advanced glycation end products (AGEs) stiffens and embrittles collagen fibers, thus increasing bone fragility and fracture risk. Despite the crucial role of AGEs in bone ageing, the relationship between AGEs and BMD is poorly understood. We hypothesized that an accumulation of AGEs, a marker of impaired bone quality, is related to decreased BMD.

Material and Methods: Prospectively collected data of 107 patients undergoing open posterior lumbar fusion at a single academic institution was analyzed. Standardized lumbar QCT measurements were performed on preoperative CT scans using the L1/2 average. Intraoperative bone biopsies from the posterior superior iliac spine were obtained and analyzed with confocal fluorescence microscopy for fluorescent advanced glycation end products (fAGEs), both trabecular and cortical, representing non-enzymatic collagen cross-linking. Pearson's correlation coefficients were calculated to examine crude relationships between BMD at L1/L2 and fAGEs, stratified by biological sex. Multivariable linear regression analysis with adjustments for age, sex, body mass index (BMI), diabetes, and HbA1c was used to investigate associations between BMD at L1/L2 and fAGEs. Statistical significance was defined as $p<0.05$.

Results: 127 patients (51.2% female) with a mean age of 61.2 years and a BMI of 29.9 kg/m2 were included in the final analysis, excluding patients with anti-osteoporotic drug therapy. In the univariate analysis, cortical fAGEs increased with decreasing BMD at L1/L2 ($r = -0.32$; $p = 0.021$), but only in men. In the multivariate analysis, trabecular fAGEs increased with decreasing BMD at L1/L2 after adjusting for age, sex, BMI, Diabetes Mellitus, and HbA1c. ($\beta = 0.99$; $p = 0.04$)

Conclusion: This is the first study to assess BMD and in-vivo non-enzymatic collagen cross-linking as a marker of bone quality in lumbar fusion patients. QCT-derived BMD measurements were found to be significantly associated with collagen properties in bone, such as fAGEs, which embrittle bone tissue. Our results enhance our understanding of bone health by suggesting that spine surgery patients with deficits in bone quantity may also have deficits in bone quality.

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AN INVESTIGATIONAL STUDY OF THE NEUROHISTOPATHOLOGIC RESPONSE FOLLOWING EPIDURAL APPLICATION OF A NOVEL HEMOSTATIC AGENT - AN IN VIVO OVINE LAMINECTOMY MODEL

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Background Context: Despite routine intra-operative utilization of hemostatic agents, the potential for inflammation and compression of neural structures, fibrosis, and neurotoxicity remain a clinical concern. Epidural fibrosis resulting from operative site hemorrhage creates chronic pain and is often refractory to treatment.

Purpose: The objective of the current study was to investigate the hemostatic and neurohistopathologic responses following direct epidural application of a novel powder-based hemostat using an in-vivo model.

Methods: A total of 18 sheep underwent laminectomies at the L3 and L5 lumbar vertebral levels and randomized into one of three treatments: 1) Laminectomy alone (Sham); 2) Absorbable gelatin sponge and thrombin (Control Article); or 3) Porcine collagen, bovine chondroitin sulfate, and human-pooled plasma thrombin (Test Article). Time intervals included 15 days (n=8) and 90 days (n=10). Intraoperative bleeding severity was quantified at baseline and 3-, 6- and 10-minutes post-application according to a published surface bleeding severity scale (SBSS). Hemostasis was defined as a grade of 0 (None/Dry) with additional grades, ranging from 1 (Minimal/Oozing) to 5 (Extreme/Gushing). Experimental endpoints included metabolic panels, cerebrospinal fluid assays, comprehensive histopathology of systemic and operative level spinal cord tissues according to ISO 10993 standards.

Results: No statistical differences in target bleeding site dimensions (mm) and mean arterial pressure (mmHg) at baseline between treatment groups were observed ($p>0.05$). SSBS scores at 3-minutes post-application were significantly less for the Test Article (0.0 ± 0.0) versus Control Article (0.6 ± 0.5) and Sham (1.0 ± 0.7) ($p=0.000$). The success of intraoperative hemostasis was significantly higher for the Test (100%) and Control (90%) Articles versus Sham (50%) ($p=0.002$). Clinical panels and systemic histopathology were unremarkable. The spinal canal indicated no evidence of cord compression and less epidural fibrosis in Test and Control Article versus Sham. For all groups and time intervals, spinal cord histopathology exhibited non-specific axonal degeneration and dystrophy with slightly higher than average microgliosis scores in the Sham and Control versus Test Article treatment.

Conclusion: The current study provides an in-vivo model for assessing neurohistopathology in response to hemostatic agents and serves as the first to document microgliosis in the spinal cord secondary to laminectomy. Importantly, this finding was secondary to the surgical procedure and not associated with hemostatic treatment. The novel powder-based hemostatic agent analyzed in the current study reduced the time to hemostasis compared to conventional treatment, without evidence of significant neural or systemic histopathology. The preclinical scientific safety and efficacy data from the current investigation provides the basis for subsequent randomized control clinical trials.

Operative Treatment	Surface Bleeding Severity Scale (SBSS)*				Hemostatic
	Baseline	3 minutes	6 minutes	10 minutes	
Sham	1.6 (0.7)	1.0 (0.7)	0.7 (0.5)	1.0 (0.0)	4/8 (50%)
Control Article	1.3 (0.5)	0.6 (0.5)	0.7 (0.5)	0.3 (0.4) **	9/10 (90%)
Test Article	1.5 (0.7)	0.0 (0.0) **	N/A	N/A	18/18 (100%)
p-value	p=0.572	p=0.000	p=1.000	p=0.012	p=0.002

Mean SBSS scores are indicated with one standard deviation in parentheses ().
* Bleeding severity from grades 0 (none/dry), with additional grades from 1 (Minimal/Oozing) to 5 (Extreme/Gushing).
** Indicates significance from all treatments at that time period.

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COMPARISON OF THE BIOLOGICAL ACTIVITY OF EXTRACELLULAR VESICLES VERSUS ENTIRE MSC SECRETOME IN PRO-INFLAMMATORY ANNULUS FIBROSUS CELL CULTURES

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Introduction: Extracellular vesicles (EV) secreted by mesenchymal stem cells (MSC) cultured under basal conditions have been shown to reduce cell apoptosis and inflammation in intervertebral disc (IVD) degeneration models and to promote extracellular matrix synthesis and proliferation of IVD cells [1]. However, previous investigations demonstrated that priming MSC with interleukin (IL)-1β improves the pro-anabolic effect of the entire MSC secretome on IVD [2,3]. Therefore, we investigated the impact of EV versus entire secretome from IL-1β-primed and non-primed MSC on annulus fibrosus (AF) cells.

Methods: Human MSC were cultured with or without 1 ng/mL IL-1β for 48h