of iontophoresis are not its ability to deliver drugs through the skin, but rather to control the precise dose (bioavailability) of the drug and patient intolerance of the stimulation. Because of the limitations of other delivery methods, iontophoresis is likely to be a topic of much future research.

Contraindications and Precautions for Electrical Currents for Tissue Healing

The standard contraindications and precautions for all electrical stimulation, as described in detail in Chapter 11, also apply to using electrical currents for tissue healing. For more detailed information on these contraindications and precautions, refer to the section on contraindications and precautions for the application of electrical currents in Chapter 11.

In addition to the standard contraindications for all electrical stimulation, do not use electrical currents for wound healing when there is concern for malignancy. Iontophoresis should also not be used after the application of any physical agent that may alter skin permeability such as heat, ice, or ultrasound. Heat causes vasodilation and increased blood flow that can accelerate dispersion of the drug from the treatment area. In addition, all contraindications and precautions for the drug being delivered must be observed.

Several theories have been suggested for how HVPC retards edema formation associated with inflammation. The negative charge can repel negatively charged serum proteins, essentially blocking their movement out of blood vessels. The current may also decrease blood flow by reducing microvessel diameter, although negative polarity stimulation has not been shown to have an effect on microvessel diameter.[69] Alternatively, the current may reduce pore size in microvessel walls, thereby preventing large plasma protein from leaking through the pores.[70] In the normal histamine response to acute trauma, these pores would be enlarged. However, since both negative polarity and positive polarity HVPC decrease microvessel permeability, some other mechanism likely underlies the reduced edema formation associated only with negative polarity stimulation.

Edema Due to Lack of Muscle Contraction

The use of electrical stimulation to control edema caused by lack of muscle contractions is also discussed in Chapter 12 as one of the clinical applications of neuromuscular electrical stimulation (NMES). In this circumstance, the electrical stimulation is applied to produce muscle contractions in order to reduce edema caused by poor peripheral circulation due to lack of motion.[71]

Lack of muscle contractions, particularly in a dependent limb, causes edema to form in the distal extremities because the muscles fail to pump fluid proximally through the veins and lymphatics. Contraction of the limb muscles is needed to compress the veins and lymphatic vessels to promote return flow of fluid from the periphery. If the muscles do not contract, fluid in the form of edema accumulates. An area with this type of edema will appear pale and will feel cool. Edema of this type can be treated by applying motor-level electrical stimulation to the muscles around the main draining veins. Motor-level electrical stimulation, in conjunction with elevating the legs, has been shown to increase popliteal blood flow in subjects with a history of lower limb surgery or thromboembolism[72] and to reduce the increase in foot and ankle volume produced in healthy volunteers after standing motionless for 30 minutes.[70] In contrast, sensory-level electrical stimulation has not been found to be effective for this application.[67] To control edema, NMES should be applied in conjunction with elevation and followed by use of a compression garment (see Chapter 20).

The improvement in blood flow produced by NMES[73] can also accelerate tissue healing and help reduce the risk of deep venous thrombosis (DVT) formation. Motor-level NMES of the calf muscles has been found to be 1.7 to 3 times more effective than intermittent pneumatic compression for promoting venous circulation, suggesting this could be a more convenient and effective way to prevent DVTs.[74] Even NMES of just the foot is as effective in promoting venous circulation and preventing DVTs as intermittent pneumatic compression.[75]

TRANSDERMAL DRUG DELIVERY: IONTOPHORESIS

The use of an electrical current to promote transdermal drug penetration is known as **iontophoresis.** Iontophoresis has been used for more than 100 years to deliver therapeutic drugs while avoiding some of the side effects of oral, nasal, or parenteral routes of administration. When taken orally, some drugs produce gastrointestinal distress, and others are incompletely absorbed.[76] Nasal delivery allows absorption of some low-concentration drugs, and many individuals find this route of administration uncomfortable. Additionally, injections and infusions carry risks of injection site reactions. Therefore, transdermal delivery is an attractive alternative if the compound can get through the skin and can be absorbed at sufficiently high rates and concentrations to be effective.

Iontophoresis is the use of low-amplitude DC to facilitate transdermal drug delivery. The use of iontophoresis was first reported in the early 1900s.[77,78] Iontophoresis works in part because like charges repel, and therefore a fixed-charge electrode on the skin can "push" the charged ions of a drug through the skin. Iontophoresis, similar to phonophoresis, may also promote transdermal drug penetration by increasing the permeability of the outermost layer of the skin, the stratum corneum, the main barrier to transdermal drug uptake. The most common use of iontophoresis in rehabilitation is to apply the antiinflammatory corticosteroid, dexamethasone.[79] Iontophoresis may be preferred over oral delivery if the patient is nauseated or vomiting; over nasal delivery, which can leave a bad taste in the patient's mouth and has low bioavailability; and over injections, which can be painful and may cause bleeding, infection, and traumatic injury.

Clinical Pearl

Iontophoresis uses low-amplitude DC to facilitate delivery of medications through the skin.

The depth to which a drug is delivered by iontophoresis is uncertain. Most studies have demonstrated penetration to a depth of 3 to 20 mm.[80] For example, lidocaine could be detected 5 mm below the surface of the skin in humans when delivered by iontophoresis together with epinephrine to maintain local vasoconstriction and thus keep the drug in the local area.[81] Other studies have also found that iontophoresis can be used to deliver drugs systemically by having them cross the skin barrier to the bloodstream, which then distributes them throughout the body.[82]

For an electrical current to facilitate transdermal drug penetration, the current must be at least sufficient to overcome the combined resistance of the skin and the electrode being used.[83] The amount of electricity used for performing iontophoresis is described according to charge, in milliamp minutes (mA-min). This is the product of the current amplitude, measured in milliamps, and the time, measured in minutes. The number of milliamp minutes depends on the specific electrode being used and is determined by the manufacturer of the electrode. At the present time, most studies and manufacturers support using 40 to 80 mA-min for each iontophoresis treatment.[82,84]

Many drugs can be delivered by iontophoresis as long as they can be ionized and are stable in solution, they are not altered by the application of an electrical current, and their ions are small or moderate in size. Different drugs have been used to treat different pathologies (Table 14.1). At the present

processes including embryogenesis, regeneration, and wound healing.[4] Galvanotaxis can cause specific cells including neutrophils, macrophages, lymphocytes, and fibroblasts to move to an injured healing area because these cells carry a **charge**.[5,6] Recent research suggests that calcium ion flow from the anode (positively charged pole) to the cathode (negatively charged pole),[7] calcium and sodium channel responses,[8] and stimulation of adenosine triphosphate (ATP) release[9] may underlie cathode-directed galvanotaxis.

The process of galvanotaxis appears to be a normal, healthy response to tissue injury that can be augmented with appropriate electrical stimulation.[10] When skin and cell membranes are intact, there is an electrical charge across them as a result of the action of the sodium/potassium pumps. As soon as tissue is injured, rupturing cell membranes, charged ions leak out of the cells, causing the center of the wound to become electrically charged relative to the surrounding uninjured tissue.[11,12] This charge difference is commonly termed a *skin battery*, producing an electrical current of injury that activates healing.[13] This current has been demonstrated in children with accidental finger amputations.[14] This electrical potential difference steadily declines over time, returning to normal only after the wound closes. Electrical stimulation with a monophasic pulsed or direct current applied to the wound is thought to promote wound healing by replicating or supplementing the effects of this skin battery.

Macrophages, epidermal cells, and inactive neutrophils are attracted to the anode, whereas lymphocytes, platelets, mast cells, keratinocytes, neural progenitor cells, fibroblasts, and activated neutrophils are attracted to the cathode.[9,15,16] In order to attract the most appropriate cell types for the phase of tissue healing, it is generally recommended that the negative electrode be used to treat infected or inflamed wounds and the positive electrode be used if necrosis without inflammation is present and when the wound is in the proliferative stage of healing.[17]

Clinical Pearl

In general, the negative electrode should be used to promote healing of inflamed or infected wounds, and the positive electrode should be used to promote healing of wounds without inflammation.

CELL ACTIVATION

Not only does electrical stimulation attract cells to an injury site, it also activates these cells. Most of the research in this area has been carried out using fibroblasts, the cells that make collagen to close a wound. Electrical stimulation activates fibroblasts, enhancing their replication and their synthesis of DNA and collagen, upregulating growth factor pathways, and inducing them to become myofibroblasts.[18-21] Fibroblasts and the collagen they produce are essential for the proliferation phase of tissue healing. It is proposed that the electrical current pulse triggers calcium channels in the fibroblast cell membrane to open. The open channels then allow calcium to flow into the cells, increasing intracellular calcium levels to induce exposure of additional insulin receptors on the cell surface. Insulin can then bind to the exposed receptors, stimulating the fibroblasts to synthesize collagen and DNA.[22,23] Electrical stimulation also modulates fibroblast gene expression. This includes genes involved in many processes such as cell adhesion, remodeling, and spreading; cytoskeletal activity; extracellular matrix metabolism; production of cytokines, chemokines, and growth factors; and signal transduction.[24] These processes may all contribute to tissue healing. Cellular responses to electrical currents are voltage dependent, with maximum calcium influx and protein and DNA synthesis occurring with high volt pulsed **current** (HVPC) with a peak **voltage** in the range of 80 to 90 V. Both higher and lower voltages have less effect. Electrical stimulation can also promote epidermal cell and lymphocyte migration, proliferation, and function,[25] possibly by increasing vascular endothelial growth factor (VEGF) production or release.[26] VEGF stimulates the development of microcirculation near the wound, which enhances delivery of oxygen and nutrients.

Although most studies using electrical stimulation for wound healing have used a monophasic pulsed current, there is evidence that alternating and biphasic currents may have some benefit.[27] Since these currents do not have a net charge effect on the tissue, they cannot exert effects through galvanotaxis but it is possible that biphasic pulsed currents activate cells

ANTIMICROBIAL EFFECTS

Electrical stimulation may also promote tissue healing through its antimicrobial activity. Monophasic currents, both microampere level **direct current (DC)** and HVPC, have been shown to kill bacteria in vitro, whereas alternating current (AC) has not been found to affect bacterial growth or survival.[17,28,29] This effect of DC and HVPC is likely due to electrolytic generation of hypochloric acid.[30] However, most research indicates that to inhibit bacterial growth, an electrical current must be applied at much higher voltages or for much longer times than used in the clinical setting.[30-35] Therefore this mechanism is not likely to contribute strongly to the benefits seen with standard electrical stimulation for wound management. However, recent research suggests that monophasic or direct current electrical stimulation enhances the activity of some antibiotic agents against bacteria in biofilms, where they are usually resistant to antibiotics.[36,37]

ENHANCED CIRCULATION

It is possible that electrical stimulation also facilitates tissue healing by increasing circulation during or after the stimulation.[38] This effect appears to be augmented when stimulation is applied in a warm room.[39,40] Over time, there may be some increase in circulation due to acceleration of angiogenesis via VEGF.[41] However, it is unlikely that stimulation increases circulation through vessels already in the area because, in general, muscle contractions are required for electrical stimulation to increase circulation, and tissue healing has been shown to be enhanced by submotor levels of stimulation.[42-45]

Clinical Applications of Electrical Stimulation for Soft Tissue Healing

CHRONIC WOUNDS: PRESSURE ULCERS, DIABETIC ULCERS, VENOUS ULCERS

A number of studies and systematic reviews support the benefits of electrical stimulation for enhancing wound healing.[17,46-49] In 2002, the U.S. Centers for Medicare and Medicaid Services approved payment for electrical stimulation to treat chronic