



# Incorporating loading variability into *in vitro* injury analyses and its effect on cumulative compression tolerance in porcine cervical spine units



Jackie D. Zehr, Liana M. Tennant, Jack P. Callaghan\*

Department of Kinesiology, University of Waterloo, Waterloo, Ontario, Canada

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## ABSTRACT

During repetitive movement, low-back loading exposures are inherently variable in magnitude. The current study aimed to investigate how variation in successive compression exposures influences cumulative load tolerance in the spine. Forty-eight porcine cervical spine units were randomly assigned to one of six combinations of mean peak compression force (30%, 50%, 70% of the predicted tolerance) and loading variation (consistent peak amplitude, variable peak amplitude). Following preload and passive range-of-motion tests, specimens were positioned in a neutral posture and then cyclically loaded in compression until failure occurred or the maximum 12 h duration was reached. Specimens were dissected to classify macroscopic injury and measurements of cumulative load, cycles, and height loss sustained at failure were calculated. Statistical comparisons were made between loading protocols within each normalized compression group. A significant loading variation  $\times$  compression interaction was demonstrated for cumulative load ( $p = 0.026$ ) and cycles to failure ( $p = 0.021$ ). Cumulative compression was reduced under all normalized compression loads (30%  $p = 0.016$ ; 50%  $p = 0.030$ ; 70%  $p = 0.020$ ) when variable loading was incorporated. The largest reduction was by 33% and occurred in the 30% compression group. The number of sustained cycles was reduced by 31% ( $p = 0.017$ ), 72% ( $p = 0.030$ ), and 76% ( $p = 0.009$ ) under normalized compression loads of 30%, 50%, and 70%, respectively. These findings suggest that variation in compression exposures interact to reduce cumulative compression tolerance of the spine and could elevate low-back injury risk during time-varying repetitive tasks.

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## 1. Introduction

Cumulative compression loading in the lumbar spine is strongly associated with the development of low-back disorders (Coenen et al., 2013; Kumar, 1990; Norman et al., 1998). Previous *in vitro* studies have demonstrated that compression magnitude (Coenen et al., 2012; Parkinson and Callaghan, 2007b) and posture (Drake et al., 2005; Gooyers et al., 2012; Parkinson and Callaghan, 2009) influence cumulative load tolerance and thus alter low-back injury risk. However, a seemingly important loading characteristic yet to be incorporated into *in vitro* analyses is the inherent variability of successive compression exposures experienced during repetitive motor tasks (Beach, 2012; Beach et al., 2012; Granata et al., 1999; van Dieën et al., 2001). Intra- and inter-individual

low-back loading variation can result from adaptive movement strategies and is a debated feature of healthy and pathological spine systems (Claeys et al., 2011; Lorimer and Hodges, 2006; Marras, 2000). As such, knowledge about the effects of loading variability on cumulative compression tolerance could advance understanding of low-back injury mechanisms.

*In vitro* tests on functional spinal units (FSUs) have shown that repeated compression with a neutral posture frequently leads to fatigue failure in bone (i.e., endplate and/or vertebral fracture) (Parkinson and Callaghan, 2007b; van Dieën et al., 1999), while intervertebral disc injury (i.e., disc herniation) is expected when repetitive compression exposures are coupled with flexed lumbar postures (Callaghan and McGill, 2001a; Parkinson and Callaghan, 2009). Under compression loading, these injuries are thought to be a consequence of buckling in the supportive trabecular bone (Brinckmann et al., 1989; McGill, 2002; Moore, 2000) and delamination of the posterior annulus fibrosis resulting from posterior displacement of the nucleus pulposus (Callaghan and McGill,

\* Corresponding author at: Department of Kinesiology, University of Waterloo, Waterloo, ON N2L 3G1, Canada.

E-mail address: [jack.callaghan@uwaterloo.ca](mailto:jack.callaghan@uwaterloo.ca) (J.P. Callaghan).

2001a; Lu and Hutton, 1996), respectively. In many cases, these injuries were contrived in a laboratory via the application of cyclic compression wherein the peak cycle-to-cycle amplitude was fixed throughout the test duration and typically scaled to a percentage of the predicted ultimate compressive tolerance.

When, for example, performing full-body manoeuvres (e.g., lifting), the variation in compression exposures differs from the “representative” *in vitro* loading paradigm. Peak compression magnitudes arising from flexible movement behaviors are expected to fluctuate by 10–40% during moderately constrained repetitive tasks (van Dieën et al., 2001). Considering this variation, it is possible that the effects of mechanical loading induced by variable task performance may be an important and potentially overlooked loading feature when studying cumulative compression low-back injury mechanisms. Therefore, the purpose of this study was to examine the effect of peak compression variability on cumulative load tolerance of porcine cervical spine FSUs. It was hypothesized that variable compression loading would reduce cumulative tolerance and consequently the number of tolerated loading-unloading cycles. This investigation was designed to compare custom compression waveforms that were constructed to have an equal average peak compression magnitude and total cumulative load. The first waveform had consistent inter-cycle peak amplitudes and the second waveform had inter-cycle peak amplitudes that randomly varied about the specified loading magnitude.

## 2. Methods

### 2.1. Specimen preparation

Forty-eight FSUs (24 C3C4; 24 C5C6) were excised from porcine cervical spines that were acquired from an abattoir. Porcine FSUs were used as a surrogate for human lumbar FSUs due to the anatomical, functional, and biomechanical similarities (Busscher et al., 2010; McLain et al., 2002; Yingling et al., 1999). All specimens were kept frozen ( $-20^{\circ}\text{C}$ ) during storage and were thawed overnight prior to dissection of surrounding muscle and fat away from the osteoligamentous structure. Care was taken to preserve the posterior spinal elements, including the facets and surrounding capsule tissue during dissection. Specimen selection was based on the degenerative state of visible intervertebral discs. Quality of the exposed superior and inferior intervertebral discs was assessed using the grading scale developed by Galante (1967). Only non-degenerated specimens (Grade 1) were included in this investigation. Following dissection and assessment, digital callipers were used to measure the anterior-posterior depth (A) and the medial-lateral width (B) for calculation of endplate area using the equation for surface area of an ellipse ( $\pi/4 * A * B$ ) (Callaghan and McGill, 1995). The mean area of the two exposed endplates represented the tested FSU.

Specimens were placed between aluminum cups such that the midplane of the exposed intervertebral disc was parallel to the cup surface. The exposed endplates were mounted to the cups using dental plaster (Dentstone, South Bend, IN, USA) together with a partially inserted screw that perforated each cup and penetrated the endplate center. The aluminum cup fastened to the superior vertebra was mounted to a torque cell (T120-106-1 K, Sensor Data Technologies, Sterling Heights, MI) that was attached in series with the actuator of a servohydraulic materials testing system (Model 8872, Instron Canada, Toronto, ON) while the cup attached to inferior vertebra was placed over a bearing covered surface (Fig. 1). This experimental setup facilitated load application to the superior vertebrae and the four-point mounting of the superior aluminum cup to the torque cell prevented motion about the FSUs lateral bend axis.

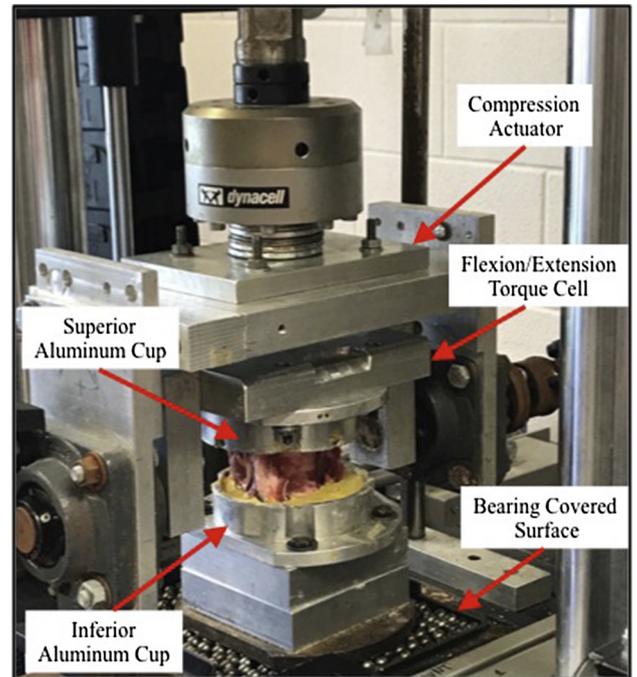
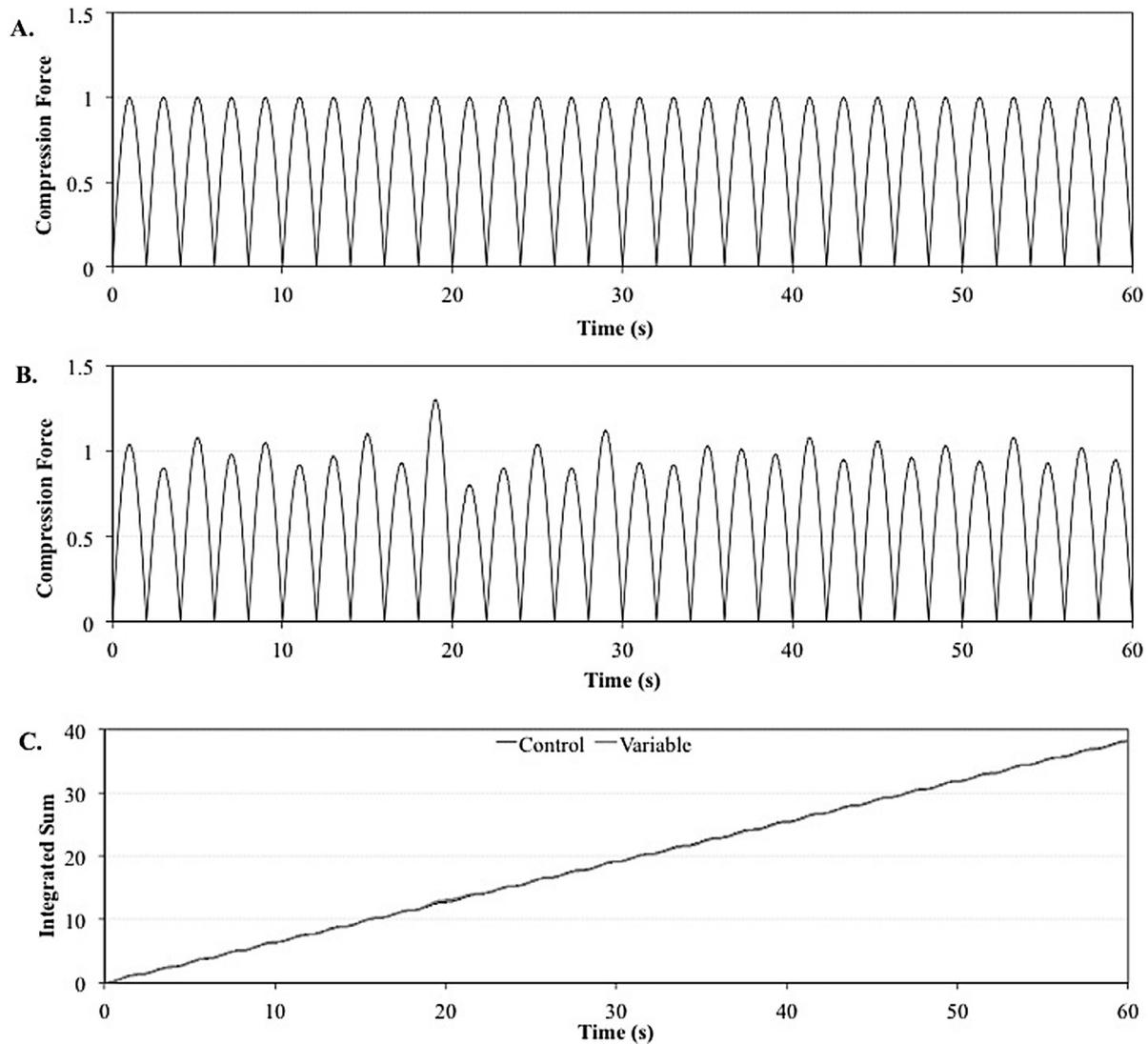


Fig. 1. Experimental setup and placement of the fixated FSU within the materials testing system.

### 2.2. Cyclic loading protocol

Prior to testing, specimens were preloaded with 300 N of compression for 15 min to eliminate post-mortem tissue swelling (Callaghan and McGill, 1995). During this preload test, a separate servomotor (AKM23D, Kollmorgen/Danaher Motion, Radford, VA) attached perpendicular to the flexion/extension torque cell rotated the FSU to a position of elastic equilibrium (i.e., the control program searched for a position minimizing the external moment) (Gunning et al., 2001). Specimen-specific range-of-motion was then determined by rotating the FSU about its flexion/extension axis ( $0.5^{\circ}/\text{s}$ ) while under a compression load of 300 N. Five repetitions of this test were performed to obtain the moment-angle histories. The average mid-point between the linear boundaries of the moment-angle curve obtained from the final three repeats of the flexion-extension test was taken as the FSU's neutral flexion/extension posture (Thompson et al., 2003). The neutral flexion/extension posture unique to each FSU was used and remained fixed for cyclic compression testing.

Each specimen was randomly assigned to one of six groups. These groups corresponded to compressive load (30%, 50%, and 70% of the estimated ultimate compressive tolerance (UCT)) and cyclic loading protocol (consistent amplitude, variable amplitude). The UCT of each FSU was estimated using a validated equation that is based on average endplate area (Parkinson et al., 2005). Both cyclic loading conditions consisted of a custom sinusoidal waveform that had a 2 s loading duration for a loading frequency of 0.5 Hz. The control waveform had consistent inter-cycle amplitudes while the variable waveform had inter-cycle amplitudes that randomly varied about the assigned mean normalized peak compression by a maximum of  $\pm 30\%$  (Fig. 2). This variation should not be construed as variation about the UCT estimation and was optimized to ensure a comparable cycle-to-cycle cumulative load with the consistent amplitude waveform (Fig. 2c). The selected variation range was estimated based on documented variability in joint compression during repetitive lifting (van Dieën et al., 2001) and established cumulative load weighting factors



**Fig. 2.** Consistent amplitude waveform (A), variable amplitude waveform normalized to a mean peak compression load of 1 (B), and the integrated sum of both waveforms (C). The mean peak compression and cumulative compression of each waveform were equal. The similarity in cycle-by-cycle cumulative load is demonstrated by the integrated sum of both waveforms plotted as a function of time. Both waveforms contained 30 loading-unloading cycles and were repeated until failure was detected. It should be noted that the example waveforms do not include the bias load (300 N) included during testing.

(Parkinson and Callaghan, 2007b, 2008). Both input waveforms were scaled based on the input average peak compression and a bias load of 300 N was included to represent the approximate mass of the human trunk during upright standing.

Cyclic loading was performed in load control until failure occurred or the maximum test duration of 12 h. (21,600 cycles) was reached. FSUs were encapsulated with plastic-backed saline soaked gauze in attempt to prevent specimen dehydration during the loading protocol. Throughout the loading protocol, compressive force and vertical displacement data were sampled at 10 Hz.

### 2.3. Failure analysis

The cycle at which failure occurred was identified by a step-like increase in displacement that was paired with a step-like decrease in average cycle stiffness (Parkinson and Callaghan, 2007b, 2008, 2009). Following the testing of specimens, dissection was performed to locate and classify the morphology of macroscopic vertebral failure. All fractures were classified as an endplate crack, step, stellate, or crush (Brinckmann et al., 1988; Gallagher et al., 2006). Specimens without visible evidence of failure were

classified as survivors. In addition to documentation of macroscopic failure, the following dependent measures were obtained: number of cycles to failure, absolute height loss at failure, and cumulative compression load to failure. Cumulative load was defined as the time integrated compression force and calculated using a trapezoidal integration technique. Height loss was determined as the absolute difference in baseline vertical displacement between the initial cycle and the cycle of injury. The employed method does not partition height loss due to bone failure from intervertebral disc height loss (Gooyers and Callaghan, 2015). Therefore, disc height was not recorded before or during testing and reported height changes represent the overall FSU height loss.

### 2.4. Statistical analyses

The following statistical analyses were performed using RStudio software (Version 1.0.136, RStudio Inc., Boston, MA, USA). To evaluate specimen randomization, a two-way analysis of variance (ANOVA) was used to assess group differences in endplate area and applied load magnitude. A separate two-way ANOVA was performed to examine the effects of compression magnitude (3 levels)

and loading variability (2 levels) on each dependent measure (described above). An additional unpaired *t*-test was conducted to examine mean differences between failed specimens exposed to the consistent and variable protocols within the 30% UCT group. This *posteriori* analysis was limited to the 30% UCT group since all specimens within the 50% and 70% UCT groups failed, meaning that differences between failed specimens were captured by the two-way ANOVA test. For all statistical analyses, alpha was set *a priori* to 0.05, and where applicable, a Tukey's *post hoc* test with Bonferroni corrections was performed.

### 3. Results

The results are presented for each dependent variable where a statistically significant effect was detected. Reported percentages refer to the relative change resulting from loading variation or compression magnitude. No significant main effect or interaction between compression magnitude and loading variation was detected for absolute height loss at failure ( $p > 0.086$ ).

#### 3.1. Randomization

Randomization was deemed effective given that no there were significant differences detected in endplate area nor mean peak compression magnitude between experimental groups (Table 1).

#### 3.2. Cycles to failure

A statistically significant interaction effect was detected for the number of cycles to failure ( $p = 0.021$ ). In each normalized compression group, the variable loading protocol led to a significant reduction in the number of tolerated cycles (Table 2). The most noteworthy reductions occurred at higher normalized compression loads, with a 72% ( $p_{adj} = 0.030$ ) and 76% ( $p_{adj} = 0.009$ ) reduction observed within the 50% and 70% UCT groups, respectively. The *posteriori* comparison of specimens with identified failure within the 30% UCT group revealed a statistically significant difference in cycles to failure between variation protocols ( $p = 0.032$ ). On average, failed specimens in the variable loading group fractured in 7915 cycles, which is approximately 3524 cycles fewer than FSUs assigned to the consistent loading group.

During consistent and variable compression loading, FSUs in the 30% UCT loading group withstood significantly more loading-

unloading cycles than FSUs assigned to the 50% UCT group [consistent = 13975 (85%); variable = 10656 (97%)], which tolerated significantly more cycles than FSUs subjected to a 70% UCT loading magnitude [consistent = 2461 (94%); variable = 699 (97%)] (Table 3).

#### 3.3. Cumulative compression

A statistically significant interaction effect was also observed for cumulative compression tolerance ( $p = 0.026$ ). FSUs that experienced consistent peak compression loading tolerated greater cumulative loads within all compression groups compared to the variable loading protocol at an equal average normalized peak load (30%  $p_{adj} = 0.016$ ; 50%  $p_{adj} = 0.030$ ; 70%  $p_{adj} = 0.020$ ) (Table 2). The absolute difference in cumulative compression between loading variation protocols was greatest within the 30% UCT group by a magnitude of 22.7MN-s, which equates to a 33% reduction during variable loading. Although, the relative differences in cumulative load tolerance were greater within the 50% (73%) and 70% (75%) UCT groups, the absolute reductions during variable loading were 12.1 MN-s and 0.6 MN-s, respectively. The *posteriori* analysis on specimens with identified failure within the 30% UCT group demonstrated a statistically significant difference in cumulative tolerance between loading protocols ( $p = 0.039$ ). The mean cumulative load tolerated by the fractured specimens in each group was 29.6 MN-s and 47.9 MN-s for the variable and consistent loading, respectively.

The magnitude of tolerated compression was significantly greater in the 30% UCT group than the 50% UCT group by approximately 52.5 MN-s (76%) during a consistent peak loading magnitude (Table 3). A significant difference of 15.9 MN-s (95%) was also noted between 50% UCT and 70% UCT loading during consistent peak compression exposures. A similar trend was observed for variable peak compression magnitudes. That is, the cumulative compression tolerance during the 30% UCT loading was 41.9 MN-s (92%) greater than the 50% group (Table 3). The cumulative compression tolerance was significantly greater during 50% UCT than 70% UCT loading by a magnitude of 4.4 MN-s (96%).

#### 3.4. Post failure analysis

Failure was detected in approximately 90% of the tested FSUs. In these 43 incidences, failure occurred within the vertebral endplate. Resulting endplate fractures with a crack morphology were observed most frequently (67%), while stellate (10%), step (8%),

**Table 1**  
Mean (standard deviation) endplate area and applied compression for the combinations of amplitude variability and normalized compression load (% UCT).

Loading protocol	Endplate area (mm <sup>2</sup> )						Compression force (kN)					
	30%		50%		70%		30%		50%		70%	
Consistent	726.6	(49.0)	726.7	(47.3)	720.0	(63.5)	3.3	(0.1)	5.3	(0.3)	7.7	(0.3)
Variable	727.5	(73.9)	729.4	(18.8)	720.9	(40.8)	3.4	(0.2)	5.3	(0.1)	7.8	(0.4)

There were no significant between-group differences between endplate area ( $p_{adj} > 0.05$ ).

There were no significant differences in applied compression force between amplitude variability conditions within each normalized compression group ( $p_{adj} > 0.05$ )

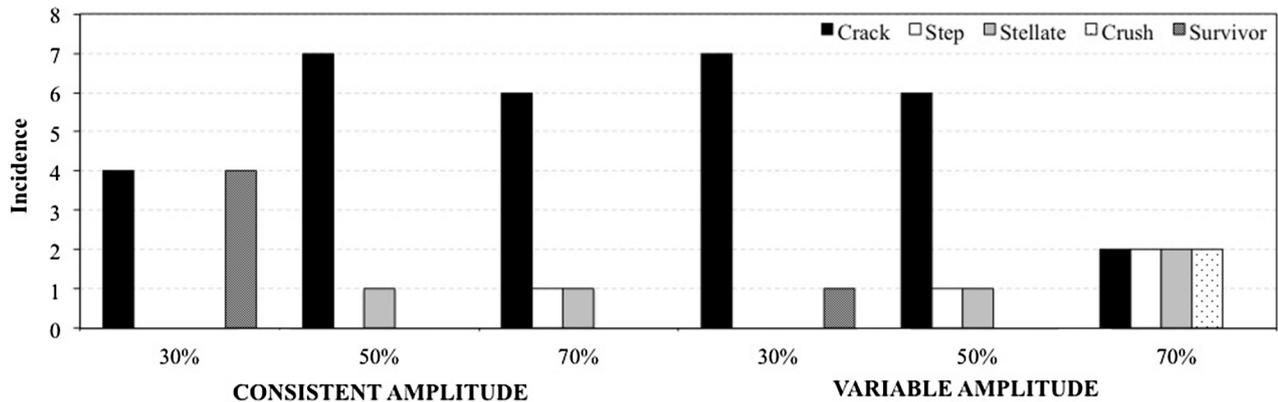
**Table 2**  
Dependent measures obtained at the cycle of failure during the consistent and variable loading protocols. All values represent the mean and the standard deviation is indicated in parentheses.

	Consistent						Variable					
	30%		50%		70%		30%		50%		70%	
Injury cycle (#)	<b>16519.5</b>	<b>(5865.0)</b>	<b>2543.6</b>	<b>(846.3)</b>	<b>82.5</b>	<b>(94.5)</b>	<b>11375.9</b>	<b>(6946.2)</b>	<b>719.9</b>	<b>(166.3)</b>	<b>20.0</b>	<b>(17.0)</b>
Cumulative load (MN-s)	<b>69.2</b>	<b>(24.7)</b>	<b>16.7</b>	<b>(5.1)</b>	<b>0.8</b>	<b>(1.0)</b>	<b>46.5</b>	<b>(29.2)</b>	<b>4.6</b>	<b>(1.6)</b>	<b>0.2</b>	<b>(0.1)</b>
Height loss (mm)	5.1	(1.1)	3.9	(2.8)	3.1	(2.1)	5.2	(2.1)	4.1	(1.9)	4.2	(2.2)

Boldface values indicate that a statistically significant mean difference ( $p_{adj} < 0.05$ ) was found between amplitude conditions (i.e., consistent vs. variable) of the same mean normalized peak compression load.

**Table 3**  
Adjusted *p*-values for between-compression group comparisons during the consistent (non-bolded) and variable (bolded) compression protocols. All comparisons were statistically significant ( $p_{adj} < 0.05$ ).

	Cumulative compression			Cycles to failure		
	30%	50%	70%	30%	50%	70%
30%	X	0.041	0.019	X	0.007	< 0.001
50%	<b>0.038</b>	X	0.009	<b>0.005</b>	X	0.010
70%	<b>0.023</b>	<b>0.036</b>	X	<b>0.001</b>	<b>0.004</b>	X



**Fig. 3.** Incidence of vertebral endplate fractures and their morphology for each experimental condition.

and crush (4%) fractures were limited to when the average peak normalized load was 50% or greater (Fig. 3). The incidence of fracture within the cranial and caudal endplate was approximately 60% and 28%, respectively and both endplates fractured in 12% of cases. For the five occurrences where fracture was observed within the cranial and caudal endplates, both fractures had crack morphologies.

A total of five FSUs tolerated the 12 h loading protocol (Fig. 3). All survivors were exposed to a mean normalized peak load of 30% UCT, with four FSUs undergoing the consistent protocol and one FSU experiencing the variable protocol. In all cases, evidence of intervertebral disc damage or prolapse was not observed.

#### 4. Discussion

Analysis of loading variation within normalized compression groups demonstrated that variable compression exposures reduced the cumulative load tolerated by intact neutrally positioned porcine cervical spine FSUs. The compression variation imposed in this study also effected the number of cycles to fracture occurrence in a similar manner. At the identified cycle of injury, height loss was not significantly different between variable and consistent loading, regardless of the normalized mean peak compression magnitude. Similar to previous studies (Parkinson and Callaghan, 2007b, 2008), an inverse relationship between compression magnitude and cumulative compression tolerance was demonstrated for both consistent and variable loading. Taken together, our findings suggest that peak low-back compression variation of up to 30% could increase injury potential during repetitive motor tasks.

The demonstrated effects of loading variation between successive loading exposures in the current study echo a similar point made previously by van Dieën and colleagues (2001). Despite the mean peak compression exposure remaining well within the margin of safety limits of what was an assumed fixed injury threshold, the cited research group proposed that a randomly incurred high compression exposure can exceed the tissue tolerance threshold,

thereby facilitating plastic deformation. This high load cycle was termed an “outlier” load and was incorporated into the variable loading protocol used in the current study at cycle 10 (Fig. 2b). The reported effects of the tested variation should be taken conservatively, as greater amounts of loading variation are expected to occur during less constrained motor tasks (van Dieën et al., 2001). Practically, the examined loading variation could represent flexible movement strategies for moderately constrained motor tasks or performance of prolonged and/or repetitive tasks associated with nominal low-back compression (e.g., sitting, bending, walking, running, carrying, light lifting etc.) (Alessa and Ning, 2018; Callaghan and McGill, 2001b; Callaghan et al., 1999; McGill et al., 2013; Zehr et al., 2018a; Zehr et al., 2018b) coupled with intermittent and abrupt performance of tasks associated with higher-risk low-back compression loads (i.e., heavy lifting, tool/equipment handling, patient transfer/repositioning, etc.) (Beach et al., 2012; Gooyers et al., 2018; Marras et al., 2009; Prairie et al., 2016).

Of the two common theoretical injury paradigms (i.e., acute vs. chronic) (Kumar, 2001; McGill, 1997), our findings point to an intermediate pathway for cumulative low-back injury. That is, a combination of repetitive sub-threshold loading (i.e., chronic) and random higher load exposures (i.e., acute) reduced cumulative compression tolerance in this study. A potential reason for the reduction in cumulative load tolerance observed with the variable loading protocol at all tested compression magnitudes may, in part, be explained by existing weighting factors, which are used to adjust compressive load magnitudes based on their potential for low-back injury development (Parkinson and Callaghan, 2007b, 2008). According to the non-linear relationship between weighting factors and normalized peak compression, the intermittent high compression cycles are associated with a larger weighting factor compared to the average peak compression quantity, and thus elevate cumulative injury risk. For example, this is highlighted by our results within the 30% UCT group, where a 30% variation from the average peak compression load of 3.4 kN (mean estimated UCT = 10.54 kN) led to peak compression exposures of 4.4 kN (i.e., outlier cycle), which equates to 41.9% UCT. These randomly

incurred high compression cycles exceed the 37.5% UCT weighting factor threshold and would therefore be adjusted by a factor that is greater than one for the assessment of cumulative compression injury risk.

Previous reports suggest possible benefits of biomechanical variability from inherent motor variation on musculoskeletal health (Davids et al., 2003; Hamill et al., 2012; Mathiassen, 2006). Given that a maximum force variation of a single magnitude was evaluated in the present study (i.e., 30%), the findings should not be interpreted as evidence for eliminating mechanical variation during repetitive movement, but rather, imply that an optimal amount of variation might exist, especially during repetitive moderate-to-high compression exposures. Though it was not explicitly examined in this study, further research may be warranted to understand and establish optimal variation bandwidths that could preserve and prolong low-back tissue health. This point also raises concern over loading exposure calculation approaches that rely on a single task cycle to quantify exposure and risk of injury.

Given that the tested FSUs were positioned in a neutral posture and lateral bend motion was restricted, the occurrence of endplate failure in all observed injury incidences was expected (Brinckmann et al., 1988; Gallagher et al., 2006; MacLean et al., 2007; McGill, 2002). For a given normalized average peak compression magnitude, the number cycles to failure recorded in this study were greater than previous findings (Hansson et al., 1987; Holmes and Hukins, 1994; Parkinson and Callaghan, 2007a), but within the reported variance ranges (Parkinson and Callaghan, 2007a). Feasible explanations for this include a longer testing duration (Hansson et al., 1987; Holmes and Hukins, 1994) and a possible 11% error in the equation used to predict UCT (Parkinson et al., 2005), which could over-/under-estimate applied compression loads. Further, in consideration of the overall height loss reported in this study, lumbar facet joints may have experienced greater stresses due to the possible intervertebral disc space narrowing (Dunlop et al., 1984). While facet failure was not observed in this study, Dunlop and colleagues (1984) opined that the associated elevation in facet joint stress could be a potential source of pain development. Normalized mean peak compression loads of >50% UCT resulted in the occurrence of stellate, step, and crush fracture morphologies. In addition to being associated with higher axial compression, these morphologies are related to high-grade disc quality and the absence of shear exposure (Gallagher et al., 2006), both of which were controlled for in the present study.

The authors acknowledge that this study is subject to two main limitations. The first limitation is the use of porcine cervical spine FSUs as a surrogate for human lumbar spine FSUs. Although differences exist, human and porcine spine FSUs have structural and functional similarities (Busscher et al., 2010; McLain et al., 2002; Oxland et al., 1991; Yingling et al., 1999), and the porcine model is commonly used for *in vitro* testing in attempt to control for the potential confounding effects of diet, age, size, and disease, thus enhancing sample homogeneity. Further, the mechanical fatigue response of the tested porcine FSUs is expected to be similar to that of a healthy human vertebrae given the documented architectural similarities in vertebral body trabecular bone supporting the endplate (Haddock et al., 2004; Lin et al., 1997). Though factors related to bone quantity (i.e., bone mineral content) and quality (i.e., osteoporotic tissue) can influence UCT (Brzoska et al., 2004; Burkein et al., 2001), these factors are not believed to have had an appreciable effect on the study outcomes. This is due to the fact that bone quality was indirectly accounted for in the employed method for predicting specimen-specific UCT and because porcine specimens were acquired at a mature adolescent age (i.e., 5–18 months) (Reiland, 1978).

The second limitation is that the continuous testing duration of 12 h did not account for the possible effects of physiological tissue

repair that may occur during rest periods from repeated compression exposures. Moderate rest has been identified as an important component for mitigating cumulative low-back injury risk (Marras et al., 2014), while extended periods of rest did not alter the tolerated cumulative load (Parkinson and Callaghan, 2007a). For the 70% UCT group, the possible effects of rest are believed to be negligible given that all specimens failed in <1000 cycles. A loading duration of 1000 cycles has been used previously to represent a single, one hour bout of repeated high-intensity exertion (Hansson et al., 1987). For the 30% and 50% UCT groups, the absence of recovery periods should be considered when interpreting the results. However, there is no known reason to believe that physiological repair processes would differ between consistent and variable loading exposures of the same magnitude. It is also important to note that potential postural changes related to muscular fatigue during repetitive task performance (Sparto et al., 1997) were not included in this study since a neutral FSU posture was maintained for the entire loading protocol. *In vivo*, fatigue has been shown to elicit greater lumbar flexion (Sparto et al., 1997) and isolated spinal units with higher amounts of flexion had a lower ultimate compressive strength (Gunning et al., 2001). Therefore, greater flexion associated with fatigue may have further reduced the number of tolerated cycles and type of failure observed in this study.

In summary, our findings suggest that the expected normal variation in spine loading during lifting may significantly reduce cumulative compression tolerance in the spine. The loading variation imposed in the current study also reduced the number of cycles to failure at each normalized compression magnitude, but a significant difference was not observed for height loss at failure. The most notable difference in cumulative load tolerance between consistent and variable loading conditions occurred within the 30% UCT group, and this difference may be explained by the possible effects of non-linear weighting factors for the evaluation of cumulative injury risk.

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## Conflict of interest

The authors have no conflicts of interest to declare including research and financial affiliation influencing any matter included in this manuscript.

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