INTEGRA® DERMAL REGENERATION TEMPLATE

Information for Patients and their Families

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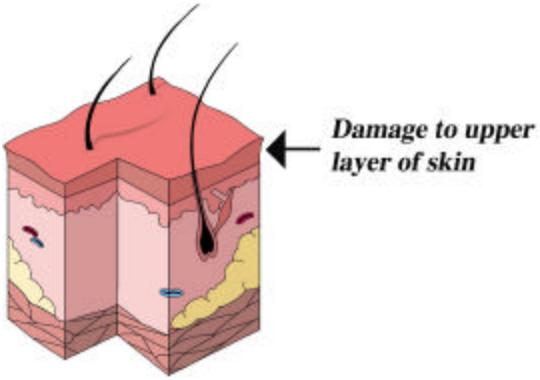
INTRODUCTION

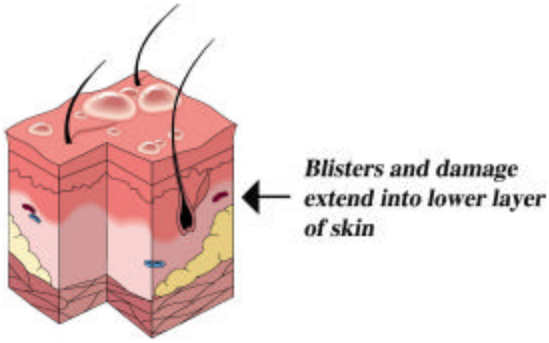
Your physician has prescribed INTEGRA Dermal Regeneration Template for the treatment of either a burn or scar contracture (the shortening and often thickening of functioning muscle). This Patient Guide will help you to understand what INTEGRA does and your role in the success of this treatment program.

The information contained in this brochure on INTEGRA Dermal Regeneration Template is not intended to replace the advice and directions of your health care practitioner.

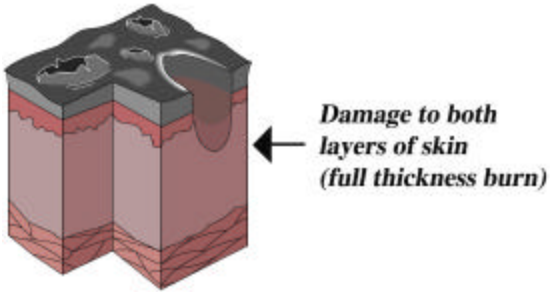
Human skin consists of two layers: the thin, outer layer called the epidermis and the much thicker underlayer called the dermis. When damaged, the epidermis is capable of healing itself. When there is complete loss of the dermis, it heals by scar formation rather than by regeneration (connective tissue repair). Severe burns involve the loss of both epidermis and dermis.



First Degree Burn



Second Degree Burn



Third Degree Burn

The treatment of severe burns usually requires skin grafting. This involves taking skin with both epidermis and dermis from unburned sites on the patient's body (donor sites), and grafting the donor site skin onto the burn wound. Patients who suffer severe burns often do not have sufficient donor site skin to immediately cover the burn wound.

The treatment of scar contractures involves surgically removing the scar (excise the scar) and applying a graft to the excised wound site to cover the wound. Again, a donor site is required and a second wound site is created at the skin graft donor site.

WHAT IS INTEGRA DERMAL REGENERATION TEMPLATE MADE OF?

INTEGRA® Dermal Regeneration Template has two layers:

1. A thick underlayer made of pure collagen (protein) from cows and a substance called glycosaminoglycan made from shark cartilage. Collagen and glycosaminoglycan are natural components of our skin.
2. A thin outer layer made of silicone.

WHAT PATIENTS CAN BENEFIT FROM INTEGRA DERMAL REGENERATION TEMPLATE?

- Any patient with severe burns where it is desirable to minimize donor site wounds (using the patient's own skin to apply to wounds)
- Any patient undergoing repair of scar contractures where it is desirable to minimize donor site wounds or if they have failed other treatments

WHO CANNOT USE INTEGRA® DERMAL REGENERATION TEMPLATE?

- Use of INTEGRA® is contraindicated in patients with a known hypersensitivity (allergy) to bovine collagen, chondroitin or silicone materials.
- INTEGRA® should not be used in the presence of infection.

NOTE: There have been no clinical studies evaluating the use of INTEGRA® in pregnant women.

WHAT OTHER CHOICES OR TREATMENTS ARE AVAILABLE?

The other choices for treatment are autologous (made from the patients skin) skin flaps and/or full or split-thickness skin grafts. A skin graft or split-thickness autograft requires taking skin from an unaffected portion of the patient's body and grafting this skin to the surgical wound. The area from where the skin graft is taken is called a donor site. The donor site wound requires coverage with a wound dressing to cover the wound and prevent infection.

HOW IS INTEGRA® DERMAL REGENERATION TEMPLATE USED?

Patients Who Have Acute Burns

When a patient is burned, their skin becomes so damaged that it must be removed surgically to prevent infection. After the surgeon removes the damaged skin, INTEGRA® is used as a graft and shaped to the exact size and shape of the skin area it is to replace. INTEGRA® is surgically secured with surgical sutures or staples. The INTEGRA® areas are then covered with bandages. There are usually two layers of protective bandages.

Patients Who Have Scar Contractures:

In patients with severe scar contractures, the exact same procedure is used. The only difference is the surgeon is removing scar tissue.

HOW DOES INTEGRA DERMAL REGENERATION TEMPLATE WORK?

INTEGRA® helps repair the damaged tissue. When placed on a wound where the burned or scarred skin has been removed, INTEGRA® provides scaffolding (support framework) for the blood vessels and other cells to regrow a new layer of dermis, while the collagen is absorbed into the body. The silicone layer helps close the wound and prevent fluid loss. In approximately 14 to 21 days, the silicone layer can be removed and an ultra-thin graft of only the patient's epidermis is applied to the wound area. INTEGRA® immediately closes the burn wound and or eliminates the need for deep donor site wounds. A benefit of INTEGRA® is that it does not require the use of a full-thickness autograft to cover the new dermis. This thin graft allows for a minimal donor site wound that heals faster.

The long-term benefit of INTEGRA® is the regeneration of the dermal tissue.

HOW IS INTEGRA DERMAL REGENERATION TEMPLATE APPLIED TO MY BURN OR CONTRACTURE WOUND?

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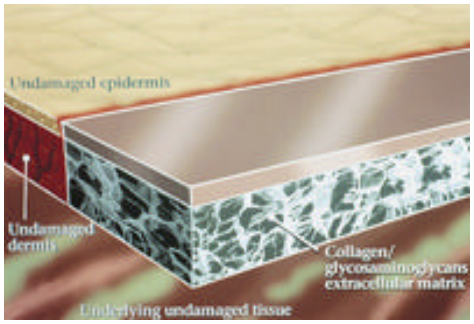
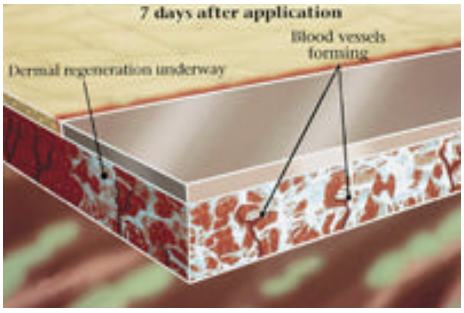
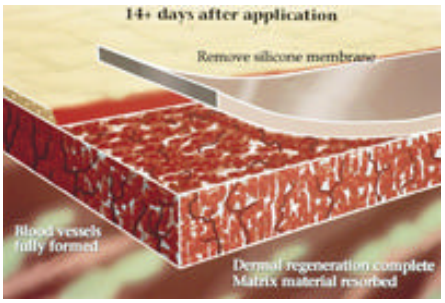


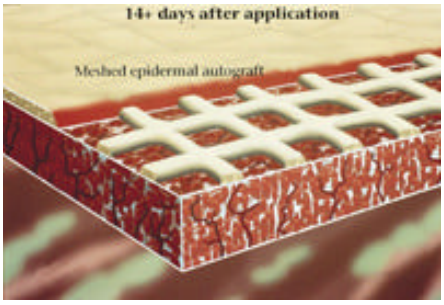
Cross section view of INTEGRA® Dermal Regeneration Template.



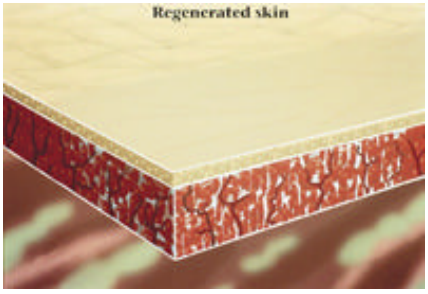
Dermal regeneration underway.



Blood vessels fully formed.



A thin meshed autograft is applied over the neodermis.



After several weeks, the epidermal layer is formed and the wound bed is now completely covered and healed.

WHAT CAN I DO TO HELP MY BURN OR WOUND TO HEAL?

It is essential that you follow all of your healthcare provider's instructions. You need to attend your scheduled appointments so that your healthcare provider can check your progress and assess your treated area.

Postoperative Care

The physician and nurses will monitor and treat all your INTEGRA® sites while you are in the hospital.

Home Care

When you are home, you will not be changing your bandages. You will either be returning to the hospital clinic or a home health nurse will visit you. Be prepared to make frequent visits to the hospital because proper wound care is very important to successful grafting.

You should be aware of any signs of infection, which can occur. Call your physician immediately if you notice any signs of infection. Signs of infection include a fever and swelling, odor, discharge, or pain in the INTEGRA® site.

If you are home, **you MUST keep the INTEGRA® sites completely dry**. This is an important warning. It might be impossible to take a bath, shower or swim without getting the wound wet. Please consult your doctor about how to bathe during this time or about any other problems you may have.

Good general health helps burns and wounds to heal. Be sure to eat a well balanced diet to help provide the nutrients that help the skin to heal. Avoid tobacco products because the nicotine can hinder blood flow to the wound site.

If you have any questions concerning diet or wound care, ask your health care provider for information.

WHAT ARE THE RISKS OR COMPLICATIONS WITH INTEGRA DERMAL REGENERATION TEMPLATE?

Adverse events that occurred in the burn studies can be found in Appendix B:

The main adverse event was infection (sepsis), a common complication in burn patients. Infection rates reported were consistent with those reported in the literature (published articles) for autograft (healthy skin from another place on your body). Infection can also lead to loss of the Integra. The other adverse events reported were also similar in type and nature to those observed with burn patients in general.

If there are any further questions, a technical representative is available to speak to you at 1-877-Ethicon or 1-877-384-4266.

APPENDIX A

WHAT DID THE CLINICAL STUDIES SHOW?

Burn Patients

INTEGRA template has been evaluated in over 1,200 wound sites in 444 burn patients evaluated in a series of 4 studies.

In a multicenter clinical trial, 149 patients were evaluated for safety and 106 patients (with 136 comparative wound sites) were included in an assessment of efficacy (how well it works). The area of wound site that supported the new skin graft is called "take". Take was the mean (average) effectiveness variable (characteristic) studied. INTEGRA template had successful take (take >10%) in 69% of the wound sites (94 of 136). For this group of wound sites with successful take, the mean take was 81%, and the median take (middle value in a set of measurements) was 90%. INTEGRA template failed to take (take =10%) in 31% of the wound sites (42 of 136 comparative wound sites). For this group, the mean take was 1.7% and the median take was 0%.

Postapproval Study in Burns

A Postapproval Study of INTEGRA template evaluated the safety and effectiveness in 216 patients, 841 wound sites. Effectiveness was measured by graft take. Overall mean average percent take for INTEGRA template was 76.2% and the median percent take for INTEGRA template was 98%. The mean (average) take of epidermal autograft was 87.4% with median take of 95%. The rate of infection in the study patients was 16.3% (13.2 superficial and 3.1 invasive). Patient deaths were 13.9%.

Data analysis indicated that deaths were related to patient age, percent total body surface area burned, presence of inhalation injury, and presence of infection at a non-INTEGRA template wound site. The rate of infection at an INTEGRA template wound site was not a significant risk factor for deaths.

Scar Contracture Patients

Contracture Reconstructive Surgery Study

This study evaluated the clinical and histologic (tissue) outcomes in 20 consecutive patients with 30 sites whose scars and contractures were treated with INTEGRA template. The mean (average) take was derived from the adverse event data and was calculated to be 94.2% for INTEGRA template and 86.3% for epidermal autograft.

APPENDIX B

Adverse events reported in the previous studies are as follows:

Coded Symptom	**Multicenter N=149 (% frequency)**	**Anatomic Site N=59 (% frequency)**	**Meshed vs Sheet N=20 (% frequency)**
Death	37(24.8%)	19 (32.2%)	3 (15%)
Sepsis	17 (11.4%)	4 (6.8%)	1 (5.0%)
Apnea	13 (8.7%)	5 (8.5%)	0 (0.0%)
Pneumonia	10 (6.7%)	0 (0.0%)	0 (0.0%)
Heart Arrest	7 (4.7%)	6 (10.2%)	0 (0.0%)
Kidney Failure	5 (3.4%)	4 (6.8%)	0 (0.0%)
Respiratory Distress	3 (2.0%)	0 (0.0%)	0 (0.0%)
Infection	2 (1.3%)	0 (0.0%)	0 (0.0%)
Lung Disease	2 (1.3%)	0 (0.0%)	0 (0.0%)
Dyspnea	1 (0.7%)	1 (1.7%)	0 (0.0%)
Adrenal Insufficiency	1 (0.7%)	0 (0.0%)	0 (0.0%)
Agitation	1 (0.7%)	0 (0.0%)	0 (0.0%)
Convulsion	1 (0.7%)	0 (0.0%)	0 (0.0%)
Hematemesis	1 (0.7%)	0 (0.0%)	0 (0.0%)
Hemoptysis	1 (0.7%)	0 (0.0%)	0 (0.0%)
Liver Cirrhosis	1 (0.7%)	0 (0.0%)	0 (0.0%)
Nonadherence	1 (0.7%)	0 (0.0%)	0 (0.0%)
Shock	1 (0.7%)	0 (0.0%)	0 (0.0%)
Skin Discoloration	1 (0.7%)	0 (0.0%)	0 (0.0%)
Asystole	0 (0.0%)	0 (0.0%)	1 (5.0%)
Cerebral Artery Infarct	0 (0.0%)	1 (1.7%)	0 (0.0%)
Metastatic Ovarian Cancer	0 (0.0%)	1 (1.7%)	0 (0.0%)
Peritonitis	0 (0.0%)	1 (1.7%)	0 (0.0%)
Sarcoidosis	0 (0.0%)	0 (0.0%)	1 (5.0%)
Third Degree Burn	0 (0.0%)	1 (1.7%)	0 (0.0%)
Multisystem Failure	0 (0.0%)	3 (5.1%)	0 (0.0%)

TABLE 1

APPENDIX C

Incidence of adverse events occurring in =1% of the safety population in the Postapproval Study are as follows:

Adverse Events	**n/N (%)**
Sepsis	50/216 (23.1%)
Death	30/216 (13.9%)
Infection	6/216 (2.8%)
Thrombophlebitis	6/216 (2.8%)
Kidney Failure	6/216 (2.8%)
Necrosis	5/216 (2.3%)
Hemorrhage	5/216 (2.3%)
Heart Arrest	4/216 (1.9%)
Apnea	4/216 (1.9%)
Pneumonia	4/216 (1.9%)
Allergic Reaction	3/216 (1.4%)
Fever	3/216 (1.4%)
Multisystem Failure	3/216 (1.4%)
Atrial Fibrillation	3/216 (1.4%)
Gastrointestinal Hemorrhage	3/216 (1.4%)
Kidney Abnormal Function	3/216 (1.4%)

TABLE 2

APPENDIX D

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

	Reconstructive Surgery Study N=30 Sites	Retrospective Contracture Reconstruction Survey N= 127 sites
Adverse event	n/N (%)	n/N (%)
Infection	0/30 (0.0%)	26/127 (20.5%)
Fluid under Silicone Layer	0/30 (0.0%)	18/127 (14.2%)
Partial graft loss (INTEGRA)	0/30 (0.0%)	2/127 (1.6%)
Failure to take (INTEGRA)	0/30 (0.0%)	8/127 (6.3%)
Shearing/Mechanical shift (loss of INTEGRA)	1/30 (3.3%)	6/127 (4.7%)
Hematoma	5/30 (16.7%)	3/127 (2.3%)
Granulation tissue formation	0/30 (0.0%)	4/127 (3.1%)
Delayed Healing	0/30 (0.0%)	1/127 (0.8%)
Separation of the Silicone Layer	0/30 (0.0%)	1/127 (0.8%)
Seroma	0/30 (0.0%)	1/127 (0.8%)
Pruritis	0/30 (0.0%)	1/127 (0.8%)
Epidermal autograft loss >15%	2/30 (6.7%)	7/127 (5.5%)
Epidermal autograft loss <15%	7/30 (23.3)	9/127 (7.1%)

TABLE 3

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