Systematic Review of Ultrasound-Assisted Lipoplasty
Update & Reappraisal

ASERNIP-S REPORT NO. 17

Australian Safety & Efficacy Register of New Interventional Procedures – Surgical
The Royal Australasian College of Surgeons
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Safety and Efficacy Classification for Ultrasound-Assisted Lipoplasty

The ASERNIP-S Procedure Classifications were revised in August 1999 by the ASERNIP-S Management Committee. As such, each of the four procedures already assessed by ASERNIP-S was allocated a new classification from the following list:

1. Safety and efficacy is established. Procedure is equal to, or better than the nominated gold standard. Procedure may be introduced into practice.

2. The safety and efficacy of the procedure cannot be determined due to an incomplete and/or poor quality evidence-base. One of the following recommendations is made:
   
   2.1 An audit is required.
   2.2 A Controlled Clinical Trial, preferably prospective with concurrent controls, is required.
   2.3 A Randomised Controlled Clinical Trial is required.

3. Safety and efficacy of procedure is shown to be unsatisfactory. Procedure should not be used.

The new classification for Ultrasound-Assisted Lipoplasty is 2.1. An audit is required to assess both safety and efficacy.

The ASERNIP-S Ultrasound-assisted Lipoplasty Review Group recommends that ultrasound-assisted lipoplasty should not be performed to contour female breast tissue.

References to previous classifications remain unchanged in the document.

2000 Update: Following the 2000 update of the Ultrasound-Assisted Lipoplasty review, the safety and efficacy classification remains unchanged.

________________________________________________________________________________________

Important Note: The information contained in this report is a distillation of the best available evidence located at the time the searches were completed as stated in the protocol. Please consult with your medical practitioner if you have further questions relating to the information provided, as the clinical context may vary from patient to patient.
The Systematic Review of Ultrasound-assisted Lipoplasty, Recommendations and Safety and Efficacy Classification were ratified by the ASERNIP-S Management Committee:

ASERNIP-S Management Committee Meeting
August 8th 1999

The Council of the Royal Australasian College of Surgeons in October 1999
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Review Protocol

Ultrasound-Assisted Lipoplasty

March 1999
(Revised and updated July 2000)

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South Australia
Protocol Update (July 2000)

1. **Background**

The original protocol (see following pages) established the search and inclusion criteria for literature on ultrasonic assisted lipoplasty (UAL). The literature searches were undertaken in January 1999. As insufficient evidence was available at that time to assess the safety and efficacy of UAL, literature searches will be repeated at annual intervals to determine whether any significant changes have occurred in the evidence base. This first update covers the sixteen month period following the primary search.

2. **Objectives**

To identify literature relating to UAL that was published in the period following the primary literature search and to critically appraise this literature with respect to the safety and efficacy of UAL in comparison to traditional lipoplasty techniques.

3. **Inclusion Criteria**

Papers were selected for inclusion in the updated systematic review on the same basis as described in the original protocol, with the exception that suction-assisted lipoplasty was not included as a valid type of intervention by itself (i.e. the paper had to also address, or only address, ultrasound-assisted lipoplasty).

Because of the theoretical concerns raised in the original systematic review, the update was broadened to include experimental papers on the mutagenic potential of ultrasound. To be included, papers had to specifically address the issue of potential DNA damage owing to ultrasonic effects.

4. **Study Design**

The study designs or papers selected for inclusion in the updated systematic review were identical to those deemed suitable in the original protocol.

5. **Additional Information**

The ASERNIP-S review process has altered during the period between the primary systematic review and the update. Originally the review was divided into two sections – a narrative review undertaken by the review surgeon and a methodological assessment undertaken by the ASERNIP-S researcher. These two approaches have now been synthesised with the review and updates now being undertaken by the ASERNIP-S researcher, in consultation with the advisory surgeon (previously review surgeon). The ASERNIP-S researcher brings the necessary evidence-based surgery and critical appraisal skills to the task, whilst the advisory surgeon provides the invaluable clinical expertise that is required.
6. **Search Strategies**

Literature databases were updated to include the period 1/99 – 4/2000

**Databases searched:**
- SilverPlatter Medline (WinSpirs)
- Ovid Current Contents
- The Cochrane Collection (The Cochrane Library CD 1999, Issue 4)
- Lexis-Nexus Embase

**Search Terms:**
- Search strategies were devised by the ASERNIP-S Researcher and Protocol Surgeon.

Search terms used:

**Ultrasound-Assisted Lipoplasty** –
Terms and text unchanged (see original protocol).

**Traditional Lipoplasty** –
Terms and text deleted and no search performed (see original protocol).

**Mutagenic Potential of Ultrasound** –
The search terms entered were:

ultraso* and cavitation and (dna or genetic) and (English in la) and (py=1980-2000)

<table>
<thead>
<tr>
<th>Results of Literature Searches: searched 19/4/00</th>
<th>Ultrasonic Assisted Liposuction</th>
</tr>
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<tbody>
<tr>
<td><strong>Medline</strong></td>
<td>01/1999-2000</td>
</tr>
<tr>
<td><strong>Current Contents</strong></td>
<td>01/1999-2000 (Wk 16)</td>
</tr>
<tr>
<td><strong>Embase</strong></td>
<td>01/1999-01/2000</td>
</tr>
<tr>
<td><strong>Cochrane Collection</strong></td>
<td>CD 1999, Issue 4</td>
</tr>
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<td><strong>References</strong></td>
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</tr>
<tr>
<td><strong>References</strong></td>
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<tr>
<th>Results of Literature Searches: searched 27/4/00</th>
<th>Mutagenic Potential of Ultrasound</th>
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</tr>
<tr>
<td><strong>Current Contents</strong></td>
<td>1993-2000 (Wk 17)</td>
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<tr>
<td><strong>Embase</strong></td>
<td>No date restriction-01/2000</td>
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<tr>
<td><strong>Cochrane Collection</strong></td>
<td>CD 1999, Issue 4</td>
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<td><strong>References</strong></td>
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<tr>
<td><strong>References</strong></td>
<td>24</td>
</tr>
<tr>
<td><strong>References</strong></td>
<td>41</td>
</tr>
<tr>
<td><strong>References</strong></td>
<td>0</td>
</tr>
</tbody>
</table>
7. **Literature Databases:**

Exclusions by ASERNIP-S Researcher:
- 138 references were included in the updated UAL database.
- 81 references were duplicates.
- 53 references were excluded because they did not meet the inclusion criteria.
- 2 references were already included in the original narrative review.
Therefore 2 references were deemed appropriate for updating the review.

- 96 references were included in the new Biological Effects of Ultrasound database.
- 43 references were duplicates.
- 34 references were excluded because they did not meet the inclusion criteria.
Therefore 19 references were deemed appropriate for updating the review.

Thus a grand total of 21 references were deemed appropriate for updating the review.

8. **Methods of the Review**

The methods used in the update were similar to those employed in the original protocol, with the exception that all the research tasks and document preparation were conducted by the ASERNIP-S researcher.
Original Protocol

1. **Objectives**

To review the literature comparing traditional techniques of liposuction with ultrasound-assisted lipoplasty (UAL) to establish the best evidence for recommendations on the safety and efficacy of UAL.

2. **Background**

The development of traditional liposuction two decades ago provided plastic surgeons with a technique to remove localised areas of fat with small suction cannulae introduced through small incisions\(^1\). This “dry” technique of fat removal has been largely replaced with a “wet” technique (also called tumescent) which involves the preparatory infiltration of fluids to help disperse the fat and thereby assist its removal. The tumescent approach allowed larger volume liposuction with reduced blood loss\(^2\). Traditional liposuction has a low complication rate and a high patient satisfaction rate.

The concept of UAL involves the ultrasonic liquefaction of fat by cellular fragmentation\(^3\). A fatty emulsion is then extracted by low-vacuum suction. Proponents of UAL claim that it provides a more selective destruction of larger volumes of adipose tissue than traditional methods, it is less physically demanding for the surgeon, with minimal blood loss and little bruising for the patient\(^4\). Ultrasound-assisted lipoplasty also removes denser fibrous tissue and breast parenchyma than traditional liposuction\(^5\).

However, in addition to the equipment being more expensive, UAL has a different thermal effect on tissues, takes longer to perform, has the potential for oil emulsion retention, as well as having a longer learning curve\(^6,7\). It is therefore necessary to determine the safety and efficacy of this new liposuction technique.

3. **Inclusion Criteria for considering studies for this review**

   a. **Types of participants:**

   Adult patients in any case setting described as having excess deposits of undesirable subcutaneous tissue were included. As the assessment of “excess and undesirable” may differ between trials, it was not possible to apply a standard definition to any study population.

   If patients were recruited with deposits of subcutaneous tissue from a metabolic, pharmacological or known pathological condition, then they were included only if the results for patients with localised subcutaneous tissue collections were presented separately.
b. **Types of intervention:**

   Ultrasound-assisted lipoplasty
   Suction-assisted lipoplasty

c. **Types of outcome measures:**

   Primary outcomes:
   - Independent measures of contour improvement
   - Surgical complications
   - Duration of operation
   - Blood loss
   - Patient recovery
   - Surgeon fatigue

   Secondary outcomes:
   - Costs
   - Pain
   - Reliability and acceptability
   - Quality of life

4. **Study Design**

   **Types of studies:**

   Trials were included if the allocation of patients was described as randomised. Controlled clinical trials and case reports were considered only in the absence of randomised controlled trials.

   There was no restriction on date of publication. Initially only studies published in the English language were included. Otherwise, references were only excluded if they did not meet the inclusion criteria.

   **Search strategy for identification of any existing reviews:**

   The trials register of the Cochrane Collaboration was searched for randomised trials of ultrasound-assisted therapies. In addition, contact was made with companies who manufacture or distribute ultrasonic-assisted liposuction devices for any unpublished or ongoing studies.

   Databases were searched and continually monitored to identify publications that met this study’s inclusion criteria. Such databases included Medline, Embase, Current Contents and the Cochrane Library Database.
5. Literature Search Strategy for Review

Databases searched:
- SilverPlatter Medline (WinSpirs)
- Ovid Current Contents
- The Cochrane Collection (The Cochrane Library CD 1998, Issue 4)
- Lexis-Nexus Embase

Search Terms:
- Search strategies were devised by the ASERNIP-S Researcher and Protocol Surgeon.

Search terms used:

Ultrasound-Assisted Lipoplasty –
(ultraso* and (liposuction or lipoplasty or lipectomy)) and English language

Traditional Lipoplasty –
(liposuction or lipoplasty or lipectomy) and English language

NB: * is a truncation symbol, which receives variations of the indicated text.
ultraso* retrieves eg. ultrasound, ultrasonic ,ultrasonics or ultrasonically
The symbol is * (Medline), $ (Current Contents), ! (Embase).

<table>
<thead>
<tr>
<th>Results of Literature Searches: searched 8/1/99</th>
</tr>
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<tbody>
<tr>
<td>Ultrasonic Liposuction</td>
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<tr>
<td><strong>Medline</strong></td>
</tr>
<tr>
<td>1984-12/1998</td>
</tr>
<tr>
<td>38 references</td>
</tr>
<tr>
<td><strong>Current Contents</strong></td>
</tr>
<tr>
<td>1993-12/1998</td>
</tr>
<tr>
<td>32 references</td>
</tr>
<tr>
<td><strong>Embase</strong></td>
</tr>
<tr>
<td>1974-12/1998</td>
</tr>
<tr>
<td>27 references</td>
</tr>
</tbody>
</table>

| Traditional Liposuction                        |
| **Medline**                                   |
| 1984-12/1998                                 |
| 877 references                                |
| **Current Contents**                          |
| 1993-12/1998                                 |
| 376 references                                |
| **Embase**                                    |
| 1974-12/1998                                 |
| 808 references                                |
Literature Databases:

Ultrasoundlipo – 39 references formed this database in Reference Manager after exclusions of duplicates and articles that clearly did not meet the inclusion criteria.

6. Methods of the Review

Titles and abstracts of publications identified by the search strategies were assessed by the ASERNIP-S Researcher in terms of their relevance and design, according to the selection criteria. After satisfying this initial assessment, full versions of articles were obtained and checked by the Review Surgeon to identify those that fit the inclusion criteria. Using a data extraction checklist, the Review Surgeon categorised the studies to be included, and excluded those that did not meet the criteria. The Review Surgeon added additional background material if considered necessary.

7. Formulation of Recommendations of Safety and Efficacy

Based upon data from the review process, recommendations by the Review Surgeon in the form of a Draft Review were made on the safety and efficacy of ultrasound-assisted lipoplasty. The Draft Review was then disseminated amongst members of the Review Group who reviewed the document according to particular expertise. Any concerns were then discussed at the Review Group teleconference.
REFERENCES


Review Update (July 2000)

The original ASERNIP-S narrative review was written by Mr Rod Cooter and the original ASERNIP-S methodological assessment was written by Dr Wendy Babidge. Both of these documents follow this section, in which the updated literature is addressed. Since the update includes both an update of the original search terms to include more recent literature and a new section on the mutagenic potential of ultrasound, these two elements are addressed separately below.

Results of the update of the original literature search
The updated literature search using the search terms from the original protocol resulted in 2 new papers being added to the database. Two other papers also uncovered had already been included in the original review and was thus excluded from further consideration.\textsuperscript{1,2} Both of the new studies were level IV evidence case series (see Methodological Assessment Report below) and are summarised in Table 2000.1.

One of these studies included patients treated with both UAL and/or SAL, although no comparisons were made between treatment groups.\textsuperscript{3} Both studies reported results on blood loss, with one reporting a mean reduction of hematocrit of 2.35% per 100cc of fat aspirated,\textsuperscript{2} and the other a mean hematocrit loss of 19.1% (range +15 to –52) and mean albumin loss of 19.7% (range +12 to –50) at 1 week postop.\textsuperscript{4} Authors of one of the studies noted that the amount of blood loss could not be accounted for by the volume of blood in the aspirate, which suggests that most of the blood loss occurs postoperatively in the body’s tissues and that this blood loss can be significant.\textsuperscript{4}

Few serious complications were related. One study was concerned principally with the efficacy of a dual-plane type of lipoplasty in which UAL was used to treat the superficial fatty layer while SAL was used upon the deep layer.\textsuperscript{3} It reported no complications and related decreases in truncal circumference and of the depth of the fatty layer which endured up to at least 3 months.

In all, these 2 additional papers would appear to add little to the discussion of UAL’s relative merits when compared to the traditional SAL and would not seem to warrant a revision of the ASERNIP-S review group’s original conclusions away from a classification of 2.

Results of the new literature search on the mutagenic potential of ultrasound
The new literature search resulted in 19 new papers being added to the database. All except for 1 of these were level II evidence in which ultrasound was applied to \textit{in vitro} collections of cells or DNA. The exception was a level III-2 paper that compared workers who had undergone long term occupational ultrasound exposure to unexposed controls.\textsuperscript{5} All of these studies are summarised in Table 2000.2.

Overwhelmingly, the \textit{in vitro} studies demonstrate that insonication of liquids such as phosphate buffered saline can produce reactive chemicals, particularly in the form of OH radicals or hydrogen peroxide, that in turn can result in DNA strand breaks and point mutations.\textsuperscript{6-18} Strand breaks can also apparently be induced by the mechanical forces induced by cavitation, although these are much more likely to occur in cells that have been lysed and are therefore unviable and have few long-term
Strand breaks have been observed both in DNA unshielded by cellular membranes and also nucleated DNA, at least some of which has been observed to occur in cells that remained viable after insonication. There is also some evidence that rapidly dividing cells are more easily damaged by cavitation than stable phase cells. The only in vitro study not to demonstrate any evidence of DNA damage from ultrasound used a procedure in which the target cells were suspended in phosphate-buffered solution to which methylcellulose had been added with the specific intention of preventing cavitation. However, as was pointed out in the original ASERNIP-S review, it would appear to be difficult to extrapolate the results of these studies to make realistic estimates about the mutagenic risks of ultrasound in vivo. They also seem to add little to that review’s recommendations that appropriate animal studies be conducted along the lines of those being performed in relation to cellular phone microwave radiation risk.

As mentioned previously, the only in vivo study turned up by the updated literature search that examined the mutagenic risks of ultrasound, compared nonsmoking men who underwent daily occupational ultrasound exposure for a mean period of 5 years with unexposed controls. The ultrasonically exposed group had significantly more micronucleated lymphocytes than the control group and the authors concluded that human chromosomes 1, 9, 15, 16 and Y might be more susceptible to DNA damage caused by ultrasound. Exposure frequencies for the subjects in this study ranged from 2.5 to 7.5 MHz, with maximum power ranging from 0.8 to 4.9 W/cm². Unfortunately, since the study was not able to randomise its subjects and the exposure condition was retrospective, it is not possible to rule out some other unknown cause to explain this interesting and provocative result.

There would appear to be inadequate evidence at the moment to ascertain the degree of mutagenic and carcinogenic risk associated with ultrasound in vivo, whether at diagnostic or therapeutic power levels. While the potential for risk clearly exists, there is inadequate evidence to decide if it is real in the clinical setting. It would seem that only carefully controlled animal studies may begin to shed some light upon this problem.

Andrew Chapman
ASERNIP-S Researcher
July 2000
<table>
<thead>
<tr>
<th>Ref #</th>
<th>Year</th>
<th>Authors</th>
<th>Study Location</th>
<th>Study Type</th>
<th>Study Level</th>
<th>Procedure Type</th>
<th>Equipment Type</th>
<th>Time of ultrasound application</th>
<th>sample size</th>
<th>Statistics used</th>
<th>Follow-up</th>
<th>Adverse Outcomes</th>
<th>Comments on efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1999</td>
<td>Albin R; de Campo T</td>
<td>CO, USA</td>
<td>Case series IV</td>
<td>N</td>
<td>SAL; SAL &amp; UAL. Tumescent technique. &gt;5000cc aspirate from all patients.</td>
<td>Lysonix 2000</td>
<td>Not stated</td>
<td>SAL: 31; SAL &amp; UAL 150. Of these 181, 45 had blood loss calculated by measuring hematocrit preop and on day 5 post op.</td>
<td>Regression analysis on liposuction volume &amp; calculated blood loss.</td>
<td>Day 5 and week 12.</td>
<td>Calculated blood loss ranged from 56cc to 2,426cc. Complications: SAL - 1 deep vein thrombosis following 20,675cc aspirate; SAL &amp; UAL - 1 pulmonary embolus on day 2 following 16,485cc aspirate and 1 pulmonary embolus on day 24 following 21,775cc aspirate. Minor complications for whole series: 0 skin burns, 0 infections, 1 transfusion (thrombosis patient), 3 prolonged pain, 6 foam blisters.</td>
<td>Calculated blood loss correlated non significantly (0.32) with aspirate volume. Apparently blood lost is in the tissues and not through the aspirate; therefore blood loss could be underestimated in studies which measure blood in aspirate (blood in aspirate was not measured here though).</td>
</tr>
<tr>
<td>3</td>
<td>1999</td>
<td>Lee Y; Hong JJ; Bang C</td>
<td>Seoul, Korea</td>
<td>Case series IV</td>
<td>N</td>
<td>Dual plane abdominal lipoplasty: SAL for deep layer; UAL for superficial layer</td>
<td>Surgitron 2000</td>
<td>Not stated</td>
<td>35 (32F)</td>
<td>None stated.</td>
<td>3 months</td>
<td>Mean hematocrit reduced by 2.35% per 100cc of fat removal. No perioperative or postoperative complications such as skin loss, seroma, infection, hematoma, paresthesia or pigmentation.</td>
<td>Mean fat in aspirate = 68%. Truncal circumference decrease at epigastric &amp; subumbilical level of 3% &amp; 4% at month 1 and 4% &amp; 6% at month 3. Mean decrease in fatty layer (ultrasoundography) of 25% &amp; 40% at month 1 and 29% &amp; 44% at month 3. Mean body weight decrease of 1.4kg at month 1 and 1.7kg at month 3.</td>
</tr>
<tr>
<td>4</td>
<td>1999</td>
<td>Troilius C</td>
<td>Malmo, Sweden</td>
<td>Case series IV</td>
<td>N</td>
<td>UAL. Tumescent technique.</td>
<td>Lysonix 2000</td>
<td>Typical times for various anatomical sites given: 5-20 min each.</td>
<td>28</td>
<td>None stated.</td>
<td>1 week.</td>
<td>Mean albumin loss 26.9% (+5-53) at day 1, and 19.7% (+12-50%). Mean hematocrit loss 24.3% (+7-50) at day 1, and 19.1% (+15-52)</td>
<td>Mean fat in aspirate = 72%. Blood loss appeared to be related to the area treated rather than the volume of aspirate, although no test of significance performed.</td>
</tr>
<tr>
<td>1</td>
<td>1999</td>
<td>Trott SA; Rohrich RJ; Beran SJ; Kenkel JM; Adams WP; Robinson JB</td>
<td>TX, USA</td>
<td>Case series IV</td>
<td>N</td>
<td>UAL. Superwet technique. Intermediate to deep plane. SAL used to remove fat. SAL only for knees</td>
<td>Lysonix 2000</td>
<td>Mean 4.0 minutes (0-11)</td>
<td>21 (16F)</td>
<td>Paired t-tests; Fisher's exact; Pearson's corr; Kendall's Tau-Beta corr. Alpha = 0.1.</td>
<td>3 follow ups: mean time: 1) 14 days (9-21); 2) 45 days (39-51); 3) 71 days (40-90).</td>
<td>No neuromas. Two paresthesias of abdomen, one resolving within 10 weeks and the other at 12 weeks. One hyperalgesia of the flank resolving at 12 weeks.</td>
<td>SAL treated knees tended to have less hypesthesia than SAL &amp; UAL treated abdomen/flank/thigh. Some indication that greater volumes of aspirate correlated with increasing hypesthesia. No difference in subjective hypesthesia between SAL and SAL &amp; UAL treated areas.</td>
</tr>
<tr>
<td>Ref #</td>
<td>Year</td>
<td>Authors</td>
<td>Study Location</td>
<td>Study Level</td>
<td>Procedure</td>
<td>Ultrasonic frequency</td>
<td>Subjects</td>
<td>Results</td>
<td>Conclusions</td>
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<tr>
<td>19</td>
<td>2000</td>
<td>Ashush H; Rozenszajn LA; Blass M; Barda-Saad M; Azimov D; Radnay J; Zipori D; Rosenschein U</td>
<td>Ramat-Gan; Rehovot; Tel Aviv, Israel</td>
<td>II</td>
<td>US applied at 22.4 and 103.7 W/cm². Compared with gamma irradiated and nonirradiated controls</td>
<td>750 KHz</td>
<td>HL-60 &amp; leukemia cells K562, U937 and M1/2 suspended in RPMI solution.</td>
<td>No free radicals detected. Higher level US produced DNA strand breaks, decrease in cell metabolic activity, and apoptosis similar to gamma irradiation.</td>
<td>Suggests US might be used to treat carcinoma.</td>
<td></td>
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<tr>
<td>6</td>
<td>1992</td>
<td>Doida Y; Brayman AA; Miller MW</td>
<td>Shiga, Japan; Rochester, New York, USA</td>
<td>II</td>
<td>US applied at 35 W/cm² for 2 min. in tube rotating at 30 RPM. Insonated or sham insonated at 3 deg C or 37 deg C.</td>
<td>1.06 MHz</td>
<td>Chinese hamster V79 cells in Eagles minimal essential medium, either chilled to 3 deg C or maintained at 37 deg C.</td>
<td>O₂ concentration 10% greater in 3 deg C than 37 deg C medium. Plating efficiency reduced in 3 deg C culture (16% v 47%). Mutation rate increased versus sham controls of 81% for 37 deg C groups and 114% for 3 deg C.</td>
<td>Lower medium temperature increases cavitation and hence mutation rate. Mutations appear to be due to insonating of medium.</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>7</td>
<td>1998</td>
<td>Doida Y; Marcello KR; Brayman AA; Cox C; Barne S; Miller MW</td>
<td>Shiga, Japan; Rochester, New York, USA</td>
<td>II</td>
<td>US applied at 35 W/cm² in continuous wave for 30 min to PBS to create sonochemicals. Some samples included Albunex (microbubble contrast agent). Cells suspended for 15 min. in exposed or sham PBS. Other cells exposed or sham to 3 Gy xrays at 46 R/min.</td>
<td>1 MHz</td>
<td>Chinese hamster V79 cells in Eagles minimal essential medium</td>
<td>Xray exposure produced a very much greater specific mutation rate; US with or without Albunex produced significantly greater specific mutation rate than sham US or sham Xray.</td>
<td>Sonochemicals have a mutagenic potential.</td>
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<td>6</td>
<td>1984</td>
<td>Dooley DA; Sacks PG; Miller MW</td>
<td>Rochester, New York; Lycoming, New York; Albany New York, USA</td>
<td>II</td>
<td>US applied for 1 min. at 0.5, 1, 3, 5, 10, 20, 30 W/cm²; and 1 to 5 min. at 5 W/cm² (all at 37rpm); also 1 min. at 10 w/cm² at 4 bar hydrostatic pressure. Sham US and gamma irradiation also.</td>
<td>1.07 MHz</td>
<td>Mouse mammary sarcoma cells EMT6/Ro suspended in isotonic or phosphate buffered saline at 400,000 cells/ml</td>
<td>Fraction of intact &amp; surviving cells min. at approx. 5 W/cm². Thymine base damage maximum at approx. 10 W/cm² &amp; increases with duration of exposure. No evidence of immediate DNA degradation. Radical scavengers stopped thiamine base damage.</td>
<td>At least part of collapsing bubble occurs intracellularly. Thiamine base damage results from production of free radicals.</td>
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<td>9</td>
<td>1995</td>
<td>Forytkova L; Hrazdira I; Mornstein V</td>
<td>Brno, Czech Republic</td>
<td>II</td>
<td>US applied for 10 min on rotating tube (5 RPM) at 0.1 or 0.5 or 1.0 W/cm². DNA synthesis measured using 3H-thymidine.</td>
<td>0.8 MHz</td>
<td>Ehrlich ascitic tumor cells cultured in mouse female hybrids for 10-12 days then suspended in Krebs solution.</td>
<td>Rate of DNA synthesis increased sig at 0.1 W/cm² &amp; decreased sig at 0.5 and 1.0 W/cm². Large sig decrease in synthesis if solution cooled to 5 deg C then insonated at ambient (37 deg C) temp without thermal equilibrium being achieved. Smaller sig decrease if cooled then warmed, or just insonated at ambient temp. If incubated for 1 hr at 37 deg C no sig difference in synthesis. No sig diff if cells suspended in insonated solution.</td>
<td>US at low levels can stimulate DNA synthesis; at higher (but not extraordinary) levels, DNA synthesis is inhibited.</td>
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<td>10</td>
<td>1995</td>
<td>Fuciarelli AF; Sisk EC; Thomas RM; Miller DL</td>
<td>Richland, WA, USA</td>
<td>II</td>
<td>US applied to aliquots rotating at 60rpm for 15, 30 and 60 min.</td>
<td>2.17 MHz</td>
<td>Calf thymus DNA in phosphate buffered saline bubbled with 3:1 Argon:Oxygen at 2.4 mg/ml</td>
<td>Purine and pyrimidine products of OH radicals detected; correlated with residual hydrogen peroxide, not duration of US exposure.</td>
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<td>5</td>
<td>1999</td>
<td>Garaj-Vrhovac V; Kopjar N; Besendorfer V; Papes D</td>
<td>Zagreb, Croatia</td>
<td>III-2</td>
<td>US max power = 0.8-4.9 W/cm²; max spatial peak pulse average intensity = 60-110 W/cm²; max spatial peak-temporal average intensity = 1.9-20 mW/cm²</td>
<td>2.5-7.5 MHz</td>
<td>20 non-smoking men aged 28-52. Group 1 (n=10) occupational exposure to US daily for mean 5 years (1-10); Group 2 (n=10) control.</td>
<td>Micronucleated lymphocytes: Group 1 9-35; Group 2 2-7; p&lt;0.05</td>
<td>Human chromosomes 1, 9, 15, 16 &amp; Y may be more susceptible to DNA damage caused by US.</td>
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<td>11</td>
<td>1985</td>
<td>Kondo T; Yoshii, G</td>
<td>Fuku; Osaka, Japan</td>
<td>II</td>
<td>US applied from 0 to 3.1 W/cm²</td>
<td>1.2 MHz</td>
<td>1) Calf thymus DNA at 0.4 mg/ml. 2) Mouse L cells in monolayer culture. 3) KI-starch &amp; sucrose solutions.</td>
<td>Iodine release at intensities &gt;1.5(2.8) W/cm² where 1.5=spatial average intensity; 2.8=spatial peak intensity; reduction of DNA molecular weight &gt;1.5(2.8) W/cm²; sucrose hydrolysis &gt;0.5(0.8) W/cm². Relative 14C-TdR incorporation decreased gradually at intensities &gt;1.5(2.8) W/cm².</td>
<td>Changes in DNA synthesis takes place independently of collapse cavitation and may be due to stable cavitation.</td>
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<td>12</td>
<td>1985</td>
<td>Kondo T; Arai S; Kuwabara M; Yoshii G; Kano E</td>
<td>Fukui; Ebetsu; Sapporo, Japan</td>
<td>II</td>
<td>US applied from 0 to 3.1 W/cm²</td>
<td>1.2 MHz</td>
<td>5ml DNA solution irradiated.</td>
<td>Double strand breaks (dsb) increased with intensity &gt; 1.5 W/cm²; single strand breaks (ssb) increased with intensity &gt; 2.3 W/cm². Hydrogen bond rupture observed at pH &gt; 3.5. No cross links observed at energy levels up to 1200 J/cm² and intensity &gt; 3.1 W/cm². Template activity decreased at intensities &gt; 1.5 W/cm², except for low energy (240 J/cm²). Addition of free radical scavengers reduced ssb but not dsb, also preserved template activity above 2.3 W/cm².</td>
<td>Cavitation occurs at frequencies &gt; 1.5 W/cm². Main DNA lesions induced by ultrasound are dsb &amp; ssb; dsb induced by mechanical shearing, ssb by free radical formation</td>
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<td>20</td>
<td>1988</td>
<td>Kondo T; Kano E</td>
<td>Fukui, Japan</td>
<td>II</td>
<td>US applied to solution. Gases bubbled through continuously - Ar, O₂, N₂ or N₂O at 30 ml/min. [Other non-DNA procedures also performed to separate cell cultures - not summarised here].</td>
<td>1.0 MHz</td>
<td>Calf thymus DNA</td>
<td>Number of dsb increased in linear fashion with duration of exposure to US for Ar, O₂, and N₂, but no dsb detected for N₂O.</td>
<td>Number of dsb is due to mechanical effects of US. N₂O appears to produce low temperature cavitation; effect remains to be elucidated.</td>
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<td>13</td>
<td>1993</td>
<td>Kondo T; Kodaira T; Kano E</td>
<td>Fukui, Japan</td>
<td>II</td>
<td>US applied to cell suspensions saturated with O₂, Ar or N₂O, rotating at 30rpm. Solutions of 5,5-dimethyl-1-pyrroline-N-oxide (DMPO) and 3,3,5,5-tetramethyl-1-pyrroline-N-oxide (M₄PO) also sonicated.</td>
<td>1.0 MHz</td>
<td>Mouse mammary carcinoma FM3A cells.</td>
<td>Free radicals produced in O₂ and Ar solutions but not in N₂O. US above 3.6 W/cm² resulted in reduced free radical formation and increasing cell survival. DNA ssb observed in Ar cell solution; no dsb in Ar or N₂O solution. No repair of ssb observed after 30min at 37 deg C.</td>
<td>Cavitation begins to decline at higher US levels owing to radiation pressure. Free radicals important in ssb production where US is time is long and/or intensity high.</td>
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<td>14</td>
<td>1997</td>
<td>Lejbkowicz F; Salzberg S</td>
<td>Haifa; Ramat-Gan, Israel</td>
<td>US applied at 0.33 W/cm$^2$ from 0 to 4 min.</td>
<td>20 kHz</td>
<td>Human foreskin fibroblast or amniotic fluid epithelial cells used as controls. Three cancer cell lines used: breast with progesterone/estrogen receptors; breast without; melanoma; lung carcinoma.</td>
<td>Normal cell viability unaffected up to 4 min. exposure. Breast carcinoma and melanoma greatly reduced cell viability up to 4 min. exposure; lung carcinoma moderately reduced cell viability up to 4 min. exposure. Similar results for cloning efficiency.</td>
<td>Ultrasound has cytotoxic characteristics.</td>
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<td>15</td>
<td>1989</td>
<td>Miller DL; Reese JA; Frazier ME</td>
<td>Richland, WA, USA</td>
<td>US applied at 0-4 deg C to rotating tube system: 1) 53 mW/cm$^2$ pulsed no cavitation; 2) 470 mW/cm$^2$ continuous with chemically inactive cavitation; 3) 10.8 W/cm$^2$ pulsed no cavitation; 4) 161 W/cm$^2$ continuous with transient cavitation; 5) 94 W/cm$^2$ continuous no cavitation. Controls: sham or gamma ray.</td>
<td>1) 6.2 MHz; 2) 1.7 MHz; 3) 1.48 MHz; 4) 1.45 MHz; 5) 8 MHz</td>
<td>Fresh human leucocytes.</td>
<td>Significantly more ssb in condition 4 No support for mutagenic risk with diagnostic US (1). Cavitation may lead to ssb, but uncertain if cells affected are viable.</td>
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<td>21</td>
<td>1991(1)</td>
<td>Miller DL; Thomas RM; Frazier ME</td>
<td>Richland, WA, USA</td>
<td>US applied in rotating tube exposure system, for 10 min at 0-8.0 W/cm$^2$. Positive controls irradiated with 60Co gamma rays at dose rate of 2 Gy/min.</td>
<td>1.61 MHz</td>
<td>Chinese hamster ovary cells suspended in phosphate-buffered saline at 1.0-1.5x10(6) cells ml</td>
<td>SSBs increased with increasing continuous intensity, but cell viability decreased at a dramatically greater rate also. Burst mode exposure produced similar results but with viability decreasing at a slower rate.</td>
<td>Ultrasound can produce ssb via cavitation, but whether these ssb occur in viable cells is unclear.</td>
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<td>16</td>
<td>1991</td>
<td>Miller DL; Thomas RM; Frazier ME</td>
<td>Richland, WA, USA</td>
<td>II</td>
<td>US applied to PBS (with or without bubbling with Argon gas) in rotating tube exposure system to produce sonochemicals (H2O2). Cells exposed to solution. Positive controls treated with H2O2 or 2Gy/min gamma ray radiation.</td>
<td>1.61 MHz</td>
<td>Chinese hamster ovary cells suspended in phosphate-buffered saline.</td>
<td>SSBs correlated with length of time PBS sonicated; greater effect for argon bubbling. H2O2 also induced SSBs. SSBs occurred in viable cells. Addition of catalase or cysteamine (to break down H2O2) stopped effect. 30 min of 16 microM H2O2 on ice equivalent to 1 Gy of gamma rays.</td>
<td>H2O2 produced by cavitation appears to be able to cause ssb in viable cells.</td>
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<td>17</td>
<td>1995</td>
<td>Miller DL; Thomas RM; Buschbom RL</td>
<td>Richland, WA, USA</td>
<td>II</td>
<td>Solution bubbled with O2 or Ar for 1 hr at 10-15 deg C. Test solution = 1ml cells, 1ml O2 solution, 3ml Ar solution. US applied at 25 deg C, minimal rotation of tube. After US solution rotated on ice for 30 min to allow H2O2 reaction, then catalase added to remove residual H2O2. Half solution allowed to incubate at 30 deg C for 30 min to allow ssb repair.</td>
<td>2.17 MHz</td>
<td>Chinese hamster ovary cells suspended in phosphate buffered saline supplemented with histidine (to enhance H2O2 effects).</td>
<td>Comet assay used (because of extreme sensitivity) to detect DNA breaks in cells. At 0.58 MPa pressure, significant DNA damage produced which was repaired; at 0.82 MPa sig. damage only partially repaired. Increased exposure time also decreased rate of repair.</td>
<td>Inertial cavitation from US can induce DNA strand breaks in surviving cells. H2O2 may not be the only cause: possibly remains of lysed cells, other sonochemicals, or some aspect of direct cavitation. US was extreme in this experiment, though.</td>
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<td>18</td>
<td>1996</td>
<td>Miller DL; Thomas RM</td>
<td>Richland, WA, USA</td>
<td>II</td>
<td>US applied at 37 deg C at 0.58 MPa for 4 min. 0.82 MPa for 2 min. 0.82 MPa for 4 min. Lithotripter shocks applied at 37 deg C to solution through which O2 &amp; Ar (1:3) had been bubbled for 1 hour at 10-15 deg C. Reaction period of 10 min. after US or shock to allow sonochemicals to react with cells, then catalase added. Part of sample left to incubate at 28 deg C to allow ssb repair; other part put on ice to prevent repair. Ssbs assessed by comet analysis.</td>
<td>2.17 MHz and lithotripter with 27.3 MPa peak pressure.</td>
<td>Chinese hamster ovary cells suspended in PBS with calcium and histidine (to enhance H2O2 effects).</td>
<td>Significant strand break repair for all warm US conditions. DNA strand breaks demonstrated in cells which remained viable after US. Lithotripter did not produce significantly different results from the sham.</td>
<td>Continuous US induces DNA strand breaks in viable cells. It also produces sonochemicals more efficiently than lithotripter shocks.</td>
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<td>23</td>
<td>1991</td>
<td>Tolsma SS; Madsen EL; Chmiel J; Martin AO; Bouck NP</td>
<td>Chicago, Illinois; Madison, Wisconsin, USA</td>
<td>II</td>
<td>US applied at max power (various depending on machine). Cells plated and grown for 4 days to expose mutants.</td>
<td>Various, not stated Mainly diagnostic US.</td>
<td>Cells suspended in PBS with methylcellulose to prevent cavitation. 1) Subclone J6S1 of the SN-10 clone of BHK21/cl13; 2) human foreskin fibroblasts.</td>
<td>No cells demonstrated mutation with clinical machines, or a non-clinical transducer delivering higher pressure US or a lithotripter.</td>
<td>No evidence US induces mutations &amp; methylation changes. Chromosomal rearrangements or change in number not excluded though</td>
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<td>22</td>
<td>1998</td>
<td>Vollmer AC; Kwakye S; Halpern M; Everbach EC</td>
<td>Swarthmore, PA, USA</td>
<td>II</td>
<td>US applied to 1ml samples placed in 200 RPM centrifuge for 5 min at 500 W/cm2. Cells suspended in solution prepared with cavitation micronuclei.</td>
<td>20 Hz (using 1 MHz transducer)</td>
<td>E. Coli containing pUCD615 plasmid with luxCDABE cassette fused to a specific promoter.</td>
<td>1) E.Coli showed heat effects greater than sham but less than ethanol treatment; 2) E.Coli demonstrated increasing stress response with increasing cavitation; 3) rapidly growing cells were more sensitive to US stress than slow growing.</td>
<td>Rapidly dividing cells are more easily damaged by cavitation than stable phase cells</td>
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ASERNIP-S

Draft Review

on the Safety and Efficacy of

Ultrasound-Assisted Lipoplasty

July 1999

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**Introduction**

Ultrasound-assisted lipoplasty (UAL) is a relatively new surgical innovation available to Australasian surgeons. While traditional Suction-assisted lipoplasty (SAL) has been widely practised with low complication rates and high patient satisfaction levels, proponents of UAL claim it offers several advantages over traditional lipoplasty. Experience with this new technique in Europe and the United States of America has generally been positive but some reservation exists about the long-term effects of ultrasonic energy interaction with living tissue\(^1\). Initial reports also raised concerns about high seroma rates, longer operating times, and skin burns\(^2-4\).

It is the purpose of this review to summarise existing international experience with UAL to provide a framework for recommendations on the safety and efficacy of this new liposuction technique. This will enable Australasian surgeons to make informed decisions about the procedure so that the Australasian patient population can be treated with maximal safety.

The review is prefaced with an overview of traditional SAL to place into perspective the potential advantages and disadvantages of the more novel UAL.
Overview of Suction-Assisted Lipoplasty

Suction-assisted lipoplasty (SAL) is a commonly used procedure for the removal of subcutaneous fat deposits and remodelling body contours.

The basic procedure involves a subcutaneous cannula connected to a power source, which generates sufficient suction to remove the fat without causing significant damage to neurovascular structures traversing the adipose tissue. To facilitate fat removal a number of modifications and refinements have been proposed and adopted in various ways as the technique of liposuction evolved.

Initially SAL was described as a “dry” procedure in which subcutaneous fat was mechanically avulsed with cannulae and external massage used to evacuate the fatty residue; however, this was brutal and haemorrhagic, so various “wetting” techniques became popular to prepare the fat with subcutaneous solutions.

The sharp tips of early cannulae facilitated fat removal at the expense of significant blood loss and neuropraxias from indiscriminate damage to neurovascular structures. Nowadays the cannulae for routine SAL are blunt tipped with side hole ports.

Suction-assisted lipoplasty is performed at one atmosphere of suction to minimise the risk of damage to vital structures within the fat, while still providing a sufficiently negative pressure to evacuate disrupted fat globules\(^5\).

Like any other surgical intervention, SAL has the potential to cause a range of complications. These may be related to:

- **Anaesthesia employed**
  - Infiltration solution - lignocaine toxicity
  - Intravascular fluid shifts - hypovolaemic shock

- **Operator techniques**
  - Cannula pathways
  - Scarring
  - Contour defects
  - Haematomas
  - Seromas
  - Skin loss
  - Paraesthesias, pain

- **General complications**
  - Swelling, bruising, impaired physical activity
  - Infection
  - Embolism – Thrombus
    - Fat

Almost all complications of SAL can be averted if due care is given to patient selection, sensible choice of subcutaneous infiltration solution, careful operator technique, restriction of fat removal to modest volumes of tissue, and appropriate aftercare.
Suction-assisted lipoplasty has become one of the most common procedures performed for recontouring body shape. Apart from fairly predictable complications if reasonable guidelines are not followed, the procedure is safe and effective with a high rate of satisfaction.

The term “ultrasound” refers to mechanical vibrations of frequencies above the limit of human hearing, \((i.e.\, above \,16 \,kHz)\). Ultrasound-assisted lipoplasty involves the application of ultrasonic energy to subcutaneous adipose tissue in order to fragment the fat cells and facilitate the removal of fat as a liquefied aspirate. The fat is then removed in the same manner as SAL, so the pivotal difference between UAL and SAL is the application of ultrasonic energy. While this report will focus on techniques that deliver ultrasonic energies internally, it is possible to utilise external ultrasonic energy applied transcutaneously as a prelude to the cannula extraction of fat\(^6\,^8\).

In a surgical sense, the use of ultrasonic energy to aspirate tissue was not novel, because several other surgical applications existed. These include phacoemulsification of cataracts, ultrasonic aspiration of intra-cranial tumours, as well as applications in liver and renal surgery.

Although UAL has been performed for over a decade in Europe and South America since its introduction by Zocchi of Italy\(^9\,^10\), only recently has it gained popularity elsewhere. Guaranteed benefits of UAL over SAL include: less injury to nerves and blood vessels, less overall tissue trauma, minimised blood loss, lesser diameter of channels formed in adipose tissue, smooth tunnels created in adipose tissue, more even shaping of overlying skin surfaces, accurate positioning of probe, and spot-specific tissue removal\(^11\).

In contrast to these positive claims are the disadvantages that include: more operating room time, more expensive equipment, skin necrosis and burns, fat necrosis and fibrosis, hyper-pigmentation, sensory alteration and a longer learning curve\(^12\).

Ultrasound-assisted lipoplasty equipment includes an ultrasonic generator that transmits electrical energy to a hand piece containing a piezo-electric crystal that converts the incoming electrical signal into a mechanical vibration at ultrasonic frequency. When the attached probe is in contact with fat, the adipocytes are lysed into an emulsion. The probe may be either a hollow cannula through which low-pressure suction can evacuate lipoaspirates, or a solid probe style that requires subsequent aspiration of emulsified fat through a separate hollow cannula, as per SAL.

After excitation by an electric field, the crystal in the hand piece produces sound waves in the ultrasonic frequency range of 20kHz to 30kHz. This sound wave energy or mechanical energy is imparted to the probe tip as a rapid piston-like action forward and backward in a longitudinal direction with cyclical displacement in the order of 100 microns.

When applied to adipose tissue these alternating waves cause compression and rarefaction that results in micro-cavities or bubbles. These bubbles can expand with each cycle until a critical diameter is reached beyond which they implode with disruption of the cell and the instantaneous generation of high levels of energy in various forms such as heat and light\(^13\), as well as the liberation of free radicals and other chemicals.
For more detailed accounts of the physics of ultrasonic energy using tissue fragmentation, refer to articles by Cimino and Bond\textsuperscript{14,15}, and the 1999 article by Zocchi\textsuperscript{16}. 
Safety and Efficacy of Ultrasound-Assisted Lipoplasty

General Considerations

The earliest clinical data on UAL were reports by Scheflan and Tazi\textsuperscript{17} describing their experience in 800 patients, and Kloehn’s\textsuperscript{18} commentary on over 600 patients. Scheflan and Tazi reported 4% fat necrosis and fibrosis, 6% sensory alteration (which they speculated might result from sensory nerve damage by ultrasound), 4% skin necrosis and 4% skin pigmentation. Kloehn’s complication rate was less than 3%, with the most common problem being surface irregularities and asymmetries. Thermal and friction burns at incisional sites were also recorded prior to the use of a skin protector.

More recently, comparative studies of UAL and SAL led Fodor and Watson\textsuperscript{12}, and Igra and Satur\textsuperscript{19}, to conclude that no benefit could be attributed to UAL. In contrast, however, Kenkel \textit{et al}\textsuperscript{20}, used a porcine model to compare the tissue effect of SAL and UAL and concluded that UAL treatments generated more lipid aspirate per haemoglobin lost, and better preservation of vascular structures.

Some enthusiastic supporters of UAL report their large clinical experiences with few complications and strongly endorse the safety and efficacy of this technique\textsuperscript{21-23}. Most however caution that there is a learning curve associated with the procedure and that proper hands-on instructional courses are essential\textsuperscript{21}.

These considerations bear particular relevance to large volume lipoplasties (\textit{i.e.} > 5 litre lipoaspirates) for which significant preoperative and postoperative attention to detail is required to avoid problems\textsuperscript{24}.

Subcutaneous Wetting Solutions

One of the major changes in liposuction over the past few years has been in the preparation of the fat layer with various solutions. The history of subcutaneous infiltrations preparatory to liposuction is well covered in an historical overview by Bussien and Maillard\textsuperscript{25}, who document the main contributors and define their individual formulae. It is appropriate to consider these solutions carefully, because SAL is more effective if the adipose tissue is infiltrated to tumescence, and perhaps more importantly, UAL’s effectiveness is critical to such an environment. From a safety and efficacy perspective, the solutions to be infiltrated are of prime importance in the light of a recent report by Rao \textit{et al}\textsuperscript{26} on liposuction deaths related to these infusions.
Enthusiastic proponents of large volume fat removals have used increasingly large volumes of wetting solutions, and as the volume of lipoaspirate has steadily increased in day surgery lipoplasties, so too has the amount of lignocaine and adrenaline. To clarify nomenclature of wetting solutions, Fodor\textsuperscript{27} has delineated the following terms:

- The wet technique
- The superwet technique
- The tumescent technique

The “wet” approach is when 200 - 300 cc of isotonic solution, usually containing adrenaline in low dose, is infused subcutaneously into each site regardless of the volume of aspirate.

In the “superwet” technique, the volume of wetting solution equals the proposed aspirate volume; the isotonic infusate (e.g. Ringer’s lactate) contains low dose adrenaline (e.g. 1:1,000,000 to 1:2,000,000). As this type of liposuction is usually performed under general anaesthesia, local anaesthetic is not included in the infusate.

The “tumescent” technique uses the wetting solution as the primary mode of anaesthesia by the addition of large amounts of lignocaine. Tissue turgor is used as the endpoint of subcutaneous infiltration, which may lead to volumes of infusate far in excess of the volume of aspirate.

Proponents of the tumescent technique advocate that the mechanical and pharmacological properties of this subcutaneously injected fluid prevent the massive shifts of intravascular fluids usually seen in liposuction under general anaesthesia. With tumescence under local anaesthesia, only small amounts of IV fluid may be advisable\textsuperscript{28}.

Care must be taken to recognise that the fluid and lignocaine load of the tumescent technique can be dangerously large, particularly when combined with sedative anaesthetic agents (e.g. midazolam) that are degraded by the same saturable system of hepatic metabolism as lignocaine. Once saturation occurs, lignocaine levels rise sharply because absorption exceeds elimination\textsuperscript{26}. Signs of lignocaine toxicity may be masked by the concomitantly administered neurolepts.

However, large doses of lignocaine under local anaesthesia have been used in tumescent anaesthesia without signs of toxicity. This may be explained by fat partitioning of the lignocaine and its subsequent removal in the lipoaspirate\textsuperscript{29}. Caution is advised in the extrapolation of this data to the routine clinical situation, because lignocaine levels may reach peak plasma levels several hours after infusion\textsuperscript{26}.

For patient safety in all types of lipoplasty, and particularly UAL, which is usually performed with tumescent techniques, the composition and volume of subcutaneous wetting solutions should be based on good evidence as per the recommendations of Bussien and Maillard\textsuperscript{25} (see over page).
In choosing an appropriate tumescent formula, there are several controversial options:

- Isotonic or hypotonic,
- Normal saline or lactated Ringer’s solution,
- The doses of lignocaine, adrenaline and bicarbonate, and
- The temperature of the fluid to be infiltrated\textsuperscript{25}.

Surprisingly, large volumes of solution containing high concentrations of lignocaine have been infiltrated rapidly with peristaltic pumps. Although a slow infusion of 35 mg/kg of lignocaine has been accepted as safe, (even though this far exceeds the recommended maximum of 7 mg/kg for lignocaine administered with adrenaline), dermatologic surgeons have reported safety with 55mg/kg with one report allegedly demonstrating “safety” using 70-90 mg/kg\textsuperscript{30}.

After careful consideration of these variables, and based upon a three-year experience with ultrasonic liposuction, Bussien and Maillard\textsuperscript{25} make the following recommendations:

- \textbf{Lactated Ringer’s solution} be used as the subcutaneous infiltration solution because it mirrors the composition of the interstitial compartment.
- \textbf{Lignocaine} be used as the standard local anaesthetic at a maximum dose of 35 mg/kg if infused over 45 minutes into the subcutaneous fat.
- \textbf{Adrenaline} 0.5 mg/l to 1.0 mg/l be used for vasoconstriction to retain the lignocaine and the adrenaline at the site of infiltration.
- \textbf{Sodium bicarbonate} 8.4%: 5 mEq/l be used to adjust the solution’s pH to the pKa (pH 7.9) of lignocaine.
- \textbf{Room temperature infusions} are preferred.

\textit{Fluid Resuscitation Guidelines}

From an analysis of 53 consecutive patients undergoing liposuction, Trott \textit{et al}\textsuperscript{31} suggest the following guidelines for fluid resuscitation:

\textbf{Small volume liposuctions ($< 4$ litre aspirates)}

Give IV maintenance fluid plus subcutaneous wetting solution.

\textbf{Large volume liposuctions ($> 4$ litre aspirates)}

Give IV maintenance fluid plus additional 0.25 cc of crystalloid per cc of aspirate removed after 4 litres plus subcutaneous wetting solution.

Other authors\textsuperscript{28,32} however, caution against embarking on major fluid replacements without due regard for the type of anaesthetic used.

\textit{Ultrasound Related Issues}

The precise mechanism in which ultrasonic energy interacts with living tissue is only partially understood. It is this incompleteness in our understanding that underpins the reticence of some clinicians to fully embrace this technology\textsuperscript{1}.
It is known that the interaction of ultrasound with human tissues *in vivo* produces three different effects:

i. Thermal

ii. Cavitational

iii. Direct tissue interactions

While there are numerous medical uses of ultrasound, the desired and undesired effects are determined by such variables as:

- Frequency,
- Power intensity,
- Peak amplitude,
- Duration of exposure, and
- Whether it is delivered as a pulse or in a continuous fashion.

For example, in tumour ablative therapy, an externally focused ultrasonic beam (frequency: = 1 MHz, power 0.5 – 3 W/cm\(^2\)) uses the thermal effects to cause spot-specific tissue heating. In contrast, ultrasonic diagnostic imaging (frequency: 1 - 10 MHz, power < 0.05 W/cm\(^2\)) relies on the absorption and scattering differences at tissue boundaries to generate images. Ultrasound-assisted lipoplasty (frequency: 20 - 50 kHz, power 10 – 300 W/cm\(^2\)) has the cavitational effect as its principal mode of action\(^{11}\).

### i. Thermal Effects

Absorption of ultrasound in human tissue depends on the molecular composition of that tissue, with the absorption coefficient increasing as a function of protein content. For water and body fluids, there is little absorption in acoustic conditions so there is little risk of heating\(^{33}\). Tumescent conditions for ultrasonic liposuction create an essentially fluid medium allowing for little absorption and theoretically little heat gain, but the extent of ultrasound-induced tissue heating depends on the balance of heat gain and heat loss.

Vascularity and tissue composition determine heat loss rate, and as perfusion is poor in fatty tissue, heat dissipation may be limited and the net effect may be tissue overheating. Tissues with higher collagen composition have higher acoustic absorption coefficients and as liposuction is usually performed within areas of adiposity bounded by skin and fascia, care must be exercised to avoid “end hits” of the ultrasonic probe against these structures to avert thermal damage.

In response to concerns of heat-related problems and following reports of burns and ischaemic skin injuries in the literature, Ablaza *et al*\(^{34}\) investigated whether significant temperature elevations occurred in the clinical setting. Using subcutaneous transducers, they measured temperatures in the area of liposuction; before infusing tumescent fluid, after tumescent fluid infusion, and at five-minute intervals until the UAL was completed.

Although subcutaneous temperatures did rise with the application of ultrasonic energy, the average subcutaneous temperatures remained below the core temperature at all time intervals.
The recommendations from that study were:

i. Room temperature tumescent fluid enhances the thermal safety zone without lowering core body temperature.

ii. Although heat is a natural by-product of the energy transfer involved in UAL, the risk of thermal injury is negligible when experienced operators (i.e. qualified surgeons who have successfully completed a training course in UAL) perform the procedure. Ablaza et al\textsuperscript{34}, interpret the previously reported ischaemic skin injuries to be the result of damage to the subdermal plexus, rather than a thermal injury. They caution that a complete understanding of UAL techniques with strict adherence to the basic principles of flap vascularity should ensure safe and effective UAL performance.

ii. Cavitation Effects

Cavitation is the generation, growth and collapse of bubbles in a sound field. During the pressure phases of a sound wave, stable bubbles of dissolved gas in living tissues will grow and shrink due to the cycles of compression and decompression; this is termed “stable cavitation”. If the pressure changes between cycles of compression and decompression are sufficiently large, gas pockets form within the tissues, and contract within the sound field, and shearing forces can fragment the cells\textsuperscript{11,35}.

A more violent form of cavitation, called “transient cavitation”, occurs when higher acoustic energies cause the gas bubbles to collapse during the compression phase of vibration. This sudden, violent collapse of the gas bubbles generates locally intense shock waves with the release of dramatic amounts of heat and pressure\textsuperscript{11}.

The mechanism of cavitation and other non-thermal effects are poorly understood, as all forms of cavitation have only been studied in simple liquids and cell suspensions. These are not truly representative of living tissues that are linked via cellular structures to form a more complex structure, which in turn may be susceptible to greater damage than a single cell. The paucity of \textit{in vivo} toxicity work means little information is available about the effects of cavitation in human tissue. However, cavitation effects can result in sufficient energy to disrupt chemical bonds and produce chemically reactive free radicals with the potential to interfere with DNA and thereby lead to chromosomal damage. Although this has never been observed in either patients or laboratory animals, several studies have been undertaken in cell culture experiments where cells are isolated from the effect of surrounding tissue, so that thermal effects are less likely than cavitation effects.

The potential carcinogenic potency of chemically active free radicals has to be considered whenever cavitation occurs within cells\textsuperscript{33}. Genetic effects include chromosomal aberrations as well as point mutations and sister chromatid exchanges (SCEs). Although chromosomal aberrations and point mutations are clinically adverse, the significance of SCEs is not clear. Liebeskind et al\textsuperscript{36} attested that ultrasound of diagnostic intensities can affect the DNA of animal cells. \textit{In vitro} acoustic shock studies on mammalian cells with the generation of inertial cavitation have demonstrated the production of ultraviolet light, which is known to be mutagenic. Such observations in cell lines cannot be directly extrapolated to mammalian tissue\textsuperscript{33}.
There is the potential also for the demyelination of peripheral nerves from the cavitational effects of UAL. However, a study comparing the sensory changes of SAL and UAL found no significant difference at ten weeks postoperatively\textsuperscript{37}.

iii. Direct Tissue Interactions

In an effort to understand the physical effects of UAL on adipose tissue, Adamo \textit{et al}\textsuperscript{35} compared the results of UAL (20 kHz, 65 W delivered by solid titanium probes) and SAL by a microscopic analysis of the evacuated tissue using a small study of five patients treated by each technique. They analysed samples of the evacuated material by centrifuging samples at 300 rpm followed by an examination of the supernatant with optical and scanning electron microscopy. This facilitated an examination for signs of cellular damage, signs of cavitation, and gas micro bubbles. The SAL derived tissue was composed of fat globules in their original organised form, whereas the UAL sonicated tissue showed cells ruptured at several sites with all the intercellular junctions destroyed. No evidence of the cavitation phenomenon was noted.

While postulating that the UAL effects are produced by micro-streaming tissue movement, Adamo \textit{et al}\textsuperscript{35} suggest that a direct ultrasonic effect on tissue produces disruption of macromolecules and cellular structures and may produce accelerated chemical reactions, free radicals and chromosomal disruption.

These researchers cautiously recommended that further research was needed to clarify the end-points of sonication:

i. Its effectiveness, and
ii. The possibility of hazards lest we expose “the patient to a physical agent that we have not thoroughly investigated”\textsuperscript{35}.

Certainly when ultrasonic energy was used in the treatment of malignancies in the past, vascular complications were frequent, and occasionally massive metastases resulted. Recent evidence on the stimulation by therapeutic ultrasound of angiogenic factors, \textit{e.g.} interleukin-8 (IL-8), basic fibroblast growth factor (bFGF) and vascular endothelial growth factor\textsuperscript{38} (VEGF), suggest that ultrasonic energies can stimulate cellular activity.

When one probes more deeply into the potential effects of the violent collapse and intense heat generated during the bubble implosions, the potential for problematic interaction becomes evident. These released free radicals could cause DNA damage\textsuperscript{39}. However although the genotoxic effects have been demonstrated \textit{in vitro}, the special conditions under which these effects have occurred may not be representative of a clinical situation.

Recent evidence would suggest that ultrasound could alter cell division rates and influence apoptosis. Using an 8 MHz scanner on 12 mice for 15 minutes, there was a 22\% reduction in the rate of cell division in cells of the small intestine and a doubling of apoptosis when examined 4½ hours after ultrasound exposure. One hypothesis for these observations was that ultrasound might be switching on the p53 gene that helps cells recognise DNA damage; the cells may stop dividing or undergo programmed cell death\textsuperscript{40}. 

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In view of these observations, it seems sensible to advise against the use of UAL to contour breast tissue. Interestingly, Maillard et al\textsuperscript{5} have reported such an application for UAL but they caution that:

i. While highly improbable, a theoretical spread of an \textit{in situ} breast cancer may be possible, and

ii. The long-term ultrasonic effects on fat and breast tissue have not been studied\textsuperscript{5}.

Concerns linger about the long-term complications that may arise from UAL as a consequence of tissue exposure to:

- \textbf{Sonoluminescence} (conversion of sonic energy into light)\textsuperscript{13},
- \textbf{Sonochemistry} (which produces free radicals)\textsuperscript{35}, and
- \textbf{Thermal effects}\textsuperscript{1}.
Recommendations

General

Ultrasound-assisted lipoplasty is not a replacement for SAL but complements it by allowing body contouring in areas not possible with SAL\textsuperscript{41}. Ultrasound-assisted lipoplasty has proven benefit in the contouring of fibrous areas and in scarred secondary liposuction cases. It also reduces surgeon fatigue and allows more thorough fat removal in the fibrous male patient\textsuperscript{21}. As with any new surgical procedure, adequate training, experience and attention to detail are the keys to predictable success. Because of the significant differences between UAL and SAL, and the potential complications associated with UAL, special training is considered an imperative prerequisite to performing UAL safely and effectively\textsuperscript{42}.

Training

In March 1995, the major American plastic surgery organisations formed a task force to evaluate the safety and efficacy of UAL and to develop an educational curriculum to introduce and teach this new technology. To acquire UAL “privileges” it was recommended that:

\textbf{Surgeons not fully trained in UAL techniques should successfully complete a training course of didactic lectures as well as a laboratory component with cadaveric dissection. The course should cover instrumentation and a demonstration of ultrasonic equipment and techniques to ensure safety.}

Technical

Specific to UAL is the recommended use of submaximal amplitude settings except in very fibrous zones, and adherence to well defined end points for the ultrasonic phase of the operation. Suggested end points include loss of resistance to cannula movement and change in aspirate colour from yellow to pink\textsuperscript{2}. By avoiding excessive applications of internal ultrasound energy, cavity formation and hence, seroma development should be lessened. Although some authors advocate shortened treatment times (from 15 to 20 minutes per site to 2 to 5 minutes per site) to decrease the incidence of post operative swelling and dysesthesia, others doubt the clinical effectiveness of such a truncated exposure time\textsuperscript{2}.

Patient Selection

The selection of patients for any liposuction procedure should be limited to those in good health and close to their ideal weight. Furthermore, liposuction should be restricted to specific areas of excess fat that have not reduced with diet and exercise\textsuperscript{43}.
Informed Consent

The omnipresent medico-legal issues of informed consent and risk minimisation require that patients be given factual information on SAL and UAL, particularly if UAL is used to complement SAL. Some risks are common to both techniques, and some are unique to each technique. Preoperative information should cover the following topics:\(^{42}\);

**Thermal Injury**

Risks include:
- Incision site burns from friction,
- Ultrasound-induced thermal injuries,
- Dermal ‘end-hits’.

Precautions to reduce risk;
- Skin protectors to overcome skin burns at incisions\(^{18}\),
- Adequate wetting solution,
- Cannula tip control with constant movement\(^{21}\),
- Time limitation of ultrasound energy,
- Lower amplitude settings.

**Skin Necrosis**

Risks include;
- Thermal or ischaemic skin loss.

Precautions to reduce risk;
- Maintaining adequately ‘wet’ subcutaneous environment,
- Avoidance of aggressive undermining of skin in a superficial plane.

**Seromas**

Risks include;
- Fat liquefaction and cavity formation.

Precautions to reduce risk;
- Thorough evacuation of fatty emulsion,
- Insertion of drains in large volume lipoplasties (> 1.5 litres),
- Conservative liposuction in areas of marked skin laxity,
- Appropriate compression garments postoperatively.
Contour Irregularities

Risks include:
- Uneven skin contours from insufficient removal,
- Grooving or tunnelling defects from over enthusiastic removal in focal superficial regions,
- Skin laxity.

Precautions to reduce risk:
- Accurate markings preoperatively,
- Adequate wetting solutions,
- Attention to liposculpting technique,
- Avoidance of aggressive superficial treatment.

Infiltration Solution Related Problems

Risks include:
- Hypovolaemia,
- Fluid overload,
- Lignocaine toxicity,
- Adrenaline overdose,
- Electrolyte imbalances,
- Hypothermia,
- Death from combinations of the above risks.

Precautions to reduce risk:
- Sensible lipoaspirate volumes to limit lignocaine infused subcutaneously to 35mg/kg,
- Physiological solutions,
- Sodium bicarbonate to bring solution’s pH to the pKa of lignocaine,
- Adrenaline limited to ≤ 0.5 to 1 mg/litre,
- Room temperature solutions\(^{34}\),
- Safe fluid resuscitation\(^{31}\).

Nerve Damage

Risks include:
- Hypoaesthesias,
- Dysaesthesias.

Precautions to reduce risk:
- Restricting UAL energy application times,
- Avoid prolonged superficial treatments,
- Advise patients that by 10 weeks 90% of liposuction patients will have normal sensation\(^{37}\).
Ultrasound-Induced Biological Effects

Risks include:
- Potential chromosomal damage from DNA disruptions,
- Carcinogenic potential of chemically active free radicals,
- Altered cell division,
- Architectural distortions of breast tissue impeding breast cancer screening.

Precautions to reduce risk:
- Avoid prolonged exposures to ultrasonic energy in one location,
- Use UAL only as an adjunct to SAL,
- Exclude pregnancy,
- Avoid female breast recontouring with UAL.

It is theoretically possible that cavitational activity in adipose tissue may generate free radicals and other reactive molecules that could interact with DNA to produce an endotoxic effect. Some consider this risk to be negligible because the adipocytes would need to:

- Survive the cavitational pressures and heat,
- Avoid being removed by aspiration, and
- Be stimulated to undergo replication, even though adipocytes are considered to be terminally differentiated cells\(^{11}\).

A liposuction site however, is not composed solely of adipocytes. Moreover, some tissues such as glandular tissue have a high propensity for cellular replication and for this reason UAL would be best avoided for breast contouring.

Anaesthetic Related Problems

Risks include:
- General anaesthetic, regional anaesthetic, neurolept anaesthetic, local anaesthetic.
- Pressure points and neuropraxias.

Precautions to reduce risk:
- Attendance of a specialist anaesthetist with experience in anaesthesia for liposuction patients,
- Appropriate monitoring and resuscitation equipment,
- Formal agreements between day surgeries and major centres for transfer in case of emergency,
- Thorough understanding of the fluid shifts with various types of anaesthesia\(^{28}\),
- Appropriate patient positioning\(^{44}\).
Bruising and Postoperative Pain

Risks include:
- Significant bruising and pain,
- Long term skin staining by haemosiderin.

Precautions to reduce risk;
- Careful evacuation of liposuction sites.,
- Compressive garments applied at end of procedure.
- If anatomically feasible, analgesia with regional blocks incorporating long acting local anaesthetics, taking due care with the cardiotoxicity of local anaesthetics like bupivacaine.
- Adequate regular oral analgesia.

Skin Scarring

Risks include;
- Longer incisions for UAL (compared to SAL) to accommodate skin protector.

Precautions to reduce risk;
- Judicious placement of incisions,
- Meticulous skin closure and scar management.

Documentation

In addition to preoperative and postoperative photographs, clinical examination data and operative details should be recorded accurately with worksheets such as those prepared for the Lipoplasty Effectiveness And Patient Safety (LEAPS) study being conducted by the American Society of Plastic and Reconstructive Surgeons Plastic Surgery Education Foundation (ASPRS/PSEF) in the USA. Documentation of intraoperative fluid loss from each anatomical zone by analysing the lipoaspirates has also been suggested to gauge blood loss.
Conclusion

In conclusion, the technical aspects of UAL can be carried out safely if certain fundamental principles are observed:\(^\text{46}\);

- Appropriate patient selection,
- Appropriate anatomical sites,
- Attention to operative technique,
- Careful selection of infiltrating solutions,
- Adequate fluid management,
- Good patient monitoring and documentation,
- Postoperative compression garments.

Caution

While UAL appears to be a technically safe and efficacious procedure, there remains the persisting doubt about potential hazards long term, as a result of the high-energy interactions with tissue\(^1\). This is particularly so for female breast contouring.

Future Research

Future \textit{in vivo} studies could be undertaken on a transgenic animal model that has a high propensity to develop chromosomal aberrations in response to exogenous factors. Exposure to UAL level energies could be followed by an analysis of any chromosomal alterations to determine whether the UAL treated group had more DNA damage when compared with animals in a control group not exposed to UAL. This type of animal model\(^{47,48}\) is currently available and is central to an ongoing study to elucidate the \textit{in vivo} effects of mobile phone signals. The importance of undertaking such a study is underpinned by the uncertainty of the significance of the ultrasonic tissue effects, particularly at the levels delivered to human tissue with UAL.
**Procedure Classification**

ASERNIP-S allocates each procedure a classification from the following list:

I. Safety and efficacy is established. Procedure may be used.

II. The procedure is sufficiently close to a procedure of established safety and efficacy to give no reasonable grounds for questioning the safety and efficacy. The procedure may be used subject to continuing audit.

III. Safety and efficacy of the procedure is not yet established. The procedure requires further evaluation and may be used only as part of systematic research; comprising either an observational study or a controlled clinical trial.

IV. Safety and/or efficacy of the procedure is shown to be unsatisfactory. Procedure should not be used.

The assigned ASERNIP-S classification for Ultrasound-assisted Lipoplasty is II.

**Review Group Comments**

The ASERNIP-S Ultrasound-assisted Lipoplasty Review Group recommends that ultrasound-assisted lipoplasty should not be performed to contour female breast tissue.
REFERENCES


METHODOLOGICAL ASSESSMENT REPORT

ULTRASOUND-ASSISTED LIPOPLASTY

Dr Wendy Babidge
Research Coordinator, ASERNIP-S

July 1999
Introduction

Closed liposuction began in the late 1970’s and since then, modifications have been made to the original idea. A significant improvement was the use of tumescent infiltration of the treatment areas prior to liposuction. In the early 1990’s, Zocchi described the use of ultrasonic energy for the destruction of adipose tissue. The technique is thought to be based on the phenomenon of ‘cavitation’ whereby ultrasound energy causes vapour bubbles in liquid to implode, thereby disrupting tissues. Cavitation acts on the fluid in fat cells and if used correctly is thought not to effect vascular, nerve or connective tissue components.

Ultrasonic energy must be applied in a ‘wet’ environment. The tumescent technique has surpassed the earlier techniques of ‘dry’ (no infiltrating fluid), ‘wet’ (a few hundred millilitres of normal saline and lignocaine) and ‘super wet’ (larger volumes of infiltrating fluid). The tumescent technique utilises large volumes of infusate (> one volume wetting solution: one volume aspirate) to pressurise the tissues and is used both with suction-assisted lipectomy (SAL) and ultrasound-assisted lipectomy (UAL). This solution is aimed at being osmotically similar to that of the interstitial compartment, and commonly Lactated Ringer’s solution is used. Bicarbonate is added as a buffer. Lignocaine is added as a local anaesthetic to a maximal dose of 35 mg/kg infused as a dilute solution over 45 minutes (care must be taken to avoid toxicity). Adrenaline can also be added to cause vasoconstriction, retain the anaesthetic at the site of infiltration and purportedly, to reduce bleeding.

In ultrasonic lipectomy a tumescent solution is infused, and following ultrasound treatment the liquefied fat is evacuated by suction. The proposed advantages of this technique include reduced trauma and blood loss, allowing massive fat removal in obese patients. It was recognised early that there was a steep learning curve for use of this technique.

Safety Issues

Potential complications of SAL include adverse effects on intravascular fluid volume (including hypotension and hypovolaemic shock), coagulation (including pulmonary embolism and thrombosis), nerves and nerve conduction, and circulation to skin; excessive blood loss, haematoma or seroma and infection. In the tumescent technique there is a risk of systemic lignocaine toxicity. Other risks include those to operating theatre personnel, who may be exposed to infectious or chemical contaminant aerosols.

The biological effects associated with the generation of ultrasonic energy are thought to be exerted by thermal mechanisms, which cause localised heating. Alternatively non-thermal mechanisms such as cavitation result in intense heat production and generation of free radicals and other chemically reactive species, which potentially can cause genotoxic effects in cells adjacent to those destroyed by the cavitation. Evidence of these has been found in cell lines in vivo under specialised conditions. However, there are no validated models for predicting whether such cavitation effects are likely in human tissues. Bond and Cimino found no evidence of cavitation in fresh pig tissue exposed to ultrasound energy.

Ultrasound aspiration devices have been used in other surgical techniques including liver resection for cancer, laparoscopic cholecystectomy, laparoscopic removal of intraperitoneal masses, laparoscopic adrenalectomy, removal of central nervous system tumours and transurethral resection of the prostate. It is important with any surgical technique that...
patients are aware of all potential risks including theoretical concerns regarding the long-term effects of ultrasonic energy exposure\textsuperscript{10}.

From the systematic searches defined in the protocol for the review of ultrasound-assisted lipoplasty the studies have been stratified based on their level of evidence (see pages 7 - 8).

<table>
<thead>
<tr>
<th>Hierarchy of evidence – NH&amp;MRC</th>
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<td>III-3</td>
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<td>IV</td>
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Two studies\textsuperscript{16,25} have been added to those originally obtained, by searching Current Contents from Week 1 to 28, 1999, to update the previous searches. The most common complication that arose in the tabulated studies included thermal entry site burns\textsuperscript{11-13} which should be avoidable if appropriate care is taken, seromas\textsuperscript{4,13,14}, Reston foam (placed between treated area and overlying compressive garment) blisters\textsuperscript{4,14} and temporary neuropraxia\textsuperscript{11}. No deaths were reported in this series, however there are literature reports of a small number of cases of death with SAL\textsuperscript{15} where lignocaine toxicity or lignocaine-related drug reactions were thought to play a part. With the UAL procedure three deaths were reported from different countries\textsuperscript{5}, with one death due to an inappropriately high dose of lignocaine having been administered.
<table>
<thead>
<tr>
<th>Ref #</th>
<th>Year</th>
<th>Authors</th>
<th>Study Location</th>
<th>Study Type</th>
<th>Study Level</th>
<th>Procedure</th>
<th>Equipment Type</th>
<th>Time of ultrasound application</th>
<th>Sample Size</th>
<th>Statistics used</th>
<th>Follow-up</th>
<th>Adverse Outcomes/Comments on Safety</th>
<th>Comments on efficacy</th>
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<tbody>
<tr>
<td>11</td>
<td>1997</td>
<td>Igra H; Satur NM</td>
<td>CA, USA</td>
<td>RCT: (randomisation of treatment site; computer generated); blinded non-operating surgeon</td>
<td>II</td>
<td>UAL vs SAL</td>
<td>Morwell Ultrasound: Ultrasonic Aspirator system, irrigated cannula</td>
<td>Not stated</td>
<td>28 (25F)</td>
<td>Paired student t-test(volume fat), non-parametric sign test (physician/patient rating)</td>
<td>Day 2-4; 1 week, 1, 3, 6 months</td>
<td>3.6% temp. neuropaxia, 3.6% thermal entry injury; physician/patient ratings mostly nsd (UAL:SAL).</td>
<td>Easier cannula motion for operating physician (UAL); nsd volume fat removed (UAL:SAL).</td>
</tr>
<tr>
<td>17</td>
<td>1997</td>
<td>Cook-WR Jr</td>
<td>CA, USA</td>
<td>RCT (treatment side randomised); operating physician blinded, patients not blinded</td>
<td>III-1</td>
<td>SAL +/- external US one side following infusion of tumescent solution; IM sedation (not IV sedation or GA)</td>
<td>External US (Rich-Mar): 2W/cm², 1 MHz</td>
<td>10 - 15 min per body area</td>
<td>30 (25F)</td>
<td>Not performed</td>
<td>Day 2 post-op</td>
<td>No complications seen, external US side less bruising/swelling (18/30 cases).</td>
<td>External US side-easier on surgeon (21/30), less patient discomfort (16/30), aspirate looser &amp; milky white (external US side).</td>
</tr>
<tr>
<td>20</td>
<td>1998</td>
<td>Podor PR; Watson J</td>
<td>CA, USA</td>
<td>RCT (treatment side randomised); patients blinded</td>
<td>III-1</td>
<td>UAL vs SAL</td>
<td>Surgitron 3000: Sebbin, Lysonix 2000 (94 cases)</td>
<td>&lt; 10 minutes per region</td>
<td>100 UAL/73F, 63/100; 10 patients randomly selected for independent evaluation</td>
<td>McNemar Chi squared test Day 3-4, 7-10; 1-3 months longest 22mo</td>
<td>No complications - seromas, skin burns; UAL - less blood loss, better for fibrotic areas; post-op. ecchymosis most moderate, UAL disadvantage - longer incision, nsd postop. ecchymosis/swelling</td>
<td>No differences in post-op. skin retraction/contraction or sensory pigmentation changes/surface irregularities between 2 sides; UAL - post-op discomfort mostly minor, UAL - increased op. time, increased learning curve, UAL not superior to SAL.</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>1997</td>
<td>Havoonian HH; Luftman DB; Menaker GM; Moy RL</td>
<td>CA, USA</td>
<td>RCT (treatment site randomised) non-blinded</td>
<td>III-1</td>
<td>SAL +/- external US one side following infusion of tumescent solution</td>
<td>1 MHz Rich-Mar Model X US unit</td>
<td>Approx. 10 min over treatment area</td>
<td>10</td>
<td>Not performed</td>
<td>1, 3, 7, 12 week</td>
<td>No intraop complications; 4/10 less swelling/bruising, 5/10 less postop. pain</td>
<td>US side: 5/10 operate ease, 3/10 higher degree skin retraction, higher av. volume supernatant fat in US.</td>
</tr>
<tr>
<td>21</td>
<td>1997</td>
<td>Adamo C; Mazocchi M; Rossi A; Scuderi N</td>
<td>Rome, Italy</td>
<td>Prospective comparative study (2 arms)</td>
<td>III-2</td>
<td>UAL vs suction lipoplasty (SAL); manual compression for fat removal</td>
<td>Brand not stated: 20kHz, 65W, solid probe</td>
<td>Not stated</td>
<td>10 - (5 + 5)</td>
<td>Not performed</td>
<td>Not stated</td>
<td>No adverse outcomes; need to assess possible hazards of US - accelerated chemical reactions, chemical changes, free radical formation, chromosome disruption.</td>
<td>SAL &gt; infiltrate per unit time than UAL; UAL disruption of fat cells while SAL intact fat cells.</td>
</tr>
<tr>
<td>12</td>
<td>1998</td>
<td>Kenkel JM; Robinson JB Jr; Beran SJ; Tan J; Howard BK; Zocchi ML; Rohrich RJ</td>
<td>TX, USA; Torino, Italy</td>
<td>Animal (pig) controlled comparative study (2 arms) &amp; non-liposuction control</td>
<td>III-2</td>
<td>UAL+/+sheath, non-liposuction control (under GA)</td>
<td>Mentor Contour Genisis</td>
<td>Not stated</td>
<td>8, 4 (+sheath), 3 (+sheath), 1 (non-liposuction control)</td>
<td>Independent t-test; repeated measures analysis of covariance</td>
<td>Not applicable</td>
<td>1 pig thermal entry site burn (12.5%); sheath requires GA; no biochemical evidence of fat, muscle, nerve damage; UAL + sheath - less Hb lost, less blood per triglyceride lost.</td>
<td>UAL more lipid aspirated and better preservation of vascular structures. SAL: more aspirate per unit time; UAL sheath has protective effect.</td>
</tr>
<tr>
<td>Ref #</td>
<td>Year</td>
<td>Authors</td>
<td>Study Location</td>
<td>Study Type</td>
<td>Study Level</td>
<td>Procedure</td>
<td>Equipment Type</td>
<td>Time of ultrasound application</td>
<td>Sample Size</td>
<td>Statistics used</td>
<td>Follow-up</td>
<td>Adverse Outcomes/Comments on Safety</td>
<td>Comments on efficacy</td>
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<tr>
<td>16</td>
<td>1999</td>
<td>Albin R; deCampo T*</td>
<td>Not stated</td>
<td>Controlled series (historic controls)</td>
<td>III-3</td>
<td>Large volume liposuction UAL, SAL</td>
<td>Lysonix 2000</td>
<td>Not stated</td>
<td>181; 31 SAL, 150 UAL</td>
<td>Not stated</td>
<td>Not stated</td>
<td>0.6% deep vein thrombosis, 1.1% pulmonary emboli</td>
<td>Not stated</td>
</tr>
<tr>
<td>4</td>
<td>1996</td>
<td>Ablazer VJ; Gingrass MK; Perry RN; Fisher J and Maxwell GP</td>
<td>TN, USA</td>
<td>Prospective case series</td>
<td>IV</td>
<td>UAL; (50 GA, 4 epidural, 1 LA + sedation)</td>
<td>Medical Device Alliance Inc.</td>
<td>mean: 51 min (10-118 min)</td>
<td>55/96 temperature measured (45F)</td>
<td>Not stated</td>
<td>Day 1, 5; 2, 4, 6 week; then 3 - 9 months (mean 3.4 months)</td>
<td>Seroma, 12 (22%), Reston foam blister (16%), scrotal haematoma (2%); plastic sheath minimise skin burns, use UAL in 'wet' environment, minimal elevation of subcutaneous temperature, advocate use of room temperature tumescent fluid.</td>
<td>None</td>
</tr>
<tr>
<td>22</td>
<td>1996</td>
<td>Budo JA</td>
<td>Large, Belgium</td>
<td>Prospective case series</td>
<td>IV</td>
<td>UAL; (45 GA, 11 LA)</td>
<td>Lipectron US Lancet, Medicon US liposuction device</td>
<td>Not stated</td>
<td>56 (54F)</td>
<td>Not performed</td>
<td>Not stated</td>
<td>Blood loss insignificant (max. 50ml), UAL less pain/haematoma, more postop. swelling.</td>
<td></td>
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<tr>
<td>23</td>
<td>1998</td>
<td>Lack EB</td>
<td>IL, USA</td>
<td>Prospective case series</td>
<td>IV</td>
<td>UAL (non-water cooled cannula), post suction by SAL, IV sedation, skin protector</td>
<td>Not stated</td>
<td>Range 1 - 8 min per area</td>
<td>6 (4F)</td>
<td>Not performed</td>
<td>1, 4 week</td>
<td>Considerable morbidities - numbness, swelling, pain, seroma, necrosis, bruising (higher than that reported for SAL).</td>
<td>Skin retraction effects not proven, no reduction in blood loss compared with reviews, UAL more complicated machinery, but more selective exeresis, treat difficult areas.</td>
</tr>
<tr>
<td>24</td>
<td>1997</td>
<td>Maillard GF; Schefflan M; Bussein R</td>
<td>Switzerland, Israel</td>
<td>Single case report</td>
<td>IV</td>
<td>UAL then SAL (Breast) (IV sedation)</td>
<td>Not stated</td>
<td>Not stated</td>
<td>1</td>
<td>Not performed</td>
<td>1, 6 week</td>
<td>Postop oedema, possible risk of spread of in situ breast cancer, aspirate little blood, no haematoma/ bruising at 1 week.</td>
<td>Symmetry nearly achieved at 6 weeks.</td>
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<tr>
<td>14</td>
<td>1998</td>
<td>Maxwell GP; Gingrass MK</td>
<td>TN, USA</td>
<td>Consecutive case series</td>
<td>IV</td>
<td>UAL, (94% GA; LA &amp; Epidural)</td>
<td>SMEI, Sonic Sculpture, Sobin, Surgitron Series 2000, Lysonix 2000</td>
<td>29 min (abdomen), 14’ min (hip), 12’ min (thigh)</td>
<td>250 (209F)</td>
<td>Not performed</td>
<td>1, 2, 4 week; 3, 6 months</td>
<td>Reston foam blisters (14%), seroma (11%), abdominal skin necrosis (1.2%).</td>
<td>Suggest final contouring with SAL; UAL learning curve.</td>
</tr>
<tr>
<td>13</td>
<td>1998</td>
<td>Rohrich RJ; Beran SJ; Kenkel JM; Adams WP Jr; DiSpaltro F</td>
<td>TX, USA</td>
<td>Consecutive case series</td>
<td>IV</td>
<td>3 stage technique - Infiltration, UAL, SAL</td>
<td>Lysonix 2000</td>
<td>2 - 11 minutes</td>
<td>114 (91F)</td>
<td>Not performed</td>
<td>Day 5; 3, 6 week; 3, 6 months</td>
<td>1% abdominal dysesthesia (due to long US time), 2.6% abdominal seromas (long US &amp; inadequate fat emulsion evacuation), 1% access site skin burn.</td>
<td>Aspiration rates: SAL - 58ml/min, UAL 36ml/min.</td>
</tr>
<tr>
<td>Ref #</td>
<td>Year</td>
<td>Authors</td>
<td>Study Location</td>
<td>Study Type</td>
<td>Procedure</td>
<td>Equipment Type</td>
<td>Time of ultrasound application</td>
<td>Sample Size</td>
<td>Statistics used</td>
<td>Follow-up</td>
<td>Adverse Outcomes/Comments on Safety</td>
<td>Comments on efficacy</td>
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<tr>
<td>19</td>
<td>1998</td>
<td>Tebbetts JB</td>
<td>TX, USA</td>
<td>Consecutive case series</td>
<td>IV</td>
<td>UAL (GA as outpatient)</td>
<td>Lysonix 2000, dual E &amp; aspiration functions</td>
<td>1 - 6 min per side</td>
<td>70 (58F)</td>
<td>Not performed</td>
<td>Day 1, 2, 3; 1. 3 week; 3. 7 months</td>
<td>No peri/postop. Complications relating to US, no seromas, skin burns/blistering, vascular insufficiency, skin loss, neuralgia, skin pigmentation, infection, haematoma.</td>
<td>Reduce surgeon fatigue, no malfunction with US generator, probe replaced after 42 cases, Total UAL op. Time &lt; traditional SAL times.</td>
</tr>
<tr>
<td>25</td>
<td>1999</td>
<td>Trott SA; Beran SJ; Kenkel JM; Adams WP Jr; Robinson JB Jr*</td>
<td>TX, USA</td>
<td>Case series</td>
<td>IV</td>
<td>UAL (3 stages)</td>
<td>Not stated</td>
<td>Not stated</td>
<td>21</td>
<td>Not stated</td>
<td>2, 6, 10 week</td>
<td>In general – SAL areas normal by 6 week, UAL by 10 week; 90% all patients normal sensation by 10 weeks.</td>
<td>Not stated</td>
</tr>
</tbody>
</table>

* Abstract only sighted; Abbreviations: RCT - randomised controlled trial, UAL - ultrasound-assisted lipoplasty, SAL - suction-assisted lipoplasty, US - ultrasound, GA - general anaesthetic, LA - local anaesthetic, IV - intravenous, F - female, nsd - no significant difference, op - operative.
Efficacy Issues

The ultrasonic probe moves easily through tissue and thus requires less force to be applied by the surgeon compared to the standard SAL technique. It has therefore been considered safer and more efficacious due to reduced surgeon fatigue. A technique of lipoplasty entirely performed by UAL has proven to take longer than SAL, however much larger volume lipoplasties are possible via this technique due to the reduced blood loss. It has been suggested that UAL should be used to complement SAL and not necessarily to replace it.

In the tabulated studies, reduced surgeon fatigue is noted for the UAL procedure, however generally increased operating times, slower aspiration rates and the increased learning curve, were noted. Ultrasound-assisted lipoplasty has been reported to be useful in areas difficult to treat and in fibrotic tissue.

Conclusions

Despite the fact that four of the tabulated studies were randomised controlled trials, they were of poor quality. In two studies only, the assessing physician/surgeon was blinded and in one only, the patients were blinded as to which side was treated with ultrasound. However in all cases, most measures were subjective and without blinding their worth is dubious. In two of these studies external ultrasonic energy was applied to the infiltrated treatment area, however no other reports of this technique are evident in the current review. In other controlled studies, small patient numbers or historical controls were used. The remaining eight studies were case series and a single case report.

It is evident that the UAL procedure requires more extensive and rigorous evaluation. The prospects of the potential damaging effects of ultrasound energy application need investigation. Given the already widespread use of UAL it is considered imperative to collect data on this procedure, particularly focusing on safety issues. A prospective multi-centre cohort study to be conducted over a six-month period, with a single treatment group is soon to begin in the United States of America. It is anticipated to enrol about 2,000 patients from 40 - 50 plastic surgery practices. It may be worthwhile for ASERNIP-S to consider coordinating selected Australian surgeons who are performing ultrasound-assisted lipoplasty for participation in this study.
REFERENCES


