



**Australian Government**  
**Department of Health and Ageing**



Horizon Scanning Technology  
Prioritising Summary  
Low frequency ultrasound debridement  
February 2007



**Australian  
Safety  
and Efficacy  
Register  
of New  
Interventional  
Procedures -  
Surgical**



**Royal Australasian  
College of Surgeons**

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The production of this Horizon scanning prioritising summary was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from health departments in all states and territories, the Australia and New Zealand governments; MSAC and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

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# PRIORITISING SUMMARY

**REGISTER ID:** S000014

**NAME OF TECHNOLOGY:** LOW FREQUENCY ULTRASOUND DEBRIDEMENT

**PURPOSE AND TARGET GROUP:** PATIENTS SUFFERING FROM CHRONIC LEG ULCERS

## STAGE OF DEVELOPMENT (IN AUSTRALIA):

- |   |   |
|---|---|
| <input checked="" type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established  |
| <input type="checkbox"/> Experimental             | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational          | <input type="checkbox"/> Should be taken out of use   |
| <input type="checkbox"/> Nearly established       |   |

## AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- |  |             |     |
|--|-------------|-----|
| <input type="checkbox"/> Yes                       | ARTG number | N/A |
| <input type="checkbox"/> No                        |             |     |
| <input checked="" type="checkbox"/> Not applicable |             |     |

## INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Europe	✓		
United Kingdom	✓		
United States	✓		

## IMPACT SUMMARY:

Low frequency ultrasonic debridement can be conducted with a range of devices. The studies included within this summary utilised either a custom investigational ultrasonic applicator, the Sonoca 180 Ultrasonic Debridement Device (Söring Inc., Germany), or the MIST™ Therapy System (Celleration Inc., United States). This procedure can be performed by a nurse with adequate training in the treatment of chronic wounds/ulcers.

## **BACKGROUND**

Chronic ulceration of the lower limb is a major cause of morbidity in most human populations and therefore results in significant economic burden as well. Most leg ulcers develop as a result of predisposing conditions, with chronic venous insufficiency accounting for the majority (60 – 90%) of chronic leg ulcers (Weichenthal et al. 1997). A large majority of chronic venous ulcers respond to appropriate compression therapy; however there are some forms of ulcers that are refractory to all forms of therapy (Tan et al. 2006). Previous studies have established that wound healing is dependent on adequate wound-bed preparation; including tissue debridement and infection control (Breuing et al. 2005). Wound debridement has been shown to accelerate healing compared to conservative treatment, and the reduction of bacterial load and bioburden achieved is considered critical for undisturbed wound healing and successful skin grafting. Previous studies have concluded that therapeutic ultrasound is capable of accelerating wound healing, while more recent studies have revealed that low frequency ultrasound (20 – 120 kHz) may be capable of accelerating healing via debridement with lower levels of pain or discomfort (Tan et al. 2006). The non-thermal effects of ultrasound that aid debridement are cavitation, formation of gas bubbles and streaming, unidirectional, steady mechanical force applied to all exposed surfaces.

## **CLINICAL NEED AND BURDEN OF DISEASE**

As stated previously, chronic leg ulceration is a major cause of morbidity and is common within the western population, affecting more than 1% of the population (Tan et al. 2006, Weichenthal et al. 1997). In the United Kingdom, the treatment cost of chronic leg ulcers is greater than £1 billion a year. There is no data on the collective impact of prevalence, incidence and economic burden of wounds in Australia. However, studies have shown that the prevalence of leg ulcers in Australia is increasing (Baker et al. 1991), and therefore so is the cost to the healthcare system.

## **DIFFUSION**

There is no published data reporting the use of ultrasound debridement for chronic leg ulcers in Australia. If low frequency ultrasound is proven to be safe, efficacious and comparably better than current debridement techniques, it is likely to be adopted rapidly into the healthcare system.

## **COMPARATORS**

- *Sharp debridement*  
This technique utilises handheld knives (Goulian/Weck or Watson) and is the current standard for wound debridement.
- *Autolytic debridement*  
Autolysis uses the body's own enzymes and moisture to re-hydrate, soften and finally liquefy hard eschar and slough. It is often a slow and unpredictable process. Patients with ongoing necrosis can get septic, develop invasive infection, become malnourished and experience pain.
- *Enzymatic debridement*  
This technique utilises chemical enzymes, fast acting products that produce slough of necrotic tissue. It appears to be effective in patients with minimal necrotic, load but is time consuming and labour intensive.
- *Mechanical debridement*  
Utilising the 'wet to dry' technique where a moist dressing is applied and peeled off when dry to remove debris and tissue. This is a painful and non-specific process.
- *Laser debridement*

Lasers appear to be efficient and precise when utilised in tissue ablation, however they carry the risk of thermal damage to healthy tissue.

- *Maggot therapy*  
Maggots are utilised to ingest and break down necrotic tissue. While this technique is effective, it carries a high level of patient and nursing non-acceptance.
- *Water debridement*  
This technique utilises a high pressure water jet, such as the Versajet™ hydrosurgery system, to debride wounds.

### SAFETY AND EFFECTIVENESS ISSUES

A recent randomised controlled trial (Ennis et al. 2005) evaluating the safety and efficacy of low frequency ultrasound (LFU) debridement (40 kHz) enrolled 133 patients with recalcitrant diabetic foot ulcers. However due to losses to follow-up and protocol violations, a final population of 55 patients was deemed suitable for evaluation. All patients received standard wound care treatment with complete dressing changes 3 times a week. Patients randomised to LFU treatment received 4 minute treatment sessions where the device transferred the ultrasound vibrations (40 kHz, 0.1 W/cm<sup>2</sup> to 0.5 W/cm<sup>2</sup>) to the wound via a stream of ultrasound generated mist from a transducer horn made on titanium alloy. The device was held 5 – 15 mm away from the wound. For the sham treatment group, a custom sham device was produced for this study to achieve identical performance parameters. At 12-weeks post-treatment, 11/27 (40.7%) patients in the LFU group achieved complete healing, compared to 4/18 (14.3%) patients in the sham treatment group (p = 0.0366) (Table 1).

**Table 1: Proportion of wound healed at 12-weeks follow-up assessment.**

	Efficacy group (n=55)			Intent-to-treat (n=133)		
	LFU	Sham	Total	LFU	Sham	Total
<b>Closed (n, %)</b>	11 (40.7%)*	4 (14.3%)*	15 (27.3%)	18 (26%)	14 (22%)	32 (24%)
<b>Not closed (n, %)</b>	16 (59.3%)	24 (85.7%)	40 (72.7%)	52 (74%)	49 (78%)	101 (76%)
<b>Total (n)</b>	27	28	55	70	63	133

\* Fisher's exact test p = 0.0366, Chi square p = 0.022

Ennis et al. (2005)

Time to healing was significantly shorter for the LFU group (mean: 9.12 ± 0.58 weeks; median: 11 ± 0 weeks) compared to the sham group (mean: 11.74 ± 0.22 weeks, median: 12 ± 0.82 weeks) (log rank p < 0.0144). Initial, post-debridement quantitative culture biopsies taken at enrolment showed that 86% of the LFU group had > 100,000 colonies/g of tissue compared to 93% in the sham group; however this difference was not statistically significant. Utilising intention-to-treat analysis, a total of 193 adverse events were reported for the 133 patient cohort. However there were no statistically significant differences in the number or severity of adverse events between the two groups. The investigators stated that 83% of the reported adverse events were not related to the study or sham treatment devices. Four patients experienced pain during treatment, 3 (10.7%) in the sham group and one (3.7%) in the LFU group. Wound infection was observed in two LFU patients (7.4%) (Ennis et al. 2005).

The randomised controlled trial by Weichenthal et al. (1997) examined the safety and effectiveness of low frequency ultrasound debridement for chronic leg ulcers in 38 patients. Patients randomised to receive conventional treatment (n = 18, one patient excluded due to arterial vascular disease) received topical application of fibrinolytic agents, antibiotics or other antiseptic agents, and occlusive dressings. Meanwhile, patients randomised to LFU treatment (n = 19) received 30 kHz ultrasound with an intensity of 100mW/cm<sup>2</sup> surface area for 10 minutes, three times a week utilising a custom experimental ultrasound applicator mounted on a foot bath (transducer positioned 5 cm from ulcer). Following ultrasound therapy, patients received conventional treatment as well. One patient (5%) from the LFU

group experienced severe pain during treatment, while 7 patients (37%) experienced moderate pain, the remaining patients (58%) experienced little to no pain during treatment. The following table presents the ulcerated area before and during treatment for both patient groups:

**Table 2: Ulcerated area before and during treatment with low frequency ultrasound treatment**

Treatment group	Ulcerated area (cm <sup>2</sup> )		
	Before therapy	3 weeks	8 weeks
<b>Controls</b>	14.8 ± 10.2	14.7 ± 10.4	13.4 ± 12.1
<b>Low frequency ultrasound</b>	10.6 ± 7.8	8.3 ± 6.4*	6.2 ± 5.9**

Values are expressed as mean ± standard deviation; \*p < 0.005; \*\*p < 0.01

Weichenthal et al. (1997)

The results (Table 2) indicate that a significant reduction in ulcer size was achieved in the LFU group at weeks 3 and 8 of treatment while the controls did not achieve significant reduction in ulcer size. Overall, the response (ulcer size reduction) was shown to be significantly better within the ultrasound group (96%) compared to controls (75%) at 3 weeks treatment (p < 0.005). This observation was sustained at 8 weeks with 87% of LFU patients experiencing ulcer size reduction compared to 57% in controls (p < 0.025). It is interesting to note that after 8 weeks of LFU treatment, 3 patients did not experience any further change, while 6 patients experienced 10 – 50% reduction in size, 8 patients experienced 50 – 99% reduction in size and 1 patient had complete healing (100% reduction). Reduction of ulcer size was not found to be related to age, post-thrombotic status or duration of the ulcer before study entry. In addition, the authors noted that there was no influence of the pre-treatment ulcer area on the relative reduction of ulcer size in both groups (Weichenthal et al. 1997).

A recent case series by Tan et al. (2006) examined the benefits of 25 kHz LFU in 19 patients with chronic leg ulceration. LFU treatment was applied for 10 – 20 seconds per probe head area (1 cm x 1 cm) onto the edges and surfaces of the ulcers, and patients received a minimum of 5 treatments at an interval of 2 to 3 weeks. Isotonic normal saline was utilised as a coupling/irrigation medium between the handheld probe and the ulcer. One patient was excluded due to non-compliance. Three patients (15.8%) experienced mild pain at the start of the treatment; however there was a noticeable reduction in pain on subsequent treatments with no pain reported by the third treatment session. No major complications were observed throughout the study. The outcomes of LFU treatment at 12-weeks post-treatment are presented in Table 3.

**Table 3: Outcomes at 12-week follow-up after low frequency ultrasound treatment**

Ulcer type	No.	Mean		No. of treatment	Percentage heal
		Initial ulcer size (cm <sup>2</sup> )	Duration per treatment (min)		
Rheumatoid	3	3.6 ± 2.6	9.6	18	33
Sickle	2	4 ± 1.13	10	13	100
Venous	13	6.56 ± 3.39	10.25	72	31 <sup>∞</sup>
<b>Total</b>	<b>18*</b>			<b>103</b>	<b>38.9</b>

\*One patient excluded due to non-compliance to protocol and was excluded from analysis

<sup>∞</sup>One additional patient achieved complete healing outside the 12-week follow-up period

Tan et al. (2006)

Complete healing was achieved in 38.9% of patients at 12-weeks post-LFU treatment. However, 55% of patients showed no visible changes in the ulcer area during the treatment period. In all patients who achieved complete healing, a response to LFU treatment was noted within the first 5 sessions. At the end of the 16-week follow-up period, one additional patient began to show gradual reduction in ulcer size, finally achieving complete healing at 21 weeks (Tan et al. 2006).

Breuing et al. (2005) provided further support on the effectiveness of LFU therapy in a group of 17 patients with acute and chronic wounds of varying aetiology. These patients also received adjunct wound therapy, which included moist dressings, alginate and Panafil. A total of nine wounds (47%) healed primarily or were sufficiently debrided to receive skin grafting or flap procedure, while six wounds (29%) achieved greater than 50% healing. The remaining 2 wounds achieved 20% and 30% healing of the original wound area. It should be noted that due to the varying aetiology of wounds within this patient cohort, the frequency of treatment varied substantially, ranging from twice weekly to fortnightly sessions and the average number of treatments per wound ranged from 6 to 15 over the 3-month period (Breuing et al. 2005).

## **COST IMPACT**

The studies included in this summary utilised different equipment to achieve LFU debridement. Two studies, Breuing et al. (2005) and Tan et al. (2006) utilised the Sonoca 180 Ultrasonic Debridement Device (Söring Inc., Germany), meanwhile Weichenthal et al. (1997) utilised a custom experimental 30 kHz ultrasound applicator mounted to a foot bath. The randomised controlled trial by Ennis et al. (2005) utilised the MIST™ Therapy System (Celleration Inc., United States). We were unable to obtain the costs of these devices.

The Medicare Benefits Schedule reimbursement fees for wound debridement are listed in Table 4:

**Table 4: Medical Benefits Schedule of fees for procedures related to wound debridement (Medicare Australia 2006)**

<b>Category</b>	<b>Item Number</b>	<b>Benefit (AUD)</b>	<b>Number of Claims (July 2005 to June 2006)</b>
Debridement of wound of soft tissue, traumatic, deep or extensively contaminated, under general anaesthesia or regional or field nerve block, including suturing of that wound when performed.	30023	\$288.10	13798
Debridement of extensively infected post-surgical incision or Fournier's Gangrene, wound of soft tissue, under general anaesthesia or regional or field nerve block, including suturing of that wound when performed.	30024	\$288.10	207

## **ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS**

No issues were identified from the retrieved material.

## **OTHER ISSUES**

No issues were identified from the retrieved material.

## **HEALTHPACT CONCLUSION**

The evidence available indicates that LFU debridement is capable of promoting significant wound healing compared to conventional wound dressing with antiseptic agents. HealthPACT has recommended that further assessment of this technology is no longer warranted.

- |  |  |
|--|--|
| <input type="checkbox"/> Horizon Scanning Report | <input type="checkbox"/> Full Health Technology Assessment |
| <input type="checkbox"/> Monitor                 | <input checked="" type="checkbox"/> Archive                |
| <input type="checkbox"/> Refer                   | <input type="checkbox"/> Decision pending                  |

### **SOURCES OF FURTHER INFORMATION:**

Celleration Inc. MIST therapy system. Last updated 2006. <http://celleration.com/products.htm> [Accessed December 2006].

Söring Inc. Sonaca. Last updated 2006. <http://www.soering.de/> [Accessed December 2006].

Peschen M, Weichenthal M, Schopf E, Vanscheidt W. Low-frequency ultrasound treatment of chronic venous leg ulcers in an outpatient therapy. *Acta-dermato-venereologica* 1997; 77(4): 311-314.

### **LIST OF STUDIES INCLUDED**

Total number of studies            4  
Level II and level IV intervention evidence

### **SEARCH CRITERIA TO BE USED:**

Debridement  
Ultrasonic therapy/methods\*  
Wound healing  
Ultrasound

### **REFERENCES:**

Baker SR, Stacey MC, Joop-McKay AG, Hoskin SE, Thompson PJ. Epidemiology of chronic venous ulcers. *British Journal of Surgery* 1991;78(7): 864-867.

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Ennis WJ, Formann P, Mozen N, Massey J, Conner-Kerr T, Meneses P. Ultrasound therapy for recalcitrant diabetic foot ulcers: Results of a randomised, double-blind, controlled, multicenter study. *Ostomy Wound Management* 2005; 51(8): 24-39.

Medicare Australia. Last updated 2006. <http://www9.health.gov.au/mbs/> [Accessed December 2006].

Tan J, Abisi S, Smih A, Burnand KG. A painless method of ultrasonically assisted debridement of chronic leg ulcers: A pilot study. *European Journal of Vascular and Endovascular Surgery* 2006 [Epub ahead of print].

Weichenthal M, Mohr P, Stegmann W, Breitbart EW. Low-frequency ultrasound treatment of chronic venous ulcers. *Wound Repair and Regeneration* 1997; 5(1): 18-22.