

UltraMIST[®]

| Ultrasound Healing Therapy

Clinical Evidence Summary





DESCRIPTION AND INDICATIONS FOR USE

Description: The UltraMIST® System delivers low frequency ultrasound to the treatment site using a noncontact fluid (e.g., saline).

Indications for Use: MIST Systems produce a low energy ultrasound-generated mist used to promote wound healing through wound cleansing and maintenance debridement by the removal of fibrin, yellow slough, tissue exudates, and bacteria.

CONTRAINDICATIONS, POTENTIAL COMPLICATIONS, AND WARNINGS

Contraindications: Do not use near electronic implants/prosthesis (e.g., near or over the heart or over the thoracic area if the patient is using a cardiac pacemaker); on the lower back during pregnancy or over the pregnant uterus; over areas of malignancies.

Potential Complications: Tingling, redness

Warnings: UltraMIST® applicator is designed as a single patient-use disposable unit to avoid contamination. Do not resterilize or reuse applicators. Reusing the applicator and/or fluid may result in infection and degraded performance. Do not allow the treatment wand or applicator to contact the patient's skin directly. Risk of burns – do not touch the metal tip of the treatment wand during operation.

For UltraMIST System and supply ordering, refurbishments, technical support, product information, product complaints, adverse reaction reporting, and customer service, please email order@sanuwave.com, or call 770-419-7525.

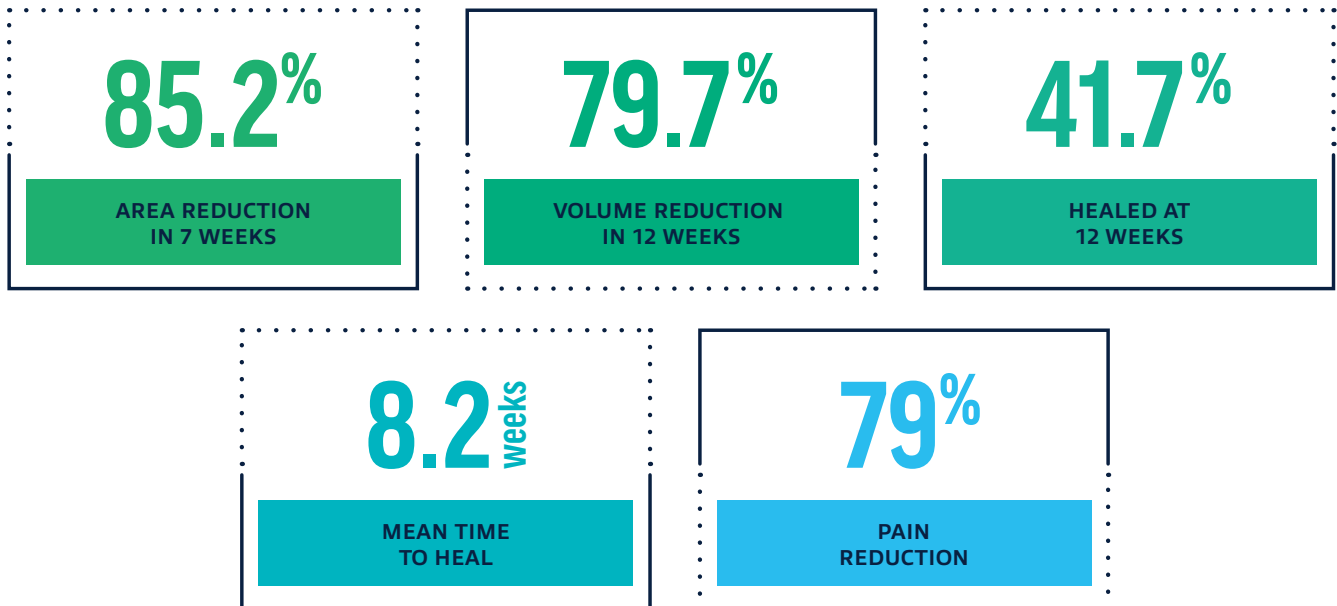
Please refer to the UltraMIST Package Insert for complete product information.

CLINICAL EVIDENCE SUMMARY

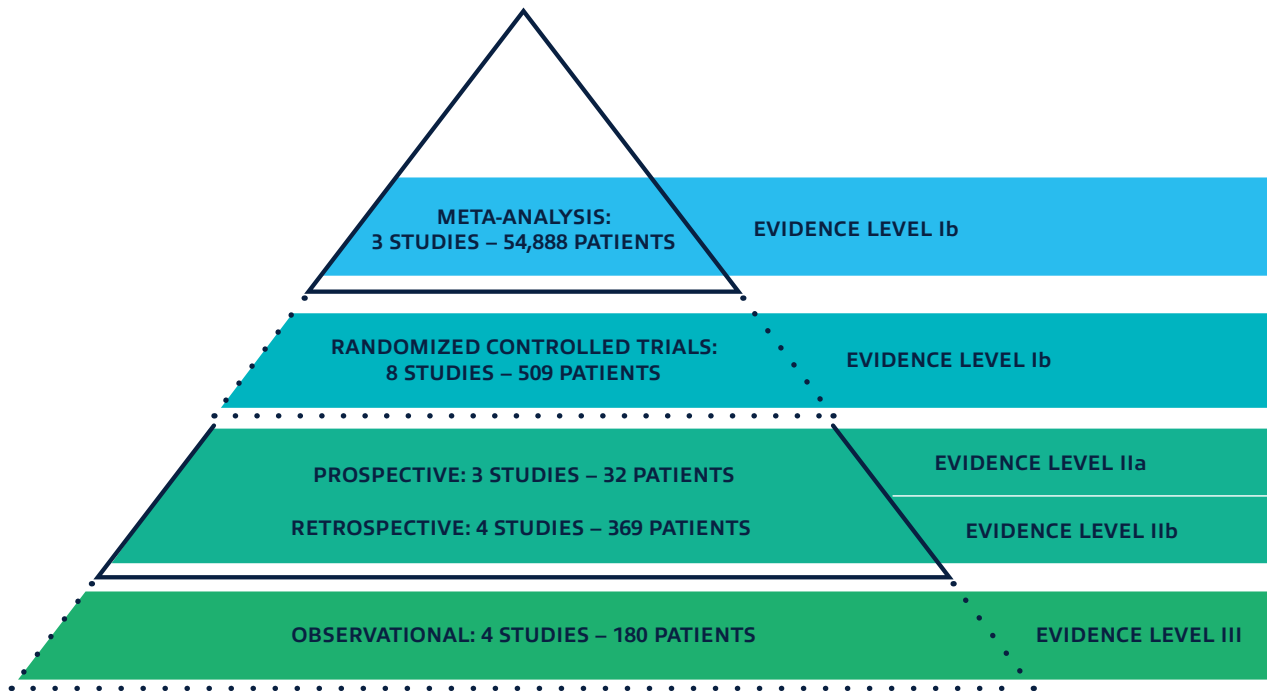
MIST Therapy was introduced into the market in late 2004. The data in this summary was compiled utilizing MIST Therapy. UltraMIST is the next generation of MIST Therapy and maintains the same mechanism of action as the MIST Therapy used these studies. MIST Therapy has been investigated in a variety of Level I-III Clinical Studies including three (3) meta-analysis, eight (8) randomized controlled trials, three (3) prospective, four (4) retrospective, and four (4) observational studies.

In the meta-analysis using only MIST Therapy ultrasound clinical data, eight (8) peer-reviewed studies with consistent designs for treatment and control wound groups were pooled to review the effects of MIST Therapy on healing time, wound size, volume, and pain. Driver et al. concluded that “MIST Therapy demonstrates remarkable consistency of reduction in wound area, volume, pain and healing times across a wide range of wounds.”

Meta-Analysis Findings (Source Driver et al.):



SUMMARY OF CLINICAL DATA



- **Meta-Analysis:** A study of randomized trials with homogeneous results.
- **Randomized Control Trial (RCT):** A study in which patients are randomly assigned to the treatment or control group and are followed prospectively.
- **Prospective Studies:** A study in which patient groups are separated nonrandomly by exposure or treatment, with exposure occurring after the initiation of the study.
- **Retrospective Studies:** A study in which patient groups are separated nonrandomly by exposure or treatment, with exposure occurring before the initiation of the study.
- **Observational Studies:** Research based on following a group of individuals before and after an intervention or service. Each person has their own baseline and control, but there is no formal control (i.e., comparison) group.

TABLE OF CLINICAL EVIDENCE LEVEL I STUDY DETAILS - META-ANALYSIS

LEVEL OF EVIDENCE	PUBLICATION AUTHOR JOURNAL	WOUND POPULATION	MEASUREMENT	MIST RESULT	STANDARD OF CARE RESULT	TREATMENT DURATION	STATISTICS
Ib	Noncontact Low-Frequency Ultrasound Therapy in the Treatment of Chronic Wounds: A Meta-Analysis Driver VR, Yao M, Miller CJ <i>Wound Regeneration and Repair</i> 2011	N=538 Wounds, (463 Treated With MIST)	Wound Closure (N=429)	41.7%	24%	12 Weeks	95% CI (Confidence Interval)
			Wound Area Reduction (N=188)	85.2% Reduction	Not Reported	Mean 7 Weeks	95% CI
		Diabetic Foot, Ischemic, Neuropathic, Venous, Multifactorial Etiology, Pressure, Surgical, Traumatic	Wound Volume Reduction (N=278)	79.7% Reduction	Not Reported	Mean 12 Weeks	95% CI
			Pain Reduction (N=139)	79% Reduction	Not Reported	From Baseline	Not Reported
Ib	Seeking effective interventions to treat complex wounds: an overview of systemic reviews. Tricco A, Antony J, Vafaei A <i>BMC Medicine</i> 2015	54,000	AMSTAR Score ≥ 8	AMSTAR Score ≥ 8 Promising Technology	NA	NA	AMSTAR Score ≥ 8
Ib	Low-frequency ultrasound (20-40 kHz) as an adjunctive therapy for chronic wound healing: a systematic review of the literature and meta-analysis of eight randomized controlled trials. Voigt J, Wendelken M, Driver, V et al <i>Int J Low Extrem Wounds</i>	N=519 Wounds, (444 Treated With MIST)	Complete Healing % Wound Area Reduction	95% Heal at 3 Months 63% >50% Size at 3 Months	29% Sham	12 Weeks	p=0.2 p=0.001

TABLE OF CLINICAL EVIDENCE LEVEL I STUDY DETAILS - RANDOMIZED CONTROL TRIALS

LEVEL OF EVIDENCE	PUBLICATION AUTHOR JOURNAL	WOUND POPULATION	MEASUREMENT	MIST RESULT	STANDARD OF CARE RESULT	TREATMENT DURATION	STATISTICS
Ib	A Prospective, Randomized, Controlled Trial Comparing the Effects of Noncontact, Low-Frequency Ultrasound to Standard Care in Healing Venous Leg Ulcers Gibbons GW, Orgill DP, Serena TE, Novoung A, O’Connell JB, Li WW, Driver VR <i>Ostomy Wound Management</i> 2015	N=112 Enrolled N=81 Randomized	Mean % Wound Area Reduction	61.6% Reduction	45% Reduction	4 Weeks	p=0.02
		Venous Leg Ulcers	Pain VAS Measurement	80% Reduction	20% Reduction		p=0.01
Ib	Prospective, Randomized, Controlled Trial Comparing the Effects of Noncontact, Low-Frequency Ultrasound to Standard Care in Healing Healing Split Thickness Donor Sites Prather JL, Tummel EK, Patel AB, Smith DJ, Gould LJ <i>Journal of American College of Surgeons</i> 2015	N=33 Enrolled N=27 Randomized	Time to First “No Drainage”	12.1 Days	21.3 Days	NA	p=0.04
			Time to 2 Consecutive Visits With No Drainage	16.1 Days	28.1 Days		p=0.02
		Split-Thickness Donor Sites	Time to Adjudicated Fully Epithelialized	18.2 Days	27.5 Days		p=0.03
			Recidivism at 6 Weeks	8%	45%		p=0.06

Level I Study Details continued on next page

TABLE OF CLINICAL EVIDENCE LEVEL I STUDY DETAILS - RANDOMIZED CONTROL TRIALS CONTINUED

LEVEL OF EVIDENCE	PUBLICATION AUTHOR JOURNAL	WOUND POPULATION	MEASUREMENT	MIST RESULT	STANDARD OF CARE RESULT	TREATMENT DURATION	STATISTICS
Ib	Noncontact Low-Frequency Ultrasound Therapy Compared with UK Standard of Care for Venous Leg Ulcers in a Single-Centre, Assessor-Blinded Randomized Control Trial White J, Ivins N, Wilkes A, Carolan-Rees G, Harding KG <i>International Wound Journal</i> 2015	N=47 Enrolled N=36 Randomized	Wound Area	47% Reduction	39% Reduction	Study Population Too Small to Demonstrate Statistical Significance	p=0.565
		Venous Leg Ulcers	Pain	-14.4 Points	-5.3 Points		p=0.078
Ib	Comparison of High-Frequency and MIST Ultrasound Therapy for the Healing of Venous Leg Ulcers Beheshti A, Shafiqh Y, Parsa H, Sangivand A. <i>Advances in Clinical and Experimental Medicine</i> 2014	N=90	Wound Area Reduction	63.7% at 4 Months	46.4% at 4 Months	12 Weeks Followed by SOC	p=0.01
		Venous Leg Ulcers	Mean Time to Healing in Months	5.7	8.13		p<0.0001
			Pain Reduction	55.4% Reduction at 4 Months	33.7% Reduction at 4 Months		p<0.0001
Ib	High-Frequency and Noncontact Low-Frequency Ultrasound Therapy for Venous Leg Ulcer Treatment: A Randomized, Controlled Study Olyaie M, Rad FS, Elahifar MA, Garkaz A, Mahsa G <i>Ostomy Wound Management</i> 2013	N=90	Wound Area Reduction	72.8% at 4 Months	55.4% at 4 Months	12 Weeks Followed by SOC	p=0.04
		Venous Leg Ulcers	Mean Time to Healing in Months	6.65	8.5		p<0.05
			Pain Reduction	47.1% Reduction at 4 Months	17.7% Reduction at 4 Months		p=0.001
Ib	A Pilot Study Evaluating Noncontact Low Frequency Ultrasound and Underlying Molecular Mechanisms on Diabetic Foot Ulcers Yao M, Hasturk H, Kantarci A, Gu G, Garcia-Lavin S, Fabbi M, Park N, Hayashi, H, Attala K, French M, Driver V <i>International Wound Care Journal</i> 2012	N=12	Wound Area Reduction	86% Reduction	39% Reduction	4 Weeks	p<0.05
Ib	Treatment of Ischemic Wounds With Noncontact, Low-Frequency Ultrasound: The Mayo Clinic Experience, 2004-2006 Kavros SJ, Miller JL, Hanna SW <i>Advances in Skin & Wound Care</i> 2007	N=70	>50% Wound Area Reduction	63% Achieved >50% Reduction	29% Achieved >50% Reduction	12 Weeks	p<0.001
		Ischemic, Neuropathic, Venous, Multifactorial					
Ib	Ultrasound Therapy for Recalcitrant Diabetic Foot Ulcers: Results of a Randomized, Double-Blind, Controlled Multicenter Study Ennis WJ, Formann P, Mozen N, Massey J, Conner-Kerr T, Meneses P <i>Ostomy Wound Management</i> 2005	N=55	Wound Closure	40.7%	14.3%	12 Weeks	p<0.0366
		Diabetic Foot Ulcers					

TABLE OF CLINICAL EVIDENCE LEVEL II STUDY DETAILS

LEVEL OF EVIDENCE	PUBLICATION AUTHOR JOURNAL	WOUND POPULATION	MEASUREMENT	MIST RESULT	STANDARD OF CARE RESULT	TREATMENT DURATION	STATISTICS
II a	Healing Rate of Chronic and Subacute Lower Extremity Ulcers Treated With Contact Ultrasound Followed by Noncontact Ultrasound Therapy: The VIP Ultrasound Protocol Viana L, Pompeo M	N=11	Wound Size Reduction	>99% Improvement	NA	12 Weeks	p=0.02
II a	A Prospective Pilot Study of Ultrasound Therapy Effectiveness in Refractory Venous Leg Ulcers Escandon J, Vivas AC, Perez R, Kirsner R, Davis S <i>International Wound Journal</i> 2012	N=10 Venous Leg Ulcers	Wound Area Reduction	45% Reduction	Failure to Improve in Previous 30 Days	4 Weeks	p<0.0039
II a	The Impact of Noncontact, Nonthermal, Low-Frequency Ultrasound on Bacterial Counts in Experimental and Chronic Wounds Serena T, Lee SK, Lam K, Attar P, Meneses P, Ennis W <i>Ostomy Wound Management</i> 2009	N=11 Pressure Ulcers (Stage III)	Wound Volume Reduction Wound Area Reduction	20% Reduction 26% Reduction	NA	2 Weeks	Not Reported
II b	Effects of Noncontact Low-Frequency Ultrasound on Healing of Suspected Deep Tissue Injury: A Retrospective Analysis Honaker JS, Forston MR, Davis EA, Wiesner MW, Morgan JA <i>International Wound Care Journal</i> 2012	N=85 (127 sDTI) Deep Tissue Injuries (Pressure Ulcers)	Wound Evolution/Resolution at Hospital Discharge Severity Scale Assessment	Resolved 18% Stage II 62% DTI 5% Stage III, IV unstageable 15%	2% 21% 30% 48%	10 MIST Treatments Over 21 Days	Not Reported p<0.000
II b	Expedited Wound Healing with Noncontact, Low-Frequency Ultrasound Therapy in Chronic Wounds: A Retrospective Analysis Kavros SJ, Liedl DA, Boon, AJ, Miller JL, Hobbs JA, Andrews KL <i>Advances in Skin and Wound Care</i> 2008	N=210 Ischemic, Venous, Neuropathic, Multifactorial	Wound Closure	53% in Mean of 147 Days	32% in Mean of 134 Days	SOC Followed by 90 Days MIST Treatment or Until Healed	p=0.0009
II b	Use of Noncontact Low-Frequency Ultrasound in the Treatment of Chronic Foot and Leg Ulcerations Kavros SJ, Schenck EC <i>J of American Podiatric Medical Assn</i> 2007	N=51 Chronic Lower Leg and Foot Ulcers, Multifactorial, Arterial, Diabetic	Wound Closure Wound Volume Reduction	51% 94.9± 9.8% Reduction	0% Patients Were Treated With SOC Prior to Starting MIST 37.3± 18.6% Reduction	MIST Mean 5.5±2.8 Weeks SOC Mean 9.8±5.5 Weeks	p<0.05 p<0.0001
II b	Evaluation of Clinical Effectiveness of MIST Ultrasound Therapy for the Healing of Chronic Wounds Ennis WJ, Valdes W, Gainer M, Meneses P. <i>Advances in Skin and Wound Care</i> 2006	N=23 (29 Wounds) Diabetic, Ischemic, Venous, Pressure, Postoperative, Inflammatory	Wound Closure	MIST Only 69% MIST Assisted*** 73.3%	<15% Area Reduction in 2 Week Prior to MIST	6.82 Weeks 10.47 Weeks	Not Reported Not Reported

TABLE OF CLINICAL EVIDENCE LEVEL III STUDY DETAILS

LEVEL OF EVIDENCE	PUBLICATION AUTHOR JOURNAL	WOUND POPULATION	MEASUREMENT	MIST RESULT	STANDARD OF CARE RESULT	TREATMENT DURATION	STATISTICS
III	Adjuvant Use of Acoustic Pressure Wound Therapy* for Treatment of Chronic Wounds Cole PS, Quisberg J, Melin MM <i>J Wound Ostomy Continence Nursing</i> 2009	N=41 (52 Wounds)	Wound Closure	38%	<15% Wound Area Reduction in 2 Weeks Prior to MIST	Mean 6.8 Weeks	Not Reported
			Wound Area Reduction	88% Reduction		Mean 7.6 Weeks	p<0.0001
		Pressure, Venous, Arterial, Surgical, Traumatic, Other	Wound Volume Reduction	100% Reduction			p<0.0001
			Pain Visual Analog Scale*	2.9 Reduction	NA		p<0.0001
III	A Retrospective Analysis of Acoustic Pressure Wound Therapy*: Effects on the Healing Progression of Chronic Wounds Haan J, Lucich S <i>J American College of Certified Wound Specialists</i> 2009	N=48 (50 Wounds)	Wound Closure	24%	<15% Wound Area Reduction in 2 Weeks Prior to MIST	Mean 4.2 Weeks	Not Reported
		Pressure, Venous, Arterial, Surgical, Traumatic, Neuropathic, Other	Wound Area Reduction	92% Reduction		Mean 5.5 Weeks	p<0.0001
			Pain Visual Analog Scale*	1.8 Reduction	NA		p<0.0001
III	Noncontact Ultrasound Therapy for Adjunctive Treatment of Nonhealing Wounds: Retrospective Analysis Bell AL, Cavorsi J <i>PT Journal</i> 2008	N=76	Wound Closure	18%	<15% reduction in 2 weeks prior to MIST	Median 3.6 Weeks	Not Reported
			Wound Area Reduction	79% Reduction		Median 4.3 Weeks	p<0.0001
		Pressure, Venous (28), Arterial, Surgical/Traumatic (25), Other	Pain Visual Analog Scale*	1.8 Reduction	NA		p=0.001
III	The Effect of Noncontact, Low-Intensity, Low-Frequency Therapeutic Ultrasound on Lower-Extremity Chronic Wound Pain: A Retrospective Chart Review Gehling ML, Samies JH <i>Ostomy Wound Management</i> 2007	N=15 Venous, Ischemia, Sickle cell	Pain Visual Analog Scale*	80% Reduction (8.07±1.91 to 1.67±1.76) VAS	Baseline	2-4 Weeks	p=0.0003

*Visual Analog Scale is used to assess pain with a 10-point numeric pain scale.

**Acoustic Pressure Wound Therapy, Noncontact Low Frequency Ultrasound, and MIST Therapy are all interchangeably used in the clinical studies.

***Addition of Apligraf.