INTRODUCTION: Postoperative peridural fibrosis (PPF) following
spinal surgery has been suggested to result in "failed back surgery" or
recurrence of pain [1]. Many investigators have studied the effects of a
variety of synthetic and biologic materials on the reduction of PPF [2, 3].
However, little is known about a material with both hemos
staphic and scar preventive effects. A new gelatin and thrombin-based heomastatic agent
has been developed and clinically applied for controlling intra-operative
bleeding [4]. The purpose of the present study was to examine anti
adhesion properties of this new material in a canine laminectomy model
using biomechanical, biochemical and histological analyses.

METHODS: Laminectomy: Nine adult mongrel dogs were used. All
procedures were approved by the Institutional Animal Care and Usage
Committee. Using a cutting burr drill, a hemilaminectomy (20 x 10 mm)
with annulus puncture was performed at L1/2 (rt), 2/3 (lt), 4/5(rt), and
5/6(lt). One level out of L1/2 and 2/3, and another level out of L4/5 and
3/4 were chosen randomly for treatment using the gelatin with thrombin-
based heomastatic agent (FloSeal®, Baxter Biosci., IL) as an anti
adhesion agent (experimental group). On these sites, the agent was
applied to fill the laminectomy defect, while the control sites received no
 treatment other than tamponade (control group). After eight weeks, all
animals were euthanized. The spine was cut into a L1-3 complex for
biomechanical, biochemical and gross analyses, and a L4-6 complex for
histological analyses.

Biomechanical Analyses: The pedicle and lamina containing the dural
tube were cut and removed from the vertebral body. The spinous process
was placed in a holder (Fig. 1-C). Then, the dural tube was
grasped by a custom made dural gripper (Fig. 1-A, 1-B), which was
connected to a linear actuator with load cells (ELFS-T3E-100N/L10F,
Entron, NJ.). While peel-off force was constantly applied to the dural
tube (Fig. 1-D), the strength of the dural adhesion to the scar tissue was
measured. Stiffness was calculated from a linear portion of the load
-displacement curve.

Gross Analyses: Aafter biomechanical testing, the sections were
examined blindly using number rankings for the amount (0 = no, 1 =
small, 2 = medium, 3 = large amount of scar) and tenacity (0 = no, 1 =
slight, 2 = moderate, 3 = tenacious adhesions) of scar [2].

Biological Analyses: DNA Content: The scar tissue attaching to the dura was obtained in 3
mm thicknesses. After papain digestion, the DNA content was measured
using the Hoescht 33258 dye method and fluorometry [5].

Collagen Content: The content of hydroxyproline, as a measure of
collagen, was measured using reverse phase HPLC [6].

Crosslinked Collagen: Collagen-specific crosslinks were quantified
using HPLC [6].

Histological Analyses: The L4-6 complexes were processed for
decalcified histology. Axial sections at the disc levels and 7 mm caudal
to the discs were obtained and stained with H&E and Golmis’s
trichrome. The dura and nerve root involvement of the scar was
examined using a number ranking (0: no involvement – 3: major
involvement with nerve degeneration). Then, the ratio of the dural
adhesion length to the circumferential length of the dura was measured
using public domain NIH image software.

Statistical Analysis: Two-tailed unpaired t-tests were used.

RESULTS: Biomechanical Analyses: Peel-off stiffness in the
experimental group was significantly smaller than in the control
group (64.8% of the control, p = 0.032). When values were standardized by the
width of adhesion, the stiffness demonstrated a pronounced difference (p
= 0.014). Peel-off strength in the experimental group was 82.2 % of that in the
control group, but statistical significance was not detected (p = 0.36).

Gross Analyses: No significant difference was detected in the score for
the tenacity of the scar, while the score for amount of the scar
demonstrated a strong tendency towards a smaller score in the
experimental group (Table).

Biological Analyses: Although no significant difference was detected in
DNA and collagen contents, there was a strong tendency towards
lower collagen crosslinks in the experimental group (p = 0.07, Table).

Histological Analyses: The dura and nerve root involvement score and
the % adhesion length showed no significant differences between the
two groups (Table).

DISCUSSION: This study demonstrated that the application of a new
gelatin with thrombin-based heomastatic agent can decrease the
tenaciousness of adhesion at the interface between the dura and
the epidural scar. This was also biochemically supported by the decreased
collagen crosslinks, indicating an immaturity of the scar tissue in the
experimental group. Because the complications of PPF are mainly
encountered in revision spine surgery, as dural tears and nerve root
injuries [7], these results support potential advantages of applying the
new agent at the sites of laminectomy. The heomastatic property of the
agent may have reduced the postoperative dural adhesion at the interface
between scar tissue and dura by reducing collagen crosslink formation.
Gelatin might have contributed to reducing the amount of scar tissue in
the defect after laminectomy. Utilization of the combined properties of
heomastasis and the prevention of scar formation in the defect may
provide synergic effects for the anti-adhesion of the dura. Microstructural studies will be required to elucidate the individual anti
adhesion mechanisms of the heomastatic agent and gelatin.


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part by NIH grants, P01-AR48152 and P50-AR9239.

Table. Biomechanical, Gross, Biochemical and Histological Analyses

<table>
<thead>
<tr>
<th>Biomechanical Analyses</th>
<th>Control</th>
<th>Exp.</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stiffness (N/mm)</td>
<td>2.15 ± 0.68</td>
<td>1.39 ± 0.69</td>
<td>0.032</td>
</tr>
<tr>
<td>Strength (N)</td>
<td>6.11 ± 3.05</td>
<td>5.03 ± 2.73</td>
<td>0.360</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Gross Analyses</th>
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<th>Exp.</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score for Amount of the Scar</td>
<td>3.0 ± 0.0</td>
<td>2.8 ± 0.3</td>
<td>0.077</td>
</tr>
<tr>
<td>Score for Tenacity of the Scar</td>
<td>4.1 ± 0.6</td>
<td>3.3 ± 1.4</td>
<td>0.102</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Biochemical Analyses</th>
<th>Control</th>
<th>Exp.</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>DNA content/ Dry wt. (µg/µg)</td>
<td>9.1 ± 2.9</td>
<td>8.2 ± 1.6</td>
<td>0.403</td>
</tr>
<tr>
<td>Hydroxyproline/ Dry wt. (µg/µg)</td>
<td>3.0 ± 0.6</td>
<td>4.4 ± 0.3</td>
<td>0.247</td>
</tr>
<tr>
<td>Pyridinoline/ Hydroxyproline (Collagen Crosslinks) (µg/µg)</td>
<td>1.6 ± 0.3</td>
<td>1.2 ± 0.5</td>
<td>0.073</td>
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</table>

<table>
<thead>
<tr>
<th>Histological Analyses</th>
<th>Control</th>
<th>Exp.</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dura and Nerve Involvement Score</td>
<td>1.1 ± 1.0</td>
<td>1.5 ± 1.0</td>
<td>0.181</td>
</tr>
<tr>
<td>%Adhesion Length</td>
<td>27.7 ± 7.5</td>
<td>26.2 ± 5.1</td>
<td>0.493</td>
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