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ORIGINAL ARTICLE

Analysis of bone mineral density distribution at trabecular bones in thoracic and lumbar vertebrae using X-ray CT images

Tatsuro Hayashi · Huayue Chen · Kei Miyamoto · Xiangrong Zhou · Takeshi Hara · Ryujiro Yokoyama · Masayuki Kanematsu · Hiroaki Hoshi · Hiroshi Fujita

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Abstract The number of participants in thoracic or abdominal examinations using multi-detector-row CT (MDCT) has been increasing recently. If the degree of progress of osteoporosis can be estimated using these images, it may be useful as it will allow predictions of vertebral fractures without an additional radiation exposure. The aims of this study were to investigate segmental variations in bone mineral density (BMD) distributions of thoracic and lumbar vertebral bodies and to show specific differences according to age and gender. A large database including 1,031 Japanese subjects for whom MDCT was used to examine various organs and tissues was utilized in this study for trabecular BMD at thoracic and lumbar vertebrae. In relationship to vertebral level, L3 had the lowest trabecular BMD. BMD tended to gradually increase from L3 to T1 in all age categories. Also, there was a moderate correlation between vertebrae whose distance from each other was great whereas there was a high correlation between adjacent vertebrae. It may be appropriate to use an arbitrary vertebra as a first approximation for assessing vertebrae that are in the area of predilection for the fracture; however, to better understand their behavior, it may be necessary to measure BMD directly in this region. This study showed trabecular BMD distribution at healthy thoracic and lumbar vertebrae in Japanese subjects and specific differences in age and gender. Improved knowledge about vertebral BMD may help with the diagnosis of primary osteoporosis using MDCT.

Keywords Vertebral trabecular bone · Bone mineral density (BMD) · Vertebra · Osteoporosis · Quantitative computed tomography (QCT)

T. Hayashi (✉) · X. Zhou · T. Hara · H. Fujita
Department of Intelligent Image Information,
Division of Regeneration and Advanced Medical Sciences,
Graduate School of Medicine, Gifu University,
1-1 Yanagido, Gifu 501-1194, Japan
e-mail: hayashi@fjt.info.gifu-u.ac.jp

H. Chen
Department of Anatomy, Division of Disease Control,
Graduate School of Medicine, Gifu University, Gifu, Japan

K. Miyamoto
Department of Reconstructive Surgery for Spine, Bone,
and Joint, Graduate School of Medicine,
Gifu University, Gifu, Japan

R. Yokoyama · M. Kanematsu
Department of Radiology Services,
Gifu University Hospital, Gifu, Japan

M. Kanematsu
Department of Radiology,
Gifu University Hospital, Gifu, Japan

H. Hoshi
Department of Radiology, Division of Tumor Control,
Graduate School of Medicine, Gifu University, Gifu, Japan

Introduction

With osteoporosis, skeletal sites where trabecular bone is predominant, such as the vertebrae, the bone of the forearm, and femoral neck, are vulnerable to fracture. Countermeasures against this disorder have become an increasingly important public health problem because of the rapidly aging populations. Early diagnosis of bone loss is important for the prevention of vertebral fractures because therapeutic drug treatments are the most effective before the decrease of BMD affects bone fractures [1].

A definition of bone quality that includes bone mineral density (BMD) was proposed by Bouxsein et al. [2]

because loss of bone mass is the most significant contributor to an increase in fracture risk. A greater understanding of all aspects of bone quality is required to improve diagnostic techniques for osteoporosis [1].

In recent years, much research using micro-computed tomography (μCT), which analyzes trabecular bones by architectural parameters such as trabecular bone pattern factors, has been reported [1, 3–8]. Because of the high radiation doses involved, it has not yet been possible to use this technique on human subjects in vivo. Work is in progress to adapt the μCT scanning technique so that it can be used in vivo for human clinical applications. However, McDonnell et al. [1] predict that, although it may be possible in the future to obtain high-resolution μCT images in vivo at clinically relevant sites, such scans will be confined to relatively small areas of bone. The prior knowledge on BMD distribution at trabecular bones in thoracic and lumbar vertebrae on X-ray CT images may help to establish the determination of vertebral level to be scanned by μCT. Noninvasive bone mass measurement by peripheral quantitative computed tomography (pQCT), which is characterized as inexpensive, precise, and involving low doses of radiation [9], has also been studied [10]. Sawada et al. [10] attempted to monitor response to alendronate therapy at the distal radius in postmenopausal women.

Recently, the number of participants in thoracic or abdominal examinations using multi-detector-row CT (MDCT) has been increasing. Thoracic or lumbar vertebrae are included in these images. If the degree of progress of osteoporosis can be estimated using these images, it may be useful for participants as it will allow predictions of vertebral fractures without additional radiation exposure. As a similar consideration, Lenchik et al. [11] reported a method of measuring the trabecular bone mineral density (BMD) of thoracic vertebrae that uses cardiac-gated CT, which was primarily intended for the measurement of coronary vascular calcium.

However, at this time, the diagnostic criterion for primary osteoporosis using MDCT is not clear. Its establishment requires exploration of the BMD distribution using many subjects. Research exploring the BMD of vertebrae using dual X-ray absorptiometry (DXA), based on thousands of subjects (images), has been reported [12, 13]. Various studies exploring the BMD of vertebrae using QCT have also been reported [3, 11, 14–27]. For instance, Bouxsein et al. [14] explored the BMD of L1–L3 vertebral bodies (including both cortical and trabecular bone) from 687 study subjects. Sigurdsson et al. [15] also reported the BMD of L1–L2 vertebral bodies (including both cortical and trabecular bone and areal BMD) from 1,715 study subjects. Research focused on the vertebral level has reported some findings, such as high BMD correlations of adjacent vertebrae in thoracic and lumbar vertebrae [18], and a difference of BMD distribution in cervical and sacral vertebrae in comparison to thoracic and lumbar vertebrae [17–19]. However, only a small number of study subjects were analyzed. The analysis of BMD at different vertebral levels is necessary because osteoporotic vertebral fractures have been shown to occur most commonly in the midthoracic spine, and to a lesser extent in the thoracolumbar junction, as described by Smet et al. [28]. If the BMD of one vertebra is known, the BMD of other vertebrae may be estimated using our knowledge of BMD correlations. This observation suggests that the BMD of vertebra outside the scope of CT images can be estimated (e.g., by estimating the BMD of the thoracolumbar junction using CT images from thoracic examination).

The aims of this study were to investigate segmental variations in BMD distribution of thoracic and lumbar vertebral bodies (vertebral trabecular bones) and to show specific differences according to age and gender. To improve our understanding of bone fragility, we attempted to answer three key questions: (1) Does BMD of the vertebrae differ by gender at each vertebral level? (2) Does the correlation between BMD and age show a different pattern at each vertebral level? (3) Can the BMD of the other vertebrae be estimated using the BMD of one vertebra? Improved knowledge of BMD correlations among thoracic and lumbar vertebrae may help establish the diagnostic criteria for primary osteoporosis using MDCT. Parts of this research have been described in previous articles [24, 25].

Materials and methods

Study subjects

The study sample consisted of the first 1,750 enrolled Japanese men and women with CT images from 2002 to 2006, scanned for the purpose of examinations of various organs and tissues. The CT images included all thoracic and lumbar vertebrae (LightSpeed Ultra; GE Yokogawa Medical Systems, Tokyo, Japan) and were scanned for each subject using standard settings (120 kV, auto mAs, 1.25-mm-thick slice, pitch = 0.49–0.88 mm) routinely used clinically. Slice intervals were modified to the same value as the pitch using sinc interpolation to keep each voxel in an isotropic size in three dimensions (3-D).

Of the 1,750 individuals with CT data available, 719 were excluded because of normal variants, bone pathology, vertebral fractures, or reasons other than mild degenerative changes at vertebrae, as confirmed by radiologists or anatomic experts. The study subjects consisted, therefore, of 1,031 individuals: 490 men and 541 women. The study subjects were then subdivided into four age categories to observe age differences. The age categories were 40 or

years or less (mean age = 30 years), 41–55 years (mean age = 50 years), 56–70 years (mean age = 63 years), and older than 71 years (mean age = 76 years). The distribution of our database is shown in Table 1. This research was approved by the Institutional Review Board of Gifu University.

Inhomogeneity of vertebral trabecular bones

Local measurement of BMD is possible using MDCT because of its high resolution. However, clinical assessment is limited to one or two thin slices, and QCT is generally performed in the central part of the vertebral body. If the BMD of the vertebral body is not homogeneous, an understanding of the lower BMD location inside the vertebral body may be helpful to clinical diagnosis. To investigate this, we have previously analyzed local BMD at the T12–S1 vertebral bodies using 80 CT images [25]. As shown in Fig. 1, BMD was compared in eight volumes of interest (VoI). As a result, we confirmed that low BMD was measured in the front and central regions at the lumbar vertebrae. For similar research about the inhomogeneity of vertebrae, Banse et al. [20], Cody et al. [21], and Briggs et al. [29] have also investigated correlations between BMD and vertebral regions using pQCT, QCT, and DXA, respectively. Referring to these reports, the general trend of vertebral trabecular BMD at other local sites or the global site can be predicted from the measurement value of BMD at one typical site. In this research, the BMD of trabecular bones at the central region of the vertebral body was measured as the typical site.

Table 1 Distribution of our database (subjects)

Gender	Age (years)				Total
	Under 40	41–55	56–70	Over 71	
Male	78	102	188	122	490
Female	76	146	217	102	541

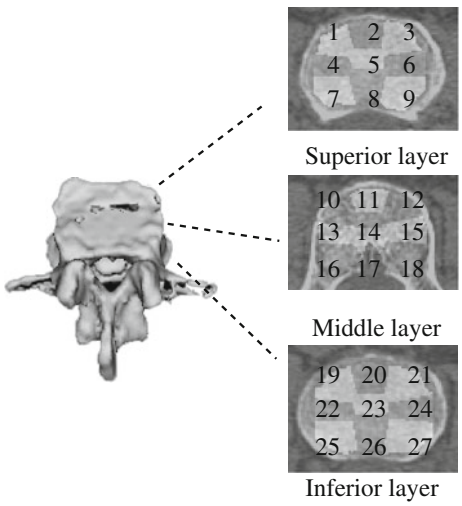

Fig. 1 Volumes of interest in the vertebral body: anterior, *1–3*, *10–12*, *19–21*; posterior, *7–9*, *16–18*, *25–27*; superior, *1–9*; inferior, *19–27*; left, *1, 4, 7, 10, 13, 16, 19, 22, 25*; right, *3, 6, 9, 12, 15, 18, 21, 24, 27*; central, *14*; whole, *1–27*

Inputting VoIs at vertebral bodies

In the current study, the central region was defined as the center, which was divided into three equal sections (i.e., number 14 in Fig. 1), and the BMD of each region was investigated. We inputted VoI using the following five steps.

1. The vertebral canal regions were segmented based on the CT number and skeletal structures [30].
2. The central locations of the right and left sides of the vertebral canal in each slice were calculated, and a sagittal sectional image based on the centerline of the vertebral canal was generated. We defined the generated image as a median plane image of the spine. An example of reconstructing the median plane image of the spine is shown in Fig. 2. Figure 2a shows one slice of a sagittal section in a volumetric X-ray CT image. Figure 2b,c indicates the segmented vertebral canal in one slice of cross sections of T11 and L3, respectively (white circle denotes the segmented vertebral canal.). Figure 2d shows the median plane image of the spine. Although there is no guarantee that the vertebral bodies of T1–L5 can be seen in only one slice of the sagittal sections of the original CT image, T1–L5 can always be seen in the median plane image of the spine, as seen in the upper thoracic vertebrae in Fig. 2.
3. VoIs of the thoracic and lumbar vertebrae were inputted manually, using the median plane image of the spine (Fig. 3a). Inputted VoIs are shown by the white regions in Fig. 3a.
4. Axial sectional images of the original CT image corresponding to the center of each vertebra were referenced, and then we determined the right and left range of the VoI. Input examples of the range of the right and left at T11 and L3 are shown in Fig. 3b,c.
5. The VoI inputted at step 3 was extended to the range inputted at step 4. Examples of VoI obtained by the above method are shown in Fig. 3d,e. Figure 3d,e shows a 3-D view of the inputted VoI from the lateral and anterior sides, respectively. 3-D volumetric VoI can be checked from this figure. The mean CT number in VoI with the CT number of each vertebra was identified in the present study.

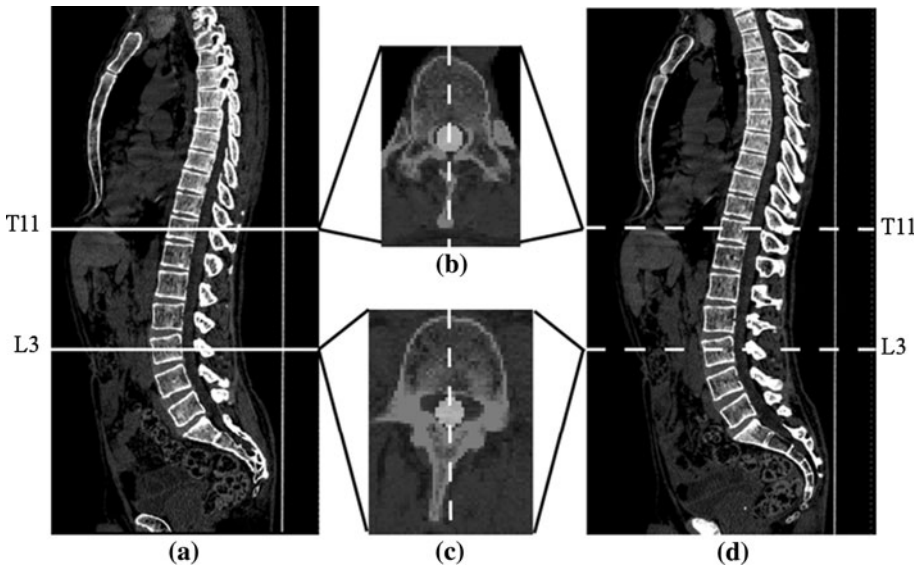

Fig. 2 Generating the median plane image of the spine. **a** One slice of sagittal section in computed tomography (CT) images. **b**, **c** One slice of cross sections of T11 and L3 in CT images, respectively (*white circle* denotes a segmented vertebral canal). **d** Median plane image of the spine

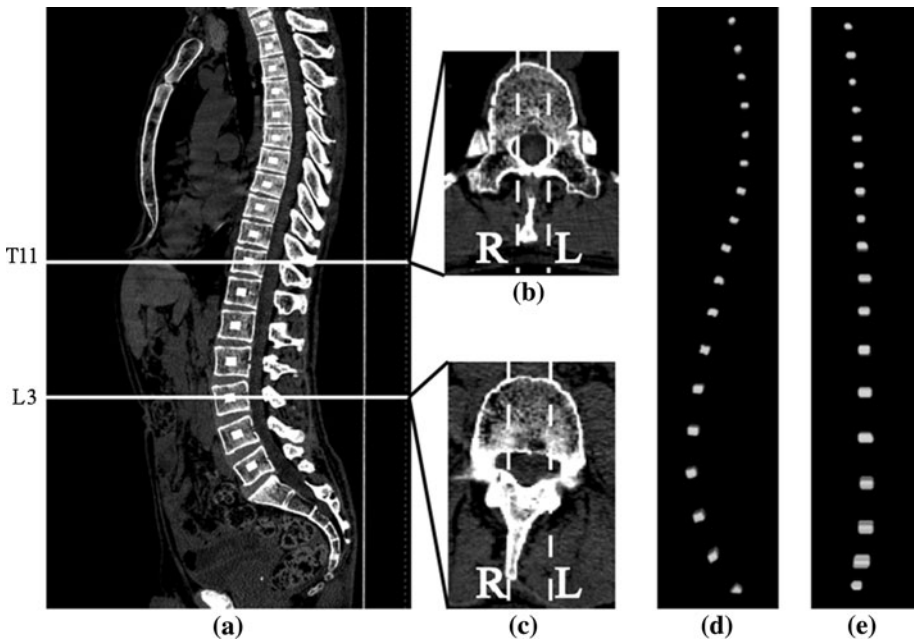

Fig. 3 Volume of interest (VoI) setting. **a** Inputted VoI using the median plane image of the spine (inputted VoIs are shown by the *white regions of square dots*). **b**, **c** Input examples of the range of the right (R) and left (L) at T11 and L3 (*white dashed lines* show the border of VoI). **d**, **e** Three-dimensional (3-D) view of the inputted VoIs from the lateral and anterior sides, respectively

Estimation of BMD

It is impossible to measure BMD using the established method proposed by Cann et al. [31] (e.g., QCT) because the purpose of our CT data was not the diagnosis of osteoporosis. Instead of using "traditional" QCT, we fixed the standard phantom (B-MAS 200; Kyoto Kagaku, Kyoto, Japan) under the human body phantom (Fig. 4) and exposed it to the same radiation dose as that used in diagnosis to calibrate the CT Hounsfield units to equivalent bone mineral concentrations. The standard phantom contained calibration cells of 0, 50, 100, 150, and 200 mg/cm^3 with equivalent concentrations of calcium hydroxyapatite. As a result, we estimated BMD as follows:

$$\mathrm{BMD}\,(\mathrm{mg/cm^3}) = \frac{\text{CT number}\,(\text{H.U.}) - 3.55}{1.13} \quad (1)$$

Statistical analysis

A free software R (version 2.7.2) [32] that provided many statistical analysis tools has been used. Welch's *t* test was used to determine if gender was related to vertebral BMD. A Lowess smoother was used to find the relationship between vertebral BMD and age. The relationship of BMD among thoracic and lumbar vertebrae was studied using Pearson's product-moment correlation coefficient. In addition, a Tukey multiple comparison test was used to find any significant differences in BMD at vertebral levels.

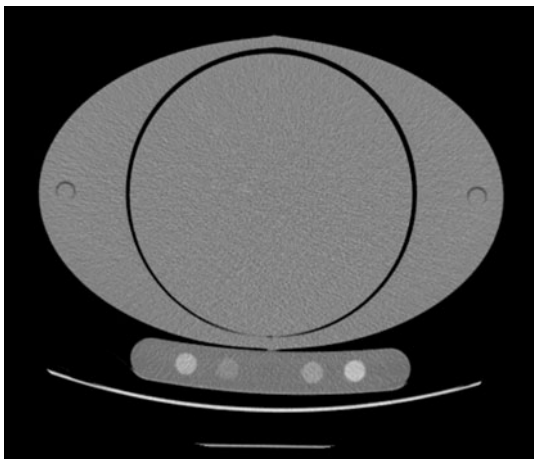

Fig. 4 Phantoms on computed tomography (CT) image. Measurement regions are from the *left* to *right*: 150, 50, 0, 100, 200 mg/cm^3

$P = 0.05$ was considered the cutoff for significance in all statistical analyses.

Results

Trabecular BMD distributions of vertebral bodies

Table 2 shows the trabecular BMD of thoracic and lumbar vertebral bodies. In Table 2, BMD in mean mg/cm^3 is described by ± standard deviation. In addition, difference in BMD values between men and women in each age category and at each vertebral level, as determined by Welch's *t* test, is also shown. Among these vertebrae in both genders, a standard deviation of measured BMD ranged approximately from 30 to 50 mg/cm^3. With a 95% confidence interval of mean BMD, many of the vertebrae were approximately within the mean of ±10 mg/cm^3 (maximum, 12 mg/cm^3). As a general trend, BMD declined with increase in age of these vertebrae in both genders. For each vertebral level, we found L3 had the lowest BMD. Moreover, in vertebrae further from L3, higher BMD was found in all age categories in both genders. Regarding gender differences, vertebral BMDs were approximately significantly different in age categories over 41 years, whereas they were not approximately significantly different in the 40-or-younger age category. In addition, in the ≥56 years categories, women had lower vertebral BMD than men of the same category, whereas in the 55-or-younger age categories, women had higher vertebral BMD than the men of the same category.

Relationship between vertebral BMD and age

To find a relationship between vertebral BMD and age, a scatter diagram was used. In addition, a Lowess smoother, essentially a type of moving average, was used to explore the data. In Fig. 5, scatter diagrams of T3, T7, L1, and L3 are shown. Compared with those under age 50, BMD of the four vertebrae at more than 50 years of age greatly declined for women. It is thought that our results can be explained by the common tendency of low BMD in postmenopausal women (over 50 years of age). For men, BMD of L1 and L3 declined at an almost constant rate with aging, whereas BMD of T3 and T7 over 60 years of age greatly declined. Moreover, we found that BMD of T3 had great variability, compared with that of L1 or L3, for both genders.

Comparison of trabecular BMD among thoracic and lumbar vertebrae

Pearson's product-moment correlation coefficient was used to explore the correlations among vertebral BMDs. Vertebral correlations based on T7, T12, and L3 (osteoporotic vertebral fractures are observed most commonly in T7 and T12, and L3 is often used in studies of vertebrae) are shown in Fig. 6. On the whole, we found that the further the vertebrae were from each other, the weaker were their correlations of vertebral BMD, and vice versa.

In addition, a Tukey multiple comparison test was used to explore significant differences of BMD among thoracic and lumbar vertebrae ($P < 0.05$). Significant differences based on T7, T12, and L3 among thoracic and lumbar vertebrae are shown in Fig. 7. The results shown in Fig. 7 indicate that there were no significant differences among T6–T10 as compared with T7. Moreover, there were no significant differences between T11–L2 as compared with T12 as well as L1–L5 as compared with L3, in all age categories in both genders. Therefore, among these vertebrae, if the BMD of one vertebra is known, the BMD values of the other vertebrae can be used in place of the undetermined value of a target vertebra.

Discussion

Loss of bone mass is the most significant contributor to an increase in fracture risk. Research on vertebral BMD using QCT has been carried out by various investigators [3, 11–27, 29–31, 33]. In other research studies, the relationships among BMD, age, and gender, which are the risk factors of vertebral fractures by osteoporosis, have been investigated [1, 12–15, 17, 18, 22–25, 27]. Moreover, there are some sites at which osteoporotic vertebral fractures tend to occur most commonly [28], and research into the relationship between BMD and vertebral level has also been done [16–19, 24, 25, 30].

Table 2 Trabecular bone mineral density (BMD) [mean ± standard deviation (mg/cm^3)] of vertebral bodies in each age and gender category

Level	Age (years)											
	–40			41–55			56–70			71–		
	Male ($n = 78$)	Female ($n = 76$)	*P*	Male ($n = 102$)	Female ($n = 146$)	*P*	Male ($n = 188$)	Female ($n = 217$)	*P*	Male ($n = 122$)	Female ($n = 102$)	*P*
T1	214.2 ± 45.1	235.7 ± 44.3	<0.01*	193.7 ± 39.9	207.6 ± 45.9	0.01*	189.4 ± 44.3	169.3 ± 46.1	<0.01*	168.3 ± 42.8	142.4 ± 39.4	<0.01*
T2	211.2 ± 43.7	221.6 ± 41.9	0.13	191.8 ± 43.7	201.3 ± 48.5	0.11	192.3 ± 50.0	164.7 ± 43.4	<0.01*	165.0 ± 45.3	137.9 ± 43.5	<0.01*
T3	212.7 ± 44.5	218.5 ± 39.8	0.40	190.8 ± 48.7	199.4 ± 49.1	0.17	196.6 ± 56.4	164.4 ± 45.7	<0.01*	162.5 ± 48.9	133.8 ± 43.0	<0.01*
T4	206.4 ± 45.4	212.5 ± 39.1	0.38	183.3 ± 44.5	196.2 ± 46.1	0.03*	183.4 ± 50.5	162.4 ± 46.0	<0.01*	153.4 ± 48.1	122.7 ± 38.6	<0.01*
T5	200.9 ± 41.5	209.2 ± 37.4	0.20	175.1 ± 37.4	189.4 ± 44.5	0.01*	174.3 ± 50.0	153.3 ± 45.0	<0.01*	144.6 ± 40.3	114.6 ± 37.5	<0.01*
T6	195.1 ± 41.5	202.6 ± 39.0	0.25	165.7 ± 35.5	180.3 ± 44.9	<0.01*	161.8 ± 45.7	144.4 ± 41.2	<0.01*	134.1 ± 39.0	105.9 ± 38.5	<0.01*
T7	188.2 ± 40.0	196.6 ± 37.6	0.18	157.2 ± 34.9	173.9 ± 42.8	<0.01*	151.7 ± 42.6	136.7 ± 39.1	<0.01*	122.4 ± 36.7	98.0 ± 37.4	<0.01*
T8	187.6 ± 41.3	194.6 ± 37.8	0.28	154.0 ± 35.9	170.2 ± 43.3	<0.01*	149.2 ± 44.1	133.5 ± 40.3	<0.01*	119.8 ± 36.2	97.1 ± 36.3	<0.01*
T9	194.0 ± 41.3	197.9 ± 37.8	0.55	158.4 ± 34.5	176.3 ± 43.2	<0.01*	151.1 ± 43.7	135.0 ± 42.0	<0.01*	125.6 ± 37.2	96.9 ± 37.7	<0.01*
T10	192.8 ± 41.6	200.2 ± 41.3	0.27	155.2 ± 35.9	172.0 ± 44.1	<0.01*	149.1 ± 41.0	134.3 ± 40.6	<0.01*	123.1 ± 36.1	98.5 ± 37.6	<0.01*
T11	183.2 ± 41.0	190.2 ± 39.3	0.28	145.7 ± 36.3	161.5 ± 39.8	<0.01*	130.6 ± 38.2	122.4 ± 36.9	0.03*	109.0 ± 33.9	89.2 ± 37.1	<0.01*
T12	176.0 ± 40.0	182.1 ± 38.8	0.34	138.0 ± 33.6	153.5 ± 37.5	<0.01*	120.3 ± 33.5	113.9 ± 34.3	0.06	95.7 ± 30.6	82.6 ± 34.2	<0.01*
L1	175.6 ± 40.0	180.7 ± 38.3	0.42	134.2 ± 34.4	149.2 ± 37.5	<0.01*	116.7 ± 34.3	108.3 ± 34.2	0.01*	91.1 ± 32.4	78.6 ± 31.4	<0.01*
L2	172.2 ± 40.6	176.0 ± 36.8	0.54	129.7 ± 36.3	144.1 ± 39.0	<0.01*	112.6 ± 35.8	103.4 ± 35.7	0.01*	91.6 ± 33.7	76.4 ± 32.8	<0.01*
L3	166.7 ± 40.1	171.0 ± 37.9	0.49	126.2 ± 37.2	137.4 ± 39.6	0.02	106.1 ± 36.3	95.7 ± 36.0	<0.01*	85.9 ± 35.8	69.9 ± 32.3	<0.01*
L4	170.1 ± 40.1	176.0 ± 40.0	0.38	128.9 ± 38.2	140.0 ± 42.2	0.03	109.5 ± 36.4	98.2 ± 36.1	<0.01*	88.8 ± 32.9	74.5 ± 34.9	<0.01*
L5	177.8 ± 46.1	181.6 ± 44.2	0.60	135.1 ± 39.6	150.1 ± 42.1	<0.01*	120.5 ± 37.1	105.3 ± 37.8	<0.01*	99.9 ± 33.8	81.6 ± 38.5	<0.01*

P values show the differences between genders by Welch's *t* test

* Significant difference between male and female ($P < 0.05$)

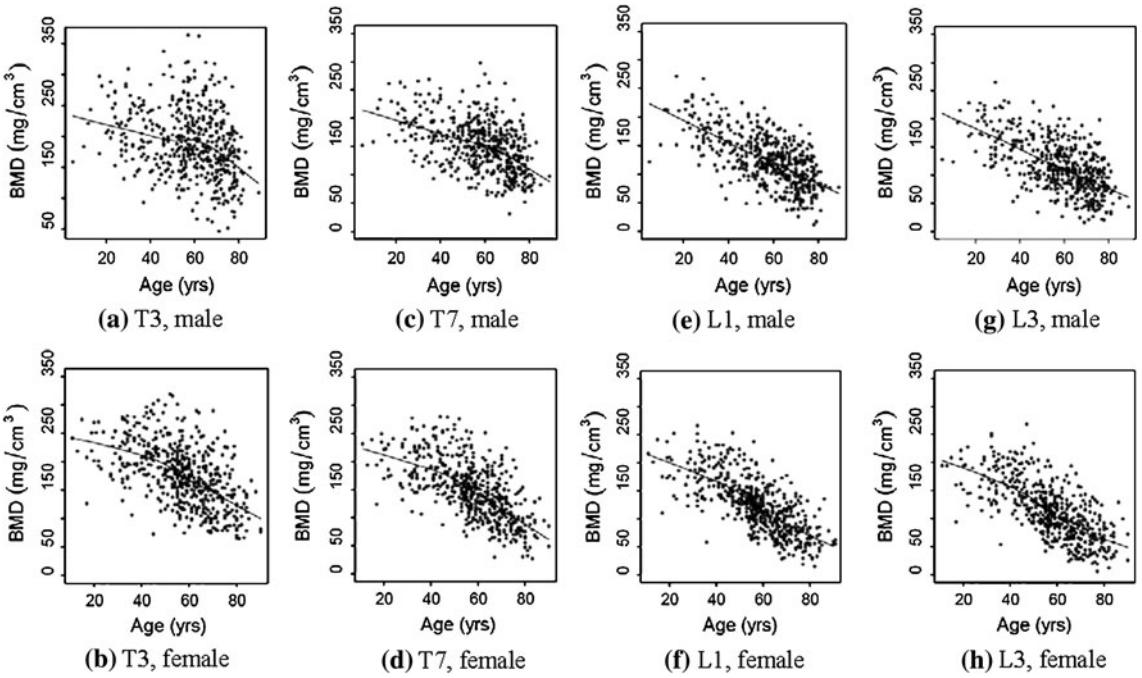

Fig. 5 Relationship between vertebral bone mineral density (BMD) and age at vertebral trabecular bones of T3, T7, L1, and L3 (**a–h**). Lowess nonparametric regression lines were added to each diagram

Weishaupt et al. [17] researched the trabecular BMD of C2, C5, T12, and L4, which they analyzed in 50 healthy volunteers (25 women, 25 men; mean age = 31.7 years). They found the trabecular BMD of C2 and C5, as measured by QCT, to be significantly higher than the trabecular BMD of T12 and L4 in both genders. Yoganandan et al. [18] have analyzed the trabecular BMD of C2–T1 and L2–L4 from 57 male subjects (mean age, 25 years; 568 vertebrae) using QCT, and indicated that lumbar vertebrae cannot act as the best surrogates for neck vertebrae, from a trabecular bone density perspective. Lu et al. [19] have analyzed the trabecular BMD of L1–S2 from 13 male subjects (mean age = 31 years) using pQCT, and found that the BMD of the S1 vertebra was significantly greater than that of the upper lumbar, lower lumbar, and S2 vertebrae. Singer et al. [16] have analyzed the trabecular BMD of thoracolumbar vertebral bodies (T1–T12 and L1–L5) in 18 subjects (8 women, 10 men; mean age = 66 years) using QCT. However, they did not classify their study's subjects into gender or age categories, and it was therefore not known how the BMD of each vertebral level was affected according to age and/or gender.

An investigation based on many cases is highly useful, from a statistical perspective. Bouxsein et al. [14] have analyzed the BMD of L1–L3 from 687 subjects (368 women, 319 men; age range = 17–88 years) using QCT, and Sigurdsson et al. [15] have analyzed the BMD of L1 and L2 from 1,715 subjects (807 women, 908 men; age range = 67–93 years) using QCT. However, it was unknown how vertebral BMD at each level was distributed because they only investigated some levels of vertebrae. The present study has analyzed the trabecular BMD of the thoracic and lumbar vertebrae (T1–T12 and L1–L5). These values include sites where osteoporotic vertebral fractures are common. These vertebrae, from 1,031 subjects (541 women, 490 men; age range = 17–88 years), were studied to demonstrate segmental variations in BMD at various vertebral levels and according to specific differences in age and gender.

In relationship to the vertebral level, Singer et al. [16] have demonstrated that L3 had the lowest trabecular BMD among thoracic and lumbar vertebrae and BMD tended to increase gradually from L3 to T1. Regardless of age and/or gender, the present study has also demonstrated the same tendency (Table 2). Yoganandan et al. [18] have found that the correlation weakens as one proceeds from the lumbar to the cervical spine, and vice versa. The present study has demonstrated the same tendency (Fig. 6). This finding indicates that estimating the BMD of distant vertebrae existing beyond the scope of CT images is difficult. For example, if the BMDs of T7 and T12 are estimated using the L3 BMD in CT images from abdominal organ examinations, the estimated accuracy of T7 BMD ($r = 0.79$) would be inferior to that of T12 ($r = 0.92$) because it is farther from L3. That is to say, it may be appropriate to use an arbitrary vertebra to make BMD measurement easier: this can be used as a first approximation, to assess vertebrae that are in the area of predilection for fracture. Nonetheless, to better understand the behavior of the target vertebrae, it

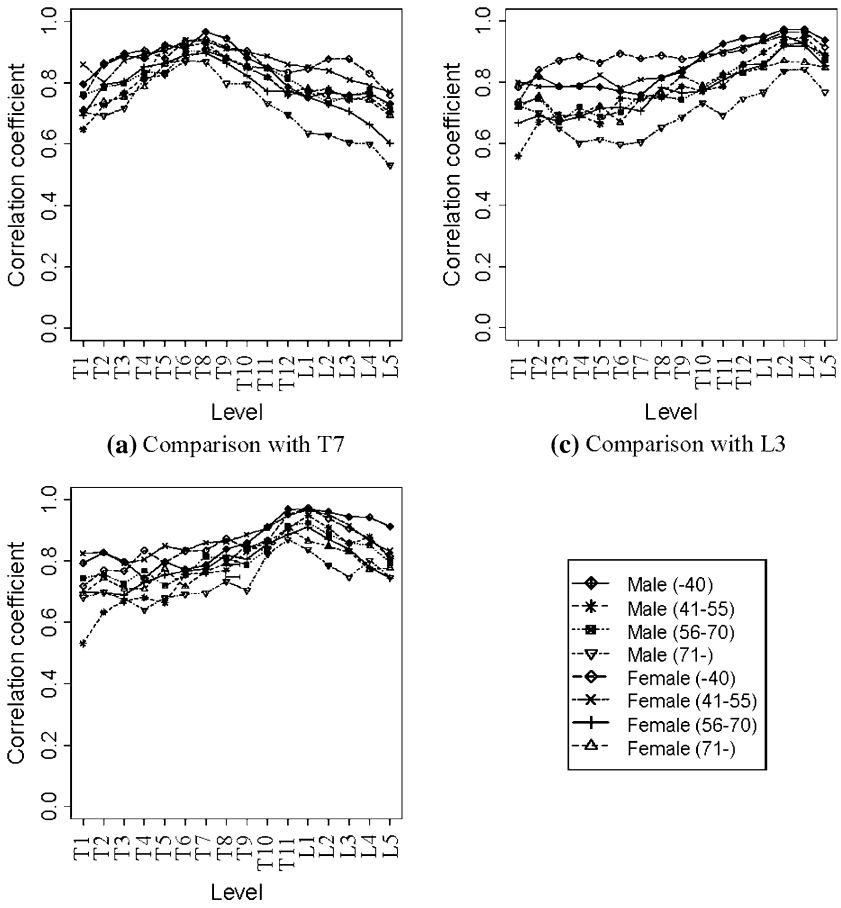

Fig. 6 Correlation of BMD of thoracic and lumbar vertebrae with T7, T12, and L3 (**a–c**, respectively)

might be necessary to obtain BMDs directly from this region.

In terms of the relationship between BMD of vertebrae according to age, various investigators have reported the deterioration of BMD with aging [1, 12–15, 22–25]. We confirmed that this tendency applied to all thoracic and lumbar vertebrae (see Table 2). In terms of the relationship between the BMD of vertebrae according to gender, the rate of bone loss accelerates for women for a period after menopause as a result of estrogen deficiency, which causes increased turnover rates and increased osteoclast activity [1]. To demonstrate this finding, we compared the perimenopausal trabecular BMD of vertebrae using a Tukey multiple comparison test. We defined perimenopausal subjects as 41–50 years old and compared them with postmenopausal subjects (51–60, 61–70, and 71–80 years old) (Table 3). Table 3 shows the following three findings: For women, trabecular BMD at the thoracic and lumbar vertebrae of perimenopausal subjects was significantly less deteriorated than that of postmenopausal subjects (51–60, 61–70, and 71–80 years old). For men, there were no significant differences in trabecular BMD of the thoracic and lumbar vertebrae between the 41- to 50-year-olds and the 51- to 60-year-olds. However, there were significant differences between those aged 41–50 years and the elderly (61–80 years old). As seen in men 61–70 years of age, trabecular BMD at the lumbar vertebrae had a tendency to deteriorate faster than did the thoracic vertebrae.

In general, peak bone mass for women is less than that for men [34], which is caused primarily by the sizes of bones rather than by differences in bone density [26, 33]. When QCT has been used, however, Bonjour et al. [33] have reported that there is no significant gender difference in the BMD at the end of pubertal maturation. Ebbesen et al. [23] have found that women had the highest densities in their younger decades. The present study is in agreement with Ebbesen et al. regarding this tendency (see Table 2).

We acknowledge several limitations of the current study. One major limitation is the uncertainty of vertebral BMD estimations. Subjects and a standard phantom were separately scanned using MDCT because our database was not obtained by "traditional" QCT. In other words, the BMD of this research was dependent on the CT number. Cann and Cenant [31] used a standard phantom to solve some problems, such as the effect of secular changes on X-ray tubes or that of differences among the software programs used by MDCT scanners.

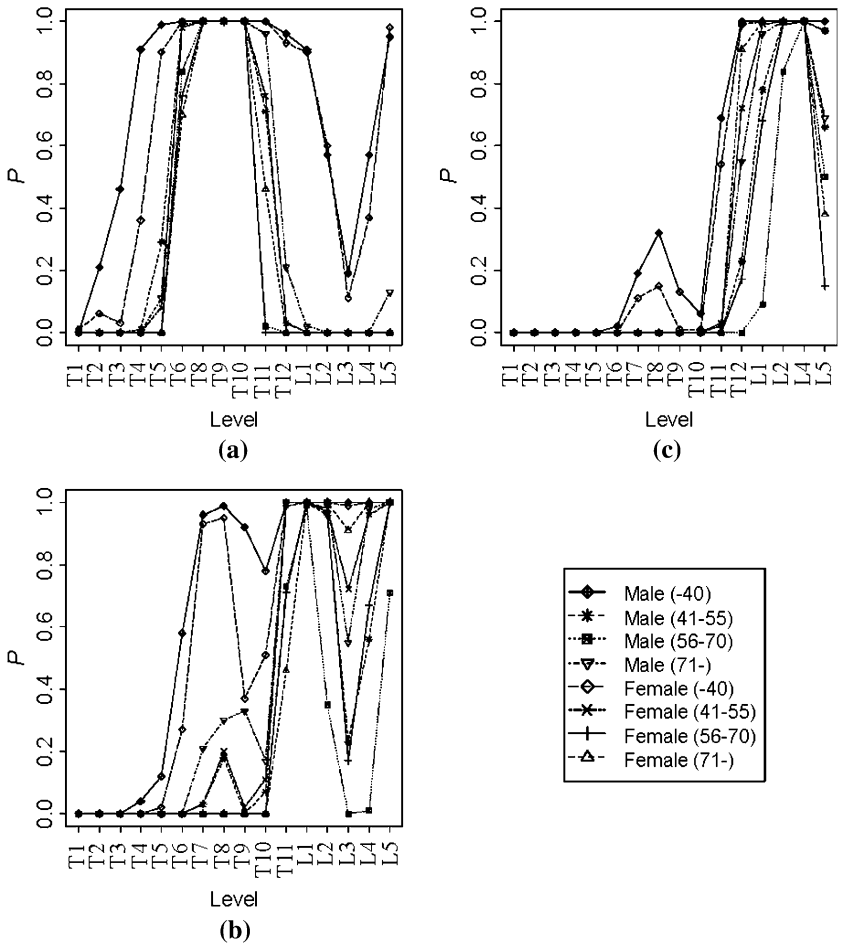

Fig. 7 Significant difference of thoracic and lumbar vertebral trabecular BMD with T7, T12, and L3 ($P < 0.05$): comparison with T7 (**a**), T12 (b), and L3 (**c**)

However, MDCT scanners are improving day by day. Nishihara et al. [35] compared the variation of CT numbers from MDCT scanners with the variation of BMD from the technique established by Cann and Cenant. They proposed that direct estimation using CT numbers was nearly satisfactory for predicting the degree of progress of osteoporosis because a CT number and a BMD from one MDCT scanner were almost at the same level of reproducibility. Moreover, Rho et al. [36] reported that there were good correlations ($r^2 > 0.6$) between the mechanical property of the vertebral trabecular bones and CT numbers. In fact, the previously mentioned BMD distributions among thoracic and lumbar vertebrae based on CT numbers in the present study showed the same tendency as that found by Singer et al. [16].

Furthermore, we compared our BMD results with those measured by other researchers (Table 4). Compared to Yoganandan et al. [18], although our measured vertebral BMD at T1 was higher than that measured in their study, the BMD at L2–L4 showed good agreement. On the other hand, compared to Tanno et al. [22], Ito et al. [3], and Weishaupt et al. [17], except for the BMD at L2 and L3 of women less than 40 years old, the BMD measured in the present study showed a low value. Here, it is necessary to note that the measurement sites in the present study were in the central region, which has low BMD. In our previous research, we have found that the central region is about 13 mg/cm^3 lower than that of the vertebral trabecular bones [25]. In addition, there are differences according to ethnicity, nutrition, environment, and genetics of the study subjects [37]. Taking these facts into consideration, BMD as measured in the present study seems to agree approximately with other research. Basically, a QCT study should be performed to measure BMD in the lumbar vertebrae using the reference phantom to avoid the beam hardening effect and to preserve reproducibility. However, because the results of this study were not adjusted by using a reference phantom, measurement errors may have been included. Furthermore, the subjects included in our study were "not-healthy" hospital control and included patients with cancer and in postoperative condition. For the interpretation of the results of this study, we should be wary that there are possibilities of inclusion of measurement errors.

Another limitation was that there was no subject with vertebral fractures. Further study in both subjects with and subjects without vertebral fractures needs to be performed.

Table 3 Correlation of trabecular BMD of thoracic and lumbar vertebral bodies between 41–50 years and other age categories

Level	Age (years)					
	51–60		61–70		71–80	
	Male ($n = 112$)	Female ($n = 159$)	Male ($n = 126$)	Female ($n = 129$)	Male ($n = 113$)	Female ($n = 82$)
T1	1.0	<0.01*	0.7	<0.01*	0.02*	<0.01*
T2	0.85	<0.01*	0.90	<0.01*	0.01*	<0.01*
T3	0.89	<0.01*	1.00	<0.01*	0.01*	<0.01*
T4	0.89	<0.01*	0.99	<0.01*	0.01*	<0.01*
T5	0.61	<0.01*	0.87	<0.01*	<0.01*	<0.01*
T6	1.00	<0.01*	0.40	<0.01*	<0.01*	<0.01*
T7	1.00	<0.01*	0.21	<0.01*	<0.01*	<0.01*
T8	1.00	<0.01*	0.18	<0.01*	<0.01*	<0.01*
T9	1.00	<0.01*	0.23	<0.01*	<0.01*	<0.01*
T10	0.97	<0.01*	0.12	<0.01*	<0.01*	<0.01*
T11	0.66	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*
T12	0.45	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*
L1	0.60	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*
L2	0.77	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*
L3	0.50	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*
L4	0.41	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*
L5	1.00	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*

Correlation was computed by Tukey multiple comparison test

* Significant difference between male and female ($P < 0.05$)

Table 4 Comparison of mean BMD at vertebral trabecular bones reported in the present study and by other research groups

Group name	Other research groups				Present study			
	Age (years)	Gender	Vertebral level	BMD (mg/cm^3)	Age (years)	Gender	Vertebral level	BMD (mg/cm^3)
Yoganandan et al. [18]	Mean 25	Male	T1	194.3	Under 40	Male	T1	214.2
	Mean 25	Male	L2	173.9	Under 40	Male	L2	172.2
	Mean 25	Male	L3	169.7	Under 40	Male	L3	166.7
	Mean 25	Male	L4	173.1	Under 40	Male	L4	170.1
Tanno et al. [22]	Under 40	Male	Avg. L2 and L3	190.0	Under 40	Male	Avg. L2 and L3	169.4
	Under 40	Female	Avg. L2 and L3	170.0	Under 40	Female	Avg. L2 and L3	173.5
	41–64	Male	Avg. L2 and L3	150.0	41–64	Male	Avg. L2 and L3	122.7
	41–64	Female	Avg. L2 and L3	150.0	41–64	Female	Avg. L2 and L3	125.8
	Over 65	Male	Avg. L2 and L3	110.0	Over 65	Male	Avg. L2 and L3	91.9
	Over 65	Female	Avg. L2 and L3	100.0	Over 65	Female	Avg. L2 and L3	77.5
Ito et al. [3]	Mean 64	Female	L3	103.9	56–70	Female	L3	95.7
Weishaupt et al. [17]	Mean 30	Male	T12	184.9	Under 40	Male	T12	176.0
	Mean 30	Female	T12	193.1	Under 40	Female	T12	182.1
	Mean 30	Male	L4	180.1	Under 40	Male	L4	170.1
	Mean 30	Female	L4	186.2	Under 40	Female	L4	176.0

Other limitations were that we did not refer to the relationship between vertebral size and BMD. Singer et al. [16] reported that the trabecular BMD of vertebrae was poorly correlated with failure load but was more highly correlated with failure stress. Furthermore, when the trabecular BMD was multiplied by the vertebral body cross-sectional area, the relationship to failure load was considerably improved. Therefore, analysis including the cross-sectional area needs to be performed through further study.

In summary, the present study measured the trabecular BMD of thoracic and lumbar vertebrae from 1,031 subjects who had undergone MDCT. Relationships between BMD,

age, and gender were shown statistically. The improved knowledge about the trabecular BMD of thoracic and lumbar vertebrae obtained in the present study may help establish diagnostic criteria for primary osteoporosis using MDCT. Further studies with vertebral BMD, such as comparisons of BMD with or without vertebral fractures, and analytical comparisons between BMD and vertebral size, are needed to develop a better understanding of vertebral fractures.

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