Intervertebral Disc Degeneration Reduces Vertebral Motion Responses

Christopher J. Colloca, DC,* Tony S. Keller, PhD,† Robert J. Moore, PhD,‡ Robert Gunzburg, MD, PhD,§ and Deed E. Harrison, DC||

Study Design. A prospective *in vivo* experimental animal study.

Objective. To determine the effects of disc degeneration and variable pulse duration mechanical excitation on dorsoventral lumbar kinematic responses.

Summary of Background Data. In vitro and in vivo biomechanical studies have examined spine kinematics during posteroanterior loading mimicking spinal manipulation therapy (SMT), but few (if any) studies have quantified SMT loading-induced spinal motion responses in the degenerated intervertebral disc.

Methods. Fifteen sheep underwent a survival surgical procedure resulting in chronic disc degeneration of the L1–L2 disc. Ten age- and weight-matched animals served as controls. Uniform pulse dorsoventral mechanical forces (80 N) were applied to the L3 spinous processes using 10-, 100-, and 200-ms duration pulses mimicking SMT. L3 displacement and L2–L1 acceleration in the control group were compared with the degenerated disc group.

Results. Dorsoventral displacements increased significantly (fivefold, P < 0.001) with increasing mechanical excitation pulse duration (control and degenerated disc groups). Displacements and L2–L1 acceleration transfer were significantly reduced (~19% and ~50%, respectively) in the degenerated disc group compared with control (100- and 200-ms pulse duration protocols, P < 0.01).

Conclusion. Dorsoventral vertebral motions are dependent on mechanical excitation pulse duration and are significantly reduced in animals with degenerated discs.

Key words: biomechanics, degeneration, intervertebral disc, manipulation, mobilization. Spine 2007;32: E544-E550

The intervertebral disc (IVD) is a known pain generator among patients with low back pain, and the IVD is therefore a primary target of intervention for clinicians apply-

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Address correspondence and reprint requests to Christopher J. Colloca, DC, 11011 S. 48th St., Suite 220, Phoenix, AZ 85044; E-mail: christopher.colloca@asu.edu

ing manual therapies.¹ Progressive degenerative changes of the IVD are associated with increased age, trauma, and abnormal postural loading.² Indeed, a large proportion of the population who receive manual therapies have some degree of disc disease.¹ To influence the peripheral pain generator, patients with discogenic disease commonly undergo spinal manipulative therapy (SMT) with the primary goal of normalizing loads and improving spinal mobility.³

A wide range of manual techniques have been developed providing clinicians with choices of force amplitude, speed, and vector among other variables of SMT delivery in patient care. Force-time characteristics, including the applied force magnitude, speed, and/or frequency, have therefore been attributed to the underlying mechanisms of SMT.⁴ Both *in vitro*^{5,6} and *in vivo*^{7,8} biomechanical studies have examined segmental and intersegmental displacements and vibration responses during SMT, but few (if any) studies have quantified SMTinduced spinal kinematics in the degenerated IVD.

The purpose of this experimental study was to examine the *in vivo* motion behavior of the normal disc and degenerated disc ovine lumbar spine subjected to varying mechanical excitation force-time profiles. Disc degeneration was established using a validated animal model.⁹ We hypothesized that vertebral kinematics would be reduced in animals with disc degeneration.

Materials and Methods

Twenty-five adolescent Merino sheep (mean, 47.2 kg; SD, 5.1 kg) were examined. Fifteen sheep (mean, 47.7, kg; SD, 4.9 kg) underwent a survival surgical procedure designed to experimentally model chronic disc degeneration.⁹ The remaining 10 animals (mean, 46.5 kg; SD, 5.6 kg) served as controls. Control and degenerated disc animals underwent a comprehensive biomechanical assessment designed to characterize segmental/intersegmental displacement/acceleration responses to varying force-time mechanical excitation protocols mimicking SMT. The disc degeneration procedure and biomechanical assessment protocol were approved by the Animal Ethics Committees and Institutional Review Board of the Institute of Medical and Veterinary Science (Adelaide, South Australia).

Disc Degeneration Model. Under general anesthesia (1 g thiopentone; 2.5% halothane), the lumbar spine was approached *via* a direct lateral left-side retroperitoneal approach. In each animal, a controlled stab incision was made in the left posterolateral anulus fibrosus midway between the endplates of the L1–L2 disc.⁹ Incisions were made with a number-15 scalpel blade directed transversely through the outer aspect of the posterior anulus towards the midline and inserted to the hilt

From the *Department of Kinesiology, Biomechanics Laboratory, Exercise and Sport Science Research Institute, Arizona State University, Tempe, AZ, and State of the Art Chiropractic Center, Phoenix, AZ; †Departments of Mechanical Engineering and Orthopaedics and Rehabilitation, University of Vermont, Burlington, VT; ‡Adelaide Centre for Spinal Research, Institute of Medical and Veterinary Science, Adelaide, South Australia; \$Department of Orthopaedic Surgery, Eeuwfeestkliniek Hospital, Antwerpen, Belgium; and ||Chiropractic Biophysics Non-profit, Inc., Evanston, WY.

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Figure 1. Fluoroscopic image of the L1–L2 ovine spine showing the accelerometer pins and location of lesion marked using a wire suture. The L1–L2 intervertebral disc was the site of the stab incision lesion. Inset shows actuator stylus over L3 and accelerometers attached to pins at L1 and L2.

of the scalpel handle (a depth of 5 mm). Fluoroscopic control was used to check the posterior limit of the blade. Care was taken to protect both the spinal cord and the exiting nerve root during the stab incision procedure. The injured disc level was marked by means of a wire placed around the associated transverse process. The wound was closed in layers, and the animals received an intramuscular antibiotic injection 2 mL/50 kg (consisting of procaine penicillin 250 mg/mL, streptomycin 250 mg/mL, and procaine HCl 20 mg/mL). Each animal recovered in an air-conditioned indoor facility on a 12-hour light/dark cycle for 3 days and was then transferred to an outdoor facility. Animals were kept on a paddock for 20 weeks, which allowed the posterior anular lesion-induced disc degeneration to mature.

Biomechanical Testing Procedures. Sheep were fasted for 24 hours before surgery, and anesthesia was induced with an intravenous injection of 1 g thiopentone. General anesthesia was maintained after endotracheal intubation by 2.5% halothane and monitored by pulse oximetry and end-tidal CO_2 measurement. Animals were ventilated and the respiration rate was linked to the tidal volume keeping the monitored CO_2 between 40 and 60 mm Hg. Biomechanical testing and kinematic measurement procedures have been described previously,^{8,10–13} but a brief description follows.

Following general anesthesia, the animals were placed in a prone-lying position with the abdomen and thorax supported by a rigid wooden platform and foam padding, respectively, thereby positioning the lumbar spine parallel to the operating table and load frame; 10-g piezoelectric triaxial accelerometers (Crossbow Model CXL100HF3, Crossbow Technology, Inc., San Jose, CA) were attached to intraosseous pins that were rigidly fixed to the L1 and L2 lumbar spinous processes under fluoroscopic guidance (Figure 1). The accelerometers are high-frequency vibration measurement devices that feature low noise (300- μ g rms), wide bandwidth (0.3–10,000 Hz) and low nonlinearity (<1% of full scale) and are precision calibrated by the manufacturer. The x-, y-, and z-axes of the accelerometer

and cranial-caudal or axial axes of the vertebrae. Only dorsoventral acceleration (z-axis motion) responses are reported in this study.

With the animals in a standardized prone-lying position, the bony preeminence of the L3 spinous process was exposed using electrocautery. Using a custom, computer-controlled mechanical testing apparatus, dorsoventral forces were applied directly to the L3 spinous process using a 12.7-mm-diameter actuator stylus equipped with a slotted tip that cradled the exposed spinous process bone surface. To simulate impulsive and manual SMT force-time profiles, 3 mechanical excitation pulse durations (10, 100, and 200 ms) were examined. In each case, an 80 N peak force with a 10 N preload was applied, and 5 trials were performed for each mechanical excitation protocol. The order in which the mechanical testing protocols were performed was randomly determined.

The dorsoventral L3 force, actuator displacement, L1, and L2 vertebral accelerations were recorded at a sampling frequency of 5000 Hz using a 16-channel, 16-bit MP150 data acquisition system.

Pathologic Examination of Intervertebral Discs. Following the experimental protocol, the sheep were killed by intravenous injection of 6.5-g pentobarbitone sodium and their lumbar spines were removed en bloc by transecting the thoracolumbar junction and the midsacrum. Individual motion segments were isolated by cutting midway through the adjacent vertebral bodies with a bandsaw and fixed in 10% buffered formalin for a minimum of 72 hours before being decalcified in a solution containing 9.5% nitric acid and 10% edetic acid (EDTA). The specimens were cut into 6 parasagittal slices of equal thickness. Slices showing the anulus lesion and a contralateral slice were processed into paraffin wax for histomorphometric examination. Tissue sections were cut at a nominal thickness of 5 μ m, stained with hematoxylin and eosin, and independently examined without knowledge of each animal's identity. Intervertebral discs from all subjects were graded on a 1 to 4 scale of degeneration (1 = normal; 2 = mildly degenerated; 3 =moderately degenerated; 4 =severely degenerated) with respect to the overall condition of the disc (grade), as well as morphologic characteristics of the anulus fibrosus, nucleus pulposus, vertebral endplates, and subchondral bone.¹⁴

Data Reduction and Analysis. The actuator displacement (mm) and vertebral intersegmental (L2–L1) dorsoventral acceleration transfer were computed for each mechanical excitation trial. Effects of mechanical excitation pulse duration on the dorsoventral motion response (L3 displacement or L2–L1 acceleration transfer) were assessed using a repeated measures analysis of variance (ANOVA) (P < 0.05, significant difference). Statistical comparisons were performed between normal and degenerated animals and across mechanical test protocols within the normal and degenerated animal groups.

Results

Histologic Analysis

The macroscopic and microscopic features of the discs in this study closely resemble those described in a previous ovine study of rim lesions.⁹ Among the animals subjected to the chronic lesion, macroscopically there was unequivocal evidence of the anular incision in the incised disc with extension of the lesion to involve the central



Figure 2. Low power mid sagittal photomicrographs of ovine L1–L2 lumbar intervertebral discs. A normal disc serving as a control in the current study is shown on the left, illustrating the normal arrangement of the anulus fibrosus and the central nucleus pulposus. The injured disc (right) is shown 20 weeks following anular incision and is characterized by extensive disruption of the anterior anulus, anterior migration of the nucleus pulposus, and medial contraction of the posterior anulus fibers. Markedly thickened repair tissue is present in the vicinity of the initial anular incision. Small transverse fissures and irregular thickening of the calcified zone are also observed at the vertebral body endplate in the injured disc.

nucleus pulposus in all cases (Figure 2). The lesion resulted in substantial loss of height due to breakdown of disc matrix. Microscopically, all discs showed advanced repair of the most peripheral anular fibers or in some case, more organized collagenous scar tissue. In most cases, there was radial and circumferential extension of the initial anular lesion with secondary displacement of the nucleus towards the anterior aspect, resulting in prominent inversion of the posterior anular fibers from their usual concave orientation. In most cases, the nucleus showed substantial migration with early clefting of the matrix in some cases.

The degenerated model discs were consistently at a stage of moderate to advanced degeneration compared with the normal discs (Table 1). In all normal subjects, the anulus fibrosus was graded as 1, whereas the degenerated group scored 3.30 (SD, 0.48). The nucleus pulposus averaged 1.40 (SD, 0.52) for the normal group compared with the degenerated group score of 2.60 (SD,

0.52). Vertebral body endplate and subchondral bone differences were less remarkable among the normal and degenerated groups. All normal group L1–L2 discs were graded as 1, whereas the mean score of the degenerated group was 3.10 (SD, 0.57). With the exception of 2 degenerated disc animals who were graded as 2, all of the incised discs were generally graded either as 3 (moderately) or 4 (severely) degenerated.

Mechanical Excitation Response

Typical force-time, displacement-time, and L2–L1 intersegmental acceleration responses produced by the uniform pulse duration mechanical excitation are illustrated in Figure 3. The uniform force pulse resulted in a haversine-like dorsoventral displacement response at the point of contact (L3). Dorsoventral displacement tended to lag behind the force by a few milliseconds. Intersegmental (L2–L1) dorsoventral vertebral accelerations showed

 Table 1. Grading of Histologic Changes in the L1–L2 Lumbar Discs of the 10 Normal and 15 Degenerated Model

 Specimens Examined

AF		NP		EP		SCB		Grade	
Normal	Lesion								
1	3	1	2	1	1	1	1	1	3
1	3	1	2	1	1	1	1	1	3
1	3	2	3	1	1	1	1	1	3
1	3	1	2	1	1	1	1	1	3
1	4	1	3	1	2	1	1	1	4
1	4	1	3	1	1	1	1	1	4
1	3	2	3	2	1	1	1	1	2
1	3	2	2	1	1	1	1	1	3
1	3	2	3	1	1	1	1	1	3
1	4	1	3	1	2	1	2	1	3
	4		2		3		2		3
	3		2		1		1		3
	3		2		1		1		3
	4		3		1		1		4
	2		3		1		1		2
Mean	3.30	1.40	2.60	1.10	1.20	1.00	1.10	1.00	3.10
SD	0.48	0.52	0.52	0.32	0.42	0.00	0.32	0.00	0.57



Figure 3. Typical actuator force, actuator displacement, and intersegmental (L2–L1) acceleration response obtained during the application of a uniform pulse mechanical excitation (100–ms pulse duration). The load was ramped from 0 N to a preload of approximately 10 N before the application of the 80 N variable pulse duration mechanical stimulation. Top, normal disc. Bottom, degenerated disc.

large amplitude motions during both the onset and removal of the uniform force pulse.

The 10-ms (80 N) mechanical excitation protocol produced the lowest L3 dorsoventral displacement re-

sponse (normal = 3.69 mm; degenerated = 3.51 mm), whereas the 100-ms (80 N) mechanical excitation protocol produced the greatest L3 dorsoventral displacement response (normal = 17.84 mm; degenerated =



Figure 4. L3 dorsoventral displacement response for the 3 variable pulse duration mechanical excitation protocols. Bars indicated mean (SD) for the normal disc group (gray) and degenerated disc group (black). *P* values for significant across group (normal *vs.* degenerated) differences are indicated.

14.49 mm) (Figure 4). Both the 100- and 200-ms mechanical excitation protocols resulted in significantly greater (approximately fivefold, repeated-measures ANOVA, P < 0.001) L3 dorsoventral displacements in comparison to the 10-ms SMT protocol (both control animal and degenerated disc animal groups). Compared with the normal disc group, animals in the degenerated disc group showed significantly reduced (approximately 19%) L3 dorsoventral displacement responses for the 100- and 200-ms mechanical excitation protocols (repeated-measures ANOVA, P < 0.01).

Intersegmental acceleration responses were opposite of that observed for the displacement responses; namely, the intersegmental acceleration response was greatest for the shortest duration mechanical excitation pulse protocol (Figure 5). Compared with the normal disc group, animals in the degenerated disc group showed a significantly reduced (approximately 50%) L2–L1 acceleration



Mechanical Excitation Pulse Duration

Figure 5. Lumbar intersegmental (L2–L1) acceleration response for the 3 variable pulse duration mechanical excitation protocols. Bars indicated mean (SD) for the normal disc group (gray) and degenerated disc group (black). *P* values for significant across group (normal *vs.* degenerated) differences are indicated.

Discussion

In the current study, an established animal model of disc degeneration⁹ was used that produces a clinically relevant healing response that is well established after 12 weeks.¹⁵ Analogous to disc degeneration in humans,¹⁶ the healing response of the ovine disc was associated with anular disruption, nuclear migration, and granulation tissue formation in the outer anular region of the ovine disc. Previous investigations have demonstrated biomechanical and biochemical similarities between sheep and human intervertebral discs.¹⁷ Thus, the ovine animal model is deemed to be a valid model to investigate biomechanical responses to dorsoventral mechanical excitation.

Mechanical excitation pulse durations selected for the current study were chosen to closely resemble SMT thrusts delivered in clinical practice. Specifically, the 10-ms thrusts mimic the speeds of mechanical force manually assisted adjusting instruments,¹⁸ whereas the 100and 200-ms pulse durations more closely resemble speeds of high velocity low amplitude SMTs.^{19,20} In addition, the loads imparted to the ovine spine were 25% of the animal body weight, which is consistent with loads commonly delivered among those practicing SMT.^{19,20} We found shorter pulse duration (10 ms) mechanical excitation produced larger adjacent segment vertebral motions in comparison to longer pulse duration mechanical excitation (100 or 200 ms). Similar findings of adjacent vertebral motion in response to mechanical force manually assisted SMTs have also been reported in human subjects in vivo.7,8,11 Impulsive forces (pulse durations <25 ms) are known to produce an abrupt change in velocity, which causes the spine to vibrate freely.⁴ This is especially true in viscoelastic structures such as the spine. Given the putative effects of impulsive-type chiropractic adjustment procedures,^{21–24} the enhanced vibration response observed during very short duration forces may represent one mechanism for impulsive-type SMTs.

Animals with degenerated discs showed significantly decreased dorsoventral displacement and L2-L1 intersegmental accelerations, which supports our hypothesis that vertebral kinematics would be reduced in animals with disc degeneration. However, statistically significant disc degeneration-related changes in segmental and intersegmental kinematics were not observed for the shorter duration (10 ms) mechanical excitation pulse protocol, which in this study seems to reflect the fact that impulsive loading produces a more variable kinematic response. In addition, Increasing pulse duration from 100 to 200 ms did not appreciably change the amount of dorsoventral displacement at the segmental contact point (L3) or adjacent segment motion at L1-L2. This suggests that spinal manipulation treatment strategies that use shorter duration SMTs (100 ms) are biomechanically more efficient since appreciably less energy is delivered to the spine. Further work examining the dynamic mechanical response of the normal and degenerated spine will assist in the understanding both the etiology of spinal disorders and putative effects of spinal manipulative therapy among different patient populations.

This is the first study demonstrating differences in vertebral kinematics for specimens with degenerated discs, an important finding for clinicians. Clinicians practicing SMT cognitively and kinesthetically gauge the amount of force they deem appropriate for a particular patient or condition based on biomechanical (*i.e.*, anatomic) and clinical (*i.e.*, pain tolerance) variables alike. Knowledge that degenerated functional spinal units will undergo substantially less dorsoventral motion for a given dorsoventral force, as demonstrated in the current study, provides clinicians with important biomechanical information that can be considered in practice.

Measurement of vertebral movement using intraosseous pins equipped with accelerometers^{7,8,11} and other invasive motion measurement devices^{25,26} has been previously shown to be a precise measure of spine segmental and intersegmental motion, but invasive procedures currently have limited clinical utility. Noteworthy, however, was our finding that decreases in dorsoventral displacement associated with the degenerated disc model mirrored the reduced acceleration transfer across the disc lesion. This corroborates the findings of others who have demonstrated increased stiffness among dehydrated or degenerated discs *in situ*.¹⁶ The ability to noninvasively detect biomechanical changes in degenerated discs in vivo using an indenter over the spinous processes may have implications for the development of quantitative biomechanical spinal assessment strategies.

Conclusion

Dorsoventral vertebral kinematics are dependent on mechanical excitation pulse duration and are significantly reduced in animals with degenerated discs. Further work is needed to identify "optimal" force-time profiles for spinal manipulative therapies and assessment strategies. Characterization of changes in the kinematic characteristics of the spine using spinal manipulative-like thrusts may assist in assessment of clinical outcomes.

Key Points

• We found that the kinematic responses of the ovine lumbar spine were sensitive to the duration of the applied mechanical excitation force.

• Compared with the normal disc group, animals in the degenerated disc group showed significantly (P < 0.01) reduced (~19%) L3 dorsoventral displacements for the 100- and 200-ms duration mechanical excitation protocols.

• Compared with the normal disc group, animals in the degenerated disc group showed significantly (P < 0.01) reduced (~50%) L2–L1 acceleration transfer during 100- and 200-ms mechanical excitation protocols.

• Characterization of spine kinematics during dorsoventral mechanical excitation mimicking spinal manipulative-like thrusts may assist in assessment of clinical treatment and outcomes for back disorders.

References

- Lisi AJ, Holmes EJ, Ammendolia C. High-velocity low-amplitude spinal manipulation for symptomatic lumbar disk disease: a systematic review of the literature. J Manipulative Physiol Ther 2005;28:429–42.
- 2. Adams MA. Biomechanics of back pain. Acupunct Med 2004;22:178-88.
- Burton AK, Tillotson KM, Cleary J. Single-blind randomised controlled trial of chemonucleolysis and manipulation in the treatment of symptomatic lumbar disc herniation. *Eur Spine J* 2000;9:202–7.
- Keller TS, Colloca CJ, Beliveau JG. Force-deformation response of the lumbar spine: a sagittal plane model of posteroanterior manipulation and mobilization. *Clin Biomech* 2002;17:185–96.
- Gal J, Herzog W, Kawchuk G, et al. Movements of vertebrae during manipulative thrusts to unembalmed human cadavers. *J Manipulative Physiol Ther* 1997;20:30–40.
- Maigne JY, Guillon F. Highlighting of intervertebral movements and variations of intradiskal pressure during lumbar spine manipulation: a feasibility study. J Manipulative Physiol Ther 2000;23:531–5.
- Nathan M, Keller TS. Measurement and analysis of the in vivo posteroanterior impulse response of the human thoracolumbar spine: a feasibility study. *J Manipulative Physiol Ther* 1994;17:431–41.
- Keller TS, Colloca CJ, Gunzburg R. Neuromechanical characterization of in vivo lumbar spinal manipulation: I. Vertebral motion. J Manipulative Physiol Ther 2003;26:567–78.
- Osti OL, Vernon-Roberts B, Fraser RD. 1990 Volvo Award in experimental studies. Anulus tears and intervertebral disc degeneration: an experimental study using an animal model. *Spine* 1990;15:762–7.
- 10. Colloca CJ, Keller TS, Gunzburg R. Neuromechanical characterization of in

vivo lumbar spinal manipulation: II. Neurophysiological response. J Manipulative Physiol Ther 2003;26:579–91.

- Colloca CJ, Keller TS, Gunzburg R. Biomechanical and neurophysiological responses to spinal manipulation in patients with lumbar radiculopathy. *J Manipulative Physiol Ther* 2004;27:1–15.
- Keller TS, Colloca CJ. Dynamic dorsoventral stiffness assessment of the ovine lumbar spine. J Biomech 2007;40:191–7.
- Colloca CJ, Keller TS, Harrison DE, et al. Spinal manipulation force and duration affect vertebral movement and neuromuscular responses. *Clin Biomech* 2006;21:254–62.
- Berlemann U, Gries NC, Moore RJ. The relationship between height, shape and histological changes in early degeneration of the lower lumbar discs. *Eur Spine J* 1998;7:212–7.
- Gries NC, Berlemann U, Moore RJ, et al. Early histologic changes in lower lumbar discs and facet joints and their correlation. *Eur Spine J* 2000;9:23–9.
- Costi JJ, Hearn TC, Fazzalari NL. The effect of hydration on the stiffness of intervertebral discs in an ovine model. *Clin Biomech* 2002;17:446–55.
- Reid JE, Meakin JR, Robins SP, et al. Sheep lumbar intervertebral discs as models for human discs. *Clin Biomech* 2002;17:312–4.
- Colloca CJ, Keller TS, Black P, et al. Comparison of mechanical force of manually assisted chiropractic adjusting instruments. J Manipulative Physiol Ther 2005;28:414–22.
- Herzog W, Conway PJ, Kawchuk GN, et al. Forces exerted during spinal manipulative therapy. Spine 1993;18:1206–12.
- Herzog W, Kats M, Symons B. The effective forces transmitted by highspeed, low-amplitude thoracic manipulation. *Spine* 2001;26:2105–10.
- Gemmell HA, Jacobson BH. The immediate effect of Activator vs. Meric adjustment on acute low back pain: a randomized controlled trial. J Manipulative Physiol Ther 1995;18:453–6.
- Yurkiw D, Mior S. Comparison of two chiropractic techniques on pain and lateral flexion in neck pain patients: a pilot study. *Chiropract Tech* 1996;8: 155–62.
- Keller TS, Colloca CJ. Mechanical force spinal manipulation increases trunk muscle strength assessed by electromyography: a comparative clinical trial. *J Manipulative Physiol Ther* 2000;23:585–95.
- Wood TG, Colloca CJ, Matthews R. A pilot randomized clinical trial on the relative effect of instrumental (MFMA) versus manual (HVLA) manipulation in the treatment of cervical spine dysfunction. J Manipulative Physiol Ther 2001;24:260–71.
- Kaigle AM, Holm SH, Hansson TH. 1997 Volvo Award winner in biomechanical studies. Kinematic behavior of the porcine lumbar spine: a chronic lesion model. *Spine* 1997;22:2796–806.
- Kaigle AM, Pope MH, Fleming BC, et al. A method for the intravital measurement of interspinous kinematics. J Biomech 1992;25:451–6.