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Intervertebral disc herniation: studies on a porcine model exposed to highly repetitive flexion/extension motion with compressive force

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Abstract

Objective. To determine whether repeated motion with low magnitude joint forces, and flexion/extension moments consistently produce herniation in a non-degenerated, controlled porcine spine motion segment.

Design. Combined loading (flexion/extension motions and compressive forces) was applied to in vitro porcine functional spinal units. Biomechanical and radiographic characteristics were documented.

Background. While most studies performed in vitro have examined uniaxial or fixed position loading to older specimens, there have been few studies that have examined whether 'healthy' intervertebral discs can be injured by low magnitude repeated combined loading.

Methods. Porcine cervical spine motion segments (C3–C4) were mounted in a custom jig which applied axial compressive loads with pure flexion/extension moments. Dynamic testing was conducted to a maximum of 86 400 bending cycles at a rate of 1 Hz with simultaneous torques, angular rotations, axial deformations recorded for the duration of the test.

Results. Herniation (posterior and posterior-lateral regions of the annulus) occurred with relatively modest joint compression but with highly repetitive flexion/extension moments. Increased magnitudes of axial compressive force resulted in more frequent and more severe disc injuries.

Conclusions. The results support the notion that intervertebral disc herniation may be more linked to repeated flexion extension motions than applied joint compression, at least with younger, non-degenerated specimens.

Relevance

While intervertebral disc herniations are observed clinically, consistent reproduction of this injury in the laboratory has been elusive. This study was designed to examine the biomechanical response and failure mechanics of spine motion segments to highly repetitive low magnitude complex loading.

Keywords: Compression; Flexion; Extension; Repetitive loading; Porcine; Herniation; Spine; Stiffness

1. Introduction

Despite disc herniation being observed clinically, there have been few in vitro studies that have achieved consistent repeatable intervertebral disc herniation, impeding the understanding of the etiology of this injury. The majority of in vitro research has examined repeated axial loading with the spine in a neutral posture [1–5] from which observed herniation was extremely rare. Typically, these studies resulted in the same compression fractures [2,4,6] seen in single cycle destructive in vitro tests (endplate or vertebral body failures). A handful of studies, somewhat inconsistently, but collectively suggest that a non-neutral spine curvature is required to produce disc herniations. The work reported here was an attempt to better understand the conditions that lead to disc herniation for ultimate implementation in injury prevention and rehabilitation strategies.

Experiments successful in producing some herniations generally examined non-neutral loading positions combined with repeated loading [6–8]. For example, Wilder et al. [6] loaded human and bovine motion segments in a combination of flexion, lateral bend, and axial twist where the bovine specimens were more

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susceptible to herniation (75%) than the older human tissue (0%). Less degenerated bovine specimens, possessing more hydraulic capability, would be more susceptible to herniation [9]. Also noteworthy were the human in vitro motion segments which were positioned in slight lateral bend with flexion to the elastic limit and cyclically loaded with a compressive force (which induced bending moments at the same time as compressive and shear loadings) [7,8]. No disc herniations were observed in the initial test condition [7]. By increasing the joint angle, as creep allowed, then increasing the compressive load once a stable position was achieved, six of 29 motion segments failed by nuclear protrusion. It has been suggested that the lumbar spine in vivo appears to have a margin of safety in forward bending [10] such that it may be unlikely that the postures required for failure in this mode would occur in vivo.

There have been few in vitro studies that have examined combined motion and load [11–13] suggesting motion warrants further study. Hardy et al. [13] used intact human lumbar spines (L1 to sacrum) with the posterior elements removed, which contribute resistance to flexion [14]. There were no disc herniations produced (without gross avulsion) with the maximum number of bending cycles required to failure reaching as high as 153 400. An additional four human lumbar motion segments were axial loaded off-centre to provide 0°–5° of flexion or 0°–4° of extension motions combined with compressive loads of 1000 N for a total of 1000 cycles at 0.25 Hz [12], but no failures were detected in any of the specimens tested. The most consistent development of disc herniation with repeated loading conditions was achieved by Gordon et al. [11]. In vitro human lumbar motion segments were flexed from a neutral posture to 7° of flexion with a small axial twist motion (<3°). All 14 of the motion segments examined failed with herniations of the intervertebral disc (either nuclear protrusion or extrusion) with an average of 40 000 loading cycles to failure. It appears that load, motion, degenerative condition, and repetition require further investigation as prerequisites to disc herniation.

The main purpose of this study was to determine the parameters necessary to consistently produce disc herniation. A secondary purpose was to examine the modulating effect of the magnitude of axial compressive force. Given the requirement for healthy young discs, controlled for age, degenerative level, size, diet, and physical activity, a porcine model was chosen.

2. Methods

The cervical spines of 26 porcine (age mean six months, weight mean 785 N) specimens (C1–C7) were obtained immediately following death. Pig cervical spines have been shown to be the section closest to human lumbar spines for anatomical and biomechanical characteristics [15]. The cantilevered head of the pig, unlike the human head and neck arrangement, is designed to accommodate ‘rooting’ behaviour which requires a large compressive load bearing structure with limited motion-similar to the human lumbar spine. All specimens were sealed in doubled polyethylene bags and stored at −20°C. Prior to testing, the frozen specimens were thawed in a refrigerator (+4°C) for 24 h [16]. Any residual coldness dissipated during dissection prior to testing. The surrounding musculature was then stripped leaving the osteo-ligamentous structures intact.

Specimens were then divided into two segments (two adjacent vertebral bodies and the intervening intervertebral discs) of C3–C4 and C5–C6. Only the C3–C4 motion segments were used for this study. The intervertebral discs of the sectioned ends of the specimens were examined for degeneration and were graded according to the scale proposed by Galante [17]. Only specimens that met the Grade 1 criteria were chosen for use (in this case-all of them). The remains of any soft tissue and discs were dissected from the cranial and caudal endplates. To assist in the documentation of progressive tracking of the nucleus leading to intervertebral disc herniation, a mixture of barium sulphate (radio-opaque), blue dye (Coomassie Brilliant Blue G-mix: 0.25% dye, 2.5% MeOH, 97.25% distilled water), and distilled water were mixed in a ratio of 2:1:2 and approximately 0.7 cm^3 was injected into the intervertebral disc’s nucleus. This mixture had sufficient resistance to diffusion over the duration of the test so that movement of the barium sulphate only occurred if a fissure was present. Specimens were then X-rayed prior to mounting to document the distribution of the nucleus in the sagittal and transverse planes. Specimens were fixed in aluminum cups using a non-exothermic dental stone (Denstone®, Miles, South Bend, IN, USA) and 19 gauge steel wires looped bilaterally around the anterior processes and the lamina of both vertebrae. Wood screws were also used to hold the specimen in the cup. The screws pierced the centre of the endplate and never protruded farther than 1 cm into the vertebral body. The fixation material covered the proximal half of the cranial vertebra and the distal half of the caudal vertebra. The mounted specimens were then placed in the testing fixture (Figs. 1(a) and (b)). The testing jig was designed to allow the centre of rotation to be moved and aligned (vertically and horizontally) with the geometric centre of the intervertebral disc at the initiation of the test. The torques applied were applied as a pure moment (not generated by a force-moment arm application) in the sagittal plane. The specimens were free to translate in the horizontal plane (X–Y table mounted beneath the specimen) and freely rotate about the vertical axis, which would allow the centre of rotation to move within the specimen during loading. This jig design allowed the

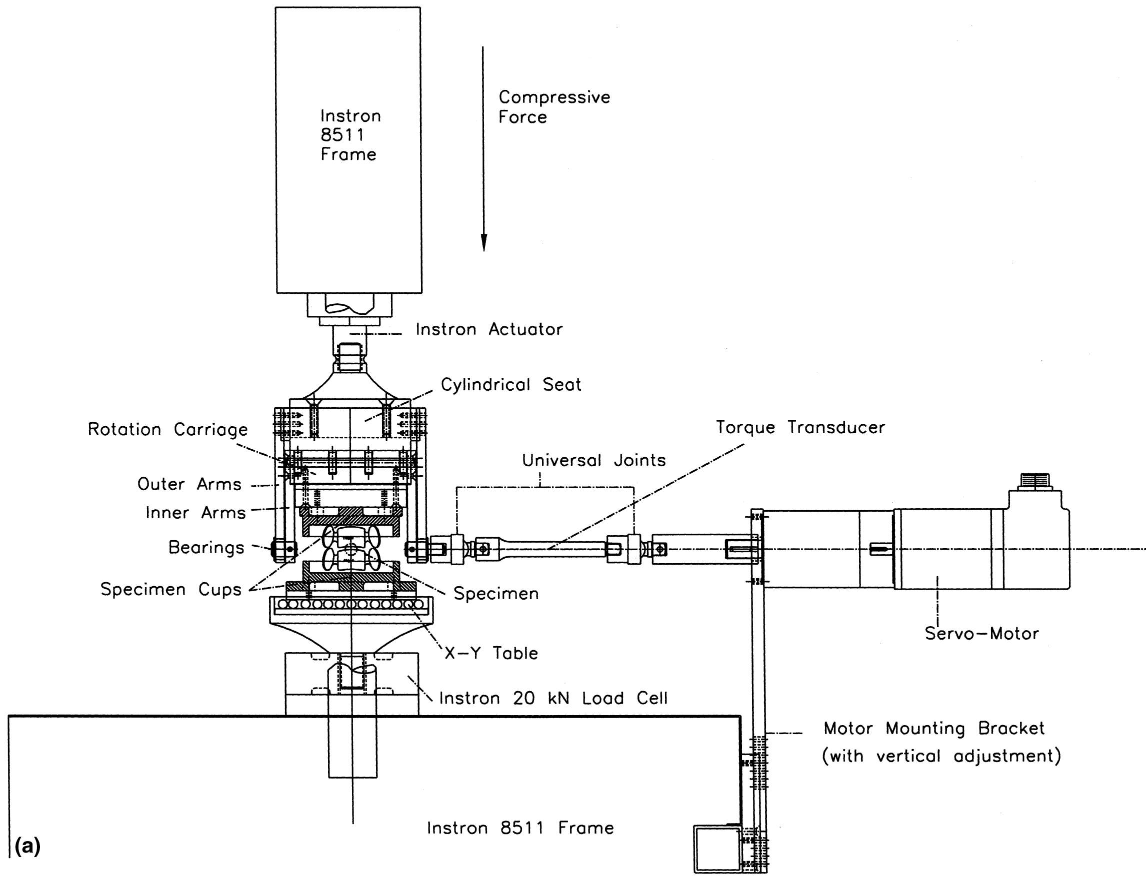

Fig. 1. Frontal (a) and sagittal (b) views of the test apparatus used to apply coupled axial compressive load and pure flexion extension moments to produce repeated flexion extension motions. The X–Y table permitted translations to better represent in vivo conditions.

specimens to deform axially in response to the applied compressive loads and only compressive loads with flexion/extension moments were applied. To prevent drying from exposure to room air specimens were wrapped in two layers of a cotton fibre plastic backed material that had been soaked in a physiologic saline solution with an additional third plastic film wrapped around the specimen. Testing was conducted in a warm environment of approximately 32.8°C (porcine body temperature approximately 39°C). A preload (260 N for 15 min) was applied to all specimens to counter any swelling that had occurred postmortem. During the preloading phase, the servomotor producing flexion/extension torques was set to zero and the angular position at the end of the preload was taken as zero position (elastic equilibrium) for each specimen. The specimens were then exposed to one of the three compressive loads examined in this study (260, 867, or 1472 N) using a servo hydraulic dynamic testing system (model 8511, Instron Canada, Burlington, Ont., Canada). Previous work using the same test apparatus and specimen population has resulted in a compressive strength of 10.5 kN in a neutral posture [18]. The moment versus angular rotation profile of each specimen was determined using four repeats of a range of motion test (RoM), flexion and extension, at a rate of 0.5°/s. The point where the torque versus angular position curve deviated from the initial linear section, similar to the neutral zone defined by Panjabi et al. [19], was chosen as the testing value (either angle or torque) for the dynamic test. The specimens were then cyclically loaded in either angular positional (rate of 45°/s) or torque control (rate was dependent on the sample and axial load, range of 10–44 $N \cdot m/s$) at a rate of 1 Hz to a maximum of 86 400 cycles using an electrical brushless servomotor (model BNR3018D, Cleveland Machine Controls, Billerica, MA, USA) and a 40:1 planetary gear head (model 34PL0400, Applied Motion Products, Watsonville, CA, USA). The servomotor was controlled using custom software which interfaced with an ISA bus motion controller (model DMC1701, Galil Motion Control, Mountain View, CA, USA). Torque was measured using a strain gauge torque transducer (model 01190-152, Sensor Developments, Lake Orion, MI, USA) and angular position data were obtained using an incremental optical encoder attached to the motor shaft (model LDA-048-1000, SUMTAK Corporations of America, Piscataway, NJ, USA). The angular position, torque, axial force, and axial defor-

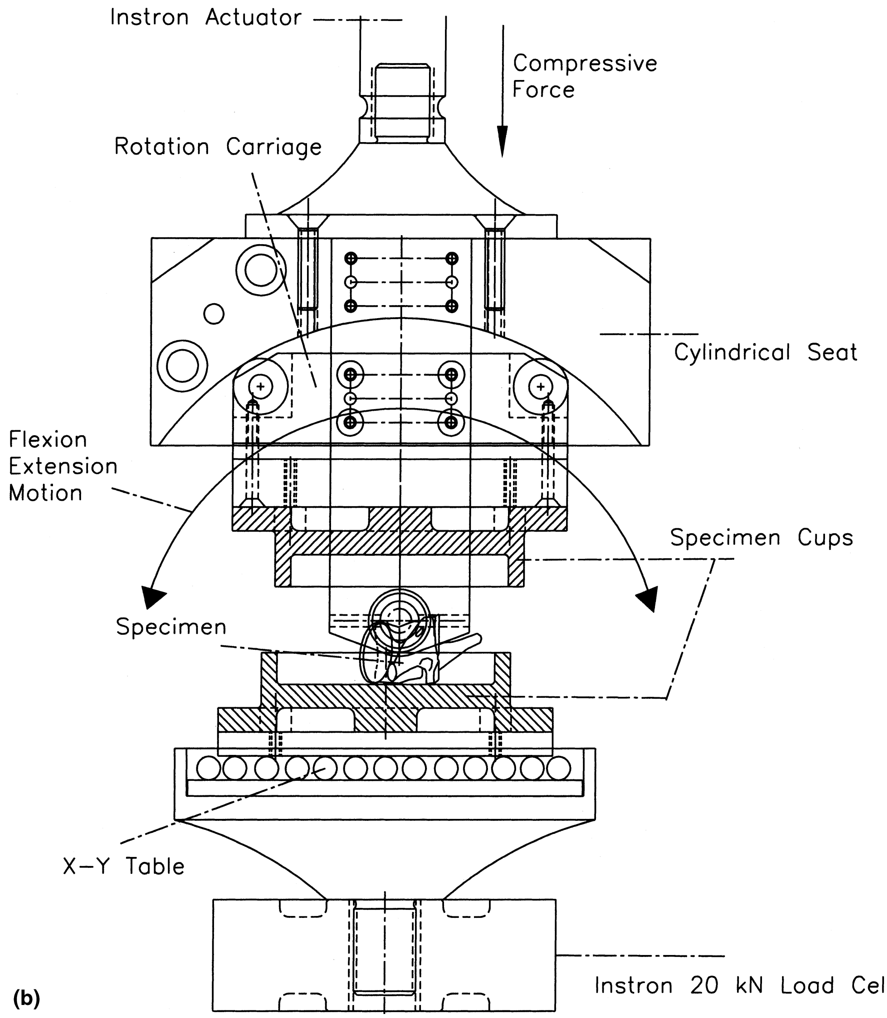

Fig. 1. (*Continued*).

mation were all A/D converted at a rate of 30 Hz for the full duration of each trial.

Following dynamic testing, four repeats of the RoM test were performed. The moments at the maximum angles achieved in the RoM test performed prior to dynamic testing were compared with the moments produced at the same joint angles from the RoM test following the dynamic testing. The specimens were X-rayed (note: several specimens were X-rayed at repeated intervals in an attempt to track disc herniations) following testing to document both sagittal and transverse plane structures. An examination of the ligamentous structure and posterior elements was conducted and any failure or damage recorded. Specimens were then dissected through the plane of the intervertebral disc and examined for any soft tissue damage, indicated by the blue dye injected prior to testing.

To determine the magnitude of angular rotations and joint torques that the C3–C4 porcine cervical joint could withstand one specimen was loaded to failure in flexion using the RoM test protocol at a rate of 0.5°/s. The specimen resisted a flexion moment of 61 N · m, an extension moment of −44 N · m, and had angular rotations of 39° and −24° in flexion and extension, respectively (note: the specimen was not taken to failure in extension due to range limits of the test setup). The intervertebral disc heights for porcine cervical spines had a pretest range of approximately 7–10 mm.

The data were reduced by pulling the peak values of the dependent variable (torque in angular positional control and angular position in torque control) in flexion and extension for each cycle of loading. The response of each specimen to the dynamic loading was examined by comparing the initial values of the dependent variable at the beginning of the test with the final values at the end of the dynamic test. Three beginning versus end values of the dependent variables were examined: peak flexion; peak extension; and range (peak flexion–peak extension). Additionally the average stiffness for the first cycle of loading was compared with the average stiffness during the last cycle. The dynamic motion segment axial creep was obtained by taking the axial displacement measured by the Instron at the zero position for specimens loaded in positional control for each cycle of loading. Since the specimens loaded in torque control tended to creep into a flexed posture, the joint angle closest to zero position that was present throughout the duration of testing was used to track axial displacement.

Data were analysed using one way analyses of variance (independent variable–axial compressive load, $\alpha = 0.05$) for tests that resulted in one measure per specimen (i.e., motion segment preload creep). Tukey's post hoc multiple comparisons were used to compare groups when a significant difference was found. Data that involved a repeated measure on a specimen (i.e., pre- vs post-dynamic test properties measured during the RoM test) were analysed using a split plot design ($\alpha = 0.05$) with a pre-post split within axial compressive load. Any significant finding of the main effects was tested post hoc using repeated *t*-tests.

There were no significant differences in the amount of motion segment creep sustained by any of the groups during the 15-min preload (Table 1). Additionally, the maximum flexion and maximum extension angles (Table 1), obtained during the RoM testing prior to dynamic testing, were not significantly different between any of the six groups suggesting successful assignment of specimens to produce homogeneous groups.

3. Results

Herniation occurred with modest levels of compression and flexion/extension moments but with a high number of motion cycles. Specimens tested in the lowest compressive force group (260 N) had nuclei that were intact after 86 400 flexion cycles (one of the five specimens demonstrated initiation of a posterior fissure that had not reached the outer boundary of the annulus). Increasing magnitudes of compressive load increased the likelihood that a herniation would develop (Table 1). All herniations that were created during testing occurred in the posterior or posterior-lateral areas of the annulus. The posterior herniation was clearly indicated in X-rays taken of specimens prior to and following testing (Figs. 2(a) and (b)). Additionally, upon post testing dissection the blue dye could frequently be seen during external examination of the posterior annulus following removal of the neural arch. A horizontal transection through the intervertebral disc revealed posterior displacement of the annulus and quite often a nuclear delamenation, indicated by the blue dye travelling circumferentially through the annulus. In contrast, specimens that demonstrated no failure had a nucleus that was still gelatinous and contained within the nuclear cavity even after 24 h of testing. X-rays taken at intervals during the testing session (Fig. 3) revealed that the annulus fibres failed first in the interior margin of the annulus at the junction between the endplate and annulus. The fissure progressed to the exterior border with an increasing number of cycles.

The only measure not significantly affected by the dynamic testing (beginning versus end effect) was the peak flexion angle of the torque control group, which demonstrated a slight increase in flexion angle over time for the 260 N condition (Table 1). All other parameters (flexion, extension, and range) within both the position and torque control groups were significantly changed with a minimum P value of 0.003 – decreases for torque control and increases for angular position control.

Increased axial compressive load demonstrated an increasing trend in axial deformation of the motion segments. The amount of axial creep was compared across the six groupings (Table 1). Only the 260 N vs 1472 N compressive load conditions within positional control were significantly different ($P < 0.01$). Both control groups exhibited an increased joint angular stiffness ($P < 0.0001$) during dynamic testing (Fig. 4). Additionally, increased magnitudes of compressive load resulted in significant increases in joint angular stiffness ($P < 0.0001$) (Fig. 4). The dynamic test had no significant effect on the flexion moments in the pre- vs post-RoM test, however, the extension moments were increased. Only the extension moments for the position control group were significantly altered ($P < 0.014$) by the dynamic testing.

4. Discussion

These data suggest that highly repetitive flexion/extension motions and modest flexion/extension moments, even with relatively low magnitude compressive joint forces, consistently resulted in intervertebral disc herniations. Larger axial compressive force resulted in more frequent and more severe disc injuries. Given the radiological documentation of progressive tracking of the nucleus, there is no doubt that disc herniation is a cumulative process that can result with modest forces if sufficient flexion/extension cycles are applied.

Lower magnitudes of applied compression increased survival time-cycles for disc injury. Specimens within the 260 N condition had only one of five specimens that demonstrated any disc injury, a tracking tear which had not reached the outer boundary of the annulus. The remaining four specimens had nucleus pulposus that were wholly intact and gelatinous after 86 400 cycles of loading. Interestingly, Goel et al. [20] also found that specimens exposed to low magnitude moments with very small compressive loads applied did not demonstrate failures after 9600 cycles. These data combined with ours suggest that increasing the magnitude of compressive load results in increased rates of disc injury. In

Table 1
Specimen data (mean and SD)[a]

Test group compressive load (N)	*n*	Number of cycles	Preload creep (mm)	RoM			Injuries [7]			Dynamic test			
				Peak flex angle (°)	Peak ext angle (°)	No damage	Track initiation	Herniation	Motion segment axial creep (mm)	Flexion		Extension	
										Begin	End	Begin	End
Torque control													
										(°)	(°)	(°)	(°)
260	3	77033	−1.53	21.17	−13.66	3	0	0	−4.50	6.18	8.19	−3.55	0.46
		(6025)	(0.36)	(0.38)	(2.30)				(0.77)	(1.09)	(0.18)	(1.42)	(0.53)
867	8	75670	−1.61	27.23	−16.34	2	2 stage 2	4 stage 3	−7.80	11.69	10.98	−3.82	3.53
		(22286)	(0.46)	(6.46)	(3.76)				(1.28)	(4.74)	(3.58)	(3.60)	(3.66)
1472	5	84220	−1.40	28.59	−11.86	1	0	4 stage 3	−7.86	16.12	12.58	−2.29	7.57
		(4875)	(0.32)	(0.63)	(1.80)				(1.20)	(3.16)	(4.06)	(1.04)	(2.80)
Angular position control													
										N · m	N · m	N · m	N · m
260	2	83700	−1.60	24.63	−12.13	1	1 stage 2	0	−5.21	3.94	5.17	−1.95	−6.08
		(3818)	(0.67)	(5.48)	(2.30)				(2.12)	(0.92)	(0.95)	(2.08)	(4.83)
867	4	70550	−1.28	22.13	−9.94	0	0	4 stage 4	−8.88	6.10	11.31	−4.02	−20.60
		(29477)	(0.13)	(1.33)	(3.24)				(2.48)	(1.40)	(2.33)	(2.51)	(2.94)
1472	4	34974	−1.43	24.25	−12.32	0	0	3[b] stage 4	−11.18	11.21	20.10	−3.03	−31.59
		(9549)	(0.31)	(1.59)	(5.92)				(2.17)	(2.53)	(3.68)	(1.85)	(3.13)

[a] Rotational measures use the following convention: positive values indicate flexion, negative values indicate extension.
[b] The fourth specimen was an endplate failure.

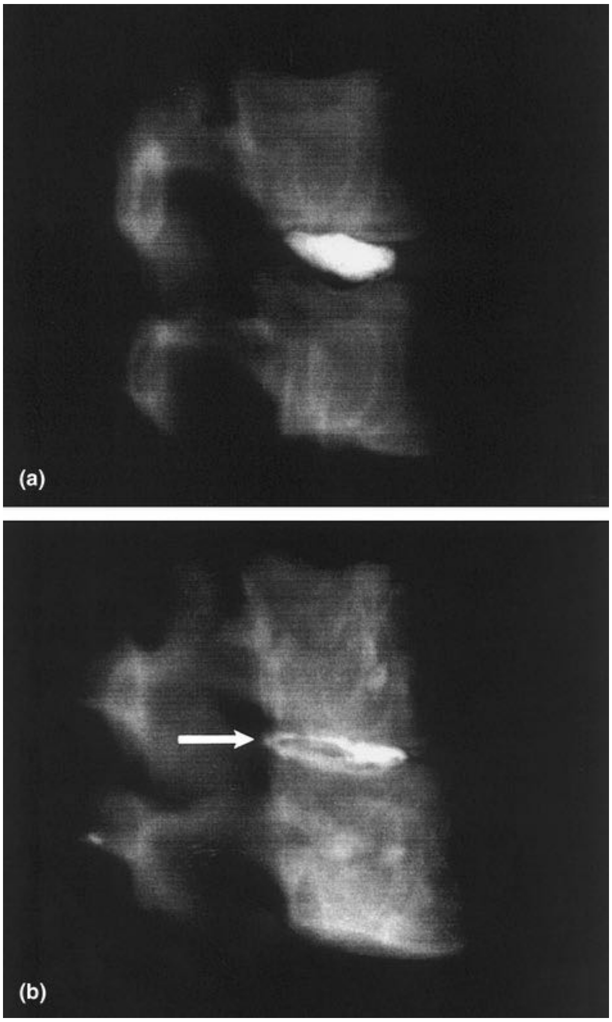

Fig. 2. An X-ray for one specimen from the angular position control group tested with a compressive load of 867 N, prior to (a) and following (b) repeated testing. The arrow indicates the posterior tracking of the radio-opaque dye indicating a herniation.

addition, the prevalence of herniations obtained in this study can partially be attributed to the use of only specimens with Grade 1 [17] intervertebral discs which have been shown to herniate more readily than more degenerated discs [9]. The failure of the annulus fibres at the endplate junction and the tracking of the fissure from the nucleus outwards agree well with the finite element modelling work done by Lu et al. [21].

Several limitations define the context of this work. The testing conditions were limited to flexion extension motions of the motion segments. While the spine moves with six degrees of freedom the largest motion present is in the sagittal plane (flexion/extension) which will provide the greatest strain to the intervertebral discs and other passive structures. The axial creep measured during the test session was measured across the entire motion segment and cannot be solely attributed to creep in the intervertebral disc. Some vertebrae showed bony damage, particularly in the higher compressive range, and one specimen had a clear endplate fracture which is indicative of damage to the trabecular structure of the vertebra and would result in a loss of overall motion segment's height. The use of porcine material to replicate postures and loads present in human loading must be reviewed. The porcine spine provides a reasonable analogue [15] of the human lumbar spine upon comparing: anatomical [22]; geometrical; and functional characteristics [15] which were found to be very similar to the human lumbar spine. In fact the pig neck is designed to bear large compressive forces (to support the cantilevered neck and "rooting" behaviour for foraging food) with modest capacity for motion – similar to the human lumbar spine but not the human cervical spine. Furthermore, healthy, young, matched human specimens are simply unavailable. While there is no question that the porcine model is simply a surrogate for human application it does offer the advantage of control over age, level of physical activity, diet, disc degeneration, and bone mineral content [5]. In terms of failure mechanics, the average bending moment (156 N·m) and flexion angle (20°) [23] at failure of human motion segments indicate larger stiffness than the porcine motion segments used in this study (61 N·m and 39° for one specimen). Perhaps the younger human spine is also more compliant (certainly the summary of Bogduk and Twomey [24] well document the increase in stiffness of the lumbar spine with age). Finally, some may equate the cyclic loading of this study with vibrational exposure but whole body vibration involves cyclic axial loading with small angular rotations. In contrast, this study examined moderate RoM with a fixed axial load such that one cannot make a link to whole body vibration exposure in humans.

The occurrence of intervertebral disc herniations in vivo reaches its peak in middle-aged individuals [9,25]. The degeneration of the annulus combined with a nucleus that is not completely fibrous presents the potential for the nucleus pulposus to breach the weakened annulus. This type of disc is typically classified as Class 2 [17]. The specimens used in this study (Class 1) were more representative of the adolescent human spine, which has a much lower occurrence of intervertebral disc herniations. The high number of cycles applied in a condensed period will undoubtedly result in some structural changes or degeneration of the involved tissues. This study has demonstrated that in healthy undegenerated discs mechanical loading can initiate, and propagate, an injury to the annulus that results in herniation if sufficient motion cycles are applied.

Regardless of the control method used, increases in stiffness were found for all test groups. The angular stiffness of all specimens increased as the specimens progressed through the loading trials. An increased stiffness of specimens during repeated dynamic testing

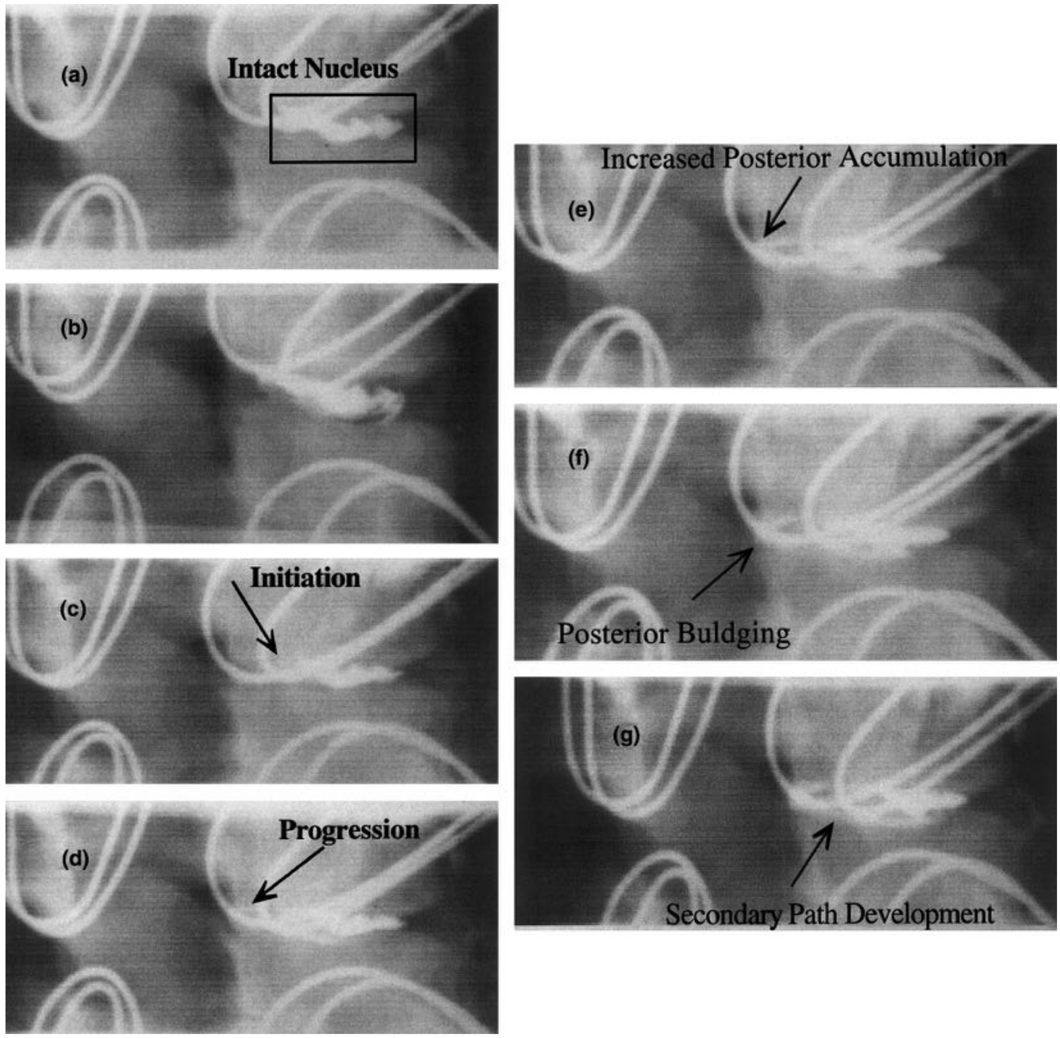

Fig. 3. Sequential X-rays taken on the same specimen illustrated in Figs. 2 (tested under angular position control with a compressive load of 867 N). (a) Prior to dynamic testing, (b) after 3850 cycles, (c) 5870, (d) 7800, (e) 10 000, (f) 12 000, (g) 14 600 cycles.

was also found in compression-flexion [20,26] and in axial compression [5] loadings.

The number of cycles applied to an in vitro structure must provide a realistic accumulation of in vivo loading. Brinckmann et al. [2] used a limit of 5000 cycles which they claimed represented an accumulation of industrial loading occurring in less than two weeks and implemented load magnitudes that ranged from 20 to 70% of the compressive strength of the specimen. The rationale behind using a two week cutoff was that repair of bone microfractures in vivo would not occur within this amount of time [2]. The proteoglycan turnover has been shown to take 500 days in dogs [27] and the collagen production to take even longer [9]. The only repair/modification mechanism that would alter the results in vivo would appear to be rest/sleep which would allow the resorption of fluid into the nucleus pulposus and the annulus. In contrast the compressive loads examined in this study were approximately 3–16% of the maximum compressive strength [28]. The moments (average of 14% of max) or rotations (average of 35% in flexion and 10% in extension of max) applied were also selected to load the specimens in the low level range which would not require straining the joints past their toe region. This loading scenario was chosen to be representative of low load repetitive tasks. Therefore, the number of cycles allowed in this study was set to a maximum of 86 400 which required a testing period of 24 h. Prolonged testing has been previously employed by other researchers, Hardy et al. [13] tested specimens for as long as five weeks (>1 million cycles) and Gordon et al. [11] tested to a maximum of 70 000 cycles over a 13 h period.

The notion that disc herniation is a progressive phenomenon where final extrusion of material appears to occur on the *n*th load cycle analogous to "the straw that broke the camels back" is consistent with the lack of a clear mechanical indicator of when disc injury occurred. All variables recorded were examined for the full time

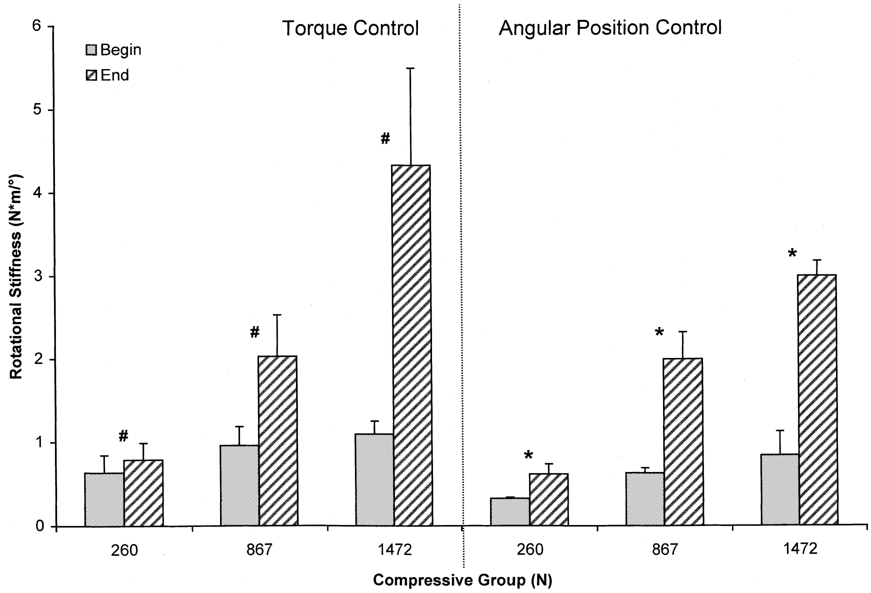

Fig. 4. Mean angular stiffness (+1 S.D.). Beginning versus end comparisons were significant for both torque and angular positional control ($P < 0.0001$). Comparisons of axial compressive load that were different within each control method ($P < 0.05$) are indicated with the same symbol.

course of testing. No acute or sudden changes were present to indicate a mechanical failure of the test specimen. Sequential X-rays (Fig. 3) of several specimens were taken which revealed a progression of injury. Using the cycle where injury initiated and where the outer annular boundary was compromised no changes were evident in the corresponding time series of the recorded variables. There were two potential methods for determining if injury had occurred. The motion segment axial creep end point in the angular positional groups (867 and 1472 N) which yielded more consistent and severe injuries had greater axial deformation (non-significant). The second test that could be useful in determining injuries was the RoM test. The angular position groups (867 and 1472 N) resulted in larger changes in the post RoM test than the corresponding torque control groups, particularly the extension moments. Both methods will require further examination paired with documentation of injuries (X-ray) to determine if they could indicate the occurrence of disc injury.

This study has shown that disc injuries and herniations can be developed during highly repetitive flexion/extension motions with modest moments and low magnitude compression With increased magnitudes of compressive load there was a corresponding increase in the number, and severity of disc injuries documented. Given our years of work loading spines in compression and shearing modes, with only the very rare observation of herniation, we have formed the opinion that high numbers of cyclic flexion extension produce cumulative damage and lead to progressive herniation. While there may be a tendency to identify an event that 'caused' an intervertebral disc herniation, this work together with our other experiments have led us to form the opinion that this is only a culminating event and that the real cause had already occurred.

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