Ultra Pure Collagen™

Dural repair

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™.

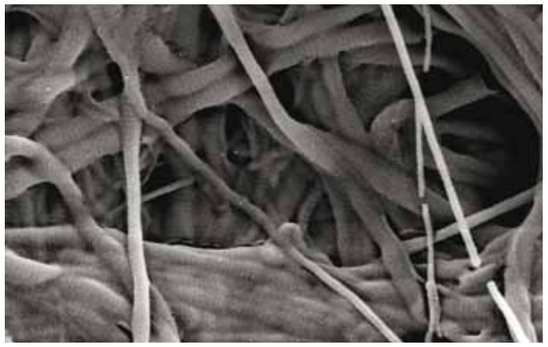


Image above: SEM (Scanning Electron Microscope) of individual collagen fibers making up the structure that defines an individual pore in the collagen matrix of DuraGen Plus™ Adhesion Barrier matrix. The ribbed appearance of the surface of each fiber that can be seen in this image demonstrates the natural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

ULTRA PURE COLLAGEN
Reduces uncertainties concerning product safety.

- Limits the risk of foreign body reaction
- Reduces the chance of encapsulation by fibrous tissue
- Mitigates the possibility of immunological response

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.

What Makes Integra LifeSciences' Collagen Ultra Pure™?

Integra LifeSciences' ultra purification method follows established and proven protocols for the removal of antigenic materials and the inactivation/ destruction of potential viral and bacterial contaminants.

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 40 times longer than suggested and thus have the potential to substantially mitigate the probability of viral or other disease transmissions.

Integra LifeSciences Ultra Pure Collagen™ technology

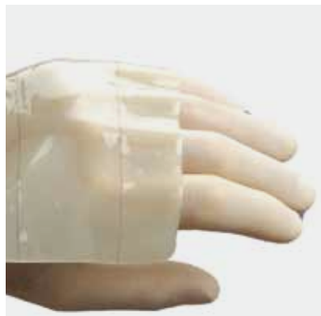
BIO-ENGINEERING WITH ULTRA PURE COLLAGEN™
Integra LifeSciences controls the physical and chemical composition to ensure each product is designed with attributes critical for ideal biological / physiological activity.

- Pore Size
- Crosslinking
- Pore Volume
- Degradation Rate

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.

Integra Lifesciences' Collagen Timeline*



1996

Burn surgery

Integra® Dermal Regeneration Template

A resorbable collagen andgylcosami-noglycan (GAG) implant that provides a scaffold for skin replacement.

2000

Neurosurgery

DuraGen® Dural Graft Matrix

A resorbable dural graft that protects against CSF leakage and provides a scaffold for dural repair.

2000

General surgery

Helitene™ Absorbable Collagen Hemostatic Agent

An absorbable collagen hemostatic agent used to help control bleeding in surgical procedures.

2003

Peripheral Nerve surgery

NeuraGen® Nerve Guide

An absorbable collagen tube designed for the repair of peripheral nerve discontinuities.

2005

Neurosurgery

DuraGen Plus™ Adhesion Barrier Matrix

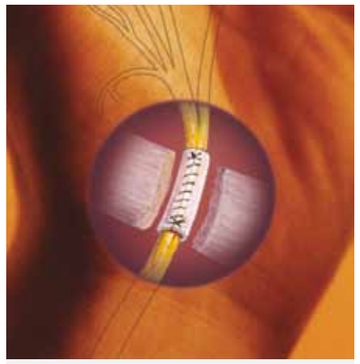
An optimized resorbable dural graft that protects against CSF leakage and provides a scaffold for dural repair.

2009

Neurosurgery

Suturable DuraGen™ Dural Regeneration Matrix

A reinforced bilayer dural graft that protects against CSF leakage and provides a scaffold for dural repair.



2007

Peripheral Nerve surgery

NeuraWrap™ Nerve Protector

An absorbable collagen implant that provides a non-constricting encasement for injured peripheral nervesfor protection of the neural environment.

2010

Orthopaedic

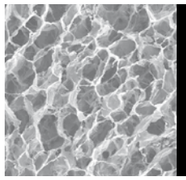
Integra Mozaik™ Osteoconductive Scaffold

A scaffold composed of collagen and tricalcium phosphate that is intended for use as a bone void filler.

Integra LifeSciences' Ultra Pure Collagen™ technology for Dural Repair

Integra LifeSciences' Dural Grafts

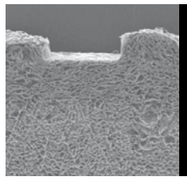
Integra LifeSciences' collagen has been bioengineered to repair the dura. Integra LifeSciences' dural grafts are resorbable implants that effectively protect against CSF leakage and serve as scaffolds for dural repair. These grafts handle and conform similar to normal soft tissue and have an outstanding safety profile.



DuraGen Plus™ Adhesion Barrier matrix has an optimized pore structure over original DuraGen® Dural Matrix and demonstrates a uniform pore structure throughout the matrix. (MAG. 100X)

DuraGen Plus™ Adhesion Barrier Matrix

DuraGen Plus™ Adhesion Barrier matrix is Integra LifeSciences' most optimized onlay graft. The DuraGen Plus™ matrix has a more uniform pore structure for superior handling over original DuraGen® Dural Graft Matrix. The increased consistency of the pore structure results in a 30% increase in tensile strength over DuraGen® Dural matrix and is important for vascularization and resorption of the graft.



Suturable DuraGen™ dural regeneration matrix contains two integrated components: an onlay matrix component and an enhanced strength component. (MAG. 100X)

Suturable DuraGen™ Dural Regeneration Matrix

Suturable DuraGen™ Dural regeneration matrix is Integra LifeSciences' reinforced onlay graft. Suturable DuraGen™ dural regeneration matrix is a bilayer collagen matrix composed of two integrated components. The enhanced strength component consists of a dense collagen fiber network that imparts strength and provides suturability. The onlay matrix component maintains the biological activity of DuraGen Plus™ Adhesion Barrier matrix and ensures conformability of the graft. Suturable DuraGen™ Dural Regeneration matrix is a versatile graft and can be sutured to the dura or used as an onlay graft.

OUTSTANDING SAFETY PROFILE
Integra LifeSciences' dural repair products have been implanted in over 750,000 patients

- Effective protection against CSF leakage with sutureless closure.
- Allows for repair of damaged tissue without scar tissue formation or encapsulation.
- Immunologically well-tolerated. No reports of foreign body reactions or graft rejections.
- Evokes minimal inflammatory response.

Mode of Action of Integra LifeSciences' Dural Grafts

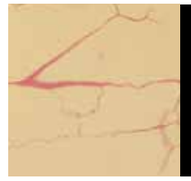
Integra LifeSciences has engineered its collagen to perform the two following functions

(1) Fibrin Clot Formation

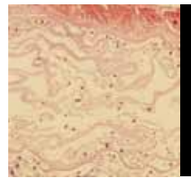
Integra LifeSciences' dural grafts provide the structure for initial clot formation. Once the collagen matrix is placed on the dural tear, proteins from the blood and the operative site permeate through the matrix and interact to form a fibrin clot. The fibrin clot stabilized within the collagen matrix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

(2) Dural Repair

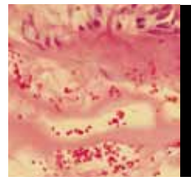
The Ultra Pure Collagen™ matrix in combination with the fibrin clot provides a biological matrix for fibroblast infiltration. Fibroblasts use the pores in the collagen matrix as a scaffold to lay down new collagen. The collagen matrix is rapidly resorbed and replaced with new dura. Integra LifeSciences'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



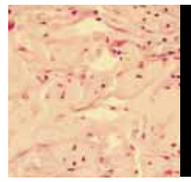
1. Cross section of dry DuraGen® Dural Matrix showing the thin eosinophillic trabeculae (MAG. 125X).



2. After rehydration and implantation, the collagen fibers are thickened. Blood plasma from the surgical fields fill the trabeculae (MAG. 125X).



3. Twelve days postimplantation, fibroblasts migrate into the DuraGen® matrix (MAG. 125X).



4. Two months postimplantation, fibroblastic infiltration and proliferation are evident. The interstices of the trabecular framework have become filled with endogenous collagen (MAG. 125X).

Attributes of Integra LifeSciences' Dural Grafts

Attributes	Functions
Ultra Pure Collagen™	Integra's dural grafts have been implanted in over 750,000 patients with no reported foreign body reaction or graft rejections.
Excellent Conformability	Conforms to complex surfaces of the brain and ensures graft approximation at the dural margin.
Fibrin Clot Formation	Fibrin clot formation within the matrix creates a rapid mechanical barrier against CSF leakage.
Engineered Porosity	The optimized pore size and distribution ensures consistent matrix hydration and uniform tissue repair throughout the matrix.
Optimized Resorption	Matrix resorbs at a similar rate that new tissue forms to prevent encapsulation.

Ultra Pure Collagen™

Dural repair

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.

Integra LifeSciences Services (France) SAS
Sales & Marketing EMEA
Immeuble Séquoia 2 ▪ 97 allée Alexandre Borodine
Parc technologique de la Porte des Alpes
69800 Saint Priest ▪ FRANCE
t +33 (0)4 37 47 59 00 ▪ fax +33 (0)4 37 47 59 99
emea.info@integralife.com ▪ **integralife.com**

Distributed by

INTEGRA
LIMIT UNCERTAINTY

Customer Service

International : +33 (0)4 37 47 59 50 ▪ +33 (0)4 37 47 59 25 (Fax) ▪ csemea@integralife.com
United Kingdom : csuk.ortho@integralife.com
France : +33 (0)4 37 47 59 10 ▪ +33 (0)4 37 47 59 29 (Fax) ▪ cs-ortho@integralife.com
Benelux : +32 (0)2 257 4130 ▪ +32 (0)2 253 2466 (Fax) ▪ custsvcbenelux@integralife.com
Switzerland : +41 (0)2 27 21 23 30 ▪ +41 (0)2 27 21 23 99 (Fax) ▪ custsvcsuisse@integralife.com

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