# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEADER</td>
<td>1</td>
</tr>
<tr>
<td>ABSTRACT</td>
<td>1</td>
</tr>
<tr>
<td>PLAIN LANGUAGE SUMMARY</td>
<td>2</td>
</tr>
<tr>
<td>BACKGROUND</td>
<td>2</td>
</tr>
<tr>
<td>OBJECTIVES</td>
<td>3</td>
</tr>
<tr>
<td>METHODS</td>
<td>3</td>
</tr>
<tr>
<td>RESULTS</td>
<td>4</td>
</tr>
<tr>
<td>DISCUSSION</td>
<td>6</td>
</tr>
<tr>
<td>AUTHORS’ CONCLUSIONS</td>
<td>6</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>6</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>6</td>
</tr>
<tr>
<td>CHARACTERISTICS OF STUDIES</td>
<td>7</td>
</tr>
<tr>
<td>DATA AND ANALYSES</td>
<td>10</td>
</tr>
<tr>
<td>Analysis 1.1. Comparison 1 Electromagnetic therapy v sham electromagnetic therapy + standard treatment, Outcome 1 Pressure ulcers healed at 2 weeks.</td>
<td>10</td>
</tr>
<tr>
<td>Analysis 2.1. Comparison 2 Electromagnetic therapy v standard treatment, Outcome 1 Pressure ulcers healed at 2 weeks.</td>
<td>11</td>
</tr>
<tr>
<td>Analysis 3.1. Comparison 3 Electromagnetic therapy v sham electromagnetic therapy, Outcome 1 Grade III pressure ulcers healed at 12 weeks.</td>
<td>12</td>
</tr>
<tr>
<td>ADDITIONAL TABLES</td>
<td>12</td>
</tr>
<tr>
<td>APPENDICES</td>
<td>13</td>
</tr>
<tr>
<td>FEEDBACK</td>
<td>14</td>
</tr>
<tr>
<td>WHAT’S NEW</td>
<td>17</td>
</tr>
<tr>
<td>HISTORY</td>
<td>17</td>
</tr>
<tr>
<td>CONTRIBUTIONS OF AUTHORS</td>
<td>17</td>
</tr>
<tr>
<td>DECLARATIONS OF INTEREST</td>
<td>18</td>
</tr>
<tr>
<td>SOURCES OF SUPPORT</td>
<td>18</td>
</tr>
<tr>
<td>INDEX TERMS</td>
<td>18</td>
</tr>
</tbody>
</table>
[Intervention Review]

Electromagnetic therapy for treating pressure ulcers

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ABSTRACT

Background

Pressure ulcers are defined as areas "of localized damage to the skin and underlying tissue caused by pressure, shear, friction and/or the combination of these". In the UK, pressure ulcers occur in 5 to 32% of hospital in patients and in 4 to 7% of people in community settings. Electromagnetic therapy, in which electrodes produce an electromagnetic field across the wound, may improve healing of chronic wounds such as pressure ulcers.

Objectives

To assess the effects of electromagnetic therapy on the healing of pressure ulcers.

Search strategy

For this second update, we searched the Cochrane Wounds Group Specialised Register (last searched October 2007); the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2008, Issue 2); MEDLINE (1966 to April 2008); EMBASE (1980 to Week 17 2008); and CINAHL (1982 to April 2008).

Selection criteria

Randomised controlled trials comparing electromagnetic therapy with sham electromagnetic therapy, or other (standard) treatment.

Data collection and analysis

For this second update, two authors independently scrutinized the results of the search to identify relevant RCTs and obtained full reports of potentially eligible studies. For the original review, details of eligible studies were extracted and summarised using a data extraction sheet. Attempts were made to obtain missing data by contacting authors. Data extraction was checked by a second author.

Main results

This update identified no new trials. Two RCTs were identified for inclusion in the original review (total of 60 participants). One was a three-armed study comparing electromagnetic therapy with electromagnetic therapy in combination with standard therapy, and with standard therapy alone, on 17 female and 13 male with grade II and III pressure ulcers. The other study compared electromagnetic therapy with sham therapy in 30 male participants with a spinal cord injury and a grade II or grade III pressure ulcer.

Neither study found a statistically significant difference between the healing rates of pressure ulcers in people treated with electromagnetic therapy compared with those in the control group.
Authors’ conclusions

The results provide no evidence of benefit in using electromagnetic therapy to treat pressure ulcers. However, the possibility of a beneficial or harmful effect cannot be ruled out, due to the fact that there were only two included trials both with methodological limitations and small numbers of participants. Further research is recommended.

Plain Language Summary

Electromagnetic therapy for treating pressure ulcers

Pressure ulcers (also called bed sores, decubitus ulcers or pressure sores) are sores on the skin caused by pressure or rubbing. They usually affect immobile people, on the bony parts of their bodies that stick out, such as hips, heels and elbows, and take a long time to heal. Electromagnetic therapy uses a field of electricity to try and encourage healing of pressure ulcers. However, the review of trials concluded there is no strong evidence to show whether electromagnetic therapy helps or hinders healing of these ulcers.

Background

According to the European Pressure Ulcer Advisory Panel (EPUAP), a pressure ulcer (also known as bed sore, bed ulcer, decubitus ulcer, and pressure sore) is “an area of localized damage to the skin and underlying tissue caused by pressure, shear, friction and/or a combination of these” (EPUAP 1999).

Pressure ulcers usually occur over bony prominences such as the sacrum, heels, hips and elbows, most often in immobile elderly people (for example elderly orthopaedic patients), patients with severe, acute illnesses (such as in people in intensive care units) and in people with neurological problems (for example those with spinal-cord injuries).

In the UK, pressure ulcers have been recorded in 5 to 32% of patients admitted to a District General Hospital (the precise rate depends on case-mix), and in four to seven percent of patients in community settings (Kaltenthaler 2001). These ulcers represent a major burden of sickness, and reduced quality of life for patients and their carers. There is a considerable cost, both to the patients (Clark 1994), and the health service (Touche Ross 1993). The annual treatment cost of pressure ulcer has been estimated to range from £1.4 to 2.1 billion, or four percent of the total health care expenditure in the UK (Bennett 2004).

Pressure ulcers present as a continuum of tissue damage from the unbroken skin with sustained redness after the release of pressure (non-blanching erythema), to destruction of the muscle and bone.

The treatment of pressure ulcers has four main elements:

1. local treatment of wounds using wound dressings and other topical applications;
2. pressure relief using beds, mattresses or cushions, and repositioning of the patient;
3. treatment of concurrent conditions that may delay healing, e.g. poor nutrition, and infection;
4. use of physical therapies, such as electrical stimulation, ultrasound, and laser therapy.

Electrical stimulation has been used for decades as a treatment for chronic wounds (Hewitt 1956) and is often applied by physical therapists. However, its role in promoting pressure ulcer healing as an adjunct to, or in the absence of, other proven therapies, is unclear.

The role of electricity in wound healing has been a topic for research since, at least, the 1940s (Burr 1940). Experimental animal studies have shown that the electric potential over a wound during healing is positive initially, but becomes negative after the fourth day of healing (Weiss 1990). It has been concluded that the proliferate phase of healing is related to a negative electric potential over the wound. However, some studies have experimented with positive wound electrodes, and others have reversed the electrodes during healing. It is hypothesised that electrical stimulation influences the migratory, proliferate and synthetic functions of fibroblasts, and also results in increased expression of growth factors (Weiss 1990). It seems likely that a moist wound environment is essential to maintain the flow of an endogenous or applied current.

The aim of electromagnetic therapy is to improve the healing of chronic wounds such as pressure ulcers. Electromagnetic therapy is distinct from most other forms of electrotherapy in that it is a field effect, and not a direct electric effect or a form of radiation (Stiller 1992). The electromagnetic spectrum covers a wide...
range of wavelengths including radio waves and X-rays. Short Wave Diathermy (SWD) is a non-ionising radiation present in the radio-waves portion of the electromagnetic spectrum. The frequency of short-wavelength radio waves ranges from 10 to 100 MHz. The radiofrequency wave band of 27.12 MHz is used for therapeutic effect in continuous SWD. Some SWD machines apply the electromagnetic energy to patients in short bursts of energy called Pulsed Short Wave Diathermy (PSWD). The interrupted, or pulsed, nature of PSWD is the only way in which it varies from continuous SWD, and these pulses result in the creation of side bands (26.95 to 27.28 MHz). So, when PSWD is applied, no SWD is delivered at that time. PSWD delivers a lower dose of SWD, and thus the tissues receive a correspondingly lower thermal load. Consequently, PSWD provides the tissues with an energy boost in the form of an electromagnetic field (Kitchen 2002). PSWD is often termed Pulsed Electromagnetic Field (PEMF) to distinguish it from SWD.

**OBJECTIVES**

The aim of this review was to assess systematically evidence for any effect of electromagnetic therapy on the healing of pressure ulcers.

We sought to answer the following questions:

1. Does electromagnetic therapy stimulate pressure ulcer healing?
2. If yes, what is the optimum treatment regimen in terms of polarity, waveform, current density, duration and frequency of treatments?

**METHODS**

**Criteria for considering studies for this review**

**Types of studies**

Trials were included if the allocation of participants to the therapies was described as randomised. There was no restriction on the basis of language, date of trial or publication status.

**Types of participants**

Studies which involved people of any age, and in any care setting, described as having a pressure ulcer were included. Studies which referred to the wounds using the synonyms decubitus, bed sore, and pressure sore were also eligible for inclusion.

**Types of interventions**

The application of electromagnetic therapy to treat pressure ulcers compared with sham electromagnetic therapy, no electromagnetic therapy, or other (standard) treatments.

**Types of outcome measures**

**Primary outcomes**

Pressure ulcer healing defined by an objective measure such as:
- rate of change in ulcer area;
- time to complete healing;
- proportion of ulcers healed within trial period.

**Secondary outcomes**

- Costs;
- quality of life;
- pain;
- acceptability of treatment.

**Search methods for identification of studies**

**Electronic searches**

In the original version and first update of the review the search strategy shown in Appendix 1 was used. For this second update of the review, we revised the search strategies and ran searches in the following databases to find randomised controlled trials (RCTs) of electromagnetic therapy: Cochrane Wounds Group Specialised Register (Search 29/4/08).

The Cochrane Central Register of Controlled Trials (CENTRAL) - The Cochrane Library Issue 2, 2008
Ovid MEDLINE 1966 to April Week 3 2008
Ovid EMBASE 1980 to 2008 Week 17
Ovid CINAHL 1982 to April Week 4 2008

The following search strategy was used in the Cochrane Central Register of Controlled Trials (CENTRAL):

#1 MeSH descriptor Electromagnetics explode all trees
#2 MeSH descriptor Electric Stimulation Therapy explode all trees
#3 (electromagnetic* or electrotherap*):ti,ab,kw
#4 (electric* NEXT current):ti,ab,kw
#5 (direct or pulsed or alternating) NEXT current):ti,ab,kw
#6 (low NEXT intensity) or (low NEXT frequency):ti,ab,kw
#7 (high NEXT voltage):ti,ab,kw
#8 ("TENS" or "NMES"):ti,ab,kw
#9 (interferential NEXT therap*):ti,ab,kw
#10 (monophasic or galvanic):ti,ab,kw
The search strategy used in Ovid MEDLINE is available in Appendix 2. This strategy was adapted where appropriate for the Ovid EMBASE and Ovid CINAHL searches. The Ovid MEDLINE search was combined with the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision); Ovid format (Higgins 2008). The EMBASE and CINAHL searches were combined with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2008). There were no restrictions on the basis of language or date of publication.

Searching other resources

For the original review and the first update, experts in the field (e.g. S.A. Cooper Vastola) and manufacturers (Diapulse and Elmedistral) were also contacted and asked to provide any information they might have about unpublished studies.

Data collection and analysis

Selection of studies

For all updates of this review, titles and abstracts of studies identified by the update search were independently checked for eligibility by two authors (AOM and HR). Full reports of articles were obtained if they appeared to satisfy the inclusion criteria of the initial assessment. Full papers were checked by two authors independently to identify those trials that were eligible for inclusion. Any disagreement was resolved by discussion and, if necessary, was referred to a third party for adjudication.

For the original review, titles and abstracts of studies identified by searching the Wounds Group Specialised Register were assessed by one author (KF) for eligibility. Full reports of articles were obtained if they appeared to satisfy the inclusion criteria of the initial assessment. Those rejected were checked by another author (NC). Full papers were checked to identify those that were eligible for inclusion (KF). This was repeated independently by another author (NC) to provide verification. Any disagreement was resolved by discussion and, if necessary, was referred to a third party for adjudication.

Data extraction and management

Details of the eligible studies were extracted and summarised using a data extraction sheet. Attempts were made to obtain any missing data by contacting the trial authors. Data from studies published in duplicate were included only once. Data extraction was undertaken by one author and checked for accuracy by a second. The following data were extracted:

1. design of study;
2. inclusion and exclusion criteria;
3. baseline characteristics (by treatment group);
4. intervention details;
5. outcome measures used;
6. results (by treatment group);
7. withdrawals (by treatment group).

Assessment of risk of bias in included studies

Each study was appraised using a standard checklist to assess the validity of the methods used. The following data relating to study quality were collected:

1. evidence that a sample size calculation was applied before trial commencement;
2. use of clear inclusion and exclusion criteria;
3. allocation concealment (A, B, C);
4. reporting of baseline comparability of treatment groups for important variables;
5. use of intention to treat analysis;
6. extent of loss to follow up;
7. blinded outcome assessment.

Data synthesis

The studies included in the review were combined by narrative overview with a quantitative summary of the result of similar trials where appropriate. For each trial with important dichotomous outcomes, e.g. ulcers healed? yes or no, a relative risk of healing with 95% confidence intervals was calculated. Where outcomes for continuous variables were presented as medians without confidence intervals, standard deviations, or some measure of the precision of the result, the median was entered into the analysis table and the data were not used in data synthesis.

RESULTS

Description of studies
See: Characteristics of included studies; Characteristics of excluded studies.

No new studies were identified by the searches for each update of the review. Two studies were excluded; one for pragmatic reasons because the original paper was unavailable (Cooper Vastola 1983) and the other because it examined micro current stimulation therapy not electromagnetic therapy (Ullah 2007).

Two studies of electromagnetic therapy for the treatment of pressure ulcers were included in the review (Comorosan 1993; Salzburg 1995).

These two studies contained a total of 60 people. The first study (Comorosan 1993) was carried out in a social care unit in Bucharest, Romania. This study was a three-arm study comparing electromagnetic therapy, a combination of sham electromagnetic therapy and standard therapy, and standard therapy alone, over a two-week treatment and follow-up period. A total of 30 people were recruited, 17 female and 13 male, aged from 60 to 84 years, with grade II (16 participants) and grade III (14 participants) pressure ulcers (the grading system used was not described). Participants were randomly allocated to one of the three groups. Five people received standard therapy; five received standard therapy plus sham diapulse treatment; and 20 people received the diapulse therapy. Diapulse therapy involved local application of electromagnetic field at a frequency of 600 pulses per second, peak power 6 (117 V, 27.12 MHz). Treatment was given for 30 minutes, twice a day. The standard therapy involved cleansing with hydrogen peroxide, and local application of talcum powder, methylene-blue in solution and antibiotic ointment (tetracycline). The outcome assessed was the percentage of ulcers healed within two weeks.

The second study (Salzburg 1995) compared electromagnetic therapy with sham electromagnetic therapy over a 12-week period, or until healing (if this was shorter than 12 weeks). The participants were volunteers admitted to a Veterans’ Administration Hospital in New York, and consisted of 30 male hospital inpatients with spinal cord injuries (20 with grade II, and 10 with grade III pressure ulcers). The treatment with electromagnetic field provided a radiofrequency of 27.2 MHz, and a pulse repetition rate of 80 to 600 pulses per second. This study also gave treatment for 30 minutes twice a day.

A clear definition of the grading of the ulcers was provided by the authors: grade II ulcers were defined as a partial-thickness skin loss involving epidermis or dermis, superficial and clinically presenting as a deep crater, abrasion, blister or shallow crater; while grade III were defined as full-thickness skin loss involving damage or necrosis of subcutaneous tissue extending down to, but not through, underlying fascia, clinically presented as a deep crater with or without undermining of adjacent tissue. The outcomes assessed were time to complete healing, rate of change in ulcer area, and proportion of ulcer healed.

### Risk of bias in included studies

Table 1 shows the methodological quality of the included studies. It was difficult to extract some of the details on methodological quality due to poor reporting. Attempts to contact the authors for clarification were unsuccessful.

Neither study stated the method of randomisation, nor conducted an intention to treat analysis. However, both studies used blinded outcome assessment. Whilst both studies reported the types of wound dressings used during the study, neither reported other concurrent interventions such as support surfaces (bed, mattresses and cushions) used. The Comorosan 1993 study did not provide information about the strategies used for randomisation, so it is not known why the three arms in the study contain an uneven distribution of patients.

### Effects of interventions

The results are presented with reference to the original questions posed by the review.

#### Does electromagnetic therapy stimulate the healing of pressure ulcers?

Both trials compared electromagnetic therapy with sham therapy, although the trial by Comorosan included a third arm in which only standard therapy was applied.

In the Comorosan 1993 trial, 17 out of 20 (85%) ulcers healed in the electromagnetic therapy group within two weeks compared with no ulcers healing in either of the other two groups (five ulcers in each); the relative risk (RR) was 10.00 (95% confidence interval (CI) 0.70 to 143.06) (Analysis 1.1; Analysis 2.1).

In the Salzburg 1995 trial, at 12 weeks, three out of five (60%) grade III pressure ulcers in the electromagnetic therapy group had healed, compared with none out of five in the sham electrotherapy group: RR was 7.00 (95% CI 0.45 to 108.26). In the electromagnetic therapy group, the ulcer area decreased by an average of 70.6%, whereas in the control group the ulcer area decreased by an average of only 20.7% (Analysis 3.1).

A median of 84% healing of grade II pressure ulcers in the electromagnetic therapy group at one week compared with 40% in the sham therapy group (P value 0.01). The median for days to complete healing was 13 days for the treatment group, compared with 31.5 days for the control group (P value < 0.001). There was no statistically significant difference in the baseline median area of ulcers between sham and electromagnetic therapy groups.

The results of the two studies could not be combined due to the different lengths of follow up (two weeks compared with 12 weeks). Secondary outcome measures such as financial costs, quality of life, pain and acceptability were not reported in either of the RCTs included.
D I S C U S S I O N

Whilst the results of both these small trials suggest that electromagnetic therapy is of benefit in the healing of pressure ulcers, neither trial reaches statistical significance and, consequently, the evidence is unreliable. Both trials contained small numbers of patients, and used different regimens of treatment over different time scales. The extent to which electromagnetic therapy contributes to healing in patients who are also receiving pressure relief and moist wound healing strategies should be explored. The trials, particularly Comorosan 1993, did not report severity of pressure ulcers and baseline comparisons adequately. Consequently, the results should be viewed as unreliable until further research involving larger numbers of patients that can be considered alongside these trials, becomes available.

A U T H O R S ' C O N C L U S I O N S

Implications for practice

There is no reliable evidence of benefit for electromagnetic therapy in the treatment of pressure ulcers. The small number of trials available for analysis (both with methodological limitations and small numbers of participants) means that the possibility of benefit, or harm, of this treatment cannot be ruled out.

Implications for research

Trials comparing electromagnetic therapy with sham therapy, or to standard care, are required to establish whether or not electromagnetic therapy improves the healing of pressure ulcers. In addition, future trials should explore whether particular sub-groups of participants are more likely than others to benefit from treatment with electromagnetic therapy, and, if the treatment is shown to be effective, to establish the point in a treatment regimen at which it should be applied.

A C K N O W L E D G E M E N T S

The authors would like to thank Ali Baba Akbari Sari and Ruth Foxlee from the Cochrane Wounds Group for this comments on the development and update of the search strategy.

The authors would also like to thank Sally Bell-Syer and Wendy Milborrow from the Cochrane Wounds Group for their support and assistance during the updating process.

R E F E R E N C E S

References to studies included in this review

Comorosan 1993  (published data only)

Salzburg 1995  (published data only)
Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers

Both studies summarised in this review were small and had methodological problems. Future trials will require:

1. participant numbers that ensure sufficient statistical power to detect true treatment effects;
2. use of true randomisation with allocation concealment (e.g. telephone randomisation, computer generated codes);
3. measures to help ensure comparability of treatments at baseline (e.g. stratification for ulcer size);
4. blinded outcome assessment;
5. use of objective outcome measurement (e.g. ulcer area, complete healing rates); and
6. use of intention-to-treat analysis.

It is also recommended that studies should clearly described the frequency and duration of treatment, location of wounds, and any treatment(s) applied concurrently with the electromagnetic therapy.

Randomised controlled trials should be adequately reported. The CONSORT statement (Begg 1996) lists 21 items that need to be reported to show readers whether or not a trial is likely to produce valid and reliable results. Further research into the relationship of electromagnetic therapy and pressure ulcer healing needs to be reported in accordance with these guidelines.

References to studies excluded from this review

Cooper Vastola 1983  (published data only)

Ullah 2007  (published data only)

Electromagnetic therapy for treating pressure ulcers (Review)

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**Additional references**

Begg 1996  

Bennett 2004  

Burr 1940  

Clark 1994  

EPUAP 1999  

Hewitt 1956  

Higgins 2008  

Kaltenthaler 2001  

Kitchen 2002  

SIGN 2008  

Stiller 1992  

Touche Ross 1993  

Weiss 1990  

*Indicates the major publication for the study*
### Characteristics of included studies  
(order by study ID)

**Comorosan 1993**

<table>
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<tr>
<th>Methods</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>30 patients on an elderly care unit with either grade II or grade III pressure sore. Grading system not defined. No report on patients' mobility status</td>
</tr>
</tbody>
</table>
| Interventions | A: (n=20) Diapulse - local application - frequency 600pps, peak power 6 (117V, 27.12 MHz), for 30 minutes 2x daily. Hepatic application - 400 pps, peak power 4 (117V, 27.12 MHz), 20 minutes 1x daily, following initial Diapulse treatment, plus conventional therapy as below  
B: (n=5) conventional therapy - H2O2 cleansing, application of talcum powder, methylene blue in solution, tetracycline ointment, plus sham Diapulse  
C: (n=5) conventional therapy |
| Outcomes | Number of ulcers healed at 2 weeks  
A: 17/20  
B: 0/5  
C: 0/5 |
| Notes | No report of concurrent pressure relief |

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors' judgement</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Unclear</td>
<td>B - Unclear</td>
</tr>
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</table>

**Salzburg 1995**

<table>
<thead>
<tr>
<th>Methods</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>30 male inpatients with spinal cord compression and a grade II (n=20) or grade III (n=10) pressure ulcer. Grading defined by authors. Patients in both stage II and III were allocated in equal numbers to the control and intervention groups</td>
</tr>
</tbody>
</table>
| Interventions | A: (n=15) electromagnetic therapy 27.12MHz, pulse repetition 80-600 pps, pulse width 65 microseconds, per pulse power range of 293 & 975 peak watts - delivered through wound dressing, 30 minutes treatment 2x daily for 12 weeks  
B: (n=15) sham treatment as above  
All ulcers dressed with moist saline gauze |
| Outcomes | Number of grade III pressure ulcers healed at 12 weeks:  
A: 3/5  
B: 0/5 |
Salzburg 1995  (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Grade II pressure ulcers - A: median of 84% healing</th>
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<tbody>
<tr>
<td></td>
<td>B: median 40% healing</td>
</tr>
<tr>
<td></td>
<td>P = 0.01</td>
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</table>

**Notes**

No report of concurrent pressure relief

**Risk of bias**

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Yes</td>
<td>A - Adequate</td>
</tr>
</tbody>
</table>

**Abbreviations**

H2O2 = Hydrogen peroxide  
n = number in sample group  
pps = pulses per second  
X = times

**Characteristics of excluded studies**  [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooper Vastola 1983</td>
<td>In the initial assessment, the title of article seemed relevant to the objective of the review. The abstract of the study was unavailable. We requested the article via an interlibrary loan and direct contact with the author and the journal publisher (Journal of American Paraplegia Society) all of which were unsuccessful. Therefore, this study was excluded for pragmatic reasons, because its content could not be verified firsthand</td>
</tr>
<tr>
<td>Ullah 2007</td>
<td>This study did not meet the inclusion criteria as it examined micro current stimulation therapy not electromagnetic therapy</td>
</tr>
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</table>
### DATA AND ANALYSES

#### Comparison 1. Electromagnetic therapy v sham electromagnetic therapy + standard treatment

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
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<tbody>
<tr>
<td>1 Pressure ulcers healed at 2 weeks</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>Subtotals only</td>
</tr>
</tbody>
</table>

#### Comparison 2. Electromagnetic therapy v standard treatment

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Pressure ulcers healed at 2 weeks</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>Subtotals only</td>
</tr>
</tbody>
</table>

#### Comparison 3. Electromagnetic therapy v sham electromagnetic therapy

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Grade III pressure ulcers healed at 12 weeks</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>Subtotals only</td>
</tr>
</tbody>
</table>

#### Analysis 1.1. Comparison 1 Electromagnetic therapy v sham electromagnetic therapy + standard treatment, Outcome 1 Pressure ulcers healed at 2 weeks.

Review: Electromagnetic therapy for treating pressure ulcers

Comparison: 1 Electromagnetic therapy v sham electromagnetic therapy + standard treatment

Outcome: 1 Pressure ulcers healed at 2 weeks

<table>
<thead>
<tr>
<th>Study or subgroup</th>
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<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Weight</th>
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<tbody>
<tr>
<td>Comorosan 1993</td>
<td>17/20</td>
<td>10.00 [0.70, 143.06]</td>
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Subtotal (95% CI): 0.0 [0.0, 0.0]

Total events: 17 (EM therapy), 0 (Sham)

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)
Analysis 2.1. Comparison 2 Electromagnetic therapy v standard treatment, Outcome 1 Pressure ulcers healed at 2 weeks.

Review: Electromagnetic therapy for treating pressure ulcers
Comparison: 2 Electromagnetic therapy v standard treatment
Outcome: 1 Pressure ulcers healed at 2 weeks

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<th>EM therapy</th>
<th>Standard therapy</th>
<th>Risk Ratio M-H Random 95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H Random 95% CI</th>
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<td>Comorosan 1993</td>
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<td>0/5</td>
<td>10.00 [0.70, 143.06]</td>
<td></td>
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</tbody>
</table>

Subtotal (95% CI)
Total events: 17 (EM therapy), 0 (Standard therapy)
Heterogeneity: not applicable
Test for overall effect: Z = 0.0 (P < 0.00001)

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Analysis 3.1. Comparison 3 Electromagnetic therapy v sham electromagnetic therapy, Outcome 1 Grade III pressure ulcers healed at 12 weeks.

Review: Electromagnetic therapy for treating pressure ulcers

Comparison: 3 Electromagnetic therapy v sham electromagnetic therapy

Outcome: 1 Grade III pressure ulcers healed at 12 weeks

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<th>Risk Ratio M H Random 95% CI</th>
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<th>Risk Ratio M H Random 95% CI</th>
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<td>Salzburg 1995</td>
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<td>0/5</td>
<td>7.00 [0.45, 108.26]</td>
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</table>

Subtotal (95% CI)

Total events: 3 (EM therapy), 0 (Sham)
Heterogeneity: not applicable
Test for overall effect: Z = 0.0 (P < 0.00001)

ADDITIONAL TABLES

Table 1. Methodological quality of included studies

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<thead>
<tr>
<th>Trial identifier</th>
<th>Pts in trial/arms</th>
<th>Incl/excl criteria</th>
<th>Sample size calc</th>
<th>Randomisation</th>
<th>Allocation Baseline features</th>
<th>Blinded</th>
<th>Outcomes</th>
<th>ITT analysis</th>
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<tr>
<td>Co-morosan 1993</td>
<td>30 participants in 3 arms</td>
<td>Inclusion criteria stated, no exclusion criteria</td>
<td>Not done</td>
<td>Method of randomisation not stated</td>
<td>Not stated</td>
<td>Some elements reported. Participants not matched at baseline for ulcer size</td>
<td>Yes</td>
<td>Appropriate</td>
</tr>
<tr>
<td>Salzburg 1995</td>
<td>30 participants in 2 arms</td>
<td>Listed</td>
<td>Not done</td>
<td>Unclear</td>
<td>Yes</td>
<td>Reported. Participants were not matched at baseline for ulcer size</td>
<td>Yes</td>
<td>Appropriate</td>
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</table>
APPENDICES

Appendix 1. Search strategy for the first update of the review

For the first update of the review, searches were carried out in the Cochrane Wounds Group Specialised Register (last searched in October 2005); the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2005, Issue 4); MEDLINE (1966 to October 2005); EMBASE (1980 to October 2005); and CINAHL (1982 to October 2005) using an updated search strategy to find randomised controlled trials (RCTs) of electromagnetic therapy.

Original Search Strategy for the Cochrane Central Register of Controlled Trials (CENTRAL)
1. DECUBITUS ULCER explode all trees (MeSH)
2. WOUND HEALING explode all trees (MeSH)
3. (bed near sore*)
4. (pressure near ulcer*)
5. (pressure near sore*)
6. (decubitus near ulcer*)
7. (chronic near ulcer* near skin)
8. #1 or #2 or #3 or #4 or #5 or #6 or #7
9. ELECTRIC STIMULATION THERAPY explode all trees (MeSH)
10. ELECTROMAGNETICS explode all trees (MeSH)
11. electromagnetic*
12. (electric* near stimulation*)
13. (electric* near therapy)
14. (pulse* near therapy)
15. (pulsed or Diapulse*)
16. DIATHERMY explode all trees (MeSH)
17. electrotherapy
18. MICROWAVES explode all trees (MeSH)
19. #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21
20. (#8 and #19)

Appendix 2. Second review update - Ovid MEDLINE Search Strategy

1 exp Electromagnetics/
2 exp Electric Stimulation Therapy/
3 (electromagnetic$ or electrotherap$).ti,ab.
4 (electric$ adj stimulation).ti,ab.
5 (electric$ adj current).ti,ab.
6 ((direct or pulsed or alternating) adj current).ti,ab.
7 (low intensity or low frequency).ti,ab.
8 high voltage.ti,ab.
9 (TENS or NMES).ti,ab.
10 interferential therap$.ti,ab.
11 (monophasic or galvanic).ti,ab.
12 exp Diathermy/
13 exp Microwaves/
14 (diathermy or microwave$).ti,ab.
15 or/1-14
16 exp Pressure Ulcer/
17 (pressure adj (ulcer$ or sore$)).ti,ab.
18 (decubitus adj (ulcer$ or sore$)).ti,ab.
19 (bedsore$ or (bed adj sore$)).ti,ab.
20 or/16-19
21 15 and 20
Comment from Prof Comorosan September 2002

Summary
Your review analyzed two papers:
2. The effects of pulsed EM (Diapulse) on wound healing of pressure ulcers in the spinal cord injured patients. Salzberg CA. et al, Wounds, 1995; 7,1, 11-16
The reviewer’s conclusions: “Neither study found a statistically significant difference between the healing rates of electromagnetic therapy treated and control group patients. The results suggest no evidence of a benefit in using electromagnetic therapy to treat pressure sores.”
This conclusion can not be correct.
The first study (Comorosan 1993) I performed, and the results did in fact prove that Diapulse was a benefit in treating pressure sores. The study was performed in accordance with the main request of the statistical studies: randomized groups and double blind assessments. Moreover, it refers to a placebo group, compared to a control (conventional treatment) and an experimental one (Diapulse and Conventional). After controlling the patients’ baseline, the null hypothesis is implicitly assumed: there will be no statistically significant difference in the healing rates of patients receiving Diapulse therapy and those who receive placebo treatment. Evaluation of the healing process is basically a qualitative medical assessment. Apart from size, no other quantitative (reliable) parameters are available. Granulation percentage and epithelialization percentage were used to establish the classic scale of the healing process: excellent (healed), very good (75-95% healed), good (50-75% healed), fair (25-50% healed), poor (less than 25% healed) and no improvement.
The results showed:
* In the conventional treatment group of 5 patients, 4 were rated unhealed and 1 less than 25%.
* In the conventional treatment and placebo Diapulse group of 5 patients, all were rated unhealed.
* In the Diapulse treated group of 20 patients, 18 were rated healed and 2 between 75-95%.
20 cases healed versus 10 unhealed, and the reviewers statement that there is not a significant difference and no evidence of benefit from the electromagnetic therapy as one can see, is completely false and misleading.
I suggest you re-read the study, and correct the assumptions that are clearly ignoring clear-cut evidence. Based on the fact that an evaluation was made after 5 weeks for the untreated Diapulse group and only 3 weeks for the Diapulse treated group, there was significant benefit for the treated group.
In the second published study (Salzburg 1995), the authors concluded that, “Diapulse treatment significantly improved healing.” Strong evidence of 30 spinal cord injured patients, treated successfully with Diapulse therapy is presented, again in a randomized double-blind study. The baseline comparison of active Diapulse treatment versus placebo included each ulcer’s area, granulation percentage...
and epithelialization percentage and was assessed by P-value, based on Mann-Whitney U tests. The authors used chi-square statistics for categorical variables and t-test for normal distribution. For the entire group of 30 participants (20 stage II and 10 stage III), a clear acceleration of wound healing was recorded.

After controlling the size, granulation and epithelialization, Diapulse treatment was found to be independently associated with percent healed at one week (P = .002) and days to 100% healing (P = 0.007).

Somehow these data were ignored. Average percentage healing achieved at one week was 77% in the treated group (standard deviation of 21%) versus 40% in the control group (standard deviation of 28%). This translates into an advantage of 3 to 1 for the active Diapulse treated group. Again, ignoring this strong evidence, it was considered devoid of statistical significance and judged to be without therapeutic merit.

Reply

Clinical decision making should give due weight to the research evidence, and that weight is determined by the volume and validity of the research. The validity of a study is the extent to which its design and conduct are likely to prevent systematic errors or bias (Moher et al, 1995). The criteria by which we assessed the validity of the primary research studies were pre-determined and peer reviewed, and are also internationally accepted as important criteria by which to judge studies which aim to evaluate the clinical effects of interventions. It is only by making rigorous, systematic assessment of the primary studies using criteria which have been determined a priori, and peer reviewed, that we can minimise biases in the review process and be sure of identifying biases in the primary research which may lead to invalid study results.

Generally, Cochrane Reviews tend to use the following broad criteria when assessing the internal validity of primary research studies (usually RCTs):

- Protection against selection bias. An unpredictable allocation sequence must be generated e.g. by computer algorithm, and then this sequence must be concealed from investigators who are enrolling patients. Knowledge of impending assignments can cause selective enrolment of patients based on prognostic factors (Schulz et al.). We therefore look to the trial report, and try to contact investigators possible, to satisfy ourselves that there was true randomisation with allocation concealment. We also look for evidence that the randomisation was successful in providing treatment groups which are balanced for important prognostic variables (particularly baseline wound size in wound care studies, since wound size is known to predict time to heal).

- Protection against performance and detection bias. Performance bias occurs if any additional therapeutic interventions are provided to one of the comparison groups. Blinding of patients and care providers helps prevent this kind of bias as well as reducing the chance of differences in placebo responses between the groups. Detection bias may arise if knowledge of the patient assignment can influence the measure of outcome.

- Protection against attrition bias. Protocol deviations and loss to follow up may lead to exclusion of patients after they have been allocated to treatment groups. Such 'lost' patients are unlikely to be representative of all patients in a study as is also the case with patients who do not 'adhere' to the treatment. All patients should be analysed in the groups to which they were randomised on an 'intention to treat' principle, so maintaining the randomisation and avoiding selection bias.

I would like to address our assessment of the internal validity of each of the papers in this review separately.


Allocation to the three treatment groups in this study was described as randomised, however, we always look for a report of how this randomisation was achieved in order to satisfy ourselves that selection bias was avoided. There was no such description nor explanation of why there were 20 patients in the treatment group and five patients in each of the other therapy groups (obviously having unequal treatment groups is a potentially valid approach but the allocation must be by a random process). The lack of a description of the process of allocation also meant that we were unable to ascertain the degree of allocation concealment - which also protects against selection bias (see above). However if you can provide us with information we will happily consider it.

During our validity assessment we also look for evidence of successful randomisation demonstrated by treatment groups which are balanced at baseline for important prognostic factors such as wound size. Balanced allocation is frequently not achieved in studies as small as this. Tests for ‘significant’ differences are unhelpful in detecting baseline differences since a) they are underpowered, and b) any differences have by definition arisen by chance if the patients were randomised. Whilst you did not report the average baseline wound area in your paper, your recent correspondence has just prompted us to calculate it from Tables 2, 3 and 4 in your paper. The median baseline ulcer area in the conventional treatment group was 3.9cm2, 9cm2 for the placebo treatment group, and 3.8 cm2 for the electromagnetic treatment group. This baseline difference biases the evaluation in favour of the electromagnetic treatment group.

Percentage reduction in wound area is a measure that is itself biased in favour of the treatment group with the smallest average wound size at baseline (since a change in area or volume will be a larger percentage of a smaller wound than a bigger wound), whereas actual
changes in size bias towards larger wounds. Time to complete wound healing is also a measure which would bias the study in favour of the active treatment group since smaller wounds take longer to heal. The baseline inequalities in this study were not adjusted for in the analysis.

Turning now to the possibility of performance and detection bias in this study, whilst clinicians and technicians were reportedly blinded to Diapulse and sham Diapulse therapy, it would not have been possible to blind to the third therapy. Furthermore you do not state who measured outcome (was it “the clinician”? Was there only one?). We are sure you are aware of the biases that can occur due to lack of blinding. One of our major concerns with regard to detection bias is the lack of information reported on outcome assessment.

When an outcome relies on the judgement of a clinician (the primary outcome of this study was described as a ‘qualitative medical assessment’) and that clinician is aware of the allocation of the patient being assessed then interpretation of the clinical findings may be biased. Qualitative outcome measures such as this are of dubious validity anyway, especially when wound healing is relatively easy to measure objectively (by measuring time to complete healing or serial measures of wound size). In our opinion a better approach would be to present the actual reduction in area for each group along with confidence intervals to allow interpretation of the differences in healing and the associated precision.

We would welcome any information that might give us further clarity on how the outcome assessment was undertaken. Incidentally we are even more confused now given that your letter states that the evaluation was made after five weeks for the untreated Diapulse group and only three weeks for the Diapulse treated group. How could these assessments have been made at different times if the assessor was blinded? Why does the published paper state in the Abstract that there was a maximum two week treatment period; but in Tables 2, 3 and 4 that the duration of treatment was is variously one, two, three, four, five, six and eight weeks!

From your data we calculated the relative risk (RR) for healing with Diapulse therapy. The Cochrane Collaboration recommends that RRs are produced for dichotomous data whenever the event rate is greater than 30%. As you will be aware from reading the review the RR for healing in your trial was 10, (95% CI 0.7-143.7). Whilst the result of this seems to favour the use of Diapulse therapy to heal pressure sores, the wide confidence intervals, which include 1, indicate a lack of statistical significance. Unfortunately your trial was extremely small, resulting in a lack of statistical power to detect a clinically important treatment effect as statistically significant (the result for the main comparison are consistent with a RR anywhere between 0.7 i.e. in favour of conventional treatment, to 143.7 in favour of electromagnetic therapy). This together with the baseline difference in wound area means that whilst there may be a real treatment effect your trial does not provide convincing evidence of it.


We were unable to obtain assurance of random sequence generation or allocation concealment from Salzberg’s written report. The allocation process for people with Stage II ulcers did not result in a balanced allocation between the two treatment groups although this was corrected for in the analysis (whilst the statistical tests for differences were not significant the differences are not unimportant). The low power of the study, again due to low sample size, is compounded by the separation of Stage II and Stage III patients which is, in effect, a subgroup analysis. Such subgroup analyses should be pre-planned, and in this case it is severely underpowered, but is the basis of the “statistically significant” difference in the original report. No baseline data were provided for patients with Stage III pressure ulcers, therefore we were unable to judge the success of the randomisation. However, these patients account for 33% of the patients in the study and they are effectively lost from the overall analysis. Readers cannot exclude chance or bias as possible causes of the treatment difference. We calculated the RR of healing for people with Stage III pressure ulcers as 7 (95% CI 0.45,108.26). Whilst this result is in the direction of benefit from Diapulse, there is no statistically significant difference.

The substantial questions about the internal validity of the two studies reviewed, and the small size of these studies, means that whilst both studies show results in the same qualitative direction (that of benefit of electromagnetic therapy), it would have been wrong to draw the conclusion that this is an effective treatment. This is clearly an important area for future high-quality research. Such research should involve sufficient numbers of patients to ensure a realistic chance of detecting important treatment effects, and should avoid the threats to validity so frequently observed in wound care trials. We would also urge that any further studies follow the internationally respected CONSORT statement for the reporting of RCTs.

As I am sure you are aware, the systematic reviews undertaken by the Cochrane Collaboration use an internationally agreed process, which includes pre-publication peer review of the review protocol and the finished review, and open peer review of the review at any time after publication. This peer review did not identify similar concerns to yours. I am afraid we are unable to change the conclusions of the Cochrane Review as requested.

Contributors

Professor Sorin Comorosan (Romania)
Professor Nicky Cullum (UK)
WHAT’S NEW

Last assessed as up-to-date: 28 April 2008.

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HISTORY


Review first published: Issue 4, 2000

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<td>Second update. For this second update, new searches were carried out in Cochrane Wounds Group Specialised Register (last searched in April 2008), CENTRAL (The Cochrane Library 2008, Issue 2); MEDLINE (1966 to April 2008); EMBASE (1980 to Week 17 2008); and CINAHL (1982 to April 2008). No new studies were identified. The reviewers’ conclusion remain unchanged.</td>
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<td>1 January 2006</td>
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<td>Substantive amendment. New review authors joined the review team. First update. For the first update, new searches were carried out in October 2005. No new studies were identified. One study was excluded. The reviewers’ conclusion remain unchanged.</td>
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CONTRIBUTIONS OF AUTHORS

KF and NC conducted the original review.

AOM ran the updated search and searched new databases to identify potentially relevant studies.

AOM and HR checked the studies independently for inclusion for this update.

AOM drafted the update.

HR provided comments on the update draft.

NC and KF commented on the final draft of update.

Contributions of others

Sally Bell-Syer advised on the updating procedure and edited the text.

Ruth Foxlee updated the search strategies for all databases, ran the searches, deduplicated the output and checked the references.

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources

- Department of Health Sciences, University of York, UK.

External sources

- NHS Health Technology Assessment Programme, UK.
- General Nursing Council of England and Wales Trust, UK.

INDEX TERMS

Medical Subject Headings (MeSH)

*Electromagnetic Phenomena; Electric Stimulation Therapy; Pressure Ulcer [*radiotherapy]; Randomized Controlled Trials as Topic; Wound Healing

MeSH check words

Humans