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Regional variation in vertebral bone morphology and its contribution to vertebral fracture strength

P.A. Hulme [a,*], S.K. Boyd [b], S.J. Ferguson [a]

[a] *MEM Research Center, University of Bern, Stauffacherstrasse 78, CH 3014, Bern, Switzerland*
[b] *Schulich School of Engineering, University of Calgary, Calgary, Alberta, Canada*

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Abstract

Vertebral fractures may result in pain, loss of height, spinal instability, kyphotic deformity and ultimately increased morbidity. Fracture risk can be estimated by vertebral bone mineral density (BMD). However, vertebral fractures may be better defined by more selective methods that account for micro-architecture.

Our aim was to quantify regional variations in bone architecture parameters (BAPs) and to assess the degree with which regional variations in BAPs affect vertebral fracture strength. The influence of disc health and endplate thickness on fracture strength was also determined.

The soft tissue and posterior elements of 20 human functional spine units (FSU) were removed (T9 to L5, mean 74.45±4.25 years). After micro-CT scanning of the entire FSU, the strength of the specimens was determined using a materials testing system. Specimens were loaded in compression to failure. BAPs were assessed for 10 regions of the vertebral cancellous bone. Disc health (glycosaminoglycan content of the nucleus pulposus) was determined using the degree of binding with Alcian Blue.

Vertebrae were not morphologically homogeneous. Posterior regions of the vertebrae had greater bone volume, more connections, reduced trabecular separation and more plate-like isotropic structures than their corresponding anterior regions. Significant heterogeneity also exists between posterior superior and inferior regions (BV/TV: posterior superior 12.6±2.8%, inferior 14.6±3%; anterior superior 10.5±2.2%, inferior 10.7±2.4%). Of the two endplates that abutted a common disc, the cranial inferior endplate was thicker (0.44±0.15 mm) than the caudal superior endplate (0.37±0.13 mm). Our study found good correlations between BV/TV, connective density and yield strength. Fracture risk prediction, using BV/TV multiplied by the cross sectional area of the endplate, can be improved through regional analysis of the underlying cancellous bone of the endplate of interest (R^2 0.78) rather than analysis of the entire vertebra (R^2 0.65) or BMD (R^2 0.47). Degenerated discs lack a defined nucleus. A negative linear relationship between disc health and vertebral strength (R^2 0.70) was observed, likely due to a shift in loading from the weaker anterior vertebral region to the stronger posterior region and cortical shell.

Our results show the importance of considering regional variations in cancellous BAPs and disc health when assessing fracture risk.

Keywords: Micro-CT; Vertebral body; Trabecular bone; Microstructural properties; Regional variation

Introduction

Osteoporosis is estimated to afflict 200 million women worldwide [1]. In the US alone, osteoporotic fractures are estimated to affect 24 million individuals. 1.5 million new fractures, nearly half of which are vertebral (700,000), are reported each year, outnumbering fractures of the hip and ankle combined [2–5]. Vertebral fracture may result in pain at the fracture site, loss of height due to vertebral collapse, spinal instability and in many cases a kyphotic deformity [6]. Chronic pain and kyphotic deformity may lead to depression, decreased appetite (leading to poor nutrition), decreased pulmonary function, impaired mobility and a reduction in the quality of life, the ultimate result being a significant increase in morbidity [7–10]. The World Health Organization defines osteoporosis as a bone mineral density (BMD) of more than 2.5 standard deviations below the mean of a young healthy reference population of the same gender. However, BMD only partially determines fracture risk [11]. Various investigators have found that bone quality, and hence fracture

* Corresponding author. Fax: +41 31 631 5960.
E-mail address: Paul.Hulme@MEMcenter.unibe.ch (P.A. Hulme).

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risk, is independent of BMD, as determined through dual energy X-ray absorptiometry (DEXA), and have suggested a role for micro-architecture, turnover, damage accumulation and mineralization [12–17]. DEXA itself does not account for regional variability in bone quality or vertebral geometry and may include structures that do not add to the mechanical strength of the vertebra, including posterior elements and osteophytes [18]. Furthermore, osteoporosis drug treatment strategies have shown poor correlations between BMD and the risk of vertebral fracture [19–24]. Hence, vertebral fracture risk may be better defined by more selective methods.

Regional vertebral morphology has been examined using histological methods [11] or using micro-CT measurement of bone cores [25,26], but few studies consider the analysis of the vertebral body as a whole [27]. Bone volume for vertebrae has been determined to be between 6.5% and 16% [11,15,25,28]. Observed age-related architectural changes to the cancellous bone include: a decrease in bone volume compared with the total vertebra volume (BV/TV), a shift from plate-like trabeculae to more rod-like structures (SMI), a decrease in connectivity density (Conn.D), an increase in orientation of trabeculae along the axis of principle loading (DA), an increase in trabecular separation (Tb.Sp) and a corresponding decrease in trabeculae number (Tb.N) [11,29–31]. Trabecular thickness (Tb.Th) has been reported to increase or decrease with age [11,31]. An increase in trabecular thickness has been explained as either adaptive remodeling of the remaining vertical trabeculae or removal of the thinner struts resulting in an increase in mean trabecular thickness [15,26,32]. The etiology of these structural changes remains unclear, whether it is excessive osteoclastic resorption or incomplete osteoblast activity resulting in perforation and thinning of trabecular elements [31,33,34]. However, the net result is a reduction in vertebral fracture strength.

The aim of this study was to describe the regional morphology of the elderly human thoracolumbar vertebra using micro-CT and to relate its derived bone architecture parameters (BAP) to vertebral failure. The micro-CT gantry allows for entire functional spine units (FSU) to be scanned non-destructively, allowing subsequent material tests to be performed using physiologically relevant loading configurations. We hypothesize that the bone architecture parameters (BAP) of the less dense anterior and central vertebral body regions will be a better predictor of failure than those of the whole vertebra or DEXA measurements [25,28]. We extended our regional analysis to determine if BAPs can help explain the reported preferential failure of the superior endplate [35]. Additionally, we considered the role of disc health on endplate thickness, the underlying trabecular bone and vertebral failure.

Methods

Sample preparation

The surrounding soft tissue and posterior elements of 22 osteoporotic cadaveric human functional spine units (FSU) were removed (average 74.45± 4.25 years). Vertebrae were grouped as follows: one T9–T10, three T11–T12, five T12–L1, five L1–L2, four L2–L3, two L3–L4 and two L4–L5. Previous investigators have found little difference between male and female bone morphology and no major difference in BV/TV between T9 and L5 (1% T9 to L5, 0.5% T11 to L5). Since morphologic changes due to the aforementioned confounding factors are minimal, we pooled all the vertebrae together for analysis [15,26,36]. Our study population consisted of vertebrae that were used in a preceding experiment that involved submaximal uniaxial compressive loading of the FSU. Six of 22 specimens had polymethylmethacrylate (PMMA, Vertecem, Synthes, Switzerland) present in the caudal vertebra. Morphology was assessed prior to cement injection. Bone mineral density (BMD) was assessed using dual energy x-ray absorptiometry (DEXA) (Discovery C, Hologic, Bedford, MA).

Impressions were made of the cranial and caudal endplates in semi-cured bone cement (Sulfix, Sulzer Orthopaedics Ltd). A jig ensured that the two end caps were parallel to each other. The molded end caps only extended to the cortical rim, thereby not adding any structural strength to the FSU. Specimens were stored in air evacuated polyethylene bags at −20 °C until testing.

Micro-CT scanning and determination of morphology

All measurements were performed on a microcomputed tomography system (XtremeCT, Scanco Medical AG, Bassersdorf, Switzerland). Scans ranged from 770 to 990 slices with a nominal isotropic resolution of 82 μm (field of view 125 mm, 1536×1536 pixels, integration time 200 ms). Scans were performed in air, before mechanical testing. Total scan time per specimen approached 30 minutes. Regions of interest (ROI) were identified for trabecular bone and endplate thickness analysis. The region for trabecular bone analysis included the cancellous bone from just below the cranial endplate to just above the caudal endplate, separated into 10 regions (Fig. 1). ROI were filtered using a Laplace–Hamming filter and segmented using a global threshold. Bone architecture parameters (BAP) analyzed included (Image Processing Language, v4.29d, Scanco Medical AG, Bassersdorf, Switzerland): bone volume ratio (BV/TV), connectivity density (Conn.D), structure model index (SMI), trabecular number (Tb.N), trabecular thickness (Tb.Th), trabecular separation (Tb.Sp) and degree of anisotropy (DA) (Table 1). Trabecular thickness, number and separation were based on direct measures using a distance transformation and not using trabecular model assumptions [37].

Endplate thickness was determined using a region of interest (ROI) that encompassed only the endplate. A Gaussian filter (sigma 0.8, support 1) was used to reduce noise. The segmentation threshold was chosen to preserve as much of

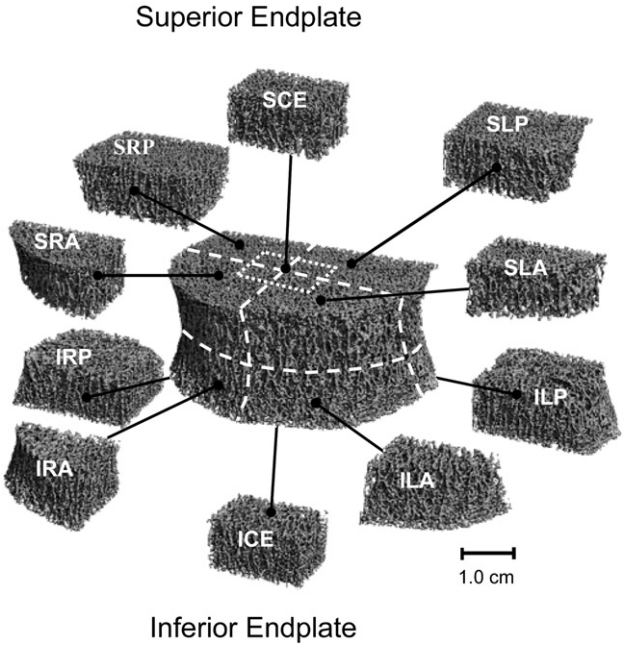

Fig. 1. Regions of the vertebra for which bone architecture parameters were determined. Regions were composed of superior (S), inferior (I), anterior (A), posterior (P), left (L), right (R) and central (CE) regions.