

Regional trabecular morphology assessed by micro-CT is correlated with failure of aged thoracic vertebrae under a posteroanterior load and may determine the site of fracture

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Abstract

Introduction: Spinal mobilization is commonly used in the treatment of patients with back pain, including individuals with osteoporosis. Previous data indicated that traditional predictors of skeletal failure—lateral or anteroposterior bone mineral density (BMD) by dual energy X-ray absorptiometry (DXA) or geometry of the spinous process or vertebral body—do not predict failure load during posteroanterior spinal mobilization. Morphological differences and inhomogeneities in BMD may have important effects on vertebral strength but integral BMD values by DXA cannot reflect these potentially important differences. We investigated the determinants of spinal fracture using μ CT.

Materials and methods: We measured failure load and failure site in 11 T5–8 cadaveric specimens (mean age 78 years) when a posteroanterior load was applied at the spinous process of T6 using a servohydraulic material testing machine. Radiography and CT scan were used to verify failure site. We observed no damage to the adjacent T7 vertebrae following the T6 posteroanterior failure test. The T7 vertebrae were sectioned to produce regional samples of the spinous process, the lamina and a vertebral body core. Each sample was scanned with μ CT to measure bone microarchitectural parameters. We segmented and analysed four trabecular regions (spinous process base and middle, central lamina and central vertebral body). We used one-way repeated measures ANOVA to compare regions and computed Pearson correlations to assess the relation between PA failure load of T6 and the morphological parameters of T7.

Results: The BV/TV at the base or middle of the T7 spinous process (fracture sites), Tb.N and Tb.Th at the base were significantly correlated with posteroanterior failure load of T6 (BV/TV base: $r=0.74$, $p=0.01$; BV/TV middle: $r=0.73$, $p=0.01$; Tb.N base: $r=0.64$, $p=0.03$; Tb.Th base: $r=0.65$, $p=0.03$). The Tb.Th of the lamina was significantly greater than Tb.Th of the spinous process base ($p=0.002$).

Conclusions: Whereas previous data indicated that BMD by DXA was not a good predictor of posteroanterior failure load, regional BV/TV of the spinous process base and middle regions, the sites of fracture, are correlated with posteroanterior failure load. Trabecular thickness differed significantly between the base of the spinous process and the lamina, and may have influenced the site of fracture.

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Introduction

Manual therapy techniques such as spinal mobilization are commonly used by physical therapists, osteopaths and chiropractors in the treatment of back pain [1–4]. These techniques are also used in individuals with osteoporosis [5,6] despite clinicians' concerns about fracture as a complication of treatment [5]. There is evidence that spinal mobilization may be therapeutic in that it can reduce spinal pain [7–10], stimulate sympathetic nervous system activity [9–11] and promote motor activity [9]. One spinal mobilization technique used very commonly in clinical practice is posteroanterior (PA) mobilization [12–14]. It can be applied at an individual spinous process to produce extension [14,15] (Fig. 1). Our previous work suggests that the posterior elements are at risk under a PA load in the midthoracic spine of older adults with low bone density [15]. Specifically, when midthoracic cadaveric spine segments are subjected to a PA load simulating the PA mobilization technique, the spinous process is the site of failure [15] (Fig. 2).

For patients with osteoporosis, it is important to assess fracture risk prior to beginning potentially beneficial therapies such as spinal mobilization. Bone mineral density (BMD) by DXA is an obvious candidate for risk assessment, yet, despite its strong correlation with axial compressive failure load [16,17], BMD of the whole thoracic vertebra is not correlated with failure load during PA spinal mobilization [15]. BMD by DXA is an integrated measure of the entire vertebra, whereas these particular fractures occur in the posterior elements [15]. An integral BMD value cannot reflect potentially important differences in geometry, structure or inhomogeneities in density, which may all influence vertebral strength [18–20]. For example, trabecular microarchitecture also contributes to bone strength and fracture risk [20–23] and researchers have improved prediction of bone strength by including measures

of microarchitecture [24]. In recent years high-resolution digital imaging techniques, such as micro-computed tomography (μ CT), have permitted detailed quantitative nondestructive analysis of 3D microscopic bone structure [25,26]. Analysis of 3D μ CT images provides direct measurement of trabecular thickness (Tb.Th), trabecular number (Tb.N) and trabecular separation (Tb.Sp) which is model-independent [27]. Studies report high correlations between morphometric analysis performed with μ CT and conventional histology [25,28].

The relations between bone mass and vertebral strength in loading modes other than axial compression have not been well-established [29]. The controlled PA loading mode and reproducible fracture site provides a model which is well suited to the investigation of regions of damage and probable failure in bone. The spinous process has long been considered a site nearly devoid of trabecular bone. The micro-structural properties of the spinous process and lamina have not previously been examined, nor has their influence on bone strength, yet spinal mobilization is frequently applied at these sites. For example, during PA loading at the most posterior aspect of the spinous process of T6, as occurs during PA spinal mobilization, the posterior side of the spinous process base is primarily under tension and the anterior side is compressed resulting in a complex loading pattern. The thickness of the cortex in these two compartments (posterior and anterior) may be related to PA failure load [30]. Observing regional bone morphology may improve our understanding of the determinants of spinal fracture, such as why the vertebrae fractured at the spinous process as opposed to at the lamina. Using μ CT, it is now possible to measure regional vertebral trabecular morphology and cortical thickness and investigate the relation to bone strength.

Thus, the primary objective of this study was to measure morphological parameters, including trabecular bone volume ratio (BV/TV), Tb.N, Tb.Th, Tb.Sp and structure model index (SMI) using μ CT in four regions of thoracic vertebrae and to correlate those measures with PA failure load at the adjacent vertebra. This design is acceptable in that there is no evidence to suggest that PA failure load would differ significantly between T6 and T7 in the same spine segment. The specific aims were to (a) compare trabecular morphological measures of the spinous process base with that found at the central lamina and middle spinous process regions, as a possible determinant of the fracture site; (b) assess the relation between BV/TV of the central vertebral body with the spinous process base; and (c) measure cortical thickness in the posterior and anterior compartments of the spinous process base, and to correlate those measures with PA failure load.

Materials and methods

Eleven fresh-frozen (unembalmed) human cadaveric spines were obtained from our institution's Department of Anatomy. Sample size for this study was calculated assuming beta equal to 0.2 (power equal to 0.80) and alpha equal to 0.05 and was based on previous published data on the relationship between vertebral body compressive strength and vertebral BMD by DXA [16,17,31]. Assuming the correlation coefficient under the null hypothesis is 0.0 and the correlation coefficient under the alternative hypothesis is 0.80, the sample size

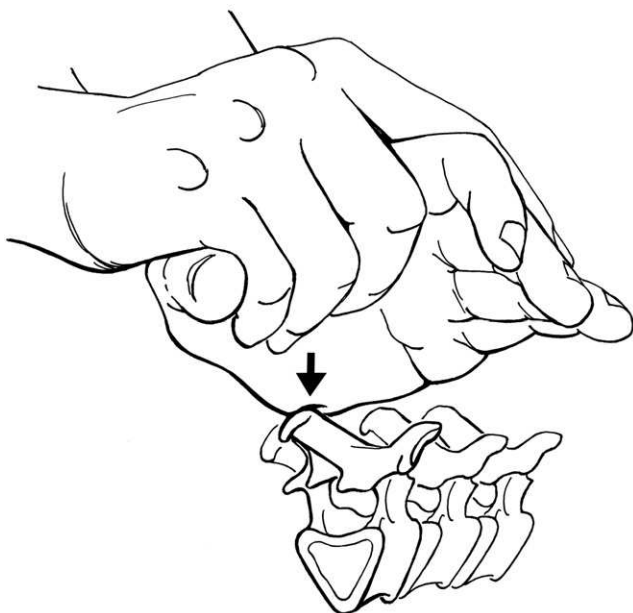


Fig. 1. Diagram of hand contact during posteroanterior (PA) mobilization in the midthoracic spine.

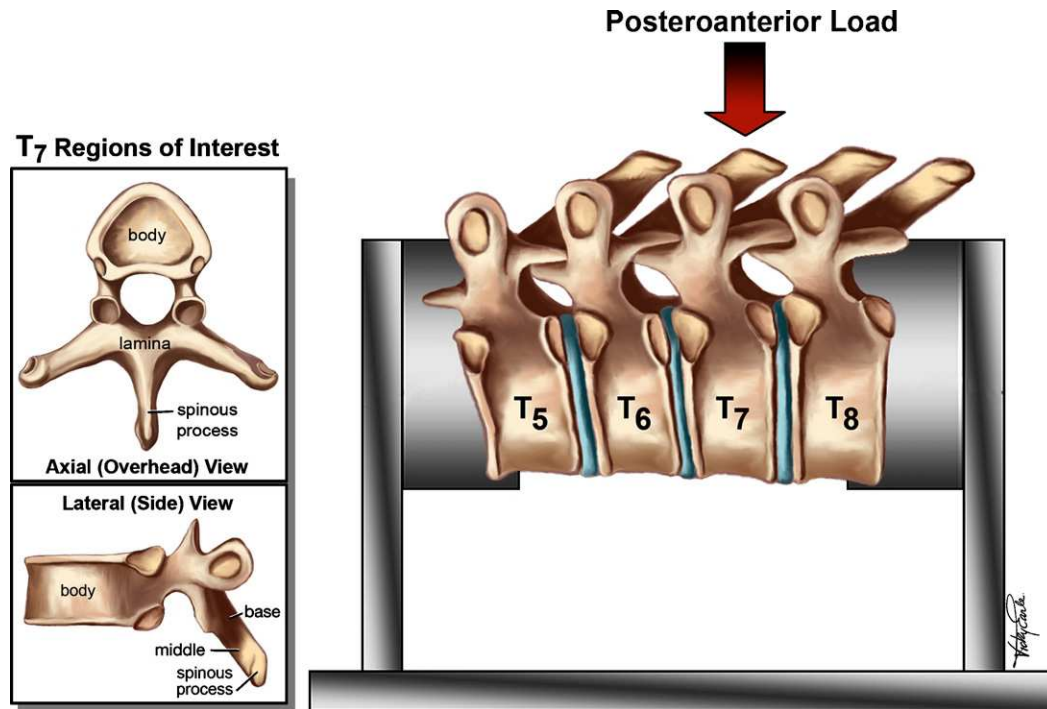


Fig. 2. Schematic of posteroanterior (PA) loading at the T6 spinous process in T5–T8 cadaveric spine segments and T7 regions of interest in the axial and lateral views. Fractures with PA loading occurred at the base or middle of the T6 spinous process. Trabecular bone was analyzed, using μ CT, in four regions of the adjacent T7 vertebrae: the vertebral body, the lamina and the base and middle of the spinous process. Cortical thickness was measured at the base of the T7 spinous process.

needed was 10. Specimen donors included five females, five males, and one of unknown gender. Age at death ranged from 62 to 93 years, mean 78 years. This study was approved by our Institutional Clinical Ethics Review Boards. Each specimen was dissected to isolate a segment consisting of T5–T8 with intact disc and ligaments. The isolated segments were stored frozen at -20°C until testing.

Lateral and AP radiographs were taken of each specimen prior to testing. No specimen showed any sign of malignancy. One specimen had a 20% wedge compression fracture of T8.

Mechanical testing

Steel (24 gauge) wire was secured to the pedicles of T5 and T8 of each spine segment. Each specimen was embedded in dental cement such that half of the vertebral bodies of T5 and T8 and the attached steel wire were fixed in cement. Thus, the T5 transverse processes were fully embedded and half of the T8 transverse processes were embedded. The T5–6 and T7–8 facet joints remained free, as did all parts of T6 and T7. The specimen was oriented horizontally in the testing machine (Instron 8874, Instron Corp. Canton, MA) to facilitate the PA load application (Fig. 2). The T5 and T8 specimen mounts were clamped rigidly, such that the T6 spinous process was aligned with the linear actuator of the machine. Load was applied through a circular delrin indenter (20 mm diameter, Young's Modulus 3.1 GPa), mounted on the end of the actuator. This indenter had a 7 mm diameter groove for the spinous process and 3 mm foam (PPT, Langer Biomechanics Group Inc, New York) was attached to the bottom of the indenter to enable a distributed load transmission and to prevent slipping of the spinous process. Each spine segment was loaded to failure at a displacement rate of 2 mm/s. Load was applied in the PA direction at the most posterior part of the spinous process of T6.

Immediately after failure, we used macroscopic observation, gentle dissection, and digital photography to identify and document the fracture. We repeated lateral and AP radiography using identical settings as in the pre-test films and they were reported by the same musculoskeletal radiologist for evidence of fracture. Each specimen was also scanned with CT using 1.3 mm helical scans at an image interval of 0.6 mm on bone algorithm (display field of view: 16 cm). We generated sagittal and coronal reconstructions on the scanner

to simulate the plain radiographs. All CT scans were reported by one neuroradiologist for evidence of fracture.

The T7 vertebra, the vertebra adjacent to the vertebra that was damaged in the PA loading test described above, was dissected and sectioned with a rotating diamond blade saw (ISOMET Low Speed Saw, Buehler; blade thickness=0.30 mm) to produce regional samples of the spinous process and the central lamina, and an 8 mm diameter core was extracted from each vertebral body.

Each sample was scanned with a high-resolution μ CT scanner (SkyScan 1072, SkyScan, Belgium), providing a nominal isotropic resolution of 15 μm . A 1-mm-thick aluminum filter was employed to minimize beam hardening artifacts. Each image series was passed through a median filter (5×5 cubic kernel using ImageJ v1.31) to partly suppress the noise in the original data. We segmented four trabecular regions for each T7 vertebra (spinous process base, spinous process middle, central lamina and central vertebral body) using a global threshold value to extract the mineralized bone phase. Fig. 3 shows the spinous process base and lamina of one specimen. Both the trabecular and cortical compartments are shown.

BV/TV [32], mean Tb.Th (mm) [27,33], mean Tb.N (per mm), mean Tb.Sp (mm) and SMI [32,34] for each region was measured using standard CT Analyser software (v1.2.35.3 SkyScan). SMI is a dimensionless index estimating the relative prevalence of rods and plates in trabecular bone where an ideal plate and rod have SMI values of zero and three respectively [32,34].

Cortical thickness of the spinous process base was measured from 2D images extracted from the 3D data volume. We measured cortical thickness of the posterior compartment of the spinous process base (the side under tension during PA loading) and also at the anterior compartment (the side being compressed during PA loading). Twenty-one images, each 10 slices apart, were measured and the mean cortical thickness was calculated. Thus this measurement spanned 200 slices, the same 200 slices that were used in the trabecular analysis. Test–retest reliability was conducted by performing three measurements at each of five sites in one specimen. Reliability ranged from 0.004 to 0.045 mm (mean 0.021 mm, S.D. 0.014 mm).

Statistical analysis was performed using Stata Release 9.0 (StataCorp, College Station, TX) and R (R Development Core Team, Vienna, Austria). We fit linear models to the data and computed Pearson correlations to measure the

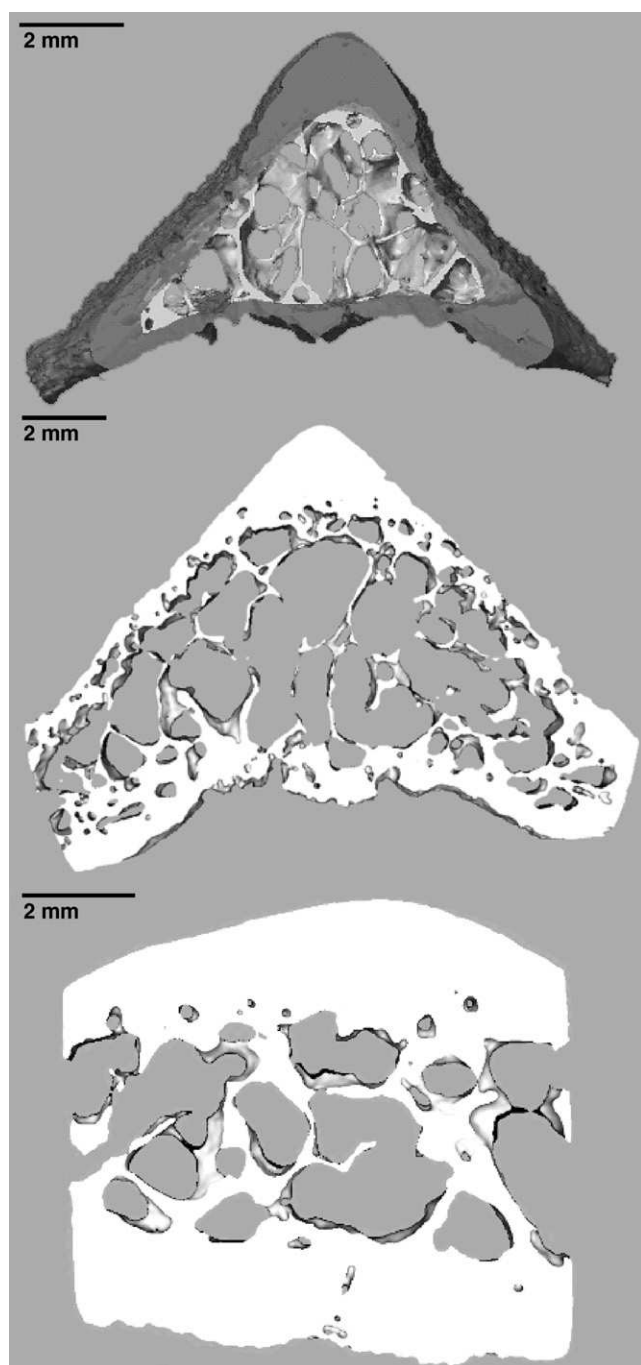


Fig. 3. Top: Three-dimensional image of the spinous process base, of one sample (15 μm nominal isotropic resolution). Both the trabecular and cortical regions are visualized. Middle and bottom: The spinous process base (middle) and lamina (bottom) of one specimen (15 μm nominal isotropic resolution). The posterior surface is superior in all three images.

linear relationship between PA failure load (N) and BV/TV, Tb.Th, Tb.N, Tb.Sp and SMI in each of the four trabecular regions, as well as PA failure load (N) and cortical thickness at the posterior and anterior spinous process base, at the midline. Pearson correlation coefficient was also computed to assess the relation between BV/TV of the central vertebral body and the spinous process base. In each case we performed diagnostic checks on the models. To assess whether the relation between failure load and each predictor was something other than linear we included a quadratic term in the model [35]; in no case did this approach significance. The residuals from the linear model were assessed graphically

using normal probability plots. No evidence of departure from normality was seen for any of the models. In an effort to better understand why the vertebrae fractured at the spinous process as opposed to at the lamina, we used one-way repeated measures ANOVA to compare trabecular BV/TV, Tb.Th, Tb.N, Tb.Sp and SMI in three regions (spinous process base, spinous process middle, and lamina) with region as the factor. Where the ANOVA was significant we used the paired *t*-test for post-hoc pairwise comparisons. We set the significance level at 0.05 a priori. For the post-hoc tests we applied a Bonferroni correction to correct for multiple pairwise comparisons. The Bonferroni correction gave us a new significance level of 0.016 ($0.05/3=0.016$).

Results

Failure load ranged from 200 to 653 N with a mean of 456 ± 148 N (S.D.). Macroscopic observation revealed fracture at the T6 spinous process in all 11 specimens. There was no evidence of damage to T7 in any specimen (by macroscopic observation, plain radiography or CT).

Range, mean and standard deviation for trabecular BV/TV, Tb.N, Tb.Th, Tb.Sp and SMI in each of the four regions (spinous process base, spinous process middle, central lamina, central vertebral body) is presented (Table 1). Mean cortical thickness of the anterior and posterior compartments of the spinous process base ranged from 0.18 to 1.34 mm (anterior) and 0.64 to 2.47 mm (posterior). Mean (S.D.) thickness was 0.65 mm (0.39 mm) and 1.64 mm (0.52 mm) for the anterior and posterior cortex, respectively.

Correlation between PA failure load and the structural parameters measured is presented (Table 2). The BV/TV at the base (Fig. 4) or middle of the T7 spinous process (fracture sites) was significantly correlated with PA failure load of T6. Tb.N and Tb.Th at the spinous process base was also significantly correlated with PA failure load. Tb.Sp at the middle of the spinous process was inversely correlated with PA failure load. BV/TV of the central vertebral body was not significantly correlated with BV/TV of the spinous process base ($r=0.60$, $p=0.05$). There were no statistically significant correlations between PA failure load and SMI, anterior or posterior cortical thickness (Table 2).

There was a trend toward decreased BV/TV from the spinous process to the lamina (linear contrast $p=0.03$). Tb.Th in each of the four regions is shown (Fig. 5). Further comparison of Tb.Th with the paired *t*-test revealed a significant difference between the spinous process base and lamina ($p=0.002$).

Discussion

The morphological analysis based on μCT showed that BV/TV of the base and middle regions of the spinous process was correlated with failure when the spinous process was subjected to a PA load. This controlled skeletal model also has clinical relevance as it simulates the commonly-used therapeutic PA spinal mobilization technique. We note that the lower Tb.Th of the spinous process base compared with the lamina may have influenced the site of fracture.

These findings extend previous investigations as the integral vertebral body BMD measured by DXA was not correlated with failure load of the spinous process [15]. That finding, taken

Table 1

Range, mean and standard deviation for trabecular BV/TV, Mean Tb.Th (mm), Mean Tb.N (per mm), Mean Tb.Sp (mm) and Structure Model Index (SMI) for each of the four trabecular regions analysed of 11 cadaveric vertebrae

Region	BV/TV			Mean Tb.Th (mm)			Mean Tb.N (per mm)			Mean Tb.Sp (mm)			Mean SMI		
	Range	Mean	S.D.	Range	Mean	S.D.	Range	Mean	S.D.	Range	Mean	S.D.	Range	Mean	S.D.
Base	0.068–0.217	0.131	0.046	0.136–0.227	0.169	0.032	0.533–1.067	0.770	0.159	0.827–1.231	1.010	0.135	1.23–2.07	1.53	0.27
Middle	0.080–0.211	0.144	0.034	0.136–0.230	0.175	0.028	0.533–1.000	0.836	0.161	0.824–1.291	0.961	0.130	1.21–2.75	1.60	0.45
Lamina	0.115–0.265	0.160	0.039	0.146–0.246	0.198	0.027	0.600–1.333	0.818	0.202	0.710–1.276	0.991	0.141	0.98–1.86	1.40	0.29
Body	0.041–0.222	0.108	0.059	0.105–0.225	0.154	0.035	0.400–1.133	0.667	0.237	0.591–1.203	0.929	0.202	0.86–2.02	1.65	0.38

together with the results of this investigation, suggests that scientists and clinicians should not rely on bone mass measures from the vertebral body if they seek information about the spinous process. Our results are relevant to both clinicians using spinal mobilization techniques applied to the spinous process and also to spinal fixation and implant research. In both of these cases DXA is often used to gain insight into vertebral strength. The results of this study suggest that trabecular bone mass and thickness at the spinous process and lamina is related to the strength at these sites, despite previous results indicating that traditional AP or lateral DXA results are not suitable for predicting strength in these regions. With respect to spinal fixation, our results extend the findings of Coe et al. [36] who found a significant correlation between BMD by DXA and loads to failure for transpedicular screws and spinous process wires, but no significant correlation between BMD and load to

failure for laminar hooks. Furthermore, the results of this study, using micro-CT, suggest that vertebral body trabecular BV/TV is not significantly correlated with trabecular BV/TV of the spinous process.

A strength of this study was the use of 3D image analysis by μ CT which allowed direct measurement of trabecular thickness, number and separation that is model-independent [32]. This avoids model-dependent errors associated with 2D analysis [32,37], and avoids errors that occur with planar methods such as DXA. Although the resolution for clinical CT scanners is improving [38], the required dose for resolving microarchitecture precludes a detailed morphological analysis of bone microstructure in the spine.

Our aim was to study the PA spinal mobilization technique that can be applied at a faster rate than we applied, but it is still slow as compared with manipulation. However, our aim was not only to measure the failure load but also to investigate the site of failure under a PA load. Due to the short delay in stopping the test once fracture occurred, a faster loading rate would have resulted in further damage between the time of initial failure and the time that the machine was stopped. Thus, our loading rate allowed for simulation of the mobilization technique but also allowed sufficient control of the experiment.

Cortical thickness of the spinous process did not predict PA failure load. Our results suggest high variability in cortical thickness in both the anterior and posterior cortex. It is possible

Table 2

Pearson correlations coefficients, with 95% confidence intervals, for postero-anterior (PA) failure load and structural parameters (BV/TV, Tb.Th, Tb.N, Tb.Sp, SMI) in each trabecular region (Base=spinous process base; Mid=spinous process middle; Lamina=central lamina; Body=central vertebral body), and cortical thickness (Ct.Th; anterior and posterior cortex at the spinous process base) in cadaveric vertebrae

Variable and region	Correlation with PA failure load (N)	
Base	r (95% CI)	
BV/TV	0.74 (0.25, 0.92)	0.01
Tb.Th	0.65 (0.08, 0.89)	0.03
Tb.N	0.64 (0.06, 0.89)	0.03
Tb.Sp	−0.40 (−0.80, 0.26)	0.23
SMI	0.00 (−0.59, 0.59)	0.90
Posterior Ct.Th	0.14 (−0.50, 0.68)	0.69
Anterior Ct.Th	0.51 (−0.12, 0.84)	0.11
Mid		
BV/TV	0.73 (0.23, 0.92)	0.01
Tb.Th	0.50 (−0.14, 0.84)	0.12
Tb.N	0.46 (−0.19, 0.83)	0.16
Tb.Sp	−0.61 (−0.88, −0.01)	0.048
SMI	0.00 (−0.59, 0.59)	0.84
Lamina		
BV/TV	0.57 (−0.04, 0.87)	0.07
Tb.Th	0.32 (−0.34, 0.77)	0.33
Tb.N	0.43 (−0.22, 0.81)	0.19
Tb.Sp	−0.51 (−0.84, 0.12)	0.11
SMI	0.01 (−0.59, 0.60)	0.80
Body		
BV/TV	0.44 (−0.21, 0.82)	0.17
Tb.Th	0.55 (−0.07, 0.86)	0.08
Tb.N	0.32 (−0.34, 0.77)	0.33
Tb.Sp	−0.52 (−0.85, 0.11)	0.10
SMI	0.00 (−0.59, 0.59)	0.95

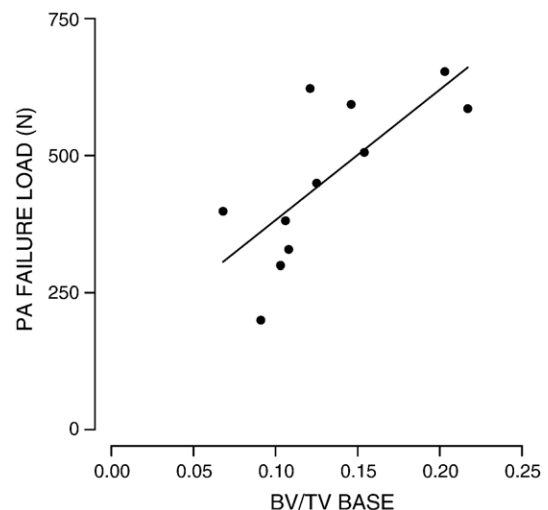


Fig. 4. Relationship between bone volume/total volume (BV/TV) of the base of the T7 spinous process and posteroanterior (PA) failure load (N) of T6 for 11 cadaveric spines. $r=0.74$, $p=0.01$.

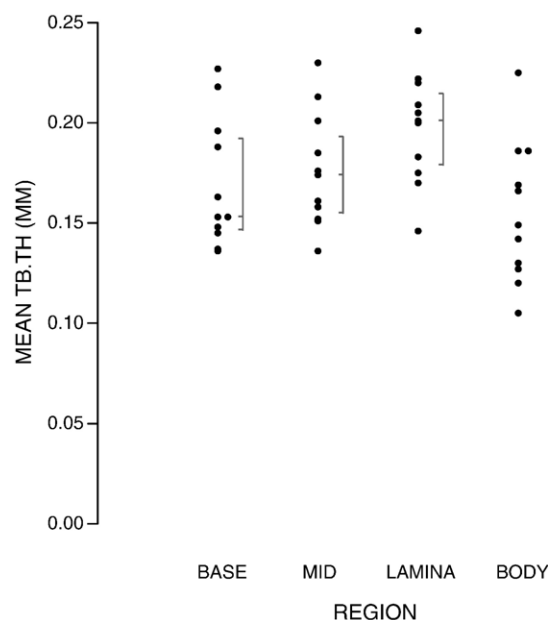


Fig. 5. Dot plot of trabecular thickness (Tb.Th; mm) in four regions of 11 specimens: spinous process base (Base), spinous process middle (Mid), lamina and vertebral body (Body). ANOVA was used to compare the spinous process base, middle and the lamina (median, lower and upper quartiles are marked). There was a significant difference.

that other spinous process cortical measures, such as cortical porosity, may predict PA failure load even though cortical thickness did not. We could not measure cortical porosity because the large size of our samples provided inadequate resolution of cortical pores. Cortical thickness in the compressed anterior compartment was more strongly correlated with PA failure load than posterior cortical thickness, although this was not statistically significant, and warrants further investigation with a larger sample size. It is also possible that PA failure load is related to a combination of trabecular and cortical bone mass and structure, and this could be tested in a larger study.

A limitation of this study was that we studied PA failure of T6 vertebrae and then investigated whether regional vertebral morphology of T7 vertebrae predicted T6 failure load. Clearly, mechanical testing and measures of morphology on the same vertebrae would have been ideal, but that was not possible because T6 was damaged. The presence of this damage to the bone precluded a meaningful measurement of the bone morphology. However, although vertebral compressive strength has been shown to increase caudally [17,39] due to the increase in the cross-sectional area of the vertebral end-plate [39], there is no evidence to suggest that PA failure load would be significantly different between T6 and T7. Further, bone mineral content (BMC) and BMD, as measured by DXA, also gradually increase caudally in the midthoracic spine but, as we found previously, lateral and AP DXA are not good predictors of spinous process failure load [15].

Whereas previous data indicated that BMD by DXA was not a good predictor of PA failure load [15], the results of this study suggest that regional BV/TV of the spinous process base and

middle regions, the sites of fracture, are correlated with PA failure load. It is noteworthy that trabecular thickness differs significantly between the base of the spinous process and the lamina, and may have influenced the site of fracture.

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