An investigational time-course study using an *in vivo* ovine laminectomy model for the neurohistopathological evaluation of hemostatic agents

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Background: Preclinical *in vivo* analysis of hemostatic agents is a fundamental requirement in the assessment of implant safety and efficacy prior to utilization in the clinical operative setting. The purpose of this study served to investigate the hemostatic, peri-operative outcomes and histopathologic responses following epidural application of a novel hemostatic agent in an ovine lumbar laminectomy model. Despite routine utilization of hemostatic agents, the potential for inflammation and compression of neural structures, fibrosis, and neurotoxicity remains a clinical concern. Epidural fibrosis resulting from hemorrhage creates chronic pain and is often refractory to treatment. Experimental endpoints, including intraoperative hemostasis, perioperative neurologic assessment, clinical pathology, and neurohistopathology, were used to evaluate the translational efficacy of this model.

Methods: Nine healthy crossbred Suffolk sheep (skeletally mature females, 1.5–2 years old, approximately 150 pounds) underwent posterior surgical lumbar laminectomies at the L3 and L5 levels followed by epidural application of a novel hydrophobically modified chitosan-based hydrogel hemostatic agent (test article). The Surface Bleeding Severity Scale (SBSS) score was recorded immediately after completion of the laminectomy at baseline, and then at 3-, 6-, and 10-minute intervals following application of the hemostatic agent. Postoperative survival analysis, specifically focused on animal recovery and neurological status was performed. Clinical pathology including comprehensive vet screens (CVS), complete blood count (CBC) with differential, and cerebrospinal fluid (CSF) assays were completed. Animals were humanely sacrificed at 12 days (n=6), 30 days (n=1), 60 days (n=1), and 90 days (n=1). Necropsy was performed at the time of sacrifice and the operative levels were axially sectioned for histopathologic evaluation.

Results: There were no neurologic, vascular, or infectious complications and animals exhibited normal recovery for this 2-level laminectomy surgical model. Complete intraoperative hemostasis was achieved in 16 out of 18 operative levels by the 3-minute interval and all 18 laminectomy levels demonstrated complete hemostasis by the 6-minute interval. Clinical pathology results were unremarkable. Histological characterization exhibited normal inflammatory and healing responses of the tissues at all postmortem time points, without evidence of abnormal spinal cord changes or infection. Residual test article was observed to decrease between the 30- and 60-day intervals, with no residual material in the epidural space observed at 90 days.

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Conclusions: This pilot study demonstrates the translational utility of the ovine model in evaluating the safety and efficacy of a novel hemostatic agent in the lumbar spine. Based on these early findings in intraoperative hemostasis, postoperative survival, and histologic analysis, additional studies of hemostatic agents using the ovine model are encouraged.

Keywords: Ovine; translational model; hemostasis; lumbar spine; laminectomy

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Introduction

Hemostasis in spinal surgery continues to be of vital importance for both the patient and surgeon (1). While a certain degree of blood loss is expected, excessive bleeding can lead to increased operative time, need for transfusions, and hindrance of the surgical field of view. Additionally, the development of postoperative epidural hematomas can cause devastating neurological deficits secondary to compression of the spinal cord and/or neural elements. To minimize these complications, topical hemostatic agents are commonly used to achieve hemostasis (2).

A variety of topical hemostatic agents are available, many of which contain a combination of animal-derived gelatin with or without thrombin. While the gelatin provides a matrix for clot formation, it is associated with swelling (3), which can potentially lead to mechanical compression and neurologic injury (4). Therefore, there is a need to identify and develop hemostatic agents that do not swell following application. A novel hydrophobically modified chitosan-based hemostatic hydrogel has been developed to address this issue.

Highlight box

Key findings

- The ovine translational model was effective in evaluating the safety and efficacy of a novel hemostatic agent in the lumbar spine.

What is known and what is new?

- Hemostatic agents are commonly used in human spine surgery.
- There is a need to assess clinical efficacy of a novel hemostatic agent using an appropriate translational animal model.

What is the implication, and what should change now?

- This pilot study demonstrated the translational utility of the ovine model in evaluating safety and efficacy of a novel hemostatic agent in the lumbar spine.

Effective translational models are essential to investigate hemostatic agents for clinical use in spine surgery. *In vivo* biological models with comparable neuroanatomy and physiology, such as the ovine model, have been widely used to evaluate the safety and efficacy of medical devices intended for clinical use in the spine (5-9).

The current translational pilot study serves to evaluate the safety and efficacy of a novel hydrophobically modified chitosan-based hydrogel hemostat following epidural application to obtain hemostasis in an *in vivo* ovine laminectomy model. Experimental endpoints included quantification of intraoperative bleeding severity, postoperative survival analysis, clinical pathology, and histopathologic assessment of spinal neural and osseous structures. We present this article in accordance with the ARRIVE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-25-10/rc) (10).

Methods

Experiments were performed under a project license (No. NAICS 424520) granted by The Institutional Animal Care and Use Committee (IACUC) at Thomas D. Morris, Inc. in compliance with the Animal Welfare Act Regulations (9 CFR), the U.S. Public Health Service Office of Laboratory Animal Welfare (OLAW) Policy on Humane Care and Use of Laboratory Animals, and the Guide for the Care and Use of Laboratory Animals (Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, 1996). A protocol was prepared before the study with registration and approval by the Institutional Animal Care and Use Committee (IACUC) at Thomas D. Morris, Inc. (Reisterstown, Maryland, USA).

A novel hydrophobically modified chitosan-based hydrogel hemostatic agent of interest (test article) was evaluated in all animals. Nine clinically healthy Crossbred Suffolk sheep (skeletally mature females, 1.5–2 years

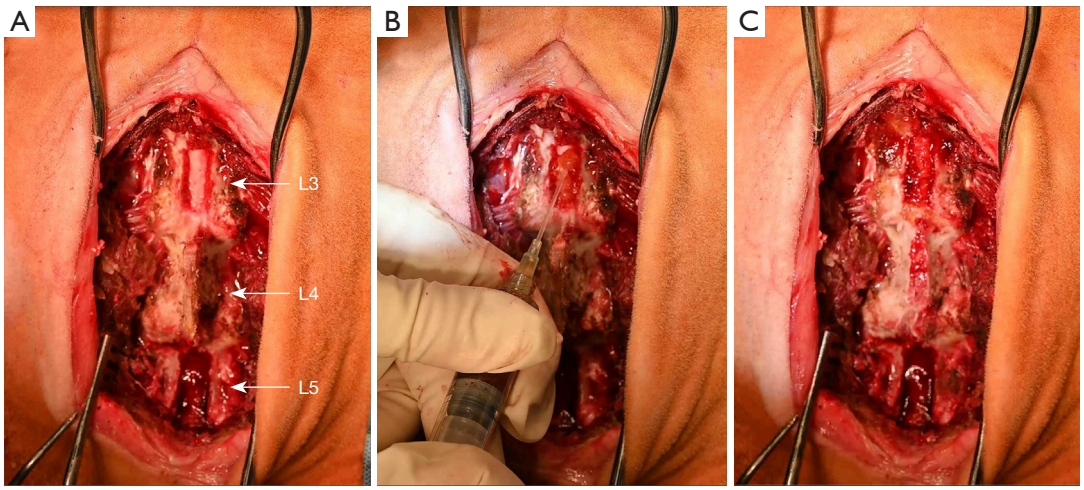

Figure 1 Intraoperative application of hemostatic agent. Intraoperative posterior view of the L3 and L5 laminectomies with intact L4 level (A). Application of hemostatic agent to the L3 site is demonstrated in (B), and hemostasis was achieved following 10 minutes of observation (C).

old, approximately 150 pounds) from a United States Department of Agriculture (USDA) approved vendor were included in this study. All animals underwent laminectomies at the L3 and L5 levels. The test article was applied directly to the entire laminectomy site, in addition to any bleeding epidural structures encountered at the time of surgery, and left in place at the time of closure. This was considered "worst case scenario", as the test article was applied in bulk directly to epidural tissues.

Surgical technique

Following adequate sedation with isoflurane and propofol and endotracheal intubation, each animal was positioned in ventral recumbency. The posterior lumbar region was aseptically prepared using chlorhexidine gluconate 4%, alcohol, and povidone-iodine. An initial skin incision was made in the dorsal midline of the low back centered over the L2–L6 levels. Following blunt dissection, three contiguous lumbar vertebral elements were exposed laterally to their facets using electrocautery. The spinous processes and laminae of the L3 (superior) and L5 (inferior) levels were resected using bone rongeurs. Following the laminectomies, the ligamentum flavum and epidural fat were removed to expose the spinal cord (*Figure 1*). The defects created were approximately 25 mm length × 12 mm wide. The 2-level laminectomy procedure was performed in lieu of a single level laminectomy to increase the operative treatment sites that were utilized per animal. The laminectomies occurred at the L3 and L5 levels, with a single intervening non-operative level (L4) preserved between the superior and inferior levels to aid in spine stability during the postoperative recovery period. All laminectomies were performed by the study surgeon and senior author (B.W.C.).

Once exposed, the entire wound was irrigated and the baseline bleeding assessment was completed. The test article was then applied directly to bony edges of the laminectomy defect and the entirety of the exposed dura mater, the outermost layer of the meninges that envelop the spinal cord. Following completion of all bleeding severity assessments and application of any additional test article, the incision was closed using 1.0 Vicryl® (fascial layer), 2.0 Vicryl® (subcutaneous and skin layers), and staples (skin). All test material applied was left in place at closure to simulate "worst case scenario". The animal was then recovered.

Bleeding severity assessment

The bleeding severity at each target bleeding site (TBS) was quantified at baseline (0 minutes after laminectomy creation) according to the validated Surface Bleeding Severity Scale (SBSS/SPOT GRADE™) described by Spotnitz *et al.*, where a score of 0= no bleeding/hemostasis, 1= minimal bleeding, 2= mild bleeding, 3= moderate bleeding, 4= severe bleeding, 5= extreme bleeding (11). The test article was then applied to the TBS, ensuring complete coverage of the entire laminectomy defect, followed by gentle manual direct pressure with moistened neurosurgical patties. Bleeding severity was assessed and SBSS scores were assigned at each TBS at 3-, 6-, and 10 minutes post-

Table 1 Evaluation for the assessment of pain in sheep and goats

Score	Description			
	Overall appearance of the animal	Overall behavior of the animal	Respiration of the animal	Spinal surgery (neurological) observation
0	Alert, eating/ruminating	Normal (bright, alert and responsive, interactive with staff)	Normal respiration	Walking without any detectable weakness
1	Depressed, ears drooped, not chewing cud	Moderate changes (quiet, alert and responsive)	Increase in rate, not due to excitement	Walking, slight weakness
2	Head down, lethargic, not chewing cud, teeth grinding	Inappetent (not eating, little if any eating observed)	Open mouth breathing	Walking, but with noticeable weakness on one side or both sides
3	Recumbent, little response when gently prodded, teeth grinding	Severe changes (isolated, prostrate, or unable to rouse)	Dyspnea or obvious respiratory distress	Recumbent and unable to rise (euthanasia indicated if persistent for >24 hours)

Clinical observation criteria for pain, including overall appearance, behavior, and respiration, as well as post-surgical observations for neurological deficits were performed twice daily. During each observation, a total evaluation score of 5 or more and/or neurological evaluation score of 2 or more would require veterinary evaluation and possible intervention.

application of the test article. If hemostasis (SBSS =0) was not achieved at the 3-minute or 6-minute time interval, additional test article was applied and the total amount was recorded.

Postoperative survival analysis

Following surgery, the animals were kept in the postoperative care pen for the remainder of their predesignated survival period. All animals received clinical observation for pain and neurologic deficits (*Table 1*) twice daily for seven days utilizing a standard protocol (12). The animals were then observed once daily for pain and ambulation for the remainder of their survival period.

In Cases 1 through 3, the intermediate-term survival periods were 30 days (n=1), 60 days (n=1), and 90 days (n=1), specifically selected to compare histopathological findings between each time point. In the remaining cases (Cases 4–9; n=6), the survival period was 12 days to evaluate short-term survival outcomes. All animals were humanely sacrificed using an intracardiac injection of chemical grade potassium chloride at the scheduled postoperative time interval.

Clinical pathology

Comprehensive vet screens (CVS) and complete blood count (CBC) with differential were performed preoperatively and prior to sacrifice to confirm that all assays were within normal limits. Additionally, cerebrospinal fluid (CSF) samples were obtained from the posterior occipitocervical junction at the time of animal sacrifice. The CSF was analyzed for color, clarity, specific gravity, white blood cells, red blood cells, protein, and glucose to identify any abnormalities resulting from the surgical procedure or the application of the test article.

Necropsy

A necropsy was performed to harvest the lumbar spine from L2 to L6 (*Figure 2*). Each specimen was dissected, examined for evidence of gross infection, and fixed in 10% neutral buffered formalin (NBF). Following 2 to 3 weeks of fixation, a partial laminectomy was performed at the intervening nonoperative L4 level, which served as the control level. The L3, L4, and L5 levels were then axially cross-sectioned into 10 mm wafer thin sections. Each wafer was then decalcified, processed, and embedded in paraffin blocks prior to sectioning (approximately 3 to 5 µm in thickness).

The heart, kidneys, liver, lymph nodes, pancreas, spleen, and brain were also examined, excised, and preserved in 10% NBF solution.

Histopathology

Specimens were mounted on slides and stained with hematoxylin and eosin (H&E) to evaluate general tissue morphology, Masson's trichrome (MT) to evaluate

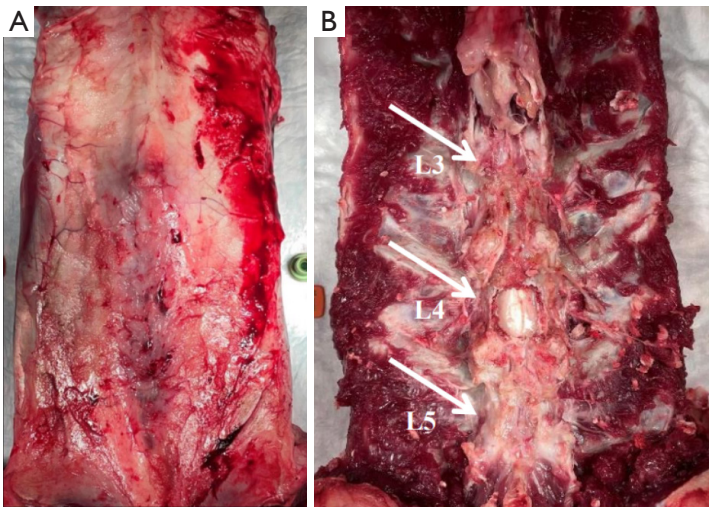

Figure 2 Sheep lumbar spine at 30-day scheduled necropsy. Following *en bloc* resection and exposure of the previous surgical site (A), laminectomy was performed at the remaining L4 level (B).

connective tissue, muscle, and the presence of fibrosis, and Ionized Calcium Binding Adaptor molecule 1 (IBA-1) for neuropathological assessment of microgliosis. Histopathological evaluation was performed by a board-certified veterinary pathologist (J.S.L.). All histology samples were scored according to International Standard ISO 10993-6 Annex E (13) in 4 regions: surgical access site (L3 and L5), epidural space (L3 and L5), spinal cord and subdural space (L3 and L5), and postmortem laminectomy at the intervening space (L4). Tissue architecture, general healing, presence of remnant hemostatic material, presence of inflammatory reaction, and/or autolysis were evaluated. Neural tissue evaluation included comments on the dura mater, spinal cord, and dorsal and ventral nerve roots.

Results

Bleeding severity

Across all laminectomy sites (n=18) for all animals, 14 levels had minimal bleeding and received an SBSS score of 1 at baseline (*Table 2*). Following application of the test article, 13 of the 14 sites achieved hemostasis with an SBSS score of 0 at the 3-minute time interval assessment. Following application of an additional 1.0 mL of test article at the 3-minute interval, the one remaining site (Case 7, L3) achieved hemostasis and received an SBSS score of 0 at the 6-minute interval assessment.

Three laminectomy sites had mild bleeding and received an SBSS score of 2 at baseline. Following application of the test article, all 3 sites achieved hemostasis and received an SBSS score of 0 at the 3-minute time interval assessment.

One laminectomy site (Case 5, L5) had moderate bleeding and received an SBSS score of 3 at baseline. Following application of the test article, the bleeding subsided to mild bleeding with an SBSS score of 2 at the 3-minute interval assessment. Following application of an additional 3.5 mL of test article at the 3-minute interval, the site achieved hemostasis and received an SBSS score of 0 at the 6-minute interval assessment. Once hemostasis was achieved, all laminectomy sites maintained hemostasis at the final 10-minute interval assessment and at the time of closure.

Postoperative survival

All animals demonstrated ambulatory function within 3 hours postoperatively. Based on postoperative cage-side clinical observations of pain and neurologic assessments, all animals exhibited normal recovery following the 2-level laminectomy procedure. Four animals (Cases 2, 3, 6, and 9) received an increase in neurological observation scores on Days 5 or 6, which after veterinary review was determined to likely be attributed to stiffness and pain secondary to surgical intervention. However, all animals either presented with either no detectable or a slight weakness during ambulation by Day 7, exhibiting normal neurological recovery for this surgical model.

Table 2 Specimen treatment arms and SBSS scores

Case number	Survival period (days)	Operative level	Test article applied (mL)	SBSS scores				
				0 minutes (baseline)	3 minutes	6 minutes	10 minutes	Hemostatic
1	30	L3	4.0	1	0	0	0	Yes
		L5	4.0	1	0	0	0	Yes
2	60	L3	2.5	1	0	0	0	Yes
		L5	2.0	1	0	0	0	Yes
3	90	L3	4.0	1	0	0	0	Yes
		L5	4.0	1	0	0	0	Yes
4	12	L3	3.0	2	0	0	0	Yes
		L5	3.8	1	0	0	0	Yes
5	12	L3	4.0	2	0	0	0	Yes
		L5	5.0	3	2	0	0	Yes
6	12	L3	5.5	2	0	0	0	Yes
		L5	2.0	1	0	0	0	Yes
7	12	L3	2.0	1	1	0	0	Yes
		L5	2.0	1	0	0	0	Yes
8	12	L3	2.0	1	0	0	0	Yes
		L5	2.0	1	0	0	0	Yes
9	12	L3	2.0	1	0	0	0	Yes
		L5	2.0	1	0	0	0	Yes

A total of 9 animal specimens were included in this study, each with a designated postoperative survival period prior to necropsy. The total amount of test article administered at each laminectomy level was recorded. The SBSS was used to grade the severity of intraoperative bleeding at set time points. SBSS, Surface Bleeding Severity Scale.

Clinical pathology

Preoperative CVS and CBC with differential results were considered unremarkable for all animals and there were no clinically significant changes when comparing the baseline and termination assays for the animals. CSF samples demonstrated mild mononuclear pleocytosis, representing a benign physiologic profile without evidence of atypical cells or infection.

At the time of necropsy, there was no evidence of wound dehiscence or gross infection in any of the specimens. The skin, fascial layers, and musculature were all noted to be healing appropriately.

Histopathologic findings

At the 12-day time point, the implant material was observed at the epidural space as well as within surgical access sites. Implant-related inflammation was characterized by lymphocytes and macrophages, with fewer giant cells. At the surgical access sites, healing was characterized by granulation tissue, fibrinous exudates, and neovascularization with fibrosis and mixed inflammatory cells, and did not appear to be adversely affected by presence of test article (*Figure 3*).

At the 30-, 60-, and 90-day time points, healing was characterized by fibrosis that tended to be replaced by new bridging bone. The fibrosis that was present was expected in this surgical model and was scored as minimal to mild, with no evidence of excessive fibrosis in reaction to the test article. Tissue response at the epidural space was associated with the procedure and characterized by granulation tissue with neovascularization and fibrosis, as well as inflammation that occasionally extended into the meninges. The amount of residual test article was observed to decrease between

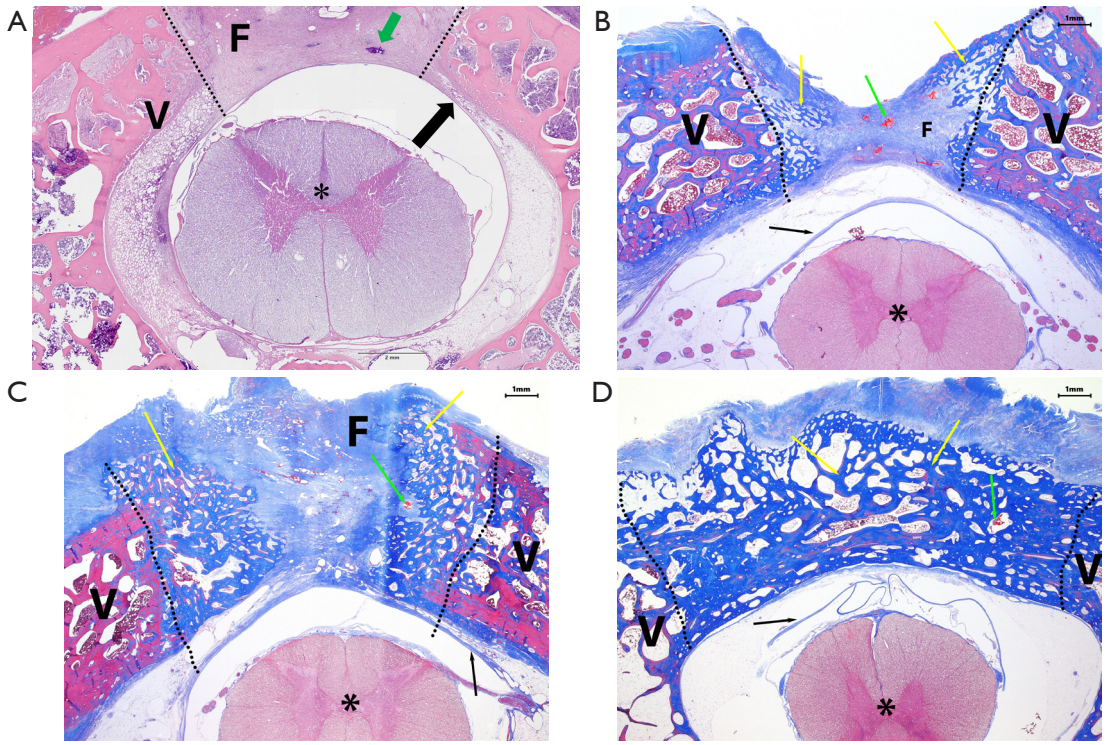

Figure 3 Histological images of the sheep lumbar vertebra. Representative cross-sectional image of the vertebral level at the 12- (A), 30- (B), 60- (C), and 90-day (D) time points. Specimens were stained with hematoxylin and eosin (A) to evaluate general tissue morphology and Masson's trichrome (B-D) to evaluate connective tissue, muscle, and the presence of fibrosis. There was no evidence of ante-mortem compression-type injuries noted at all timepoints. Laminectomy was performed between dotted black lines. Green arrow: residual test material; black arrow: dura mater; asterisk: spinal cord; yellow arrow: new bone. F, fibrosis; V, vertebrae.

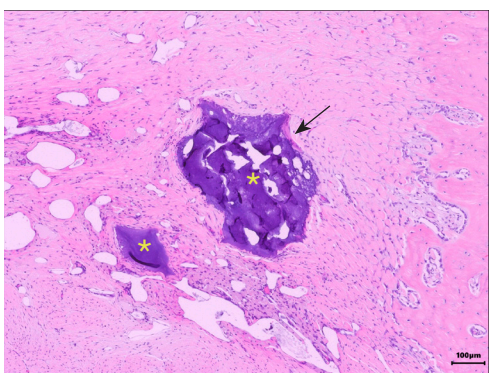

Figure 4 Histological image at the L3 level following necropsy at 60-day, demonstrating extracellular residual test article (asterisks) and multinucleated giant cell (black arrow). Specimens were stained with hematoxylin and eosin to evaluate general tissue morphology, Masson's trichrome to evaluate connective tissue, muscle, and the presence of fibrosis, and IBA-1 for neuropathological assessment of microgliosis. IBA-1, ionized calcium binding adaptor molecule 1.

the 30- and 60-day intervals and there was no evidence of residual test article in the epidural space at 90 days. Residual test article, when present, was associated with minimal numbers of macrophages, rare lymphocytes, and multinucleated giant cells (*Figure 4*).

Spinal cord changes were limited to nerve fiber degeneration and/or axonal dystrophy and microgliosis (*Figure 5*). The changes in the spinal cord and nerve roots did not appear to be associated with the implant material. There was no evidence of ante-mortem compression-related injuries in the spinal cord.

Discussion

The overall results of this study demonstrate the utility and safety of the ovine model in evaluating intraoperative bleeding severity and postoperative histopathology following epidural application of a hydrophobically

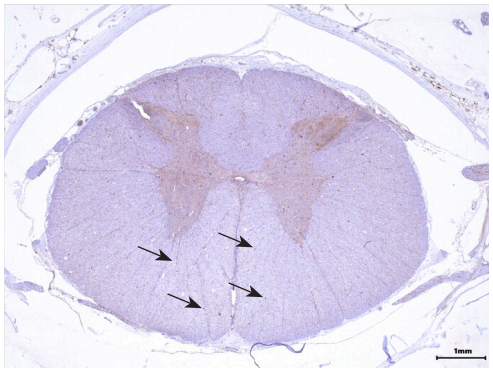

Figure 5 L3 level following necropsy at the 12-day timepoint. Note the multiple foci of microgliosis (arrows). Specimens were stained with hematoxylin and eosin to evaluate general tissue morphology, Masson's trichrome to evaluate connective tissue, muscle, and the presence of fibrosis, and IBA-1 for neuropathological assessment of microgliosis. IBA-1, ionized calcium binding adaptor molecule 1.

modified chitosan-based hydrogel hemostatic agent.

From a hematologic standpoint, the ovine model is suitable for assessing hemostasis. Studies have demonstrated that, compared to humans, sheep on average have a comparable mean corpuscular hemoglobin concentration as well as similar lymphocyte and leukocyte compositions (14,15). In addition, factors involved in the clotting cascade, and end measurements of prothrombin time, activated partial thromboplastin time, and thrombin clotting times have not been shown to be significantly different in ovine and humans (14-16). Anatomically, the neurovasculature of sheep and humans share many similarities, with the spinal cord being supplied by the anterior spinal artery, posterior spinal arteries, and radiculomedullary branches called the spinal artery plexus or vasa coronae (17-19). Therefore, the bleeding severity scores observed in this study can likely be translated to humans.

The bleeding in laminectomy procedures is usually minimal to moderate (SBSS score of 1 or 2) and while a higher number of SBSS scores of 2 were expected in this model, the majority of baseline SBSS scores of 1 as reported in this study are consistent with what would be encountered clinically. The hemostatic test article was effective in achieving homeostasis in all bleeding severities (SBSS score of 1–3) encountered in this pilot study.

There are several notable differences in the neuroanatomy of sheep compared to humans. In humans, the spinal cord terminates at the L1–L2 level and tapers

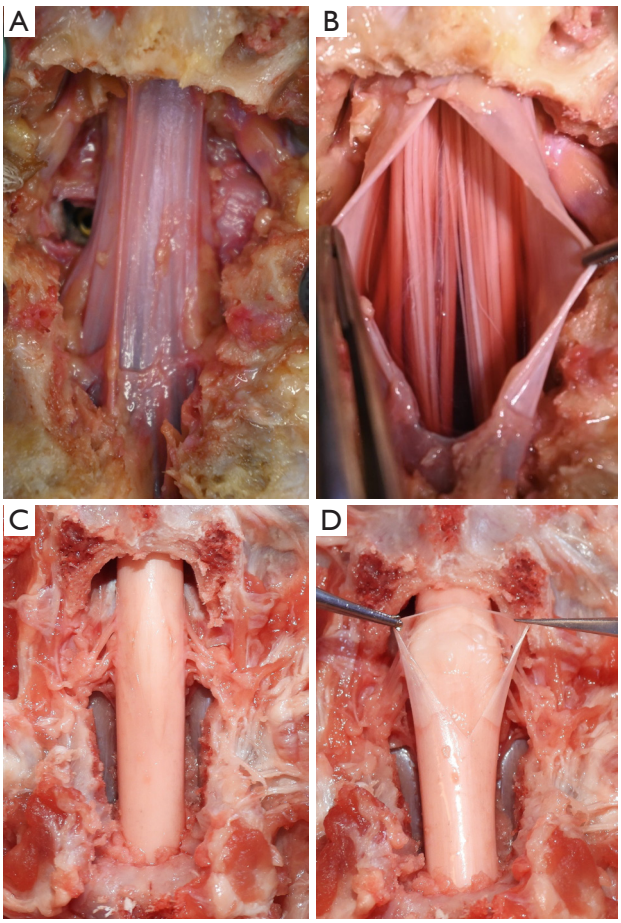

Figure 6 Comparison of human and sheep anatomy. Posterior view of a human spine cadaver (A) and sheep spine specimen (C) with visible nerve rootlets after consecutive 2-level laminectomy at the L3 and L4 levels. The human cauda equina (B) and sheep spinal cord (D) were exposed after intentional durotomy. Note the thicker and more opaque human dura mater in comparison to the sheep dura mater. The human cadaveric specimen photographed here was not part of this study, and is shown for comparative purposes.

into the conus medullaris, with nerve roots forming the cauda equina in the lumbar region (*Figure 6*). In contrast, the sheep spinal cord extends throughout the lower lumbar segments and terminates at S1–S2 (20,21). Therefore, all neurologic structures of the spinal cord are present in sheep at the lumbar level, making the ovine model an appropriate translational subject for the human spine. The absence of neurologic deficits observed during the survival period may also be taken as freedom from device-related swelling and compression of the spinal cord and neural tissue or other

neurological complications related to the test article.

In sheep, the cranial dura mater has been shown to be 2.41 times thinner than that of humans (22). Grossly, this was also observed in the lumbar spine where sheep dura mater (*Figure 6C*,*6D*) was significantly thinner than human dura mater (*Figure 6A*,*6B*). Furthermore, the intrathecal space was observed to be approximately 1mm or less between the spinal cord and dural sac, which is significantly less compared to the intrathecal space measured in a previous magnetic resonance imaging (MRI) study in healthy humans without spinal stenosis (23). With less volume for CSF, the sheep neurological structures may be more susceptible to mechanical compression and/or injury to the nerve elements. This may be acceptable in a translational model, where any neurological deficits would represent a "worst case scenario".

In terms of osseous anatomy, there are typically 6 lumbar vertebrae in sheep (L1–L6) and in some cases 7 (L1–L7) in comparison to 5 in humans (L1–L5). Likely attributed to the upright posture of humans and the need to support greater axial load, humans have larger, wider, and shorter vertebral bodies, as well as thicker vertebral discs. Notwithstanding these differences, the lumbar vertebral dimension indices and Pavlov's ratio (the depth ratio between the spinal canal and the vertebral body) in sheep spine show close similarity to humans, making the osteopathic structures in the sheep spine an acceptable translational and "worst case scenario" model for translation to humans (24).

Histopathology was consistent with time-dependent changes associated with normal healing, without evidence of epidural fibrosis, infection, or compression-related nerve damage. Overall, the histologic findings observed in the ovine specimens are also translatable. Previous studies have demonstrated that the cellular mediators involved in the inflammatory response in sheep are comparable to that of humans (14-16). All tissue reactions observed during the histopathological evaluation were expected for this surgical model and represented normal progression of healing at all time points. Test article related changes were limited to low grade lymphocyte, macrophage, and multinucleated giant cell infiltrates, which overall represents a benign inflammatory response profile. These findings suggest an early indication of excellent biocompatibility of the test article in the ovine model.

This pilot study is not without limitations. The small and variable sample sizes per survival group, and lack of experimental controls, do not allow for statistical comparisons across survival groups. While this was not the primary aim of the study, the results of this pilot demonstrate an effective proof-of-concept for larger comparative investigations powered with appropriate sample sizes. In addition, the risk for thromboembolic side effects from the hemostatic agent were not evaluated. However, all animals were closely monitored during the postoperative period and none exhibited clinical signs of symptomatic thromboembolism. Furthermore, the ovine model has several anatomic differences as previously mentioned that do not make for a perfect translational model for the human lumbar spine, including a kyphotic curvature and variations of 6 or 7 lumbar vertebrae (21,24). However, these anatomic differences may have had little consequence in the current study, as all laminectomies were performed at the L3 and L5 levels. Finally, this pilot study evaluated a single hemostatic agent chosen for its unique characteristic in mitigating risks associated with swelling, so a comparative analysis with other commonly used hemostatic agents was not performed. Based on the results of the current study, future comparative investigations using the ovine model are encouraging.

Conclusions

Application of a novel hydrophobically modified chitosan-based hydrogel hemostat was found to be effective in achieving hemostasis in this pilot study of ovine lumbar laminectomies. Postoperative survival analysis and histopathology suggest that the test article, when used and assessed under similar conditions, was safe and well tolerated in sheep. The results of this pilot study establish a framework for future, larger comparative investigations and demonstrate that the sheep lumbar laminectomy model provides a suitable translational model for the evaluation of hemostatic agents for use in the human spine.

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None.

Footnote

Reporting Checklist: The authors have completed the ARRIVE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-25-10/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-25-10/dss

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Experiments were performed under a project license (NAICS 424520) granted by The Institutional Animal Care and Use Committee (IACUC) at Thomas D. Morris, Inc. in compliance with the Animal Welfare Act Regulations (9 CFR), the U.S. Public Health Service Office of Laboratory Animal Welfare (OLAW) Policy on Humane Care and Use of Laboratory Animals, and the Guide for the Care and Use of Laboratory Animals (Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, 1996).

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