Non-Contact Ultrasound Treatment for Wounds

Policy Number: 2.01.79  Last Review: 7/2014

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for non-contact ultrasound treatment for wounds. This is considered investigational.

When Policy Topic is covered
Not Applicable

When Policy Topic is not covered
Non-contact ultrasound treatment for wounds is considered investigational.

Description of Procedure or Service
Low-frequency ultrasound (US) in the kilohertz (KHz) range may improve wound healing. Several devices are available, including the MIST Therapy® system, which delivers ultrasonic energy to wounds via a saline mist without direct skin contact.

Ultrasound (US) is defined as a mechanical vibration above the upper threshold of human hearing (greater than 20 KHz). US in the megahertz (MHz) range (1–3 MHz) has been used for the treatment of musculoskeletal disorders, primarily by physical therapists. Although the exact mechanism underlying its clinical effects is not known, therapeutic US has been shown to have a variety of effects at a cellular level, including angiogenesis, leukocyte adhesion, growth factor and collagen production, and increases in macrophage responsiveness, fibrinolysis, and nitric oxide levels. More recently, the therapeutic effects of US energy in the KHz range have been examined. It has been proposed that low frequency US in this range may improve wound healing via the production, vibration, and movement of micron-sized bubbles in the coupling medium and tissue.

The mechanical energy from US is typically transmitted to tissue through a coupling gel. Several high-intensity US devices with contact probes are currently available for wound debridement. A non-contact low-intensity US device has been developed that does not require use of a coupling gel or other direct contact. The MIST Therapy™ System (Celleration, Eden Prairie, MN) delivers a saline mist to the wound with low-frequency US (40 KHz); it includes a generator, a transducer, and a disposable applicator for discharge of prepackaged saline.

Regulatory Status
In 2005, the Celleration MIST therapy device received marketing clearance (K050129) through the U.S. Food and Drug Administration’s (FDA) 510(k) process, “to promote wound healing through wound cleansing and maintenance debridement by the removal of yellow slough, fibrin, tissue exudates and bacteria.” Several wound drainage and wound vacuum systems were listed as predicate devices. In 2004, the FDA had reclassified these devices from class III to class II at the request of Celleration (K032378).

In 2007, the AR1000 Ultrasonic Wound Therapy System (Arobella Medical) received marketing clearance, listing the Celleration MIST system and several other ultrasonic wound debridement and
hydrosurgery systems as predicate devices. The AR1000 system uses a combination of irrigation and US with a contact probe to debride and cleanse wounds. The indications are similar to that of the MIST system, listed as: “selective dissection and fragmentation of tissue, wound debridement (acute and chronic wounds, burns, diseased or necrotic tissue), and cleansing irrigation of the site for the removal of debris, exudates, fragments, and other matter.”

**Rationale**

This policy was originally created in 2007 and was updated regularly with searches of the MEDLINE database. The most recent literature search was performed for the period August 2012 through September 19, 2013. Following is a summary of the key literature to date:

**Literature Review**

The literature review focused on studies evaluating whether the addition of non-contact ultrasound (US) improves wound healing in comparison with standard treatment alone.

Two systematic reviews were published in 2011. An industry-sponsored review by Driver and colleagues considered both controlled and uncontrolled studies on non-contact low-frequency US therapy for treating chronic wounds. (1) To be eligible for inclusion, studies had to have at least 4 weeks of follow-up. Ten studies were initially identified and 2 were excluded, 1 because data were not in a form suitable for pooling and the other because follow-up time was too short. Of the remaining 8 studies, 1 was an RCT, and the remainder were observational studies (5 retrospective analyses and 2 prospective studies). A pooled analysis of findings from 7 studies (total n=429) found that a mean of 32.7% (95% confidence interval [CI]: 23.3% to 42.1%) of patients had healed wounds by a mean of 6 weeks. A pooled analysis of 4 studies (total n=188) found a mean of 85.2% (95% CI: 64.7% to 97.6%) reduction in wound area by final follow-up. The major limitation of this meta-analysis was that there were no pooled comparisons of non-contact US therapy to optimal wound care alone, or to an alternative intervention. Thus conclusions cannot be drawn about the incremental benefit of non-contact ultrasound treatment over optimal wound care alone.

The second systematic review only included randomized controlled trials (RCTs); studies could non-contact or contact ultrasound (US) for treating chronic wounds. (2) Five RCTs were identified on non-contact ultrasound, 1 of which was unpublished. The authors conducted 1 pooled analysis of study findings. This meta-analysis of 2 RCTs found a significantly smaller proportion of non-healed wounds at 3 months in the non-contact US group compared to the control group (risk ratio [RR]: 0.74, 95% CI: 0.58 to 0.95). The ability to draw conclusions from this meta-analysis is limited because only 2 RCTs were included and 1 of these used non-contact US delivered during foot bathing (i.e. it did not use a modern device). The other RCT, by Ennis and colleagues had potential methodologic limitations (see below).

Details of the 2 industry-sponsored RCTs that have assessed the incremental benefit of MIST therapy on wound healing are as follows:

In 2005, Ennis and colleagues published findings of a double-blind multicenter RCT that used MIST therapy for recalcitrant diabetic foot ulcers. (3) Most of the 133 patients (85%) were enrolled and treated at 17 different wound clinics/private practice centers. An additional 15% of patients were enrolled at 6 university medical clinics. Patients with recalcitrant foot ulcers were treated with active or sham saline mist therapy 3 times per week, with debridement as needed and a weekly evaluation by an independent investigator. Twenty-four patients were lost to follow-up, and data from 54 patients were excluded from analysis due to protocol violations (5 centers were found to have inverted the treatment distances for the active and sham devices), leaving 55 patients (41%) for the per-protocol analysis. The investigators reported significant improvement in the active treatment group (11 of 27 patients, 41%) compared to the control group (4 of 28 patients, 14%) in the proportion of wounds healed (defined as complete epithelialization without drainage). However, intent-to-treat (ITT) analysis showed no difference in wound healing (26% vs. 22%, respectively) between the active (n=70) and control (n= 63)
groups. In addition to the 59% loss to follow-up, there was a difference in the ulcer area at baseline (1.7 vs. 4.4 cm², respectively) and chronicity of wounds (35 vs. 67 weeks, respectively) that favored MIST therapy in the per-protocol groups. Due to the serious limitations of this study, these results are considered inconclusive.

In 2007, Kavros and colleagues published an open-label (non-blinded) RCT comparing 12 weeks of MIST therapy plus standard care to standard care alone in 70 patients with non-healing (2 months) foot, ankle, or leg. (4) To participate, patients need to have documented ischemia (transcutaneous oximetry of 40 mm Hg or less) and to agree to 3 times per week visits for therapy. The study found that a greater proportion of patients in the MIST therapy group (22 of 35, 63%) achieved wound healing (defined as a reduction of wound area greater than 50%) in comparison with standard of care alone (10 of 35, 29% of patients). The authors did not control for potential non-specific effects of the additional treatment sessions for patients in the non-contact US group e.g. by including a sham treatment group. In addition, although the study reported on the importance of baseline transcutaneous partial pressure of oxygen (TcPO2) on wound healing, patients with low (1–20 mm Hg) and high (21–40 mm Hg) TcPO2 levels did not appear to be equally distributed between the groups.

Since publication of the 2011 systematic reviews, 1 additional RCT was published that evaluated the incremental benefit of non-contact US on wound healing. The study, by Olyaie and colleagues, was non-blinded and was conducted in Iran. (5) Sponsorship of the study was not discussed. Ninety patients with venous leg ulcers were randomized to 1 of 3 groups (30 patients per group): standard care only; standard care plus high-frequency US; or non-contact US using MIST therapy. Patients in the 2 US groups received treatments 3 times per week for 3 months or until healing occurred. After 4 months, mean ulcer size was 3.23 cm² (standard deviation [SD]: 2.39) in the high-frequency US group, 2.72 cm² (SD: 2.16) in the non-contact US group, and 4.28 cm² (SD: 2.80) in the standard care group, p<0.04. Patients were followed for a mean of 7.5 months. The mean time to complete healing (in months) was 6.86 (SD: 2.04) in the high-frequency US group, 6.65 (SD: 1.59) in the non-contact US group, and 8.50 (SD: 2.17) in the standard care group. The difference in time to healing among the 3 groups was statistically significant, p<0.001. The authors did not report paired comparisons between the standard care and non-contact US groups. The main limitation of this trial is that it was not blinded—this could have led to differential treatment of patients in the 3 groups as they received standard care, and could have biased outcome assessment. Also, as evidenced by the complete healing of ulcers in all patients in the standard care group, it is unlikely that patients had received optimal wound care prior to enrolling in the study..

Ongoing Clinical Trials
MIST Ultrasound Therapy Compared to UK Standard Care for the Treatment of Non-healing Venous Leg Ulcers (NCT01671748) (6): This single-blind RCT is comparing MIST ultrasound therapy to standard care in the United Kingdom for treatment of non-healing venous leg ulcers. The primary outcome is change in wound area. The investigators expect to enroll 40 patients, and the expected date of study completion is November 2013.

Summary
Non-contact low-frequency ultrasound (US) in the kilohertz range is proposed to promote wound healing. The available published evidence does not permit conclusions concerning the effect of non-contact US on health outcomes compared to standard wound treatment. One blinded RCT and 2 non-blinded RCTs have evaluated the incremental benefit of commercially available non-contact US devices on wound healing. The blinded RCT had substantial methodologic flaws e.g., high dropout rate, baseline differences between groups that limit the validity of the findings. Well-designed, blinded studies that have adequate numbers of patients and that include all relevant outcomes are needed to further evaluate the efficacy of this treatment. Therefore, non-contact ultrasound treatment for wounds is considered investigational.

Practice Guidelines and Position Statements
In 2010, the Association for the Advancement of Wound Care (AAWC) published a guideline on care of pressure ulcers. (7) Non-contact ultrasound therapy was included as a potential second-line intervention if first-line treatments did not result in wound healing.

The AAWC guideline on treatment of venous ulcers, updated in 2010, states that low-frequency ultrasound treatment requires additional evidence before it can be considered an appropriate treatment. (8)

**Medicare National Coverage**
No national coverage determination.

**References**


6. Sponsored by Cardiff and Vale University Health Board in collaboration with Celleration. MIST Ultrasound Therapy Compared to UK Standard Care for the Treatment of Non-healing Venous Leg Ulcers (NCT01671748). Available online at: www.clinicaltrials.gov


**Billing Coding/Physician Documentation Information**

97610 Low frequency, non-contact, non-thermal ultrasound, including topical application(s), when performed, wound assessment, and instruction(s) for ongoing care, per day (new code 1/1/14)

Coding information on the Celleration website states that, “Providers may determine it is appropriate to use the MIST Therapy system in conjunction with or adjunctively to other wound treatment procedures (e.g., surgical or sharp debridement).” (1)

**Additional Policy Key Words**

N/A

**Policy Implementation/Update Information**

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1/1/13  No policy statement changes.
7/1/13  No policy statement changes.
1/1/14  New 2014 CPT code. No policy statement changes.
4/1/14  Removed deleted code 0183T.
7/1/14  No policy statement changes.

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