PULSED RADIOFREQUENCY ELECTROMAGNETIC FIELD FOR PAIN AND WOUND THERAPY

HEALTH TECHNOLOGY ASSESSMENT SECTION
MEDICAL DEVELOPMENT DIVISION

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DISCLAIMER

Technology review is a brief report, prepared on an urgent basis, which draws on restricted reviews from analysis of pertinent literature, on expert opinion and / or regulatory status where appropriate. **It has been subjected to an external review process.** While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of this review.

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DISCLOSURE

The author of this report has no competing interest in this subject and the preparation of this report is totally funded by the Ministry of Health, Malaysia.

EXECUTIVE SUMMARY

Background

Pain is an unpleasant sensation that can range from mild, localized discomfort to agony perception that signals the individual that tissue damage has occurred or may be occurring. Pain can be “acute” or “chronic”. Meanwhile wounds are injuries that break the skin or other body tissues which includes surgery, sutures, cuts, scratches, stitches and punctured skin.

Pain and wound require further assessment before they getting worst. Various types of treatment can be used includes drugs, complementary medicines or other alternative medicines. One of the alternative medicines used is electrical stimulations. Electric stimulations involve the transfer of an electrical current to the skin surface adjacent to the wound edge via two electrodes, with the net effect of generating a flow of ions through the wound tissues.

There are various types of electrical stimulations used for wound healing and pain therapy. The electrical stimulations include shortwave electromagnetic therapies such as pulsed shortwave radiofrequency electromagnetic field therapy or pulsed shortwave diathermy.

This technology review report is mainly focused on pulsed shortwave radiofrequency electromagnetic field therapy. Extensive numbers of clinical studies have been performed using non-thermal pulsed shortwave radiofrequency electromagnetic over the last five decades for the treatment of acute and chronic pain.

Based on the potential of the pulsed shortwave radiofrequency electromagnetic in pain therapy and wound healing, the Director of Hospital Tengku Ampuan Rahimah, Kelang has requested a review on the effectiveness, safety and cost-effectiveness of the device.

Objective/aim

To assess the safety, efficacy / effectiveness and cost-effectiveness of pulsed radiofrequency electromagnetic field (PRFE) for pain therapy and wound healing ([redacted]).

Results and conclusions

Based on the review, there were two meta-analysis, and four randomized control trials (RCTs) identified. The trials were published between 1992 to 2014. Both meta-analysis found that electrical stimulation including PRFE was effective as an adjunct therapy to accelerate wound healing (improved wound size) and reduce pain. All four RCTs also showed that PRFE can be used as an adjunct therapy for pain reduction after surgery or for leg ulcer healing. However, each

RCTs concluded that, larger-scale clinical trials were needed for further validation of the therapy.

In conclusion, the pulsed radiofrequency electromagnetic (PRFE) field seemed to have the potential as an adjunct therapy to accelerate and improve wound healing and reduce pain. However, the quality of the evidence was not satisfactory especially due to insufficient sample size and short study period.

Methods

Electronic databases were searched through Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1948 to present, and Embase 1996 to 2015 June 08. Searches were also run in PubMed, Horizon Scanning databases, FDA website and INAHTA for published reports.

Search was limited to studies published within 1990s to 2000s. Google and Google Scholar were also used to search for additional web-based materials and information about the technology. Besides, additional articles from reviewing the references of retrieved articles also included.

PULSED RADIOFREQUENCY ELECTROMAGNETIC FIELD FOR PAIN AND WOUND HEALING THERAPY

1. BACKGROUND

Pain is an unpleasant sensation that can range from mild, localized discomfort to agony perception that signals the individual that tissue damage has occurred or may be occurring. Pain can be “acute” or “chronic”. Acute pain lasts a short and chronic pain may be defined as pain that lasts beyond the healing of an injury, continues for a period of several months or longer, or frequently occurs.[1] Meanwhile wounds are injuries that break the skin or other body tissues which includes surgery, sutures, cuts, scratches, stitches and punctured skin.[2]

Pain and wound require further assessment before they get worst. Various types of treatment can be used includes drugs, complementary medicines or other alternative medicines. Rawe IM in his review stated that, pain management is a very important health care issue because of the negative impact pain has on patient quality of life and the significant associated healthcare costs involve in pain management.[3] One of the alternative medicines used is electrical stimulations. Electric stimulations involves the transfer of an electrical current to the skin surface adjacent to the wound edge via two electrodes, with the net effect of generating a flow of ions through the wound tissues.[4]

There are various types of electrical stimulations used for wound healing and pain therapy. The electrical stimulations include shortwave electromagnetic therapies such as pulsed shortwave radiofrequency electromagnetic field therapy or pulsed shortwave diathermy. Other electrical diathermies that are used clinically are microwave diathermy and ultrasound diathermy. Microwave diathermy uses radar waves that are of higher frequencies (434 and 915 MHz) than shortwave diathermy and has a lower depth of penetration. However, ultrasound diathermy employs high-frequency acoustic vibrations that are converted into heat in the body.[3]

This technology review report is mainly focused on pulsed shortwave radiofrequency electromagnetic field therapy. In the original form, continuous shortwave radiofrequency electromagnetic field had the potential to cause thermal injury. Thus, to prevent excessive heat build-up, the signal was pulsed, which allowed heat to dissipate and the resulting therapy were still found to be therapeutic. Extensive numbers of clinical studies have been performed using non-thermal pulsed shortwave radiofrequency electromagnetic over the last five decades for the treatment of acute and chronic pain.[3]

Based on the potential of the pulsed shortwave radiofrequency electromagnetic in pain therapy and wound healing, the Director of Hospital Tengku Ampuan Rahimah, Kelang has requested a review on the effectiveness, safety and cost-effectiveness of the device.

2. OBJECTIVE/AIM

To assess the safety, efficacy / effectiveness and cost-effectiveness of pulsed radiofrequency electromagnetic field for pain therapy and wound healing ([redacted]).

3. TECHNICAL FEATURES

Pulsed Radiofrequency Electromagnetic Field for Pain and Wound Therapy ([redacted])

The [redacted] (Figure 1) device carried therapeutic radiofrequency of 27.12MHz with 1000 pulses rate per second.[5] According to Code of Federal Regulations by United State of Food and Drug Authority (USFD) radiofrequency of 13MHz to 27.12MHz is intended to generate deep heat within body tissues for the treatment of selected medical conditions such as pain relief, muscle spasms and join contractures but not for malignancies treatment.[6]

The device will be placed adjacent to the affected area. Then the electrical currents that have introduced into the tissue will interacted with the radiofrequency amplifier itself with a non-linear manner. This non-linear interaction results in a demodulation on the pulsed radiofrequency field resulting in a 1 KHz electrical field component being created in the tissue. The demodulated 1KHz pulses then interact with electrically excitable cells in the tissue (nerves) through a process referred to as stochastic resonance, or noise amplified stimulation. That is, the high frequency electrical pulses add to the intrinsic electrical noise in the tissue resulting in increased nerve activation, specifically increased afferent nerve activity. Increased afferent nerve activity results in increased efferent nerve and muscle activity. Thus, improved blood circulation which may reduced pain and accelerated wound healing.[5]

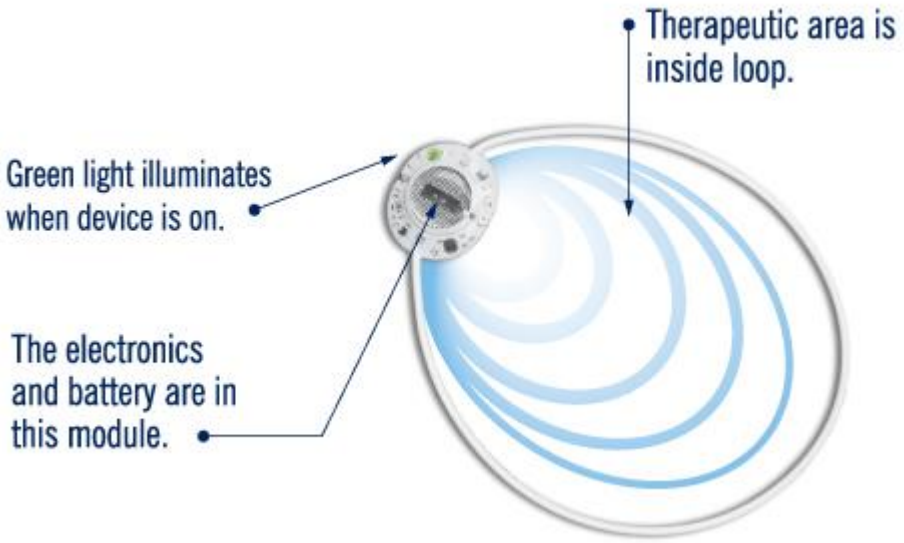

Figure 1: [redacted]

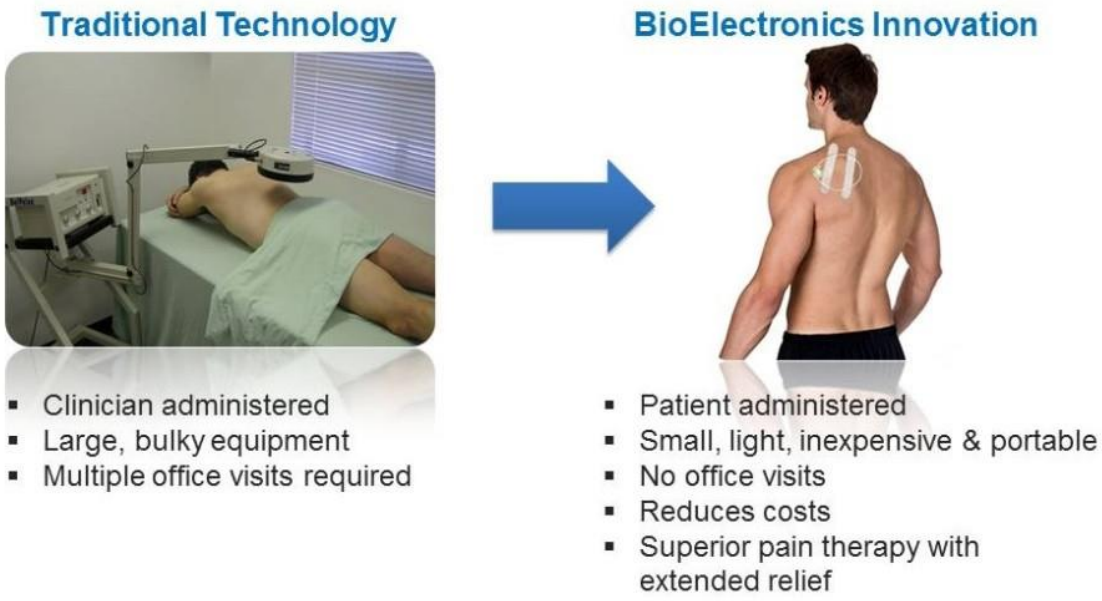

Figure 2

4. METHODS

4.1. Searching

Electronic databases were searched through Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1948 to present, and Embase 1996 to 2015 June 08. Searches were also run in PubMed, Horizon Scanning databases, FDA website and INAHTA for published reports.

Search was limited to studies published within 1990s to 2000s. Google and Google Scholar were also used to search for additional web-based materials and information about the technology. Besides, additional articles from reviewing the references of retrieved articles also included.

Appendix 1 showed the detailed search strategies.

4.2. Selection

A reviewer screened the titles and abstracts against the inclusion and exclusion criteria and then evaluated the selected full-text articles for final article selection.

The inclusion and exclusion criteria were:

Inclusion criteria

Population	Patient/general population who are having pain due to surgery / wound
Interventions	Pulsed radiofrequency electromagnetic field therapy
Comparators	Conventional therapy
Outcomes	Reduce pain / accelerated wound healing
Study design	RCT, non-randomized controlled trials, and systematic reviews
	English article

Exclusion criteria

Study design	Animal studies and laboratory studies
	Non English article

Relevant articles were critically appraised using Critical Appraisal Skills Programme (CASP) and evidence graded according to the US / Canadian Preventive Services Task Force (Appendix 2). Data were extracted from included studies using a pre-designed data extraction from (evidence table as shown in Appendix 3) and presented in tabulated format with narrative summaries. No meta-analyses was conducted for this review.

5. RESULTS AND DISCUSSION

There were two meta-analysis, and three randomized control trials (RCTs) identified. The trials were published between 1992 to 2014.

5.1. EFFICACY/ EFFECTIVENESS

The efficacy/effectiveness was divided based on outcome; the ulcer size and the pain.

Barnes et al. conducted a SR with meta-analyses in 2014 to review the effect of electrical stimulation on ulcer healing compared to usual treatment and/or sham stimulation. The SR included 21 studies with total of 866 patients. The electrical stimulations assessed were pulsed currents, direct currents and alternating currents. The types of ulcer included in the study were pressure ulcers, venous ulcers, diabetic ulcers, and arterial ulcers. The trials looked at the percentage of change in wound surface area and change in ulcer size over study period. Based on data pooling and meta-analyses of six RCTs (involved 266 patients) that evaluated electrical stimulations effects on percentage of change in ulcer size over the total studies period, the electrical stimulations significantly increased the percentage mean change in ulcer size by 24.62%, (95% CI 19.98-29.27), (I^2 = 0%, P = 0.66) when compared to standard care and/or sham stimulation. The electrical stimulations improved ulcer size by 2.42cm^2, (95% CI 1.66-3.17) compared to standard care and/or sham stimulation. However, there was significant heterogeneity across the trials (I^2 = 94%, P < 0.00001). [7, level 1]

Further analysis was carried out based on the electrical stimulations type. The analysis of five RCTs which used pulsed current showed that the percentage mean change in ulcer size increased by 28.31%, (95% CI 22.08-34.54). On the other hand, the other one trial which used alternating current, the percentage mean change in ulcer size increased by 20%, (95% CI 13.03-26.97). Based on the findings, the author stated that the electrical stimulation can be used as an adjunct treatment to accelerate healing when compared with standard care and/or sham stimulation.[7, level 1]

Meta-analysis by Barnes et al. was in line with another meta-analysis in 1999 by Gardner SE et al. The meta-analysis included 15 studies with 547 patients to compare electrical stimulation and standard wound healing. The electrical stimulations assessed were high voltage pulsed current, alternating current, low intensity direct current and transcutaneous electrical nerve stimulation. The meta-analysis also looked at the wound size and rates of healing by electrical stimulation. Based on the analysis, the mean baseline wound size for electrical stimulation was 8.8cm^2 as compared to 9.2cm^2 for control samples. Meanwhile, overall rates of

healing of electrical stimulations increased ≥40% over the control rate. The author found that the results of the meta-analysis supported electrical stimulations as an effective adjunct therapy for chronic wound healing.[8, level 1]

Brook J et al. conducted a randomized controlled double blind trial in 2012 to determine the effects of nightly use of a wearable pulsed radiofrequency electromagnetic (PRFE) device. The study involved 70 patients with plantar fasciitis. These patients were randomized into either treatment group or control group. The PRFE device was supplied to the treatment group and placebo device was supplied to the placebo group. Study conducted for seven days. They recorded the pain levels using a 0 to 10 visual analog scale (VAS) in the morning and night. At the end of the study, the VAS score decreased in both groups. However, significant decrease was showed in treatment group compared with placebo group. Although the study showed that PRFE was significant to reduce pain in plantar fasciitis, more studies warranted to confirm the initial findings.[9, level 1]

Rawe IM et al. also conducted a randomized controlled double blind study to determine postoperative pain after breast augmentation. The study involved only 18 healthy women who underwent breast augmentation purely for aesthetic considerations. Once surgery completed, each patients will be randomized either to, active group which was supplied with PRFE or placebo group which was supplied with placebo device. Upon completion of the operation, a baseline score was assessed for each patient with VAS score for seven days. The baseline score did not differ significantly between active and placebo groups. During treatment, VAS scores for active group were significantly lower than the placebo group except day two ($P = 0.23$). In term of recovery, the active group recovered to 50% of baseline pain between postoperative days two and three. Meanwhile the 50% recovery stage in the placebo group was at day six. Although the active group showed significant difference compared with placebo group, the authors agreed that larger-scale clinical trials were needed for further validation of the therapy.[10, level 1]

Jankovic A et al. conducted randomized controlled trial in order to establish the effects of frequency rhythmic electrical modulation system (FREMS) therapy as a novel treatment of painful leg ulcer healing. The study involved 35 patients with various number of leg ulcer and time duration. Those patients were randomized into FREMS group and control group. FREMS group showed that significant decrease in surface leg ulcer, pain score, score of ulcer and ulcer vicinity ($P < 0.05$) compared with control group. With that, the authors concluded that FREMS significantly facilitates the epithelisation of ulcus cruris and significantly decrease the pain level without damaging effects. Thus, they

recommended the device for treatment of chronic and painful leg ulceration of various aetiology.[11, level 1]

5.2. SAFETY

There was no retrievable evidence on safety of pulsed radiofrequency electromagnetic treatment. All studies included in the report stated that no adverse event occurred during or after the procedures. The device was received approval from United State Food and Drugs Authority and is classified under class III medical device (premarket approval).[6]

5.3 COST/COST-EFFECTIVENESS

Taylor RR et al. conducted an economic study in 2011 to estimate the cost-effectiveness of using electrical stimulation therapy with dressings and compression bandaging compared with dressing and compression bandaging alone in treating chronic, non-healing venous leg ulcers (VLUs) of more than six months duration from prospective of National Health Services (NHS) in United Kingdom (UK). Twenty one patients with non-healing VLUs involved in the study. Study duration was about 90 days to five months. At weeks 12, ultrasound assessment demonstrated a statistically significant acceleration of wound healing in 95% of patients. The ultrasound assessment looked at level of oedema in wound and width of the oedema areas. According to the Markov Model, managing patients with electrical stimulation therapy in addition to their previous care plan was expected to lead to a reduction in health-care cost of £131.00 (95% CI: £126.80; £135.10). More than 300% improvement in probability of wound healing and 6% improvement in health status of 0.017 QALYs at five months.[4]

Probabilistic sensitivity analyses highlighted the distribution in the incremental costs and QALYS due to the variability and uncertainty surrounding such as probability of moving from one health care to another, resource used, utilities and unit costs. With the cost of £40 per unit of electrical stimulation therapy it was probable that 98% cohort would be cost-effectively treated with electrical stimulation therapy up to a threshold of £20,000 per QALY. Electrical stimulation therapy was likely to be preferred to patients previous care plan even at low cost per QALY thresholds.[4]

5.4 LIMITATIONS

This technology review has several limitations. The selection of studies was done by one reviewer. Although there was no restriction in language during the search but only English articles were included in this report. Only studies published within 1990s to 2000s were included in this technology review report.

6. CONCLUSION

In conclusion, evidence showed that the pulsed radiofrequency electromagnetic (PRFE) field seemed to have the potential as an adjunct therapy to accelerate and improve wound healing and reduce pain. However, the quality of the evidence was not satisfactory especially due to insufficient sample size and short study period.

8. REFERENCES

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8. Gardner SE, Frantz RA & Schmidt FL. Effect of Electrical Stimulation on Chronic Wound Healing: A Meta-Analysis. Wound Rep Reg.1999;7:495-503
9. Brook J, Dauphinee DM, Korpinen J,, Rawe IM. Pulsed Radiofrequency Electromagnetic Field Therapy: A Potential Novel Treatment of Plantar Fasciitis. The Journal of Foot & Ankle Surgery. 2012;51:312-316
10. Rawe IM, Lowenstein A, Barcelo CR, & Genecov DG. Control of Postoperative Pain with a Wearable Continuously Operating Pulse Radiofrequency Energy Device: A Preliminary Study. Aesth Plast Surg.2012;36:458-463
11. Jankovic A & Binic I. Frequency Rhythmic Electrical Modulation System in the Treatment of Chronic Painful Leg Ulcers. Arch Dermatol Re. 2008;300:377-383
12. Rawe IM & Vlahovic T. The Use of a Portable Wearable Form of Pulsed Radio Frequency Electromagnetic Energy Device for Healing of Recalcitrant Ulcers: a Case Report. Int. Wound J.2012;9:253-258
13. Rhame EE, Levey KA & Gharibo CG. Successful Treatment of Refractory Pudendal Neuralgia with Pulsed Radiofrequency. Pain Physician.2009;12:633-638

9. APPENDIX

9.1. Appendix 1: LITERATURE SEARCH STRATEGY

Ovid MEDLINE® In-process & other Non-Indexed citations and OvidMEDLINE® 1948 to present

1. Electric Stimulation Therapy/
2. Wound Healing/
3. Inflammation/
4. Pain/
5. Occlusive Dressings/ or Wound Healing/ or Bandages/
6. Short-Wave Therapy/
7. Diathermy/ or Short-Wave Therapy/
8. inflammation$.tw.
9. pain.tw.
10. (pain$ adj1 (migratory or splitting or crushing or burning or radiating)).tw.
11. (suffering$ adj1 physical$).tw.
12. ache$.tw.
13. 3 or 4 or 8 or 9 or 10 or 11 or 12
14. diathermy#.tw.
15. (therap# adj1 short-wave).tw.
16. (shortwave adj therap#).tw.
17. wave therap# short.tw.
18. therap# electric# stimulation.tw.
19. stimulation therap# electric#.tw.
20. electric# stimulation therap#.tw.
21. (electrotherapy adj interferential current).tw.
22. electrotherapy.tw.
23. 1 or 6 or 7 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24. (dressing$ adj1 (spray-on or occlusive)).tw.
25. (occlusive adj1 (dressing$ or bandage$)).tw.
26. dressing$.tw.
27. bandage$.tw.
28. (wound$ adj1 healing$).tw.
29. 2 or 24 or 25 or 26 or 27 or 28
30. 13 and 23
31. 23 and 29
32. 13 and 23 and 29

Embase 1996 to 2015 June 08

1. pain/
2. inflammation/
3. wound/
4. inflammation$.tw.
5. pain.tw.
6. (pain$ adj1 (migratory or splitting or crushing or burning or radiating)).tw.
7. (suffering$ adj1 physical$).tw.
8. ache$.tw.
9. wound$.tw.
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. diathermy device/ or diathermy/
12. (diatherm# adj device).tw.
13. diathermy/
14. (therap# adj1 short-wave).tw.
15. (shortwave adj therap#).tw.
16. wave therap# short.tw.
17. electrostimulation therapy/
18. therap# electric# stimulation.tw.
19. stimulation therap# electric#.tw.
20. electric# stimulation therap#.tw.
21. (electrotherapy adj interferential current).tw.
22. electrotherapy.tw.
23. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24. wound healing/ or wound dressing/
25. (dressing$ adj1 (spray-on or occlusive)).tw.
26. (occlusive adj1 (dressing$ or bandage$)).tw.
27. dressing$.tw.
28. bandage$.tw.
29. (wound$ adj1 healing$).tw.
30. 24 or 25 or 26 or 27 or 28 or 29
31. 10 and 23 and 30

OTHER DATABASES	
EBM Reviews - Cochrane Central Register of Controlled Trials	Same MeSH, keywords
EBM Reviews - Database of Abstracts of Review of Effects	
EBM Reviews - Cochrane database of systematic reviews	
EBM Reviews - Health Technology Assessment	
PubMed	
NHS economic evaluation database	
INAHTA	[redacted], pulsed radiofrequency, pulsed shortwave diathermy
FDA	[redacted], pulsed radiofrequency, pulsed shortwave diathermy
Horizon scanning database	[redacted], pulsed radiofrequency, pulsed shortwave diathermy
Others (Google Scholar, Google)	[redacted], pulsed radiofrequency, pulsed shortwave diathermy

9.2. Appendix 2

HIERARCHY OF EVIDENCE FOR EFFECTIVENESS STUDIES

DESIGNATION OF LEVELS OF EVIDENCE

I Evidence obtained from at least one properly designed randomized controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)

9.2. Appendix 3 EVIDENCE TABLE

Evidence Table: **Efficacy/Effectiveness**
Question: **Is pulsed radiofrequency electromagnetic therapy able to reduce pain and accelerate wound healing?**

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
1. Barnes R, Shahin Y, Gohil R & Chetter I. Electrical Stimulation vs. Standard Care for Chronic Ulcer Healing: a Systematic Review and Meta-analysis of Randomised Controlled Trials. European Journal of Clinical Investigation. 2014; 44(4):429-440	Systematic Review with Meta-analyses Obj: to investigate the effect of electrical stimulation on ulcer healing compared to usual treatment and/or sham stimulation	1	21 studies - 866 patients . 34 randomised in 1 parallel non-placebo single blind trial . 50 randomised in 1 parallel non-placebo double blind trial . 138 randomised in 3 parallel non-placebo open trials . 8 randomised in 1 parallel placebo single blind trial . 246 randomised in 6 parallel placebo double blind trial . 390 randomised in 9 parallel placebo open trials Types of ulcer - 11 studies on pressure ulcers - 3 studies on venous ulcers - 2 studies on diabetic ulcers - 1 studies on	Electrical stimulation Current types -14 trials utilised pulsed currents - 2 trials utilised direct currents - 5 trials utilised alternating currents	Usual treatment Sham stimulation		Outcomes measures varied between trials - 12 trials examined percentage change in wound surface area over study period - 9 trials examined the change in size over study period in cm^2 Data Pooling and Meta-Analyses *Mean Percentage Change in Ulcer Size Over Total Studies* - Electrical stimulation effect on percentage change in ulcer size over total studies period was assessed in 6 RCTs (210 pts) • Percentage mean change in ulcer sized increased by 24.62%, 95% CI 19.98-29.27, P<0.00001 with no heterogeneity (I^2=0%, P=0.66) compared to standard care and/or sham stimulation • 5 trials which used pulsed current, the percentage mean change in ulcer size increased by 28.31%, 95% CI 22.08-34.54, P<0.00001 with no heterogeneity • 1 trial which used alternating current, the percentage mean change in ulcer size increased by 20%, 95% CI 13.03-26.97, P<0.00001 *Mean Percentage Weekly Change in Ulcer Size* - Electrical stimulation effect on	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
			arterial ulcers - 4 various ulcers				percentage weekly change in ulcer size was assessed in 3 RCTs (176 pts) • Electrical stimulation insignificantly increased the percentage weekly change in ulcer size by 1.64%, 95% CI -3.81 to 7.09, P = 0.56 with significant heterogeneity across trials (I^2 = 96%, P<0.00001) when compared to standard care and/or sham stimulation • In Pulsed current trials the percentage weekly change in ulcer size increased by 5.11%, 95% CI -4.26 to 14.47, P=0.28 but in alternating current trial the percentage weekly change in ulcer size decreased by 0.21%, 95% CI -7.59 to 7.16, P=0.96 *Mean Change in Ulcer Size (cm2)* - Effect on ulcer size was assessed in 6 RCTs (266 pts) - Electrical stimulation effect on ulcer size was superior to standard care and/or sham stimulation – ulcer size improved by 2.42cm^2, 95% CI 1.66-3.17, P<0.00001 compared to the 2 treatment - There was significant heterogeneity across trials (I^2=94%, P<0.00001) - Pulsed current in 3 trials decreased ulcer size by 2.53cm^2, 95% CI 1.51-3.54, P<0.00001 - Direct current in 3 trials decreased the ulcer size by 2.53cm^2, 95% CI 2.28-2.79, P<0.00001 *Mean Percentage Daily Change in Ulcer Size*	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
							- Mean percentage daily change in ulcer size – 1study with 16 pts showed that electrical stimulation insignificantly (pulsed current) improved the percentage daily change in ulcer size by 0.63%, 95% CI -0.12 to 1.37, P=0.10 when compared with standard and/or sham stimulation Discussion/conclusion - Electrical stimulation used as an adjunct treatment to accelerates healing when compared with standard care and/or sham stimulation - Electrical stimulation significantly improved mean percentage change in ulcer size over total studies period by 24.62% and significantly improved ulcer size by 2.42cm^2 - Results of the MA were in agreement with findings of previous MA by Gardner et al - Cost-effectiveness: 1 trial showed that the electrical stimulation treatment was cost-effective within the patient cohort - Cost-effectiveness: 1 study showed that electrical stimulation was cost-effective treatment adjunct in the treatment for chronic venous leg ulcer however it was dependent on number of required treatment units, the costs of the units and the degree of required nurse input – it will vary greatly between the devices tested	

Evidence Table: **Efficacy/Effectiveness**
Question: **Is pulsed radiofrequency electromagnetic therapy able to reduce pain and accelerate wound healing?**

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
2. Gardner SE, Frantz RA & Schmidt FL. Effect of Electrical Stimulation on Chronic Wound Healing: A Meta-Analysis. Wound Rep Reg.1999;7:495-503	Meta-Analysis	1	15 studies - 8 single blind RCTS - 1 RCT -5non-randomized trials - 1 descriptive study	Electrical stimulation - High Voltage Pulsed current (HVPC) radiofrequency - Alternating current (AC) - Low intensity direct current (LIDC) - Transcutaneous electrical nerve stimulation (TENS)	Standard wound healing		- Mean baseline wound size for ES samples was 8.8 cm^2 (SD=6.8; n=15) as compared to 9.2 cm^2 (SD=6.4; n=11) for control samples Overall Rates of Healing - Percent healing per week (PHW) provide a basis for quantifying the effectiveness of electrical stimulation as an adjunctive therapy for chronic wounds - Based on interval estimated, there was 90% probability that the net effect of ES was 3.7% per week or more, represents an increase of ≥40% over the control rate *Rates of Healing by ES Device* -Subtracting the overall control PHW of 9.10% from the ES PHW associated with each type of ES device, the net increase in rate of healing was 10.87% for TENS, 12.59% for continuous direct current and 15.50% for pulsed current *Rates of Healing by Chronic Wound Category* -Highest net difference in pressure ulcer with net increase of 13.30% per week for ulcers treated with ES; a 403% increase over the control rate Discussion/conclusion - Results supported ES as an effective adjunctive therapy for chronic wound -ES increases the rate of chronic wound healing 144% - ES may be more effective for healing pressure ulcers	

Evidence Table: **Efficacy/Effectiveness**
Question: **Is pulsed radiofrequency electromagnetic therapy able to reduce pain and accelerate wound healing?**

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
3. Brook J, Dauphinee DM, Korpinen J,, Rawe IM. Pulsed Radiofrequency Electromagnetic Field Therapy: A Potential Novel Treatment of Plantar Fasciitis. The Journal of Foot & Ankle Surgery. 2012;51:312-316	Multicenter Randomized Controlled Double Blind Trial Obj: to determine the effects of nightly use of a wearable PRFE device Primary diagnostic criteria: presence of tenderness at the insertion of the plantar fascia into the heel bone, either plantar medially or plantarly Subjects use the PRFE and placebo device accordingly nightly for 7 days then they will record the pain levels using a 0 to 10 visual analog scale (VAS) – VAS score were recorder in the morning (AM) and at night (PM) Study Limitations -Short time data collections (7 days) -Lack of long term follow up -Lack of intercenter analysis - No power analysis to	1	70 subjects with plantar fasciitis - 42 in treatment group - 28 in control group	Pulsed radiofrequency electromagnetic (PRFE)	Placebo - not emit radiofrequency electromagnetic field	7 days	VAS Score - Day 1 showed no difference in the score between treatment and control group - 7 days of the study showed consistency in the control group with a day 1 to day 7difference of 0.26 VAS points - AM-VAS score in the study group showed steady decline – day 1 to day 7 VAS score difference was 1.74 VAS points , for a 7.5-fold greater reduction in pain than in the control group - Means PM-VAS scores in both groups showed declines compared with day 1 VAS scores Regression Analysis - Study group showed R^2 of 0.887 (p=0.002), slope = -0.252) – significant downward slope of 0.25 VAS points/day in study group - Control group showed R^2 was 0.239 (p=0.265, slope = -0.0051) Standard Repeated Measure Analysis using SAS generalized linear model routine - Significantly different rates of improvement in morning pain between the 2 groups (p=0.03) F-test - Groups means showed significant difference (P=0.036) Student t-test - Treatment Group showed steady	

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	calculate the study size						decline in pain scores and become significantly differences at day 4 (p=0.021) compared with day 1 score - Control group no significant difference in score of day 2 to 7 compared with day 1 - Decline in control group was 1.05 VAS points or 19% - Decline in study group was 1.49 VAS points or 30% - SAS analysis of variance and F-test showed no significant difference between both group - VAS score decline in treatment group was evenly spread with a • Day 1 to day 2 decline of 0.33 VAS point • Day 2 to day 3 decline of 0.39 VAS point • Day 3 to day 7 was 0.77 VAS point -VAS score decline in control group • Day 1 to day 2 decline of 0.64 VAS point • Day 2 to day 3 additional of 0.36 VAS point • Day 3 to day 7 no additional decline in the mean VAS score (4.46 and 4.41 points respectively) - Results of PM-VAS analysis was similar to AM-VAS analysis – significant decrease for day 4 to day 7 in study group but not in control group Discussion & Conclusion No adverse effect reported 1st study use PRFE for plantar fasciitis thus additional studies warranted to confirm the initial findings	

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4. Rawe IM, Lowenstein A, Barcelo CR, & Genecov DG. Control of Postoperative Pain with a Wearable Continuously Operating Pulse Radiofrequency Energy Device: A Preliminary Study. Aesth Plast Surg.2012;36:458-463	Randomized controlled double blind study Obj: to determine postoperative pain after breast augmentation - Once surgery completes, the PRFE and placebo was activated and secured in place with a surgical bra at the same time - At completion of the operation, a baseline score was assessed for each patient - Pain score: with VAS score (0-10) with logged in AM and PM for 7 days Limitation of study - Small sample size - conflict of interest as the authors paid and link with the device company		18 healthy women who underwent breast augmentation purely for aesthetic considerations - 10 pts under active devices group - 8 pts under placebo devices group	Pulsed radiofrequency energy (PRFE) / Pulse Electromagnetic Therapy (PEMF) / Pulsed Shortwave therapy (PSWT) / Radiofrequency (RF) non-thermal diathermy	Placebo device	7 days	- Baseline score did not differ significantly between active and placebo groups - Active group: Baseline VAS scores 6.46 on the 0 to 10-point scale. Postoperative day 1 VAS score for the active group was 2.06 points lower than baseline score (P=0.02, significant difference) - Placebo VAS group: 6.80, not significantly lower than baseline score (P=0.65) - VAS score for active group was 2.40 points lower than placebo group (P=0.017, significant difference) - VAS scores in active group were significantly lower than the placebo group on all days except day 2 (P=0.23) – VAS points 1.35 (35%) lower - On postoperative day 3, placebo group VAS score 5.40 - On day 3, active group mean VAS score (2.57) was significantly lower than placebo group (P= 0.003) - Active group recovered to 50% of baseline pain between postoperative days 2 and 3 (recover faster than placebo group) - Placebo group recovered to 50% of baseline by postoperative day 6 Discussion & Conclusion Larger-scale clinical trials still are needed for further validation of the therapy	

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5. Jankovic A & Binic I. Frequency Rhythmic Electrical Modulation System in the Treatment of Chronic Painful Leg Ulcers. Arch Dermatol Re. 2008;300:377-383	Randomized Controlled Study Obj: to establish the effects of FREMS therapy as a novel treatment of painful leg ulcer healing	1	35 pts with various number of leg ulcer and time duration -Treatment group: 20 pts with 24 legs ulcers -Control group: 15 pts with 19 legs ulcers	Frequency Rhythmic Electrical Modulation System (FREMS)			- Wound healing Verge Videometer (VeV) - Pain intensity Visual Analog Scale (VAS) FREMS treatment - Significant decrease in surface leg ulcer, pain score, score of ulcer and ulcer vicinity (P<0.05) - Ulcer vicinity in FREMS group was not significant in 2nd month - VAS score decreased in all control measurements and was significant (P<0.001) - Within treatment analysis in control group, showed statistically significant decrease leg ulcer surface and ulcer score in the 3rd week and 1st month (P<0.05) - Decrease score for ulcer vicinity is statistically significant in the 1st week (P<0.02), 2nd week (P<0.01) and 3rd week (P<0.05) - VAS score decreased without significance in control group FREMS group vs Control group - Decrease surface of leg ulcer was significant in control measurement sin the 3rd week (P<0.003) at the end of 1st and 2nd month (P<0.001) - Decrease of ulcer score was correlated with decrease leg ulcer surface in control measurements in the 3rd week (P<0.006), at the end of 1st and 2nd (P<0.001) - Ulcer vicinity was significant in measurements at the end of the 2nd	

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							week (P<0.05), 3rd week (P<0.04) and after 1st month (P<0.02) - Pain decreased was statistically significant in all control measurement (P<0.001) Safety - No systemic side effects were recorded – only slight burning sensation at the site of electrode placement during FREMS treatment without residual skin signs Conclusion - FREMS significantly facilitates the epithelisation of ulcus cruris and significantly decrease the pain level (36-48 hours without damaging effects - Recommended for treatment of chronic and painful leg ulceration of various aetiology	

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6. Rawe IM & Vlahovic T. The Use of a Portable Wearable Form of Pulsed Radio Frequency Electromagnetic Energy Device for Healing of Recalcitrant Ulcers: a Case Report. Int. Wound J.2012;9:253-258	Case report	II	4 Adult African-American diabetic males with ulcer present more than 3 mths -3 pts with diabetic neuropathic ulcers - 1 pt with venous stasis ulcer - Wound were evaluate 1/7 day	PRFE (ActiPatch)	Previous treatment -multilayer compression therapy for 4 weeks -wound debridement , Promogran matrix and dry sterile dressing - debridement and application of triple antibiotic antibiotic ointment with offloading -offloading with protactive boot and debridement, promogran matrix and dry sterile dressing	6 weeks	Wounds were evaluated for - Infection, Increased depth, Drainage Results - Starting week 1: all pts have decrease in wound size - Ulcers had a steady decrease in side to side closure and in visible pre-wound oedema - Pts 2 and 3 had complete healing of their diabetic ulcers after 3 weeks of treatment - Pt 1 had venous stasis ulcer which cause pain→after 2 weeks of PRFE therapy the pain relief significantly - Pt 1 ulcer size decreased from 4 x 2.4cm to 0.7 x 0.5cm at the end of 6 week study period (decrease approximately 95% of the wound area - Ulcers for pt 2 and 3 improved rapidly with PRFE treatment recovering up to 50% of the wound area after 1 week of PRFE treatment → the ulcers progressed to complete healing after 3 weeks of PRFE treatment - Pt 4 wound size at week the beginning of treatment was 2.5 x 1.75cm → by week 4 the size decreased to 1 x 1cm approximately 73% reduction in size → by week 6 the wound size decreased to 1 x 0.5cm, 88% reduction in size Conclusions PRFE devices maybe an effective adjunct therapy for recalcitrant wounds promoting healing and reducing pain	

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7. Rhame EE, Levey KA & Gharibo CG. Successful Treatment of Refractory Pudendal Neuralgia with Pulsed Radiofrequency. Pain Physician.2009;12:633-638	Case Report	III	41 year old female with 1.5 years of sharp, burning pain of the left gluteal and perineal regions Pain rated at 9/10 – at maximum intensity Only able to sit for a maximum 10 to 15 minutes and unable to work at her desk job for more than a year	Pulse-wave Radiofrequency	(previous treatment: drugs, acupuncture, TENS)		- Pain was rated as 9/10 prior to the procedure and 2/10 post procedure - During the 3-hours interval, pt was able to sit without pain - After 2nd diagnostic left pudendal nerve block was performed 2 weeks later, pain was described as 8/10 prior to procedure and 4/10 post procedure, pain relief again lasted for several hours - Pain improved significantly and able to tolerate prolong sitting for 4 to 5 hours - 5 months after procedure, pt return to work - At 6 months post procedure pt reported significant improvement in her pain and good sitting tolerance - At 1.5 years post procedure, pt only takes 3 tabs of oxycodone-acetaminophen per day – she also able to tolerate 4 to 5 hours sitting per day	

Evidence Table: **Cost-Effectiveness**
Question: **Is pulsed radiofrequency electromagnetic cost-effective therapy to reduce pain and accelerate wound healing?**

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8. Taylor RR, Sladkevicius & Guest JF. Modelling the Cost-Effectiveness of Electric Stimulation Therapy in Non-Healing Venous Leg Ulcers. Journal of Wound Care. 2011;6(10):464-472	Economic study Obj: to estimate the cost-effectiveness of using electrical stimulation therapy + dressings and compression bandaging compared with dressing and compression bandaging alone in treating chronic, non-healing VLU of > 6 months duration from prospective of NHS in UK		21 pts with non-healing VLUs Treated with 3 active units of ES therapy plus 2 layer compression with secondary absorbent dressing if the wound was highly exuding over a periods of 10 days	electrical stimulation therapy + dressings and compression bandaging	dressing and compression bandaging alone	90 days – 5 months	-At 12 weeks ultrasound assessment demonstrated a statistically significant acceleration of wound healing in 95% of pt (look at level of oedema in wound and width of zone of the oedema) -Post hoc analysis from pt data revealed that 14% of VLUs had healed -Pain scores with VAS reduced by 70% over the period of evaluation from 5.3 to 1.6 -Exudate levels on score of 1 to 10 were reduced from mean of 5.8 to 2.8 Economic Analysis -Markov Model: managing pt with ES therapy in addition to previous care plan is expected to lead to a reduction in health-care cost of £131.0 (95% CI:£126.8;£135.1), >300% improvement in probability of wound healing and 6% improvement in health status of 0.017 QALYs at 5 months -ES therapy was a dominant treatment and potentially affords the NHS a cost-effective treatment for chronic VLUs of >6 months durations -Based on cost-effectiveness acceptability curve: • Probability of ES therapy being cost-effective at various costs per QALY thresholds • Cost of £40 per unit of ED therapy,	

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							it is probable that 98% cohort would be cost-effectively treated with ES therapy up to a threshold of £20,000 per QALY • ES therapy was likely to be preferred to pts previous care plan even at low cost per QALY thresholds Sensitivity Analysis -Deterministic sensitivity analysis demonstrated that: the relative cost-effectiveness of using ES therapy was very sensitive to the acquisition cost of • The therapy • The number of ES therapy units per treatment and • The number of nurse visits in the improved health states in both groups and number of nurse visits in worsened health states -Deterministic sensitivity analysis also demonstrated the relative cost-effectiveness of using ES therapy was less sensitive to the healing rates and relatively insensitive to changes in any other of the model's inputs Net Resource Implications and Budget Impact -Assumptions: • Assumed that prevalence of VLUs in UK was 0.2% (equate to 123,600 people presenting with VLU per annum • Assumed that 38% of the wounds were long-term, non-healing of >6 months' duration (equate to approximately 47,000 people in UK	

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							with a long-term non-healing VLU >6 months' duration - If all 47,000 pts with hard-to-heal VLU used ES therapy (3 units at £40 per unit) instead of continuing with their previous care plan alone, the expected net impact to NHS would be: • 15% reduction in NHS cost (£6.1 million) over the 1st 5 months of treatment, from £4.13 to £35.2 million • 26% reduction in the number of the nurse visits (0.6 million) over the 1st 5 months of treatment, from 2.3 to 1.7 million nurse visits - It is dependent on the number of ES therapy units per treatment, the unit cost of the device and the number of nurse visits required to manage patients in clinical practice	

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9. Stiller MJ, Pak GH, Shupack JL, Thaler S,Kenny C & Jondreau L. A Portable Pulsed Electromagnetic Field (PEMF) Device to Enhance Healing of Recalcitrant Venous Ulcers: a Double-blind, Placebo-Controlled Clinical Trial. 1992. British Journal of Dermatology. 127;147-154	Randomized controlled Study Obj: to assess the efficacy and safety of PELUT as an adjunct to non-surgical management of recalcitrant venous leg ulcers Study Protocol - 31 pts were randomized into treatment group and placebo - At week 0 pts were instructed to apply PELUT device over wound dressing for 3hrs every day for about 8-12 weeks - All pts received ancillary topical treament - Compliance: pts kept a diary listing start and stop time of each treatment application - Pts were seen in clinic at 2 weeks intervals to monitor safety and compliance - Efficacy parameters were assessed at week 0, 4, 8 (and 12)		31 pts with recalcitrant venous ulcer - 18 active treatment group - 13 placebo group End results 4 pts defaulted (1 treatment group & 3 placebo group) 12 week treatment - 11 pts from treatment group - 1 pt from placebo group	Pulsed electromagnetic limb ulcer	Placebo	8-12 weeks	Efficacy Parameters assessed a. Wound surface area • Changes in wound surface area were (P<0.0002) 47.1% decrease in treatment group 48.7% increase for placebo • 2 methods to determine week 8 wound area in pts who discontinued study prior to day 42 i) Estimation by linear extrapolation to day 56 ii) Use of the last observed wound area in place of week 8 value - Results were the same with in both method: treatment group: 47.7% decrease in wound surface area vs 42.3% increase in wound area for placebo group (P<0.0002) b. Wound depth • In treatment group the average wound depth decreased from 0.24±0.04 cm to 0.13±0.02 cm • In placebo group the average wound depth was 0.26±0.01 cm at baseline and 0.25±0.03 cm after treatment (P<0.04) c. Granulation tissue • Treatment group: average percentage of healthy granulation tissue increased from 68.1±6.4% to 83.2±4.4% • Placebo group: average percentage of healthy granulation tissue was 67.1±8.3% at week 0 and 67.5±7.7% at week 8 (P<0.04) • There was 14.1% decrease in	

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							unhealthy granulation tissue for the treatment group and 0% change for the placebo group (P<0.04) d. Clinical global assessment • 50% of the treatment group healed or 0%of the placebo group • 54% of the placebo group was rated worse compared with 0% of the treatment group (P<0.001) e. Pain Intensity • Wound site pain score in the treatment group decreased 0.21 • Wound site pain score in placebo group decreased 0.15 (P<0.04) f. 12 week treatment group • Treatment group pts exhibited 66.3% decrease in wound surface area – further improvement from week 8 (47.9%) • Placebo group pts exhibit only a slight further decrease in wound area in week 12 (42.8%) compared to week 8 (39.2%) g. Adverse effects • No reports or complaint regarding PELUT device	