Biophysical Agents: data extraction and appraisals

Search results for 2019 International Pressure Injury Guideline: Biophysical agents

Identified in pressure injury searches
n=11,177

Excluded after screening title/abstract
• Duplicate citations
• Included in previous guideline
• Not related to pressure injuries
n=8,128

Identified citations
n=3,085

Excluded after review of full text
• Not related to pressure injuries
• Not related to the clinical questions
• Citation type/research design not meeting inclusion criteria
• Non-English citation with abstract indicating not unique research for translation
n=66

Identified as providing direct or indirect evidence related to topic and critically appraised
n=20

Total references providing direct or indirect evidence related to topic
n=62

Biophysical agents keywords
Biophysical, bioagent, ultrasound, electrical stimulation, phototherapy, light therapy, vibration, electromagnetic, oxygen, laser, magnet, acupuncture, alternative therapy, negative pressure, NPWT, vacuum

Additional citations
Identified by working group members
n=36

Additional citations
Appraised for previous editions
n=42

Identified in topic-specific key word searches for full text review and critical appraisal
n=86

Excluded based on key word searches
• Not related to the topic-specific questions
n=2,999

### Biophysical Agents: data extraction and appraisals

#### Articles Reviewed for International Pressure Injury Guideline

The research has been reviewed across three editions of the guideline. The terms pressure ulcer and pressure injury are used interchangeably in this document and abbreviated to PU/PI. Tables include papers with relevant direct and indirect evidence that were considered for inclusion in the guideline. The tables are provided as a background resource and are not for reproduction.


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<table>
<thead>
<tr>
<th>Ref</th>
<th>Type of Study</th>
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<tr>
<td>(Polak et al., 2017)</td>
<td>RCT to determine if electrostimulation (ES) by high voltage monophasic pulsed current (HVMPC) differs in pressure injury healing outcomes if delivered through the cathode (CG) only compared to a combination of cathode and anode (CAG) current delivery</td>
<td>Participants were recruited in three nursing homes (n=63)</td>
<td>Participants were randomized to one of three groups: - Electrostimulation (twin-peak monophasic pulse, 154 μs, 100pps, 0.25 A 50mins/day. 5days/week) delivered through the cathode as mode of delivery attended 5 times/week in 50 minute sessions (n=23) - Electrostimulation with a combination of cathode and anode mode of delivery – regimen as for cathode only group except the cathode intervention was delivered for 1 week, followed by anode delivery for 5 weeks (n=20) - Control group receiving placebo electrostimulation with no current delivered (n=20)</td>
<td>- 7 measurements done before trial started - Wounds measured once a week in the duration of the trial - Outcome was healing achieved over total time and time until 50% healing was achieved - Follow up period of 6 weeks</td>
<td>Percent area reduction at six weeks Cumulative wound surface area reduction was 82.34% (95% CI 70.06 to 94.63) in cathode-only group compared with 70.77% (95% CI 53.51 to 88.04) in cathode-anode group. These reductions were significantly greater than in the placebo ES group (40.53%; 95% CI 23.60 to 57.46); P=0.0006 and p =0.0124 respectively. The cathode-only group and the cathode-anode group were not statistically significantly different regarding treatment results (p=0.9932). Time to 50% approximation Cathode only group had fastest time to 50% healing (1.92 weeks, 95% CI 1.62-2.23) compared to cathode-anode group (2.60 weeks, 95% CI 2.08-3.13) and placebo group (10.60 weeks, 95% CI 7.25-13.95). The differences were statistically significant between the cathode ES group and the placebo ES group (p &lt;0.05) and between the cathode+anode ES group and the placebo ES group (p &lt;0.05). But they</td>
<td>- Triple blinded trial - Outcome measure of 50% closure is not a strong indicator of effectiveness - Short observation time of 6 weeks failed to elucidate ideal regimen - Approx 9.3% dropped out of the treatment groups (not different from placebo group)</td>
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Data Tables: 2019 Guideline Update: Biophysical Agents for Treatment or Prevention of Pressure Injuries © EPUAP/NPIAP/PPPIA
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| (Polak, Kloth, et al., 2016) | RCT | To determine if electro-stimulation (ES) by high voltage monophasic pulsed current (HVMPC) delivered through the cathode (CG) improves pressure injury healing times | Participants were recruited in two nursing homes (n=49)  
Inclusion criteria:  
- Age ≥60 years  
- High risk score for pressure injury development  
- Category/Stage II or III pressure injury of up to 50 cm² present  
- Duration of pressure injury 1 to 12 months  
- Located in the pelvic girdle  
Exclusion criteria:  
- Could not receive ES  
- Conditions impeding wound healing  
- Critical wound infection | Participants were randomized to receive either:  
  - HVMPC electrostimulation delivered through the cathode as mode of delivery (ES group, n=36) or  
  - placebo electrostimulation with no current delivered (n=24)  
  - 7 measurements done before trial started  
  - Wounds measured once a week in the duration of the trial  
  - Outcome was healing achieved over total time and time until 50% healing was achieved  
  - Follow up period of 6 weeks | Percent reduction in wound size  
After 1 week the pressure injury area reduction in the ES group was 35% compared to 17.07% in the control group (p<0.032).  
Decreases in wound surface area  
Largest decrease of wound surface area at weeks 1, 2 and 3 with 35%, 32.78% and 45% achieved respectively in the ES group when compared to the control group where wound surface area reduction was 17.07%, 12.78% and 20.32% on weeks 1, 2 & 3. (p<0.032) | Outcome measure of 50% closure is not a strong indicator of effectiveness  
Short observation time of 6 weeks failed to elucidate ideal regimen  
16.7% drop out from treatment group (similar to placebo group) | Level of Evidence: 1  
Quality: High |
### Biophysical Agents: data extraction and appraisals

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| (Karsli, Gürçay, Karaahmet, & Cakci, 2017) | RCT comparing high voltage ES to low frequency ultrasound for healing pressure injuries | Participants were recruited in a medical clinic Turkey (n=35, 8 excluded due to concurrent medical diagnoses) | Participants were assigned to either:  
- HVES applied using twin peaked monophasic pulsed current with 100PPS 10-50-100 us pulse width and 2 second ramp up time in continuous mode. Intensity between 50 and 150 V. 60 minute duration 3x per week x 4-12 weeks (n=25), or  
- Ultrasound at 3 MHz 20% duty cycle and 0.3 W/cm² frequency 1 MHz in continuous mode in the wound bed for 1-2 mins. 1-1.5 W/cm² dose for 2-3 mins around the wound (n=22) | - Did not specify who was assessing wounds if consistent.  
- Did utilize wound evaluation scales to calculate dimensions  
- NPUAP Staging system  
- Follow up 4 to 12 weeks. | Wound surface area change  
- 43% decrease in wound surface area in HVES group versus 63% WSA decrease in US group  
- Analysis based on Category/Stage and intervention group showed significant improvements in Category/Stage II, III and IV pressure injuries in both treatment groups (baseline compared to follow-up)  
- Wound surface area showed significant decrease in HVES group over time (p<0.001) and in US group over time (p<0.001) | - No control group  
- All pressure injuries were Category/Stage IV were in the HVES group which may alter realistic findings |

**Participant characteristics:**  
- No statistical differences between the two groups  
- Inclusion criteria:  
- Hospitalized for neurologic rehabilitation.  
- Category/Stage II to IV pressure injury  
- Exclusion criteria:  
- Cardiac dysrhythmia or pacemaker, epilepsy, osteomyelitis, pregnancy, malignancy, and/or uncontrolled autonomic dysreflexia.  

**Participant characteristics:**  
- Majority had SCI, (TBI, CVA, myelitis and combination of SCI/TBI)  
- Duration of neurologic disease, Smoking, voiding status, ambulation level not statistically significant different between groups  
- Baseline severity of pressure injuries were significantly different, with the HVES group having significantly worse profile in terms of classification  

**Level of Evidence:** 1  
**Quality:** Low
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<td>[Lawson &amp; Petrofsky, 2013]</td>
<td>Comparative study to compare a biphasic and monophasic waveform electrical stimulation for promoting blood flow and healing rates of chronic stage III and IV pressure injuries over 4 weeks of treatment</td>
<td>Participants were recruited at an outpatient wound center in US (n=40 participants, n=20 had pressure injuries)</td>
<td>All groups received sharp debridement, hydrogel to wound bed, wet-to-dry sterile gauze, 3 times per week.</td>
<td>wound healing over 4 weeks using unreported methods</td>
<td>Percent wound healing over 4 weeks</td>
<td>No significant difference between monophasic and biphasic groups for percent wound healing</td>
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<td>All groups received electrical stimulation via Challenge 8000 device for 30 minutes in a 32°C room. The waveform was generated by a Biopac MP 100 (Biopac Systems, Goleta, CA) data analysis system delivering pulse width of 200µs, frequency 30Hz and current up to 20mA.</td>
<td>Blood flow using Laser Doppler flow meter at 5 and 10 mins pre-stimulation and at 5, 10, 15, 20, 25 and 30 minutes during stimulation and at 10 minutes post stimulation, at initial treatment, 2 weeks and 4 weeks.</td>
<td>Blood flow</td>
<td>Pressure injuries demonstrated significantly greater blood flow with biphasic current than monophasic at initial test (p&lt;0.001) and week 2 (p&lt;0.001)</td>
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<td>Participants received either:</td>
<td>Follow up for 4 weeks</td>
<td>Author conclusions: Biphasic current electrical stimulation was significantly more effective in healing neuropathic wounds vs pressure ulcers. Healing rate not significant when comparing the two currents for pressure ulcers.</td>
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<td>o biphasic waveform</td>
<td>• wound healing over 4 weeks using unreported methods</td>
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<td>Study also included 20 participants with neuropathic ulcers, results not reported here but neuropathic group had significantly better healing with biphasic ES</td>
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<td>No blinding</td>
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<td>Methods of outcome assessment not reported</td>
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<td>Quality: Moderate</td>
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<td>(Jercinovic, 1994 #17864)</td>
<td>RCT</td>
<td>Participants were people with SCI and PU (n=73 people, n=109 ulcers)</td>
<td>Individuals were randomized to received either:</td>
<td>Trial duration 4 weeks</td>
<td>mean healing rate</td>
<td>Unclear how many completed study</td>
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<td>o Low frequency, biphasic, asymmetric, charge-balanced pulsed current electrical stimulation(2 hours/day, 5 times/week) plus standard wound care. Delivered by two</td>
<td>wound area values evaluated using exponential and linear fitting</td>
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<td>No information on randomization and allocation concealment</td>
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<td>Weekly wound area changes in wound depth and tissue appearance</td>
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<td>No double blinding</td>
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<td>{Franek, 2012 #461}</td>
<td>RCT</td>
<td>n=57 (7 did not complete treatment and not considered in analysis)</td>
<td>group had ulcers with more complex tissue characteristics</td>
<td>electrodes placed on healthy skin approx 3cm from ulcer edge. Frequency 40pps, pulse duration 205us, amplitude individualized (up to 35mA) to achieve minimal muscle contraction, or Standard wound care • For all patients, initial debridement, application of standard dressing two or more times per day and antibiotic as required</td>
<td>day (linear) or 2.7% (3.6) per day (exponential)</td>
<td>• No statistical comparisons of results • Severity of pressure injuries is not reported</td>
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<tr>
<td>All participants received standard care: Range of wound dressings (e.g. non-adhesive, hydrogels, moist gauze), topical treatments, pressure-relieving surface if required. Participants received either: • Only standard care (n=24) • High-Voltage Electrical Stimulation (HVES) at 100V;100 µs; 100 Hz for 50 minutes once daily five times a week (n=26)</td>
<td>Wounds photographed on weekly basis and digital planimetry to determine wound area • Wound area measured using callipers at deepest point • Patient were followed until healing for a maximum of 6 weeks</td>
<td>• Mean PU areas decreased significantly in both groups • Mean PU area was statistically significantly different from week 3 (p=0.008) • Average granulation area increase was statistically significantly superior in treatment group only in week 5 (p=0.02) • Week 6 surface area change was 88.9% (SD=14) the treatment group and 44.4% (SD= 63.1) in the control group (p=0.00003) • Correlation coefficients between changes in wound surface area, longest length and longest width were R=0.96 and R=0.98 in the treatment and R=0.94 and R=0.89 in the control</td>
<td>• Study length of 4 years • No blinding • Lower extremity PU only • Variety of other treatments may not have been consistent between groups</td>
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<tr>
<td>{Franek, 2011 #462}</td>
<td>RCT</td>
<td>n = 58 participants</td>
<td>All patients received standard care: local bath of potassium</td>
<td>Per cent change in wound surface area</td>
<td>Both groups had statistically significant reduction in (p≤0.0001)</td>
<td>Non-blinded study</td>
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Level of evidence: 1
Quality: moderate
### Biophysical Agents: data extraction and appraisals

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<td>(Houghton, 2010 #466)</td>
<td>Single-blind RCT</td>
<td>Participants (n=67 screened, n=34 included) with SCI living in the community</td>
<td>permanganate, compresses of fibrolan, colistin, iruxol, and wet dressings containing 10% sodium chloride Participants received either: • Standard care only (n=29) • Monophasic pulsed current generator high voltage monophasic stimulation (HVMS) at 100 μs, 100 Hz, 100 V once daily, five times a week for 6 weeks (n=29)</td>
<td>• Per cent change in wound depth • Per cent change in wound volume • Per cent change in wound length</td>
<td>wound surface area, wound volume, wound depth, wound length and pus covered area • In HVMS group 8/29 PUs healed versus 4/29 PUs in control group • Relative changes: o total surface area: 85.38% in HVMS group versus 40.08% in control group o Length: 71.22% in HVMS group versus 30.38% in control group o Width: 76.09% in HVMS group versus 32.48% in control group o volume 20.69% in HVMS group versus 9.39% in control group • The Gilman Index (0.64 cm in HVMS group versus 0.28 cm in control group) indicated a difference in favor of group A (p≤0.001) • More efficient decrease of pus and greater granulation growth were observed in group A but difference was not statistically significant (p=0.07) • In HVMS group the correlation between change of total area and length of ulcers was 0.85 (p=0.002), total area and width was 0.84 (p=0.002), and total area and volume was 0.66 (p=0.01). • In control group the correlation between change of total area and length of ulcers was 0.55 (p=0.02), total area and width was 0.54 (p=0.02), total area and volume was 0.49 (p=0.04).</td>
<td>• Wide variety in participants and PU characteristics • Authors unable to confirm the mechanism by which HVMS influences healing</td>
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**Inclusion:**
- Stage I, II or III PU

**Exclusion:**
- SCI or paralysis
- ABI <0.9
- Diabetes mellitus
- Arrhythmias
- Post-steroid therapy

**Characteristics:**
- Mean age 59 to 60 yrs
- Primarily leg PU
- Mean PU duration 2 to 3 mths
- Mean PU area 4.5 to 5cm²
- Mean PU volume 0.04cm³
- About 50% participants were smokers
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| {Gentzkow, 1993 #189} | Baseline-controlled study exploring pulsed electrical stimulation for healing Category/Stage III and IV pressure injuries | Participants were recruited at a spinal cord injury center, a long term care facility and a specialist pressure injury center, all in US (n=61) | In lead in phase, pressure injuries received moist saline gauze only. Whirlpool or hyperbaric oxygen (this is the comparator group)  
For pressure injuries not progressing, treatment with pulsed electrical stimulation using Dermapulse® for two 30-minute sessions per day, | Improvement in pressure injury stage or wound character at 2 weeks  
Follow-up of 4 weeks | 60.7% improved after 2 weeks of electrical stimulation (p=0.000001)  
80.4% improved after 4 weeks of treatment  
Complete healing achieved in 23% of pressure injuries  
No safety issues occurred | • EST treatments were applied in combination with silver dressings  
• High PU recurrence rate | Level of evidence: 3  
Quality: low |

Inclusion:  
• Stage II to IV PU between 1 and 20cm² of at least 3 month duration  
Exclusion:  
• Serious comorbidity  
• Contraindications to electrical stimulation therapy (e.g. pacemaker)  
• Deep tunneling PU  
• Three or more abnormal blood values  
Characteristics:  
• Mean age 50 years  
• primarily stage IV PUs  
• mean wound duration 1.2 to 3 years

Participants received either:  
• Standard wound care (SWC)  
• Electrical stimulation therapy (EST):  
  - Silver dressing regimen to facilitate therapy  
  - 2 to 30 30 minute education sessions  
  - Individualised electrical stimulation (generally single electrode placed directly over wound with larger dispersive electrode placed 20cm away from wound), twin peak monophasic pulsed current with 50µs pulse duration at 50 to 150V intensity. 40 minutes therapy followed by 20 minutes with no therapy for an 8 hour cycle daily.

3 months assessed by digital planimetry  
Proportion of wounds achieving at least 50% reduction in wound surface area  
Wound appearance assessed using a photographic wound assessment tool  
Assessed monthly over 3 months then followed for 4 months to assess recurrence.

(70% ± 25% versus 36% ± 61%, p=0.048)  
• All stage II PUs healed in both groups  
• Proportion of wounds achieving at least 50% reduction in wound surface area significantly greater in EST group (80% versus 36%, p=0.02)  
• photographic wound assessment tool score was improved in more PUs in the EST group (75% versus 44%, p=0.07)  
• Adverse reactions included red itchy skin beneath dispersive electrode (resolved within 24 hours), one patient acquired a burn.  
• Mean treatment time was 3±1.5 hrs per day (lower than recommended time)  
• 8 subjects in each treatment group had recurrent or new PUs develop within 4 months of closure
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<td>{Kloth, 1988 #257}</td>
<td>RCT exploring pulsed electrical stimulation for healing Category/Stage IV pressure injuries</td>
<td>Participants were recruited (n=16)</td>
<td>All wounds debrided enzymatically or manually Participants were randomized to receive either • pulsed electrical stimulation high voltage, monophasic at 105Hz with intraphase duration of 50μsec and voltage just</td>
<td>Methods of wound measurement not reported</td>
<td>Percent healing per week • Electrical stimulation had greater healing per week than control group (44.80% versus −11.59%) Complete healing • All wounds in treatment grouped achieved 100% healing after mean 7.3 weeks of treatment</td>
<td>• Methods of randomization not valid • No allocation concealment • Inclusion/exclusion criteria not reported</td>
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<td>Participant characteristics: • Age range 20-89 years (mean 66-77) • Ulcers had previously been unresponsive to treatments</td>
<td>monophasic, square wave current in pulse duration of 140 μsec, 128 pulses per second at 35 millamps (n=21) • Treatment continued for at least 2 weeks but up to 4 weeks</td>
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<td>measure of healing • Comparison was baseline treatment</td>
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<td>Exclusion criteria: • Pace maker • Active phlebitis • Osteomyelitis, thrombosis, malignancy, epilepsy • Long-term steroids, chemotherapy, radiation • Pregnancy</td>
<td>Only pressure injuries without improvement in this phase received electrical stimulation. • Eschar, necrotic or exudative wounds were selected</td>
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| {Wood, 1993 #450} | RCT exploring pulsed electrical stimulation for healing Category/Stage II and III pressure injuries | Participants were recruited in four centers (n=74) | Participants were randomized to receive either:  
- pulsed low intensity direct current electrical stimulation at 300-600μA (n=43)  
- sham treatment (n=31) | Surface area calculated from cross-section diameters and from wound tracings transferred to a grid  
Response was considered as a decrease in surface area of at least 80% after 8 weeks  
Followup of 8 weeks | Percent healing per week  
Electrical stimulation had greater healing per week than control group (11.04% versus 4.10%, p<0.0001)  
Complete healing  
58% in treatment group healed by 8 weeks compared with 3% in control group (p=0.001) | Very small sample, likely not sufficient to measure significant effect  
Double blinded study  
Method of randomization and allocation concealment not reported  
Inclusion/exclusion criteria not clear | Level of evidence: 1  
Quality: Low |
| {Griffin, 1991 #202} | RCT exploring pulsed electrical stimulation for healing pressure injuries | Participants with SCI were recruited in a SCI center in US (n=20 randomized, n=17 completed and analyzed) | Participants stratified based on Category/Stage of pressure injury then were randomized to receive either:  
- high voltage pulsed electrical stimulation delivered for 1 hour/day for 20 consecutive days with frequency at 100pps, intensity at 200V (n=8)  
- sham treatment (n=9) | Measurements of wound at baseline and days 5,10,15 and 20  
Wound tracings projected to grid to calculate surface area | Healing outcomes  
Treatment group showed significantly better change in wound surface area at day 5 (p=0.03), day 15 (p=0.05) and day 20 (p=0.05) compared with sham treatment group  
100% of Category/Stage II pressure injuries in treatment group healed completely  
After 20 days, median change was ~80% in treatment group versus ~52% in control group | Sample size calculation indicated a need for 10 per group  
2 patients withdrew due to medical complications and 1 withdrew to have surgical repair  
Methods of randomization and allocation concealment not reported | Level of evidence: 1  
Quality: Low |
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</table>
| {Stefanovska, 1993 #401} | Experimental study reporting outcomes when using electrical stimulation to promote healing | Individuals in treatment group had SCI duration significantly longer (P<0.05) | • Participants received either:  
  o ES with direct currents with amplitude 600μA for two hours daily plus standard wound care  
  o ES with AC low frequency pulsed currents, biphasic with pulse duration 0.25ms and repetition rate of 40Hz, plus standard wound care  
  o Control group receiving standard wound care only  
  • For delivering ES in both groups the electrodes were placed on healthy skin on either side of the wound | • Wound area and wound depth  
• Methods of measurement not reported | • AC electrical stimulation group showed significantly greater rate of healing compared to control group (p=0.003)  
• DC group was not significantly different to control group for rate of healing  
• AC electrical stimulation was less effective for wounds with initial greater surface area  
• DC electrical stimulation was less effective for wound with initial greater depth | • Unclear how individuals were assigned to groups  
• Does not stay how wounds were measured  
• Contains detailed discussion on how to measure wound healing rate  
• Blinding not discussed  
• Unclear exactly how many participants, DC group appears to have much less |

| {Baker, 1996 #57} | RCT comparing different types of electrical stimulation | Participants were inpatients and outpatients with SCI (n=80 participants with n=192 pressure injuries) | • Participants were randomized to receive:  
  o Asymmetric biphasic electrical stimulation, phase duration 100μsec, 50 pulses/second (n=20 with n=67 wounds)  
  o Symmetric biphasic electrical stimulation, phase duration 300μsec, 50 pulses/second (n=21 with n=58 wounds)  
  o Microcurrent, 4mA amplitude, 10μsec, 1 pulse/second (n=20 with n=42 wounds) | Pressure injury healing Acetate wound tracings and wound volume performed weekly for inpatients and 2-4 weekly for outpatients | • The Asymmetric electrical stimulation was associated with significantly more individuals achieving a good response (61%) compared with good responders for Microcurrent group (56%) (p=0.02)  
• Asymmetrical (61%) and Symmetrical (70%) had similar amount of good responders but the percent healing per week was higher in the asymmetric group (63.7%±7.2 versus 50.6%±5.6, p=not reported) | • Blinded study  
• Does not report methods of randomization or allocation concealment  
• Treatment as inpatients vs outpatients may have led to other variations in care  
• Level of analysis was the wound, not the patient |
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|     |               |        | o Control group receiving sham treatment (n=19 with n=25 wounds) | Author conclusions: Asymmetric electrical stimulation is most effective for promoting healing |         | • Approx 25% of participants withdraw |}

**Clinical question 2: Pulsed electromagnetic therapy**

(Gupta, 2009 #464)

Double-blind RCT

Participants with neurological disorders who were hospitalized (n=12)

Inclusion:
- Category/Stage III or IV pressure injuries

Excluded:
- Osteomyelitis
- Non-ischaemic pressure injuries

Characteristics:
- Mean age 27 to 28 years
- Mean duration of PU 103.75±113.70 days
- A total of 24 PUs were included (13 Category/Stage IV and 11 Category/Stage III)

- All pressure injuries were debrided and treated with antibiotics as required prior to study.
- Both groups were given standard wound care including daily dressing changes.
- Participants randomised either:
  - PEMT (n=6, 13 pressure injuries) administered in ‘Pulsatron’ delivering low frequency PEMF therapy (1Hz frequency sine waves with 30 milliampere current intensity).
  - Sham therapy (n=6, 11 pressure injuries) in ‘Pulsatron’ without machine switched on

Therapy was administered for 30 sessions, 5 days a week for 6 weeks, for 45 minutes/session.

Wound healing assessed based on Bates-Jensen wound assessment (BJWAT) tool score

Staging assessed on NPUAP criteria

- Significant improvement in BJWAT scores in both PEMT group (p=0.001) and sham group (p=0.003) but no significant difference between the two groups (p=0.361)
- Both groups achieved significant healing of pressure injuries assessed on NPUAP staging criteria (PEMF group p=0.008 and sham group p=0.014) but no significant difference between the two groups (p=0.649)

- Small sample size
- Non-standard assessment of healing outcomes

Level of evidence: 1

Quality: low
### Biophysical Agents: data extraction and appraisals

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<tr>
<td>{Comorosan, 1993 #121} RCT exploring electromagnetic field therapy</td>
<td>Participants were recruited in a social care unit in Romania (n=30) Inclusion criteria: Pressure injury of long duration Participant characteristics: • Primarily in palliative end-of-life care • Age range 60-84 years • Category/Stage II and III pressure injuries • Co morbidities included SCI, CVA, dementia and atherosclerosis</td>
<td>• Participants were randomly assigned to receive: o Diapulse® sessions 1 to 2 times daily in 30 minute sessions applied through dressings at 600pps with peak power of 6, plus conventional treatment (n=20) o Conventional treatment only (hydrogen peroxide cleansing, application of talcum powder, methylene blu, tetracycline (n=5) o Sham Diapulse plus conventional therapy (n=5) o Treatment for 1-4 weeks Wounds photographed on a weekly basis Wounds were assessed on the following scale: excellent (healed), very good (75-95% healed), good 50-75% healed, fair 25-50% healed, poor &lt;25% healed, no improvement unhealed.</td>
<td>• 85% of pressure injuries in treatment group were ranked as excellent and 15% ranked as very good • 80% sham treatment group rated as no improvement and 20% ranked as poor improvement • Control group 60% no improvement and 40% poor improvement</td>
<td>• Methods of randomization and allocation concealment not reported • Double blinded study • The standard word care regimen is not used in contemporary wound care and may have impeded healing • Subjective evaluation of healing</td>
<td>Level of evidence: 1 Quality: low</td>
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<tr>
<td>{Salzberg, 1995 #377} RCT exploring PEF energy for healing Category/Stage II and III pressure injuries</td>
<td>Participants were recruited in a veteran hospital in USA (n=30) Inclusion criteria: • Category/Stage II or III pressure injury • SCI Exclusion criteria: • More than one pressure injury • Pacemaker • Cellulitis, sepsis, terminal illness, total joint replacement or other metal implant • Category/Stage I or Stage IV pressure injury Participant characteristics: All male</td>
<td>• After stratification based on pressure injury category/stage, participants received either: o Non thermal, pulsed high frequency, peak power electromagnetic energy on frequency 27.12MHz with pulse repetitions rates of 80 to 600 pulses/second and pulse width of 65microseconds and pulse power peak at 293-975 peak watts delivered through wound dressing (n=10) o Sham therapy o Treatment for up to 12 weeks All participants received saline gauze dressings</td>
<td>Pressure inures measured as width x length by a single observer All pressure injuries photographed weekly Healing for Category/Stage II pressure injuries • At 1 weeks, active therapy group had 84% of pressure injuries healed compared with 40% of sham group (p=0.01) • At one week, mean wound size was significantly smaller in active therapy group 16.5 cm² versus 2.7 cm², p=0.015 Time to healing for Category/Stage II pressure injuries Active group had significantly faster healing with mean 31.5 days to complete healing versus 13 days (p&lt;0.001) Healing for Category/Stage III pressure injuries • Active therapy group had 60% of pressure injuries healed</td>
<td>Double blind study Does not report methods of randomization or allocation concealment</td>
<td>Level of evidence: 1 Quality: moderate</td>
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### Clinical question 3: Pulsed radio frequency energy

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</table>
| (Seaborn, 1996 #386) | RCT to explore the best regimen for PEMF therapy | Participants were recruited in a non-ambulatory hospital for men (n=20) Inclusion criteria:  
- Aged 60 to 101 years  
- Trochanter or sacral pressure injuries  
Exclusion criteria: Pacemaker  
Participant characteristics:  
- Mean duration of pressure injury 13.5 weeks  
- Pressure injury descriptions indicate Category/Stage II to IV pressure injuries were involved  
- Negative swab cultures | - Participants were randomized to receive high frequency PEMF energy at 27.12MHz with pulse power 1000watts  
  - Regimen 1: magnetic field, 20 pps, 700W peak power, power density 0.036 W/cm² (n=5)  
  - Regimen 2: electric field, 20 pps, 700W peak power, power density 0.042 W/cm² (n=5)  
  - Regimen 3: magnetic field, 110 pps, 700W peak power, power density 0.199 W/cm² (n=5)  
  - Regimen 4: electric field, 110 pps, 700W peak power, power density 0.230 W/cm² (n=5)  
- All patients had 20 minute regimens daily for 5 days/week for two weeks  
- Study design was ABAB repeated measures (baseline, treatment, no treatment, treatment) | Wound surface area measured with wound tracings transferred to graph paper  
Wound measurement on a weekly basis for 5 weeks | Mean wound surface area  
- Differences in mean wound surface area was significant at 4th and 5th weeks compared to baseline (p<0.001)  
- No significant differences between regimens |  
- One person administered all treatment  
- Blinded outcome measurement  
- Small sample, with four groups there may be insufficient participants to truly measure effect | Level of evidence: 1  
Quality: moderate |
<table>
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| {Frykberg, 2011 #463} | Retrospective case series         | Database review of records of patients treated with PRFE (n=413, 28 patients had 34 pressure injuries) from 100 facilities in USA. | • Pulsed radio frequency energy administered 30 mins, x2 daily  
  • By placing applicator adjacent to wound dressing  
  • Administered by patients (community-based) or staff (facility-based)  
  • Frequency not reported. | • Per cent reduction in wound area at 4 weeks  
  • Wound healing trajectory at 4 weeks ([initial wound area-final wound area]/number days treatment)  
  • Proportion of wounds achieving ≥ 50% reduction in size at 4 weeks | • Mean per reduction cent wound surface area for pressure injuries at 4 weeks 49% ± 6% (range 100% to −386%, p<0.0001)  
  • 59% PUs achieved ≥ 50% reduction in size at 4 weeks  
  • Wound healing trajectory at 4 weeks: 0.34 ±0.60 cm²/day | • Selection bias favoured severe wounds  
  • Assumed reliable database entries  
  • Compliance with therapy regimen is known as self-administered for patients in the community  
  • Took data from a registry maintained by the product manufacturer |
| {Conner-Kerr, 2012 #458} | Retrospective record case series analysis | Data was taken from a device manufacturer’s registry consisting of cases from 99 different facilities in USA. (n=89 participants, 110 pressure injuries) | Wound and additional PU care was as per individual institution standards  
  PRFE performed by carer or participant  
  All facilities had been instructed to use Provant Therapy System by placing applicator over wound dressings for 30 minutes twice daily | • Median wound surface area reduction at 4 weeks  
  • Per cent of wound achieving 50% reduction or greater in wound surface area  
  • Rate of healing  
  • Method of assessing the outcome measures is not reported | • Median wound surface area was 9.8cm² at baseline and 4.5cm² at 4 weeks  
  • Median wound surface area reduction at 4 weeks was 44%±54%, mean 51%, range 100% to −386% (i.e. increased)  
  • 51% of wound achieving 50% reduction or greater in wound surface area at 4 weeks  
  • Wound healing trajectory at 4 weeks was 0.36±0.63cm²/day (mean 0.13, range 3.06 to −1.29)  
  • Greatest reduction in wound size was seen in Stage II PUs (median wound surface area reduction of 82%) | • No control group  
  • Database records  
  • Excluded all cases without 4 weeks of outcome data, thereby favouring treatment  
  • Adherence to instructions for administration is not checked  
  • Method of assessing the outcome measures is not reported and |
### Biophysical Agents: data extraction and appraisals

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<tr>
<td></td>
<td></td>
<td>• Median age 69 yrs (range 28 to 75)</td>
<td>• Median age 69 yrs (range 28 to 75)</td>
<td>• All received standard wound care (daily simple dressings with sterile gauze and 1% hydrophilic silver sulfadiazine cream)</td>
<td>• Infrared camera measurement, data collection by a nurse</td>
<td>may differ between facilities</td>
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<td>• 82% participants had only one PU</td>
<td>• 82% participants had only one PU</td>
<td>• Participants were randomized to receive either:</td>
<td>• Statistical analysis by a technician</td>
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<td></td>
<td>• 89% treated in inpatient facilities</td>
<td>• 89% treated in inpatient facilities</td>
<td>o Placebo laser, or</td>
<td>• Complete wound healing by a nurse and physiotherapist.</td>
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<td>• PUs ranged from 1 to 82 mths duration (median 6 mths)</td>
<td>• PUs ranged from 1 to 82 mths duration (median 6 mths)</td>
<td>o One of three different laser treatments, all provided by a physiotherapist using gallium-aluminum-arsenide diode laser, 50mW, spot size 0.1cm², average dose 4J/cm² wavelengths in one of three doses:</td>
<td>• Staging system used: EPUAP</td>
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<td>• 43% stage IV, 20% stage III, 19% stage II, 18% unstaged.</td>
<td>• 43% stage IV, 20% stage III, 19% stage II, 18% unstaged.</td>
<td>o Group 1: 940nm</td>
<td>• Follow up period: 3 months after end of study</td>
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<tr>
<td></td>
<td></td>
<td>• Ref</td>
<td>• Ref</td>
<td>o Group 2: 808nm</td>
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<td></td>
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<td>• Ref</td>
<td>• Ref</td>
<td>o Group 3: 658nm</td>
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### Clinical question 4: Phototherapy

(Taradaj et al., 2013) RCT to assess the efficacy of phototherapy (laser therapy) at different wavelengths (940, 808 and 658nm) on Category/Stage II and III pressure injury healing.

- Participants were recruited from medical setting in Poland (n=72)
- Lower extremity pressure injury

*Inclusion criteria:*
- Infection,
- Medication that interfere with wound healing
- Use of special dressings or any type of non-routine therapeutic procedure
- Nonattendance to program
- Pregnancy
- ABPI <0.8
- Diabetes mellitus
- Systemic sclerosis, cancer, paralysis
- Pressure injury requiring surgical intervention

*Exclusion criteria:*
- Infection,
- Medication that interfere with wound healing
- Use of special dressings or any type of non-routine therapeutic procedure
- Nonattendance to program
- Pregnancy
- ABPI <0.8
- Diabetes mellitus
- Systemic sclerosis, cancer, paralysis
- Pressure injury requiring surgical intervention

- Placebo laser, or
- One of three different laser treatments, all provided by a physiotherapist using gallium-aluminum-arsenide diode laser, 50mW, spot size 0.1cm², average dose 4J/cm² wavelengths in one of three doses:
  - Group 1: 940nm
  - Group 2: 808nm
  - Group 3: 658nm

Therapy for a duration based on wound size, once daily, five

- Infrared camera measurement, data collection by a nurse
- Statistical analysis by a technician
- Complete wound healing by a nurse and physiotherapist.
- Staging system used: EPUAP
- Follow up period: 3 months after end of study

<table>
<thead>
<tr>
<th>Percentage reduction of ulcer surface area</th>
<th>Group 1: 940nm laser- 33.23%</th>
<th>Group 2: 808nm laser- 71.09%</th>
<th>Group 3: 658nm laser- 33.23%</th>
<th>Placebo- 28.34%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of completely healed wounds at 1 month</td>
<td>Group 1: 940nm laser- 11.11%</td>
<td>Group 2: 808nm laser- 11.11%</td>
<td>Group 3: 658nm laser- 47.05%</td>
<td>Placebo- 11.11%</td>
</tr>
<tr>
<td>Ulcer healing rate at 3 months after end of study</td>
<td>Group 1: 940nm laser- 16.66%</td>
<td>Group 2: 808nm laser- 16.66%</td>
<td>Group 3: 658nm laser- 58.82%</td>
<td>Placebo- 16.66%</td>
</tr>
</tbody>
</table>

**Author conclusions:** Wavelength of laser beam is extremely important in wound healing process. No

**Limitations and comments:**
- No power calculation
- No conflict of interest declared.
- No commercial association with the manufactures of the equipment

**Level of Evidence:** 1
**Quality:** High
## Biophysical Agents: data extraction and appraisals

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</table>
| {Lucas, 2003 #17866} | RCT comparing phototherapy (low level laser therapy) for healing Category/Stage III pressure injuries with standard wound healing | Participants were recruited in three nursing homes in the Netherlands (n=86)  
Inclusion criteria: Category/Stage III pressure injuries | Participants were randomized to receive either:  
- Low level laser therapy (LLLT) using an irradiated area of 12cm² with total peak power at 904nm 830Hz pulse frequency mode of 150ns pulses. Laser was applied to normal peri-wound tissue with applicator held just off contact with wound surface. (n=39)  
- Control group: standard wound therapy (n=47) |  
- Absolute and relative pressure injury reduction at 6 weeks compared to baseline  
- Number of individuals developing a Category/Stage IV pressure injury | Rate of healing  
- There was no difference in rate of change in absolute improvement in wound surface area between the two groups (p=0.23)  
- There was no difference in rate of change in relative improvement in wound surface area between the two groups (p=0.42) |  
- 7% withdrawal with no reasons given, but used ITT analysis  
- Methods of randomization not reported  
- No information about potential blinding of participants  
- Outcome assessors were blinded  
- No ITT analysis | Level of Evidence: 1  
Quality: low |
| {Wills, 1983 #444} | RCT comparing phototherapy (UV light) to conventional therapy for healing pressure injuries | Participants were recruited in an aged care facility in British Columbia (n=18 randomized, n=16 analyzed)  
Inclusion criteria:  
- Superficial pressure injuries recently occurring and <5mm  
Participant characteristics>  
- 81% of pressure injuries were on sacrum or ischium  
- Age range 62 to 103 years | Participants were randomized to receive:  
- Conventional treatment plus phototherapy with UV light twice daily at dose of 2.5 minimal erythema dosage, delivered twice weekly for 10 weeks for total exposure of 7.5 minutes (n=8)  
- Conventional treatment (twice daily sterile water wound dressings) plus sham light (n=8) |  
- Time to complete healing  
- Adverse events | Time to complete healing  
Phototherapy group had a shorter time to complete healing (mean 6.26±1.6688 weeks versus 8.37±1.4142 (p<0.02) (mean difference -2.11, 95% CI -3.63 to -0.59) |  
- Randomization and allocation concealment methods not reported  
- Category/Stage of pressure injury was unclear  
- Blinding was attempted but may not have been sufficient  
- No ITT analysis  
- Small sample size | Level of Evidence: 1  
Quality: low |
## Biophysical Agents: data extraction and appraisals

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<td>{Schubert, 2001 #381}</td>
<td>RCT comparing phototherapy (infrared light) for healing Category/Stage II or III pressure injuries</td>
<td>Participants were recruited at a hospital in Sweden (n=72) &lt;br&gt; Inclusion criteria: Aged over 65 years &lt;br&gt; Category/Stage II or III pressure injuries &lt;br&gt; Orthopedic or geriatric ward inpatient Participant characteristics: 82% had a fracture &lt;br&gt; Mean age 85 years</td>
<td>• Participants were randomized to receive: &lt;br&gt; o Pulsed monochromatic infrared light at 956nm with red light at 637nm. Treatments for 9 minutes with pulse repetition frequency of 15.6Hz to 8.58kHz (n=37 randomized) or, &lt;br&gt; o Control group (n=37 randomized, n=35 analyzed) &lt;br&gt; • All pressure injuries had necrosis removed with sharp debridement and moist wound healing (e.g. hydrocolloids were used). Treatment for 10 weeks of until complete healing</td>
<td>• Pressure injury surface area &lt;br&gt; • Wound tracings on a weekly basis with planimetry used to determine surface area</td>
<td>Healing rate: &lt;br&gt; • Mean wound surface area decreased by 10% by 5 weeks, compared to 9 weeks for control group &lt;br&gt; • Healing rate in phototherapy group was 0.298 per week versus 0.200 in control group (i.e. Rate of healing was 49% greater in the phototherapy group compared to the control group.)</td>
<td>• Allocation concealment methods not reported &lt;br&gt; • No blinding of participants or outcome assessors &lt;br&gt; • 18% withdrawal rate (death and transfers, malnutrition and ulcer revisions), no ITT analysis</td>
</tr>
<tr>
<td>{Shojaei, 2008; #1473}</td>
<td>RCT comparing phototherapy (laser)</td>
<td>Participants were recruited from a veteran’s center in Iran (n=16) &lt;br&gt; Inclusion criteria: • SCI &lt;br&gt; • Category/Stage I to III pressure injuries Participant characteristics: • More than half the participants (9/16) had Category/Stage I pressure injuries (more in the phototherapy group (75% vs 37.5%))</td>
<td>Participants were recruited to either: &lt;br&gt; • Phototherapy with a gallium-aluminium-arsenide laser plus gallium-aluminium-indium-phosphate diode laser with continuous emission (IR 980 nm, 200 m continuous at dose 4-6J/cm applied alternate days for three weeks (n=8), or &lt;br&gt; • Standard treatment group (n=8)</td>
<td>• Reducing the size of pressure injuries &lt;br&gt; • Pressure injury stage before and after treatment &lt;br&gt; • Pressure injury size before and after treatment &lt;br&gt; • Difference in cure rate</td>
<td>Proportion of healed pressure injuries: &lt;br&gt; Healing rate was significant in favour of the intervention group (p=0.001) &lt;br&gt; Rate of healing: There was no significant difference between groups (p=0.236)</td>
<td>• Randomization and allocation concealment methods not reported &lt;br&gt; • No blinding of participants &lt;br&gt; • There were no withdrawals in this study &lt;br&gt; • Non-equivalent samples with respect to Category/Stage &lt;br&gt; • Small sample size</td>
</tr>
<tr>
<td>{Dehlin, 2003 #1472}</td>
<td>RCT comparing phototherapy (monochromatic)</td>
<td>Participants were recruited in eight aged care centers in</td>
<td>Participants were randomized to receive either: &lt;br&gt; • Shea score to classify pressure injuries</td>
<td>Proportion of healed pressure injuries at 12 weeks</td>
<td>Proportion of healed pressure injuries</td>
<td>Randomization and allocation concealment</td>
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<th>Quality:</th>
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<td>light therapy) to placebo for healing pressure injuries</td>
<td>Sweden and Denmark (n=164)</td>
<td>o Phototherapy with pulsed monochromatic light (infrared at 956 nm and red light at 637nm pulsed) (n=78) o Placebo therapy group: white light diode painted red (n=86)</td>
<td>• Proportion of healed pressure injuries at 12 weeks • Rate of healing • Time to complete healing</td>
<td>• Healing rate was higher in the phototherapy group compared to placebo (43.6% versus 39.5%) Rate of healing There was no difference in rate of change in wound surface area between the two groups (p=0.18)</td>
<td>methods not reported • No blinding of participants but outcome assessors were blinded • 17% withdrawal due to protocol violations or due to adverse events</td>
<td>low</td>
</tr>
<tr>
<td>Nussbaum, 1994 #334</td>
<td>RCT exploring phototherapy (ultrasound combined with ultraviolet C (UVC) light therapy) for healing pressure injuries</td>
<td>Participants recruited from a SCI center in Canada (n=20 participants with n=22 pressure injuries)</td>
<td>Participants were randomized to one of three groups: • Ultrasound/UVC: pulsed ultrasound at 3 MHz frequency, average intensity 0.2Wcm² for 5 minutes per 5cm² wound area plus UVC dose calculated based on wound appearance. US and UVS was alternated daily for 5 days/week (n=5) • Laser therapy: three times weekly administration of laser using 820nm diode and 30 superluminous diodes at energy density of 4 J/cm² (n=6)</td>
<td>• Time to complete healing • Mean percent change in ulcer size</td>
<td>Mean weekly healing rate • Overall in the study 36.54% Mean percent change in wound size Mean change was significantly greater in the US/UVC group (53.5%) compared with laser group (23.7%) and control group (32.4%, p=0.032). • No adverse events were reported</td>
<td>• Category/Stage of pressure injury was not reported • Randomization and allocation concealment methods not reported • Appears to have no blinding • 20% withdrew from study and were not analyzed</td>
<td>low</td>
</tr>
</tbody>
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<tr>
<td>{Nussbaum, 2013 #469} Double-blind RCT investigating phototherapy (ultraviolet C light therapy) for healing Category/Stage II to IV pressure injuries</td>
<td>Participants recruited from two inpatient facilities, and an outpatient wound center in Canada (n=43 participants with n=58 pressure injuries) Inclusion: • Adults over 18 years • SCI at C2 to L2 • Category/Stage II to IV pressure injuries Exclusion: • NPWT • Surgical repair in previous 3 months • Neoplasm Participant characteristics: • Primarily buttock and lower extremity PUs • Mean age 54 to 55 yrs • Mean PU size stage 2 PUs 2.44 to 4.22cm² • PU duration primarily 1-8 wks in both groups, UVC group had more PUs of 9-52 wks than placebo group and placebo group had more PUs &gt;52 wks than UVC group.</td>
<td>• Control group: standard wound care (twice daily cleansing, paraffin gauze dressing (n=9) • All participants received standard pressure relieving measures. Wound care regimen not reported. • Participants were stratified by pressure injury location and randomized to either: o Placebo UVC attained using regular light bulb and regimen as per treatment group (n=28) o Ultraviolet C light therapy (UVC) applied x3 weekly (wound edges and peri-wound irradiated for 15 seconds at ~15mW/cm² then PU irradiated on a regimen based on PU severity (n=30) • Therapy until 100% PU closure or discharge from facility</td>
<td>• Weekly wound area as per cent of baseline • Mean per cent wound area change between consecutive weeks • Weeks to wound closure Assessed weekly by wound photography and imaging software to calculate area Subgroup analysis for stage 2 and stage 3-4 PUs</td>
<td>• 13 PUs(43.3%) in UVC group and 12 (42.8%) in placebo group closed during treatment time (p=ns overall or by subgroup) • At any weekly time point, number of PUs closed was similar between groups (p=ns) • 5 PUs reopened within 1 month (p=ns between groups) • 15 PUs were unhealed after 12 months (p=ns between groups) • Stage 2 PUs showed significant healing at some weekly time points (weeks 3, 5 and 7) with respect to per cent of baseline size for UVC group versus placebo group (p&lt;0.03 to 0.05).</td>
<td>• Homogeneity between PU location and severity was considered responsible for lack of significant results. • Large drop out not included in analysis • Unit of analysis is the pressure injury, not the patient</td>
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<tr>
<td>{Durovic, 2008 #460} Prospective randomized single-blind study investigating phototherapy</td>
<td>Participants (n=40) Inclusion: • Category/Stage I to III pressure injuries</td>
<td>All participants received standard wound cleaning and dressings. Participants randomised to receive either:</td>
<td>• Surface of PU measured using callipers</td>
<td>There were significant differences between the groups at the end of the treatment regarding: • The surface of PU (experimental group 10.80 ±19.18 versus control group)</td>
<td>• Non-blinded and poorly described randomisation and inclusion criteria.</td>
<td>Level of Evidence: 1 Quality: low</td>
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</table>

(c) EPUAP/NPIAP/PPPIA Not for Reproduction
## Biophysical Agents: data extraction and appraisals

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<tr>
<td>(polarised light therapy) for healing Category/Stage I to III pressure injuries</td>
<td>no contraindications for polarised light</td>
<td>Polarized light therapy with wavelength: 400–2000 nm; degree of polarization: &gt; 95%; power density: 40 mW/cm²; light energy: 2.4 J/cm². Therapy performed for 6 minutes daily at 10cm distance for 5 days/week for 4 weeks. (experimental group, n=20)</td>
<td>Rank of PU (this outcome is not described)</td>
<td>group 22.97±15.69, p=0.00005; however, 50% of the PUs in control group were described as “closed” at baseline</td>
<td>Outcome measure of “rank of PU” not described</td>
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<td></td>
<td>no deterioration of a common disease or development of a new disease</td>
<td>No additional therapy (control group, n=20)</td>
<td>PUSH score</td>
<td>Rank of PU (experimental group 5.95±2.48 versus control group 8.6±1.05, p =0.0005)</td>
<td>Did not address if an individual assessor was involved in assessing the results</td>
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<td>Exclusion:</td>
<td>All PUs in experimental group had light (50%) or moderate (25%) exudate and more in control group had no exudate (65%) p=0.04</td>
<td>Total PUSH score (experimental group 7.35±3.17 versus control group 11.85±2.35, p=0.00003)</td>
<td>Control PUs were less severe at baseline therefore less opportunity for improvements</td>
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<td>Intended skin graft within 7 days</td>
<td>More PUs in experimental group were “closed” or epithelialized at baseline (75% versus 65%, p=0.01)</td>
<td>Outcome measure of “rank of PU” not described</td>
<td>Did not use gold standard for PU assessment (wound tracings and/or digital planimetry)</td>
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<td></td>
<td>Previous PU study participation</td>
<td>More PUs in control group had no exudate (65%)</td>
<td>Did not address if an individual assessor was involved in assessing the results</td>
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<td>Albumin levels &lt; 3.0g/dL</td>
<td>More PUs in control group were “closed” or epithelialized at baseline (75% versus 65%, p=0.01)</td>
<td>Control PUs were less severe at baseline therefore less opportunity for improvements</td>
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<tr>
<td></td>
<td>Local or general infection including pilonidal sinus or osteomyelitis</td>
<td>Steroids, immunosuppressants, antineoplastics or anticoagulants.</td>
<td>Characteristics:</td>
<td>Level of Evidence: 2</td>
<td></td>
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<td>Polarized light therapy with wavelength: 400–2000 nm; degree of polarization: &gt; 95%; power density: 40 mW/cm²; light energy: 2.4 J/cm². Therapy performed for 6 minutes daily at 10cm distance for 5 days/week for 4 weeks. (experimental group, n=20)</td>
<td>Mean age 61.86 to 68.65 yrs</td>
<td>Mean surface area using wound tracings</td>
<td>Quality: low</td>
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<td></td>
<td>No additional therapy (control group, n=20)</td>
<td>Mean PU surface area 15.10 to 19.15</td>
<td>78.9% decrease in the mean surface area of the experimental group limb (initial = 76.5 cm²; final 16.6 cm²) compared with 37.4%</td>
<td>Experimental pressure injuries had much larger baseline size</td>
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<td>More PUs in experimental group had light (50%) or moderate (25%) exudate and more in control group had no exudate (65%)</td>
<td>More PUs in control group were “closed” or epithelialized at baseline (75% versus 65%, p=0.01)</td>
<td>Participants were bed ridden patients at a teaching hospital in Nigeria (n=10)</td>
<td>All PUs were dressed with Ringer’s solution dressings.</td>
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<td>More PUs in control group had no exudate (65%)</td>
<td>More PUs in control group were “closed” or epithelialized at baseline (75% versus 65%, p=0.01)</td>
<td>Left limbs were radiated with ultraviolet radiation type B</td>
<td>Mean surface area using wound tracings</td>
<td></td>
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<tr>
<td>(Onigbinde, 2010 #467)</td>
<td>Non-randomised controlled study with participants serving as own</td>
<td></td>
<td>Mean surface area using wound tracings</td>
<td>78.9% decrease in the mean surface area of the experimental group limb (initial = 76.5 cm²; final 16.6 cm²) compared with 37.4%</td>
<td>Experimental pressure injuries had much larger baseline size</td>
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Data Tables: 2019 Guideline Update: Biophysical Agents for Treatment or Prevention of Pressure Injuries © EPUAP/NPIAP/PPPIA
## Biophysical Agents: data extraction and appraisals

### Clinical question 5: Ultrasound therapy

#### Non-contact low frequency ultrasound

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<tr>
<td>(Wagner-Cox, Duhave, Jamison, Jackson, &amp; Fehr, 2017)</td>
<td>Retrospective observational study to evaluate efficacy of non-contact low frequency ultrasound (NCLFUS) for treating SDTI</td>
<td>Inclusion: • Received NCLFUS for a DTI</td>
<td>Protocol in place for managing DTIs included: • Mandatory staff education • Skin assessment every shift by an RN • WOC nurse review all patients with DTI • NCLFUS administered as per manufacturer protocol – daily for 5 days over total surface area then 3 times weekly until resolved</td>
<td>It was unclear who performed the evaluation of DTI, or how often this was performed</td>
<td>Outcomes from NCLFUS therapy • 23% of DTI resolved • Significant decrease in size of injury from commencement to completion of therapy (24.6 cm² vs 14.4 cm², p=0.02) • Number of NCLFUS treatments was not correlated with resolution or otherwise of the DTI (p=0.40) • Change in DTI size was not correlated with age (p=0.79), BMI (p=0.30), baseline glucose</td>
<td>No control group – DTIs may have resolved naturally, particularly as there was no correlation between status and number of treatments • Small sample size • Unclear outcome measurement – Level of evidence: 4 Quality: Low</td>
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<tr>
<td>Controls comparing phototherapy (ultraviolet B) for healing pressure injuries</td>
<td>Inclusion: • Bilateral pressure injuries on lower limbs • Stable medication regimen including ciprofloxin • Aged 35 to 55 years</td>
<td>(UVR – B) every, 3 days for 6 weeks with gradual increase in session duration for ¾ to 5 minutes • The right limbs only received the normal wound dressing for 6 weeks</td>
<td>• Mean wound volume measured by lining the wound with foil • Bacterial growth assessed by Likert score (0 being no growth and 5 being very heavy growth)</td>
<td>decrease in the control group (initial = 43.8 cm²; final 27.4 cm², p=not reported) 74.7% decrease in the mean volume of the experimental group (initial = 34.9 ml; final 8.2 ml) versus 46.3% decrease in the control group (initial = 26.1 ml; final 14.0 ml, p=not reported) Significant decrease in the growth of bacteria (X² = 37.01, p&lt;0.00)</td>
<td>therefore had greater opportunity for improvement • Participants received oral ciprofloxacin that confounded results • Volumetric measurements for depth lined the wound with “foil” – not the usual gold standard • Assessed bacteria growth by Likert scoring • Category/Stage of pressure injuries not reported</td>
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</table>
| (Honaker et al., 2016) | Case-control study investigating efficacy of non-contact low frequency ultrasound for deep tissue injury | Participant characteristics:  
- Mean age 71.3±16.3 years  
- 48% females  
- Approx 71% Caucasian  
- Mean BMI 25.5±14.1  
- 27% diabetes  
- Mean Braden scale score 12.1±2.1  
- 93% urine incontinence, 96% fecal incontinence  
- Median length of stay 12.5 days (range 5 to 27) with significantly longer LOS in cohort with hospital acquired DTI, p<0.001 | Treatment group identified prospectively over 3 years (n=30)  
Control group were identified via a retrospective chart review of patients with DTPI in 2008 (n=30)  
Inclusion criteria:  
- Treatment group:  
  o diagnosis of DTPI documented  
  o hemodynamically stable  
  o ability to tolerate lateral laying position  
- Control group:  
  o diagnosis of DTPI documented by WOC nurse at two time points at least 10 days apart (if the DTI was ascribed to a PU at the second time)  
Control group care: (n=30)  
- standard PU repositioning, assistive turning device and application of trypsin-balsam of peru ointment twice daily  
  - silicon border foam dressing  
  - low air loss bed or static overlay if ICU  
  - dietitian consultation | Assessed using Honaker Suspected Deep Tissue Injury Severity Scale (HSDTISS) score that measures wound surface area (range 1–8), skin integrity (range 1–3), and wound/color tissue assessment (range 1–7) | (p=0.76), baseline albumin (p=0.97)  
- For cohort with heel DTI (n=8) there was a significant reduction in size from baseline to cessation of NCLFUS treatment (15.9cm² vs 13.4cm², p=0.045)  
- No heel DTIs fully resolved | who performed it and when was it performed |
|     |               |        |                 |                                        |         |                          |

**Efficacy of treatment**  
- The treatment group had significantly greater change in total surface area compared with control group (mean 0.96 days, range <1 to 5 days) and treatment group (mean 0.93 days, range <1 to 4 days) for timeframe between identification of DTPI to implementation of treatment  
- The treatment group had significantly greater change in mean HSDTISS (mean decrease 2.2 versus mean increase 1.6, p=0.001, r²=0.39)  
- Final category of injury was most commonly unstageable (57%) for

**Level of evidence**: 3  
**Quality**: High
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<tr>
<td>(Honaker, 2013 #896)</td>
<td>Retrospective cohort study comparing NCLFUS for STDIs with standard care</td>
<td>Retrospective record review (n = 43 cases of SDDI treated with NCLFUS and n=42 control STDIs)</td>
<td><strong>Point it met inclusion criteria</strong></td>
<td>5.32 minutes (95% CI 4.83 to 5.83)</td>
<td>the control group and Stage 2 in treatment group (50%)</td>
<td>Time before participant was discharged or a pressure injury stage could be ascribed to the evolving DTPI was longer in control group (average 11.1 days, 95% CI 8.9–13.3 days, p=not reported)</td>
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<td>Long wave-length of kHz has been hypothesized to be more effective for DTPI due to increased deep tissue penetration in comparison to the mHz waveform</td>
<td>Factors identified as predictors of HSDTISS</td>
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<td>• Length of stay (p=0.017, r²=0.10)</td>
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<td>• Treatment/control group (p=0.0001, r²=0.40)</td>
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<td>Factors identified as predictors of DTPI total surface area</td>
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<td>• Hypertension (p=0.02, r²=0.06)</td>
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<td>• Anemia (p=0.04, r²=0.60)</td>
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<td>• Treatment/control group (p=0.014, r²=0.10)</td>
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<td>Development of a new assessment tool to assess SDTI, validity and reliability not reported</td>
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<td>Tool used three scales on which total surface area, skin integrity and wound color were assessed from photos in patient records</td>
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<td>Severity score was assigned based on three scales (score 3-10)</td>
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<td>NC-LFUS group achieved significant reduction in severity score at follow up compared to the control group (t = 5.67, p &lt; 0.000)</td>
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<td>18% of SDTI in NC-LFUS resolved spontaneously versus 2% in control group</td>
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<td>Assessment of wound color using digital photography requires a validated photographic strategy – unclear if this was used.</td>
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<td>Non blinded</td>
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<td>Relies on documentation</td>
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<td>Underpowered study</td>
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</table>

**Limitations and comments**:

- Exposure criteria:
  - Treatment group:
    - Actively dying
    - Scheduled for discharge within 7 days of DTI identification
    - DTI over an electronic implant
    - Malignancy
    - Pregnancy

- Participant characteristics:
  - Mean age approx. 66 years
  - Mean length stay approx. 18 days
  - Approx 40% smokers
  - Approx 50% diabetes
  - Approx 90% anemia
  - Predominantly Caucasian
  - DTPI predominantly located at coccyx, sacrum or buttocks

- **Ref**: Honaker, 2013 #896

- **Type of Study**: Retrospective cohort study comparing NCLFUS for STDIs with standard care

- **Sample**: Retrospective record review (n = 43 cases of SDTI treated with NCLFUS and n=42 control STDIs)

- **Intervention(s)**: NCLFUS delivered with MIST™ Therapy System (Celleration) daily for 5 days then every second day (mean number of treatments = 10)

- **Outcome Measures & Length of Follow-up**: Records were reviewed either cases or controls

- **Results**: All participants received standard pressure ulcer prevention

- **Limitations and comments**: Development of a new assessment tool to assess SDTI, validity and reliability not reported

- **Participants**: Cases had NCLFUS if the SDTI was presumed to be <5 days old

- **Participant characteristics**: Control group had larger wound surface area at baseline but significance was not reported

- **Limitations and comments**: Cases had NCLFUS if the SDTI was presumed to be <5 days old

- **Participant characteristics**: No difference in severity score at baseline (p<0.913)

- **Limitations and comments**: No difference in severity score at baseline (p=0.913)
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<tr>
<td>(Serena, 2009 #895)</td>
<td>Case series exploring NCFLU for Category/Stage III pressure injuries to decrease bioburden and facilitate healing</td>
<td>Participants were recruited from 3 centers (n = 18, n = 11 eligible based on requirement for bioburden)</td>
<td>Twice daily or soft-silicone bordered foam dressing.</td>
<td>18 with higher score = greater severity</td>
<td>Mean reduction in bacterial bioburden from (4 \times 10^7) to (2 \times 10^7), (p) not reported</td>
<td>No analysis by center, No control, No blinding, Small sample size, Unclear how wound size was assessed, No statistical analysis</td>
</tr>
</tbody>
</table>

### High frequency ultrasound

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<td>(Polak, Tarada, et al., 2016)</td>
<td>RCT exploring high voltage pulsed current (ES) plus high frequency ultrasound to</td>
<td>Participants were recruited in residential care and temporary care facilities in Poland (n=90 randomized, n=77 completed and analyzed)</td>
<td>All wounds received debridement at baseline, Noncontact low frequency ultrasound (NC-LFUS) applied for duration based on wound size for three times per week for two weeks (3 minutes for wounds &lt;10cm² and 20 minutes for wounds &gt;170cm²) Treatment administered was a mean of 6 administrations for mean duration of 4 minutes/session</td>
<td>Per-protocol analysis, Wound biopsy at baseline and 2 weeks for wound culture</td>
<td>Mean reduction in bacterial bioburden from (4 \times 10^7) to (2 \times 10^7), (p) not reported, 26% reduction in mean wound area from 13.8cm² to 10.8cm² ((p) not reported), 20% mean wound volume ((p) not reported)</td>
<td>14.4% dropout, Pressure injury rather than individual was the unit of analysis</td>
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| heal pressure injuries | Inclusion criteria:  
• >60 years of age  
• Category/Stage II to IV pressure injuries of 1-50 cm² and 1-12 months duration  
• Exclusion criteria:  
• Cancer  
• electronic implants  
• necrotic or tunneling pressure injuries  
• Osteomyelitis  
• Requiring surgical intervention  
Participant characteristics: The majority of participants were aged over 80 years.  
50% of ES group and about 30% of the other two group had diabetes  
Primarily Category II pressure injuries | o Standard wound care plus electrical stimulation  
(HVMPC, 154 µs, 100 pps, 100 V, 250 µC/sec, 50 minutes/day) (n=30 randomized, n=25 completed) or  
o standard wound care plus high frequency ultrasound  
(1MHz; 0.5 W/cm²; 20%; 1–3 minutes/cm²) (n=30 randomized, n=24 completed)  
o standard wound care  
(n=31 randomized, n=28 completed)  
Treatments were administered once a day, 5 days a week for 6 weeks | • Wound measurements at baseline, week 4 and week 6  
• Did not specify who was assessing wounds if consistent.  
• Did utilize wound evaluation scales to calculate dimensions NPUAP Staging system  
• Follow up 4 to 12 weeks. | • ES group from 7.48±6.20 cm² to 2.65±4.33 cm², p<0.0001  
• control group from 9.31±7.27 cm² to 5.33±4.61 cm², p<0.0001  
• Percent area reduction at 6 weeks was 77.48±11.59% in US group, 76.19±32.83% in ES group and 48.87±53.42% in standard wound care. (p=0.014 between all three, US and ES were not significantly different to each other p=0.99, US was significantly better than control (p=0.024) and ES was significantly better than control p=0.03)  
Complete healing  
• Not significantly different between all three groups US 46.4%, ES 51.7% and standard wound care 22.6% (p=0.79) US was not significantly better than control (p=0.097) and ES was significantly better than control p=0.031) | • No patient blinding,  
• RCT comparing high voltage ES to high frequency ultrasound for healing pressure injuries  
Participants were recruited in a medical clinic Turkey (n=35, 8 excluded due to concurrent medical diagnoses)  
Inclusion criteria:  
• Hospitalized for neurologic rehabilitation.  
• Category/Stage II to IV pressure injury  
Exclusion criteria:  
• Cardiac dysrhythmia or pacemaker, epilepsy, Participants were assigned to either:  
• HVES applied using twin peaked monophasic pulsed current with 100PPS 10-50- 100 us pulse width and 2 second ramp up time in continuous mode. Intensity between 50 and 150 V. 60 minute duration 3x per week x 4-12 weeks (n=25), or  
• High frequency ultrasound at 3 MHz 20% duty cycle and 0.3 W/cm² frequency 1 MHz  
Wound surface area change  
• 43% decrease in wound surface area in HVES group versus 63% WSA decrease in US group  
• Analysis based on Category/Stage and intervention group showed significant improvements in Category/Stage II, III and IV pressure injuries in both treatment groups (baseline compared to follow-up)  
Wound surface area showed significant decrease in HVES group  
• No control group  
• All pressure injuries were Category/Stage IV were in the HVES group which may alter realistic findings  
Level of Evidence: 1  
Quality: Low |
<table>
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<tr>
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</table>
| (Polak et al., 2014) | RCT exploring the use of high-frequency ultrasound (HFUS) as part of a interdisciplinary wound care program in a geriatric population at high risk of pressure injuries | Participants were recruited in four nursing/ and care centers in Poland (n=42) | - Participants were randomized to receive either:  
  - High-frequency ultrasound (HFUS) 5 x weekly for 1-3 minutes/cm²: 1 MHz, 0.5 W/cm²/SATP, Duty cycle 20% for 6 weeks or until healed, (n=20 with n=21 pressure injuries) or | - Change in wound surface area after treatment  
  - % decrease in wound surface area at 6 weeks  
  - Wound healing rate  
  - Average weekly change in wound surface area  
  - % of wounds where wound surface area has reduced by ≥50% at 6 weeks  
  - Wound size measured by a clinician by | - Intervention group had significantly greater change in surface area compared with control group (68.8 ± 37.23 vs 37.24 ± 57.04, p = 0.047)  
- Decrease wound surface area at 6 weeks (cm²)  
  - Intervention group showed a significant improvement in wound surface area from baseline to week 6 (15.38 ± 12.92 cm² versus 6.16 ± 8.26 cm², p = 0.000069)  
- Control group showed non-significant reduction in wound surface area at 6 weeks (11.08 ± | - Small sample size of Category/Stage III pressure injuries  
- Non-blinding of patients  
- Includes data on mechanisms of ultrasound  
- No sham control  
- Care between participants may have varied |
Biophysical Agents: data extraction and appraisals

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<tr>
<td></td>
<td>RCT to evaluate the effect of continuous ultrasound therapy in healing of Category/Stage II and III pressure injuries</td>
<td>Participants were recruited in India (n=30)</td>
<td>Participants were randomized to receive either: o Continuous ultrasound (US) therapy (3 MHz; 0.8W/cm² for 10 min) applied at surrounding wound surface area (n=15), or o Control group: no additional treatment, received saline (0.9%) and sterile gauze dressing</td>
<td>Wound assessment using PUSH tool Digital photographs taken at initial of treatment, end of treatment and 20 days after last treatment session The initial ulcer area was carried out using graph papers to detect the injuries perpendicular linear dimensions</td>
<td>Wound surface area Intervention group had significantly smaller wound surface area following treatment compared to control group (0.124±0.26cm² vs 6.27±5.12cm², p=0.0003) Absolute improvement in wound surface area Intervention group had significantly better absolute improvement in wound surface area following treatment compared to control</td>
<td>• Does not report methods of randomization, allocation concealment • No blinding • Small sample size • Authors measured linear dimensions but reported area</td>
</tr>
<tr>
<td>(Shanmuga, Suryanaryan a Reddy, Venkat, Sachin, &amp; Bhagya, 2017)</td>
<td></td>
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<td>o no additional treatment (n=22 with n=23 pressure injuries)</td>
<td>copying the wound contour onto a transparent sheet and measured using a planimeter, before treatment and at week 6 EPUAP Staging system</td>
<td>/5.2cm² at baseline versus 8.28 ± 8.79 at 6 weeks, p= 0.0062) Wound healing rate % No significant difference between intervention group (38.1%) and control group (11.04 %, p = 0.083) Average weekly change in wound surface area (cm²) No significant difference between intervention group (2.63 ± 2.49cm²) versus control group (1.52 ± 2.02cm², p=0.07) % of wounds where wound surface area has reduced by ≥50% at 6 weeks No significant difference between intervention group (66.67%) and control group ( 43.48%, p=0.14)</td>
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Participant characteristics: • 17 females • age range 71 – 95 • no significant difference in population characteristics between groups

% of wounds where wound surface area has reduced by ≥50% at 6 weeks
No significant difference between intervention group (66.67%) and control group (43.48%, p=0.14)

Author conclusions: High-frequency ultrasound (HFUS) 5 x weekly for 6 weeks reduces surface area more effectively than standard care alone

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Data Tables: 2019 Guideline Update: Biophysical Agents for Treatment or Prevention of Pressure Injuries
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<tr>
<td>{McDiarmid, 1985 #302} RCT comparing high frequency ultrasound to sham therapy for healing Category/Stage I and II pressure injuries</td>
<td>Participants were recruited in three hospitals in UK (n=40)</td>
<td>Participants were randomly assigned to received either: Mental health problems, Metal implants, Malignancy, Radiotherapy in preceding 6 months, Deep vein thrombosis</td>
<td>changed 6 times per week (n=15)</td>
<td>group (9.97±5.34cm² vs 4.05±5.12cm², p=0.0072)</td>
<td>• Less than 50% (n=18) followed to complete healing, n=22 censored due death, discharge or failure to completely heal</td>
<td>Level of Evidence: 1 Quality: moderate</td>
</tr>
<tr>
<td>{McDiarmid, 1985 #302} RCT exploring phototherapy (ultrasound combined with ultraviolet C (UVC) light therapy) for healing pressure injuries</td>
<td>Participants recruited from a SCI center in Canada (n=20 participants with n=22 pressure injuries)</td>
<td>Participants were randomized to one of three groups: Mental health problems, Metal implants, Malignancy</td>
<td>Time to complete healing, Mean percent change in ulcer size</td>
<td>Complete healing</td>
<td>• Category/Stage of pressure injury was not reported</td>
<td>Level of Evidence: 1 Quality: low</td>
</tr>
</tbody>
</table>

**Participant characteristics:**

- Mean age 40-45 years (range 22-66 years)
- Primarily male
- Mean duration of pressure injury 4 months
- Mean size approx. 10cm²
- No differences between groups

**Inclusion criteria:**

- Category/Stage I or II pressure injuries
- Aged > 18 years
- Able to relieve pressure

**Exclusion criteria:**

- Malignancy
- Radiotherapy in preceding 6 months
- Deep vein thrombosis

**Outcome measures & length of follow-up:**

- Transparent film tracing
- Maximum length x maximum width for wound surface area
- No bacteriological investigations
- Pressure injury survival time
- Pressure injuries classified as ‘clean’ or ‘infected’, but the method of classification is not reported and no interrater reliability

**Results:**

- Complete healing
  - No significant difference between ultrasound group (48%) and sham therapy group (42%, p>0.05)
  - Median healing time was 32 days in ultrasound group vs 36 days in sham therapy group (p=0.80)
  - Mean weekly healing rate
    - Overall in the study 36.54%
  - Mean percent change in wound size
    - Mean change was significantly greater I the US/UVC group (53.5%) compared with laser group (23.7%) and control group (32.4%, p=0.032).
    - No adverse events were reported

**Limitations and comments:**

- Level of Evidence: 1
- Quality: moderate

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| {ter Riet, 1996 #413} | RCT investigating high frequency ultrasound for healing pressure injuries | Participants were recruited in 11 nursing homes and a hospital in Netherlands (n=88) | Participants were randomly assigned to received either:  
- Ultrasound at 3.28 MHz, 0.1Wcm² peak intensity, pulse duration of 2ms, pulse repetition frequency 100Hz, for five times per week for 12 weeks. (n=45)  
- Sham ultrasound (n=43)  
- Equipment delivered by a physical therapist |  
- Wound photography on week 1,2,4,6,8,10 and 12  
- Wound surface reduction in cm² at 12 weeks |  
**Complete healing**  
18/45 (40%) of pressure injuries healed in the ultrasound group compared with 19/43 (44%) in the sham group (p=0.61)  
**Surface area reduction**  
There was no significant difference in mean reduction in wound surface area between ultrasound group and sham group (22.91% vs 13.82%, p=0.10, adjusted difference 8.27%, 95% CI -2.31% to 18.85%)  
**Healing rate**  
There was no significant difference in mean healing rate between ultrasound group and sham group (0.18cm vs 0.13cm, p=0.18, adjusted difference 0.05cm, 95% CI -0.04 to 0.13) |  
- ITT analysis  
- Blinded outcome assessment  
- The study also investigated effect of vitamin C  
- ITT analysis reported here, Per protocol analysis was also not significant |  
- 20% withdrew from study and were not analyzed |

### Clinical question 6: Negative pressure wound therapy (NPWT)

| (Srivastava et al., 2014) | Controlled trial to compare pressure injury healing with | Participants were recruited in a trauma center in India (n=48) | All pressure injuries cleaned and packed with saline gauze, with dressings twice daily | Wound surface area, depth and tissue type (slough to red granulation tissue) | Change wound condition at week 3  
In intervention group, wound bed slough converted to granulation tissue in 33.3% pressure injuries | Unclear who performed wound assessment | Level of Evidence: 2  
Quality: high |

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## Biophysical Agents: data extraction and appraisals

| Ref | Type of Study                                                                 | Sample                                                                                                                                                                                                 | Intervention(s)                                                                                                                                                                                                 | Outcome Measures & Length of Follow-up                                                                 | Results                                                                                                                                                                                                 | Limitations and comments                                                                 |
|-----|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     | conventional dressing and with negative pressure                              | • Traumatic paraplegia  
• Age 16-60 years  
• Category/Stages 3-4 pressure injury (according to NPUAP scale)                                                                 | • Participants in intervention group received NPWT for 9 weeks (mean pressure -80 mmHg (range -60 to -120 mmHg)                                                                 | • Evaluated weeks 0, 3, 6 and 9  
• Pathologic organisms evaluated at week 0 and week 9  
• Greatest length and width measured and surface area estimated  
• Ulcer depth measured with cotton-tipped applicator  
• Exudate – subjective evaluation  
• Necrotic tissue, slough and granulation tissue were assessed by visual inspection at dressing changes. (p=0.0001) compared with no change in the control group.  
Change wound condition at week 6  
In intervention group, wound bed slough converted to granulation tissue in 73.8% pressure injuries (p=0.0001), and in 37.5% pressure injuries in the control group (p=0.0001).  
Change wound condition at week 9  
In the intervention group, slough converted to granulation tissue in 100% pressure injuries, while it was still present in 41.7% control group  
Infection status  
In week 0, 100% of pressure injuries in both groups had positive cultures for pathogenic organisms  
In week 9, 100% of the intervention group had no pathogenic organisms (p=0.0001) but 41.6% (p>0.05) had positive cultures in control group  
Ulcer size and depth  
Ulcer size and depth decreased significantly (p=0.0001) from week 0 to weeks 3, 6, and 9 in intervention group but there were no statistically significant differences for surface area or depth in the control group (p>0.05)  
Cost  
The total cost of a 9-week treatment of one PU was approximately 46% less than the costs of conventionally treated comparable ulcer. | • Subjective evaluations used without reporting interrater reliability  
• This procedure was ineffective in low sacral ulcers in which the ulcer involves the area close to the natal cleft because the adhesive dressing could not be properly applied to obtain an airtight seal.  
• Sterile foam used in the negative pressure apparatus has a tendency to disintegrate and make the secretion viscous |
### Biophysical Agents: data extraction and appraisals

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<tr>
<td>(Fulco, Erba, Valeri, Vournakis, &amp; Schaefer, 2015)</td>
<td>Pilot RCT exploring the use of poly-N-acetyl glucosamine nanofibers (sNAG) as a hemostatic agent used in conjunction with NPWT</td>
<td>Participants were undergoing ischial or sacral PU repair flap surgery at a center in Switzerland (n=26)</td>
<td>All participants had surgical wound debridement (until wound bed bleading). NPWT for 2 weeks then flap repair. Bleeding was controlled with light compression and bipolar coagulation. NPWT applied on day 2 with participants (who were not treated with antiplatelet therapy) were randomized to either: NPWT alone (n=10) NPWT with sNAG (n=10)</td>
<td>Wound base area and wound surface area measured using digital planimetry, Mean wound epithelization assessed by digital planimetry, Granulation tissue measurements performed on histological wound cross sections, Bleeding assessed by % of dressing covered in blood at day one</td>
<td>Mean wound area: superior reduction in sNAG-NPWT group versus NPWT group (second group tended to have increase in wound area), p&lt;0.05</td>
<td>Small sample size, uncertain if this study is adequately powered, Patient inclusion criteria is not defined</td>
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<td>Participants were all in the control group</td>
<td>A control group continued antiplatelet therapy with sNAG with NPWT (n=6)</td>
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<td></td>
<td></td>
<td>No significant difference in wound base area at baseline</td>
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<td></td>
<td>No significant differences between three groups on serum albumin, zinc, lymphocyte count, BMI, diabetes or CV disease</td>
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<tr>
<td>(Dwivedi et al., 2017; Dwivedi et al., 2016)</td>
<td>RCT exploring the effectiveness of negative pressure devices compared to standard wound dressings for promoting PU closure in SCI unit in a hospital in India (n=65 screened, n=60 randomized, n=16 withdrew, n=44 analyzed)</td>
<td>Participants were recruited in SCI unit in a hospital in India (n=65 screened, n=60 randomized, n=16 withdrew, n=44 analyzed)</td>
<td>Pressure ulcers were debrided prior to randomization. Participants were randomized to receive either: Standard care consisting of normal saline and sterile gauze packing changed 1-2 times daily (n=30 allocated, n=23 analyzed) or</td>
<td>Measurement using ruler at greatest length and width and cotton tip measurement of depth; PUSH tool; clinical photography; Assessment conducted weekly; Patients followed until on closure of wound or</td>
<td>Pressure ulcer length: No significant difference week 2-6 NPWT group had significantly shorter length in week 7 (p=0.04), week 8 (p=0.005) and week 9 (p=0.001)</td>
<td>Power calculation conducted but required population not explicitly stated, Appears to be non-blinded, Withdrawals were not</td>
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|     | individuals with paraplegia. | Exclusion criteria:  
• Necrotic tissue incompatible with debridement  
• Chronic osteomyelitis  
• Exposed blood vessels or nerves  
• Diabetes mellitus, rheumatoid disease, vasculitis, neuropathy, chemo or radiation therapy  
• Braden scale assessment indicating poor nutrition  
• Serum albumin <2.5g/L or hemoglobin <9.0g/L  
Participant characteristics:  
• Mean age 32.52 to 38.30 (standard care group significantly younger, p<0.05)  
• >80% male  
• Standard care group had significantly more stage III PU (56.5% versus 19.0%) and significantly less stage IV PU (53.5% vs 81%), p<0.01 | NPWT: using a sterile foam and transparent film dressing changed weekly (n=30 allocated, n=21 analyzed) until trial completion 9 weeks  
• Cost effectiveness (consumables) calculated on a daily basis based on two representative PUs from each group and multiplied for number of days to achieve granulation | • NPWT group had significantly shorter length in week 6 (p=0.01), week 8 (p=0.02) and week 9 (p=0.006)  
Pressure ulcer depth  
• Standard care group significant improvement compared to NPWT group in week 1 (p=0.001), week 2 (p=0.003) and week 3 (p=0.02)  
• NPWT significantly better than standard care group at week 9 (p=0.01)  
Other characteristics  
• NPWT group had significant better exudate scores using PUSH for weeks 3-9 (p=0.001 for all)  
• NPWT group had significantly less discharge (mls ) for weeks 2-6 (p=0.001 for all) and no discharge in weeks 7-9  
• NPWT group had significant better tissue type scores using PUSH for weeks 4-9 (p=0.001 for all)  
MMP-8 levels  
By week 3, levels were significantly lower in the NPWT group (p =0.46 at week 3, p=0.006 at week 6 and p<0.001 at week 9)  
Wound dimensions  
• By week 6, the difference between groups in length was significant (p=0.04) favoring NPWT, which continued at week 9 (p=0.001)  
• By week 9, NPWT group had 79.7% reduction vs dressing group 54.7% reduction | included in analysis  
• Groups were not similar with respect to PU stage at baseline but there was no significant difference in length, width or depth at baseline  
• No reason given for withdrawals  
• Cost only included dressing materials  
• Note: Both trials report the same study (same results week 0 and 8, same ethics number) but the participants in groups are slightly different  
• Methods of randomization and allocation concealment not reported  
• Approx 30% of participants were withdrawn for various reasons including deteriorating wound, no ITT analysis |
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<tr>
<td>(Wild, 2008 #472)</td>
<td>RCT</td>
<td>Recruited from nursing home, n=10</td>
<td>NPWT with either: &lt;br&gt;• V.A.C.® system (n=5) with dressings changed x3 weekly &lt;br&gt;• Redon surgical drain bottles (n=5) delivering pressure between –900mmHg and 0mmHg, but pressure level is uncontrolled. Dressings changed as required.</td>
<td>• Absolute and relative proportion of wound area consisting of granulation tissue, fibrin and necrosis assessed by an independent observer using Wound Healing Analysing Tool (WHAT) &lt;br&gt;• Frequency of dressing change</td>
<td>• Width became significant favoring NPWT group by week 9 (81.7% reduction vs 59.5% reduction, p=0.006 for cm reduction) &lt;br&gt;• Depth became significant favoring NPWT group by week 9 (89.4% reduction vs 78.1% reduction, p=0.01 for cm reduction)</td>
<td>• 10 participants withdrawn from NPWT group due to deterioration of wound/infection, or inability to maintain seal &lt;br&gt;• Randomization, allocation concealment and blinding not reported</td>
</tr>
</tbody>
</table>

### Wound condition
- Conversion of slough into red granulation was significantly higher in NPWT after week 6.  
- Exudate was significantly lower in NPWT group after week 3.

### Cost
- 9 week treatment cost was US$105 for NPWT and US$200 for standard care group

### Author conclusions:
NPWT is a reasonable treatment for promoting closure of stage IV PU and is cost effective in low resource setting. The treatment was not effective in low sacral ulcers due to inability to apply dressing to create an airtight seal. Sterile foam can block the drain.

- Unable to recruit sufficient participants to meet a priori power calculation  
- Study ceased early  
- Ethics not obtained (states not required in country research performed)

### Level of evidence: 1  
Quality: low
### Data Tables: 2019 Guideline Update: Biophysical Agents for Treatment or Prevention of Pressure Injuries

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<td>(de Laat, 2011 #459)</td>
<td>Prospective RCT (Nb: the RCT included two study arms – PUs and surgical wounds. Only data from PUs included in evidence table)</td>
<td>n= 12 patients with 16 PUs</td>
<td>All wounds debrided, all SCI patients managed in hospital. Random assignment to either: • Patients were assigned to either treatment with NPWT using V.A.C.® system (n=6 patients with 9 PUs) : foam dressing changed x3 weekly • sodium hypochlorite wound dressings (n=6 patients with 7 PUs): wet to moist dressings changed x3 daily</td>
<td>Mean follow-up of 8.5 days</td>
<td>• Mean change in necrotic tissue favoured V.A.C.® system but there was no statistically significant differences (p=0.598)</td>
<td>Redon system: • Seal checked two hourly • Bottles reapplied when vacuum insufficient • Bottles changed up to 10 times daily • Leakage and suction of stool • Complaints of pain from participants</td>
</tr>
<tr>
<td>(Wallin, 2011 #468)</td>
<td>Retrospective record analysis (Nb: Included patients with wounds of other aetiology. Only Consecutive selection of patients treated with NPWT in one general hospital between 2005 to 2007. n=14 patients with PUs)</td>
<td>NPWT using VAC® device with continuous sub atmospheric pressure of 125 mm Hg. Dressings changed x2 to 3 weekly or more frequently depending on exudate</td>
<td>Patient demographic Comorbidities Clinical infection Wound complications Treatment outcome: • successful: wound much improved and/or • 86% wounds treated with NPWT had positive wound swab, primarily E.Coli, Pseudomonas, Streptococci, Enterococci and Bacteroides • 50% (n=7) cases classified as successful</td>
<td>Only 14 PUs reached 50% healing within 6 weeks. Median treatment time to 50% reduction of wound volume: NPWT group 2.0 weeks (interquartile range [IQR]=1 to 2) versus sodium hypochlorite group 3.0 weeks (IQR = 3 to 4, p=0.001) Unadjusted hazard rate ratio (HRR) 0.188 (p=0.014) and HRR adjusted for baseline wound volume and smoking status was 0.833 (p=0.021) Complications associated with NPWT included clinical infection (2 wound) and 1 patient had an arterial bleed requiring surgical repair.</td>
<td>• Used wound as a point of analysis rather than patient • Used non-conventional comparative treatment that may favour NPWT • Excluded patients who did not reach 50% healing within 6 weeks from analysis</td>
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**Level of evidence: 1**

**Quality: moderate**

**Level of evidence: 3**

**Quality: moderate**
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<tr>
<td>data from PUs included in evidence table</td>
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<tr>
<td>(Ho, 2010 #465)</td>
<td>Observational study</td>
<td>Participants (n=86) with SCI recruited from 10 Veterans Affairs medical centres</td>
<td>All patients received low air loss mattress, regular turning, wound debridement, hydrotherapy, routine wound cleansing and dressing changes. At discretion of physician patients received either: NPWT (n=33) or standard wound care alone (n=53)</td>
<td>left to heal by secondary granulation; wound healed; wound bed improved and skin graft performed, unsuccessful: wound not improved, wound bed larger or worse, treatment discontinued due to complications. Follow up ranged from 24 to 48 months.</td>
<td>• Median treatment time was not significantly different (p=0.48) between cases that were successful (median 28 days ± 71 days, range 8 to 210) and those that were unsuccessful (median 23 days ± 23 days, range 4 to 75) • Patients with infectious, postoperative, and traumatic wounds had greater treatment success than those with PU (p=0.001). • In the full sample (n=87) there were complications in 10 patients including infection (n=5), breakdown of surrounding skin (n=3) and hemotoma (n=2).</td>
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| Level of evidence: 4 |
| Quality: low |

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<th>Quality:</th>
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| {Joseph, 2000 #247} | RCT comparing NPWT with standard therapy for chronic non-healing wounds     | Participants were recruited in a medical center in USA (n=24 participants with n=36 pressure injuries)                                                                 | • Sharp debridement of necrotic tissue before application of treatment  
• Participants were randomized to receive either:  
  o NPWT with open cell foam dressing and controlled atmospheric pressure, with dressing changed every two days (n= ) or,  
  o Standard wound care (saline gauze dressings changed three times daily)                                                                 | • Wound photography  
• Alginate impression molds to measure wound volume  
• Six week follow-up                                                                 | Wound dimensions                                                                 | NPWT was associated with greater reduction in wound depth (68% versus 20%, p=0.00001)  
NPWT was associated with greater reduction in wound width (62% versus 35%, p=0.02)  
NPWT was associated with greater reduction in wound volume (48% versus 39%, p=0.038)  
No significant between group differences in wound length (NPWT 46% reduction, standard care 38% reduction, p=0.38)  
Adverse events  
  • Osteomyelitis occurred in one case  
  • Calcaneal fractures occurred in two cases when patients ambulated against advice  
  • Standard wound management was related to 2 fistulas, 6 wound infections and 2 cases of osteomyelitis  
  • Rate adverse events was 44% in standard care vs 17% in NPWT)                                                                                                                     | • Unit of analysis was pressure injury, not participant  
• Reported methods of randomization and allocation concealment  
• Blinded outcome assessment                                                                                     | 1     | High                     |
| {Isago, 2003 #237}  | Cohort study evaluating response to NPWT                                      | Participants were bedridden medical patients recruited in Japan (n=10)                                                                              | Participants received treatment with a V.A.C.™ system using polyurethane foam  
Wounds debrided prior to treatment  
Pressure at 125mmHg, continuous for 48 hours then intermittent  
Second daily dressings                                                                                           | Wound length x width and depth  
Weekly wound assessment  
Surface area of wound calculation  
Bloods – white blood cells, CRP, Sodium, potassium and calcium                                                                 | Wound dimensions                                                                 | NPWT was associated with greater reduction in wound surface area over time after one week of treatment (mean reduction 55.1% by seven weeks p<0.05)  
NPWT was associated with greater reduction in wound depth after two weeks of                                                                                     | Does not report recruitment strategy  
• Minimal information on participant characteristics  
• Unclear wound severity  
• No comparator                                                                                                       | 3     | Low                      |
### Biophysical Agents: data extraction and appraisals

<table>
<thead>
<tr>
<th>Ref</th>
<th>Type of Study</th>
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<th>Outcome Measures &amp; Length of Follow-up</th>
<th>Results</th>
<th>Limitations and comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>{Deva, 2000 #148}</td>
<td>Case series exploring NPWT for Category/Stage III and greater pressure injuries</td>
<td>Participants were recruited in a plastics unit (n=30)  &lt;br&gt; Inclusion criteria: Category/Stage III and greater pressure injuries  &lt;br&gt; Participant characteristics: Mean age 50.7 years 50% had SCI and the rest were immobilized from other causes  &lt;br&gt; Mean duration of pressure injuries was 418 days (range 8 to 1650)</td>
<td>Some pressure injuries surgically debrided  &lt;br&gt; Participants received NPWT using V.A.C. device with suction at 75-125mmHg continuous for first 48 hours and thereafter intermittent</td>
<td>Complete wound healing  &lt;br&gt; Reduction in wound cavity  &lt;br&gt; Closure by skin graft or suture  &lt;br&gt; Wound photography  &lt;br&gt; Wound volume estimated based on volume of foam dressing  &lt;br&gt; Follow up for 3 months</td>
<td>• NPWT was successful for 87% of pressure injuries  &lt;br&gt; • Mean time to healing was 35 days (range 8 to 124)</td>
<td>• Unclear how representative these cases are  &lt;br&gt; • Minimal data on wound size and how success was evaluated</td>
</tr>
<tr>
<td>{Wanner, 2003 #915}</td>
<td>Quasi experiment comparing NPWT to wet-to-dry/wet-to-wet dressings</td>
<td>People with SCI (n=22) with Category/Stage II or deeper pressure injuries  &lt;br&gt; Mean size larger in NPWT at baseline</td>
<td>Surgical debridement  &lt;br&gt; Participants received treatment with either: V.A.C.™ system with a foam dressing at ~125 mmHg with dressings change every 2-7 days (n=11)  &lt;br&gt; wet-to-dry or wet-to-wet dressings with Ringer's solution (n=11)</td>
<td>Endpoint was 50% reduction in size in preparation for flap surgery</td>
<td>• Time to reach 50% reduction in size was not significantly different (27 days VAC vs 28 days control)  &lt;br&gt; • Reducing frequency of dressings decreases pain</td>
<td></td>
</tr>
</tbody>
</table>

### Clinical question 7 kinetic energy

#### Pulsatile lavage

<table>
<thead>
<tr>
<th>Ref</th>
<th>Type of Study</th>
<th>Sample</th>
<th>Intervention(s)</th>
<th>Outcome Measures &amp; Length of Follow-up</th>
<th>Results</th>
<th>Limitations and comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>{Ho, 2012 #488}</td>
<td>Double blind prospective RCT</td>
<td>Participants recruited from an inpatient facility (n=28)  &lt;br&gt; Inclusion:  &lt;br&gt; • aged &gt; 18 yrs with SCI  &lt;br&gt; • stage III and IV pelvic PUs, presenting as clean with no</td>
<td>All participants received standard care according to clinical guidelines. Participants were randomised to receive either:  &lt;br&gt; • Daily low-pulsatile lavage treatment with 1 litre of normal saline at 11 psi</td>
<td>• Length, width and depth of PU obtained weekly for 3 weeks  &lt;br&gt; • PU depth using saline injection method</td>
<td>• Random-coefficient models for analysis of linear and volume measurements revealed improvements over time for both groups  &lt;br&gt; • Small number of participants and underpowered  &lt;br&gt; • Strict exclusion criteria excluded 221 participants</td>
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<tr>
<td>Ref</td>
<td>Type of Study</td>
<td>Sample</td>
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<td></td>
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<td>Odor, necrosis, minimal exudate, no tunnelling or fistula, no cellulitis, no erythema of surrounding tissue</td>
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<td></td>
<td></td>
<td>PU maximum diameter of 3 to 15cm at baseline</td>
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<td></td>
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<td>No antibiotics within preceding 7 days</td>
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<td></td>
<td></td>
<td>No malignancy or vascular disease associated with PU</td>
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<tr>
<td></td>
<td></td>
<td>No diabetes, heart disease or renal failure</td>
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<td></td>
<td>Characteristics:</td>
<td></td>
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<tr>
<td></td>
<td>• Primarily ischial PUs</td>
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<tr>
<td></td>
<td>• No significant demographic differences</td>
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<td></td>
<td>• Mean age 55 to 57 years</td>
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<tr>
<td></td>
<td>Intervention(s)</td>
<td>Applied over 10 to 20 mins using a device designed for the procedure (n=14) or</td>
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<td></td>
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<td>Sham treatment in which no lavage was administered directly to the PU but participants were given the impression it had been (n=14)</td>
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<td></td>
<td></td>
<td>Dressings were removed before the commencement of treatment and replaced at the completion of treatment</td>
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<tr>
<td></td>
<td>Outcome Measures &amp; Length of Follow-up</td>
<td>PU healing rate over the 3-week study period</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Results</td>
<td>Time trend analysis revealed greater measurement decreases for the treatment groups</td>
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<tr>
<td></td>
<td>Limitations and comments</td>
<td>Differences in rates of change over time (95% CI) for treatment and control groups respectively (p&lt;0.001):</td>
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<tr>
<td></td>
<td></td>
<td>o Depth: −0.24 (0.09 to −0.58) cm/wk</td>
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<tr>
<td></td>
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<td>o Width: −0.16 (0.06 to −0.39) cm/wk</td>
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<tr>
<td></td>
<td></td>
<td>o Length: −0.47 (0.18 to −1.12) cm/wk</td>
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<tr>
<td></td>
<td></td>
<td>o Volume: −0.33 (0.13 to −0.80) cm^3/wk</td>
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<tr>
<td></td>
<td></td>
<td>All 95% CIs span the null value, decreasing confidence in the significance of the results.</td>
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</tbody>
</table>

**Whirlpool**

(Burke, 1998 #106)

RCT comparing whirlpool to standard wound care for healing Category/Stage III to IV pressure injuries

Participants were recruited in a veteran’s hospital in USA (n=18 participants with n=42 pressure injuries)

Inclusion criteria: Category/Stage III to IV pressure injuries

Exclusion criteria: Wound not followed for at least 2 weeks Coexisting medical conditions precluding whirlpool Clinical infection of the wound

- Whirlpool at 96 to 98°F with no jet stream directly position to a pressure injury for 20 minutes daily plus dressings as per the control group (n=24), or

- Control group: Irrigation with saline, wet-to-wet saline dressings changed twice daily (n=18)

- Follow-up for two weeks

- Ulcer dimensions over time

- Wound healing rates

- Whirlpool was associated with superior healing based cm/week (p=0.0435)

- No adverse effects were reported

- All 95% CIs span the null value, decreasing confidence in the significance of the results.

**Vibration therapy**

Data Tables: 2019 Guideline Update: Biophysical Agents for Treatment or Prevention of Pressure Injuries © EPUAP/NPIAP/PPPIA
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<tbody>
<tr>
<td>(Arashi, 2010 #456) Non-randomised blinded trial investigating vibration for accelerating PU healing</td>
<td>Participants recruited from a hospital facility. (n=31 participants with 41 PUs)</td>
<td>All participants received standard care according to the PU care guidelines.</td>
<td>More PUs in experimental group healed compared to control group (40% versus 9.5%, p=0.033)</td>
<td>• More PUs in experimental group healed compared to control group (40% versus 9.5%, p=0.033)</td>
<td>• Non blinded, non randomised study</td>
<td>Level of Evidence: 2 Quality: moderate</td>
</tr>
</tbody>
</table>

**Clinical question 8: Atmospheric**

**Topical oxygen therapy**

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>(Azimian, Nayeri, Pourkhaleghi, &amp; Ansari, 2015) Single blinded RCT investigating effectiveness of TWOT on healing PUs.</td>
<td>Convenience sample of participants recruited from two intensive care units in Iran (n=100)</td>
<td>All participants received routine care at the study site (not described).</td>
<td>Complete healing (complete epithelialization)</td>
<td>• Routine care was not reported but may have consisted of gauze dressings.</td>
<td>Level of Evidence: 1 Quality: Moderate</td>
<td></td>
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</tbody>
</table>

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# Biophysical Agents: data extraction and appraisals

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<tbody>
<tr>
<td></td>
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<td>• Category/stage II to IV PU Sacral or ischial PU</td>
<td>o direct application via a disposable of humidified high pressure oxygen (10L/min) to the wound site for 20 minutes, three times a day for 12 days. Oxygen was delivered using a disposable catheter.</td>
<td>• Experimental group had greater healing evident at every observation time point compared with control but the difference was only significant from day 6.</td>
<td>there was high interrater correlation between the two assessors</td>
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<td></td>
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<td>Exclusion criteria:</td>
<td>o Saline soaked gauze dressings changed every shift. (n=50)</td>
<td>• Experimental group showed significant reduction (p=0.001) in wound area from baseline to day 12.</td>
<td>3 participants dropped out but reason not stated (included in analysis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Peripheral vascular disease, diabetes</td>
<td></td>
<td>• Control group had no significant change in wound area from baseline to day 12 (p=0.16)</td>
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<td></td>
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<td>Participant characteristics:</td>
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<td></td>
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<td></td>
<td>• Mean age 69 to 70 years</td>
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<td></td>
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<td></td>
<td>• Mean wound area 28 to 32 cm²</td>
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<td>• Approx. half of PUs were Category II and the rest category III or IV</td>
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<td></td>
<td>• No significant differences between groups on age, gender, previous cerebrovascular disease, level of consciousness, mobility, baseline wound state or wound size.</td>
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<td></td>
<td>Hyperbaric oxygen therapy (at 3 atmospheres of pressurized air), 2 hours per day, 5 days per week plus standard wound care (n=18, n=38 pressure injuries)</td>
<td>Complete healing 58% of pressure injuries completely healed</td>
<td>No randomization and unclear method of group assignment</td>
</tr>
<tr>
<td></td>
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<td>Standard wound care only (cleansing, frequent dressing changes and mechanical debridement) (n=3, n=6 pressure injuries)</td>
<td>Reduction in wound surface area 13% of pressure injuries had a 50% or greater reduction in size</td>
<td>Poor comparative analysis</td>
</tr>
<tr>
<td></td>
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<td>Average 37 treatments</td>
<td>Control group did not have reduction in wound size</td>
<td>Unclear severity of pressure injuries</td>
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<td></td>
<td>Limited information about participants</td>
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<td></td>
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<td></td>
<td></td>
<td>*LTAPP has several active</td>
<td>Atmosphere plasma</td>
<td>Level of Evidence: 1</td>
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<td></td>
<td></td>
<td>Quality: Low</td>
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</table>

## Hyperbaric oxygen

{Rosenthal, 1971 #367} Comparative study exploring hyperbaric oxygen therapy for pressure injuries

Participates were recruited in unknown facility (n=21 participants)  
Inclusion criteria:  
Not stated  
Participant characteristics:  
Age range 15 to 67 years  
Primarily had SCI  

- Hyperbaric oxygen therapy (at 3 atmospheres of pressurized air), 2 hours per day, 5 days per week plus standard wound care (n=18, n=38 pressure injuries)  
- Standard wound care only (cleansing, frequent dressing changes and mechanical debridement) (n=3, n=6 pressure injuries)  
- Average 37 treatments  

Wound diameter and width  
Complete healing 58% of pressure injuries completely healed  
Reduction in wound surface area 13% of pressure injuries had a 50% or greater reduction in size  
Control group did not have reduction in wound size  

- No randomization and unclear method of group assignment  
- Poor comparative analysis  
- Unclear severity of pressure injuries  
- Limited information about participants  

## Level of Evidence: 3  
Quality: Low

## Atmospheric plasma

{Chuangsuwanich, RCT exploring low-temperature} Participants recruited in plastic surgery unit in Thailand

Regimen for intervention group:  
- Wound exudate and size by wound  
- Wound size reduction  
- Intervention 88.5% vs control 52.2%  
- "LTAPP has several active..."  

Level of Evidence: 1
## Biophysical Agents: data extraction and appraisals

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<th>Quality:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assadamongkol, T., Boonyawan, D. (2016)</td>
<td>atmospheric-pressure plasma</td>
<td>(n=50 RANDOMIZED, N=42 COMPLETED)</td>
<td>Standard wound care (debridement, proper wound dressing) plus unipolar low – temperature atmospheric-pressure plasma delivered using one using argon as the gas medium with direct noncontact short distance plasma, 2- to 3-mm micro beam to wound surface. Therapy administered weekly after wound dressing (N=23) Regimen for control/comparison group: Standard wound care (debridement, proper wound dressing) (N=19)</td>
<td>specialist nurse, weekly • Bacterial load by tissue culture weekly • Wound healing score PUSH Tool 3.0 • VISITRAK device for wound size • NPUAP staging guidelines, 2007 • Follow up period 8 weeks</td>
<td>P &lt; 0.001 <strong>Exudate reduction</strong> Intervention 80.8% vs control 30.4% P &lt; 0.001 <strong>Number of wounds with less bacterial load (%) week 8</strong> Intervention 88.5% Control 82.7% P=0.002 <strong>PUSH score improvement week 8</strong> Intervention 96.2% VERSUS Control 52.2% P&lt;.001 No side effects were reported <strong>Author conclusions:</strong> LTAPP group had significantly better wound healing than the control group</td>
<td>components, including charged particles, metastable-state molecules or atoms, ultraviolet ray, and reactive species, which are free radicals and some ground state molecules of oxygen such as ozone and peroxides.” • Assessing nurse blinded to treatment arm. • LTAPP is dose dependent and may vary depending on manufacturer.</td>
<td>High</td>
</tr>
</tbody>
</table>

Full references in direct and indirect evidence tables


Biophysical Agents: data extraction and appraisals


