

# Effectiveness of Vibration Therapy for Hard-to-Heal Wounds in Clinical Study: A Scoping Review

Daijiro Haba<sup>1,2</sup>, Mizuho Itabashi<sup>1,3</sup>, Nao Tamai<sup>2,4,5</sup>, Hiromi Tobe<sup>2,6</sup>, Hiromi Sanada<sup>1,2,6</sup>, Gojiro Nakagami<sup>1,2</sup>

<sup>1</sup>Department of Gerontological Nursing/Wound Care Management, Graduate School of Medicine, The University of Tokyo, Bunkyo-Ku, Tokyo, Japan; <sup>2</sup>Global Nursing Research Center, Graduate School of Medicine, The University of Tokyo, Bunkyo-Ku, Tokyo, Japan; <sup>3</sup>Department of Gerontological Nursing, Graduate School of Nursing Science, St. Luke's International University, Chuo-ku, Tokyo, Japan; <sup>4</sup>Department of Imaging Nursing Science, Graduate School of Medicine, The University of Tokyo, Bunkyo-Ku, Tokyo, Japan; <sup>5</sup>Department of Nursing, Graduate School of Medicine, Yokohama City University, Yokohama, Kanagawa, Japan; <sup>6</sup>Ishikawa Prefectural Nursing University, Kahoku, Ishikawa, Japan

Correspondence: Gojiro Nakagami, Department of Gerontological Nursing/Wound Care Management, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-Ku, Tokyo, 113-0033, Japan, Tel/Fax +81-3-5841-341, Email [gojiron@g.ecc.u-tokyo.ac.jp](mailto:gojiron@g.ecc.u-tokyo.ac.jp)

**Abstract:** Diminished peripheral blood flow at the wound site remains a key hindrance to effective wound healing. Hard-to-heal wounds are defined as wounds that fail to heal with standard therapy. Vibration therapy may help promote the healing of hard-to-heal wounds such as pressure injuries, diabetic foot ulcers, and venous leg ulcers by improving blood flow. However, evidence supporting its effectiveness on hard-to-heal wounds is inadequate. This scoping review focuses on studying the effectiveness of vibration therapy for healing hard-to-heal wounds by compiling all available research. The following databases were systematically reviewed from 1980 to 2023: MEDLINE, EMBASE, Cochrane Library, Ichu-shi-Web, IEEE, CINAHL, Scopus, Web of Science, and PEDro. The search terms included “wound”, “ulcer”, “hard-to-heal”, “vibration therapy”, and “wound healing”. Two authors independently screened the articles based on inclusion criteria, and the lead author performed data extraction and analysis. A total of 1036 articles were identified, and five articles were eligible to be included in this review. The results suggested that low-frequency and low-intensity vibration therapies helped effectively treat wounds (including pressure injuries, diabetic foot ulcers, and venous leg ulcers) by improving blood flow, relieving pain, reducing exudate, removing necrotic tissue, and increasing the expression of nitric oxide associated with wound healing. This study will inform the treatment choices of clinicians who manage patients with hard-to-heal wounds and researchers who plan to conduct clinical trials using vibration therapy. Further studies on vibration therapy must be performed to gather evidence to support the clinical application of vibration therapy to improve healing time and outcomes in individuals with hard-to-heal wounds.

**Keywords:** vibration, physical therapy, hard-to-heal wound, chronic wound, wound healing

## Introduction

### Background

Treatments of hard-to-heal wounds such as pressure injuries (PIs), diabetic foot ulcers (DFUs), and venous leg ulcers (VLUs) poses a significant challenge worldwide,<sup>1</sup> especially in aging populations.<sup>2,3</sup> These wounds, with a high prevalence (12.8% for PIs globally,<sup>4</sup> 4–27% among diabetes mellitus (DM) patients worldwide,<sup>5</sup> and 2.21 per 1000 individuals for chronic venous leg ulcers)<sup>6</sup> contribute to increased healthcare costs and impact patient quality of life and hospitalization length.<sup>7,8</sup> Risk factors such as aging, peripheral vascular disease, obesity, and diabetes exacerbate their prevalence and severity.<sup>6,9,10</sup>

Hard-to-heal wounds, defined by their failure to respond to standard treatments,<sup>11</sup> often suffer from delayed healing due to reduced blood flow at the wound site.<sup>3,12</sup> Revascularization is general treatment and helps improve peripheral blood circulation;<sup>13</sup> however, revascularization surgery is invasive and significantly increases the risk of perioperative

complications.<sup>14</sup> To address delayed healing, treatments aim to enhance peripheral circulation, leading to the development of various less invasive techniques,<sup>15</sup> including negative pressure wound therapy,<sup>16</sup> ultrasound,<sup>17</sup> electrical stimulation,<sup>18</sup> oxygen therapy,<sup>19,20</sup> and notably, vibration therapy.<sup>21</sup> Vibration therapy, in particular, stands out for its practicality and non-invasive approach, utilizing a vibration stimulus directly at the wound site to promote blood flow, easily applied through devices placed under a mattress or on a vibrating platform.<sup>22–25</sup>

Vibration therapy may be an effective treatment to facilitate the healing of hard-to-heal wounds by improving peripheral blood circulation, as has been reported in joint and muscle studies.<sup>26</sup> Employed for skeletal muscle training and increasingly in clinical settings, whole-body vibration (WBV) therapy has demonstrated numerous benefits<sup>25</sup> such as improved muscle strength,<sup>27</sup> increased bone mass,<sup>28</sup> better skin blood flow,<sup>29</sup> and reduced fat and blood glucose levels.<sup>30,31</sup> Extensively studied since the 1980s,<sup>32</sup> recent research, particularly in animal models, has highlighted its potential in wound healing<sup>32–35</sup> Studies have shown that WBV accelerates wound closure, re-epithelialization, and angiogenesis, especially in diabetic hard-to-heal animal models, by reducing tissue hypoxia and promoting tissue regeneration.<sup>36–39</sup> Notably, low-frequency and low-intensity WBV have been effective in improving both wound closure and healing quality, making it a promising therapeutic avenue for hard-to-heal wounds.

While vibration therapy's benefits in animal wound healing studies have been documented, its effectiveness in human clinical cases remains less explored.<sup>21</sup> The International Guideline 2019 by EPUAP/NPIAP/PPPIA suggests vibration therapy could offer superior healing outcomes for PIs compared to standard care.<sup>40</sup> However, currently, there are no guidelines regulating the use of vibration therapy for DFUs and VLU. Despite indications of improved healing, its clinical application is limited, possibly due to inadequate clinician familiarity, unclear dosage guidelines, and limited understanding of its healing mechanisms.<sup>41</sup> This review addresses this gap by synthesizing available research on vibration therapy in hard-to-heal wounds, aiming to enhance clinical practice and guide future studies.

## Study Rationale

There are few studies assessing the effectiveness of vibration therapy in people with hard-to-heal wounds.<sup>42</sup> Hard-to-heal wounds are defined as wounds that fail to heal with standard therapy in an orderly and timely manner.<sup>11</sup> Our study is centered on evaluating interventions for a variety of wound types commonly associated with hard-to-heal conditions, including PIs, DFUs, VLUs, and arterial leg ulcers (ALU). In defining hard-to-heal wounds, we specifically considered ulcers that had not healed over a long period since their occurrence, regardless of whether such wounds typically respond to standard treatment. We specifically characterized hard-to-heal wounds as ulcers that have not healed for an extended period following their development, irrespective of their usual response to standard treatment.

In this scoping review, we searched for studies with a wide range of study designs that reported the effectiveness of low-frequency vibration in the healing of hard-to-heal wounds. We mapped the available evidence to better understand the effectiveness of vibration therapy for wound healing. Vibration therapy includes various specifications regarding amplitudes and frequencies, which are applied intermittently or continuously through localized vibration or WBV intermittently or continuously.<sup>21</sup> The vibration device delivers a frequency measured in hertz (Hz),<sup>25</sup> typically ranging from 1 Hz to 100 Hz.<sup>42</sup> In this study, ultrasound therapy, which is also a form of mechanical vibrational energy, was excluded because ultrasound therapy involves frequency ranges above 20 kHz.<sup>21</sup>

## Study Objectives

The objectives of this scoping review were to: (a) summarize the available evidence to identify which vibration therapy was effective in terms of healing outcomes of hard-to-heal wounds, as reported in human study, and (b) identify the optimal setting for vibration therapy to promote healing of hard-to-heal wounds.

## Scoping Review Question

The following scoping review question was formulated: “What kind of vibration therapy and setting contribute to wound healing in patients with hard-to-heal wounds” “Is there any evidence suggesting that vibration therapy promotes healing of hard-to-heal wounds?”

## Material and Methods

### Protocol Design

A review protocol was not published. This scoping review was drafted using the scoping review framework of Arksey and O'Malley<sup>43</sup> and the JBI framework.<sup>44</sup> The Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews (PRISMA ScR) Checklist<sup>45</sup> were used to prepare this review.

### Eligibility Criteria

Papers published between 1980 to 2023 in English and Japanese were included in this review, regardless of the clinical setting, involving participants of all ages with hard-to-heal wounds that had undergone vibration therapy. We excluded papers that reported ultrasound therapy; treatments with high-frequency vibration of kHz and MHz; and if vibration settings were not defined in the paper.<sup>25</sup> Conference abstracts, books, letters to the editor, guidelines, protocols, and review articles were also excluded. We investigated the effectiveness of various types of vibration therapy for wounds, focusing on the reduction of wound area and improvement in healing rate or duration. We included original studies and case reports, including (1) randomized controlled trials (RCT), (2) longitudinal studies, (3) cross-sectional studies, (4) case-control studies, excluding animal experiments.

### Information Sources

To identify potentially relevant papers, the following bibliographic databases were searched with a date filter of January 1, 1980, to May 31, 2023: MEDLINE (PubMed), Ovid EMBASE, Cochrane Library (Ovid), Ichu-shi-Web, IEEE, EBSCO CINAHL, Scopus, Web of Science, and PEDro. Additional data sources were identified using Semantic Scholar. Search strategies were developed through team discussion. The final search results were exported to Mendeley for better reference management, and duplicates were removed before screening the literature by two researchers.

### Search

Search terms and Medical Subject Headings (MeSH) terms related to vibration therapy, wound, and wound healing were used and were combined using the boolean operators “AND” and “NOT”. Our primary search strategy, exemplified by the search conducted in PubMed in May 2023, was as follows:

- #1. Wound\* OR injur\* OR ulcer\* OR chronic OR hard-to-heal OR non-healing
- #2. Vibrat\* OR “vibration therap” OR “whole body vibratio” OR “local vibratio”
- #3. Ultraso\*
- #4. Wound healing [MeSH Terms]
- #5. ((#1 AND #2) NOT #3) AND #4
- #6. Limit #5 to yr = “1980–2023”

Search results from the digital search process were uploaded to reference management software, and duplicates were removed. It is important to note that multiple search engines were utilized, each with its unique search formula. Due to the extensive number of search strategies employed and their complexity, they have been detailed in the [Supplementary Material](#).

### Selection of Sources of Evidence

In the first screening of the title and abstract, the articles that included the terms “vibration therapy”, “whole-body vibration”, “local vibration”, “low-frequency vibration”, or “low-intensity vibration” and neither of “ultraso\*” or the terms related to testing such as “vibratory sense examination”, or “vibration test” were selected. The articles that included the terms “wound”, “chronic wound”, “chronic injury”, “chronic ulcer”, “hard-to-heal”, “non-healing”, “pressure ulcer”, “pressure injury”, “diabetic foot ulcer”, “diabetic foot disease” “venous leg ulcer” were selected. In the second full-text screening, original articles lacking wound healing or repair outcomes in patients were excluded.

## Data Charting Process

The search results were imported into Rayyan (Qatar Computing Research Institute, Doha, Qatar).<sup>46</sup> A data-charting form was developed by two reviewers (D.H. and M.I.) using Rayyan to determine which variables were to be extracted. Two reviewers (D.H. and M.I.) independently charted the data, discussed the results, and continuously updated the data-charting form in an iterative manner. Any disagreements were resolved through discussion between the two reviewers or through further adjudication by a third reviewer.

## Data Items

The following information was extracted: 1) article characteristics (e., study authors, year of publication, country); 2) study design/participants/age (eg, target population, the number of participants, age); 3) study subjects/ wound type (eg, details of their condition/ PI, DFU, VLU, or ALU); 4) name of vibration device used/ type of vibration (eg, local vibration and location, WBV); 5) treatment posture or vibration setting (eg, supine position, prone position, standing position); 6) vibration frequency (Hz), vibration intensity (eg, accelerations (g, m/s<sup>2</sup>), peak-to-peak voltage (Vpp)); 7) vibration protocol (eg, time, duration, wave type, frequency of treatment); 8) control treatment or option, 9) primary outcome for wound healing (eg, wound size, wound closure, duration or ratio of wound healing); 10) secondary outcome associated with wound healing; 11) adverse events; 12) conclusion.

## Synthesis of Results

We grouped the studies in the manner in which the vibration device was used in human study. The results are presented in [Table 1](#). The factors related to the vibration setting were summarized for each study, along with the study attributes, study design, wound type, and protocols. We identified a study investigating the effectiveness of wound healing in relation to certain factors and summarized the indicators of the outcomes.

## Results

### Selection of Sources of Evidence

The initial search yielded 1,273 studies. After removing the duplicates (n = 238) and including an additional study from other sources (n = 1), 1036 articles remained. After screening the title and the abstract, 1026 papers were excluded. Among the 10 remaining papers, 5 were excluded through full-text screening: one study did not investigate the effects of vibration for wound healing, and four others were ineligible due to wound type and study type. Five articles met the inclusion criteria and were included in this scoping review.<sup>24,47–50</sup> The PRISMA flowchart for this review is shown in [Figure 1](#).

### Characteristics of Sources of Evidence

The characteristics of the five included studies are shown in [Table 1](#). These studies included patients with VLUs,<sup>47</sup> PIs,<sup>24,48</sup> and DFUs.<sup>49,50</sup> All study demonstrated that both the intervention group and the control group received the same standard treatment; however, the intervention group additionally underwent vibration therapy. Wilson et al conducted a comparative pre-post study in patients with VLUs. This study used the Vibro-Pulse device (Vibrant Medical, Sheffield), which is used to deliver cycloidal multidirectional vibration therapy.<sup>47</sup> In this study, detailed vibrational conditions, including vibration frequency and intensity, were not described. However, the vibration was delivered three times a day for 30 min to patients with a minimum gap of three hours between each therapy session. All 21 patients participated in the study until the end. Thirteen patients (62%) healed completely by 12 weeks; however, the eight patients who had not healed by 12 weeks showed a reduction in ulcer size of 63–65%. Additionally, there was a reduction in pain in 17 out of 18 patients (94%) who reported pain at the start of the study, a reduction in exudate discharge in 11 out of 21 patients (52%), and a 15% reduction in total limb volume. Among these, one case involving a patient with a venous leg ulcer (VLU) that had not healed for 20 years was reported to have healed following the intervention.

In four studies, RelaWave (Global Micronics Corp, Chiba, Japan) was used to deliver local vibration therapy to treat PIs and DFUs.<sup>24,48–50</sup> The vibration settings of the RelaWave were the same in all the studies: the frequency and

**Table 1** Summary of Collected Data of Clinical Studies in This Scoping Review

Study Authors, Year, Country	Study Design /Participants /Age	Subjects /Wound Type	Vibration Device /Type of Vibration	Treatment Posture	Vibration Frequency and Intensity	Vibration Protocol	Control Treatment/ Option	Primary Outcome	Secondary Outcome	Adverse Events	Conclusion
Wilson et al 2002 (United Kingdom) <sup>47</sup>	Comparative pre-post study/N = 21 (6 male, 15 female)/ 51–93 years (mean: 74)	All had venous pathology. Ankle-brachial pressure index > 0.8. / VLU	Vibro-Pulse therapy (Vibrant Medical, Sheffield)/ Local vibration	Pad was placed under the lower leg and stabilized using a padded compression strap.	Not described (Low-frequency/ Small-amplitude setting)	Thrice daily for 30 minutes. Minimum three hours gap between treatments.	Exudate control with dressing Compression bandaging	<b>Ulcer area</b> 13 patients (62%) healed completely over 7 weeks. 8 patients (38%) who had not healed by 12 weeks showed a 63–65% reduction in ulcer size.	<b>Quality of life assessments</b> Pain: Reduction in 17 out of 18 patients (94%) reporting pain at the start of the study. Exudate: Reduction in exudate in 11 of the 21 patients (52%). Edema reduction: There was 15% reduction in limb volumes	Not described	Cycloid vibration combined with compression bandaging improved the healing of VLU and enhanced quality of life, particularly in relation to pain relief.
Arashi et al 2010 (Japan) <sup>24</sup>	Non-randomized, blinded, controlled trial/N = 39, experimental group (N = 16) (20 ulcers); control group N = 15 (21 ulcers)/ Age of experimental group/ control group: 80.0 ± 8.9/ 80.4 ± 0.3 (Mean ± Standard deviation (SD))	Identified from the hospitals' inpatients lists older than 65 years with skin redness. / PI (Category I)	RelaWave (Global Micronics Corp, Chiba, Japan)/ Local vibration	Vibrator was located underneath the PI. If PI was on a lower extremity, the vibrator was placed between a mattress and a cushion. The vibrator was placed between the mattress and bed frame for other PI locations.	47 Hz; 1.78 m/s <sup>2</sup>	Thrice daily for 15 minutes until Category I PIs healed or for a maximum of 7 days.	Nursing care according to the Japanese Society of Pressure Ulcers guidelines for local treatment of PIs.	<b>Ulcer area</b> The mean relative change/day: 20.4% in the experimental group and 6.4% in the control group (P = 0.007) <b>Healing rate</b> Treatment group: 8 healed (40.0%) and four deteriorated. Control group: 2 ulcers healed (9.5%), and 8 deteriorated. <b>Healing period</b> The Kaplan–Meier curves indicate a faster healing rate in the experimental group (P = 0.018).	Not described	Not described	The proportion of healed Category I PIs was significantly higher in the experimental group. Healing time was significantly faster in the experimental group. Relative daily changes in the wound area and delta a* were significantly greater in the experimental group.

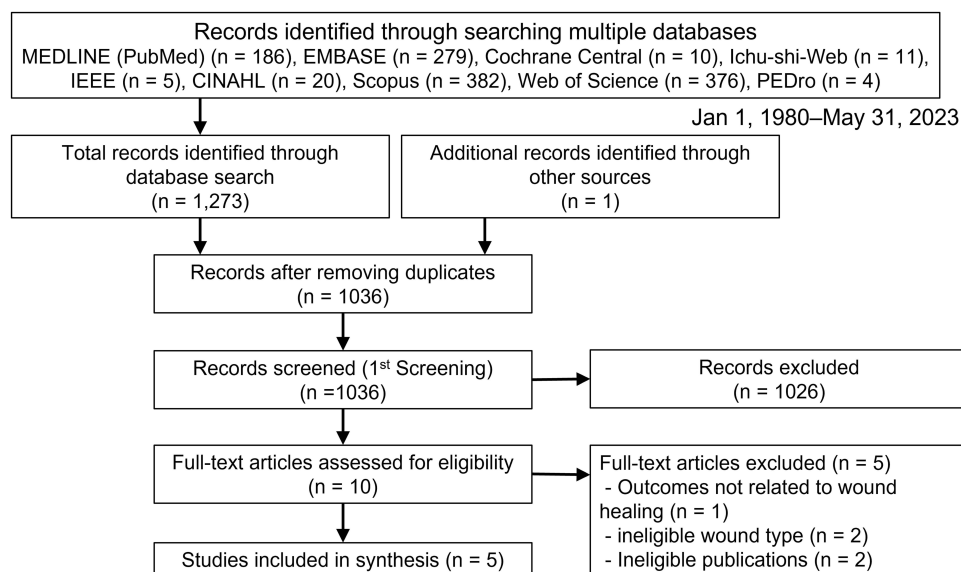
(Continued)

Table I (Continued).

Study Authors, Year, Country	Study Design /Participants /Age	Subjects /Wound Type	Vibration Device /Type of Vibration	Treatment Posture	Vibration Frequency and Intensity	Vibration Protocol	Control Treatment/ Option	Primary Outcome	Secondary Outcome	Adverse Events	Conclusion
Ueda et al 2010 (Japan) <sup>48</sup>	Quasi-experimental study/N = 31 (analysis, N = 24; experimental group, N = 13; control group, N = 11)/ Age of experimental group/ control group: 81 (77–90)/ 85 (59–97) (Mean, Minimum–Max)	Pls. More than 50% of the wound was covered with yellow or black necrotic tissue. / PI (Category III and IV)	RelaWave (Global Micronics Corp, Chiba, Japan)/ Local vibration	Vibrator was placed between a mattress and a cushion.	47 Hz; 1.78 m/s <sup>2</sup>	Thrice daily, 15 minutes, 5 weeks.	Nursing care according to the Japanese Society of Pressure Ulcers guidelines for local treatment of Pls.	<b>Wound area</b> No significant difference in the relative value of wound area between the experimental and control group at the 5th week.	<b>Proportion of necrotic tissue</b> Necrotic tissue proportion decreased faster in the experimental group (P = 0.013). Necrotic tissue proportion was significantly lower in the experimental group at weeks 2 (P = 0.027), 3 (P = 0.026), and 4 (P = 0.049).	Not described	Proportion of necrotic tissue in the experimental group decreased from week 2 to week 4 after vibration.No significant relative area of PI between the experimental and control groups.
Mahran et al 2013 (Egypt) <sup>49</sup>	Randomized, controlled trial/N = 29 (analysis, N = 29; experimental group, N = 15; control group, N = 14)/ Age of experimental group/ control group: 63.00 ± 7.28/ 65.33 ± 8.21 (Mean ± SD)	Diabetic ischemic foot ulcers with diabetes mellitus type II. / DFU	RelaWave (Global Micronics Corp, Chiba, Japan)/ Local vibration	Vibrator was placed underneath the ulcerated foot, as the feet rested on a cushion over a vibrator.	47 Hz; 1.78 m/s <sup>2</sup>	Thrice daily for 15 minutes, five days/ week for one month.	Nurse wound care and medical treatment to maintain moist environment without any granulation stimulate produce such as collagen or hormone	<b>Healing rate</b> Significant difference between the experimental and control groups in the mean value of ulcer areas after 2 and 4 weeks (P = 0.014 and 0.008, respectively).	Not described	Not described	Healed ulcer area was significantly higher in the study group. Low mechanical vibration therapy may improve the healing of DFUs.

Syabariyah et al 2023 (Indonesia) <sup>50</sup>	Randomized controlled trial/ N = 80 (analysis, N = 79; experimental group, N = 40; control group, N = 39)/ Age of experimental group/ control group: 55.20 ± 8.39/ 56.60 ± 9.03 (Mean ± SD)	Diabetic neuropathic foot ulcers with Wagner grades I-III /DFU	RelaWave (Global Micronics Corp, Chiba, Japan)/ Local vibration	Vibrator was set under the lower legs.	47 Hz; 1.78 m/s <sup>2</sup>	Thrice daily for 15 minutes after standard wound care every two days during the 12-week study period.	Only standard care	<p><b>Healing rate</b> The patients administered VWT had a shorter median healing rate of 25 days (95% CI, 20.3–29.7 days), while the subjects of the control group had a longer median healing rate of 33 days (95% CI, 25.6–40.4 days).</p> <p><b>Hazard ratio (HR)</b> Wounds healed 1.69 times faster in the vibration intervention group than in the control group (95% CI of the HR, 1.07–2.68)</p> <p><b>Wound closure area</b> There were notable improvements in the relative area reduction (%/day) (P = 0.032) and delta reduction (mm/day) of the wound closure (P = 0.021) in the vibration group compared to the control group.</p>	<p><b>NO level</b> The average NO levels after intervention were significantly higher in the vibration intervention group (2.91 mol/mL) compared to the control group (0.86 mol/mL) (P &lt; 0.001).</p>	No clinically adverse effects were found in the patients induced with VWT	VWT accelerates DFU healing. The patients administered VWT consistently require a significantly shorter hospitalization time than those who are not.
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**Abbreviations:** CI, confidence interval; DFU, Diabetic foot ulcer; NO, Nitric oxide; PI, Pressure injury; VLU, Venous leg ulcer; VWT, Vibration wound therapy.



**Figure 1** Flow chart of this scoping review. A PRISMA flowchart of the current review is shown. Finally, a total of ten articles were included in this scoping review.

horizontal vibration acceleration were 47 Hz and 1.78 m/s<sup>2</sup>, respectively. Arashi et al conducted a non-randomized blinded controlled trial in patients with Category I PIs, and vibration was delivered for 15 min three times a day until Category I PIs healed or for a maximum of 7 days. This study demonstrated that the mean relative change in the wound area per day was decreased in the experimental group (20.4%) compared to that of the control group (6.4%); eight ulcers healed (40%) and four ulcers deteriorated in the experimental group. In contrast, two ulcers healed (9.5%) and eight ulcers deteriorated in the control group.<sup>24</sup> Additionally, Kaplan–Meier curves indicated a faster healing rate in the experimental group ( $P = 0.018$ ). Ueda et al conducted a quasi-experimental study using vibration therapy, performed thrice a day for five weeks for category III and IV PIs with necrotic tissue.<sup>48</sup> There was no significant difference in the decrease in relative wound area between the experimental and control groups at week five of the study period. However, the proportion of necrotic tissue decreased more rapidly in the experimental group than in the control group at the first week ( $P = 0.013$ ), second week ( $P = 0.027$ ), third week ( $P = 0.026$ ), and fourth week ( $P = 0.049$ ). Mahran et al conducted an RCT ( $n = 29$ ) enrolling individuals with DFUs in Egypt, where vibration treatment was applied for 15 min thrice a day, five days per week, for one month.<sup>49</sup> This study found a significant difference between the experimental and control groups in the mean value of ulcer healing rate after two and four weeks ( $P = 0.014$  and 0.008), respectively. The authors concluded that low-frequency and low-intensity vibration therapy might improve the healing time of DFUs. Syabariyah et al conducted an RCT ( $n = 80$ ) including DFUs with diabetic neuropathy in Indonesia. They performed vibration wound therapy for 15 min thrice a day after standard wound care every two days for 12 weeks.<sup>50</sup> This study reported that the duration of the wounds was 2.0 ± 1.0 to 4.0 weeks for the control group and 2.0 ± 1.0 to 6.0 weeks for the intervention group, with no significant difference in wound duration between these two groups. The patients in the vibration group ( $n = 40$ ) had a shorter median healing rate of 25 days (95% confidence interval (CI), 20.3–29.7 days), while the patients in the control group ( $n = 39$ ) had a longer median healing rate of 33 days (95% CI, 25.6–40.4 days). There was one patient in the control group whose wound was not healed within the designated 12-week study period. This study also calculated the hazard ratio (HR) and found that the wounds healed 1.69 times faster in the vibration group than in the control group (95% CI of the HR, 1.07–2.68). There were notable improvements in the relative area reduction (%/day) and delta reduction (mm/day) of the wound closure in the vibration group compared to the control group ( $P = 0.032$ , 0.021, respectively). The author also evaluated the effect of vibration intervention on NO level, which is a factor of vasodilation, prior to and after the intervention. There were no differences in the NO levels between the vibration group and control group before intervention ( $P = 0.502$ ). However, the two groups had significant differences in NO levels postintervention. The average NO levels after intervention were significantly higher in the vibration intervention group (2.91 mol/mL)

compared to the control group (0.86 mol/mL), with a p-value of <0.001. These five human studies indicate that local vibration treatment promotes wound healing in PIs and DFUs in a clinical setting.

## Synthesis of results: Effects of Vibration Therapy and Appropriate Vibration Setting for Wound Healing

Four studies reported the same vibration setting, in which the frequency and horizontal vibration acceleration of the present vibrator were 47 Hz and 1.78 m/s<sup>2</sup>, respectively. The vibration was applied for 15 min three times a day. However, the treatment periods were different for each study ranging from 7 days,<sup>24</sup> every two days during the 12 week,<sup>50</sup> one month,<sup>49</sup> to 5 weeks.<sup>48</sup> In three studies, the vibrator was placed between a mattress and a cushion and was positioned underneath the wounds, and all patients lay on the bed. In another study using the same vibrator, the vibrator was set under both lower legs.<sup>50</sup> In one study that used cycloidal multidirectional vibration therapy, the vibration setting involved three therapy sessions at the patient's home, each session of 30 min, with a minimum of three hours rest period between each session.<sup>47</sup> The vibration pad was placed under the lower leg and was combined with compression therapy.

## Discussion

### Summary of Evidence

This scoping review focused on the effects of vibration therapy on wound healing in hard-to-heal wounds and aims to determine the appropriate vibration settings according to human study. To the best of our knowledge, no studies have so far summarized evidence on the effectiveness of vibration therapy on wound healing in hard-to-heal wounds. The final number of articles included in the study was five. In the clinical study, four studies reported a reduction in wound size and improvement in the healing rate. While one study did not indicate a significant difference in the wound area between the vibration and control groups, they reported a reduction in necrotic tissue in the vibration group. Taken together, the evidence from the results suggests that a combination of low-frequency (47 Hz) and low-intensity (1.78 m/s<sup>2</sup>) vibration with a treatment period of 15–30 minutes thrice daily for 5–7 days a week potentially improved processes involved in wound healing, such as improving blood flow, resulting in wound healing. The results from these ten articles suggested the promising effectiveness of vibration therapy in promoting wound healing, with low-frequency and low-intensity vibration settings being optimal for healing hard-to-heal wounds, including PIs, DFUs, and VLUs.

### Implication for Clinical Practice

Vibration therapy presents a promising option for treating hard-to-heal wounds, yet there's a notable gap between evidence and clinical practice. This scoping review highlights its effectiveness in managing PIs, VLUs, and DFUs. Clinical studies have predominantly used local vibration treatments, acknowledging that patients with hard-to-heal wounds may not be able to use WBV platforms. Research indicates that low-frequency, low-intensity vibration can effectively enhance skin blood flow, crucial for wound healing in both healthy individuals and diabetic patients<sup>24,49,51,52</sup> However, it's important to avoid long-term exposure to high-frequency and high-intensity vibrations to prevent vascular issues like Raynaud's phenomenon.<sup>53</sup> This review provides existing evidence to the clinical practice and may inform future researchers who may plan to conduct clinical trials assessing the effectiveness of vibration therapy.

### Mechanisms of Wound Healing by Vibration Therapy

One of the most important treatments to promote hard-to-heal wound healing is to improve blood flow at the wound site. The previous animal studies investigated the mechanisms of wound healing promoted by vibration therapy. They reported that vibration therapy induced regeneration of veins, promoted angiogenesis and blood perfusion, reduced tissue hypoxia, induced re-epithelialization and granular tissue formation, and induced expression of cytokines associated with wound healing.<sup>32,34,36,38,54</sup> A previous study reported that low-frequency vibration could accelerate regional blood flow through vasodilation via the production of NO<sup>22,23</sup> and wound healing in PIs.<sup>24</sup> One study in this review reported that vibration therapy increased NO levels in patients with DFUs.<sup>55</sup> However, the outcomes in this review could not explain the discrepancy between the theory and clinical practice, which is that vibration therapy cannot improve

peripheral blood flow in DFU patients due to the dysfunction of NO production and severe angiopathy, but low-frequency vibration can promote healing of DFUs.<sup>49</sup> Further studies are needed to elucidate the mechanisms underlying the promotion of peripheral blood flow in patients with DFU.

## Limitations

This scoping review has some limitations. First, we did not assess the quality of the studies systematically in this scoping review. Furthermore, these studies had small sample sizes, and there was only one paper related to the effects of vibration therapy for VLU, and there was no paper regarding to arterial leg ulcer. These limitations may have affected the evidence.

## Conclusion

This scoping review summarized the evidence regarding the effectiveness of vibration therapy for hard-to-heal wounds. Low-frequency and low-intensity local vibration therapy is useful for promoting wound healing based on evidence from human studies. The current optimal settings could be summarized as follows: local vibration at a low frequency within 47 Hz and low-intensity (1.78 m/s<sup>2</sup>) for less than 30 min, three times a day, and five weeks. The findings from this review may be used by researchers and clinicians planning to conduct clinical trials on vibration therapy to elucidate the mechanisms underlying wound healing to bridge the evidence-practice gap in this area.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

Hiroshi Sanada, Gojiro Nakagami, and the Global Micronics Corp are co-developers of RelaWave. The authors report no other conflicts of interest in this work.

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