Electrical stimulation therapy for wound healing: a WHAM evidence summary

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CLINICAL QUESTION

What is the best available evidence for electrical stimulation therapy (EST) for promoting healing in hard-to-heal wounds?

SUMMARY

Electrical stimulation therapy is a biophysical modality through which an electromagnetic current is delivered to the wound with the intention of promoting wound healing. The electrical current is thought to influence healing by increasing blood flow to the wound bed. *Level 1* evidence[1-9] of moderate certainty suggested that electrical stimulation therapy has a moderate effect in improving wound healing for hard-to-heal wounds, including pressure injuries (PIs) and diabetic foot ulcers (DFUs), when used in conjunction with standard wound care. It is best clinical practice to have appropriate qualifications and training before delivering biophysical modalities as adjuvant treatment to standard wound care.[10-12]

CLINICAL PRACTICE RECOMMENDATIONS

All recommendations should be applied with consideration to the wound, the person, the health professional, and the clinical context.

Electrical stimulation therapy could be used by appropriately trained wound clinicians as an adjuvant to standard wound care to promote healing in hard-to-heal wounds, pressure injuries and diabetic foot ulcers.

SOURCES OF EVIDENCE

This summary was conducted using methods published by the Joanna Briggs Institute.[13-16] The summary is based on a systematic literature search combining search terms related to wounds and EST. Searches were conducted in Embase, Medline, Cochrane Library and Google Scholar. Due to the volume of evidence, inclusion was limited to evidence from meta-analyses published from January 2013 to December 2023 in English. Levels of evidence for intervention studies are reported in the table below.

BACKGROUND

Electrical stimulation therapy involves applying an electrical current to the wound. The current is generally generated by a battery-type device at various electrical frequencies, amplitudes, polarities, and either in a direct, alternating or pulsed (monophasic or biphasic) current. The electrical stimulation is applied by placing at least two electrodes on the skin (with at least one applied to either the wound bed or the peri-wound skin) to conduct the electrical current through the wound tissue. The mechanism through which electrical current might promote wound healing is suggested to be promoting increased blood flow and reducing tissue oedema, which positively influences tissue oxygenation and cell proliferation.[3, 9, 22] Stimulation with an anodal electrode is used to stimulate autolysis and the inflammatory response in infected wounds, and application of the cathode electrode at the wound/peri-wound tissue is used to promote perfusion during wound granulation and epithelialisation.[19]

Level 1 evidence	Level 2 Evidence	Level 3 Evidence	Level 4 Evidence	Level 5 Evidence
Experimental designs	**Quasi-experimental Designs**	**Observational – Analytic Designs**	**Observational – Descriptive Studies**	**Expert Opinion/ Bench Research**
1.a Systematic review of RCTs[1-4, 6, 7, 9, 17-19] 1.b Systematic reviews of RCTs and other designs[5, 8, 20]	Not eligible	Not eligible	Not eligible	5.a Expert consensus and literature reviews[10-12, 21, 22]

Electrical stimulation therapy can be broadly categorised based on the response the amplitude elicits in the individual. Higher amplitudes (300-400 milliamps [mA]; e.g. electrical muscle stimulation [EMS]) generate a motor response (e.g., muscle contraction); however, this level of stimulation is generally not required in wound care.[21] Electrical stimulation therapy at an amplitude of 150-250 mA (e.g. trans-epidermal nerve stimulation [TENS]) leads to a sensory response (e.g., tingling or prickling) and at less than 100 mA the stimulation is sub-sensory (i.e. the recipient does not sense the stimulation).[21] Sub-sensory electrical stimulation at the lowest of amplitude (e.g., below 60mA) is referred to as microcurrent stimulation.[21] Most EST is delivered in sessional treatments and using a range of regimens (regularity, duration, etc.)[19].

'Electroceuticals' that deliver sub-sensory (i.e., below 100mA), microcurrents directly to the wound have been developed.[21, 23, 24] This therapy, referred to as microcurrent therapy, uses medical devices/wound dressings to generate continuous very low amplitude microcurrents that mimic natural biological electrical fields using either external electrical sources (e.g., wearable devices) or through embedded chemical reactions between silver, zinc and moisture in the wound bed.[23, 24] This evidence summary will only address evidence exploring the use of external electrical sources.

CLINICAL EVIDENCE

Electrical stimulation therapy for promoting healing in pressure injuries (PIs)

Seven meta-analyses[1-5, 7, 8] provide the best evidence on electrical stimulation for promoting healing of PIs. All the meta-analyses included randomised controlled trials (RCTs) that were evaluated for risk of bias, and the evidence on the effect of EST for healing PIs was rated as being at moderate certainty.[3] The meta-analyses included various combinations of the same RCTs (see Table 1), one of the meta-analyses also included non-randomised, controlled trials[8] and another included case series[5]. Four of the meta-analyses[2, 3, 7, 8] combined results from studies using any type of EST and four of the meta-analyses[1, 4, 5, 7] specifically reported monophasic pulsed current EST.

In most of the studies, EST was applied with one electrode on the wound bed and the second electrode placed on healthy peri-wound skin.[19] The electrical current intensity varied from eliciting a minimal motor contraction to mild tingle, and the frequencies ranged up to 100Hz.[3,19] One study[25] reported in the meta-analyses used direct current at a level below sensation (i.e. microsimulation).

The Cochrane review[3] pooled the most RCTs, combining data from 11 studies comparing any EST plus standard wound care (n = 284) to standard care with no EST (i.e., either standard care plus sham therapy or standard care alone; n = 228). The review found that the proportion of PIs that heal within 12 weeks may increase when electrical stimulation therapy is added to the treatment regimen (relative risk [RR] 1.99, 95% confidence interval [CI] 1.39 to 2.85[3]). The effect size was similar to that reported in most of the other meta-analyses.[2,5,7,8] It was uncertain if electrical stimulation therapy plus standard wound care leads to faster

Table 1. Evidence in meta-analyses on electrical stimulation therapy for complete PI healing

Reported studies	PI stage	Type of EST¥	Meta-analyses						
¥ DC = direct current; LVBPC = low voltage biphasic pulsed current; LVBPC = low voltage monophasic pulsed current; HVMPC = high voltage monophasic pulsed current; TENS = trans-epidermal nerve stimulation			Girgis 2023[1]	Chen 2023[2]	Arora 2020[3]	Zhang 2019[4]	Girgis 2018[5]	HQO, 2017[7]	Lala 2016[8]
Adunsky 2005[25]	Stage 3	DC		X	X			X	
Asbornsen 1990[26]	Not reported	TENS			X				
Baker 1996[27]	Not reported	LVBPC							X
Feedar 1991[28]	Stage 2-4	HVMPC			X				
Franek 2011[29]	Stage 1-3	HVMPC	X		X		X		
Griffin 1991[30]	Stage 2-4	HVMPC	X	X	X			X	X
Houghton 2010[31]	Stage 2-4 and unstageable	HVMPC	X	X	X		X	X	X
Jerčinović 1994[32]	Not reported	LVBPC		X					
Karba 199[53]3	Stage 3-4	LVBPC							X
Kloth 1988[34]	Stage 4	HVMPC	X						
Polak 2016a[35]	Stage 2-3	HVMPC	X	X	X		X	X	
Polak 2016b[36]	Stage 2-4	HVMPC	X	X	X				
Polak 2017[37]	Stage 2-4	HVMPC	X	X	X		X		
Polak 2018[38]	Stage 2-4	HVMPC	X	X	X				
Wood 1993[39]	Stage 2-4	LVMPC		X	X			X	

PI healing compared to standard wound care only[3] (2 RCTs, hazard ratio [HR] 1.06, 95% CI 0.47 to 2.41; *Level 1*).

Electrical stimulation therapy for promoting healing in diabetic foot ulcers (DFUs)

Three recent meta-analyses[1,17,18] reported electrical stimulation therapy for treating DFUs, combining 11 studies (see Table 3) based on outcome measures. The studies varied from low to high risk of bias, and the evidence was appraised as being of moderate certainty.[1] Only two of the studies reported completed DFU healing as an outcome measure, and the risk ratio favoured electrical stimulation therapy in addition to standard wound care compared to standard wound care alone (RR 1.43, 95% CI 0.92 to 2.24).[1] Percent reduction in DFU surface area also favoured EST (7 studies, standardised mean difference [SMD] 2.56, 95% CI 1.43 to 3.69).[18] Sub-analyses suggested similar results between pulsed current and direct current EST for treating DFUs[17, 18].

Electrical stimulation therapy for promoting healing in hard-to-heal wounds

Two meta-analyses[6,9] that combined studies on EST for promoting healing in hard-to-heal wounds of any aetiology were identified. Many of the studies were also included in the aetiology-specific meta-analyses summarised above. The most recent of the two reviews[6] included 29 RCTs at varied risk of bias that primarily investigated high voltage pulsed or alternating current EST for treating PIs, DFUs or VLUs. Pooling of the results indicated a moderate effect for EST on wound healing (SMD 0.72, 95% CI 0.48 to 1.0) and the certainty of the evidence was low. A sensitivity analysis that included only RCTs at low risk of bias showed a large effect favouring EST plus standard wound care over standard wound care alone (SMD 0.90, 95% CI 0.44 to 1.37).[6]

The second review[9] included 21 RCTs at varying risk of bias. About half of the studies focussed on PIs. The primary outcome reported in this meta-analysis was mean percent change in ulcer size, which was reported in six of the studies. The results favoured EST (mean change in size by 24.62%, 95% CI 19.98 to 29.27; certainty of evidence not reported). Pooled results for other measures of wound healing also favoured EST.[9]

CONSIDERATIONS FOR USE

- Electrical stimulation therapy should not replace best standard of wound care.[51]
- When delivering HVMPC directly to the wound, debride the wound bed then use a normal-saline moistened sterile gauze pad between the electrode and wound bed tissue to improve electrical conductivity.[19]

Table 2. Results from the meta-analyses on electrical stimulation therapy for PIs

	Any type of EST vs shame/no therapy				Monophasic pulsed current EST vs shame/no therapy			
	Chen 2023[2]	Arora 2020[3]	HQO, 2017[7]	Lala 2016[8]	Girgis 2023[1]	Zhang 2019[4]	Girgis 2018[5]	HQO 2017[7]
Complete healing	RR: 1.79 (95% CI 1.09 to 2.92)	RR: 1.99 (95% CI 1.39 to 2.85)	RR: 1.68 (95% CI 0.77 to 3.65)	RR:1.55 (95% CI 1.12 to 2.15)	RR: 2.08 (95% CI 1.42 to 3.04)		RR: 1.93 (95% CI 1.26 to 2.93)	RR: 1.66 (95% CI 1.03 to 2.67)
Reduction in surface area	Mean difference: –1.76 (95% CI –3.24 to –0.28)		Mean difference (%): 31.53 (95% CI 19.15 to 43.90)		Mean difference (%): 33.76 (95% CI 21.38 to 72.58)	Mean difference (%): 36.18 (95% CI 24.59 to 47.76)		
Percent healed	Mean difference: 29.70 (95% CI 22.43 to 36.98)							
Time to healed		HR: 1.06 (95% CI 0.47 to 2.41)						
Healing rate		Mean difference: 4.59 (95% CI 3.49 to 5.69)		Healing/ day (%): 1.32 (95% CI 0.58 to 2.05)				

- Some of the meta-analyses indicated there might be no difference in effect between EST of different waveforms (biphasic versus monophasic[17]), different current types (pulsed current versus direct current[17, 18]) or different placement of the electrodes (on the wound bed versus peri-wound skin).[6] High voltage monophasic pulsed current (HVMPC) has been explored more thoroughly than other forms of EST.[19] None of the analyses compared different treatment regimens (i.e. duration and frequency of treatment).
- Evaluate the capacity of the individual to adhere to treatment when selecting adjunct therapies, therapy device and the treatment regimen.[21]
- Standards of wound practice[10] and evidence-based clinical guidelines[11, 12] outline that health professionals should collaborate with an interdisciplinary team when selecting adjuvant therapies, and have appropriate education and training before selecting or delivering EST, or teaching individuals to self-administer.

ADVERSE EFFECTS AND COMPLICATIONS

- Some complications/adverse events are associated with treating wounds with EST. A small number of people treated with electrical stimulation therapy reported dizziness and delusions, but these were not attributed to the EST intervention.[3,6] Skin redness, irritation, slight discomfort, tingling or burning sensations have also been reported,[3,6,8] but the certainty that these events were associated with EST is low[3]. A minor burn has also been reported in one person.[6]
- Use caution when applying HVPMC to wounds in people with Raynaud's syndrome because increased wound pain has been reported.[1]

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CONFLICTS OF INTEREST

The author declares no conflicts of interest in accordance with International Committee of Medical Journal Editors (ICMJE) standards.

ABOUT WHAM EVIDENCE SUMMARIES

WHAM evidence summaries provide a summary of the best available evidence on specific topics and make suggestions that can be used to inform clinical practice. Evidence contained within this summary should be evaluated by appropriately trained professionals with expertise in wound prevention and management, and the evidence should be considered in the context of the individual, the professional, the clinical setting and other relevant clinical information.

WHAM evidence summaries are developed using methodology consistent with that published by Joanna Briggs Institute.[13-16] Evidence underpinning a WHAM recommendation is identified via a PICO search strategy, assigned a level of evidence and evaluated for risk of bias. All WHAM evidence summaries are peer-reviewed by an international Expert Reference Group. For more information on the methods and the WHAM Expert Reference Group, visit the website: www.WHAMwounds.com.

Table 3. Evidence included in meta-analyses on EST for DFUs

Study	DFU severity/description as reported in primary study	Girgis 20231	Zheng 20224	Chen 202017
Asadi 2015[40]	Wagner Classification grade 2			X
Asadi 2017[41]	Wagner Classification grade 2		X	X
Baker 1997[42]	Infected		X	X
Liani 2014[43]	Not reported		X	
Lundeberg 1992[44]	Primarily superficial DFUs		X	X
Mohajeri-Tehrani 2014[45]	Wagner Classification grade 2		X	X
Ortíz 2014[46]	Primarily Wagner Classification grade 1	X	X	
Peters 2001[47]	University of Texas Diabetic Wound Classification System grades 1A-2A	X	X	X
Petrofsky 2007[48]	Not infected		X	
Petrofsky 2010[49]	Wagner Classification grade 2		X	X
Zulbaran-Rojas 2021[50]	Primarily Wound, Ischemia, and foot Infection (WIfI) Classification stage 1/2		X	

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