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Laparoscopic fixation of biologic mesh at the hiatus with fibrin or polyethylene glycol sealant in a porcine model

Eric D. Jenkins,

Department of Surgery, Section of Minimally Invasive Surgery, Washington University School of Medicine, 660 South Euclid Avenue, Campus Box 8109, St. Louis, MO 63110, USA

Sopon Lerdsirisopon,

Department of Surgery, Section of Minimally Invasive Surgery, Washington University School of Medicine, 660 South Euclid Avenue, Campus Box 8109, St. Louis, MO 63110, USA

Kevin P. Costello,

Department of Surgery, Section of Minimally Invasive Surgery, Washington University School of Medicine, 660 South Euclid Avenue, Campus Box 8109, St. Louis, MO 63110, USA

Lora Melman,

Department of Surgery, Section of Minimally Invasive Surgery, Washington University School of Medicine, 660 South Euclid Avenue, Campus Box 8109, St. Louis, MO 63110, USA

Suellen C. Greco,

Division of Comparative Medicine, Washington University School of Medicine, 660 South Euclid Avenue, Campus Box 8109, St. Louis MO 63110, USA

Margaret M. Frisella,

Department of Surgery, Section of Minimally Invasive Surgery, Washington University School of Medicine, 660 South Euclid Avenue, Campus Box 8109, St. Louis, MO 63110, USA

Brent D. Matthews, and

Department of Surgery, Section of Minimally Invasive Surgery, Washington University School of Medicine, 660 South Euclid Avenue, Campus Box 8109, St. Louis, MO 63110, USA

Corey R. Deeken

Department of Surgery, Section of Minimally Invasive Surgery, Washington University School of Medicine, 660 South Euclid Avenue, Campus Box 8109, St. Louis, MO 63110, USA

Corey R. Deeken: deekenc@wudosis.wustl.edu

Abstract

Background—The objective of this study was to determine the acute and chronic fixation strengths achieved by fibrin or polyethylene glycol (PEG) sealants to secure biologic mesh at the esophageal hiatus in a porcine model.

Methods—For this study, 32 female domestic pigs were divided into four groups of 8 each. The four groups respectively received acute fibrin sealant, acute PEG sealant, chronic fibrin sealant,

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Correspondence to: Lora Melman; Corey R. Deeken, deekenc@wudosis.wustl.edu.

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and chronic PEG sealant. Laparoscopically, a 5.5 × 8.5-cm piece of Biodesign Surgisis Hiatal Hernia Graft (porcine small intestine submucosa) was oriented with the U-shaped cutout around the gastroesophageal junction and the short axis in the craniocaudal direction to simulate hiatal reinforcement with a biologic mesh. The mesh then was secured with 2 ml of either fibrin sealant or PEG sealant. The pigs in the acute groups were maintained alive for 2 h to allow for complete polymerization of the sealants, and the pigs in the chronic group were maintained alive for 14 days. After the pigs were euthanized, specimens of the mesh–tissue interface were subjected to lap shear testing to determine fixation strength, and hematoxylin and eosin (H&E) stained slides were evaluated for evidence of remodeling.

Results—No significant differences were observed between the acute and chronic fixation strengths or the remodeling characteristics of the two sealants. However, fixation strength increased significantly over time for both types of sealant. Evidence of remodeling also was significantly more pronounced in the chronic specimens than in the acute specimens.

Conclusions—This study demonstrated the feasibility of using fibrin or PEG sealants to secure biologic mesh at the hiatus in a porcine model.

Keywords

Fibrin sealant; Fixation strength; Laparoscopic; Paraesophageal hernia repair; Polyethylene glycol sealant; Porcine small intestine submucosa

Recurrence rates as high as 19–42% after primary laparoscopic hiatal hernia repair have been documented [1–4]. Synthetic mesh materials such as polypropylene and polytetrafluoroethylene used to reinforce the esophageal hiatus have been shown to reduce recurrence rates to 0–14% in some series [1, 4–6]. However, these materials also present a risk of increasing the incidence of dysphagia, erosion, migration, and stricture [7].

Biologic tissue-derived “mesh” materials developed recently represent an attractive alternative to synthetic materials. These biologic materials, composed of human or animal tissues such as dermis, pericardium, or small intestine submucosa (SIS), are thought to undergo a remodeling process, ultimately resulting in replacement of the mesh by host tissue. This is thought to reduce the likelihood of erosion or stricture [8, 9].

Short-term studies have demonstrated the benefits of using biologic scaffold materials to reinforce laparoscopic paraesophageal hernia repairs. Oelschlager et al. [10] published a multicenter prospective randomized trial involving 108 patients who underwent laparoscopic paraesophageal hernia repair. The patients were randomized to receive either a primary repair or a repair buttressed with a porcine small intestine submucosa mesh material. They were followed for 6 months, and the SIS material was shown to reduce recurrences and symptoms significantly and also to increase quality-of-life scores significantly. After 6 months, the patients who received a primary repair without SIS demonstrated a recurrence rate of 24%, whereas those who received SIS to buttress the repair had a recurrence rate of 9%. However, after a long-term followup period of 59 months, the recurrence rate did not differ statistically between repairs with and those without SIS reinforcement [11, 12].

Despite these benefits, the technical difficulty of suturing a biologic mesh at the hiatus precludes use of these materials by many surgeons unfamiliar with the procedure. Tacks and staples also could be used, but there is risk of injury to the aorta and pericardium because of close proximity to the hiatus [13–15]. If adequate incorporation at the hiatus could be demonstrated, the potential simplicity of using a tissue sealant for biologic mesh fixation would increase the use of these materials and ensure a better outcome for patients.

Although both fibrin and polyethylene glycol (PEG) sealants have been used in other fixation applications such as inguinal hernia repair and bowel anastomoses [16–18], the fixation strengths achieved by these sealants to secure biologic mesh at the hiatus have not been reported to date. Thus, this study aimed to determine the feasibility of using sealants at the hiatus, to quantify the fixation strengths achieved, and to evaluate the host tissue response using a semiquantitative scoring system to characterize cellular infiltration, scaffold degradation, host extracellular matrix (ECM) deposition, neovascularization, fibrous encapsulation, and inflammation.

Materials and methods

Tissue sealants

Two tissue sealants were selected for evaluation: one fibrin sealant (Tisseel, Baxter Healthcare Corporation, Deerfield, IL, USA) and one polyethylene glycol (PEG) sealant (Coseal Surgical Sealant, Baxter Healthcare Corporation). The Tisseel fibrin sealant comprises a combination of fibrinogen and thrombin, which are converted to fibrin to form an adhesive. According to the Baxter Web site (<http://www.baxterbiosurgery.com>), Tisseel is indicated for hemostasis and prevention of leaks at bowel anastomoses. However, studies have demonstrated the utility of using fibrin sealant as an alternative to traditional fixation mechanisms for hernia repair applications [14, 18–25]. For this reason, Tisseel was selected for evaluation of biologic mesh fixation at the hiatus.

The Coseal polyethylene glycol sealant is composed of a tetra-succinimidyl and tetra-thiol-derivatized polyethylene glycol [16], which combine to form a hydrogel. According to the Baxter Web site, Coseal is indicated for hemostasis, particularly during vascular reconstruction.

A unique property of Coseal is its ability to form crosslinks within its structure and to underlying tissue. Covalent bonds are thought to form between the hydrogel and the amine groups present in the collagen of the tissue. For this reason, Coseal was selected as the second tissue sealant for evaluation in this study.

It should be noted that these tissue sealants are not currently Food and Drug Administration (FDA) approved for mesh fixation, so the methods described in this study are considered “off-label” use in the United States.

Study animals

For this study, 32 female domestic pigs weighing 80–100 lb were divided into four groups. The four groups respectively received acute fibrin sealant ($n = 8$), acute PEG sealant ($n = 8$), chronic fibrin sealant ($n = 8$), and chronic PEG sealant ($n = 8$). All the animals received care in conjunction with the Division of Comparative Medicine according to the standards set by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council. The Institutional Animal Care and Use Committee at Washington University School of Medicine in St. Louis approved the experimental protocols before the start of the study [26].

Animal care and operative technique

The animals were acclimated to the facility for at least 3 days and fasted for 24 h before surgery. They were sedated with intramuscular telazol/ketamine/xylazine (telazol 4 mg/kg, ketamine 2 mg/kg, and xylazine 2 mg/kg administered 1 ml/50 lb) and maintained under anesthesia with isoflurane through endotracheal intubation. Preoperative doses of cefazolin

and Buprenex were given to the survival animals for antibiotic prophylaxis and pain control, respectively.

The animals were positioned in dorsal recumbency in the reverse Trendelenberg position, then prepped and draped using standard sterile technique. The abdominal cavity was accessed at the mid-abdomen with a Veress needle. Insufflation was achieved, and ports were placed at the mid-abdomen ($n = 1$), right subcostal ($n = 1$), epigastric ($n = 2$), and left subcostal ($n = 1$) positions. The liver was retracted using the right subcostal port. The gastroesophageal junction (GEJ) and hiatal crura were identified, and the region of the cardia was exposed with blunt dissection and electrocautery. Care was taken to spare the vagal nerves, and a Penrose drain was placed around the esophagus for retraction and exposure of the hiatus.

A simulated paraesophageal hernia repair was performed by freeing the crura and then reapproximating them using two 2-0 Ethibond sutures. Although this technique represents a porcine model of laparoscopic reinforcement of the hiatus, simulating hiatal hernia repair, it does not represent a true model of paraesophageal hernia repair. Insufflation pressure was decreased to 10 mmHg, and reverse Trendelenburg was decreased after exposure of the crura to reduce the risk of tension pneumothorax due to the natural anatomic extension of the porcine pleura posterior to the GEJ. A 5.5×8.5 -cm piece of biologic mesh (Biodesign Surgisis Hiatal Hernia Graft, a collagen matrix composed of porcine small intestinal submucosa; Cook Biotech, Inc., West Lafayette, IN, USA) was oriented with the U-shaped cutout around the GEJ and the short axis in the craniocaudal direction for hiatal reinforcement (Fig. 1).

After verifying correct placement of the mesh, it was secured with 2 ml of either polyethylene glycol sealant (Coseal Surgical Sealant; Baxter Healthcare Corporation) applied with the Coseal Extended Applicator or with 2 ml of fibrin sealant (Tisseel; Baxter Healthcare Corporation) applied with the Duplocath MIS Application Catheter (eight for each fixation method, both acute and chronic). The Penrose drain was removed after 5 min had been allowed for initial sealant polymerization.

After hemostasis was ensured, the abdomen was desufflated. For all the survival animals, the port sites were closed with 0-Prolene at the fascia and 3-0 PDS at the skin. The survival animals were recovered, allowed to return to a normal diet, and administered postoperative Buprenex for pain and cefazolin for antibiotic prophylaxis.

Euthanasia of the animals and explantation of meshes

The acute animals were maintained under anesthesia for 2 h after mesh implantation to ensure complete polymerization of the sealants. The acute animals then were humanely euthanized using pentobarbital dosed once at more than 150 mg/kg intravenously or using supersaturated KCl to effect intravenously under anesthesia. The animals from the chronic arm of the study were premedicated with intramuscular telazol/ketamine/xylazine and humanely euthanized after 14 days, as described earlier. At the time of euthanasia in both the acute and chronic phases of the study, a midline laparotomy and chevron incision was made, and the mesh was evaluated macroscopically for migration or folding. One piece of biologic mesh/crural construct (3×5 cm) was taken from each animal for biomechanical testing, and two pieces of biologic mesh/crural construct (1×1 cm) were taken from each animal for histologic evaluation.

Biomechanical testing

One specimen (3×5 cm) was recovered from each animal and subjected to lap shear testing using the Instron Series 5542 mechanical testing system (Fig. 2). At each end of the

specimen, the mesh was separated from the underlying tissue, leaving a 1 × 3-cm strip of separated mesh and tissue at each end, with a 3 × 3-cm central section in which the bonding was intact. The mesh component then was gripped in the upper grip of the Instron machine, and the tissue component was gripped in the lower grip using pneumatic grips set to a pressure of 30 psi.

Next, the construct was tested in tension at a rate of 0.42 mm/s until the mesh fully disrupted from the tissue in the central 3 × 3-cm section. The fixation strength (N/cm²) was calculated by dividing the maximum load sustained during the test by the area of the fixation interface (cm²). The results are reported as mean ± standard error of the mean.

Histology

Two specimens (1 × 1 cm) were recovered from each animal and preserved in 10% neutral buffered formalin for at least 48 h. The specimens then were processed into paraffin blocks, sectioned, and stained with hematoxylin and eosin (H&E). A veterinary pathologist evaluated each slide semiquantitatively using a scoring system adapted from Valentin et al. [27] and published previously [28]. The entire interface between the mesh and the diaphragm tissue (5–10 nonoverlapping fields) was evaluated at 100×. The scores from these 5–10 fields then were averaged to provide an overall composite score for each slide. Higher scores represent more favorable outcomes with regard to remodeling (i.e., extensive cellular infiltration, host ECM deposition, scaffold degradation, and neovascularization; low inflammation and fibrous encapsulation).

Statistical analysis

Systat version 12.0 software (Systat Software, Inc., San Jose, CA, USA) was used to perform a one-way analysis of variance (ANOVA) and Fisher's posttest, with *p* less than 0.05 considered significant.

Results

Premature death occurred due to pneumothorax during the surgical procedure for one animal and gastric bloat on postoperative day 13 for another animal, both unrelated to the mesh and tissue sealants. Both cases were excluded from the study, and two additional animals were acquired as replacements. All the other animals survived the study, and no other complications were observed.

At the time the animals were euthanized, all of the meshes in the acute group remained adherent to the diaphragm without evidence of mesh migration (Fig. 3). However, two specimens (25%) of the acute fibrin sealant group and two specimens (25%) of the acute PEG sealant group were slightly folded down along one edge and not fully adherent to the underlying diaphragm in those areas. Similarly, four specimens (50%) of the chronic fibrin sealant group and five specimens (63%) of the chronic PEG sealant group also displayed folding in some areas and a lack of adherence to the diaphragm in those areas. However, only one mesh (13%) of the chronic PEG sealant group appeared to have migrated from the original location and was attached to the left crus and the gastroesophageal junction at the time the animals were euthanized. All the other meshes remained adherent to the diaphragm without evidence of mesh migration. Adhesions between the abdominal viscera and the mesh also were present in six specimens (75%) of the chronic fibrin sealant group (1 stomach and 5 liver specimens) and in seven specimens (88%) of the chronic PEG sealant group (1 stomach, 1 esophagus, and 5 liver specimens).

Biomechanical testing

No significant differences were observed in the acute fixation strengths between the two sealants (fibrin: 0.13 ± 0.05 N/cm² vs PEG: 0.17 ± 0.03 N/cm²; $p = 0.907$). Fixation strength increased over time, and chronic fixation strengths were significantly greater than acute fixation strengths for both the fibrin and PEG sealants (fibrin: 1.59 ± 0.39 N/cm² vs PEG: 1.56 ± 0.35 N/cm²; $p = 0.001$). No significant differences in the chronic fixation strengths between the two sealants were observed ($p = 0.938$).

Histology

No significant differences were detected between the two types of sealants at the acute time point for any of the six remodeling characteristics evaluated or with regard to the overall composite remodeling score ($p > 0.05$) (Fig. 4; Table 1). The acute fibrin and PEG specimens scored identically for cell types (0.0 ± 0.0), ECM deposition (0.0 ± 0.0), scaffold degradation (0.0 ± 0.0), neovascularization (0.0 ± 0.0), and fibrous encapsulation (3.0 ± 0.0). The cellular infiltration scores were 0.3 ± 0.1 for the fibrin sealant and 0.2 ± 0.1 for the PEG sealant, and the overall composite remodeling scores were 0.6 ± 0.0 for the fibrin sealant and 0.5 ± 0.0 for the PEG sealant.

Similarly, no significant differences were detected between the two types of sealants at the chronic time point for any of the six remodeling characteristics evaluated except for scaffold degradation and with regard to the overall composite remodeling score ($p > 0.05$) (Fig. 4; Table 1). The scaffold degradation scores for the chronic fibrin sealant (1.2 ± 0.1) were significantly higher than for the chronic PEG sealant (1.0 ± 0.1) ($p = 0.031$). Chronic fibrin and PEG specimens scored identically for cellular infiltration (2.3 ± 0.1), cell types (1.5 ± 0.0), and fibrous encapsulation (0.0 ± 0.0). All the other chronic scores also were similar for the fibrin and PEG sealants: respectively, 2.1 ± 0.1 and 2.0 ± 0.1 for ECM deposition, 2.0 ± 0.1 and 1.9 ± 0.1 for neovascularization, and 1.5 ± 0.1 and 1.4 ± 0.1 for overall composite remodeling.

Significant differences were observed, however, between the chronic and acute scores for the two sealant types in every category evaluated. The two sealant types showed chronic scores significantly higher than acute scores for cellular infiltration ($p = 0.000$), cell types ($p = 0.000$), ECM deposition ($p = 0.000$), scaffold degradation ($p = 0.000$), neovascularization ($p = 0.000$), and overall composite remodeling ($p = 0.000$). In contrast, the chronic fibrous encapsulation scores were significantly lower than the acute scores for both types of sealants ($p = 0.000$).

Discussion

Although fibrin sealants have been used in inguinal hernia repair applications to secure synthetic and biologic mesh materials in both humans and animal models [14, 18–23, 29], the use of these sealants to secure mesh at the hiatus to date has been limited to synthetic meshes in one animal study and two clinical reports [17, 24, 25]. The fixation strengths achieved by these sealants have been reported in two of the animal studies using synthetic mesh materials, one in the inguinal region and one in the intraperitoneal position [14, 30].

No data currently exist for fixation strengths or the incidence of mesh migration achieved at the hiatus with the use of biologic meshes. Thus, this study aimed to determine the feasibility of using such products to secure biologic mesh at the hiatus, to quantify the fixation strengths achieved, and to evaluate the host tissue response using a semiquantitative scoring system to characterize cellular infiltration, scaffold degradation, host ECM deposition, neovascularization, fibrous encapsulation, and inflammation.

As demonstrated by this study, the acute fixation strengths achieved by fibrin (0.13 N/cm^2) and PEG (0.17 N/cm^2) sealants to attach a biologic mesh to the diaphragm in a porcine model were fairly low. However, the fixation strengths increased significantly over time to $1.59 \pm 0.39 \text{ N/cm}^2$ for the fibrin sealant and $1.56 \pm 0.35 \text{ N/cm}^2$ for the PEG sealant, indicating that both sealants achieved early tissue ingrowth and maintained fixation between the scaffold and the diaphragm during the 14-day survival period. It should be noted that one mesh (13%) in the chronic PEG sealant group migrated from the original location and was attached to the left crus and the gastroesophageal junction at the time the animals were euthanized. All the other meshes remained adherent to the diaphragm without evidence of mesh migration.

The acute fixation strengths reported for the current study are comparable with the values reported by Jenkins et al. [31], who used the same fibrin sealant (Tisseel, 500 IU/ml) to attach synthetic mesh materials to the intact peritoneum of a rabbit. These authors reported fixation strengths of 1.76–3.94 N, which when divided by the 9 cm^2 fixation interface, converts to 0.2–0.44 N/cm^2 .

In a second study, Jenkins et al. [32] also evaluated the chronic fixation strength of a similar fibrin sealant (AR-TISS, 4 IU/ml) compared with that of metallic tacks alone or a combination of suture and fibrin sealant to secure synthetic meshes in the same rabbit model with a survival period of 8 weeks. When divided by the fixation interface, the fixation strengths they reported were 0.11–0.59 N/cm^2 for the fibrin sealant alone, 1.62–2.88 N/cm^2 for the tacks alone, and 2.64–3.21 N/cm^2 for the combination of suture and fibrin sealant.

Our chronic fixation strengths measured for the Tisseel fibrin sealant ($1.59 \pm 0.39 \text{ N/cm}^2$) and the PEG sealant ($1.56 \pm 0.35 \text{ N/cm}^2$) were greater than those obtained by Jenkins et al. for the ARTISS fibrin sealant alone and comparable with their values for tacks alone and less than for their combination of suture and ARTISS fibrin sealant [31, 32]. However, it is difficult to make any accurate comparisons between the two sets of data because the two models varied in species (rabbit vs pig), type of repair (intact peritoneum vs simulated paraesophageal hernia repair), and type of mesh material (synthetic vs biologic). To our knowledge, no other studies have reported the fixation strength developed between fibrin or PEG sealants and a biologic tissue-based scaffold material at the hiatus. Thus, these data represent the best available comparisons to date.

With regard to histologic evaluation of the sealants, the acute remodeling scores generally were very low, ranging from 0.0 to 0.5 for many of the remodeling characteristics such as cellular infiltration, cell types, ECM deposition, scaffold degradation, and neovascularization, and no significant differences were detected between the two types of sealants. Scores in this range indicated that very few cells, host ECM proteins, scaffold degradations, or neovascularizations were observed. Similarly, acute scores of 3.0 indicated that fibrous encapsulation was not observed after this early evaluation period. These results are consistent with expectations for such a brief implantation period and are important baseline measurements necessary for comparison with the chronic scores observed after 14 days.

Chronic cellular infiltration scores of 2.3 ± 0.1 for both types of sealants indicated that cells infiltrated the mesh materials beyond the periphery but did not reach the center in many cases. It is likely that greater cellular infiltration would have been observed after a longer period of implantation, but even after only 14 days, significant cellular infiltration had already occurred relative to the acute specimens, indicating that neither type of sealant prevented early cellular infiltration. Cell type scores of 1.5 ± 0.0 indicated that both types of sealants elicited a similar cellular response with an equal mixture of inflammatory cells and

fibroblasts. Again, this mixture of cells was expected given the 14-day implantation period, but it also was interesting to note the presence of fibroblasts given that the acute specimens exhibited the presence of inflammatory cells only. The presence of fibroblasts indicated that the remodeling process was underway at 14 days and not hindered by the presence of either type of sealant. Chronic scores of 2.1 ± 0.1 (fibrin) and 2.0 ± 0.1 (PEG) for ECM deposition indicated the presence of host ECM proteins deposited inside the meshes beyond the periphery but not quite reaching the center of the mesh. This represented a significant improvement over the complete lack of ECM proteins observed after the acute implantation period and is consistent with what is expected after 14 days of implantation.

Chronic scaffold degradation scores of 1.2 ± 0.1 (fibrin) and 1.0 ± 0.1 (PEG) remained fairly low after 14 days, indicating that the scaffolds were only partially degraded, with the layers just beginning to be separated by cells, blood vessels, and host ECM proteins. These scores indicated a significant level of scaffold degradation compared with the fully intact acute specimens, but the mesh materials remained recognizable and generally intact even after 14 days.

Fibrous encapsulation scores were significantly reduced after chronic implantation. Scores of 0.0 ± 0.0 indicated extensive encapsulation encompassing 50–100% of the periphery of the scaffolds and significantly more encapsulation than observed in the acute group after implantation for just 2 h. Again, these results are consistent with what is expected within the first 2 weeks of normal wound healing, but longer implantation times are needed to determine whether this fibrosis diminishes over time or continues to develop into a complete encapsulation of the mesh.

Chronic neovascularization scores of 2.0 ± 0.1 (fibrin) and 1.9 ± 0.1 (PEG) indicated the presence of new blood vessels infiltrating the scaffolds beyond the periphery and beginning to make their way toward the center. This level of neovascularization represented a significant improvement over the complete lack of neovascularization observed in the acute specimens. Neovascularization was not expected to occur just 2 h after implantation. However, extensive neovascularization after 14 days of implantation is consistent with an appropriate wound healing response, indicating that neither type of sealant prevented revascularization of the scaffolds.

The composite remodeling scores comprised an average of the six subcategory scores and represented an overview of the entire remodeling response. Chronic composite remodeling scores were 1.5 ± 0.1 (fibrin) and 1.4 ± 0.1 (PEG), and these scores were significantly greater than the acute composite remodeling scores (0.6 ± 0.0 and 0.5 ± 0.0 , respectively), indicating a significant remodeling response as early as 14 days after implantation. This response consisted of six basic categories, namely, cellular infiltration, cell types, ECM deposition, scaffold degradation, fibrous encapsulation, and neovascularization.

Although few differences between the two types of sealants were observed with regard to fixation strength or histologic findings, the results of this study successfully demonstrated the feasibility of using either fibrin or PEG sealant to secure biologic mesh at the hiatus. The study results also quantified the fixation strengths and tissue responses achieved by such sealants in a porcine model of laparoscopic reinforcement of the hiatus simulating hiatal hernia repair.

A potential pitfall of this technique is loose adherence of the mesh in some areas, resulting in folding of the mesh along one edge. This did not appear related to a particular sealant because both the fibrin and PEG specimens exhibited folding at the time of acute evaluation (25% for both fibrin and PEG) and chronic evaluation (50% for fibrin and 63% for PEG). It is possible that the mesh did not make adequate contact with the sealant and the underlying

tissue during the extremely short sealant polymerization time. The sealants polymerize within a few seconds. Thus, it is critical to provide good contact between the mesh and the underlying tissue during this time to achieve full adherence of the mesh. Every effort was made to achieve full contact between the mesh and underlying tissue, but it is possible that a modification of the current technique or the inclusion of two or three sutures could alleviate this issue. Future studies should evaluate this aspect of the technique in greater detail. It also is possible that these particular tissue sealants do not provide optimal adherence between this particular type of biologic mesh and the porcine diaphragm. Future studies also should investigate other types of sealants and other types of biologic meshes to determine whether greater fixation strength can be achieved with another mesh–sealant combination in this particular anatomic location.

An additional pitfall of this technique involves adhesions of the abdominal viscera to the mesh. Adhesions between the abdominal viscera and the mesh were present in six specimens (75%) of the chronic fibrin sealant group (one stomach and five liver specimens) and in seven specimens (88%) of the chronic PEG sealant group (one stomach, one esophagus, and five liver specimens). Adhesions to a variety of hemostatic agents have been investigated, and the literature demonstrates that Coseal and Tisseel both limit the formation of adhesions in a variety of animal models ranging from rat cecal abrasion studies to rabbit pericardial abrasion studies [33–36]. Hoffmann et al. [33] also have speculated that the growth factors present in the Tisseel sealant may contribute to adhesion formation in the early postoperative period but that this may be reversed at late time points once the sealant is resorbed. Future studies should evaluate additional time points to determine whether this is the case with this particular model.

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Fig. 1. Laparoscopic view of the Biodesign Surgisis graft immediately after its attachment to the hiatus using polyethylene glycol (PEG) sealant. The short axis of the graft is oriented in the cranialcaudal direction, and the *U*-shaped cutout is visible surrounding the gastroesophageal junction (GEJ)

Fig. 2.

Lap shear testing of a Biodesign Surgisis graft attached at the hiatus using fibrin sealant (Tisseel). The free edge of the graft is clamped in the *lower* grip of the Instron machine, and the free edge of the diaphragm tissue is clamped in the *upper* grip. Tension is applied until the graft is sheared completely off the underlying tissue

Fig. 3.
When the animals were euthanized, all the grafts in the acute group remained adherent to the diaphragm without evidence of migration (acute polyethylene glycol [PEG] sealant is shown)

Fig. 4. Hematoxylin and eosin (H&E) stained slides viewed at $\times 200$ original magnification. **A** Acute polyethylene glycol (PEG) sealant. **B** Acute fibrin sealant. **C** Chronic PEG sealant. **D** Chronic fibrin sealant

Table 1

Semiquantitative mean scores for six characteristics of remodeling

	Cellular infiltration	Cell types	ECM deposition	Scaffold degradation	Fibrous encapsulation	Neovascularization	Composite score
Acute fibrin sealant	0.3 ± 0.1	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	3.0 ± 0.0	0.0 ± 0.0	0.6 ± 0.0
Acute PEG sealant	0.2 ± 0.1	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	3.0 ± 0.0	0.0 ± 0.0	0.5 ± 0.0
Chronic fibrin sealant	2.3 ± 0.1	1.5 ± 0.0	2.1 ± 0.1	1.2 ± 0.1	0.0 ± 0.0	2.0 ± 0.1	1.5 ± 0.1
Chronic PEG sealant	2.3 ± 0.1	1.5 ± 0.0	2.0 ± 0.1	1.0 ± 0.1	0.0 ± 0.0	1.9 ± 0.1	1.4 ± 0.1

Higher scores represent favorable characteristics of remodeling. The composite score is derived from the average of the six subcategory scores *ECM* extracellular matrix, *PEG* polyethylene glycol