Repair of the Dura Mater With Processed Collagen Devices

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Abstract: ***Background*: We evaluated in a canine duraplasty model how specific differences in device physicomechanical properties, porosity, and crosslinking influenced the biological performance of three processed collagen dural substitutes. *Methods*: Three collagen dural substitutes were studied: Dura-Guard, DuraGen, and Durepair. The initial strength, stiffness, and suture retention force were measured using standard mechanical test methods. The relative pore sizes of each device were assessed with a scanning electron microscope. Differential scanning calorimetry was used to measure their respective collagen denaturation temperatures. The biologic response and performance of the materials were evaluated via an acute (1 month) and long-term (3 and 6 months) canine bilateral duraplasty study. *Results*: The mechanical properties of Dura-Guard and Durepair were similar to native dura. We could not quantify the mechanical properties of DuraGen because of its fragile nature. The denaturation temperature of DuraGen and Dura-Guard differed significantly from that reported for native collagens. The denaturation temperature of Durepair was comparable with the values reported for native collagens. All three materials were tolerated well by the animals. DuraGen did not maintain its structural integrity beyond 1 month. Dura-Guard and Durepair persisted for 6 months. Durepair was populated by fibroblasts and blood vessels, whereas Dura-Guard was not. *Conclusions:* The three dural substitutes tested were found to be safe and effective in healing surgically created defects in the dura mater. Although each of these dura substitutes are composed of collagen, differences in the collagen source and processing influenced device physicomechanical properties, porosity, and the nativity of the collagen polymer. These measured differences influenced device intraoperative handling and installation as well as the post-operative biological response, where differences in device resorption, cell penetration, vascularization, and collagen remodeling were observed.** © 2007 Wiley Periodicals, Inc. J Biomed Mater Res Part B: Appl Biomater 83B: 580–588, 2007

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INTRODUCTION

Dura mater may be damaged as a result of trauma, surgery, or tumor involvement. Restoration of this occlusive, cerebrospinal fluid containment tissue routinely involves use of harvested autologous collagenous membranes, like the pericranium, fascia lata, or temporal fascia. Rather than eliciting an inflammatory or foreign body response, these native collagen grafts are immunologically accepted, reconstituted with host cells and supporting vasculature, and remodeled. The biological response to autologous collagen membranes remains an ideal to which dural graft substitutes can be compared.

Indeed, over several decades, poor biological performance has excluded from clinical use dozens of dural grafts substitutes ranging from metal foils to various synthetic polymer sheets.[1–6] In contrast, xenogeneic collagen-based dural graft substitutes have become increasingly popular. These devices are typically composed of animal collagens processed to remove cellular and other immunogenic components. For example, Dura-Guard is a strong, drapable dura implant readily sutured to surrounding tissues and is produced from processed sheets of bovine pericardium. Similarly, DuraGen, is a collagen foam used as an onlay graft on the convexity of the brain that is derived from bovine Achilles tendons.

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Here, we report a detailed physicomechanical characterization of Dura-Guard and DuraGen. We also report on Durepair, a collagen dural graft substitute derived from the dermis of fetal bovine skin. Although each of these devices is similarly composed of collagen, we evaluated in a canine duraplasty model how specific differences relating to device physicomechanical properties, porosity, and crosslinking ultimately impact the biological performance and remodeling of these implants.

MATERIALS AND METHODS

Dural Graft Substitutes

Three dural substitutes were acquired: (1) DuraGen (Integra LifeSciences, Plainsboro, NJ), a chemically cross-linked collagen foam made from bovine tendon; (2) Dura-Guard (Synovis, St. Paul, MN), a chemically cross-linked collagen material made from bovine pericardium; and (3) Durepair (TEI Biosciences, Boston, MA; distributed by Medtronic Neurosurgery, Goleta, CA), a collagen implant derived from fetal bovine dermis, which has not undergone a chemical crosslinking processing step.

Study Design and Endpoints

The initial strength, stiffness, and suture retention strength of DuraGen, Dura-Guard, and Durepair were measured using standard mechanical test methods. The relative pore sizes of each device were assessed with a scanning electron microscope. The denaturation temperature of each processed collagen graft was measured with a differential scanning calorimeter. The biologic response, remodeling, and performance of the materials were evaluated via an acute (1 month) and long-term (3 and 6 months) bilateral duraplasty study in dogs.

A total of fifteen animals, five animals per time point, were used in this Institutional Animal Care and Use Committee approved study. A dural substitute was used to repair standardized dura mater defects on the left and right hemispheres of the brain for a total of thirty implanted grafts. The animals were implanted with dural substitutes according to the following scheme: 1 month-DuraGen and Durepair, 3 month-Dura-Guard and Durepair, 6 month-Dura-Guard and Durepair.

Preoperative physical, neurological, and blood analyses were performed on each animal. To evaluate any changes in the animals following implantation, identical exams were performed on each animal at 1, 3, and 6 months postoperatively. During implantation, the devices were evaluated for their surgical handling. At each time point, the devices were explanted, evaluated grossly, and sent to an independent laboratory (NAMSA, Northwood, OH) for pathology analysis.

Mechanical Properties

The mechanical properties of the three dural substitute materials were measured using an automated materials testing system (Instron Model 5544, Canton, MA). Standard test specimens of each material were cut to 5×50 mm^2 for tensile testing and 10×10 mm^2 for suture pull-out testing. Following hydration in USP purified water, the thickness of each test specimen was measured using a digital drop micrometer (Model ID-C112E, Mititoyo, Tokyo, Japan). Uniaxial tensile tests were conducted with initial lengths of 30 mm at a crosshead speed of 30 mm/min. We report the maximum tensile strength and elastic modulus (stiffness). Suture pull-out tests were performed by threading 4-0 polypropylene suture (Prolene, Ethicon) through each sample, 3 mm from its edge, and applying tension at a crosshead speed of 20 mm/min. The reported suture pull-out force is the peak load measured when pulling the suture through the matrix.

Thermal Properties

The denaturation temperatures of the three dural substitute products and untreated, native fetal bovine skin were measured using differential scanning calorimetry (DSC 6, Perkin Elmer, Wellesley, MA). Thermal analysis was performed at a scan rate of 2°C/min over a 50–150°C temperature range for the fully hydrated specimens.

Pore Architecture

Cross-sections of DuraGen, Dura-Guard, and Durepair and were examined using a scanning electron microscope to evaluate differences in pore shape and size. The fixed, wet Dura-Guard device was critically point dried and sputter coated with gold-paladium and photographed. The dry DuraGen and Durepair samples were likewise sputter coated with gold-paladium and photographed.

Animal Model

Mixed-breed intact female hounds with an average age of 2 years and body weights of 20–29 kg were used. The animals were under the supervision of a veterinarian board, certified by the American College of Laboratory Animal Medicine, and were housed in an USDA registered animal research facility. Physical examinations were performed preoperatively and at the 1, 3, and 6 month time points. Neurological examinations were performed at similar time points by a veterinarian. This examination included evaluation of basic motor function, muscle tone, vision, pupillary light reflex, facial nerve function, and balance. Blood was drawn pre- and postoperatively for blood counts and serum chemistries.

Our surgical model was similar to the one used by Mello et al.[7] Bilateral frontotemporoparietal craniotomies were performed (Figure 1). The central portion of each exposed dura site was excised and removed to create large dural defects ($\sim 1.5 \times 2$ cm^2). Duraplasties using the commercially avail-

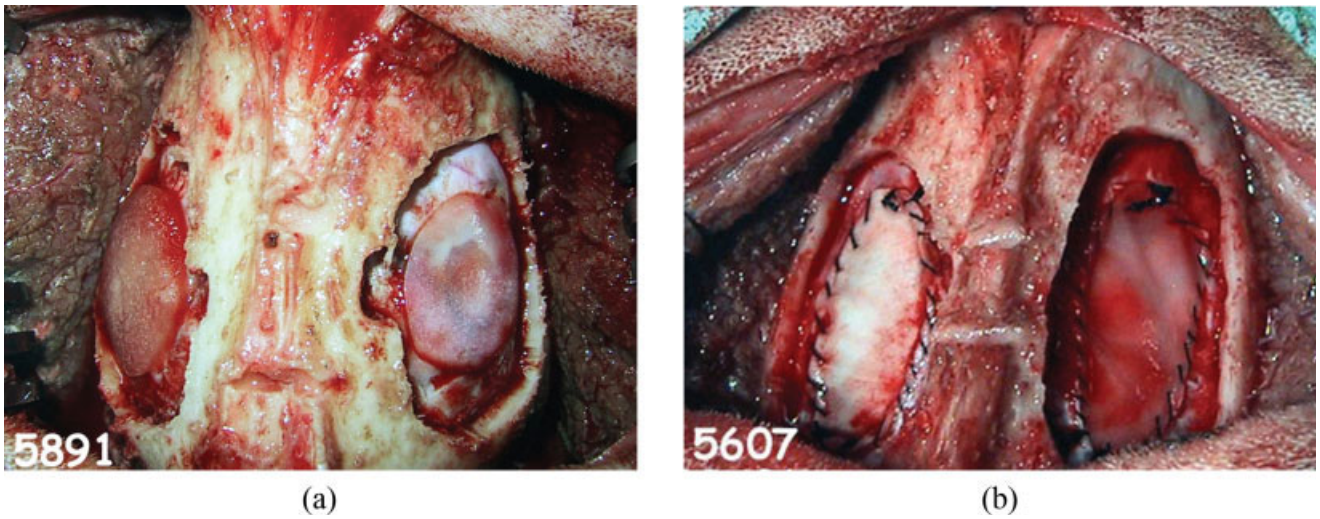

Figure 1. Canine duraplasty model. (a) DuraGen (left) and Durepair (right) being used as an onlay graft. (b) Dura-Guard (left) and Durepair (right) being sutured in place.

able devices were performed according to the manufacturers' instructions. DuraGen was used as an onlay graft, whereas Dura-Guard was sutured in place to the surrounding dura. Durepair was used as an onlay graft when the contralateral implant was DuraGen and sutured in place when the contralateral implant was Dura-Guard.

RESULTS

Mechanical and Thermal Properties

Each device's strength, stiffness (Young's modulus), thickness, and resistance to suture pull-out are summarized in Table I. For context, literature reported testing results for human dura mater are also included. Attempts at quantifying the mechanical properties of the DuraGen foam product were unsuccessful as the material was too fragile to be tested using the materials test set-up. Both Dura-Guard (average strength: 13.5 MPa) and Durepair (average strength: 22.7 MPa) were found to be as strong as the native dura that these devices repair (reported strength range: 3.28–12.76 MPa). Similarly, the stiffness of both devices (stiffness range: 69.94–81.33 MPa) was comparable with the stiffness of human dura mater (stiffness range: 21.3–192.61 MPa). On average, a loop of suture would pull through the Dura-Guard and Durepair devices at 10.02 and 12.38 N, respectively.

Table II compares the denaturation temperature of DuraGen, Dura-Guard, and Durepair to unprocessed collagenous membranes, that is, fetal bovine skin, bovine pericardia, and porcine pericardia. The reported range of denaturation temperatures of tissues in their native state is 59.5–63.9°C. The denaturation temperature of DuraGen (47.2°C) and Dura-Guard (82.3°C) differed significantly from that reported for native collagens. The denaturation temperature of Durepair

TABLE I. Mechanical Properties of Three Dural Substitutes and Reported Mechanical Data for Human Cranial Dura Mater[a]

	Thickness (mm)	Tensile Strength (MPa)	Young's Modulus (MPa)	Suture Pull-Out Force (N)
Dural substitute				
DuraGen ($n = 1$)	3.00	[b]	[b]	[b]
Dura-Guard ($n = 4$)	0.40 ± 0.00	13.50 ± 3.34	81.33 ± 20.48	10.02 ± 1.35
Durepair ($n = 10$)	0.50 ± 0.02	22.70 ± 2.83	69.94 ± 9.49	12.38 ± 2.10
Human dura mater				
Van Noort et al., 1981[8]	Not reported	3.28–7.86	21.3–48.0	Not reported
McGarvey et al., 1984[9]	Not reported	9.41 ± 1.54	61.50 ± 9.60	Not reported
Wolfinbarger et al., 1993[10]	0.58 ± 0.03	6.65 ± 0.14	69.50 ± 1.28	Not reported
Sacks et al., 1998[11]				
Parallel to fiber orientation	0.35 ± 0.04	12.76 ± 1.65	192.61 ± 23.51	Not reported
Perpendicular to fiber orientation	0.37 ± 0.04	5.21 ± 1.01	72.60 ± 10.86	

[a] Values are expressed as the mean ± standard error of the mean except for Van Noort et al., in which a range was reported.
[b] Upon hydration, DuraGen was too weak to be tested using the Instron force gauge.

TABLE II. Denaturation Temperatures of Three Collagen-Based Dural Substitutes, Fetal Bovine Skin, and Reported Thermal Transitions of Other Collagenous Tissues[a]

Material	Denaturation Temperature (°C)
DuraGen	47.2
Dura-Guard	82.3
Durepair	60.7
Fetal bovine skin	60.9
Bovine pericardium	
Sung et al., 1999[12]	63.9 ± 0.7
Porcine pericardium	
Sung et al., 2001[13]	60.7 ± 0.7
Sung et al., 1998[14]	59.5 ± 0.6
Huang et al., 1998[15]	62.7 ± 0.6

[a] Values are expressed as mean ± standard deviation.

(60.7°C) was comparable with the values reported for native collagens.

Scanning Electron Microscopy

The microstructure of the dural graft substitute matrices were quite varied (Figure 2). The largest pores ($\sim$100 μm) were seen with the DuraGen matrix. The smallest pores ($<$5 μm) were seen with the Dura-Guard matrix. The collagen fibers that make up the Durepair matrix were plainly evident forming pores in the 10–20 μm range.

Physical/Neurologic Examinations and Clinical Pathology Screening

The physical and neurologic condition of all the animals included in this study was within normal limits. One dog was euthanized intraoperatively because of a surgical complication. One animal developed a seroma over the area of the incision, which resolved spontaneously without any interventions. Blood was drawn from all animals pre- and postoperatively for complete blood counts and serum chemistries. The majority of the animals had an absolute eosinophilia and basophilia preoperatively, which was attributed to parasitism and resolved with appropriate pharmacotherapy. One animal in the 1–month-group exhibited severe leucopenia, which was attributed to a laboratory error, as the animal appeared healthy and its physical condition was not consistent with sepsis. A repeat sample was not obtained because the animal had been already euthanized.

Surgical Handling

Dura-Guard and Durepair had a firm, tissue-like consistency when compared with DuraGen, and could be handled more rigorously. All three materials readily conformed to the contour of the brain whether they were previously hydrated or hydrated *in situ*. Dura-Guard and Durepair were equivalent in the ease with which the materials could be sutured in place. DuraGen did not hold a suture well.

Pathology

One Month. In the DuraGen group, the test article could only be identified in one animal. Tissue response to the implant was minimal. An area of whispy collagen could be identified at the implant side on the trichrome stain. It did not blend into the surrounding tissue and contained plump immature fibroblasts. In the remaining four animals, the test article was not present. The material appeared to have been completely resorbed and replaced with thin, loose connective tissue [Figure 3(a)].

In the Durepair group, the test article could be clearly identified [Figure 3(b)]. The inflammatory response to all implants was minimal. Histologically, the collagen device appeared as ribbons and bundles of eosinophilic material with variable orientation. In all devices, the porous structure was observed to be diffusely infiltrated by fibroblasts and macrophages (Figure 4). Except for one explant, a superficial infiltration of blood vessels was observed into the collagen fiber makeup of the devices. No neutrophils, lymphocytes, or plasma cells were identified. The calvarial surface of the implant was covered by a thin fibrous layer measuring one to two cells thick and merged with the test articles.

Three Months. In the Dura-Guard group, the test article could be identified in all animals. The inflammatory response was minimal in three out of the five animals. In the remaining two specimens, a moderate inflammatory response characterized by macrophages and lesser numbers of lymphocytes and plasma cells at the surfaces of the devices was noted. Because this was present only in two out of the five animals, it was most likely because of surgical trauma and tissue manipulation rather than inherent implant biocharacteristics. Penetration of blood vessels and fibroblasts into the device was not observed in any of the five devices examined [Figure 5(a)]. The dura and dura repair site was not expanded to any significant extent. No new subdural or epidural masses were present.

In the Durepair group, the specimen could be identified in all of the animals. The inflammatory response was minimal in all animals. Histological features were consistent with the 1-month explants, where each device had been populated by an infiltrate of fibroblasts and lesser numbers of macrophages [Figure 5(b)]. Although vascularization was limited primarily to the surface of the device at 1 month, revascularization of the entire test articles was noted in three of the five explanted devices. The dura and dura repair site was not expanded to any significant extent. No new subdural or epidural masses were present.

Six Months. In both groups, the histologic response to the implants at 6 months was similar to that observed at 3 months. The inflammatory response to Dura-Guard was minimal in all explants. In addition, the explanted devices were not infiltrated by blood vessels nor fibroblasts [Figure 6(a)]. The inflammatory response was minimal in all Durepair explants. The collagen fiber network of the Durepair devices

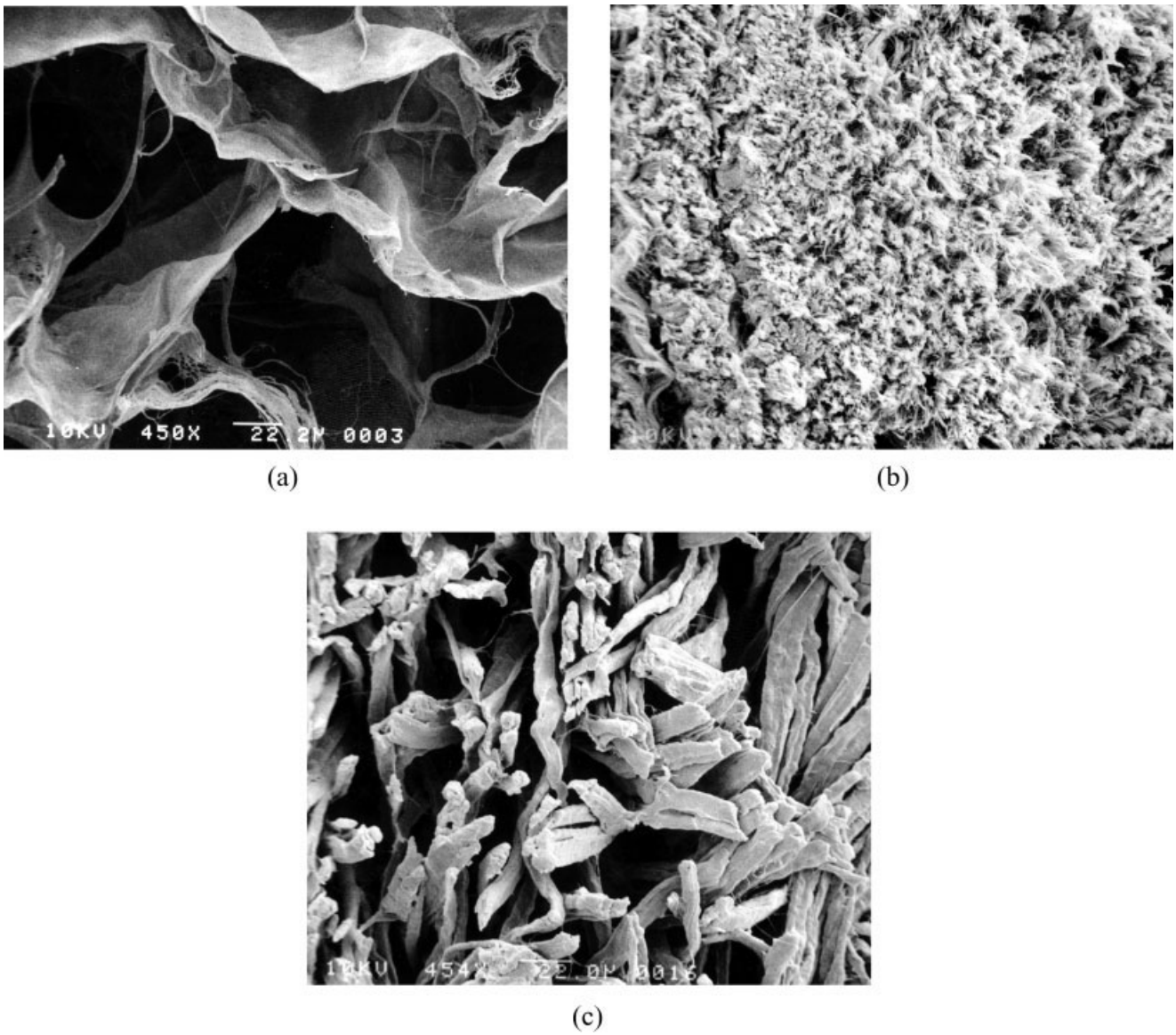

Figure 2. Scanning electron micrographs of each dural substitute (scale bar 22 μm). The collagen pore structure varied widely. The thin collagen sheets that composes DuraGen (a) creates pores on the order of 100 μm. Dura-Guard (b) is also composed of a fine network of collagen fibers that form smaller pores in the 1–5 μm range. Durepair (c) is composed of distinct collagen fibers creating an open porous structure with pores $\sim$10–20 μm in size.

remained populated by fibroblasts, lesser numbers of macrophages, and a supporting vasculature. At 6 months, there was evidence that the collagen fibers of Durepair were being remodeled by the populating cells as the definition of the collagen fibers of the implant had become less distinct. This feature was emphasized in those collagen fibers at the external surface of the devices, which appeared to have merged with the collagen fibers of the superficial fibrous tissue deposited by host cells [Figure 6(b)].

For both the Dura-Guard and Durepair, one of the five specimens revealed a small amount of pia matter and cerebrum attached to the dural substitute at the graft margin where the implants were sutured to host dura. These adhesions were not viewed to be clinically significant. For both devices, the dura and dura repair site were not expanded to any significant extent. No new subdural or epidural masses were present.

DISCUSSION

Dural Graft Technical Requirements

Reflecting on the clinical results of a number of failed dural graft substitute designs highlights the unique challenges and features the ideal dural graft substitute must possess. Metal foils were first used by Beach in 1890 for the treatment of

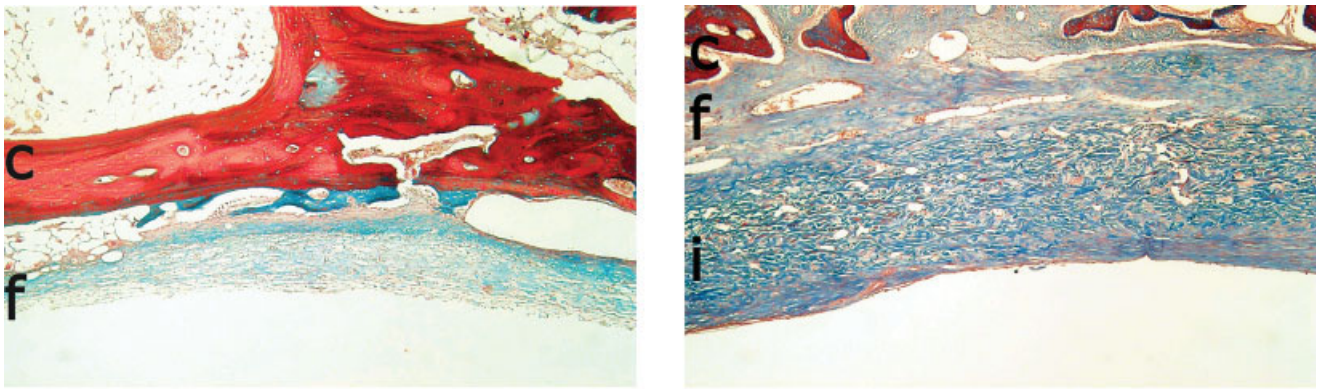

Figure 3. One month histology of DuraGen (a) and Durepair (b). DuraGen was not evident under the cranium in the histological section. A thin, loose fibrous tissue layer had formed at the implantation site. The fibrous network of the Durepair collagen implant staining blue is plainly evident. Minimal inflammation is associated with the implant, and a thin fibrous tissue layer has formed between the cranium and implant (trichrome stain; "c" designates cranium, "f" designates host fibrous tissue, "i" designates implant).

cerebral cicatrix. Polymer derived materials, such as Dacron and Orlon, subsequently gained popularity in the mid 1900's. Despite initial enthusiasm for both the metals and synthetic polymers, high infection rates, the inability of the material to integrate with the surrounding dura, foreign body encapsulation, high rate of adhesion formation, and epi- or subdural hematomas, led to their disuse.[16,17] Cellulose, a safe and biologically well tolerated plant derived polymer, was similarly abandoned as histological analysis revealed that the material performed no differently than unrepaired dura.[7]

Collagen allografts were first used by Finster in 1910.[18] The most commonly used allograft was lyophilized human dura.[19] Other tissue sources included: pericardium, dermis, peritoneum, and flexor tendons.[20] The collagen-based implant has proven popular and effective in repairing dura mater defects. However, allograft tissues, specifically allograft dura mater, fell from favor after several reports were published linking the allograft dura mater to Creutzfeldt-Jacob disease, a transmissible spongiform encephalopathy (TSE).[21–26]

As such, collagen autograft implants continue to be the preferred dural substitute. Their origin can be cranial, such as pericranium, and temporalis fascia, or from other parts of the body, such as rectus fascia and fascia lata. The native collagen dural substitute is easy to handle, strong, suturable, affordable, well tolerated by the host, incorporated into the recipient site, nonimmunogenic, and carries a low risk of infection. Its use is primarily limited by its availability, surgical morbidity, and the size of the dural defect.

The processed bovine collagen implants effectively address the limitations of availability, surgical morbidity, and the size of the dural defect. Moreover, in this *in vivo* evaluation, none of the animals developed any clinical signs consistent with CSF leak, seizures, hemorrhage, hydrocephalus, foreign body reaction, or infection. No CSF leaks were observed in any of the animals intraoperatively, postoperatively, or at necropsy, although one animal did develop a transient seroma. No adhesions were seen at 1 month with DuraGen or Durepair. No adhesions were seen at 3 months with Dura-Guard or Durepair. At 6 months, a limited number of focal adhesions were noted at the healing suture margins at comparable rates for Dura-Guard and Durepair. In our opinion, these represent an inflammatory reaction to the suture material and are not of clinical importance. No significant foreign body reaction was noted for any of these bovine collagen devices. Still, although all implants were well tolerated by the animals and were effective in repairing the dura mater defect, intraoperative handling and the biological sequelae proved unique to each implant. That is, device physicomechanical properties, cell penetration, revascularization,

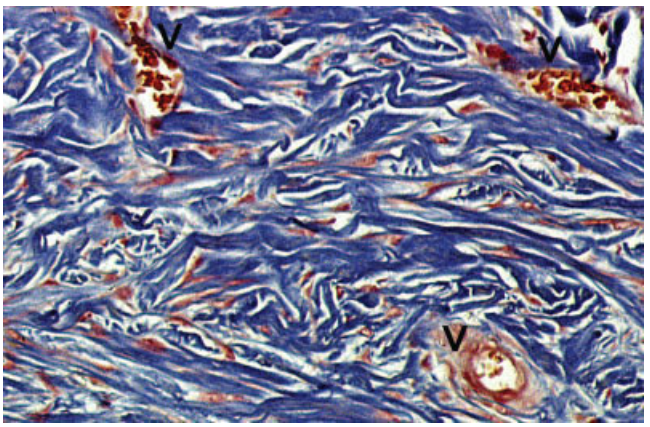

Figure 4. The collagen fiber matrix (stained blue) of the Durepair implant had been revascularized and populated by host fibroblasts at 1 month. (trichrome stain; "v" designates blood vessel).

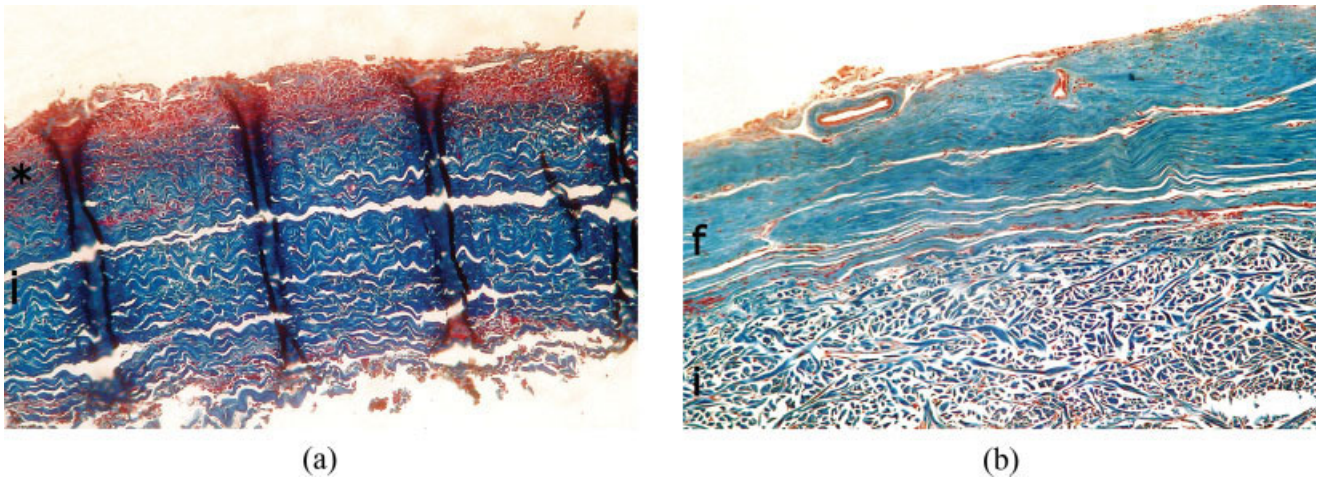

Figure 5. At 3 months post-op, differences in the biological response to the Dura-Guard (a) and Durepair (b) implants were seen. Cell penetration into the Dura-Guard implant was minimal and primarily consisted of inflammatory cells (folds in Dura-Guard section are histological artifact). On the implant side exposed to the calvaria, Durepair was overgrown with host collagenous tissue. The device was populated with host vessels and fibroblasts. Minimal inflammatory cells were present. (Trichrome stain; "*" designates inflammatory cells, "f" designates host fibrous tissue, "i" designates implant).

resorption, and remodeling of the grafts varied and were found to be related to the processing of the collagen implant.

Collagen Processing and Graft Performance

DuraGen is delicate collagen foam formed by freeze-drying a dispersion of purified, ground flexor tendons that is later chemically cross-linked. Dura-Guard is a strong collagen membrane composed of processed, intact pericardium that has been chemically crosslinked with glutaraldehyde. Durepair is a strong collagen graft of intact dermis from fetal bovine that has been processed to remove all cellular components and has not been chemically modified with crosslinking chemicals.

The success of the Dura-Guard bovine pericardium and other dense connective tissue grafts as dural substitutes can be largely attributed to their high mechanical strength, flexibility, and ability to be sutured securely in place, providing an occlusive seal to prevent CSF leaks. The physicomechanical properties of these grafts are familiar to the surgeon, as the strength and stiffness are similar to that of native human dura mater. Durepair is similarly strong, suturable, and drap-

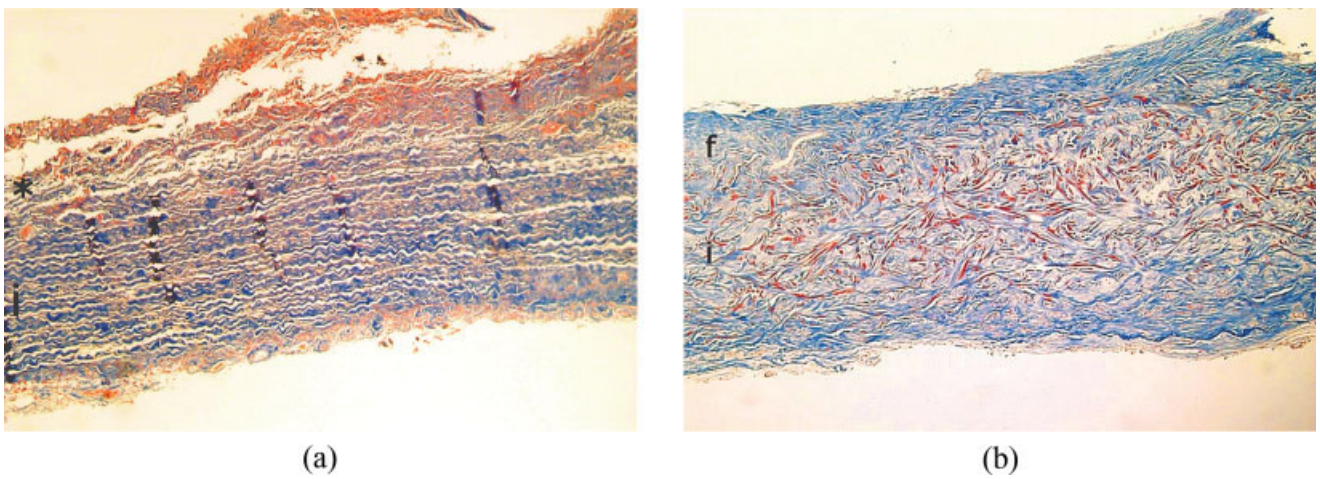

Figure 6. At 6 months post-op, differences in the biological response to the Dura-Guard (a) and Durepair (b) implants were again seen. Cell penetration into the Dura-Guard implant continued to be minimal and primarily consisted of inflammatory cells. Durepair was populated with host cells and a vasculature. The collagen fibers that make up the Durepair implant, while distinct at 3 months, were increasingly diffuse as host cells remodel the implant. Similarly, host collagen deposited on the surface on the implant was seen blending with the Durepair implant. (Trichrome stain; "*" designates inflammatory cells, "f" designates host fibrous tissue, "i" designates implant).

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able over curved surfaces. In short, Dura-Guard and Durepair mimic the physicomechanical properties of tissues because they are processed intact tissues. In contrast, the DuraGen foam is derived from ground tendon and was delicate. DuraGen could not be sutured in place, and attempts at quantifying the mechanical properties of this product were unsuccessful as the material was too weak to be tested using the materials test system. Whereas the Dura-Guard and Durepair devices are strong enough to be used at low and high CSF pressure sites, in our opinion DuraGen is suited as an onlay graft on the convexity of the brain where CSF pressures are low.

Change in the collagen denaturation temperature from that measured for native collagen is indicative of protein denaturation and/or changes in collagen crosslinking. The 10°C decrease in denaturation temperature of the collagen composing DuraGen indicates that it was partially denatured during processing. The 20°C increase in denaturation temperature of the Dura-Guard implant indicates non-native crosslinking of the collagen as a result of the glutaraldehyde processing treatment. The denaturation temperature of Durepair was found to be comparable with native, nonprocessed collagen. The collagen composing this device was neither significantly crosslinked nor denatured during processing.

Non-native crosslinking and denaturation did influence the biological response to and resorption rate of DuraGen and Dura-Guard. Being composed of denatured collagen that is more susceptible to cellular breakdown and having large pores on the order of 100 μm, the DuraGen implants were rapidly penetrated by cells and quickly resorbed within a month. A thin, weak connective tissue occupied the implant space.

Dura-Guard's restrictive pores, typically smaller than the cells attempting to penetrate the device, coupled with added, nonnative collagen crosslinks results in a long-lived collagen implant that was minimally revascularized at 1, 3, and 6 months. Similarly, there was no indication that the material was being resorbed or remodeled by host cells.

Durepair's *in vivo* performance was more akin to allograft and autograft tissue implants in that the nonchemically crosslinked, nondenatured collagen device retained its capacity to be progressively remodeled. Hallmarks of native remodeling included reconstitution of the porous collagen implant by host fibroblasts and vasculature by 1 month, followed by the concurrent deposition and integration of host collagen with the implanted collagen fibers.

Based on these results, the Dura-Guard and Durepair implants can be used where a permanent dural layer is required.

Safety of Bovine Collagen Implants

These bovine derived collagen products come in direct contact with the central nervous system. As such, there is a theoretical possibility that these collagen devices could transmit new variant Creutzfeldt-Jakob disease (vCJD), the human form of mad cow disease.

The contaminant or infectious agent responsible for transmissible spongiform encephalopathies (TSEs) and the associated progressive, degenerative neurological disease, is widely believed related to a self replicating, abnormally folded isoform of normal cellular membrane proteins called prions. Though prions can be transmitted from one host to another, they are not comparable with traditional infectious agents such as bacteria, viruses, protozoa, or fungi. What causes the abnormal prion folding to occur, why hosts cannot develop immunity to these proteins, and what factors might cause or transmit TSEs are still poorly understood.[27–29]

Better understood are the tissues which can contain infectious prions and effective methods of inactivating the infectious agents responsible for TSEs. Each of the bovine dural graft substitutes tested is derived from tissues the World Health Organization (WHO) has designated as having no detectable TSE infectivity. In addition, each manufacturer has incorporated a chemical TSE inactivation step by exposing the collagen to concentrated sodium hydroxide. Considering the steps taken by the manufacturers, the likelihood that these xenogenic collagen devices are capable of transmitting the agent responsible for TSEs appears remote.

SUMMARY

The three dural substitutes tested were found to be safe and effective in healing surgically created defects in the dura mater. Although each of these dura substitutes are composed of collagen, differences in the collagen source and processing influenced device physicomechanical properties, porosity, and the nativity of the collagen polymer. These measured differences influenced device intraoperative handling and installation as well as the post-operative, biological response where differences in device resorption, cell penetration, vascularization, and collagen remodeling were observed.

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