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Clinical Study

Regional bone mineral density differences measured by quantitative computed tomography: does the standard clinically used L1-L2 average correlate with the entire lumbosacral spine?

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Abstract

BACKGROUND CONTEXT: Quantitative computed tomography (QCT) of the lumbar spine is used as an alternative to dual-energy X-ray absorptiometry in assessing bone mineral density (BMD). The average BMD of L1-L2 is the standard reportable metric used for diagnostic purposes according to current recommendations. The density of L1 and L2 has also been proposed as a reference value for the remaining lumbosacral vertebrae and is commonly used as a surrogate marker for

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This study was approved by the Institutional Review Board (IRB#2016-0751) at the Hospital for Special Surgery.

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overall bone health. Since regional BMD differences within the spine have been proposed, it is unclear if the L1-L2 average correlates with the remainder of the lumbosacral spine.

PURPOSE: The aim of this study was to determine possible BMD variations throughout the lumbosacral spine in patients undergoing lumbar fusion and to assess the correlation between the clinically used L1-L2 average and the remaining lumbosacral vertebral levels.

STUDY DESIGN/SETTING: This is a retrospective case series.

PATIENT SAMPLE: Patients undergoing posterior lumbar spinal fusion from 2014 to 2017 at a single, academic institution with available preoperative CT imaging were included in this study.

OUTCOME MEASURES: The outcome measure was BMD measured by QCT.

METHODS: Standard QCT measurements at the L1 and L2 vertebra and additional experimental measurements of L3, L4, L5, and S1 were performed. Subjects with missing preoperative lumbar spine CT imaging were excluded. The correlations between the L1-L2 average and the other vertebral bodies of the lumbosacral spine (L3, L4, L5, S1) were evaluated.

RESULTS: In total, 296 consecutive patients (55.4% female, mean age of 63.1 years) with available preoperative CT were included. The vertebral BMD values showed a gradual decrease from L1 to L3 and increase from L4 to S1 (L1=118.8 mg/cm^3, L2=116.6 mg/cm^3, L3=112.5 mg/cm^3, L4=122.4 mg/cm^3, L5=135.3 mg/cm^3, S1=157.4 mg/cm^3). There was strong correlation between the L1-L2 average and the average of the other lumbosacral vertebrae (L3-S1) with a Pearson's correlation coefficient (r=0.85). We also analyzed the correlation between the L1-L2 average and each individual lumbosacral vertebra. Similar relationships were observed (r value, 0.67−0.87), with the strongest correlation between the L1-L2 average and L3 (r=0.87).

CONCLUSIONS: Our data demonstrate regional BMD differences throughout the lumbosacral spine. Nevertheless, there is high correlation between the clinically used L1-L2 average and the BMD values in the other lumbosacral vertebrae. We, therefore, conclude the standard clinically used L1-L2 BMD average is a useful bone quantity measure of the entire lumbosacral spine in patients undergoing lumbar spinal fusion.

Keywords: Regional BMD differences; Bone mineral density; Computed tomography; Osteoporosis; Quantitative computed tomography; QCT; Dual-energy X-ray absorptiometry; DXA; Lumbar spine; Spinal fusion

Introduction

Quantitative computed tomography (QCT) of the lumbar spine is increasingly used as an alternative to dual-energy X-ray absorptiometry (DXA) in assessing bone mineral density (BMD) [1−3]. Several advantages of QCT over DXA have been described in the literature. QCT has the ability to provide three-dimensional (3D) BMD information (in mg/cm^3) compared to the two-dimensional DXA information (in g/cm^2) [1,2]. In contrast to DXA, QCT is less susceptible to the negative effects of confounding factors such as variations in bone size and overlying densities including osteophytes, aortic calcification and high body mass index (BMI) [1,3−10]. In addition, QCT can selectively measure trabecular or cortical bone density depending on the region of interest, whereas DXA cannot differentiate between different bone architectures. Trabecular bone is metabolically more active than cortical bone and a more sensitive marker for changes in overall bone strength [1,11].

Routine reporting of lumbar spine BMD by 3D QCT only includes the density information of 2 selected vertebrae, L1-L2, as the standard metric for the past decade [12]. Prior to that, studies using the original QCT methodology (single-slice QCT) would analyze 3 to 4 consecutive vertebrae in the range of T12-L4 [12−17]. However, with the advancements in CT technology and the introduction of spiral scans, it was agreed to only assess the BMD of the first 2 lumbar vertebrae. The main reason for limiting the number of scanned vertebrae was to reduce the radiation exposure [12].

As in the years before, the current 2015 International Society for Clinical Densitometry (ISCD) official guidelines state that only L1-L2 should be scanned using 3D QCT [18]. The average L1-L2 BMD is then used for radiologic diagnosis of osteopenia and osteoporosis as defined by the American College of Radiology [19]. The average density of L1-L2 has also been proposed as a reference value for the remaining lumbosacral vertebrae [17]. However, the L1-L2 BMD may not fully capture substantial BMD differences throughout the lumbosacral spine. This might lead to an underestimation of fracture risk due to low BMD values at unmeasured spinal levels [20].

Significant regional BMD differences within the spine have been previously described [21−23]. However, there is a paucity of literature regarding BMD information for each lumbar vertebra and the first sacral vertebral body. This information would be of particular importance in lumbar fusion patients since L1-S1 are common sites for pedicle screw fixation. To the best of the authors' knowledge, there is no large series of QCT measured BMD in lumbar fusion patients, although these patients frequently undergo preoperative assessment of BMD in an attempt to determine bone status and predict ultimate strength of fixation [24,25].

Moreover, the correlation of the clinically used L1-L2 average with the remaining lumbosacral levels is not well-established in this patient population. Hence, there is a need to quantify the BMD of the entire lumbosacral spine and to assess whether the L1-L2 average correlates with the remaining lumbosacral vertebrae.

The aim of this study was to determine possible BMD variations throughout the lumbosacral spine in patients undergoing lumbar fusion surgery and to assess the correlation between the clinically used L1-L2 average and the remaining lumbosacral vertebral levels.

Material and methods

Patient population

This study was approved by the hospital institutional review board. Patients who underwent posterior lumbar spinal fusion from 2014 to 2017 at a single, academic institution were eligible for inclusion. Subjects with missing preoperative lumbar spine CT imaging were excluded. In addition, individuals were excluded from the current study if they had a history of prior spinal fusion, history of fracture and vertebral augmentation, since these conditions would impact the QCT measurement at the affected level. Inpatient and outpatient charts were reviewed. Collected demographic and clinical information included age, gender, BMI, ethnicity, and operative details.

QCT measurements

Standard QCT measurements were utilized to evaluate BMD at the L1 and L2 vertebra as shown in Fig. 1 [18]. In addition, experimental measurements were performed at L3, L4, L5, and S1. A BMD value was obtained using Mindways QCT Pro software (Mindways Software, Inc., Austin, TX, USA). The measurement method uses an elliptical region of interest manually fixed over the interior space of the individual vertebral body on an axial CT image being analyzed. Special attention was made to maximize the area of the region of interest while also avoiding contact with adjacent cortical bone or any other free-standing, high

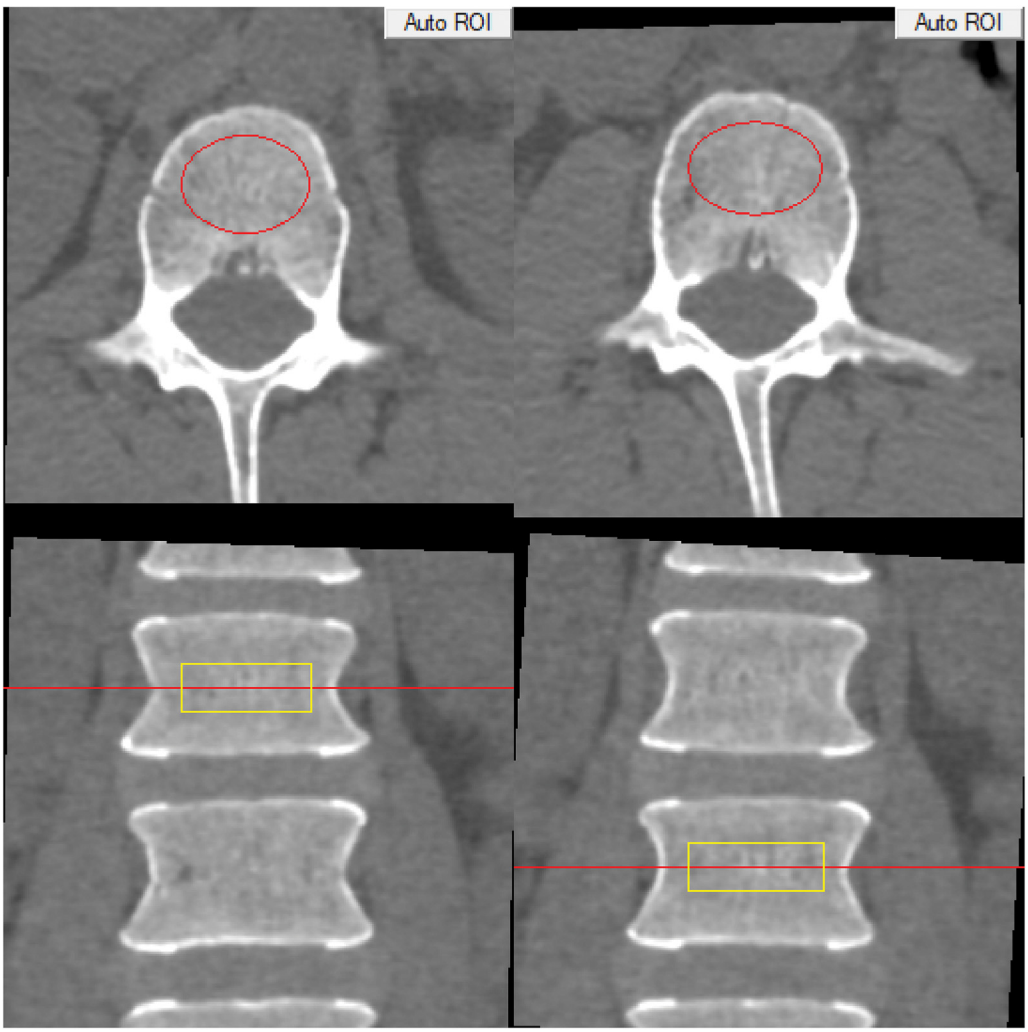

Fig. 1. Axial and coronal view of the L1 and L2 region of interest (ROI).

Table 1
Description of the study population (N=296)

Gender, N (%)	
Females	164 (55.4)
Males	132 (44.6)
Age, yrs, mean (SD)	63±13
BMI, (kg/m^2), mean (SD)	28±5.6
Ethnicity, (%)	
Caucasian	262 (88.5)
African American	11 (3.7)
Other	16 (5.4)
N/A	7 (2.4)
Fused Level, (%)	
L1-L2	6 (2.0)
L2-L3	35 (11.8)
L3-L4	105 (35.5)
L4-L5	211 (71.3)
L5-S1	133 (44.9)

density artifacts seen in the vertebra. The methods used to determine regions of interest have been previously described in detail [17,26].

All preoperative CT scans were performed without the use of a phantom (calibration device with known hydroxyapatite concentrations simultaneously scanned with the patient at the time of the image acquisition). As such, the Hounsfield unit value derived from each phantomless measurement was subsequently converted to BMD (in mg/cm^3) using a calibrated conversion factor as determined by barometric quality assurance (QA) data specific to the make and model of the CT machine utilized for image acquisition. All QA phantom data required for this step was provided by Mindways (Mindways Software, Inc., Austin, TX, USA). This novel conversion technique is known as asynchronous QCT [27]. It has been validated [28] and used in previous studies [29,30]. The ISCD states that the synchronous phantom calibration can be replaced by asynchronous calibration if CT scanner stability is maintained [18]. According to the American College of Radiology, the BMD of L1-L2 as measured by QCT can be categorized using thresholds as either osteoporotic, osteopenic, or normal if the value is <80 mg/cm^3, ≥80 mg/cm^3 and ≤120 mg/cm^3, or >120 mg/cm^3, respectively [19].

Statistical analysis

Descriptive statistics were summarized as mean ± standard deviation (SD) for normally distributed continuous variables, median ± interquartile range (IQR) for non-normally distributed continuous variables and count (frequency) for categorical data. Pearson correlation analysis was performed to assess the correlation between the L1-L2 BMD average and the other vertebral bodies of the lumbar sacral spine (L3, L4, L5, and S1). Pairwise comparison of each level of BMD measures was conducted. Bonferroni correction was used for multiple comparisons. The significance level was set at p<.05. All the analyses were performed using Stata 14 SE Software (StataCorp, College Station, TX, USA).

Table 2
Summary of bone mineral density (BMD) data (mg/cm^3)

Spinal region (level)	Mean	Standard deviation
L1	118.8	37.2
L2	116.6	39.7
L3	112.5	42.0
L4	122.4	46.8
L5	135.3	46.0
S1	157.4	57.0

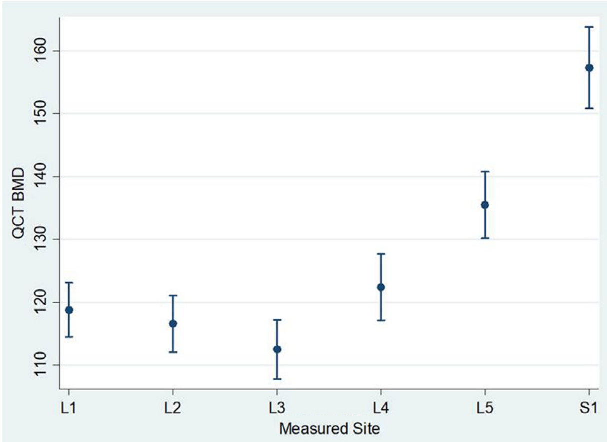

Fig. 2. Mean quantitative computed tomography (QCT) bone mineral density (BMD) (in mg/cm^3) with standard error (SE) bar of the lumbosacral vertebrae.

Results

In all, 296 consecutive patients (55.4% female) undergoing primary lumbar fusion procedures from 2014 to 2017 with available preoperative CT imaging were included. The patient population was 88.5% Caucasian with a mean age of 63.1 years and mean BMI of 28.0 kg/m^2. Demographic and clinical characteristics are displayed in Table 1. The majority of patients underwent fusion procedures at caudal levels (L1-L2 [2.0%], L2-L3 [11.8%], L3-L4 [35.5%], L4-5 [71.3%], and/or L5-S1 [44.9%]).

The mean BMD of the lumbosacral spine from L1 to S1 was 127.2 mg/cm^3. Detailed QCT BMD information of each individual lumbosacral measurement is displayed in Table 2. The vertebral BMD values showed a gradual decrease from L1 to L3 and increased from L4 to S1 (L1=118.8 mg/cm^3, L2=116.6 mg/cm^3, L3=112.5 mg/cm^3, L4=122.4 mg/cm^3, L5=135.3 mg/cm^3, S1=157.4 mg/cm^3) (Table 2, Fig. 2). BMD did not vary significantly between L1 and L2 (p=.249), L2 and L3 (p=.056), and L1 and L4 (p=.078). All other observed BMD differences within the lumbosacral levels were statistically significant (Table 3).

Although significant variation in densities were observed, our data demonstrated a strong correlation between the clinically used L1-L2 average and the

Table 3
Pairwise comparison of bone mineral density (BMD) of L1, L2, L3, L4, L5, and S1

p Value	L1	L2	L3	L4	L5	S1
L1	-	0.249	0.002	0.078	<0.001	<0.001
L2			0.056	0.004	<0.001	<0.001
L3				<0.001	<0.001	<0.001
L4					<0.001	<0.001
L5						<0.001
S1						-

Table 4
Correlation coefficients of the L1-L2 bone mineral density (BMD) average and BMD of each individual lumbosacral vertebra as well as the L3-S1 BMD average

	L1-L2 average	p Value
L3	0.869	<.001
L4	0.672	<.001
L5	0.713	<.001
S1	0.723	<.001
L3-S1 average	0.854	<.001

average of the other lumbosacral vertebrae (L3-S1) with a Pearson's correlation coefficient, r=0.85. We also examined the correlation between the L1-L2 average and each individual lumbosacral vertebra. Similar relationships were observed (correlation coefficient, 0.67 −0.87) with the strongest correlation between the L1-L2 average and L3 (Table 4).

Multivariate regression analysis demonstrated that after controlling for confounding factors (age, sex, BMI, race, and bone medication use) the L1-L2 average is still significantly associated with the remaining lumbosacral vertebrae (p<.001). Additional analyses were performed to determine if the observed correlations held in subgroups including gender, age, BMI, BMD, and bone medication use. For all the subgroups, the L1-L2 average remained significantly correlated with the remaining lumbosacral vertebrae.

Discussion

To our knowledge, this is the first study investigating the BMD heterogeneity within the entire lumbar spine and the first sacral vertebra. Our results support previous reports describing considerable differences in mean BMD throughout the spine. BMD as a function of vertebral level gradually decreased from L1 to L3 and increased from L4 to S1. Nonetheless, we found high correlation between the standard clinically used L1-L2 BMD average and the BMD values of the other lumbosacral vertebrae. As the closest vertebra to the standard measurement site, L3 showed the strongest individual correlation to the L1-L2 average. Although still strongly correlated, the Pearson's correlation coefficients were smaller for the L4, L5, and S1 vertebra. This might be of importance, since the majority of patients in our cohort underwent fusion procedures at L4-L5 (71.3%) and/or L5-S1 (44.9%).

Bone strength and fracture risk are known to depend on 2 factors, bone quantity and bone quality. Bone quantity is derived from bone density and size, whereas bone quality depends on factors such as micro- and macro-architecture, material properties, and bone turnover [31,32]. Since a single direct measurement of overall bone strength is currently unavailable, it is common clinical practice to assess bone strength indirectly using BMD, which is a bone quantitative marker [11]. In clinical and research settings, quantitative BMD assessments are commonly performed at the lumbar spine with DXA or QCT [33]. For both modalities, lumbar spine BMD values are usually presented as an averaged value of selected vertebrae [2,7,17,20].

For patients undergoing 3D QCT examinations, the ISCD recommends to only scan the first 2 lumbar vertebrae [18]. Following these recommendations, the L1-L2 BMD is the standard reportable metric on QCT reports. However, given reported BMD variations throughout the entire spinal column, limiting the number of scanned vertebrae to L1-L2 might lead to an underestimation of actual BMD at unmeasured lumbosacral levels [20]. A review of the literature reveals that several studies attempted to quantify these spinal regional BMD differences. Previous reports include different spinal regions (cervical, thoracic, lumbar) and measurement methods (DXA, QCT) [2,20−22]. We compared these previous findings to the results of this study.

Our results are largely in agreement with the QCT study published by Budoff et al. [2]. Including patients who underwent simultaneous thoracic and abdominal CT scans, BMD values showed a gradual decrease from L1 to L3 and an increase from L4 to L5. Measurements of S1 were not included, however, BMD data of the thoracic spine were available. They reported that the BMD of the thoracic spine is significantly higher compared to the lumbar spine. Higher thoracic bone density was also observed by Wong et al. [22].

Likewise, Yoganandan et al. described a decrease in BMD from rostral to caudal along the entire spine [21]. In their study of healthy male volunteers, the mean BMD of the cervical spine (C2-C7) was 256.0 mg/cm^3, 194.3 mg/cm^3 for the first thoracic vertebra, and 172.2 mg/cm^3 for the lumbar spine (L2-L4). In contrast, the mean BMD of the lumbosacral spine from L1 to S1 in our study was 127.2 mg/cm^3. A possible explanation for this BMD discrepancy is the mean age of their cohort was 25.0 years, representing the BMD of a younger population. In addition, we did not exclude patients with BMD levels diagnostic of osteopenia or osteoporosis. When performing a subgroup analysis of only patients with normal (>120 mg/cm^3) bone density from our cohort, there were 123 patients (52.8% female), with mean age 56 years and L1-L2 average BMD of 153.9 mg/cm^3. This value is much closer to their reported BMD in younger, healthy male patients. A gradual BMD decrease after the age of 25 years has been described in the literature, which may further explain the differences between our results [34].

In addition to the decrease in mean BMD caudally, Yoganandan et al. also found that the variability in BMD was higher in the cervical spine compared to the lumbar spine. Interestingly, they did not find any intersegmental differences in BMD between the three examined vertebral levels of L2, L3, and L4 [21]. This is in contrast to our study. Although there was no statistical difference between L2 and L3, we found the BMD of L4 to be significantly higher than L2 or L3. The detected BMD difference between the levels in the present study might be due to the larger sample size of 296 patients compared to the 57 individuals in the study by Yoganandan et al. In addition, since BMD differences between different levels have been shown to be related to aging [2], the older mean age of our larger study cohort might have made such differences more apparent.

Potential explanations for the regional differences within the lumbosacral spine are scarce in the existing literature. Possible factors that might cause BMD variation according to Wolff's law include differences in bone size, in-vivo loads, range of motion, and vertical orientation of the vertebral body [23]. Also, a relationship of degree of lumbar lordosis to BMD has been reported and might have a variable effect on individual vertebrae [35].

The majority of previous studies examined regional BMD differences in patients without obvious spinal pathology [2,20−22]. To the best of the authors' knowledge, there is no study focusing on patients referred for lumbar spine surgery. This is surprising, since preoperative assessment of lumbar BMD is particularly important in this patient group. It is unclear if regional BMD data obtained from the general population can be used in lumbar fusion patients, which are more likely to have decreased activity due to low back pain, less exercise, and potentially more exposure to steroid injections. All of those factors could potentially affect bone density [36−40]. Whether those factors result in regional or global BMD loss remains unclear. However, the observed trends in BMD variation in this lumbar fusion cohort are comparable to those observed in nonfusion patients [2].

Preoperative assessment of lumbar fusion patients commonly involves CT scanning of the lumbar spine. Asynchronous QCT, as it was used in this study, makes use of preexisting CT images and thereby does not result in additional radiation exposure or increase in cost for the patient [21]. From a spinal instrumentation perspective the clinically used L1-L2 average may be an appropriate and safe approximation to assess the BMD also of lower lumbosacral levels. The majority of patients in this cohort underwent fusion procedures at caudal levels (L4-L5 [71.3%] and/or L5-S1 [44.9%]), which correlates with a higher prevalence of degenerative conditions occurring at L4-L5 and L5-S1 [41]. Guglielmi et al. [5] and Ito et al. [10] demonstrated that trabecular BMD measured by QCT (in contrast to DXA) is not falsely elevated in the presence of degenerative changes. They concluded that assessment of BMD by volumetric QCT may be suggested in patients with degenerative changes of the spine. Using the L1-L2 average as a reference for caudal levels might not result in an underestimation of BMD, since L5 and S1 had significantly higher BMD values. The implications of higher BMD values in the lower lumbar spine on spinal instrumentation should be investigated in future prospective studies.

This study has several unique strengths. It is a systematic assessment of level-specific BMD in a large sample of both men and women undergoing lumbar posterior spinal fusion. Unlike other studies that only provide data on a select number of lumbar vertebrae, we assessed the entire lumbar spine including S1 as these levels are common sites of spinal instrumentation. Most importantly, due to the use of asynchronously calibrated QCT, preoperative CT scans could be used to obtain BMD information. This dual use of readily available CT images avoided additional radiation exposure for the patients.

Our study has a number of limitations. First, due to the cross-sectional study design, possible BMD changes of each vertebral level over time and their impact on the applicability of the L1-L2 BMD average could not be assessed. The subjects in this study are representative of patients who receive surgical treatment for degenerative lumbar spine pathology. This clearly adds to the clinical relevance of our findings, since L1-S1 are common sites for pedicle screw fixation. However, our data does not permit any conclusions about nonsurgical patients. Furthermore, our patient cohort was derived from a single tertiary-care orthopedic referral hospital which might limit the generalizability of our results to other patient populations. Since DXA measurements (the current gold standard modality) were not available for the entire patient cohort, a comparison of the two modalities was not possible. In addition, CT imaging was performed on different CT machines over the study period, but the use of QA data specific to the make and model of each machine mitigates the measurement variability this may introduce.

Conclusions

This study reports the BMD of L1-S1 from 296 patients undergoing lumbar posterior spinal fusion using QCT. BMD was the lowest at L3 and steadily increased caudally. There was high correlation between the average L1-L2 BMD and the remaining lumbosacral segments with the strongest correlation at L3. In summary, the L1-L2 BMD is a useful tool in clinical practice to estimate the overall lumbosacral spine bone density in patients undergoing posterior lumbar spinal fusion and correlates well to each individual lumbosacral vertebra. The clinical and surgical implications of variable bone density throughout the lumbosacral spine should be investigated in future studies. It also remains to be determined whether a single-level vertebral QCT measurement (of L1 or L2) could be used instead of the L1-L2 average in order to further reduce radiation exposure to the patient. The average L1-L2 QCT BMD is highly correlated with the bone density through the entire lumbosacral spine, thus, clinicians can confidently utilize L1-L2 average and gain valuable information about the other lumbosacral segments without the need for additional radiation exposure.

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