IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Ultrasound (US) is defined as a mechanical vibration above the upper threshold of human hearing (greater than 20 KHz) and has been used primarily by physical therapists in the megahertz (MHz) range (1–3 MHz) for the treatment of musculoskeletal disorders. Recently, non-contact ultrasound treatment devices, which administer low frequency ultrasound in the kilohertz range via a saline mist, have been proposed for use in wound healing, including pain management and debridement. Their proposed mechanism of action is the production, vibration, and movement of micron-sized bubbles in the saline and wound tissue.

Regulatory Status

Devices with 510(k) clearance from the US Food and Drug Administration (FDA) include the following:

- The MIST Therapy® System, a non-contact ultrasound device, which uses an ultrasound transducer or wand, by Celleration® Inc.
- The Qoustic Wound Therapy System™ model AR1000 by Arobella Medical LLC. In contrast to MIST system, the AR1000 device uses a contact probe to treat wounds.
MEDICAL POLICY CRITERIA

Non-contact low-frequency ultrasound is considered investigational for the treatment of all wounds.

SCIENTIFIC EVIDENCE

The principal outcomes associated with treatment of wounds, particularly chronic wounds, are complete wound closure, improvement in the rate or quality of healing (such as the minimization of scarring), treatment of infection, and patient-centered outcomes such as improvements in function or mobility, and minimization of pain. Outcomes relating to the use of a non-contact low-frequency ultrasound devices for the treatment of wounds are best understood when comparing use of a non-contact low-frequency ultrasound device to a sham device among patients with similar wound type (i.e., burn or chronic diabetic ulcer) receiving standardized wound care regimens. Therefore, data from adequately powered, blinded, randomized sham-controlled trials are required to control for bias and determine whether any treatment effect from non-contact low-frequency ultrasound devices provides a significant advantage over standard wound care.

Literature Appraisal

The published literature on non-contact low-frequency ultrasound devices is limited to industry-sponsored randomized controlled trials, a systematic review based upon 2 of these trials, and several observational studies.

Systematic Reviews

A systematic review, also published in 2011, examined the literature on non-contact or contact ultrasound for treating chronic wounds. Five RCTs were identified on non-contact ultrasound. One of these studies was unpublished, 2 were the trials described above, and 2 were older studies from the 1990s that involved the delivery of ultrasound while the wounded area was in a footbath. They conducted one pooled analysis of findings on efficacy of non-contact ultrasound. Two RCTs, the Ennis et al. study on MIST therapy and one on ultrasound delivered during foot bathing were included. The studies included a total of 75 patients; the Ennis study contributed 55 of these. A pooled analysis found a significantly smaller proportion of non-healed wounds at 3 months in the non-contact ultrasound group compared to the control group (risk ratio [RR]: 0.74, 95% CI: 0.58 to 0.95). The limitations of the Ennis study which are included in the above description of this trial (e.g., high dropout rate, baseline differences between groups, etc.) limits the ability to draw conclusions about the efficacy of treatment in the pooled analysis.

Randomized Controlled Trials (RCTs)

Two industry-sponsored RCTs assessed the benefit of MIST therapy on wound healing. Both trials, had considerable limitations. A third RCT published in 2013 did not discuss its sponsorship. In the first trial, 133 patients with recalcitrant foot ulcers were treated with active or sham saline mist therapy 3 times per week. Although the study reported improvement in the healing rate in patients treated with the active MIST Therapy, several design flaws undermine the validity of the study findings:
• There was a large loss to follow-up (18%) and large exclusion due to violation of the protocol (41%), potentially undermining randomization and comparability of treatment groups. Consequently, the treatment responses observed could have been confounded by differences in demographic, clinical or other characteristics between the groups.
• Intention-to-treat analysis showed no difference in wound healing between the active and sham groups.
• The active and sham treatment groups were significantly different at baseline, with larger ulcer area (4.4 vs. 1.7 cm²) and longer chronicity of wounds (67 vs. 35 weeks) in the sham group, suggesting that there may have been a baseline difference affecting the outcome.

In the second trial, 70 patients with nonhealing (2 months) lower-extremity wounds were randomized to 12 weeks of standard of care alone or standard of care plus MIST therapy.[4] The study reported improved rates of healing in patients treated with the active MIST therapy, but several design flaws undermine the validity of the findings:

• The small study population (<100) limits the ability to rule out the role of chance as an explanation of findings.
• The randomization scheme was not explained. Inadequate randomization of study participants may result in unequal distribution of potential confounders, such as clinical characteristics.
• Although the study reports on the importance of baseline transcutaneous oxygen levels (TcPO2) on wound healing, patients with low (1–20 mm Hg) and high (21–40 mm Hg) TcPO2 levels were not equally distributed between the two treatment groups, suggesting that there may be a baseline difference affecting the outcome.
• The outcome of interest was defined as a reduction of wound area greater than 50%. The clinical significance of partial wound healing and its significance in predicting complete wound closure were not adequately explained.
• The nonblinded design increases the likelihood of placebo effect.

In the third trial, 90 patients with chronic wounds, including venous leg ulcers, were randomized into standard care (N=30), high-frequency ultrasound (N=30), or noncontact low frequency ultrasound (N=30).[5] Therapy was provided 3 times a week for 12 weeks, or until healed. The study reported improved rates of healing in patients treated with both methods of ultrasound compared to standard care alone; however, there were no differences between the ultrasound groups. In addition, there were several methodological limitations:

• The main limitation of this trial is that it was not blinded, and this may have led to differential treatment of patients in the 3 groups as they received standard care, and could have biased outcome assessments.
• The small study population (<100) limits the ability to draw firm conclusions.
• The wound surface in the study was measured by tracing the margins of the open wound. The use of more precise imaging and histopathological assessment methods may have enhanced study accuracy.
• Also, as evidenced by the complete healing of ulcers in all patients in the standard care group, it is unlikely that patients received optimal wound care prior to enrolling in the study.

Nonrandomized Studies
A number of nonrandomized studies described experiences of MIST therapy-treated wound patients.[6-22] While these studies contribute to the body of knowledge by providing direction for future research, evidence from these studies is unreliable due to inherent design flaws, such as non-random allocation of treatment and lack of appropriate comparison groups.

Clinical Practice Guidelines

In 2010, the Association for the Advancement of Wound Care (AAWC) published a guideline on care of pressure ulcers[23] on-contact ultrasound therapy was included as a potential second-line intervention if first-line treatments did not result in wound healing, although the strength of the evidence supporting this decision was low (Level C), indicating a lack of sufficient studies on this topic.

The 2012 AAWC guideline on treatment of venous ulcers stated that low-frequency ultrasound treatment requires additional evidence before it can be considered an appropriate treatment. [25][25]

Summary

Currently available scientific evidence does not permit conclusions concerning the effect of non-contact low-frequency ultrasound devices on wound healing, particularly in comparison to standard wound therapy; therefore, the use of these devices is considered investigational. Well-designed, blinded studies with additional subjects that include all relevant outcomes are needed to adequately evaluate this treatment.

REFERENCES


**CROSS REFERENCES**

[Electrostimulation and Electromagnetic Therapy for the Treatment of Wounds](#), DME, Policy No. 83.09

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