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Bioresorbable Film for the Prevention of Adhesion to the Anterior Spine After Anterolateral Discectomy

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Keywords

Postoperative adhesions, Discectomy, Polylactide film, Antiadhesion barrier

Abstract

Background context

The development of scar tissue and adhesions postoperatively is a natural consequence of healing but can be associated with medical complications and render reoperation difficult. Many [biocompatible](#) products have been evaluated as barriers or deterrents to adhesions.

Purpose

To evaluate the efficacy of a bioresorbable polylactide film as a barrier to adhesion formation after anterolateral [discectomy](#).

Study design

Experimental study.

Methods

Seven, skeletally mature female sheep underwent a retroperitoneal approach to the anterolateral [lumbar spine](#). A discectomy was performed at two levels with an intervening unoperated disc site. One site was treated with a polylactide film barrier (Hydrosorb Shield; MacroPore [Biosurgery](#), San Diego, CA) affixed with tacks manufactured from the same material. The second site was left untreated. Treatment and control sites were randomly assigned. Postmortem analysis included scar tenacity scoring on five spines and histological evaluation on two spines.

Results

The application of the Hydrosorb film barrier allowed a definite dissection plane during scar tenacity scoring and there was a significant difference in the development of adhesions to the disc between the control and treated sites. Histological evaluation revealed evidence of barrier formation to scar tissue and no significant adverse inflammatory reactions.

Conclusions

Hydrosorb Shield appears to be an effective postoperative barrier to scar tissue adhesion after anterolateral discectomy. The use of polylactide tacks was beneficial to affix the barrier film in place. Safety issues associated with delayed healing or adverse response to the film or tacks were not observed. Hydrosorb film may be useful as an antiadhesion barrier facilitating dissection during [surgical revision](#) in anterior approaches to the spine. Further studies are

indicated to evaluate the performance of the bioresorbable material as an antiadhesion barrier in techniques of [spinal fusion](#) and disc replacement.

Introduction

Postoperative [fibrosis](#) is a natural consequence of wound healing. Fibrosis, which can lead to adhesions between healing tissues, is a problem that is seen in a wide array of surgical specialties. Adhesions that form postoperatively have been associated with “failed back syndrome,” [bowel obstruction](#), chronic pain, and infertility [1], [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [19], [20], [21], [22], [23], [24], [25]. In addition, subsequent surgeries are made more challenging and can lead to organ injury because of attachment between structures that are usually independent of one another. Extensive research has been conducted into the mechanism of adhesion formation. It is believed that after surgery there is a decreased concentration and activity of [fibrinolytic](#) activity, resulting in deposition of [fibrin](#) matrix on which organized collagen, and thus, scar formation can occur [1], [2], [3], [6], [7], [8], [11], [14], [15], [20], [23], [26], [27]. Because of the [morbidity](#) associated with unwanted or excessive adhesion between tissues, multiple strategies have been used and studied to prevent adhesion formation. Many of these have included pharmacologic or biochemical methods of impairing scar tissue formation. Others have included the use of a physical barrier to adhesion attachment to the tissues of concern [2], [6], [9], [13], [20], [22], [24], [25], [28], [29], [30], [31], [32], [33], [34], [35], [36], [37], [38], [39], [40], [41], [42], [43], [44], [45], [46], [47], [48], [49], [50], [51], [52], [53], [54], [55], [56], [57], [58], [59], [60], [61], [62], [63].

There are several [preclinical studies](#) evaluating safety and efficacy associated with the use of a bioresorbable polylactide film (70:30 poly-l-lactide-co-d,l-lactide barrier film; Hydrosorb Shield; MacroPore [Biosurgery](#), San Diego, CA) as a barrier to adhesion formation. Most of these studies have shown that this bioresorbable film is efficacious in minimizing adhesion after various procedures including hemisternotomy and pericardiumotomy, [pelvic](#) surgery, spinal [laminectomy](#), abdominal surgery, and bowel [anastomosis](#) surgery [2], [9], [22], [64], [65]. Most recently, a study of Hydrosorb Shield revealed its efficacy as a barrier to adhesion between the paraspinal musculature and [dura mater](#) of the spinal cord in sheep without inhibiting healing of an [iatrogenically](#) induced dural tear with [cerebrospinal fluid](#) leakage [46]. In the current study, the safety and efficacy of this film, as well as affixing tacks made of the same material, were investigated in an anterolateral [discectomy](#) model, an anatomical location not previously studied for this material.

Materials and methods

Animal care and use

Seven skeletally mature, female, Rambouillet–Columbian cross sheep were used in this study. The care and use of these animals were approved by and in compliance with the Colorado State University Animal Care and Use Committee.

Anesthesia and pain management

The sheep were sedated with 7.5 mg of diazepam IV (Hospira, Inc., Lake Forest, IL, USA) and 4 mg/kg of [ketamine](#) IV (Ketavet; IVX Animal Health, Inc., St. Joseph, MO, USA), and [anesthesia](#) was maintained with [isoflurane](#) at 1.5% to 3% in 100% oxygen at 2 l/min (IsoFlo; Abbott Laboratories, North Chicago, IL, USA). The sheep were given 15 mg/kg of atracurium IV (Mayne Pharma, Inc., Paramus, NJ, USA) intraoperatively to facilitate muscle dissection and retraction. Respiration was controlled with a mechanical ventilator to maintain [normocapnia](#) and adequate oxygenation.

Fentanyl patches (5 and 10 mg) (Mylan Laboratories, Inc., Morgantown, WV, USA) were applied 24 hours preoperatively and maintained for 3 days. In addition, phenylbutazone 1 g per os (VetOne; Bimeda, Inc., LeSueur, MN, USA) was administered daily from one day preoperatively to 3 days postoperatively. Before skin incision, 8 ml of [lidocaine](#) 2% (Hospira, Inc., Lake Forest, IL, USA) was injected into the [subcutaneous tissues](#) along the length of the incision site.

Operative procedure

The sheep were placed in right lateral recumbency and were clipped and prepared for aseptic surgery from the last rib to the ilium in the cranial to caudal direction and from the posterior midline to halfway to the anterior midline. A retroperitoneal [surgical approach](#) to the spine was performed. The psoas major muscle was dissected from the left anterolateral aspect of the [intervertebral disc](#) and the two adjacent [vertebral bodies](#) that comprised a single study site. Each study site was separated by an undissected segment to separate treatment and control levels. One site was used for autonomous control and the other site for treatment ([Table 1](#)). Two small drill holes (anterior and posterior) using a Steinmann pin were made in the vertebral bodies on both sides of the intervertebral disc at both the treatment and control sites. A bioresorbable tack made of the same material as the barrier film was placed in each drill hole at the control site. The annulus fibrosus and nucleus pulposus of the intervertebral disc were disrupted with an 18-g hypodermic needle and the outer annulus [fibrosis](#) was removed using [discectomy](#) forceps.

Table 1. Results of scar tenacity scoring

Sheep number	Spinal level and treatment	Score 1 (LSK)	Score 2 (JWT)	Score 3 (WCW)
1	L2–L3 treatment	2.5	2.5	3
	L4–L5 control	4	4	4
2	L1–L2 control	3.5	3.5	3
	L3–L4 treatment	1	1	2
3	L1–L2 control	3	3	3
	L3–L4 treatment	0	0	2
4	L2–L3 control	3	3	4

Sheep number Spinal level and treatment Score 1 (LSK) Score 2 (JWT) Score 3 (WCW)

5	L4–L5 treatment	0	0	3
	L2–L3 treatment	1	1	3
	L4–L5 control	2	2	4

Average \pm standard deviation; control, 3.27 ± 0.68 ; and treatment, 1.47 ± 1.17 .

Scar tenacity score: 0, no adhesions present; 1, thin membranous threads, easily detachable; 2, slight adhesion, some [blunt dissection](#) required; 3, moderate adhesions, blunt dissection, or some sharp dissection; and 4, tenacious adhesions, sharp dissection required.

At the treatment site, a sheet (approximately 3.5 cm \times 1.5 cm \times 0.02 mm) of 70:30 poly-l-lactide-co-d,l-lactide barrier film (Hydrosorb Shield; MacroPore [Biosurgery](#), San Diego, CA, USA) was placed to overlay the disrupted intervertebral disc and adjacent vertebral bodies. Hypodermic needles (25 g) were placed through the film into the drill holes to provide temporary fixation of the film, then individually removed, and replaced with a bioresorbable tack. Once all four tacks were applied, the muscle [fascia](#), subcutaneous tissues, and skin were approximated in a routine manner.

Evaluation of the antiadhesion efficacy of the barrier

At 8 weeks postoperatively, the sheep were euthanized with 20 ml of pentobarbital sodium euthanasia solution. The [lumbar spines](#) were removed *en bloc* with the anterolateral spinal muscles undisturbed. Two of the spines were submitted for histological evaluation. The remaining five spines were evaluated grossly for scar tenacity. The degree of difficulty in removing the muscle and the amount of scar tissue directly in contact with the [surgical site](#) was scored by three independent, blinded observers. Two of the observers (LSK and JWT) were present for the dissection at postmortem. The third observer (WCW) made scoring evaluations by digital videotape of the dissections. The evaluation scale used for scar tenacity scoring is shown in [Table 1](#). The scoring system used has been previously described [\[66\]](#). For data analysis, SPSS for Windows 11.5 was used (SPSS, Inc., Chicago, IL, USA).

Histological evaluation

The disc spaces of all spinal levels were sectioned in the sagittal plane, at a slight angle to the left anteriorly in the coronal plane, to produce four tissue slabs for analysis. The two medial slabs were routinely processed for decalcified histology and tissue embedding was performed. Tissue blocks were cut on a rotary [microtome](#) to produce thin sections between 6 and 10 μ m in thickness. To evaluate the [host response](#) seen in tissues adjacent to the polylactide film and tacks the sections were stained with [hematoxylin](#) and [eosin](#), [toluidine blue-O metachromasia](#), and Mallory–Heidenhain stains. Approximately, 5 to 10 sagittal plane sections through two lateral slabs were processed for undecalcified samples. [Differential staining](#) using a proprietary trichrome-based stain was used to permit histological differentiation in the undecalcified histology.

Images of the decalcified and undecalcified histology were scanned using [image analysis](#) system software (Image Pro Plus Software v 5.0; Media Cybernetics, Silver Spring, MD, USA) on a PC workstation. The host response to the polylactide film and tacks was characterized using ASTM F981 “Standard Practice for Assessment of Compatibility of Biomaterials for Surgical Implants with Respect to Effect of Materials on Muscle and Bone” [66]. The scoring values for the ASTM guidelines are found in [Table 2](#).

Table 2. Scoring system for inflammatory reaction to the polylactide film and tacks

Number of elements	Score (quantitative)	Score (qualitative)
0	0	None
1–5	0.5	Very slight
6–15	1	Mild
16–25	2	Moderate
26 or more	3	Marked

From the ASTM F981 “Standard Practice for Assessment of Compatibility of Biomaterials for Surgical Implants with Respect to the Effect of Materials on Muscle and Bone.”

Analysis of the sections was based on the following criteria: characterization of the type and orientation of tissues adjacent to the polylactide film and tacks; presence or absence of tissue planes with and without the film and tacks that might create a surgical dissection plane and eliminate or reduce adhesions adjacent to disc tissues after discectomy; and characterization of the host response to the polylactide film and tacks.

Results

There were no implant- or surgery-related complications associated with this study and all sheep were ambulating and eating on the first postoperative day. In addition, there was no evidence of [systemic disease](#) or wound infection or dehiscence in any sheep.

Scar scores

The scar tenacity scoring results and parameters defining the scores are shown in [Table 1](#). There was complete agreement between the two observers who were present and scored the dissection at postmortem (LSK and JWT). The remote observer (WCW), tended to assign higher scar scores to treatment sites, with, 3 samples scored 2 grades higher and 1 scored 3 grades higher; the remaining 6 of 10 samples were scored the same or within 1 grade. Overall the control sample scores averaged 3.27 (standard deviation, 0.68), and the film-treated sample scores averaged 1.47 (standard deviation, 1.17).

Because each animal had a film-treated and untreated (control) sample, the scoring data were considered to be related (paired) samples. Therefore, a Wilcoxon signed-ranks test was performed on the 15 pairs of data (5 animals x 3 scorers). For each of the 15 pairs the treated

score was less than the untreated score (zero ties). The difference in the treated and control scores was significant at $p < .001$. Photographs of the dissection of control and treatment sites are found in [Fig. 1](#), top and bottom, respectively.

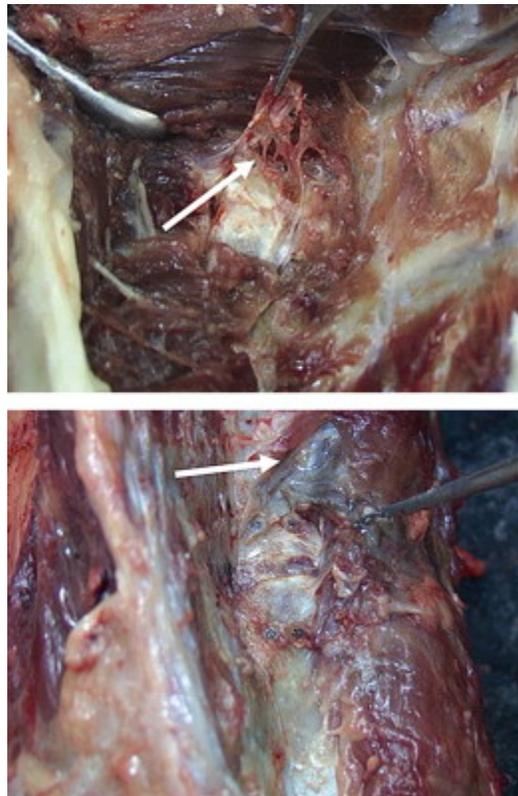


Fig. 1. Postmortem dissection of the untreated (control) [discectomy](#) site. (Top) The tissues were difficult to remove and adhesions (arrow) to the [periosteum](#) and outer annulus [fibrosis](#) were observed. Postmortem dissection of the treated discectomy site. (Bottom) The tissues were easily detached by gentle elevation because of the presence of the Hydrosorb film. The elevated tissue is indicated by the arrow.

Histological results

Histology was unable to determine the tenacity of tissues to the disc or other anatomic structures. However, histology was evaluated for the presence/absence of tissue planes that might create a surgical dissection plane and eliminate or reduce adhesions adjacent to disc tissues after [discectomy](#) with and without the polylactide film and tacks. Sections of the control (untreated) disc spaces confirmed disruption of the anterolateral annulus and the presence of fibrovascular tissues in direct contact with Sharpey's fibers of the annulus ([Fig. 2](#), top, left). No adhesions between distinct tissue planes/layers adjacent to the polylactide film-treated levels were observed. Formation of an organized collagen fiber matrix, which ran cranial to caudal, was observed external to the polylactide film by histology. This layer was not in contact with the anterior aspect of the disc space ([Fig. 2](#), top, right). Thus, in the film-treated levels, no adhesions to the anterior aspect of the disc were recognized in decalcified sections. Histology

further revealed that when the tacks were found in bony tissues, no intervening fibrous interface was observed adjacent to the tacks in the bone. Fibrovascular tissues and formation of organized collagen fiber matrices were observed adjacent to the heads of the tacks that were seen external to the bony cortex. The polylactide film was fragmented and surrounded by [fibroblasts](#) and fibrovascular tissues ([Fig. 2](#), top, right and bottom, left). Exostoses adjacent to the anterior treatment sites were not observed by microradiography or histology. No osteoclastic resorption was observed adjacent to the polylactide tacks or polylactide film. [Bone density](#) as visualized on microradiographs identified no changes in [bone mineralization](#) adjacent to the polylactide tacks and film.

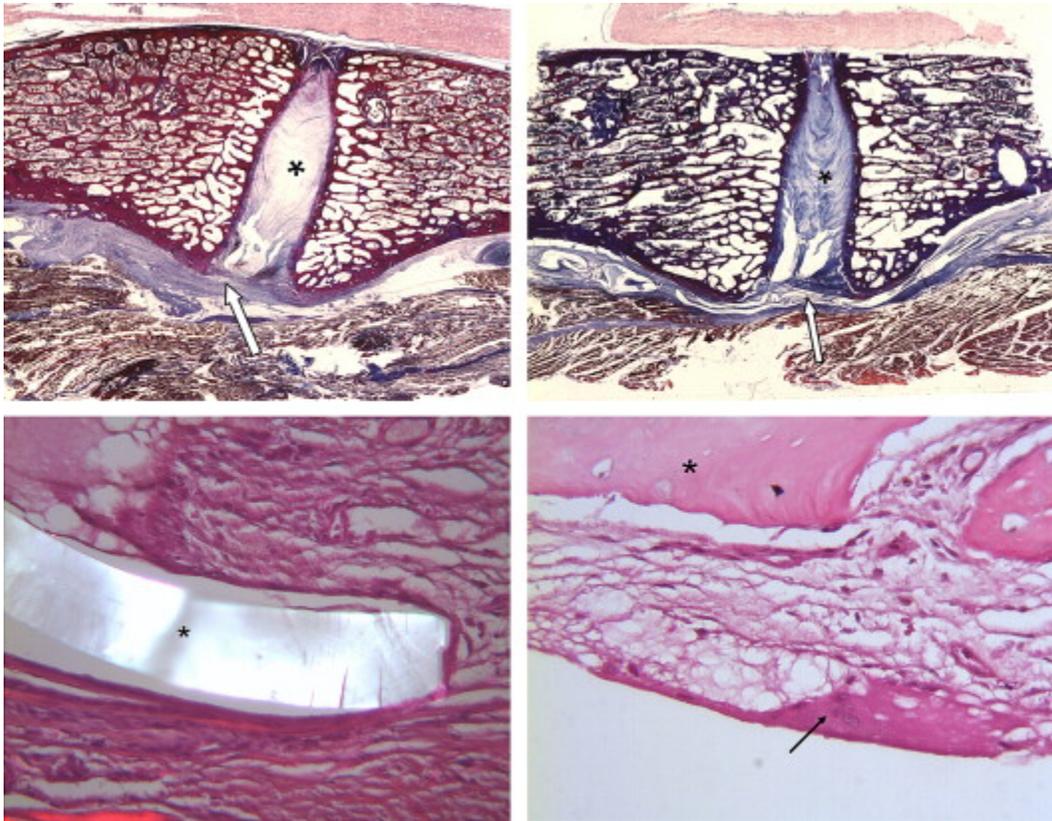


Fig. 2. Histology of the untreated (control) [discectomy](#) site showing fibrous connective tissues (indicated by arrow) adjacent to the discectomy site and adhered to the [periosteum](#). (Top, left) The [intervertebral disc](#) is indicated by the asterisk. Mallory–Heidenhain stain, 3x original magnification. Histology of the treated discectomy site. The operated region has been protected from [fibrosis](#) and adhesions by the Hydrorsorb film (indicated by arrow). The discectomy injury is evident as a cleft in the intervertebral disc (indicated by asterisk). (Top, right) Mallory–Heidenhain stain, 3x original magnification. Partially polarized light photomicrograph demonstrating a fibrous tissue interface with [fibroblasts](#) in fibrous tissues adjacent to the birefringent polylactide film (indicated by asterisk). (Bottom, left) [Hematoxylin](#) and [eosin](#) (H&E) stain, partially polarized light, 200x original magnification. Histology image demonstrating a single foreign body giant cell (indicated by arrow) at the interface of the polylactide film. (Bottom, right) The vertebral end plate is indicated by the asterisk. H&E stain, 313x original magnification.

No inflammatory response was observed in tissues anterior to the disc in untreated control levels. No acute inflammatory response was observed adjacent to the film or tacks. In one of the two treated levels examined by histology, no inflammatory response was observed adjacent to the polylactide tacks. An occasional single foreign body giant cell was observed on the surface of the polylactide film ([Fig. 2](#), bottom, right). This was an infrequent finding. Based on these findings, the [host response](#) to the polylactide film and tacks would be best interpreted/characterized as “very slight reaction” by ASTM F981-04 [\[66\]](#).

Discussion

A multitude of studies have been performed to evaluate the use of various products as antiadhesion barriers [\[2\]](#), [\[6\]](#), [\[9\]](#), [\[10\]](#), [\[13\]](#), [\[20\]](#), [\[22\]](#), [\[24\]](#), [\[25\]](#), [\[27\]](#), [\[28\]](#), [\[30\]](#), [\[31\]](#), [\[32\]](#), [\[33\]](#), [\[36\]](#), [\[37\]](#), [\[38\]](#), [\[39\]](#), [\[40\]](#), [\[41\]](#), [\[42\]](#), [\[43\]](#), [\[44\]](#), [\[45\]](#), [\[46\]](#), [\[47\]](#), [\[48\]](#), [\[49\]](#), [\[50\]](#), [\[52\]](#), [\[53\]](#), [\[54\]](#), [\[55\]](#), [\[56\]](#), [\[57\]](#), [\[59\]](#), [\[60\]](#), [\[61\]](#), [\[62\]](#), [\[64\]](#), [\[65\]](#), [\[67\]](#), [\[68\]](#), [\[69\]](#), [\[70\]](#). Although scar formation is a normal part of the healing process, excessive scarring or scarring in regions where adhesions cause anatomical dysfunction (eg, intestinal adhesions) is detrimental. The purpose of this study was to evaluate a bioresorbable 70:30 poly-L-lactide-co-D,L-lactide barrier film (Hydrosorb Shield, MacroPore [Biosurgery](#), San Diego, CA, USA) as a barrier to adhesion in an anterior [discectomy](#) model. The use of this product has been previously reported to have efficacy in surgical scenarios to reinforce soft tissue, for temporary wound support, and to minimize soft-tissue adhesions in the [viscera](#) [\[2\]](#), [\[9\]](#), [\[22\]](#), [\[64\]](#), [\[65\]](#). In addition, this film has been studied in several models evaluating efficacy against [peridural](#) adhesion in [laminectomy](#) and [laminotomy](#) models [\[24\]](#), [\[46\]](#), [\[64\]](#).

Nonparametric statistical analysis (sign test) demonstrated a significant difference in the control and film-treated scar scores ($p < .001$). It should be noted, however, that this study included a small number of animals, and only a single time period was evaluated. Evaluation of scar scoring from video has both advantages and disadvantages. The advantages include the ability to re-evaluate the video multiple times to determine the scar score. However, visualization is limited and the barrier film margins and relationships to scar tissue may not be as easily determined as by direct observation. The area of interest is more difficult to observe on video recording and the remote observer has a more difficult task in assessing the scar scoring. In summary, a larger number of sites (treated/control), perhaps at additional time points, and direct observation of all scar scoring would address the limitations of the present study.

On histological analysis, the barrier film was associated with slight inflammatory reactions. This is not unexpected for a few reasons. First, although it is general accepted that most commonly used, marketed bioresorbable material do not incite significant inflammation, some degree of inflammation may be expected by the process of having a foreign object in the surgical-altered tissues. Macrophagocytic inflammation would be expected to be involved in the breakdown and bioresorption of this material. Second, a slight amount of inflammation is within acceptable limits. The benefit that was observed with the use of Hydrosorb Shield in this study was the lack or decreased amount of adhesion to the disc and adjacent [vertebral body](#) end plates, both on scar scoring and histological evaluation. In addition, the tacks made from an identical material did not induce any pathology associated with their elevated profile and remained well seated in the cortex of the vertebral bodies without evidence of [osteolysis](#) on histology.

Previous studies have shown that the polylactide film does not elicit an acute or chronic inflammatory response [9], [22], [24], [46], [65]. In a cardiac model after 4 weeks, there was a mild inflammatory response with isolated [lymphocytes](#) and giant cells, with no evidence of an acute or chronic inflammatory reaction to the film [9]. In this same cardiac model at 49 weeks there was no gross or [palpable](#) presence of implanted polylactide material, histology did not reveal the presence of any residual polymer, and there was no evidence of inflammation or foreign body reaction [71]. The data at 49 weeks confirmed the earlier results in the cardiac model that the polylactide film effectively controlled adhesions. With the same film in a [pelvic](#) adhesion model [22], there was only a mild inflammatory response at 4 weeks, which was reduced by 12 weeks. At both 4 and 12 weeks the film significantly reduced the formation on pelvic adhesions. The adhesion data also suggested that soft-tissue attachments did not form continuously throughout the postoperative healing period and that some early soft-tissue attachments did not persist during the healing period [22]. Therefore, the 8-week time point for the present study was based on allowing sufficient time for postoperative adhesions to occur, if adhesions were to occur at all in either treated or control animals, and the previous published studies demonstrating that the film degraded without eliciting either an acute or chronic inflammatory response.

In summary, the findings of this study demonstrate that Hydrosorb Shield applied as described is an efficacious barrier to adhesions in an ovine anterior discectomy model in the sheep. Histological evaluation identified fibrous attachment to the [intervertebral disc](#) in the absence of the barrier film, and a lack of fibrous attachment in sites where the barrier film was present. A dissection plane was easily identifiable at sites where the film was present. This is especially helpful in situations where [surgical revision](#) may be required. The film and the tacks were in the process of resorption at the termination of this 8-week study. In this study, the film barrier and tacks presented no apparent safety issues related to their placement near the paraspinal tissues and intervertebral disc. The current study evaluated the performance of the polylactide barrier film after anterolateral [lumbar discectomy](#) in the ovine model only. Based on the encouraging results in this model, future studies could be conducted to evaluate the performance of the bioresorbable barrier film after disc replacement or [spinal fusion](#). The risks and benefits with the use of the barrier in these procedures are not known. Long-term efficacy in preventing adhesion in anterolateral spine in the human patient has not been reported and results may differ from animal models.

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