Treating intractable postamputation pain with wearable, non-invasive, non-thermal, pulsed shortwave (radiofrequency) therapy: a randomized, double-masked, sham-controlled, crossover pilot study

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INTRODUCTION
Pulsed shortwave (radiofrequency) therapy (PSWT) is a non-invasive, non-pharmacologic analgesic used for over 7 decades. The mechanism of action involves multiple factors and is only partially understood. Over-the-counter, lightweight, battery-operated, single-use, wearable devices that are cleared by the US Food and Drug Administration have minimal medical risks and no systemic side effects.

One uncontrolled series suggests that PSWT may decrease postamputation pain. Consequently, we conducted a pilot study to investigate the use of non-thermal PSWT for postamputation pain. We aimed to better inform the planning of a subsequent definitive trial by (1) determining the feasibility of and optimizing a study protocol; and (2) estimating the treatment effect of 4 weeks of PSWT on postamputation phantom and residual limb pain.

METHODS
This study was prospectively registered at clinicaltrials.gov (NCT05392803) and approved by the local institutional review board.

Adult patients with a lower limb amputation distal to the hip that occurred at least 12 weeks prior to enrollment were offered enrollment. They had to experience phantom and/or residual limb pain of 3 or higher on a Numeric Rating Scale (NRS) at least daily for the previous 2 months. Exclusion criteria were an implanted pulse generator, pregnancy, and incarceration.

Following written, informed consent, two devices (Model 088, BioElectronics Corporation, Frederick, Maryland, USA; see figure in online supplemental eAppendix)—both with the same randomization (active or sham in a double-masked fashion)—were sent to each participant through the postal service (1000 pulses per second, pulsed width 100 microseconds, peak spatial power density of 73 microwatts/
The patients self-applied the devices to their residual limb (figure 1) and held their normal analgesic regimen unchanged for 70 days. After 28 days, the participants removed the initial two devices and were provided two crossover devices of the alternative treatment group (active or sham) to be applied on day 35.

A convenience sample was used, and standard descriptive statistics summarized the treatment effect.

**RESULTS**

Twenty-three participants were enrolled and randomized, with 14 electing to continue (table 1, figure 1). After 28 days, in participants who received active treatment (n=7), phantom pain intensity decreased by a median (IQR) of 2.0 (0, 5.5) vs 0 (−0.3, 0) in patients given sham (n=7); and

<table>
<thead>
<tr>
<th>Initial treatment</th>
<th>Active (n=7)</th>
<th>Sham (placebo) (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57 (14)</td>
<td>61 (22)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>57% (4)</td>
<td>29% (2)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>180 (9)</td>
<td>172 (9)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>84 (21)</td>
<td>68 (18)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26 (6)</td>
<td>23 (4)</td>
</tr>
<tr>
<td>Lower extremity amputation</td>
<td>100% (7)</td>
<td>100% (7)</td>
</tr>
<tr>
<td>Trans-femoral</td>
<td>43% (3)</td>
<td>100% (7)</td>
</tr>
<tr>
<td>Trans-tibial</td>
<td>57% (4)</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Continuous phantom limb pain at baseline</td>
<td>73% (8)</td>
<td>71% (5)</td>
</tr>
<tr>
<td>Continuous residual limb pain at baseline</td>
<td>7% (1)</td>
<td>7% (1)</td>
</tr>
</tbody>
</table>

Values are reported as mean (SD) or percentage (number of subjects).

Figure 2  Effects of 28 days of non-thermal pulsed shortwave therapy on postamputation residual and phantom limb pain. Pain severity was measured using a Numeric Rating Scale, with 0 being no pain and 10 being the worst imaginable pain. The participants’ overall perception of the change in pain was measured with the Patient Global Impression of Change which is a 7-point ordinal scale requiring the participant to rate the current intensity of residual limb pain compared with their pre-treatment baseline: 1 for ‘very much worse’ to 7 for ‘very much improved’ (4 is ‘no change’). Data expressed as median (dark horizontal bars) with 25th–75th (box), 10th–90th (whiskers), mean (diamonds), and outliers (circles). Statistics were not applied to the data due to the relatively small sample size.
for residual limb pain: 2.5 (0, 5.3) for active vs 0 (−0.5, 0) for sham. At 28 days, the participants who received active treatment reported a Patient Global Impression of Change for their phantom pain of 6.0 (4.0, 7.0) vs 4.0 (4.0, 4.0) for sham; and for residual limb pain of 5.5 (4.0, 7.0) for active vs 4.0 (4.0, 4.0) for sham.

The remainder of the results include the five participants who received active treatment on their crossover for a total of 12 active participants (figure 1). By day 7, the participants who received active treatment experienced a decrease in residual and phantom limb pain intensity as well as Patient Global Impression of Change which continued through day 28 (figure 2). The participants who received active treatment had less physical and emotional interference at the end of the treatment period on day 28 with a median (IQR) Brief Pain Inventory (interference scale 0–70, lower=better) of 13 (0, 34) vs 22 (17, 23) for the sham group.

No device-related side effects or other adverse events were identified.

DISCUSSION

This pilot study provides information to guide the accurate planning of a definitive clinical trial. Patients receiving active treatment demonstrated improvements in both phantom and residual limb pain for the duration of treatment. Additionally, we identified the conduct of the study would be feasible given participants’ adherence to the study protocol and success of the data collection instruments at the designated time points. We conclude that further study is warranted given that we identified a beneficial treatment effect in the setting of a low cost and low-risk intervention.

Trial registration number

NCT05392803 (principal investigator: Brian M. Ilfeld, MD, MS; initial posting: May 16, 2022).

Contributors

BM helped conceive the study, wrote the protocol, acquired the required study devices, implemented the investigation, oversaw data collection, interpreted the results, and wrote the initial draft of the manuscript. BJC and ANQ contributed to data management, manuscript preparation, and manuscript revision. JJF and ETS contributed to protocol design and manuscript revision. BA contributed to protocol design, protocol implementation, data collection and management, and manuscript revision.

Funding

Funding for this project was provided by the University California San Diego Department of Anesthesiology (San Diego, California, USA). The contents of this article are solely the responsibility of the authors and do not necessarily represent the official views of the funding entity. None of the authors has a personal financial interest in this research.

Competing interests

BMI, IJF, ETS, and BA: The University of California San Diego has received funding and/or product from the following companies for other research studies of these authors: Epimed International (Dallas, Texas, USA), SPR Therapeutics (Cleveland, Ohio, USA), InfuTronix (Natick, Massachusetts, USA), Avarus Medical (Irvine, California, USA), Masimo (Irvine, CA, USA), and Varian Medical Systems (Palo Alto, California, USA). BJC: The University of California San Diego has received product from Masimo (Irvine, CA, USA) for other research studies. ANQ: No conflicts to disclose.

Patient consent for publication

Obtained.

Ethics approval

This study involves human participants and was approved by the University of California San Diego, protocol number 803348. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review

Not commissioned; externally peer reviewed.

Supplemental material

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REFERENCES


