Australian Government

Department of Health and Ageing

Australia and New Zealand Horizon Scanning Network

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AN INITIATIVE OF THE NATIONAL, STATE AND TERRITORY GOVERNMENTS OF AUSTRALIA AND THE GOVERNMENT OF NEW ZEALAND

National Horizon Scanning Unit
Horizon scanning prioritising summary

Volume 8, Number 2:

SonoPrep Ultrasonic Skin Permeation system for skin preparation prior to cutaneous penetration.

February 2005

AHTA

Adelaide Health Technology Assessment

Electronic copies can be obtained from http://www.horizonscanning.gov.au

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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: **000138**

NAME OF TECHNOLOGY: **SONOPREP® ULTRASONIC SKIN PERMEATION SYSTEM**

PURPOSE AND TARGET GROUP: **SKIN PREPARATION WITH ULTRASOUND PRIOR TO CUTANEOUS PENETRATION**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☒	Yet to emerge	☐	Established
☐	Experimental	☐	Established *but* changed indication or modification of technique
☐	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐	Yes	ARTG number	
☒	No	☐	Not applicable

INTERNATIONAL UTILISATION:

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

IMPACT SUMMARY:

The Sontra Medical Corporation provides the SonoPrep® Ultrasonic Skin Permeation System with the aim of pre-treating skin prior to the application of topical anaesthetic. The device is not yet available in Australia but was approved for clinical use in the United States in August 2004 (US Food and Drug Administration, 2004).

BACKGROUND

Topical anaesthetics are used to reduce local pain caused by cutaneous procedures such as venipuncture injections and lumbar punctures and require at least 30 – 60 minutes to achieve localised numbness. The SonoPrep® Ultrasonic Skin Permeation System device aims to significantly reduce this waiting time to analgesia. The SonoPrep® Ultrasonic Skin Permeation System is indicated for the rapid production of local dermal anaesthesia using topical over the counter (OTC) lidocaine (4%). Lidocaine is used as a skin preparation prior to transdermal drug delivery and/or to extract interstitial fluid for diagnostic purposes, eg glucose monitoring.

The SonoPrep® device consists of a battery operated power and control unit, a hand piece containing the ultrasonic probe, a coupling medium disposable cartridge and a return electrode. The SonoPrep® device applies a relatively low ultrasonic frequency energy to the skin for 15 seconds. The ultrasonic horn contained in the hand piece vibrates at 55,000 times per second (55KHz) and applies the energy to the skin through the liquid coupling medium to create cavitation bubbles that expand and contract. Ultrasonic cavitation disorganises the lipid bi-layer of the stratum corneum, creating reversible micro-channels in the skin through which fluids and analytes can be extracted and large molecules, such as medications, can also be delivered (Sontra Medical 2004). Once the level of skin permeation is achieved, based on a

reduction in skin impedance that is measured by current moving through the return electrode, the device automatically shuts itself off (Sontra Medical 2004).

Increasing skin permeability (sonophoresis), to allow for transdermal drug delivery, has some advantages compared to conventional drug delivery methods (oral or injection). They include steady delivery and better patient compliance, reduced gastrointestinal degradation in the patient and/or reduced necessity for a first-pass metabolism by the liver (Lavon and Kost 2004).

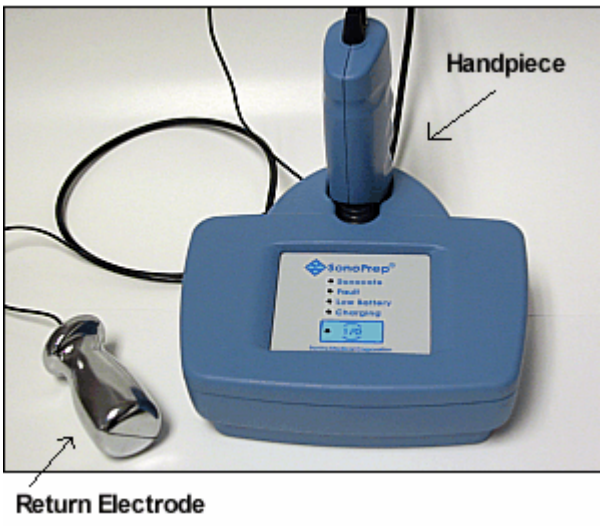

Figure 1. SonoPrep® Skin Permeation Device, (Printed with permission: Sontra Medical Corporation, 2004)

CLINICAL NEED AND BURDEN OF DISEASE

SonoPrep® can be applied to a wide range of patient groups. Published studies of the device have reported its use in the following populations: diabetic patients requiring continuous glucose monitoring and for patients requiring cutaneous anaesthesia in an Emergency Department setting. It is not possible to quantify the number patients requiring cutaneous anaesthesia prior to a needle insertion or intravenous procedure. In particular, the Sonoprep® pre-treatment followed by the application of a eutectic mixture of local anaesthetics (EMLA) cream, would have likely relevance to child patient groups where injections can be difficult to administer.

DIFFUSION

The SonoPrep® is not currently approved for use outside of the United States. The company is seeking international approval, including Australia in 2005 (personal communication, Sontra company representative). It was not possible to ascertain how widely used the device is in the United States at the time of writing this summary, as the device was approved by the FDA in August 2004.

COMPARATORS

The existing comparators are conventional drug delivery methods such as oral administration and subcutaneous or intravenous injection.

EFFECTIVENESS AND SAFETY ISSUES

See complete volume of Prioritising Summaries for definitions of Levels of Evidence.
The SonoPrep® was tested in a randomised controlled trial (level II Intervention evidence) in an Emergency Department setting on 104 adult patients prior to receiving intravenous cannulation (Becker et al 2004). This study shows that in conjunction with EMLA, the SonoPrep® was better than no local anaesthetic cream in reducing pain during intravenous cannulation.

One group of patients received SonoPrep® treatment and a five minute application of topical anaesthetic (4% liposomal lidocaine cream) prior to cannulation , while the control group received IV insertion with no ultrasound or topical anaesthetic. The cannulation site was observed after ultrasound treatment, after removal of the topical anesthetic and 20 to 36 hours following ultrasound treatment. Pain scores were dichotomised using a cut-off of "greater than three" vs. "less than or equal to three" on a Visual Analogue Scale . Pain scores for both groups in this study are as follows:

	Control (n = 49)	Sonoprep® treated (n = 45)
Pain ≤ 3	18 (37%)	36 (80%)
Pain >3	31 (63%)	9 (20%)

P <0.0001

The authors conclude that treatment with the SonoPrep® decreased time to anaesthesia from 30 minutes to five minutes as the pain scores in the treatment group at five minutes of topical anaesthetic application indicated less pain. The EMLA cream used for this study was intended to take 30 minutes to achieve localised numbness.

A randomised, double blinded crossover trial (level II Intervention evidence) compared the onset and effectiveness of cutaneous anaesthesia using ultrasound pre-treatment with the Sonoprep® or no pre-treatment in 42 healthy volunteers (Katz et al 2004). This study assessed four treatment groups: ultrasound pre-treatment with the SonoPrep® and onset of cutaneous analgesia with EMLA cream at 5, 10 and 15 minutes; and the application of EMLA cream at 60 minutes, without SonoPrep® pre-treatment. A placebo cream was applied to the control group, utilising the same pre-treatment (or no pre-treatment) and time conditions (see Table 1).

Each person was assessed for adverse events and any notable effect on skin appearance immediately after the intervention and at 24-48 hours after treatment. There were no adverse events arising from treatment with the device. Cutaneous anaesthesia was assessed by pain score with a 20 gauge needle prick and patient preference for EMLA or placebo cream. Results from this study are presented in table 1 below.

Table 1. Comparison Between Effectiveness of EMLA and Placebo Creams with SonoPrep® pre-treatment at 3 time points and at 60 minutes without pre-treatment: Pain Score

	5 min (with SonoPrep®) (n = 20)	10 min (with SonoPrep®) (n = 22)	15 min (with SonoPrep®) (n=20)	60 min (withoutSonoPrep®) (n = 22)
Pain score				
EMLA cream	0.30 (0.31)	0.20 (0.26)	0.12 (0.20)	0.30 (0.38)
Placebo cream	0.74 (0.29)	0.64 (0.31)	0.74 (0.31)	0.65 (0.33)
Treatment difference				
Mean difference	- 0.44	- 0.44	- 0.62	- 0.35
95% CI	- 0.69 to – 0.20	-0.67 to – 0.20	-0.87 to – 0.38	- 0.58 to –0.12
Difference P value				
ANOVA test	0.0004	<0.0001	<0.0001	0.001
Van Elteren test	0.004	0.0006	0.0002	0.006

Data for pain score are mean (SD). The pain score was the mean of 5 individual pin pricks, each scored by the subject either 1 ("sharp"), 0.5 ("less sharp"), or 0 ("dull"). Treatment difference in mean pain score (EMLA cream – placebo cream). A negative value indicates less pain (better efficacy) with EMLA than placebo cream.

Compared to the usual 60 minute duration required to produce an anaesthetic effect for EMLA cream alone, the efficacy of EMLA cream with the SonoPrep® at all the time points performed at least as well at producing pain relief and eliciting patient preference. The study authors concluded that the SonoPrep® produced rapid onset of anaesthesia with EMLA cream as early as five minutes compared to standard time of 60 minutes without ultrasound treatment.

Although both of these studies have assessed rapid onset of local anaesthesia through the stratum corneum, the SonoPrep® has not been tested in clinical procedures requiring deeper penetration of the cutaneous structures.

In addition, the SonoPrep® has been tested (level IV Intervention evidence) in diabetic patients to assess whether transdermal glucose monitoring can be achieved with ultrasonically permeated skin (Chuang et al 2004). In this clinical pilot study glucose biosensors were placed over 20 skin sites in 10 people treated with the SonoPrep®, with blood glucose readings taken every 20 minutes over an 8-hour period. There were no reported adverse reactions from the use of the device. Although the Sonoprep® was shown to enable transdermal glucose monitoring with the use of the glucose flux biosensor in this study, the accuracy of this approach to measuring blood glucose has not been compared with other continuous measurement devices or the self-monitoring method.

COST IMPACT

The SonoPrep® system has a list price of $US1,995 and procedure trays are $8. Each tray is for single patient use and provides the materials for treating up to three sites on the same patient. The lidocaine is sold separately at $US200 for a case of 50 – 1gram pouches, enough for treating between 3 and 4 locations. The manufacturer allows the SonoPrep® to be available on a loan basis: when $2400 is spent on procedure trays and/or lidocaine pouches the purchaser receives the use of the SonoPrep® for free on the condition that product is used. The reduction in time to achieve cutaneous anaesthesia could potentially result in quicker treatment times in a hospital setting.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

It is worth noting the ethical imperative to reduce pain in people when it is possible to do so. In addition, early effective topical anaesthesia for children may relieve attendant anxieties associated with cutaneous penetration in all types of medical settings.

OTHER ISSUES

No issues were identified/raised in the sources examined.

CONCLUSION:

A randomised, controlled trial with the SonoPrep® comparing its use with EMLA cream alone in achieving local anaesthesia and in reducing pain associated with percutaneous interventions is currently being conducted. SonoPrep® has potential for use for diabetic patients

HEALTHPACT ACTION:

It is recommended that the following a Horizon Scanning Report be conducted.

SOURCES OF FURTHER INFORMATION:

Becker, B., Helfrich, S., Baker, E., Lovgren, K., Minugh, A., Machan, J.T. (2004) 'Ultrasound with topical anesthetic rapidly decreases pain of intravenous sticks.' Presented at the Society for Academic Emergency Medicine, May15-17, 2004, Orlando, FL.

Chuang, H., Taylor, E. & Davison, T. W. (2004). 'Clinical evaluation of a continuous minimally invasive glucose flux sensor placed over ultrasonically permeated skin', *Diabetes Technol Ther,* 6 (1), 21-30.

Katz, N. P., Shapiro, D. E. Herrmann, T.E., Kost, J., Custer, L.M. (2004). 'Rapid onset of cutaneous anesthesia with EMLA cream after pretreatment with a new ultrasound-emitting device', *Anesth Analg*, 98 (2), 371-376.

Lavon, I. & Kost, J. (2004). 'Ultrasound and transdermal drug delivery', *Drug Discov Today*, 9 (15), 670-676.

Mitragotri, S. & Kost, J. (2000). 'Low-frequency sonophoresis: a noninvasive method of drug delivery and diagnostics', *Biotechnol Prog*, 16 (3), 488-492.

http://www.sontra.com/technology/

SEARCH CRITERIA TO BE USED:

Anesthesia, Local/adverse effects
Anesthetics, Local/administration & dosage/adverse effects/ pharmacology
Diagnostic Techniques and Procedures
Drug Delivery Systems
Glucose/metabolism
Ultrasonics