



Australian Government
Department of Health and Ageing



Horizon Scanning Technology Prioritising Summary

**AlloDerm® for deep superficial and full
thickness burns**

December 2005



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



**Royal Australasian
College of Surgeons**

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

This Horizon scanning prioritising summary was prepared by staff from the Australian safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S).

Horizon Scanning Technology Prioritising Summary

Name of Technology:

AlloDerm® (LifeCell Corporation, Branchburg, NJ, USA)

Purpose and Target Group:

AlloDerm® is an allograft (a transplant of tissue from one individual to another) derived from donated human skin tissue. It is used in patients with deep superficial and full thickness burns in order to reduce the need for a full thickness skin autograft (transplant of tissue taken from another site on the patient's body).

Stage of Development (in Australia):

 Not yet emerged in Australia

- Experimental
- Investigational
- Nearly established
- Established
- Established but changed indication or modification of technique
- Should be taken out of use

AlloDerm is not listed or registered in the Australian Register of Therapeutic Goods.

International Utilisation:

COUNTRY	LEVEL OF USE		
	Trials underway	Limited use	Widely diffused
United States of America			✓
China	✓		

Impact Summary:

Background

Skin is made up of three layers: the epidermis (outer layer), the dermis, and the subcutaneous tissues. The type and severity of a burn is dependent on the number of skin layers affected. Superficial or first degree burns only involve the epidermis. This is the most common type of burn, with sunburn falling into this category. Partial thickness or second degree burns are very painful as they involve the epidermis and some of the dermis. This type of burn may be broken down into superficial or deep, depending on how much of the dermis is involved. The full thickness or third degree burn is the most severe as it involves all three layers of the skin. This type of burn is painless and numb to touch because the nerve endings, blood vessels, hair follicles and sweat glands have all

been destroyed. Third degree and deep second degree burns are not able to heal by skin auto-regeneration and require skin grafts. (Better Health Channel 2005)

This prioritising summary details the use of AlloDerm for the treatment of deep second and third degree burns that require skin grafting. AlloDerm dermis provides skin properties such as tensile strength, durability and elasticity to replace the skin that has been lost in burn injury (LifeCell 2004). It is made from cadaveric skin that has had the epidermis, fibroblasts and endothelial cells of the dermis removed. This yields an acellular, immunologically inert allograft dermis that retains the native structure and composition of the dermal matrix, including the collagen, elastin, proteoglycans and the basement membrane complex (LifeCell 2004). The result is that AlloDerm is immediately recognised as human tissue and is able to be rapidly revascularised into the surrounding tissue, resulting in skin that grows and ages normally. The long term benefit of AlloDerm is that it functions as the burn patient's own skin, thereby replacing lost dermis, significantly reducing scarring, restoring mobility and minimising the use of autografts, which reduces donor site morbidity (LifeCell 2004).

Clinical Need and Burden of Disease

In Australia, fires, burns and scalds account for a relatively small proportion of injury related deaths. Burn injury can have serious long term physical and social effects, as well as economic consequences. In 2002, 1.5% of all injury related deaths were caused by burns, with males having higher death rates (72 males per 100,000) than females (43 females per 100,000) (Australian Institute of Health and Welfare 2004). Young children and the elderly are particularly vulnerable to serious injury and death from fire, burns and scalds.

The impact of burn injuries on the health economy is great. Approximately 6,248 people were hospitalised for burns in public hospitals in Australia between 2001 and 2002 (Australian Institute of Health and Welfare 2004). During this time, the mean length of hospital stay of patients with burns and frostbite was 7.3 days, with an estimated cost of AU\$36 to AU\$132 million.

Estimated Speed and Geographic and Practitioner Use Patterns of Diffusion in the Health System

AlloDerm is currently not in use in Australia, but is anticipated to be introduced into clinical practice by 2006 (Dr. Greenwood, personal communication 2005).

LifeCell Corporation (Branchburg, NJ, USA) introduced AlloDerm to the market in 1994. AlloDerm has since been used in more than 700,000 grafts and implants for a variety of applications, including plastic reconstructive, general surgical, burn and periodontal procedures, and to improve the cosmetic and functional results of skin grafts. AlloDerm is widely used in the United States, with donated human skin being supplied by tissue banks that comply with the standards of the American Association of

Tissue Banks. The US Food and Drug Administration (FDA) has classified AlloDerm as a banked human tissue because it is minimally processed and not significantly different in structure from the natural material.

Existing Comparators

Currently, the most conservative and common surgical treatment for third degree and deep second degree burns is a split-thickness skin autograft. This involves taking the epidermal layer and a portion of the dermis from an uninjured area on the patient's body. However in patients with severe burns, there are often not enough uninjured donor sites available to provide an adequate autograft.

The following treatments for burns patients have been designed to reduce the amount of skin that needs to be harvested from the patient for an autograft:

- TransCyte™ (Advanced Tissue Sciences Inc.) – extracellular matrix of allogenic human dermal fibroblasts. (Available in Australia)
- Integra® (Integra Life Science Corp.) – non-living extracellular matrix of collagen and chondroitin-6-sulfate. (Available in Australia)
- BioBrane® (Dow Hickman/Bertek Pharmaceuticals) – silicone, nylon mesh and collagen composite. (Available in Australia)
- Apligraf® (Organogenesis, Inc., Canton, MA, USA) - living allogeneic bi-layered construct containing keratinocytes, fibroblasts and bovine collagen. (Available in Australia only in clinical trials)
- Dermagraft® (Advanced Tissue Sciences Inc.) – living allogenic dermal fibroblasts. (Not available in Australia)
- Orcel® (Ortec International, Inc.) – collagen seeded with allogenic fibroblasts and keratinocytes. (Not available in Australia)

The above treatments can only be used as a temporary skin substitute until the epidermis has healed because they are rejected from the body once the healing process is complete.

Estimated Cost Impact

The cost of AlloDerm in Australia is not available. According to Bührlen and Hüsing (2003), the cost AlloDerm is approximately €8.66 per cm² (approx. \$AU 13.81).

The reimbursement fees, as stated by the Medicare Benefits Schedule, for free grafting of split skin range from AU\$574.25 to AU\$1,465.95 for patients who have burns to at least 9% and no more than 50% of their total body surface area (Medicare Australia 2005a).

This fee only involves excision of burnt tissue. In the July 2004 to July 2005 financial year, there were 18 claims to Medicare in this group of patients for the following item numbers: 45460, 45461, 45464, 45471, 45415 and 45418 (Medicare Australia 2005b).

Efficacy and Safety Issues

List of Studies Found

Total number of studies	7
Randomised controlled trials	1
Non-randomised comparative studies	3 (5 articles)
Case series studies	3
Case reports	4

The studies included in this summary are highlighted in bold in the reference list.

Safety and efficacy data from five non-randomised comparative studies, one case series study and two case reports have been selected for inclusion in this summary. There is an overlap of patients in Sheridan and Choucair (1997) and Sheridan *et al.* (1998), and a probable overlap of patients between Wainwright (1995) and Wainwright *et al.* (1996).

A prospective randomised study by Munster *et al.* (2001) presented data from 17 patients with freshly excised burn wounds who were randomised into two groups. The first group received AlloDerm that was overgrafted with a thin split thickness autograft. The second group received AlloDerm covered with a fresh frozen allograft obtained from a skin bank. Both patient groups also had a similar sized standard thickness autograft placed next to the test site as a control. After a week, the allograft covering the AlloDerm was removed in the second patient group and replaced with a thin split thickness skin graft. The 'take rate' of a graft is an important outcome measure in burns surgery. Munster *et al.* (2001) concluded that there was no statistically significant difference in take rate between any of the grafts. However, the thin graft donor sites healed faster (8.4 days) than the standard thickness sites (12.7 days) ($P < 0.001$).

Wainwright *et al.* (1996) presented a non-randomised comparative study of 43 patients with burns to a mean of 30.5% of their total body surface area. Burns were treated with a test site of AlloDerm and a thin autograft overlay, which was compared with a control site of split thickness autograft on an adjacent part of the patient's body. AlloDerm was grafted on average 10.2 days post-burn (range 2 to 37 days), and patients were followed postoperatively for 200 days. Wainwright *et al.* (1996) noted that the physicians did not find the grafting procedure difficult. Perioperative care was the critical factor for a successful graft, and shear stress forces were minimised by restricting dressing changes to 5 to 7 days after graft application. One patient died postoperatively from a non-burn related cause, so only 42 patients were described. Six of the 42 patients had take rates of more than 80% for the control site and less than 80% for the AlloDerm site ($P =$

0.0143). At day 14, the postoperative take rates were 78.4% for AlloDerm, 74.2% for the thin autograft overlay and 89.7% for the control site. Wainwright *et al.* (1996) noted that the patients with a take rate of less than 80% for AlloDerm had epithelialised spontaneously. In comparison, Tsai *et al.* (1999) reported a take rate of between 80% and 100% (average 91.5%) 14 days after surgery with AlloDerm.

A number of other studies used AlloDerm to reduce the depth of the donor site autograft in an effort to minimise donor site morbidity and infection. Tsai *et al.* (1999) presented a case series of 12 patients with major burns to their wrist, ankle, knee, elbow, cubital fossa and popliteal fossa. It took approximately 6 to 7 days for complete re-epithelialization of the split thickness donor site and 13 to 18 days (average 15.6 days) for complete re-epithelialization of the AlloDerm site. Lattari *et al.* (1997) presented a case series study in which three patients with burns to their hands or feet received AlloDerm overgrafted with a thin split thickness autograft. None of the patients experienced the donor site infection, hyper or hypopigmentation, hypertrophic scarring or blistering that is often associated with a thicker autogenous skin graft.

Cosmesis and functionality of the burn site is another important factor in burns surgery. Wainwright (1995) presented a non-randomised comparative study of two patients with full thickness burn injury. The report compared a test site of AlloDerm and a thin autograft overlay with a control site of normal split thickness skin graft on the same patient. The AlloDerm sites had a smoother, less elevated surface, increased elasticity, and better cosmesis, compared to the control site. However, the latter developed occasional traumatic blistering at days 60 and 90. Wainwright *et al.* (1996) found that all patients and 8 out of 12 physicians regarded the AlloDerm test site and the thinner overlying autograft to be equivalent to, or better than, the control site. Tsai *et al.* (1999) stated that the overall cosmesis with AlloDerm was judged as fair to good, with surgeons suggesting that wounds had a better cosmetic outcome and smoother surface compared to conventional meshed split thickness skin grafts. Gore (2005) presented a retrospective non-randomised comparative study of 28 elderly patients, with 10 receiving AlloDerm and 18 being treated with conventional skin grafts. At three months, the patients treated with AlloDerm were slightly more functionally dependent (86%) than those in the conventional group (83%) but this was not significant. Similarly, Tsai *et al.* (1999) reported that physicians and patients rated the movement of skin over joint sites as being in the near normal range after AlloDerm grafting. According to Lattari *et al.* (1997), the AlloDerm transplants exhibited excellent elasticity and good pigmentation, with minimal scarring or wound contracture.

A limited number of complications relating to AlloDerm grafting were presented in the studies. Wainwright *et al.* (1996) reported that only 3/42 (7.1%) patients required regrafting due to infection at both the AlloDerm test and control site. Kraut *et al.* (1995) reported on three patients (age range 15 to 91 years) who were treated with AlloDerm. The 91 year old patient was the only one to develop a complication, which was heavy

seeding of the graft with *Enterococcus*. This resulted in a significant portion of the graft being lost. Other complications noted in this patient included increased shear forces and pressure on the posterior torso. In a non-randomised comparative study of six children (Sheridan and Choucair 1997) with burns to an average of 68.7% of their bodies, one patient suffered a MARSAs infection (methicillin- and aminoglycoside-resistant *Staphylococcus aureus*). The bacterial colonisation of small open areas in the graft resulted in infection to both the study and control site. Both sites were resurfaced.

Ethical Issues

No issues were identified from the retrieved material. AlloDerm production complies with FDA human tissue regulations and the procedural guidelines of American Association of Tissue Banks. The skin donor is tested with FDA licensed tests to rule out AIDS, hepatitis B and C, HIV types 1 and 2 and syphilis. After the AlloDerm is processed, it is individually checked under a microscope to ensure a disease-free graft.

Cultural or Religious Considerations

No issues were identified from the retrieved material.

Other Issues

The Australian Red Cross Blood Service runs a skin bank in Australia, however as this is a government organisation, it is unsure as to how accessible donated skin is to a private company, such as Alloderm's manufacturer LifeCell.

Recommendation:

Limited evidence exists on the safety and efficacy of AlloDerm. However, the evidence available indicates that AlloDerm is reasonably effective in treating burns. AlloDerm appears to have a take rate that is similar to thin autografts, good cosmetic results, few side effects and allows patients to regain functionality that is similar to or better than thin autografts. Long-term safety and efficacy data on AlloDerm will provide greater insight into the value of this procedure as well as identify any complications that may occur. Based on the evidence available on this procedure, it is recommended that the following be conducted:

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

Note: 'Bioengineered skin substitutes for the management of burns: a systematic review' and 'Bioengineered skin substitutes for the management of wounds: a systematic review' are currently in progress as ASERNIP-S reviews.

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Search Criteria:

A search of MEDLINE, PubMed, *The Cochrane Library*, the Current Controlled Trials metaRegister, the UK National Research Register, the International Network for Agencies for Health Technology Assessment, relevant online journals and the Internet was conducted in September 2005.

Search terms used were:

‘Alloderm’, ‘Burn*’, ‘Allograft’ and ‘LifeCell’

This Horizon Scanning Prioritising Summary was prepared by Miss Catherine Easterbrook from the NET-S Project, ASERNIP-S for the Health Policy Advisory Committee on Technology (Health PACT), on behalf of the Medical Services Advisory Committee (MSAC) and the Australian Health Ministers' Advisory Council (AHMAC).