Integra®

DuraGen® Family
Dural Regeneration Matrices

Limit uncertainty with proven solutions for CSF leak prevention and natural dural repair.

INTEGRA®
LIMIT UNCERTAINTY

Products for sale in Europe, Middle-East and Africa only.

A Pioneer in Collagen Regeneration Matrices

For almost forty years, Integra and its predecessors have been leading the development and manufacturing of collagen implants and advanced regenerative technologies. In the early 1970's the first collagen matrix to improve skin restoration of severely burned patients was developed. This advanced matrix led to a revolution in understanding the science behind the biological response and role of extracellular matrices in tissue regeneration. This science along with expertise in collagen processing and manufacturing resulted in DuraGen® dural regeneration matrix.

- **Integra pioneered regenerative medicine.**
- **Over 10 million collagen implants.**
- **1 million implants and counting.**
- **Integra created the onlay dural graft paradigm.**

Integra DuraGen® Family

Dural Regeneration Matrices
Conforms intimately to complex surfaces.

What is DuraGen® Matrix?

DuraGen® matrix is one of the safest and most effective onlay grafts for the restoration and repair of dura mater.

- DuraGen® matrix is made from a controlled collagen source and is treated with a proprietary process designed to remove antigenic components, yielding our **Ultra Pure Collagen™ Technology**.

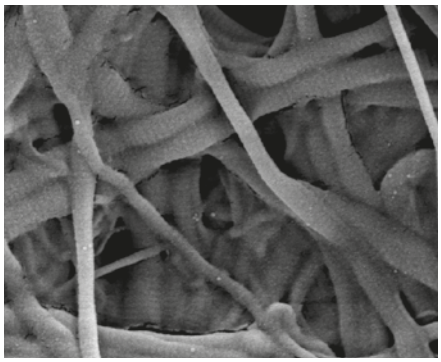
- It is conformable and contours instantly and effectively to the complex surfaces of the brain and spinal cord, rapidly forming a biological seal to protect against cerebrospinal fluid (CSF) leakage: 1 day post-implantation, a fibrin clot has formed within the matrix creating a watertight barrier.

How does the Duragen® matrix work?

The onlay nature of DuraGen® matrix revolutionized duraplasty.

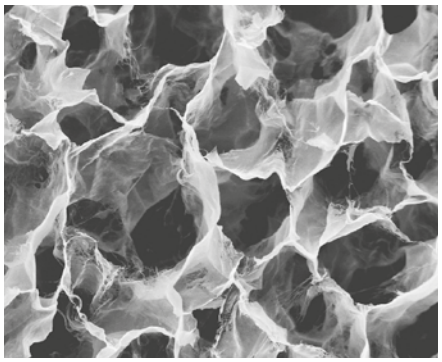
- The highly porous collagen scaffold promotes rapid fibrin clot formation.
- DuraGen® matrix rapidly provides watertight closure to prevent CSF leakage while promoting natural dural growth.

THE DURAGEN® MATRIX WAS ENGINEERED WITH THE IDEAL BALANCE OF STRENGTH AND FLEXIBILITY TO ENSURE OPTIMAL HANDLING, SEALING, AND RESORPTION-LEAVING THE PATIENT WITH A NATURAL DURAL REPAIR.



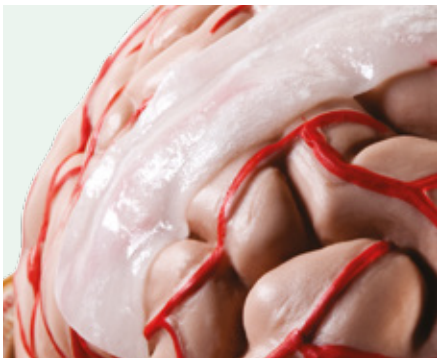
It Starts with Ultra Pure Collagen™ Technology

- Harvested, processed, and purified to limit the risk of infection, immunological response, and foreign body reaction, thereby reducing the chance of fibrotic encapsulation.
- In almost 40 years of Ultra Pure Collagen™ Technology use, there have been no confirmed reports of foreign-body reactions or rejections.
- Integra's Ultra Pure Collagen™ Technology is the foundation of DuraGen® matrix.



Precisely Engineered Porosity

- Platelets infiltrate the matrix and initiate fibrin clot formation, forming an effective layer that prevents CSF leakage and initiates the dural repair process.
- The pore size is optimized to allow fibroblasts to rapidly enter the matrix and lay down natural collagen fibers.
- The optimized 99% porosity, even distribution, and pore interconnectivity promote uniform tissue regeneration throughout the matrix.



Excellent Conformability and Handling

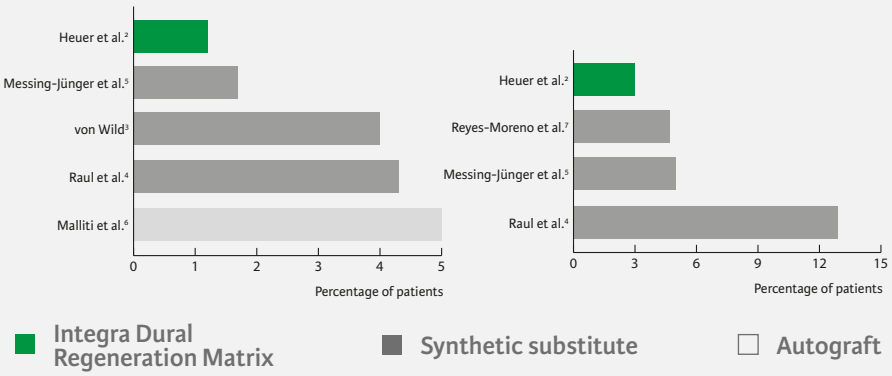
- Offers optimal conformability and ease of handling.
- DuraGen® matrix is quickly and easily hydrated prior to implantation or *in situ*.
- Upon hydration, DuraGen® matrix becomes a pliable membrane that conforms to the existing dura and remains in place through surface tension and fibrin clot formation, eliminating the need for sutures.

Integra's Dural Regeneration Matrices are specially designed to meet your cranial and spinal needs.

Safety Profile

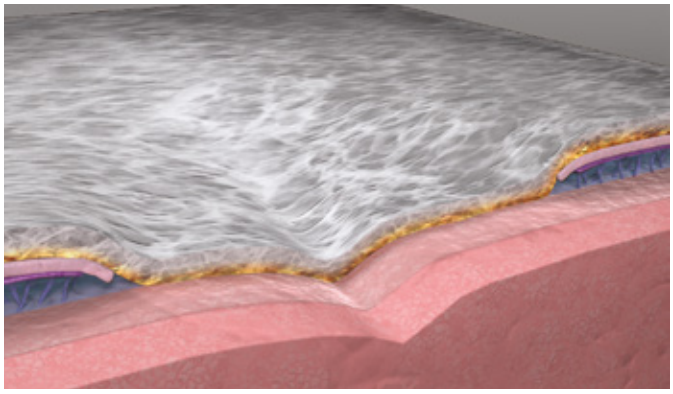
- Better safety profile than synthetic dural substitute[1-6] – minimization of postoperative complications.
- Infection rate comparable to other methods of dural closure.[1-5]
- Effectiveness proved against CSF leakage.[1,3,4,6]
- Inhibition of fibrosis and prevention of adhesion.[8]

Incidence of infection



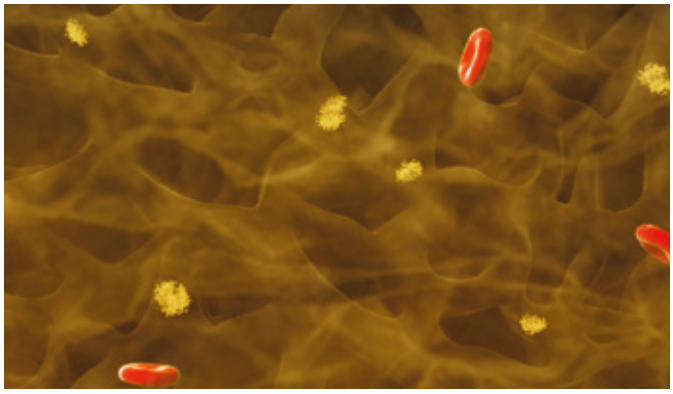
Scientific Superiority

1 Excellent Conformability and Adherence



- The hydrated graft conforms closely to the complex surfaces of the exposed brain or spinal cord.
- Matrix rapidly fills with the patient's blood and plasma exudate.

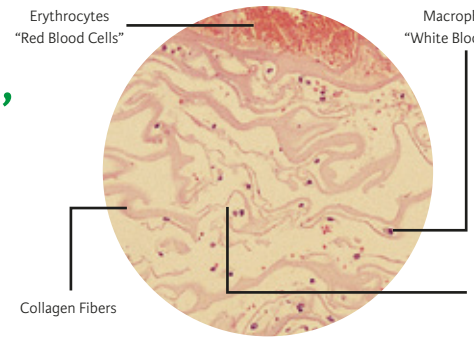
2 Rapid CSF Leak Prevention



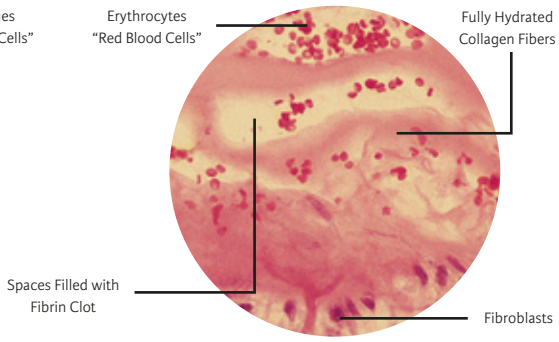
- Type 1 collagen matrix rapidly initiates platelet aggregation.
- Upon contact with the collagen matrix, platelets degranulate and release clotting factors that initiate fibrin clot formation.
- The fibrin clot creates a watertight barrier and binds the implanted matrix to the patient's dura.

In Vivo Dural Repair Continuum

By 60-days post-implantation, new dural tissue has formed.

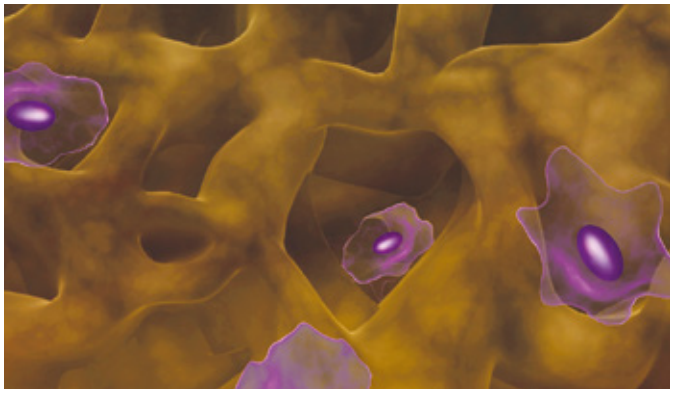


1 Day Post Implantation
Fibrin clot formed within matrix creating watertight barrier



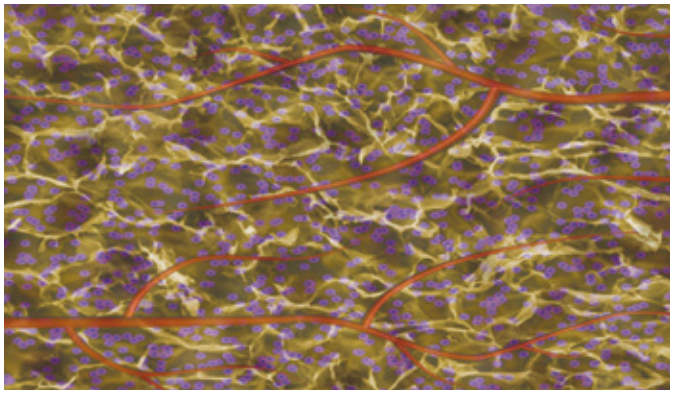
3 Days Post Implantation
Fibroblasts infiltrate and attach to graft matrix to lay down new collagen

3 Rapid Fibroblast Infiltration

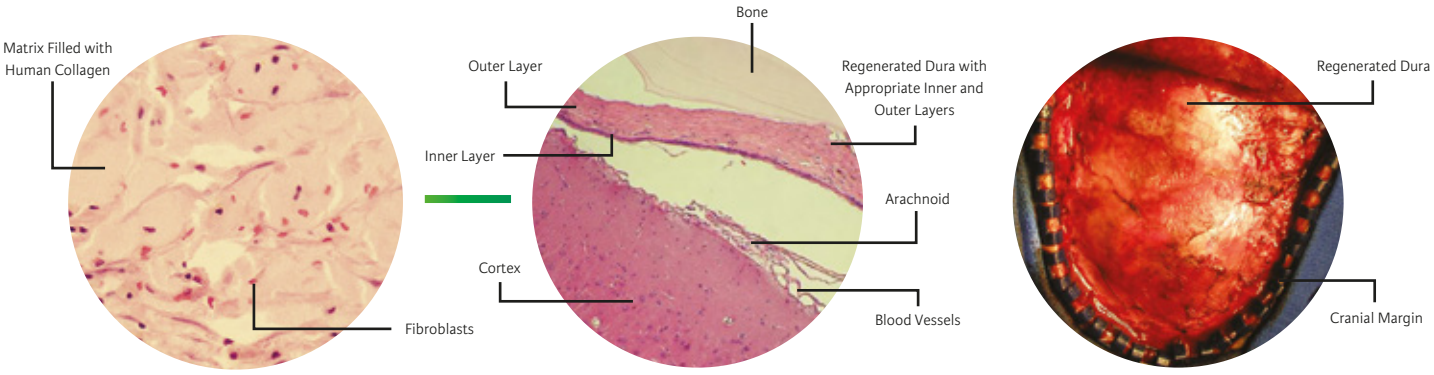


- Ultra Pure Collagen™ Technology, in combination with the open pore structures, promotes fibroblast activity and acts as a scaffold for cells to deposit new collagen.
- The graft structure features pores of 50 to 150 microns, within the optimal size for rapid fibroblast infiltration.
- Fibroblasts begin to migrate into the matrix 2 to 3 days after implantation and start the process of laying down new collagen.

4 Uniform Tissue Formation



- Within two weeks of implantation, a neodural membrane has formed between the dural margins to permanently close the dural defect.
- After 6-8 weeks, the implant is resorbed and replaced by dura.
- After 1 year, the neodura has developed into mature dura.



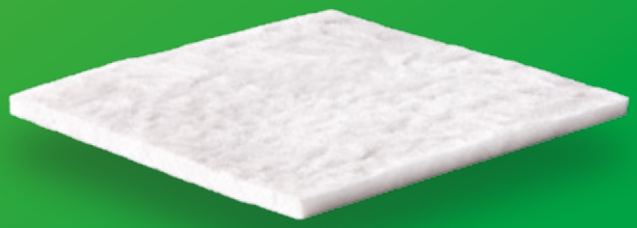
60 Days Post Implantation
Collagen matrix has been resorbed and replaced with dura

26 Weeks Post Implantation
Dura as seen in secondary cranioplasty procedure 6-months after decompressive hemicraniectomy*

*G. Heuer, M. Stiefel, E. Maloney-Wilensky, S. Danish, C. Dolinskas, P. LeRoux. *DuraGen is an Effective Dural Substitute: Clinical Experience in 100 Patients.* American Association of Neurological Surgeons Annual Meeting, April 2003.

Integra®
DuraGen® Matrix
The Leading Family of Dural Repair Products

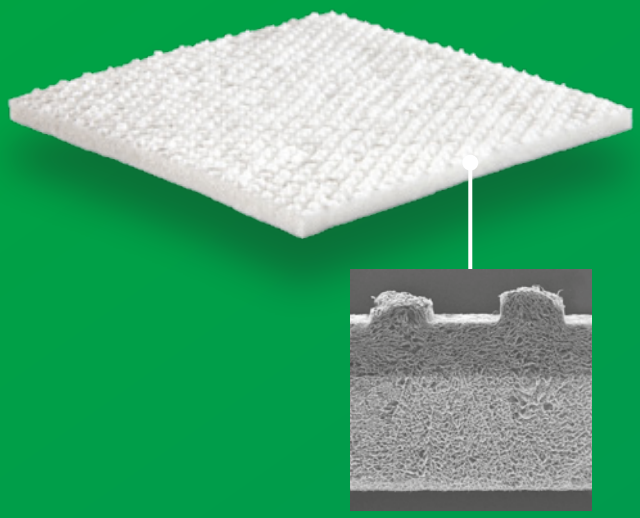
Limit uncertainty with one of the most innovative line of products for optimal dural repair:



PLUS: *Reliability*

DuraGen Plus™ matrix has an excellent safety record and provides industry-leading conformability and resorption. The improved consistency of DuraGen Plus™ matrix* offers increased tensile strength for optimized handling during challenging neurosurgery cases. Clinically proven to limit CSF leakage, DuraGen Plus™ matrix is also indicated to be used as an adhesion barrier in spinal procedures.

*compared with DuraGen® matrix, the 1st generation of Integra Dural Regeneration Matrices.



SUTURABLE: *Adaptability*

Suturable DuraGen™ matrix provides the benefits of DuraGen Plus™ matrix with the added versatility of accommodating both suture and onlay techniques. Suturable DuraGen™ matrix is a bilayer collagen graft with enhanced strength and support, providing the ability to suture without losing the conformability and resorption you demand from a dural graft.

DuraGen Plus™ Indications

DuraGen Plus Adhesion Barrier Matrix is indicated as an onlay graft for the repair and restoration of dural defects in cranial and spinal surgical procedures. DuraGen Plus matrix is also indicated as an adhesion barrier for the inhibition of post-surgical peridural fibrosis. DuraGen Plus matrix readily conforms to the surface of the brain, spinal cord and overlying tissues. DuraGen Plus matrix may be used to close dural defects following traumatic injury, excision, retraction or shrinkage. DuraGen Plus matrix may be used to supplement primary closure.

DuraGen Plus™ Contraindications

DuraGen Plus matrix is not designed, sold or intended for use except as described in the indications for use and is contraindicated in the following situations:
- For patients with a known history of hypersensitivity to bovine - derived materials.
- For primary repair of spinal neural tube defects; anterior spinal surgery with dural resection (e.g., transoral surgery).
- Should be used with caution in infected regions.
- Not recommended to cover dural defects involving mastoid air cells.
- Not recommended for large defects at the skull base following surgery.

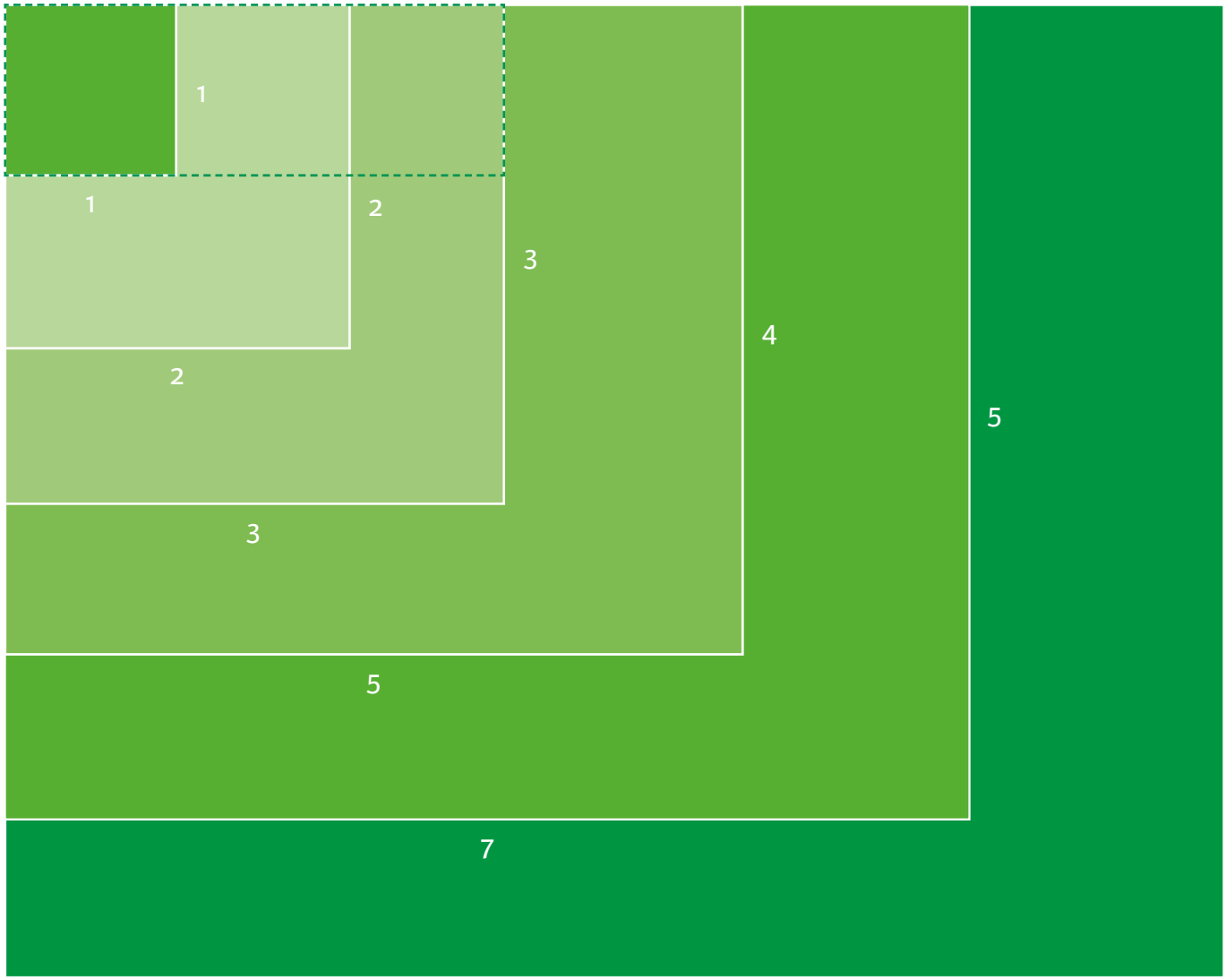
Suturable Duragen™ Indications

Suturable DuraGen is indicated as a dural substitute for the repair and restoration of dural defects in cranial and spinal surgical procedures. Suturable DuraGen readily conforms to the surface of the brain and overlying tissues. Suturable DuraGen may be used to close dural defects following traumatic injury, excision, retraction or shrinkage. Suturable DuraGen may be used to supplement primary closure.

Suturable Duragen™ Contraindications

Suturable DuraGen is not designed, sold or intended for use except as described in the indications for use and is contraindicated in the following situations:
- For patients with a known history of hypersensitivity to bovine derived materials.
- Should be used with caution in infected regions.

Integra®
DuraGen® Matrix
Product Sizes to Meet Your Surgical Needs



Sizes shown in inches at actual size

DuraGen Plus™ Dural Regeneration Matrix

Reference	Size	Units
DP-1011-I	1 in x 1 in (2.5 cm x 2.5 cm)	1
DP-5011-I	1 in x 1 in (2.5 cm x 2.5 cm)	5
DP-1013-I	1 in x 3 in (2.5 cm x 7.5 cm)	1
DP-5013-I	1 in x 3 in (2.5 cm x 7.5 cm)	5
DP-1022-I	2 in x 2 in (5 cm x 5 cm)	1
DP-5022-I	2 in x 2 in (5 cm x 5 cm)	5
DP-1033-I	3 in x 3 in (7.5 cm x 7.5 cm)	1
DP-5033-I	3 in x 3 in (7.5 cm x 7.5 cm)	5
DP-1045-I	4 in x 5 in (10 cm x 12.5 cm)	1
DP-1057-I	5 in x 7 in (12.5 cm x 17.5 cm)	1

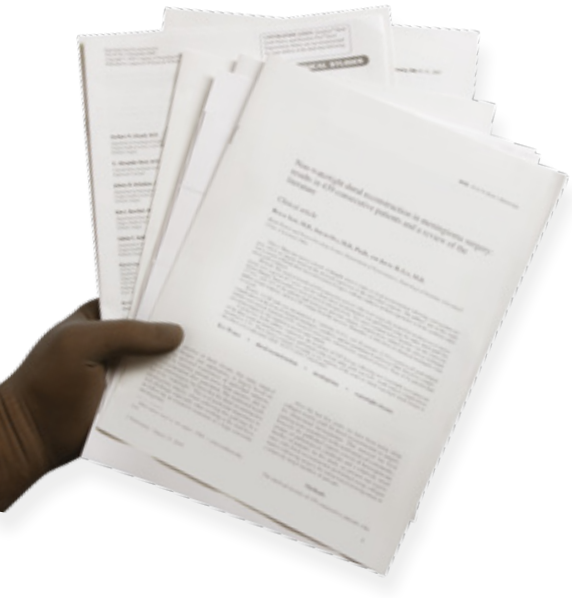
Suturable DuraGen™ Dural Regeneration Matrix

Reference	Size	Units
DURS-1391-ITL	1 in x 3 in (2.5 cm x 7.5 cm)	1
DURS-2291-ITL	2 in x 2 in (5 cm x 5 cm)	1
DURS-3391-ITL	3 in x 3 in (7.5 cm x 7.5 cm)	1
DURS-4591-ITL	4 in x 5 in (10 cm x 12.5 cm)	1

References

1. **G. Heuer, M. Stiefel, E. Maloney-Wilensky, S. Danish, C. Dolinskas, P. LeRoux.** *DuraGen is an Effective Dural Substitute: Clinical Experience in 100 Patients.* American Association of Neurological Surgeons Annual Meeting, April 2003.
2. **K. von Wild.** *Examination of the safety and efficacy of an absorbable dura mater substitute (Dura Patch) in normal applications in neurosurgery.* Surg Neurol 52:418-425, 1999.
3. **JS. Raul, J. Godard, F. Arbez-Gindre, A. Czorny.** *Use of polyester urethane (Neuro-Patch) as a dural substitute. Prospective study of 70 cases.* Neurochirurgie 2003 May;49(2-3 Pt1):83-9.
4. **AM. Messing-Jünger, J. Ibáñez, F. Calbucci, M. Choux, G. Lena, I. Mohsenipour, F. Van Calenbergh.** *Effectiveness and handling characteristics of a three-layer polymer dura substitute: a prospective multicenter clinical study.* J Neurosurg. 2006 Dec;105(6):853-8.
5. **M. Malliti, P. Page, C. Gury, E. Chomette, F. Nataf, FX. Roux.** *Comparison of deep wound infection rates using a synthetic dural substitute (neuro-patch) or pericranium graft for dural closure: a clinical review of 1 year.* Neurosurgery 2004 Mar;54(3):599-603.
6. **I. Reyes-Moreno, R. Verheggen.** *Time-sparing and effective procedure for dural closure in the posterior fossa using a vicryl mesh (Ethisorb).* Neurocirugia 2006 Dec;17(6):527-31.
7. **I. Haq, Y. Cruz-Almeida, EB. Siqueira, M. Norenberg, BA. Green, AD. Levi.** *Postoperative fibrosis after surgical treatment of the porcine spinal cord: a comparison of dural substitutes.* J Neurosurg Spine 2:50–54, 2005.
8. **P. Narotam, A. Gousseau, G. McGinn.** *Collagen Matrix (DuraGen) for duraplasty following cranial and spinal surgery.* 35th Canadian Congress of Neurological Sciences, Ottawa, Canada, June 2000.

Integra®
DuraGen® Matrix
Unsurpassed Clinical Data



Over 1,400 patients in 10 published clinical studies

- 0% Foreign body response
- 0% – 5.6% Infection rate
- 0% – 7.1% Leakage rate

Integra's DuraGen® products have more published human clinical data than any other collagen-based dural graft. Clinical studies have shown effective protection against CSF leakage with sutureless closure and no reports of foreign body reactions or graft rejections.

Summary outcome statistics derived from the following 10 clinical studies:

1. **Danish SF, et al:** *Experience with acellular human dura and bovine collagen matrix for duraplasty after posterior fossa decompression for Chiari malformations.* J Neurosurg Pediatrics 104:16-20, 2006.
2. **Harvey RJ, et al:** *Closure of large skull base defects after endoscopic transnasal craniotomy.* J Neurosurg 111 (2) : 371-379, 2009.
3. **Horaczek JA, et al:** *Collagen matrix in decompressive hemicraniectomy.* Neurosurgery 63 (1 suppl.1): ONS 176-ONS 181, 2008.
4. **Lee JH, et al:** *Dural reconstruction in meningioma surgery in, Lee JH (ed): Meningiomas: Diagnosis, Treatment an Outcome.* London: Springer, 2009, pp 619–624.
5. **Litvack ZN, et al:** *Dural augmentation: Part I: evaluation of collagen matrix allografts for dural defect after craniotomy.* Neurosurgery 65 (5): 890-897, 2009.
6. **Narotam PK, et al:** *Collagen matrix (DuraGen) in dural repair: analysis of a new modified technique.* Spine 29 (24) :2861-2867, 2004.
7. **Narotam PK, et al:** *Collagen matrix duraplasty for cranial and spinal surgery: a clinical and imaging study.* J Neurosurg 106 (1): 45–51, 2007.
8. **Narotam PK, et al:** *Collagen matrix duraplasty for posterior fossa surgery: evaluation of surgical technique in 52 adult patients.* J Neurosurg 111 (2): 380-386, 2009.
9. **Sade B, et al:** *Non-watertight dural reconstruction in meningioma surgery: results in 439 consecutive patients and a review of the literature.* J Neurosurg 114 (3) :714-718, 2011.
10. **Stendel R, et al:** *Efficacy and safety of a collagen matrix for cranial and spinal dural reconstruction using different fixation techniques.* J Neurosurg 109 (2): 215-221, 2008.

DuraGen® Family Regenerative Matrices

- Made from Ultra Pure Collagen™ Technology.
- Precisely engineered porosity for complete and natural repair.
- Excellent conformability & handling.

1 Million Implants and Counting

Integra DuraGen® graft provides the confidence of utilizing a dural matrix which has been implanted over one million times.

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
Phone: +33 (0)4 37 47 59 00 ▪ Fax: +33 (0)4 37 47 59 99
emea.info@integralife.com ▪ **integralife.eu**

EC REP

Customer Services
International: +33 (0)4 37 47 59 50 ▪ +33 (0)4 37 47 59 25 (Fax) ▪ csemea@integralife.com
France: +33 (0)4 37 47 59 10 ▪ +33 (0)4 37 47 59 29 (Fax) ▪ custsvcfrance@integralife.com
United Kingdom: +44 (0)1 264 345 780 ▪ +44 (0)1 264 363 782 (Fax) ▪ custsvcuk@integralife.com
Germany: +49 (0) 2102 5535 6200 ▪ +49 (0)2 102 5536 636 (Fax) ▪ custsvcgermany@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

Integra LifeSciences Corporation
311 Enterprise Drive
Plainsboro, NJ 08536 ▪ USA

Distributed by

INTEGRA® LIMIT UNCERTAINTY

Last modification: 07/2012 ▪ Class III

CE 0086 BSI