INTEGRA® DERMAL REGENERATION TEMPLATE

The first and only FDA approved tissue engineered product proven to regenerate dermis.
Outcomes

CASE 1
Left: Two-year-old neck scar contracture before INTEGRA template treatment
Right: Neck 1.5 years after contracture release and treatment with INTEGRA® template

CASE 2
Left: 14-year-old chest scar contracture before INTEGRA template treatment
Right: Chest 1 year after contracture release and treatment with INTEGRA template

CASE 3
Left: Hand scar contracture before INTEGRA template treatment
Right: 5 weeks after release and treatment with INTEGRA template patient regained functional use of hand
INTEGRA template promotes regeneration of dermal tissue

INTEGRA template has two layers: a thin outer layer of silicone and a thick inner matrix layer of pure bovine collagen and glycosaminoglycan (GAG). Both collagen and GAG are normal components of human skin. In INTEGRA, the collagen is obtained from bovine tendon collagen and the glycosaminoglycan is obtained from shark cartilage.

INTEGRA template indication

INTEGRA template is indicated for the postexcisional treatment of life-threatening, full-thickness or deep partial-thickness thermal injuries where sufficient autograft is not available at the time of excision or not desirable due to the physiological condition of the patient.

INTEGRA template is also indicated for the repair of scar contractures when other therapies have failed or when donor sites for repair are not sufficient or desirable due to the physiological condition of the patient.

• INTEGRA template is soft and pliable, facilitating greater range of motion even in difficult anatomic areas
• INTEGRA template grows with the patient
• INTEGRA template helps to restore function and joint mobility
Structure of INTEGRA template

Designed to promote organized regeneration of dermal tissue

SILICONE LAYER

- Enables immediate wound closure
- Controls fluid loss
- Provides mechanical protection
- Provides a bacterial barrier
- Water vapor transmission rate similar to that of normal skin

3-DIMENSIONAL MATRIX LAYER

- Cross-linked collagen and glycosaminoglycan
- Functions as an extracellular matrix
- Promotes cellular growth and collagen synthesis
- Biodegrades while being replaced by autologous dermal tissue
How INTEGRA template works

**DAY 0: CONTRACTED SCAR**
Scar contracture caused by tissue injury.

**DAY 1: EXCISION OF CONTRACTURE SCAR**
The contracture scar is completely excised to viable tissue.

**DAY 1: APPLICATION**
INTEGRA template is applied to the excised viable wound bed. The first phase of integration, imbibition, begins within minutes when wound fluids invade the matrix and fibrin fosters adherence to the wound bed.

**DAY 7-14: NEODERMAL FORMATION**
Fibroblasts, lymphocytes and macrophages migrate into the matrix. Later, endothelial cells begin forming the neovascular network.
As healing progresses, endogenous collagen is deposited by the fibroblasts, replacing the collagen/glycosaminoglycan layer of INTEGRA template. The color of the neodermis starts to change from red to pale yellow.

**DAY 21+: COMPLETE NEODERMAL FORMATION AND SILICONE REMOVAL**
When the neodermis has formed and vascularization is adequate, the silicone layer is removed. INTEGRA template is incorporated without rejection and biodegrades, leaving autologous dermis in place.

**DAY 21+: EPIDERMAL AUTOGRRAFT**
A thin (approximately 0.004”–0.006”) epidermal autograft (sheet or meshed and expanded) is applied over the neodermis.

**DAY 28-56: REGENERATED SKIN**
Engraftment and wound closure is complete. Neovascularization is well established. In a clinical trial evaluation, the neodermis was indistinguishable histologically from collagen in normal dermis.
INTEGRA template as an alternative

The unique bilayer system provides immediate wound closure and promotes dermal regeneration

- Silicone layer water vapor transmission rate similar to that of normal skin\(^6,7\)
- 3-dimensional matrix with optimized properties\(^2,11\)
  - Promotes cellular growth and organized regeneration of dermal tissue
  -Minimizes inflammatory response
  - Controlled degradation rate by collagenase
  - Controlled pore diameter
  - Controlled pore volume fraction
  - Defined collagen fiber dimensions
  - Specified collagen/glycosaminoglycan ratio (type 1 bovine tendon collagen/chondroitin-6-sulfate)

The Reconstructive Ladder

**Wound Closure**
- **Primary:**
  - Direct approximation: (z-plasty)
- **Secondary:**
  - Spontaneous healing: (granulation)
- **Tertiary:**
  - Delayed wound closure: (infected)

**Grafts**
- Split-thickness
- Full-thickness
- Autografts, Allografts, Xenografts

**Flaps**
- Axial
- Arterial
- Local 'Distant
  - Random pattern
  - Cutaneous
  - Myocutaneous

**Skin Expansion**
- Single
- Sequential

**Bone, Tendons, etc ...**

**Complicated**

**INTEGRA template (could be an alternative)**

**Simple**

**INTEGRA template (could be an alternative)**

**INTEGRA template (could be an alternative)**

**INTEGRA template (if donor sites could be a problem)**
INTEGRA template can be used as an alternative for standard split-thickness autograft

- The INTEGRA template neodermis is covered with a thin epidermal autograft (0.004"–0.006")
- Donor site heals faster than a standard autograft site (10 days ± 6 days vs. 14 days ± 8 days)³

The benefits of thin donor sites³
- Heal faster with minimal scarring³
- Can be reharvested more frequently than standard donor sites³
- Epidermal graft can be meshed and expanded up to 5:1, preserving additional donor areas

INTEGRA template requires thin donor sites

Depth of donor sites for epidermal autografts average less than half the thickness of standard donor sites³

Dermal Regeneration: The Lasting Advantage

Regeneration of functional dermis benefits the patient⁵
- INTEGRA template acts as a scaffold to promote permanent regeneration of functional dermis
- Restoring the dermis is vital to restoring cosmetic appearance and proper function after closing a large skin defect
- Dermis provides skin elasticity, tear resistance and texture, and acts as a sliding layer over the subcutaneous fascia to allow mobility without adhesion
Additional outcomes with INTEGRA template

INTEGRA template can successfully increase treatment options in a number of situations:

- **Infants and children**: when skin is thin and areas for harvesting are limited
- **The elderly**: when additional donor site wounds would cause unacceptable added stress to thin, friable skin
- **Hypertrophic scarring**: when there is a tendency to form hypertrophic or keloid scars
- **Difficult grafting situations**: when donor sites are limited due to the extent of the defect or patient condition, or when functional outcome is particularly important

A 26-year-old patient with extensive full-thickness face burn. The entire face was treated with INTEGRA template.

A: Left eye treated with INTEGRA template applied

B: Six weeks after INTEGRA template application, the eyelid has healed but still remains sewn shut

C/D: 1 year post INTEGRA template application, the eyelid is fully functional and the patient can open and close the eye

Eyelids: acute treatment and functional restoration with INTEGRA template

Chin: release of contracted hypertrophic scar with INTEGRA template in pediatric patient

Ear: reconstruction of ear contraction with INTEGRA template in elderly patient
Neck Contracture Reconstruction
After Conventional Treatment

A: Neck contracture after conventional treatment and prior to INTEGRA template application
B: Release of contracted scar
C: Silicone has been removed after complete neodermal formation
D: Released neck 5 months after INTEGRA template application—Hyperpigmentation will decrease over time

Pediatric Elbow Reconstruction of Contracted Scar

A: Scald burn on 18-month-old child resulted in a contracted scar at the elbow
B: At 13 years of age the scar was released and treated with INTEGRA template
C: After neodermal formation and silicone removal, a thin meshed and slightly expanded autograft was applied over the neodermis
D: One year after INTEGRA template application there was no contracture and pinching demonstrates tissue pliability
INTeGRA Basic Science
Incidence of adverse events occurring in ≥1% of the safety population in the Postapproval Study are as follows:

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Postapproval Study n/N (%)</th>
<th>Reconstructive Contracture Reconstructive Contracture Survey n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>50/216 (23.1%)</td>
<td>26/127 (20.5%)</td>
</tr>
<tr>
<td>Death</td>
<td>30/126 (13.9%)</td>
<td>18/127 (14.2%)</td>
</tr>
<tr>
<td>Infection</td>
<td>6/216 (2.8%)</td>
<td>2/127 (1.6%)</td>
</tr>
<tr>
<td>Thrombophlebitis</td>
<td>6/216 (2.8%)</td>
<td>8/127 (6.3%)</td>
</tr>
<tr>
<td>Kidney Failure</td>
<td>6/216 (2.8%)</td>
<td>12/127 (9.5%)</td>
</tr>
<tr>
<td>Necrosis</td>
<td>5/216 (2.3%)</td>
<td>6/127 (4.7%)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>5/216 (2.3%)</td>
<td>4/127 (3.1%)</td>
</tr>
<tr>
<td>Heart Arrest</td>
<td>4/216 (1.9%)</td>
<td>2/127 (1.6%)</td>
</tr>
<tr>
<td>Apnea</td>
<td>4/216 (1.9%)</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4/216 (1.9%)</td>
<td></td>
</tr>
<tr>
<td>Allergic Reaction</td>
<td>3/216 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>3/216 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>Multisystem Failure</td>
<td>3/216 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>3/216 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal Hemorrhage</td>
<td>3/216 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>Kidney Abnormal Function</td>
<td>3/216 (1.4%)</td>
<td></td>
</tr>
</tbody>
</table>

In these clinical trials, data were collected regarding wound infection. The consequences of infection at sites treated with INTEGRA template included partial or complete loss of take (incorporation into the wound bed) of INTEGRA template. Infection rates in sites treated with INTEGRA template in the three clinical trials supporting the PMA ranged from 14 to 55%. The overall infection rate for the Postapproval Study was 16.3%.

**Contracture Reconstruction Patients**

The following adverse events were reported in a Reconstructive Surgery Study involving 20 patients with 30 anatomical sites and a Retrospective Reconstruction Contracture Survey involving 89 patients and 127 anatomic sites.

**Incidence of Adverse Events in the Reconstructive Contracture Surgery Study and Retrospective Contracture Reconstruction Survey**

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Reconstructive Surgery Study N = 30 Sites</th>
<th>Retrospective Contracture Reconstructive Contracture Survey N = 127 sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>0/30 (0.0%)</td>
<td>26/127 (20.5%)</td>
</tr>
<tr>
<td>Partial graft loss (INTEGRA)</td>
<td>0/30 (0.0%)</td>
<td>18/127 (14.2%)</td>
</tr>
<tr>
<td>Failure to take (INTEGRA)</td>
<td>0/30 (0.0%)</td>
<td>12/127 (9.5%)</td>
</tr>
<tr>
<td>Shearing/Mechanical shift (loss of INTEGRA)</td>
<td>1/30 (3.3%)</td>
<td>6/127 (4.7%)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>5/30 (16.7%)</td>
<td>3/127 (2.3%)</td>
</tr>
<tr>
<td>Granulation tissue formation</td>
<td>0/30 (0.0%)</td>
<td>4/127 (3.1%)</td>
</tr>
<tr>
<td>Delayed Healing</td>
<td>0/30 (0.0%)</td>
<td>1/127 (0.8%)</td>
</tr>
<tr>
<td>Separation of the Silicone Layer</td>
<td>0/30 (0.0%)</td>
<td>1/127 (0.8%)</td>
</tr>
<tr>
<td>Seroma</td>
<td>0/30 (0.0%)</td>
<td>1/127 (0.8%)</td>
</tr>
<tr>
<td>Pruritis</td>
<td>0/30 (0.0%)</td>
<td>1/127 (0.8%)</td>
</tr>
<tr>
<td>Epidermal autograft loss &gt;15%</td>
<td>2/30 (6.7%)</td>
<td>7/127 (5.5%)</td>
</tr>
<tr>
<td>Epidermal autograft loss &lt;15%</td>
<td>7/30 (23.3%)</td>
<td>9/127 (7.1%)</td>
</tr>
</tbody>
</table>

There were no infections reported in the Reconstructive Surgery Study and the reported infection rate was 20.5% in the Retrospective Contraction Reconstruction Survey. No deaths were reported.

**HOW SUPPLIED**

The sale of INTEGRA template is restricted to clinicians who have completed a company sponsored training program.

INTEGRA template is available in the following sizes:

- 2 inch x 2 inch (5 cm x 5 cm)
- 4 inch x 5 inch (10 cm x 12.5 cm)
- 4 inch x 10 inch (10 cm x 25 cm)
- 8 inch x 10 inch (20 cm x 25 cm)

The bilayer sheets consist of collagen with an outer removable silicone covering identified by black chevron-style pouch. Store flat at 2°– 30°C. Protect from freezing.

**CAUTION:** Federal law restricts this device to sale by or on the order of a physician or practitioner with appropriate training.

Please refer to the clinical training materials for complete instructions for use.

For product ordering information, technical questions, or reimbursement issues please call 877-444-1122 or 609-275-0500.