Skin Grafting

Biomaterials

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Overview

- Structure and function of skin
- History
- Reasons for a skin graft
- Traditional methods
- Modern solutions
- Future advancements
Structure of the Skin

- Skin is the largest organ of the body
- Epidermis
  - Outermost protective layer
- Dermis
  - Binds epidermis to underlying tissue
- Hypodermis
  - Attaches skin to muscles
Functions of the Skin

- Thermo-regulation
- Blood reservoir
- Protection
- Cutaneous sensations
- Metabolism and nutrient storage
- Excretion and absorption
Properties of Skin

- **Composition**
  - $\sim 3\%$ elastin
    - $E \approx 1 \text{ MPa}$
  - $< 10\%$ collagen
    - $E \approx 1 \text{ GPa}$
  - $< 60\%$ water

- **Elastic modulus of skin**
  - 0.657 MPa in the direction close to the long axis of the arm
  - 0.130 MPa in the perpendicular direction
History of Skin Grafts

- 3000 – 2500 BCE in ancient India: reconstruction of noses amputated for judicial punishment
- Italy in 1442 CE, Brancas developed a novel technique
- Tagliacozzi published Brancas technique 100 years later and received credit
- 1804 Baronio: first successful autograft using the backs of sheep
- Rejection of transplanted skin mediated by the body's immune system discovered in 1943
Reasons for a Skin Graft

- Severe second and third degree burns
- Diabetic foot ulcers
- Venous leg ulcers
- Epidermolysis bullosa
- Reconstruction after surgery

Left: 3rd degree burn
Below: Venous leg ulcer
Traditional Skin Grafts

- **Autograft**: skin is transplanted from one part of the patient's body to another.
- Skin is meshed to cover a greater surface area (from 1:1 up to 9:1).
- **Two types**
  - Split-thickness
  - Full-thickness

Visit [www.skingrafter.com](http://www.skingrafter.com) to see a video of the traditional autograft.
**Advantages**
- Usually not rejected by immune system
- Same colour, texture and topography
- Minimal risk of disease transmission (e.g. HIV, Hepatitis)

**Disadvantages**
- Severely burned victims may not have enough skin to autograft
- Possible infection and wound contracture
- Requires secondary surgical wound
When there is not enough skin to autograft there were two alternatives:

- **Xenograft**
  - Tissue transplanted from one species to another

- **Allograft**
  - Tissue transplanted from one person's body to another person

**Advantages**
- Readily available, no secondary surgical wound

**Disadvantages**
- Immune system rejection, potential disease transmission

![Skin graft harvesting diagram](image)}
Modern Solutions

- Bioengineered skin has cut death rates from 100 percent to 40 percent in patients with severe burns over more than 70 percent of their bodies.
- Progress has been driven by the need for a more biocompatible skin substitute.
- Complexity and uniqueness of each individual’s skin makes it impossible to create a single material that works in all circumstances.
- Several approaches have been taken to create a working synthetic skin.
- Material must be readily available for life threatening conditions.
## Properties of Biomaterials

<table>
<thead>
<tr>
<th>Material</th>
<th>Tensile Strength</th>
<th>Elastic Modulus</th>
<th>Strain at Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collagen</td>
<td>75 MPa</td>
<td>1300 MPa</td>
<td>9.0 %</td>
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<tr>
<td>Silicone</td>
<td>2.4 MPa</td>
<td>700 %</td>
<td>700 %</td>
</tr>
<tr>
<td>Chitin</td>
<td>50 MPa</td>
<td>45 000 MPa</td>
<td>1.3 %</td>
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<tr>
<td>Keratin</td>
<td>50 MPa</td>
<td>5000 MPa</td>
<td>2.0 %</td>
</tr>
</tbody>
</table>
Epicel by Genzyme Biosurgery

- Introduced in 1987
- Permanent skin replacement product for patients with life threatening burns
- Grown from a patient's own skin cells (autologous keratinocytes) which are “co-cultured” with mouse cells (irradiated murine cells) to form epidermal autografts
- Not rejected by patient’s immune system
Starting with a biopsy of healthy skin about the size of a postage stamp, enough skin can be grown in a time period of as little as 16 days to cover the entire body.

Cells from biopsy of healthy skin are placed into individual cultures and are provided with nutrients so that they can grow to the approximate size of a playing card. Once they are ready, the pieces are attached to a surgical dressing and applied to the patient.

Biomaterials: human keratinocytes and mouse cells.
Dermagraft by Smith & Nephew

- A cryopreserved human fibroblast-derived dermal substitute
- Used for chronic diabetic foot ulcers
- Composed of fibroblasts, extracellular matrix, and a bioabsorbable scaffold
- Derived from the foreskin tissue of circumcised newborns
- Human fibroblasts are seeded onto a bioabsorbable polyglactin mesh scaffold
- Fibroblasts proliferate to fill the interstices of this scaffold and secrete human dermal collagen, matrix proteins, growth factors and cytokines, to create a three-dimensional human dermal substitute containing metabolically active, living cells
- A disadvantage is that no lymphocytes, hair follicles, blood vessels or macrophages are present
- Biomaterials
  - Human cells and a bioabsorbable polyester (polyglactin)
Dermagraft Application Process

1. Preparation
2. Application
3. Fixation
4. Sterilization
5. Suture
6. Closure
AlloDerm by Lifecell

- An acellular dermal matrix derived from donated human skin tissues from tissue banks
- Human donor tissue undergoes a process that removes epidermis and other cells that can lead to tissue rejection, without damaging the matrix
The tissue is preserved via a freeze drying process that prevents ice crystals (which can damage the sample) from forming.

All that remains is a framework (growth factor binding sites and blood vessel architecture) which aids the body in its own tissue regeneration process.

Unlike scar tissue, regenerate tissue is essentially normal tissue.
AlloDerm shows exceptional biomechanical strength on its own and at junctions with other materials. This makes it a good biomaterial for skin grafts.
Apligraf by Organogenesis Inc.

- Apligraf is a living, bi-layered skin substitute
- Like human skin, it has 2 primary layers, a dermis and an epidermis
- Epidermal layer is composed of human keratinocyte cells
- Dermal layer is made up of human fibroblast cells and bovine type 1 collagen
- Matrix proteins and cytokines found in human skin are present in Apligraf.
- Human keratinocytes and fibroblasts are derived from neonatal foreskins.
- Foreskin is decontaminated and digested by enzymes.
- Used for chronic ulcers:
  - Diabetic foot ulcers
  - Venous leg ulcers
- Shelf life of 10 days.
Integra by Johnson & Johnson Wound Management

- Integra Dermal Regeneration Template
  - A bilayer skin replacement system

- Used for
  - Immediate treatment of severe burn injuries
  - Surgical replacement of scar tissue to improve function or mobility (scar contracture release)
**Biomaterials**

- Epidermal substitute layer is made of a thin polysiloxane (silicone) layer.
- Dermal replacement layer is made of a porous matrix of cross-linked bovine tendon collagen fibers and glycosaminoglycan (chondroitin-6-sulfate).
The healing process of synthetic skin

A patch of synthetic skin is placed on top of damaged tissue. The patch contains chemicals that trigger growth of new blood vessels and proteins for skin regeneration.

7 days after application

Blood vessels forming

14+ days after application

Remove silicone membrane

Restated blood flow

14+ days after application

Meshed skin graft

35+ days after application

Regenerated skin

The skin graft eventually creates a smooth surface of regenerated skin.
Future Advancements

- A major area of research is tissue engineering
- Some researchers believe that tissue engineering holds enormous potential but is limited by the use of scaffolds
- Chitosan-gelatin artificial skin is an area of recent interest
- Spray-On skin cells have made an appearance in Australia
- Cell sheets from inkjet printers may one day become an industry standard as well
Skin Printing

- Researchers at the Medical University of South Carolina hope to use old inkjet printers to create artificial skin.
- The printer spray nozzles release proteins and skin cells onto a specialized gel forming sheets of skin.
Spray-On Skin Cells

- Spray-on technique was pioneered in Australia several years ago and is now being tested in the U.K.
- It is thought to reduce scarring and speed up the healing process in patients with extensive burns.
Chitosan-Gelatin

- Chitosan is a bio-polysaccharide derived from chitin
  - A polymer from the exoskeleton of shellfish
- Gelatin is a partially denatured derivative of collagen
- Innovative absorbable scaffold for tissue replacement
- Superior qualities include:
  - Ideal pore size
  - Excellent water retention ability
  - Aids in cell proliferation
  - Does not shrink after application (e.g. collagen based scaffolds shrink to 40% of their original size)
  - Antimicrobial and wound healing properties
- When Chitosan is combined with DL-Lactic Acid some of its properties are enhanced

- Biocompatible
  - Non-toxic
  - Biodegradable
  - Natural polymer

- Chitosan contains positive charges which cause the negative surface of cells to bind tightly with it
Water uptake ability calculated using:

\[ E_{sw} = \left(\frac{W_{w} - W_{d}}{W_{d}}\right) \times 100 \]

- \( E_{sw} \) is the percentage water adsorbed by the scaffolds at equilibrium
- \( W_{w} \) is the weight of the wet sample
- \( W_{d} \) is the weight of the dry sample
Summary

- The science of skin grafting has radically progressed since its origin in ancient India.
- The last decade has seen the emergence of several novel synthetic skin products.
- These advances have been made possible by a greater understanding of biomaterials and their interactions with the human body.
- Hopefully as we strive to create better biomaterials we will develop more advanced skin healing methods.
Thank you for listening

Any questions?
References

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