Because we are committed to limiting uncertainty, Integra continues to develop new products in regenerative technology.

Specifications

- An established product line with proven results.
- Outstanding safety profile.
- Implanted in over 750,000 patients.
How was Integra LifeSciences’ Collagen Matrix Created?

For over thirty years, Integra LifeSciences has been a leader in developing and manufacturing high quality collagen implants.

In the early 1970’s, John F. Burke, MD, chief of Trauma Services at Massachusetts General Hospital and Shriners Burns Institute, identified the need to improve skin restoration of severely burned patients. While patient related donor skin was an option, immunorejection was a critical issue. Dr. Burke theorized that an artificial means to cover the skin might offer positive results without the potential for donor skin rejection.

Dr. Burke collaborated with Dr. Ioannas Yannas, a professor at MIT with a specialization in material sciences and physical chemistry, to develop a biocompatible product to improve wound healing. With Dr. Burke’s expertise in wound management and Dr. Yannas’ knowledge of collagen, a collagen matrix was created. Initial experimentation with the matrix not only resulted in improved wound healing, but also supported the regeneration of the dermis. These findings confirmed the concept of tissue regeneration using a collagen based matrix.

This creation of a biocompatible, porous collagen matrix by Integra LifeSciences, led to an evolution in the science of collagen processing and manufacturing. Thirty years and over ten million implantations later, Integra LifeSciences continues to develop innovative collagen implant solutions for a number of clinical applications including general surgery, burn surgery, neurosurgery, plastic and reconstructive surgery, oral surgery, and peripheral nerve/tendon surgery.

What Makes Integra LifeSciences’ Collagen Unique?

Integra LifeSciences is the only company to manufacture its products from Ultra Pure Collagen™.

Collagen Sourcing
Each Integra LifeSciences product made with collagen derived from bovine deep flexor tendon, used specifically for its highly collagenous composition (95% collagen).

Bovine tendon is known to be one of the purest sources of Type I collagen that is commercially available.

Collagen Purification
After a mechanical breakdown, the collagen is further purified using proprietary treatments to ensure an ultra pure base material.

Advanced Bioengineering
The Ultra Pure Collagen™ matrix is specifically engineered for each clinical application.

Developing and Manufacturing
Each Integra LifeSciences collagen product is purified, engineered, and manufactured by Integra LifeSciences.

Processing and Manufacturing the Ultra Pure Collagen™ matrix
With over three decades of processing and manufacturing experience, Integra LifeSciences has the ability to take a product from concept to commercialization. Integra LifeSciences has complete ownership and control of the design and manufacturing to ensure consistent, reliable, and safe products.

Purification Process
Integra LifeSciences places its collagen through a proprietary purification process which deactivates viruses and bacteria, substantially reducing the risk of transmission of bovine spongiform encephalopathy (BSE) and mitigating the risk of inflammatory response.

Integra LifeSciences’ collagen products are processed ad times longer than suggested and thus have the potential to substantially mitigate the probability of viral or other disease transmissions.

Image above: SEM (Scanning Electron Microscope) of individual collagen fibers making up the structure that defines an individual pore in the collagen matrix of DuraGen Plus™ Adhesion Barrier matrix. The ribbed appearance of the surface of each fiber that can be seen in this image demonstrates the natural banded structure of native collagen fibers.

Ultra Pure Collagen™
Dural repair

PRODUCTS FOR SALE IN EUROPE, MIDDLE-EAST AND AFRICA ONLY
Integra Lifesciences’ Collagen Timeline*

1996
Burn surgery
Integra® Dermal Regeneration Template
A resorbable collagen and glycosaminoglycan (GAG) implant that provides a scaffold for skin replacement.

2000
General surgery
Helitene™ Absorbable Collagen Hemostatic Agent
An absorbable collagen hemostatic agent used to help control bleeding in surgical procedures.

Neurosurgery
DuraGen Plus™ Adhesion Barrier Matrix
An optimized resorbable dural graft that protects against CSF leakage and provides a scaffold for dural repair.

2005
Neurosurgery
DuraGen® Dural Graft Matrix
A resorbable dural graft that protects against CSF leakage and provides a scaffold for dural repair.

Peripheral Nerve surgery
NeuraWrap™ Nerve Protector
An absorbable collagen implant that provides a non-constricting encasement for injured peripheral nerves for protection of the neural environment.

2007
Peripheral Nerve surgery
NeuraGen® Nerve Guide
An absorbable collagen tube designed for the repair of peripheral nerve discontinuities.

2009
Neurosurgery
Suturable DuraGen™ Dural Regeneration Matrix
A reinforced bilayer dural graft that protects against CSF leakage and provides a scaffold for dural repair.

2010
Orthopaedic
Integra Mozaik™ Osteoconductive Scaffold
A scaffold composed of collagen and tricalcium phosphate that is intended for use as a bone void filler.
Mode of Action of Integra LifeSciences’ Dural Grafts

Integra LifeSciences has engineered its collagen to perform the two following functions:

1. **Fibrin Clot Formation**
   Integra LifeSciences’ dural grafts provide the structure for initial clot formation. Once the collagen matrix is placed on the dural tear, proteins from the blood and the operative site permeate through the matrix and interact to form a fibrin clot. The fibrin clot stabilized within the collagen matrix provides a rapid mechanical barrier against CSF leakage.

2. **Dural Repair**
   The Ultra Pure Collagen™ matrix in combination with the fibrin clot provides a biological matrix for fibroblast infiltration. Fibroblasts use the pores in the collagen matrix as a scaffold to lay down new collagen. The collagen matrix is rapidly resorbed and replaced with new dura. Integra LifeSciences’ dural grafts are completely replaced with endogenous tissue within 8-12 months.

Attributes of Integra LifeSciences’ Dural Grafts

<table>
<thead>
<tr>
<th>Attributes</th>
<th>Functions</th>
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<tbody>
<tr>
<td>Ultra Pure Collagen™</td>
<td>Integra’s dural grafts have been implanted in over 750,000 patients.</td>
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<tr>
<td>Excellent Conformability</td>
<td>Conforms to complex surfaces of the brain and ensures graft approximation at the dural margin.</td>
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<tr>
<td>Fibrin Clot Formation</td>
<td>Fibrin clot formation within the matrix creates a rapid mechanical barrier against CSF leakage.</td>
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<tr>
<td>Engineered Porosity</td>
<td>The optimized pore size and distribution ensures consistent matrix hydration and uniform tissue repair throughout the matrix.</td>
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<tr>
<td>Optimized Resorption</td>
<td>Matrix resorbs at a similar rate that new tissue forms to prevent encapsulation.</td>
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Integra’s background about Collagen

- Integra LifeSciences has leveraged over 30 years of science and innovation in the development of collagen technology.

- Integra LifeSciences’ extensive collagen purification process, advanced bio-engineering proficiency, and manufacturing experience add value to our products designed for protection, regeneration and repair of human tissue in various clinical applications.

- Ultra Pure Collagen™ is the base material of implants used successfully in over 10 million procedures worldwide.

- Ultra Pure Collagen™ has been used in general surgery, burn surgery, neurosurgery, plastic and reconstructive surgery, peripheral nerve/tendon surgery & orthopedic surgery.