Noncontact Warming Therapy, Ultrasound Therapy, and Fluorescence Imaging for Wounds (for Idaho Only)

Policy Number: CS132ID.C
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Instructions for Use

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Related Policies
None

Application

This Medical Policy only applies the state of Idaho, including Idaho Medicaid Plus plans.

Coverage Rationale

State-Specific Criteria

For medical necessity clinical coverage criteria for low frequency ultrasound therapy for treating wounds, refer to the Idaho Medicaid Provider Handbook, Therapy Services, Chapter 5.1: Active Wound Care Management (OT/PT).

Non State-Specific Criteria

Warming therapy or noncontact normothermic wound therapy (NNWT) is unproven and not medically necessary for treating wounds due to insufficient evidence of efficacy.

Noncontact real-time fluorescence wound imaging for bacterial presence is unproven and not medically necessary due to insufficient evidence of safety and/or efficacy.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
0598T	Noncontact real-time fluorescence wound imaging, for bacterial presence, location, and load, per session; first anatomic site (e.g., lower extremity)

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CPT Code	Description
0599T	Noncontact real-time fluorescence wound imaging, for bacterial presence, location, and load, per session; each additional anatomic site (e.g., upper extremity) (List separately in addition to code for primary procedure)
97610	Low frequency, non-contact, non-thermal ultrasound, including topical application(s), when performed, wound assessment, and instruction(s) for ongoing care, per day

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HCPCS Code	Description
A6000	Noncontact wound-warming wound cover for use with the noncontact wound- warming device and warming card
E0231	Noncontact wound-warming device (temperature control unit, AC adapter and power cord) for use with warming card and wound cover
E0232	Warming card for use with the noncontact wound-warming device and noncontact wound warming-wound cover

Description of Services

Warming therapy or noncontact normothermic wound therapy (NNWT) uses a noncontact wound cover and a warming unit to apply radiant heat and maintain 100% relative humidity in a wound. The intent is to raise the wound temperature to increase blood flow and oxygen to the wound.

MolecuLight *i:X*® is a handheld fluorescence imaging device for real-time detection of bacteria in wounds; the violet light illumination captures and documents the presence of bacteria in the wound and surrounding areas. The device provides clinicians with information about the fluorescent characteristics of a wound to assist them in making improved diagnostic and treatment decisions.

Clinical Evidence

Warming Therapy

The safety and efficacy of warming therapy or noncontact normothermic wound therapy (NNWT) for the treatment of chronic wounds has not been established in the published medical literature. Limitations of the existing studies include small samples, a lack of controls and/or randomization, and short follow-up times.

Yue et al. (2018) conducted a systematic review to assess the effects of local warming therapy (LWT) in treating chronic wounds. The inclusion criteria included randomized controlled trials (RCTs) that recruited people with chronic wound(s) [pressure ulcers, venous leg ulcers, arterial ulcers, diabetic foot ulcers (DFUs) and arterial ulcers] comparing the effects of LWT with standard wound care or other wound-healing interventions. Primary outcomes included time to healing assessed using appropriate survival analysis, proportion of people with DFUs undergoing amputation of the lower limb at any level, including single toes, and proportion of wounds with complete healing. Secondary outcomes consisted of change in wound size, with change expressed as absolute change or relative change; healing rate; quality of life measured by a validated scale. No RCTs comparing the effects of LWT with standard wound care or other wound-healing interventions amongst people with chronic wound(s) were found. It was therefore not possible to undertake a meta-analysis. The authors concluded that this review highlights the lack of robust evidence for the use of LWT in the treatment of chronic wounds. Thus, no definitive conclusions regarding using LWT for treating chronic wounds can be drawn from this review.

Thomas et al. (2005) conducted a randomized controlled comparative study on forty-one participants with a stage 3 or stage 4 truncal pressure ulcer > 1.0 cm^2. The experimental group was randomized to a radiant-heat dressing device and the control group was randomized to a hydrocolloid dressing, with or without a calcium alginate filler. They were followed until healed or for 12 weeks. Eight participants (57%) in the experimental group had complete healing of their pressure ulcer compared with seven participants (44%) with complete healing in the control group (p = .46). The authors concluded that although a 13% difference in healing rate between the two arms of the study was found, this difference was not statistically significant. This was a small sample size study.

Karr (2003) performed a randomized pilot study to evaluate the use of NNWT in the treatment of wounds associated with osteomyelitis. The study consisted of two arms. The control arm (n = 11) received standard wound care, which resulted in

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complete ulcer healing at an average of 127 days. The treatment arm (n = 5) received NNWT, which resulted in complete ulcer healing at an average of 59 days, or 54% faster than in the control arm. The authors concluded that although NNWT is not a direct treatment for osteomyelitis, this new treatment option results in accelerated healing of wounds associated with osteomyelitis. However, this difference did not reach statistical significance, and median wound healing times did not differ between groups.

Ellis et al. (2003) evaluated 33 participants with full-thickness pressure sores who were randomized to receive standard care or radiant heat therapy with a Warm-Up® device. The Warm-Up® device eradicated bacteria in six participants within 2 weeks of starting treatment compared to none in the standard care group. The significance of this study is limited by small sample size.

Noncontact Real-Time Fluorescence Wound Imaging

The safety and efficacy of handheld, noncontact imaging devices that can visualize fluorescent bacteria and measure wound surface area in real-time has not been established in the published literature. All fluorescence wound imaging devices, regardless of FDA approval, require further clinical studies for evaluation to ensure their safety and efficacy are validated. While some evidence exists for the predictive characteristics of the method compared to conventional wound cultures, the clinical utility of the method in improving care and participants' outcomes is unclear.

Oropallo et al. (2025) conducted a prospective, single-center cohort study aimed to evaluate the association between high bacterial colonization and wound associated pain in venous ulceration using MolecuLight i:X™ for bacterial detection. The authors evaluated 46 adults with venous ulceration of the lower extremity self-reporting a wound-associated pain score of ≥ 4 on a scale of 1 to 10. Before any treatments were performed (e.g., debridement), subjects rated their pain during the study visit, and fluorescence images were captured. Regions of pain and positive fluorescence signals were sketched onto a printed wound image. Fluorescence imaging was repeated post procedurally, and subjects re-rated their pain either at the end of the study visit or over the phone the following day. Semiquantitative analysis involved visual estimation of the percentage overlap between regions of fluorescence and pain in the wound bed. Wilcoxon matched pairs signed rank tests and Mann-Whitney t tests assessed changes in pain scores post procedurally. Fluorescence from elevated bacterial loads and biofilm was present in every venous ulcer assessed, usually covering ≤ 50% of the wound bed and commonly colonizing the wound edges. Regions of pain were more extensive than regions of fluorescence within the wound bed, and some degree of overlap was identified in 40 of 46 participants (87%). This overlap was often substantial (29 participants with > 25% overlap and 16 with > 50% overlap). Overall mean pain scores were 8.17 before the procedure and 6.87 after the procedure, corresponding with a 1.30-point reduction that was statistically significant ($p < .0001$). Pain score reduction was higher when participants rerated their pain one day after debridement (3.40-point reduction; $p = .004$). In conclusion, the authors observed that fluorescence signals from clinically significant bacterial colonization and biofilms were commonly present in painful venous lower extremity ulcerations. Regions of patient-reported pain and positive fluorescence frequently overlapped, suggesting a relationship between the two. Wound-associated pain scores were immediately reduced after objectively targeted bacterial removal via real-time fluorescence imaging, with an even greater reduction observed by the next day. The authors concluded that MolecuLight i:X imaging device offers a practical method to enhance the management of venous ulcers through its noninvasive, real-time fluorescent visualization. Understanding the association between chronic bacterial presence and pain in venous ulcers can inform treatment and management strategies, potentially enhancing patient quality of life and satisfaction, promoting healing, and reducing complications. This study has limitations. First, the relatively small sample size may limit the generalization of the results. Data collection was limited to treatment during a single appointment, which does not account for the full scope of wound management. Longitudinal studies should be conducted to establish the role of imaging-informed treatment in the context of consistent, multidisciplinary management of chronic venous ulcers.

Hanson-Viana et al. (2024) conducted a single-center, prospective observational study to investigate the use of real-time fluorescence imaging device, MolecuLight i:X™, as a predictive tool for skin graft integration through detection of common pathogens associated with burn wound infection and graft failure. This study included adult burn patients with previously infected wounds that were deemed clinically and microbiologically clean and were therefore candidates for grafting. Prior to grafting, a fluorescence imaging assessment (blinded to the surgical team) localized areas positive for moderate-high bacterial loads (> 104 CFU/gr). The most common pathogens found in the initial infection were P. aeruginosa (40%), E. coli (16%), and E. cloacae (13%). Intra-operatively, a standard swab sample from the recipient site was collected by the surgical team. Postoperatively, areas positive/negative for fluorescence and areas of graft take and failure were overlapped and measured (cm2) over a 2D schematic. The performance and accuracy of fluorescence imaging and swab sampling in relation to graft outcomes were assessed. A total of 38 participants were enrolled in this study with 73% (n = 28) male, and the mean age was 42 years ±SD13 years. The most common burn causes were direct fire contact (73%, n = 28), electrical (18%, n = 7), and contact burns (8%, n = 3). Six participants had comorbidities: three participants with psychiatric disorders (schizophrenia, depressive disorder, substance withdrawal syndrome), one with hypertension, and three with type 2 diabetes. The mean total body surface area (TBSA) involvement was 14.5 ±12.4% (range 0.8 –

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40.2%). Twenty-five of the 38 subjects enrolled had complete graft take while 13 had partial graft losses. There were no total losses. Fluorescence imaging was positive in 100% of losses versus 31% (4/13) of the swab microbiology. Fluorescence imaging was found to have a sensitivity of 86%, specificity of 98%, PPV of 72%, NPV of 99%, and an accuracy of 94% for predicting any type or range of graft loss in the entire cohort. Meanwhile, the sensitivity of microbiology from swab samples was 30%, with a specificity of 76%. The authors concluded that real-time fluorescence imaging of bacterial and biofilm presence and location can identify areas of the wound bed where grafts are most likely to fail or succeed with high sensitivity and specificity. Better diagnostic methods that flag pre-infection states and enable proactive bacterial and biofilm management may lead to better outcomes and support the viability of early excision. Further studies, however, are needed to prove the association of fluorescence imaging with other burn wound outcomes, including research that compares fluorescence imaging with other advanced microbe typification methods, or investigates variations in graft take between beds prepared using fluorescence guidance and those following standard care protocols.

Mayer et al. (2024) conducted a prospective, single-blind clinical trial to evaluate the diagnostic accuracy of clinical signs of biofilm (CSB), bacterial fluorescence imaging (MolecuLight™), and wound blotting (Saraya®, Osaka, Japan) against biofilm identification as validated by gold standard scanning electron microscopy (SEM) imaging and microbiology. In this study, 40 chronic hard-to-heal wounds underwent the following assessments: (1) clinical signs of biofilm (CSB), (2) biofilm blotting, (3) fluorescence imaging for localizing bacterial loads, wound scraping taken for (4) SEM to confirm matrix encased bacteria (biofilm), and (5) PCR (Polymerase Chain Reaction) and NGS (Next Generation Sequencing) to determine absolute bacterial load and species present. The authors used a combination of SEM and PCR microbiology to calculate the diagnostic accuracy measures of the CSB, biofilm blotting assay, and fluorescence imaging. Study data demonstrate that 62.5% of wounds were identified as biofilm-positive based on SEM and microbiological assessment. By employing this method to determine the gold truth, and thus calculate accuracy measures for all methods, fluorescence imaging demonstrated superior sensitivity (84%) and accuracy (63%) compared to CSB (sensitivity 44% and accuracy 43%) and biofilm blotting (sensitivity 24% and accuracy 40%). Biofilm blotting exhibited the highest specificity (64%), albeit with lower sensitivity and accuracy. Using SEM alone as the validation method slightly altered the results, but all trends held constant. The authors concluded that this trial provides the first comparative assessment of bedside methods for wound biofilm detection. The authors report the diagnostic accuracy measures of these more feasibly implementable methods versus laboratory-based SEM. Fluorescence imaging showed the greatest number of true positives (highest sensitivity), which is clinically relevant and provides assurance that no pathogenic bacteria will be missed. It effectively alerted regions of biofilm at the point-of-care with greater accuracy than standard clinical assessment (CSB) or biofilm blotting paper, providing actionable information that will likely translate into enhanced therapeutic approaches and better patient outcomes. This study has limitations. The biofilm prevalence reported here is likely an underestimation due to a small sample size. The microbiological analyses herein were semiquantitative, whereas quantitative analysis could have provided more insights, particularly in the cases that were inconclusive for biofilm. The threshold used in the microbiological analysis was set as 10^5 CFU/g of tissue due to processing lab standards. If this threshold had been set lower, the results of this analysis could provide more information. The MolecuLight™ device detects bacteria at a lower threshold (starting at 10^4 CFU/g), which differs from this threshold. Due to product supply constraints, only 35/40 subjects included were exposed to wound blotting. This meant that sensitivity and specificity were calculated with a slightly smaller sample size. When sample sizes are small, the confidence interval around the sensitivity and specificity widens, indicating greater uncertainty. Finally, while efforts were made to choose the most suitable validation method, there is currently no consensus on the definitive method for detecting biofilms. If an alternative diagnostic standard emerges in the future, it could impact the accuracy of the current bedside measures that have been selected.

Armstrong et al. (2023) conducted a post-hoc multicenter clinical trial analysis of 138 DFUs to evaluate fluorescence (FL)-imaging role in detecting biofilm-encased and planktonic bacteria in wounds at high loads. The sensitivity and specificity of clinical assessment and FL-imaging were compared across bacterial loads of concern (10^4 –10^9 CFU/g). Quantitative tissue culture confirmed the total loads. Bacterial presence was confirmed in 131/138 ulcers. Of these, 93.9% had loads > 10^4 CFU/g. In those wounds, symptoms of infection were largely absent and did not correlate with, or increase proportionately with, bacterial loads at any threshold. FL-imaging increased sensitivity for the detection of bacteria across loads 10^4 –10^9 ($p < .0001$), peaking at 92.6% for > 10^8 CFU/g. Imaging further showed that 84.2% of ulcers contained high loads in the peri-wound region. The authors anticipate that the definition of chronic inhibitory bacterial load (CIBL) will spark a paradigm shift in DFU wound assessment and management that encourages and enables earlier intervention along the bacterial-infection continuum, thereby preventing sequelae of infection and supporting improved DFU outcomes. The authors concluded that FL-imaging of bacterial burden has potential for facilitating early bacterial intervention, monitoring treatment effectiveness during and after debridement, aiding antimicrobial stewardship to limit antibiotic and antimicrobial dressing prescriptions, and improving wound healing outcomes. Clinicians had limited experience using FL-imaging in a clinical context before the study; this may have lowered the sensitivity of FL-imaging to detect bacteria at loads > 10^4 CFU/g (sensitivity previously reported to range from 72% to 100%). Limitations of the imaging technology described include a limited (1.5 mm) depth of excitation and the inability to detect non-porphyrin-producing bacteria, including all species from the Streptococcus, Enterococcus, and Finegoldia genres, although these rarely occur mono-

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microbially in chronic wounds. Additional limitations are that this study focused primarily on high bacterial load as a contributor to wound pathogenicity, but there are additional systemic factors which delay DFU healing and increase infection risk (e.g., peripheral artery disease, poor glycemic control, neuropathy). As the number of datapoints for each bacterial load threshold ranges from n = 14 to 34, these results should be interpreted with caution. The clinical utility of the technology to improve patient-centered outcomes was not assessed in this study. Finally, there is risk of bias and a potential conflict of interest as this clinical trial was funded by MolecuLight, Inc.

Chen et al. (2023) conducted a meta-analysis to assess the effect of ultrasound-supported wound debridement (USSD) in subjects with diabetic foot ulcer (DFU). A comprehensive literature examination through January 2023 was implemented and 1873 linked studies were appraised. The picked studies contained 577 subjects with DFUs in the studies' baseline, 282 of them were using USSD, 204 were using standard care, and 91 were using a placebo. Odds ratio (OR) in addition to 95% confidence intervals (CIs) were used to calculate the consequence of USSD in subjects with DFUs by the dichotomous styles and a fixed or random effect model. The USSD applied to DFU caused a significantly higher wound healing rate compared with the standard care (OR, 3.08; 95% CI, 1.94–4.88, $p < .001$) with no heterogeneity ($I^2 = 0\%$) and the placebo (OR, 7.61; 95% CI, 3.11–18.63, $p = .02$) with no heterogeneity ($I^2 = 0\%$). The USSD applied to DFUs caused a significantly higher wound healing rate compared with the standard care and the placebo. Though precautions should be taken when commerce with the consequences as all of the picked studies for this meta-analysis was with low sample sizes. A limitation to this meta-analysis is potential selection bias because a number of the studies involved in the meta-analysis were not covered. In addition, bias may have been increased due to the inclusion of missing or erroneous data from prior studies. The findings of this study need to be validated by well-designed studies. Further investigation is needed before clinical usefulness of this procedure is proven. [Authors Rastogi et al. (2019), and Yao et al. (2014), who were previously cited in this policy, are included in this meta-analysis].

Derwin et al. (2023) conducted a prospective observational study to investigate wound area reduction (WAR) outcomes in a complex wound population composed of non-healing acute and chronic wounds. The relationship between bacterial autofluorescence signals and WAR was investigated. Area measurements were collected both manually and digitally, and both methods were compared for accuracy. Twenty-six participants with 27 wounds of varying etiologies were observed twice weekly for two weeks. Digital wound measurement, wound bacterial status assessment, and targeted debridement were performed through a point-of-care fluorescence imaging device (MolecuLight® i: X, MolecuLight Inc, Toronto, Canada). The wound area reduction (WAR) rate was calculated using baseline and last visit measurements. Statistical analyses, including t-tests, Fisher exact tests, the Wilcoxon signed rank test for method comparison, and ANOVA for bacterial subgroups, were applied as pertinent. The overall average WAR was −3.80 cm^2 or a decrease of 46.88% (manual measurement), and −2.62 cm^2 or a 46.05% decrease (digital measurement via MolecuLight® device). There were no statistically significant differences between the WAR of acute and chronic wounds ($p = 0.7877$). A stepwise correlation between the WAR and bacterial status classification per fluorescence findings was observed, where persistent bacteria resulted in worse WAR outcomes. An overestimation of wound area by manual measurement was 23% on average. The authors concluded that fluorescence imaging signals were linked to WAR outcome and could be considered predictive. Wounds exhibiting bacterial loads that persisted at the end of the study period had worse WAR outcomes, while those for which management was able to effectively remove them demonstrated greater WAR. Manual measurement of the wound area consistently overestimated wound size when compared to digital measurement. However, if performed by the same operator, the overestimation was uniform enough that the WAR was calculated to be close to accurate. Notwithstanding, single wound measurements are likely to result in overestimation. Limitations to this study include being conducted at a single site, and a small, heterogeneous sample in relation to the age and wound etiology. Therefore, caution is needed in generalizing the results. Further research with randomized controlled trials is needed to validate these findings.

Ramirez-GarciaLuna et al. (2023) conducted a multi-center prospective study of 66 outpatient wound care participants using hyperspectral imaging to collect visible light, thermography, and bacterial fluorescence images. Wounds were assessed and screened using the International Wound Infection Institute (IWII) checklist for clinical signs and symptoms (CSS) of infection. Principal component analysis was performed on the images to identify wounds presenting as infected, inflamed, or non-infected. The model could accurately predict all three wound classes (infected, inflamed, and non-infected) with an accuracy of 74%. They performed best on infected wounds (100% sensitivity and 91% specificity) compared to noninflamed (sensitivity 94%, specificity 70%) and inflamed wounds (85% sensitivity, 77% specificity). The authors concluded that combining multiple imaging modalities enables the application of models to improve wound assessment. Infection detection by CSS is vulnerable to subjective interpretation and variability based on clinicians' education and skills. Enabling clinicians to use point-of-care hyperspectral imaging may allow earlier infection detection and intervention, possibly preventing delays in wound healing and minimizing adverse events. Limitations to the research include a lack of systematic, objective infection measurements, such as tissue biopsies, as the classification of infected vs. non-infected wounds was clinically done. The findings of this study need to be validated by well-designed studies. Further investigation is needed before clinical usefulness of this procedure is proven.

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Rahma et al. (2022) conducted a single center (multidisciplinary outpatient clinic), prospective pilot, randomized controlled trial (RCT) to estimate comparative healing rates and decision-making associated with the use of bacterial autofluorescence imaging in the management of diabetic foot ulcers (DFUs). This RCT included participants with an active diabetic foot ulcer (DFU) and no suspected clinical infection. Consenting participants were randomly assigned 1:1 to either treatment as usual informed by autofluorescence imaging (intervention), or treatment as usual alone (control). The primary outcome was the proportion of ulcers healed at 12 weeks by blinded assessment. Secondary outcomes included wound area reduction at 4 and 12 weeks, patient quality of life, and change in management decisions after autofluorescence imaging. Between November 2017 and November 2019, 56 participants were randomly assigned to the control or intervention group. The proportion of ulcers healed at 12 weeks in the autofluorescence arm was 45% (n = 13 of 29) vs. 22% (n = 6 of 27) in the control arm. Wound area reduction was 40.4% (autofluorescence) vs. 38.6% (control) at 4 weeks and 91.3% (autofluorescence) vs. 72.8% (control) at 12 weeks. Wound debridement was the most common intervention in wounds with positive autofluorescence imaging. There was a stepwise trend in healing favoring those with negative autofluorescence imaging, followed by those with positive autofluorescence who had intervention, and finally those with positive autofluorescence with no intervention. The authors concluded that assessing the use of autofluorescence imaging in DFU management, their results suggest that a powered RCT is feasible and justified. Autofluorescence may be valuable in addition to standard care in the management of DFU. There are a number of limitations to this study. First, it was a pilot study and, therefore, was not powered to show a difference in the primary outcome. Although the results suggest an improvement in the primary outcome measure in the autofluorescence arm, the results must be viewed with some caution, and a fully powered study is required to determine whether there is definitive evidence that the use of autofluorescence to guide standard care is superior to standard care alone. Second, the randomization was performed using serial opaque envelopes by stratification group which may present a greater risk of selection bias. Finally, although all attempts were made to minimize differences in baseline characteristics and the provision of standard care between the randomization groups, there may have been differences in the treatment received and patient concordance based on knowledge of randomization strategy. Further investigation is needed before clinical usefulness of this procedure is proven.

In participants with longstanding diabetic foot ulcers (DFUs), Ai-Jalodi et al. (2021) conducted a multi-center, prospective pilot study evaluating the time to healing over 12 weeks. The aim of this study was to assess the efficacy and safety of a porcine peritoneum-derived matrix in DFU treatment. In addition to weekly assessments for wound size, investigators analyzed bacterial burden using the MolecuLight i:X (MLiX) wound imaging device and bacterial protease (BPA) testing. Participants received a weekly application of Meso Wound Matrix Scaffold (MWM), a lyophilized porcine peritoneum-derived matrix (DSM Biomedical Inc., Exton, PA, US) for up to eight weeks. Descriptive statistics were chosen for this analysis. A total of 12 male participants and three female participants with an average age of 57 years were enrolled over a two-month period. The average wound duration was 30 weeks. Due to unrelated health issues, four participants were withdrawn. For the study endpoint of complete wound closure at 12 weeks, six (55%) of the remaining 11 participants achieved complete closure, and four (36%) participants healed during the 8-week treatment period. The average number of cellular- and/or tissue-based product (CTP) applications was six. Participants who healed all had negative BPA by nine weeks and no fluorescence on MLiX, indicating low bacterial load. The authors concluded this small pilot study indicated that participants with longstanding DFUs may respond to a porcine peritoneal-derived CTP. In this study, the CTP appears to have inhibited bacterial growth in the wound; however, further research is needed. The limitations of this pilot study include the small sample size, the lack of a control arm, and the loss of four of the 15 participants to unrelated adverse events. The bacterial results require further study before drawing any conclusions. Further research with randomized controlled trials is needed to validate these findings.

A clinical evidence assessment by ECRI suggests the evidence for the use of the MolecuLight i:X Fluorescence Imaging System is inconclusive. Studies provide insufficient evidence to determine improvement in patient outcomes. While the evidence might suggest the MolecuLight i:X Fluorescence Imaging System may be helpful for identification of wounds with bacterial loads, additional RCTs are needed to confirm the safety and efficacy of the device (ECRI 2021; updated 2024). Le et al. (2020, included in ECRI report above), conducted a prospective multicenter observational study on the use of MolecuLight i:X for 350 participants. Wounds underwent clinical signs and symptoms (CSS) assessment using the International Wound Infection Institute (IWII) checklist immediately followed by fluorescent imaging with the MolecuLight device. CSS assessment missed approximately 85% of bacterial loads that were greater than 10^4 CFU/g which can be indicative of infection. The authors found the use of the MolecuLight device resulted in higher sensitivity and accuracy of the detection of the bacteria. Limitations of the study included underreporting of bacteria diversity with the culture analysis, limited experience by clinicians in using the MolecuLight device and funding of the study by MolecuLight, Inc. The authors recommend the MolecuLight device be used in combination with CSS assessment and that evidence from larger longitudinal studies would be beneficial. The clinical utility of the technology to improve patient-centered outcomes was not assessed in this study.

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Farhan and Jeffery (2020) conducted a single-center observational study to assess the MolecuLight i:X device for efficacy in pediatric burn wounds and the overall feasibility of the device. Ten participants were recruited, and the device was utilized on sixteen different wounds to assess for the presence or absence of clinical signs and symptoms of infection; swabs were obtained to confirm the findings. The authors found the device demonstrated ability to visually identify significant bacterial growth and high compliance for use of the device. The authors conclude that these findings may pave the way for including bacterial fluorescence imaging use into the pediatric burn population. The clinical utility of the technology to improve patient-centered outcomes was, however, not assessed in this study.

Chew and associates (2020) stated that early diagnosis of wound infections is crucial as they have been shown to increase patient morbidity and mortality. These researchers examined the use of MolecuLight i:X to identify infections in acute open wounds in hand trauma. In a prospective cohort study, data was collected from participants who attended the hand trauma unit over a 4-week period before having surgery. Wounds were inspected for clinical signs of infection and auto-fluorescence images were taken using the MolecuLight i:X device. Wound swabs were taken, and results interpreted according to report by microbiologist. Auto-fluorescence images were interpreted by a clinician blinded to the microbiology results. A total of 31 participants were included and data collected from 35 wounds; three wounds (8.6%) showed positive clinical signs of infection, 3 (8.6%) were positive on auto-fluorescence imaging and 2 (5.7%) of wound swab samples were positive for significant infection. Auto-fluorescence imaging correlated with clinical signs and wound swab results for 34 wounds (97.1%). In one case, the clinical assessment and auto-fluorescence imaging showed positive signs of infection, but the wound swabs were negative. The authors concluded that auto-fluorescence imaging in acute open wounds may be useful to provide real-time confirmation of bacterial infection and thus guide management.

A pilot study performed by Pijpe et al. (2019) compared the detection of bacteria in burn wounds between a bacterial fluorescence imaging device MolecuLight i:X and standard microbiological swabs. A total of 14 participants with 20 wounds participated in the study. Wounds were swabbed three times: once with a standard swam, once with a high-fluorescent area swab, and finally with a non-fluorescent (nF) area swab. Proportion agreement of the microbiological results was calculated and the accuracy of the device to detect relevant bacteria was assessed. The diagnostic accuracy of the bacterial fluorescence imaging device to detect relevant bacteria in burn wounds was moderate and the reliability was equal to standard swabbing. Further research in larger sample sizes is needed for safety and efficacy of the fluorescence imaging device.

Raizman et al. (2019) conducted a prospective comparative study aimed to assess the accuracy, clinical incorporation, and documentation capabilities of a handheld bacterial fluorescence imaging device (MolecuLight *i*:X). In a clinical trial, trained clinicians digitally measured and captured fluorescence images to assess for presence moderate to heavy loads of bacteria in 50 wounds. The results showed wound measurement was accurate 95%. A positive signal for bacterial fluorescence was demonstrated 72%. Sampling of wounds was found to under-report bacterial loads relative to fluorescence-guided curettage samples.

In a pilot study, Serena et al. (2019) evaluated 19 wounds for diagnostic accuracy of wound bacteria when bacterial fluorescence imaging (MolecuLight i:X) was used in combination with clinical evaluation of signs and symptoms (CSS). CCS criteria for wounds to determine the presence or absence of moderate-to-heavy bacterial loads were done using the NERDS (non-healing, exudate, red and bleeding surface or granulation tissue, debris, and smell) and STONEES (size, temperature, osteomyelitis, new areas, exudate, erythema, and smell) method. Then fluorescence images of the wound were acquired along with determination of bacterial presence or absence. Biopsies were obtained under local anesthetic and sent to lab for confirmation; all lab staff were blinded to the wound's assessment outcomes. Four out the 19 participants (21%) were identified as positive (for moderate-to-heavy bacterial loads) based on clinical signs and symptoms alone. The use of fluorescence imaging in combination with CSS assessment led to 2.5–3.2-fold improvements in reported diagnostic accuracy measures as compared with CSS assessment alone. The authors concluded the data in this pilot study suggests that current standard of care assessment for wounds fails to identify many wounds with moderate-to-heavy bacterial loads, leaving participants with undetected and untreated bacteria. The addition of bacterial fluorescence imaging improved sensitivity and accuracy of assessments for detecting moderate-to-heavy bacterial loads. Limitations of this study included small sample size thus not statistically significant and lack of follow-up. Future larger sample studies are needed.

In a prospective observational study, Hurley et al. (2019) swabbed 43 wounds from 33 participants. The authors wanted to establish the accuracy of the wound imaging device at detecting bacteria. All data was collected in the outpatient wound care clinic setting. Participants over 18 were recruited with a variety of wounds; patients on antibiotics for wound infection were excluded. Images from the wounds were captured with the handheld fluorescent device; upon visualization of bacteria, areas of red or cyan fluorescence indicating bacteria were swabbed and sent to the lab for culture and sensitivity testing. Of the swabs taken, 95.4% were positive for bacteria growth and nine different species of bacteria were identified. Limitations included device incompatibility for wounds with active bleeding, dressings that contained silver (a potent

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antimicrobial) and sample size. Despite these limitations, the authors concluded the device as safe, effective, and accurate for use. Further research should be directed to its application in other environments such as preoperative and perioperative settings.

For information on current clinical trials studying the use of MolecuLight i:X and bacterial growth, go to www.clinicaltrials.gov. (Accessed March 20, 2025)

Clinical Practice Guidelines

Association for the Advancement of Wound Care (AAWC)

Members of the Association for the Advancement of Wound Care (AAWC), Wound Healing Society, and the Canadian Association for Enterostomal Therapy formed the International Consolidated Guidelines Taskforce in 2015, to update the AAWC Venous Ulcer Guidelines to the collaborative, intersociety, endorsed International Consolidated Venous Ulcer Guideline. This clinical practice guideline contains systematically developed recommendations intended to optimize patient care and assist physicians and other health care practitioners and participants to make decisions about appropriate health care for venous ulcer (VU) clinical care.

Recommendations include the following:

- Low frequency ultrasound may support healing, reduce pain, and improve QOL of non-healing venous or mixed etiology venous ulcers.
- Use ultrasound stimulation in combination with adequate patient-appropriate compression and moisture-retentive dressings to add possible VU healing benefit, but be aware that limited evidence supports cost effectiveness, enduring benefit, or parameters of application.
- Warming therapy has insufficient evidence of healing efficacy to inform VU management decisions about its use as an adjunct to optimal patient-appropriate compression and moisture-retentive dressings (AAWC, 2015; Couch et al., 2017).

The AAWC also indicates that ultrasound stimulation may be used in combination with adequate patient-appropriate compression and moisture-retentive dressings to add possible VU healing benefit but be aware that limited evidence supports enduring benefit or parameters of application (AAWC, 2015).

In 2010, the AAWC released a guideline on the care of pressure ulcers. While noncontact ultrasound therapy was included as a potential second-line treatment if first-line treatments failed to induce wound healing, the strength of the evidence supporting this decision was low (Level C), indicating that there is limited evidence for this technology.

American Podiatric Medical Association

The American Podiatric Medical Association in collaboration with the Society for Vascular Surgery and the Society for Vascular Medicine developed a 2016 clinical practice guideline for the management of diabetic foot. Their recommendations do not include warming therapy, noncontact normothermic wound therapy (NNWT) or low frequency ultrasound for the treatment of wounds (Hingorani et al. 2016).

National Institute for Health and Care Excellence (NICE)

A National Institute for Health and Care Excellence (NICE) Medtech innovation briefing [MIB212] concluded that there is limited evidence to show whether MolecuLight i:X reduces wound closure time or improves antibiotic stewardship (2020).

The National Institute for Health and Care Excellence (NICE) guideline for diabetic foot problems prevention and management recommends one or more of the following as standard care for treating DFUs: offloading; control of foot infection; control of ischemia; wound debridement; and wound dressings. NICE recommends that negative pressure wound therapy should be considered after surgical debridement for DFUs, on the advice of the multidisciplinary foot care service. Dermal or skin substitutes as an adjunct to standard care can be considered when treating DFUs, only when healing has not progressed, and on the advice of the multidisciplinary foot care service (NICE, 2019; updated 2023).

In a National Institute for Health and Clinical Excellence (NICE) guidance for MIST Therapy® System for the Promotion of Wound Healing in Chronic and Acute Wounds, NICE states that the MIST Therapy® System shows potential to enhance the healing of chronic, hard-to-heal, complex wounds, compared with standard methods of wound management. However, the amount and quality of published evidence on the relative effectiveness of the MIST Therapy® System is not sufficient, at this time, to support the case for routine adoption of the MIST Therapy® System (NICE, 2011, Reaffirmed April 23, 2025).

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U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Warm-Up® Active Wound Therapy (Augustine Medical, Inc.) received 510(k) approval from the FDA on March 28, 1997, as a wound and burn occlusive heated dressing. Refer to the following website for more information (use product code MSA): http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed April 23, 2025)

The Mist Therapy® System is regulated by the FDA as a Class II device and is classified as an ultrasound wound cleaner. This device was approved via the FDA 510(k) process in April 2004. In May 2005, FDA granted marketing clearance to Celleration for the MIST Therapy® System 5.1 with an expanded indication. The approved indication for use is to produce "a low-energy ultrasound-generated mist to promote wound healing through wound cleansing and maintenance debridement by the removal of yellow slough, fibrin, tissue exudates, and bacteria." In 2014 the FDA approved the UltraMIST® System (K140782), a smaller, sleeker, and user-friendly design. Refer to the following website for more information: http://www.accessdata.fda.gov/cdrh_docs/pdf5/K050129.pdf. (Accessed April 23, 2025)

Refer to the following website for additional devices (use product code NRB): https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed April 23, 2025)

The U.S. Food and Drug Administration (FDA) cleared The MolecuLight i:X® device under its 510(k) premarket notification process as substantially equivalent to predicate devices. For additional information refer to the following: https://www.accessdata.fda.gov/cdrh_docs/pdf19/K191371.pdf. (Accessed April 23, 2025)

Refer to the following website for additional devices (use product code QJF or FXN): http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed April 23, 2025)

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Policy History/Revision Information

Date	Summary of Changes
12/01/2025	**Supporting Information** • Updated *Clinical Evidence* and *References* sections to reflect the most current information • Archived previous policy version CS132ID.B

Instructions for Use

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