NHS
Blood and Transplant

dCELL® Human Dermis

Tissue Services for all your allograft requirements

dCELL® Human Dermis

What is dCELL® Human Dermis

dCELL® Human Dermis is a decelluralised dermal skin allograft produced from split thickness skin grafts (which comprise the epidermis and upper part of the dermis), retrieved from deceased tissue donors. All epidermal and cellular components from the dermis are removed in a patented sequential decellurisation process.

How it is sourced

dCELL® Human Dermis is obtained from deceased tissue donors within the UK, whose families choose to altruistically donate their relatives tissues for the benefit of others after death.

How it is prepared

The donated split skin grafts undergo a multi-step process that removes the epidermis and any donor cells and cell remnants for the graft, a procedure known as decellularisation. The particular decellularisation we use is known as 'dCELL®', and was developed by our long term collaborators at the University of Leeds. The dCELL® process involves sequentially incubating the skin grafts in different reagents to achieve this goal:

- incubation in a hypertonic solution, to remove the epidermis
- incubation in a hypotonic solution, to lyse dermal cells
- incubation in a detergent solution, to remove cell remnants
- incubation in a solution of nuclease enzymes, to remove nucleic acids.

These steps result in a graft matrix that comprises the structural proteins of dermal matrix, which retains the vascular channels to facilitate re-vascularisation of the graft following application, and the basement membrane which facilitates re-epithelialisation of the graft.

After decellularisation, the dermis grafts are sterilised with gamma irradiation, after impregnation with a dilute solution of glycerol to protect the dermal tissue from irradiation induced damage. It has been shown with *in vitro* and *in vivo* validation that this process results in a graft which is non toxic, biocompatible, and non-immunogenic.

What are the advantages of decellularisation?

Cellular skin allografts, such as those used to treat severe burn wounds, can only temporarily engraft to a wound, as the donor cells within the graft provoke an immune response which results in the graft being rejected. By removing donor cells and cell remnants, decellularisation treatment produces a graft which consists of much less immunogenic extracellular matrix, which can serve as a permanent implant, providing a scaffold that can be repopulated with the recipient's cells. This scaffold retains the essential structures of normal skin, including vascular channels and a basement membrane which is essential for regeneration of the epidermis. These structures can only be replicated in a graft material which is prepared from donated human tissue.

How safe is dCELL® Human Dermis?

In addition to the already discussed screening and testing applied to donors, the decellularisation protocol removes cells that can harbour intra-cellular viruses and prions. The inclusion of a sterilisation treatment results further reduces the already remote possibility of disease transmission. In over 60 years of tissue banking, there has never been a documented case of disease transmission via a graft provided by a tissue bank in the UK, and as a processed and sterilised graft, dCELL® Human Dermis is in the lowest risk category.

How does it work?

As a decellularised graft, dCELL® Human Dermis fully integrates into the wound bed after application, replacing lost dermal tissue. It provides a scaffold into which the recipient's cells can grow, becoming vascularised and supporting the generation of a new epidermis, ultimately regenerating into normal skin.

Clinical use of decellularised dermis

NHSBT Tissue Services's dCELL® Human Dermis has been evaluated by the University Hospital of South Manchester for it's ability to heal chronic leg ulcers with a number of different aetiolgies.[1]

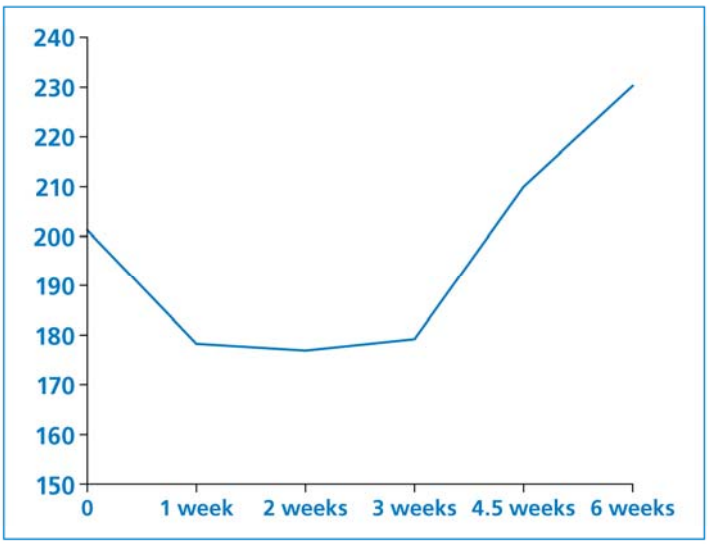
20 patients were treated, with chronic ulcers ranging in age from three months to 40 years. At six months follow up, complete healing was accomplished in 60% of patients, with a reduction in ulcer size averaging 69% found in all the remaining patients.

Table 2 Treatment outcomes of patients with chronic leg ulcers treated with dCELL® Human Dermis

Patient	Age	Ulcer aetiology	Ulcer Duration	Initial size (cm^2)	% healing at six months
1	71	Venous	13 years	23.24	23.5
2	86	Venous	3 years	7.73	83.5
3	92	Venous	18 months	8.33	100
4	60	Venous	4 years	4.27	100
5	74	Arteriovenous	40 years	36.22	61
6	88	Arteriovenous	4 years	9.61	73.5
7	66	Venous	2 years	14.77	80.5
8	55	Venous, traumatic	4.5 years	40.75	73
9	72	Venous	15 months	5.46	100
10	81	Venous	2 years	35.05	70
11	60	Venous	4 months	2.04	100
12	45	Diabetic	5 months	3.63	100
13	68	Diabetic, arterial	4 months	8.69	100
14	66	Venous	15 years	2.88	100
15	62	Venous	7 months	1.45	100
16	46	Venous	1 year	2.49	100
17	66	Venous	8 months	2.64	83.5
18	79	Diabetic	6 months	23.74	100
19	83	Venous	1 year	8.14	100
20	54	Venous	3 months	1.06	100

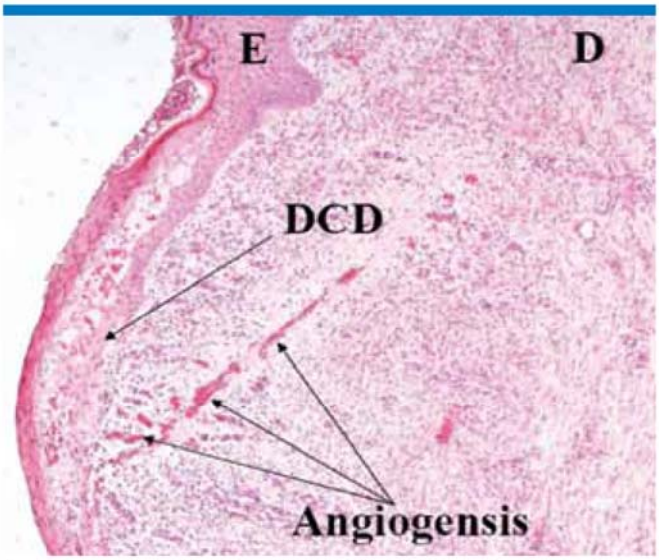
Measurements of blood flow in the wound bed using fluorescent laser perfusion imaging demonstrated integration and revascularisation of the dermis. Within two weeks of application, the graft is fully integrated and unable to be distinguished from the patient's native tissue.

Figure 1 Mean haemoglobin flux in the wound bed over time; an initial decrease is seen following application of the graft, followed by an increase as the graft revascularises



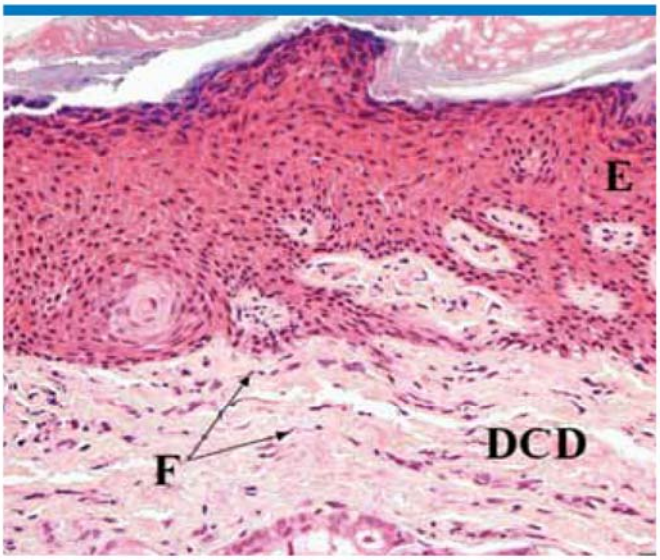
Histological samples taken from the healing wounds demonstrate re-vascularisation of the graft, re-cellularisation of the dermis, and regeneration of the epidermis within six weeks of application. The graft effectively provides the scaffold for regeneration of living skin.

Figure 2 Biopsy samples taken six weeks after graft application, showing the formation of new blood vessels



D = dermis, E = epidermis, DCD = dCELL® Human Dermis

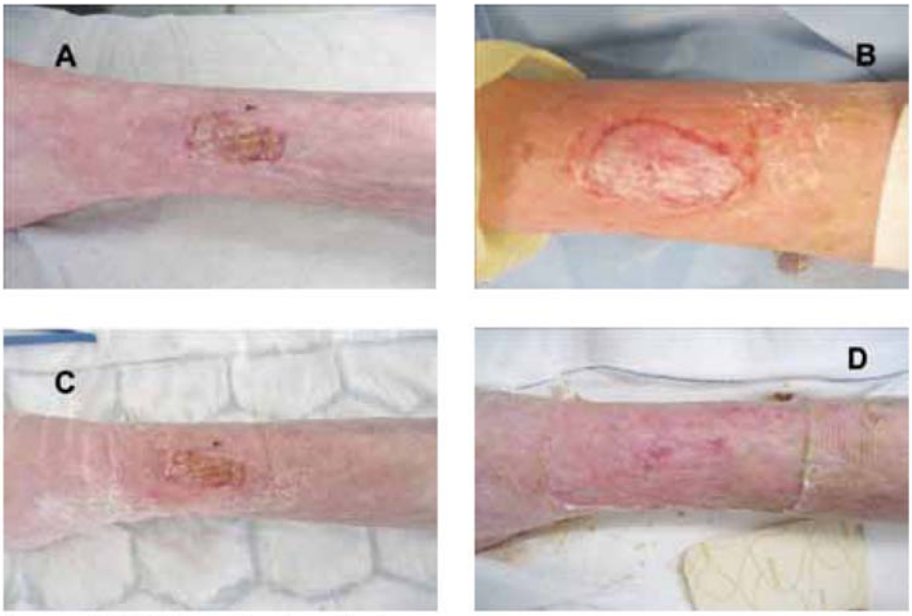
Figure 3 Recolonisation of the dermis with fibroblasts, and regeneration of the epidermis



E = epidermis, DCD = dCELL® Human Dermis, F = fibroblasts

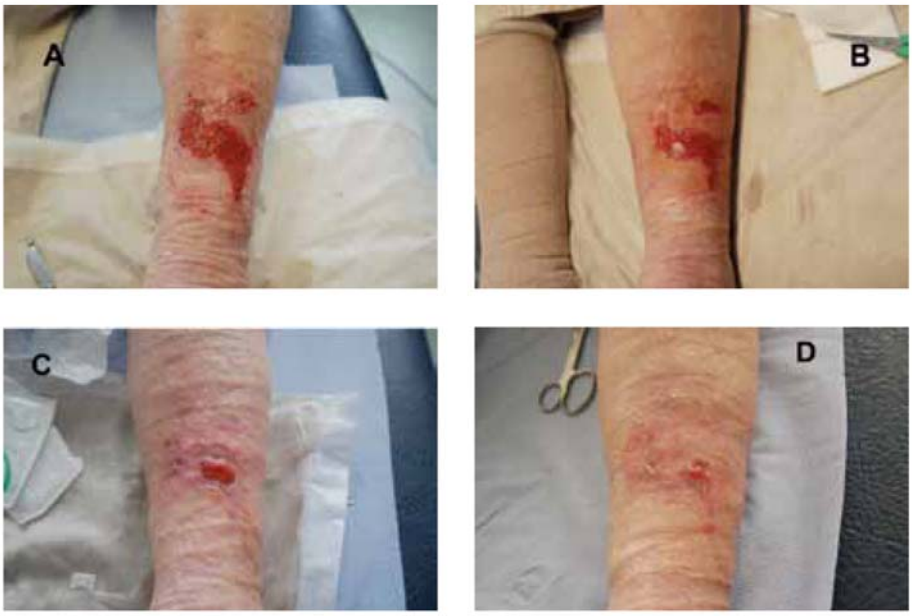
This results in the complete or partial healing of the ulcer, even in elderly patients with long standing, chronic ulcers.

Figure 4 92 year old patient with an 8cm^2 venous ulcer, extant for 18 months



A – pre-dCELL® Human Dermis application
B – immediately post application
C – 2 weeks post application
D – 10 weeks post application

Figure 5 79 year old patient with a 23cm^2 diabetic ulcer, extant for six months



A – pre-dCELL® Human Dermis application
B – 3 weeks post application
C – 4.5 weeks post application
D – 8 weeks post application

Clinical benefits, Contraindications and precautions, Graft application, Supply and storage

Clinical benefits

The key clinical benefits of using dCELL® Human Dermis for the healing of topical wounds includes:

- single stage treatment
- use of a normal human skin template that facilitates re-vascularisation and re-epithelialisation of the skin
- more resistant to infection than synthetic wound dressings
- permits the use of thinner autografts, with consequent reduced donor site morbidity, when used in the treatment of burns.

Contraindications and precautions

dCELL® Human Dermis is contraindicated for use in patients with known sensitivities to any of the antibiotics and reagents listed on the package insert.

Consideration should be given to the underlying medical condition of the patient when selecting patients for application of dCELL® Human Dermis. Any medical condition that may compromise healing, such as immune deficiency, immunosuppression, or poor blood supply to the site of engraftment, may delay or prevent healing. If the graft is to be implanted in a site which is known to be contaminated or infected, or at risk of becoming contaminated or infected, appropriate local and/or systemic anti-infective measures should be considered.

Other topical indications

- Scar contracture revision[2]
- Excision of cutaneous malignancies[3]
- Eyelid reconstruction[4]
- Dental soft tissue grafting[5]
- Treatment of severe burns[6].

Graft application

The following treatment protocol has been shown to result in successful treatment of chronic leg ulcers with dCELL® Human Dermis:

- debridement of the wound bed down to healthy tissue
- soak the dCELL® Human Dermis graft in sterile saline for 15 minutes
- cut the graft to size using sterile scissors
- apply directly to the wound bed, epidermal side upwards, securing in place with surgical adhesive
- apply a standard dressing over the graft (use of negative pressure therapy for the initial week may speed up graft incorporation and healing).

Detailed notes and instructions for use are provided with the graft.

Supply and storage

All grafts supplied by NHSBT Tissue Services can be stored at room temperature until the expiry date shown on the label. A HTA license for storage is not required as dCELL® Human Dermis is acellular.

In order to comply with HTA traceability requirements, each Trust is required to have a signed service level agreement with NHSBT before tissue can be supplied. This is to ensure compliance with the legal requirement for traceability of the tissue after it has been issued, to ensure that tissue can be tracked from the donor to the recipient.

NHSBT has considerable expertise in the HTA requirements and our Customer Care Team will be able to advise and help with this.

On request all grafts are issued on a next day delivery, although a same day delivery for a small additional charge is available for urgent requests.

References

References

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