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Ex Vivo and *In Vivo* Assessment of Vertebral Strength and Vertebral Fracture Risk Assessed by Dual Energy X-Ray Absorptiometry

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1. Introduction

Osteoporosis is defined as a skeletal disorder characterized by loss of bone mass, decreased bone strength and resulting in increased risk of bone fracture. The disease is progressive with age, especially in postmenopausal women [1]. Osteoporotic hip fractures and vertebral fractures have become a major social problem because the elderly population continues to increase. Hip fractures account for about 10% of all osteoporosis-related fractures [2]. Hip fractures are particularly devastating and have a particularly negative impact on morbidity. Survivors often suffer severe and prolonged physical and social limitations, and fail to recover normal activity [3]. Vertebral fractures affect approximately 25% of postmenopausal women [4]. Vertebral fractures can be associated with chronic disabling pain and incur loss of normal activity.

In addition to this increased awareness of osteoporosis as a significant health problem, there has been the emergence of several novel drugs that appear to be effective at reducing the risk of fracture, such as bisphosphonates. Consequently, clinicians and researchers are emphasizing the importance of early detection of osteoporosis, aggressive fracture prevention, and monitoring of patients who have high risk of fractures. Fracture risk associated with osteoporosis consisted of bone strength reduction and tendency to fall, therefore it is essential to measure bone strength to assess the risk of fracture. Bone strength reflects the integration of bone density and bone quality, which are influenced by bone architecture, bone turnover, accumulation of damage, and mineralization [5].

Traditionally, measurement of areal bone mineral density (aBMD) by dual energy X-ray absorptiometry (DXA) has served as the means by which to best diagnose osteoporosis and evaluate fracture risk [6]. In 1994, the World Health Organization (WHO) published a set of diagnostic criteria to define osteoporosis in postmenopausal Caucasian women, using aBMD values measured by DXA [7]. Measurement of aBMD by DXA has been the standard method for diagnosing osteoporosis, in addition to assessing fracture risk and therapeutic effects. However, a variety of problems exist with DXA, which include its relatively high cost, the absence of DXA in many communities, especially in less-developed countries.

Therefore, aBMD by DXA is not a suitable screening method for fracture risk in terms of accessibleness and cost. In addition, the correlations between bone strength and aBMD by DXA are reported to be 0.51-0.80 [8-11], which indicates aBMD only accounts for 50 to 80% of bone strength. And the application of aBMD measurements in isolation cannot identify individuals who eventually experience bone fracture because of the low sensitivity of the test [12].

Recently, quantitative ultrasound (QUS) is emerging as a relatively low-cost and readily accessible alternative means to identify osteoporosis, evaluate fracture risk, and initiate osteoporosis treatment. More recently, finite element (FE) method based on data from computed tomography (CT) has been used to assess bone strength, fracture risk, and therapeutic effects on osteoporosis.

2. Dual energy X-ray absorptiometry (DXA)

In the 1960s, a new method of measuring aBMD, called single-photon absorptiometry (SPA), was developed. In this method, a single-energy photon beam is passed through bone and soft tissue to a detector. The amount of mineral in the path is then quantified. This method most commonly uses a gamma-ray source coupled with a scintillation detector, which together scan across the area of interest [13]. The amount of the bone mineral in the tissue traversed by a well collimated gamma-ray beam is derived from its attenuation through bone plus soft tissue relative to that through soft tissue alone. The overall thickness of the soft tissue is standardized, usually by immersing the limb in water or cuffing with a fluid-filled bag. The value obtained is proportional to the bone mineral content of the segment scanned. The value may be divided by the bone width (yielding a result in g/cm) or by an estimate of the cross-sectional area to give a value for bone mineral density in g/cm^2. The technique has been applied to the femur, humerus, metacarpal, os calcis, hand and foot, but the most commonly used site is the forearm. The most frequently used source is ^{125}I (27keV), but has the major drawback of a relatively short half-life (60 days).

Accuracy may be compromised by a non-uniform thickness of fat, which has attenuation characteristics different from those of water or lean soft tissue. In some equipment, the program assumes the fat to be a uniform shell around the bone and makes a correction, but the correction requires a number of assumptions that influence the accuracy of the method. The heterogeneity of surrounding tissues is nevertheless considerably less than that of tissue surrounding axial sites such as the spine. Although true *in vivo* estimates of accuracy have not been made, errors in cadaveric studies of excised bone have sufficiently low to make the technique attractive for screening [14].

The radiation dose of SPA is very low and applied to a small volume of tissue, giving an effective dose equivalent of < 1μSv. Typical scanning times are 10-15 minutes. Single-energy X-ray absorptiometry (SXA) is a newly developed technique suitable for scanning appendicular sites. It avoids the need for isotopes and is likely to replace SPA.

The proximal femur and the vertebral bodies, with their associated processes, are very irregular bones that are difficult to delineate. Furthermore, they are surrounded by a widely varying amount of fat and muscle mass. The ratio of bone mass to soft tissue is thus lower in the spine or hip than in the forearm, and standardization of soft tissue by immersion in water is not feasible for these sites. These and other factors limit the use of SPA or SXA to

the appendicular skeleton. The development of dual-photon absorptiometry (DPA) and, more recently, dual-energy X-ray absorptiometry (DXA) have resolved at least some of these problems. The different thickness of soft tissue can be accommodated by simultaneous measurement of the transmission of gamma-rays of two different energies, which makes the techniques applicable to any part of the body, but particularly the lumbar spine and hip.

The theory underlying DPA and DXA requires that there are only two components present – bone and soft tissue of uniform composition. In practice, fat forms a further component with attenuation characteristics that differ from those of water, muscle and most organs. A uniform layer of fat is unimportant, but fat is distributed non-uniformly in the region of the lumbar spine and may cause errors of up to 10% in spinal bone mineral. Errors can also be introduced by fat within the vertebral bone marrow.

Total body bone mineral can be measured by DPA, but instrumental problems are greater because of the wide range of count rates and the non-uniform distribution of fat, which introduces errors. However, total body bone mineral measured by neutron activation analysis. As with SPA, the radiation dose for DPA is low, the effective dose equivalent for part-body examinations being only a few microsieverts (µSv).

Recently, sources of gamma radiation have been replaced by X-ray generators. The necessary pairs of effective energies can be obtained either by K-edge filtering, using cerium or samarium, or by rapidly switching the generator potential. The advantages of these approaches are a higher beam intensity and therefore faster scan, improved spatial resolution with easier identification of vertebrae, and better precision. The absence of source decay also eliminates problems associated with decreasing count rates over the lifetime of the source.

Like DPA, DXA determines bone mineral density from an anterior-posterior image. The sites most commonly measured are the lumbar spine, generally L2-L4, including the intervertebral discs. Other sites include the hip, forearm, whole body and skeletal segments. The error in reproducibility *in vitro* is 1-2%. DXA has been reported to have a high short-term and long-term precision *in vivo*, which is about twice that of DPA. This has led to its widespread use in studies of osteoporosis.

A recent development has been scanning of the lumbar spine in the lateral position, which has the advantage of eliminating the posterior arch and the spines of the vertebrae as well as aortic calcification from the measurement. Its limitations are the increased soft tissue mass and overlap of the projected image by the ribs and pelvis, so that only one or two vertebrae are measured. Lateral scanning provides a measurement of vertebral depth which, together with the antero-posterior area, can provide a volumetric measurement for calculating bone mineral mass per unit volume. Whether this volumetric density measure is a better predictor of fracture is unknown. The technique may be useful in assessment of bone density in children, allowing accurate assessment of vertebral size. The precision error of measurement of the vertebral body and mid-slice *in vivo* is of the order of 2% [15]. DXA has now largely replaced DPA for screening because of its greater precision, ease of use and freedom from several technical artifacts. The WHO defines osteoporosis as a value for aBMD by DXA 2.5 standard deviation (SD) or more below the mean for young Caucasian adult women (T-score diagnostic criteria of -2.5), based on data that this criterion identified 30% of all postmenopausal women as having osteoporosis, more than half of whom would have sustained a prior fracture [7].

3. Quantitative computed tomography (QCT)

In quantitative computed tomography (QCT), a thin transverse slice through the body is imaged. Under appropriate conditions, the image can be quantified to give a measure of volumetric bone mineral density (vBMD) (mg/cm^3), and cancellous bone can be measured independently of surrounding cortical bone and aortic calcification. Developments have been concentrated in two directions: the construction of special equipment using a radionuclide source for measurements of the forearm, and the adaptation of X-ray CT machines installed for general radiology to measure vBMD. The attraction of the technique is that cancellous bone can be examined separately from cortical bone. It also gives a true value for mineral density (mg/cm^3) unlike other techniques.

A dedicated forearm scanner was first described in the mid 1970s [16,17]. The photon source is ^{125}I and is mounted in a gantry with a sodium iodide scintillation detector. A linear scan is performed at each of 48 angular positions. Computer reconstruction generates an image in which a region of interest in the cancellous bone of the distal ulna is selected. Since 1980s, QCT has been used as a means for non-invasive quantitative determination of bone mineral of the spine [18,19].

A lateral plane projection scan is necessary for precise slice positioning through the centers of the vertebrae. Comparison between the CT Hounsfield numbers and a calibration standard scanned simultaneously allows bone density to be expressed in terms of the equivalent concentration of the material of the standard. Regions of interest within the vertebral bodies are selected: circular, elliptical, rectangular or other chosen areas are selected to include all the cancellous bone just inside the cortex. The relationship between the observed CT number and the true attenuation coefficient is subject to short- and long-term variation, so that it is necessary to scan the patient and a calibration standard simultaneously. Recently, simple standards with fewer components based on suspensions of calcium hydroxyapatite in plastic have been adopted. Comparison between the standard and the Hounsfield numbers of the trabecular region of the vertebral bodies allows bone density to be expressed in terms of the equivalent concentration of the material of the standard.

Investigators reported the prediction of vertebral body compressive strength using QCT. In 1985, McBroom et al. [20] showed a strong positive correlation between QCT and apparent density of the vertebral trabecular bone but could find only suggestive, not quite significant, correlations between QCT and the vertebral body compressive strength. Cann et al. [21] showed that QCT evaluation of vertebral trabecular bone mineral density is a useful tool for determining the patients with increased risk of vertebral fracture. The positive correlations between QCT and vertebral body compressive strength in cadaver studies are 0.72-0.74 [22,23].

The biggest source of error in X-ray CT systems is fat within the bone marrow: accuracy errors of up to 30%. The accuracy can be improved by carrying out scans at two different potentials (dual energy techniques); typically, 80 and 120 kVp are used. Kalender et al. [24] claim an accuracy error of 5% *in vitro*, but errors *in vivo* are likely to be larger. The effective radiation doses equivalent for QCT are 0.3 mSv for single energy techniques and 1 mSv for dual energy techniques, respectively [25].

4. Quantitative ultrasound (QUS) bone assessment method

QUS bone assessment method has been recently introduced as an alternative for peripheral bone mass assessment, reflecting bone strength, bone density, and bone elasticity or fragility, and may be superior to aBMD by DXA [26]. The advantages of this method over X-ray-based techniques, which include low cost, portability, and no radiation exposure, have encouraged the use of this method for defining a stage of development of osteoporosis and evaluating bone fracture risk.

There are several reports for assessing bone conditions *in vivo* using QUS method and apparatus. QUS devices can be classified mostly into 3 groups, related to the type of ultrasound transmission. Trabecular sound transmission is best for measuring the heel [27]. Cortical transverse transmission currently only is used in phalanx contact devices [28]. And cortical axial transmission presently is being investigated for use in phalanges, the radius, and the tibia [28]. Heel devices currently appear to have the most clinical applications, where QUS are being used and evaluated for the prediction of fracture risk, the diagnosis of osteoporosis, the initiation of osteoporosis treatment, the monitoring of osteoporosis treatment, and osteoporosis case finding. For these purposes, the recommended parameter of interest in clinical routine is a composite score, e.g., heel stiffness index or Quantitative Ultrasound Index (QUI) combining the results of broad-band ultrasound attenuation (BUA) and speed of sound (SOS), as measured in meters per second.

At the present time, there is good evidence that QUS can discriminate those with osteoporotic fractures from age-matched controls without osteoporotic fracture [29,30]. The power of heel QUS to predict fracture observed in cross-sectional studies has been confirmed prospectively in some populations as defined by sex, age, and ethnic background. This is particularly true of heel QUS and for hip and spinal fractures. However, because of methodological issues, it is difficult to compare studies. Nonetheless, it is possible to make the following generations. Using QUS of the heel, the increase in relative risk for each standard deviation decrease in stiffness index (SI) is approximately 2.0 for the hip and spine and roughly 1.5 for all fractures combined [31-41].

The evidence from studies is good that the heel QUS SI using QUS devices is predictive of hip fracture risk in Caucasian and Asian women over age 55 and of any fracture risk in Asian women over age 55. Cortical axial transmission devices have no prospectively proven clinical utility, although clinical use in adults of phalanx QUS devices using cortical transverse transmission is also limited. These results for heel QUS are roughly the same as for DXA by BMD in terms of hip and spine fracture risk per SD decrease [12,42]. Discordant results between heel QUS and DXA, which are not infrequent, are not necessarily an indication of methodological error but rather due to the independence between the 2 techniques.

Diagnosing osteoporosis using QUS is less supported by evidence and more complicated and problematic than assessing fracture risk. To start with, the T-score diagnostic criteria of -2.5, classically used for DXA aBMD, cannot be applied to QUS without discrepancies in the numbers of women diagnosed with osteoporosis because of tremendous variations in QUS measurements by skeletal site, because different QUS devices yield different results, and because of the relatively poor correlation between heel QUS and hip/spine DXA measurements. If the prevalence of osteoporosis is defined as -2.5 SD from the mean

threshold for QUS, even within the same sample population, different QUS instruments and different skeletal sites generate prevalence estimates that vary as much as 10-fold, such as prevalence estimates among Caucasian women over age 65 ranging from 4 to 50% [43-46]. To overcome this dilemma, there is a need for predefined, device-specific diagnostic thresholds. One recommended system suggests calibrating QUS measurements with DXA results, the latter used as the "gold standard," so that an upper QUS threshold is set to identify osteoporosis with 90% sensitivity and a lower threshold is set to identify osteoporosis with 90% specificity [47]. Using such a system, one could identify osteoporosis with high probability in patients whose results fall below the lower threshold for QUS, where specificity exceeds 90%; between the upper and lower thresholds, the diagnosis of osteoporosis would be considered quite equivocal, so that another means of measurement, like DXA aBMD, would be highly recommended; and above the upper threshold for QUS, where the sensitivity of a value below the threshold is 90%, osteoporosis would be deemed unlikely.

Except in the case of a low-energy fractures of the hip or spine, when the fracture alone is adequate to require treatment, all currently published recommendations for the initiation of treatment for osteoporosis are based on DXA aBMD values; in no instance, to date, are the results of QUS the definitive parameter. Despite this, several studies have demonstrated high levels of correlation between heel trabecular sound transmission and aBMD at matched skeletal sites [48-50]. Moreover, both SOS and BUA, standard QUS measurements, are dependent on overall bone strength which, in turn, is related to bone density, architecture and turnover, and the extent of bone mineralization [48,50,51-56]. These factors likely work together to maintain the overall quality and strength of bone and to prevent fractures and other bone failure. QUS parameters of heel trabecular transverse transmission are highly correlated with bone strength [57-62]. Consequently, it is conceivable that QUS guidelines for treatment initiation could be created, especially if combined with the use of clinical risk factors [63]. But no randomized clinical trials have been published examining whether individuals identified as high risk for fracture by QUS respond to treatment.

5. Finite element (FE) method based on data from computed tomography

The finite element (FE) method, an advanced computer technique of structural stress analysis developed in engineering mechanics, was first introduced to orthopaedic biomechanics in 1972 to evaluate stressed in human bones [64]. Since then, this method has been used to study the mechanics of human bones [65]. In the early 1990s, the FE method of analyzing a bone for fracture risk using 3-dimensional CT data was developed.

The object of this method is to measure non-invasively the strength of an individual bone in an individual patient. This measurement can then be used to determine whether or not the bone will fracture under specified loading conditions such as those normally seen in daily living. It can also be used to estimate fracture risks under abnormal loading conditions such as occur in falling, jumping or during athletic events or heavy training regimens. This method uses the distribution of physical properties of bone measured non-invasively in an individual and mathematical analysis of that distribution to predict the risk that a bone may fracture under applied loads. The use of such methods relates to the clinical disease of osteoporosis, or in general metabolic bone diseases. In a primary application, 3-dimensional CT data acquired using a conventional CT scanner are used to determine the distribution of

bone mineral density, this distribution is used to define bone material properties, and the FE method of analysis is used to determine structural properties of the whole or a part of the bone. This information is then used to predict risk of fracture under specified loading conditions. Specifically, the distribution of bone material properties determined non-invasively is used as input to a FE analysis of structural strength, and other parameters such as loading conditions and boundary conditions are also included in the model as needed. Using mathematical methods contained in commercially-available or specially written computer programs, the model of a bone can be incrementally loaded until failure, and the yield strength determined.

A FE method based on data from CT has been applied to predict proximal femoral fracture [66-70]. CT-based FE method appears more predictive of femoral strength than QCT or DXA alone [66] and can predict proximal femoral fracture location [68]. Nonlinear FE method demonstrated improved predictions of femoral strength [69]. For the spine, CT-based nonlinear FE method was clinically applied to assess vertebral strength [71] and cadaver studies have been performed to evaluate the accuracy of CT-based FE method [72-77]. The cadaver studies have verified CT-based FE method predicts failure loads and fracture patterns for 10-mm-thick vertebral sections [72] and can predict *ex vivo* vertebral compressive strength better than aBMD [73,74] and QCT alone [75]. CT-based nonlinear FE method can accurately predict vertebral strength, fracture sites and distribution of minimum principal strain *ex vivo* [77]. Based on verification by the cadaver studies, FE method has been applied clinically to the assessment of chronic glucocorticoid treatment at the hip [78], as well as teriparatide and alendronate treatment for osteoporosis at the lumbar spine [79], proving useful for assessing medication effects on bone strength.

A study assessing vertebral fracture risk and medication effects on osteoporosis *in vivo* with CT-based nonlinear FE method showed that analyzed vertebral compressive strength had stronger discriminatory power for vertebral fracture than aBMD and vBMD, and detected alendronate effects at 3 months earlier than aBMD and vBMD [80]. The CV (coefficient of variation) for the measurement of vertebral compressive strength was 0.96% *ex vivo*. The effective radiation dose for assessing vertebral compressive strength is 3 mSv.

CT-based FE method predicts compressive bone strength accurately and is useful for assessing the risk of fracture and therapeutic effects on osteoporosis, and provides unique theories from a biomechanical perspective. This method also predicts bone strength under specified loading conditions such as those normally seen in activities of daily living [81,82].

6. Assessment of vertebral strength *ex vivo* by DXA

This study was conducted at Tokyo University in Tokyo, Japan. The study protocol was approved by the ethics committee.

Twelve thoracolumbar (T11, T12, and L1) vertebrae with no skeletal pathologies were collected within 24 hours of death from 4 males (31, 55, 67, and 83 years old). Causes of death for the four donors were myelodysplastic syndrome, pneumonia, adult T-cell leukemia, and bladder cancer, respectively. All of the specimens were obtained at Tokyo University Hospital with the approval of the ethics committee and with informed consent. They were stored at –70 C° after each step in the protocol. The vertebrae were disarticulated,

and the discs were excised. Then the posterior elements of each vertebra were removed by cutting through the pedicles. The vertebrae were immersed in water and aBMD (g/cm²) of the vertebrae were measured by DXA (DPX; Lunar, Madison, WI, USA) in the supine position.

To assess vertebral strength, a quasi-static uniaxial compression test of each vertebra was conducted. To restrain the specimens for load testing, both upper and lower surfaces of the vertebrae were embedded in dental resin (Ostron; GC Dental Products Co., Aichi, Japan) so that the two surfaces were exactly parallel. Then the embedded specimens were placed on a mechanical testing machine (TENSILON UTM-2.5T; Orientec, Tokyo, Japan) and were compressed at a cross-head displacement rate of 0.5 mm per minute. A compression plate with a ball joint was used to apply a uniform load onto the upper surface of the specimen. The applied load was measured by a load cell (T-CLB-5-F-SR; T. S. Engineering, Kanagawa, Japan). The load was recorded using MacLab/4（AD Instruments, Castle Hill, NSW, Australia）at a sampling rate of 2 Hz. The measured vertebral strength was defined as the ultimate load achieved. Pearson's correlation analysis was used to evaluate correlations between the measured aBMD by DXA and the measured vertebral strength by mechanical testing.

The result from the *ex vivo* assessment, aBMD by DXA ranged from 0.287 to 0.705 g/cm², while the measured vertebral strength by mechanical testing ranged from 1.54 to 4.62 kN. There were significant linear correlations between aBMD and the measured vertebral strength ($r = 0.915$, $p < 0.0001$) (Fig. 1).
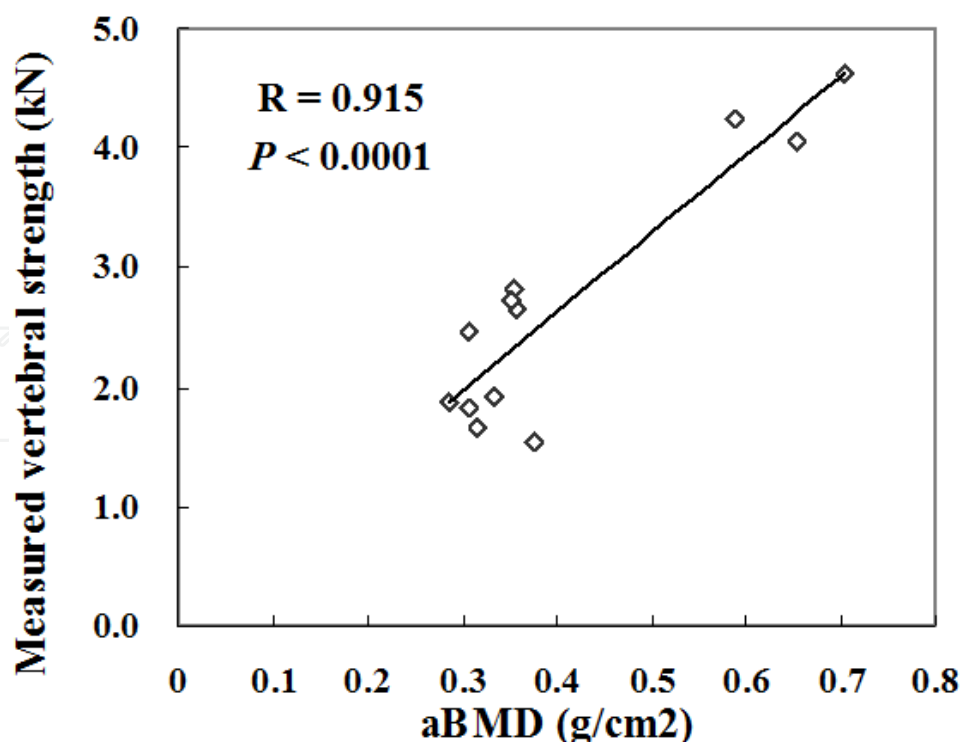

Fig. 1. The experimentally measured vertebral strength versus aBMD measured by DXA. They were significantly correlated.

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7. Assessment of vertebral fracture risk *in vivo* by DXA

This study was conducted at Tokyo Metropolitan Geriatric Medical Center in Tokyo, Japan. The study protocol was approved by the ethics committee and each participant provided written informed consent in accordance with the Declaration of Helsinki.

The inclusion criteria included ambulatory postmenopausal Japanese women aged between 49 and 85 years old. Exclusion criteria included women with any disorders of bone and mineral metabolism other than postmenopausal osteoporosis, those who had any recent or current treatment with the potential to alter bone turnover or bone metabolism. Vertebral fracture was diagnosed based on lateral spine radiography. Radiographic vertebral fracture was defined if either the anterior or central height was ≥20% less than posterior height. A total of 123 eligible participants were enrolled in this cross-sectional study. For all participants, aBMD of the anteroposterior (AP) lumbar spine (L2-4) were measured by DXA (DPX; Lunar, Madison, WI, USA).

Logistic regression analysis was performed to estimate risk factors for vertebral fracture. L2-4 aBMD was assessed using sensitivity and specificity curves to determine the optimal cut-off point as the vertebral fracture threshold. For each statistical analysis, differences were considered significant at $p<0.05$. Statistical analysis was performed using StatView for Windows version 5.0 software (SAS Institute, Cary, NC, USA).

The 123 women enrolled in the *in vivo* clinical study had a mean age of 71.8 ±7.4 years, mean height of 149.4 ±5.6 cm, and mean weight of 50.2 ±7.4 kg. Measured L2-4 aBMD was 0.816 ±0.191 g/cm². Subjects were classified on the basis of prior vertebral fracture. Among the 123 women, 75 subjects did not have any vertebral fractures (nonfracture group) and 48 subjects already had vertebral fractures (fracture group). The average aBMD of the non-fracture group was 0.860 ± 0.166 g/cm², which was greater than that of the fracture group at 0.759 ± 0.207 g/cm² (Mann-Whitney *U* test, $p = 0.0255$).

Vertebral fractures were present in 39.0% of the total study population. Among the fracture group, vertebral fractures spontaneously developed in 29 women (spontaneous fracture group) and were caused by trauma in 19 women (traumatic fracture group). Among the 19 subjects in the traumatic fracture group, 18 women developed fracture following a fall from standing height, and 1 woman developed fracture following a fall down stairs. To exclude factors of trauma, 75 subjects in the nonfracture group and 29 subjects in the spontaneous fracture group were compared. aBMD (Mann-Whitney *U* test, $p=0.0033$) was significantly decreased in the spontaneous fracture group compared with the nonfracture group. Logistic regression analysis after adjustment for age and body weight revealed that aBMD reduction as risk factors associated with spontaneous vertebral fracture, the odds ratio per SD decrease was 1.83 with 1.13-3.26 of 95% confidence interval ($p=0.0238$). aBMD was also assessed by sensitivity and specificity curves. The nonfracture group and spontaneous fracture group (104 women in total) were assessed in a cross-sectional manner. The optimal point on the sensitivity and specificity curves used as the fracture threshold to predict spontaneous vertebral fractures for aBMD was 0.816 g/cm² with 69.0% sensitivity and 72.0% specificity (Fig. 2).

8. Discussion

Bone strength primarily reflects bone density and bone quality, which are influenced by bone architecture, turnover, accumulation of damage, and mineralization [5]. Previous
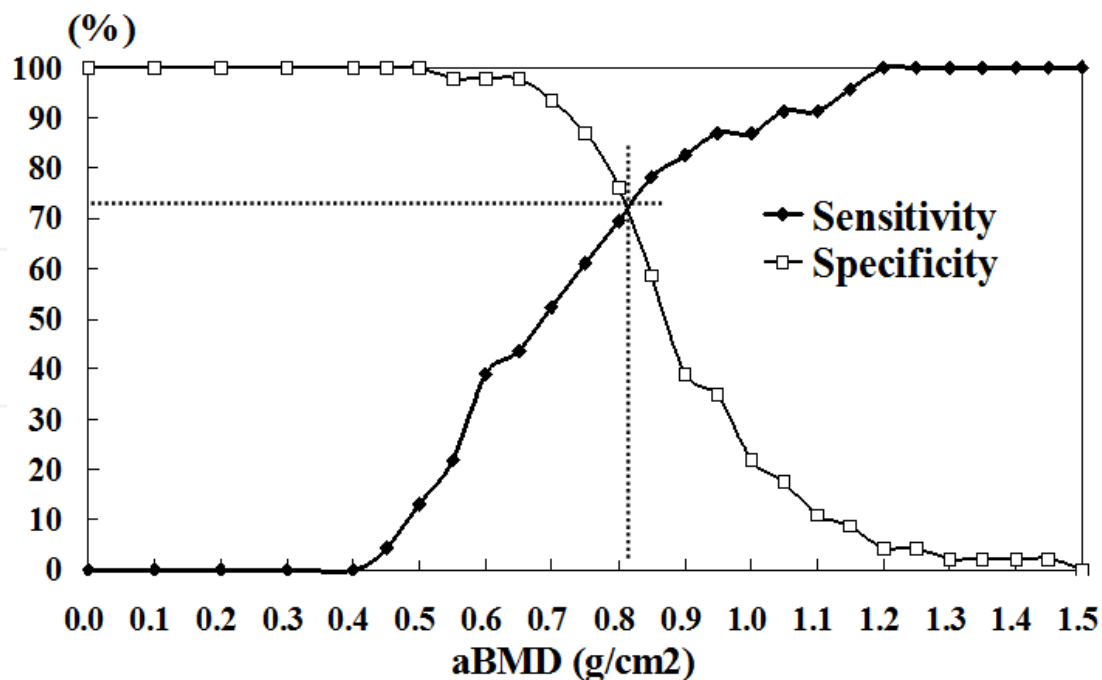
Fig. 2. Sensitivity and specificity curves to determine the optimal cut-off point of aBMD measured by DXA to predict spontaneous vertebral fracture.

studies showed that aBMD explained 50-80% of vertebral strength [8-11] based on data that the correlations between aBMD and the measured vertebral strength were 0.51 to 0.80. In this study, the correlations between the measured values of aBMD and the vertebral strength were 0.915 and better than the previous studies. This *ex vivo* study showed that aBMD measurements in isolation might assess vertebral strength well.

In the treatment of osteoporosis, the target is to assess fracture risk and prevent fractures. This *in vivo* study showed that aBMD had high discriminatory power for spontaneous vertebral fracture. The cut-off value of aBMD for predicting vertebral fractures without trauma was 0.816 g/cm², equivalent to -2.62 SD compared to young healthy Japanese women. Low trauma fractures such as a fall from a standing height are due to osteoporosis. The present assessment excluded the traumatic fracture group. Therefore, the threshold value was not for diagnosing osteoporosis, but for assessing spontaneous vertebral fracture risk.

This *ex vivo* and *in vivo* study showed that aBMD was a good parameter of vertebral strength and vertebral fracture risk. However, aBMD in isolation can only assess bone density and can not assess bone quality. Therefore, accuracy of assessing vertebral strength by aBMD is limited.

To improve accuracy of assessing vertebral strength and vertebral fracture risk, new method has been developed. CT-based nonlinear FE method can accurately predict vertebral strength, fracture sites and distribution of minimum principal strain *ex vivo* [77]. Based on verification by the cadaver studies, FE method has been applied clinically. A study assessing vertebral fracture risk and medication effects on osteoporosis *in vivo* with CT-based nonlinear FE method showed that analyzed vertebral compressive strength had stronger discriminatory power for vertebral fracture than aBMD and detected alendronate effects at 3 months earlier than aBMD [80].

This method assesses bone geometry and heterogeneous bone mass distribution as well as aBMD, but cannot detect microdamage and bone turnover. In clinical application, other parameters such as age and bone turnover markers should be included to assess the risk of fracture and therapeutic effects. Methods for assessing fracture risk and therapeutic effects on osteoporosis in the future might include other parameters as well as CT data.

Prediction by FE method with a smaller element size using the data from CT scans with a thinner slice thickness and a smaller pixel size is more accurate. On the other hand, thinner CT slices lead to more radiation exposure in the clinical situation. To decrease radiation exposure as much as possible during CT scanning, optimization of the element size of the FE method was performed by assessing the accuracy of the FE method simulation [83]. With the limited resolution of currently available CT scanners, the micro-architecture of the bone cannot be precisely assessed. Micro-CT and synchrotron micro-CT visualize bone microstructure. However, obtaining micro-CT scans of a whole vertebra *in vivo* would be impossible with the currently available scanners. Also, use of thinner CT slices to obtain images leads to more radiation exposure. With future developments, FE method based on micro-CT data with less radiation dose might be promising.

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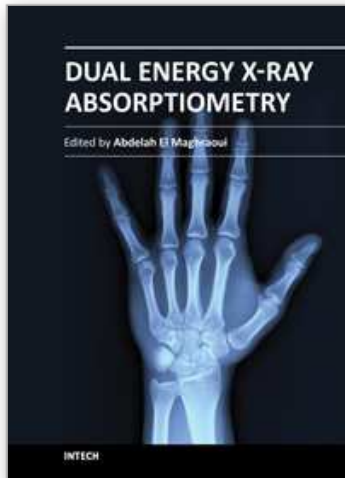
Dual Energy X-Ray Absorptiometry

Edited by Prof. Abdelah El Maghraoui

The World Health Organization (WHO) has established dual-energy x-ray absorptiometry (DXA) as the best densitometric technique for assessing bone mineral density (BMD) in postmenopausal women and has based the definitions of osteopenia and osteoporosis on its results. DXA enables accurate diagnosis of osteoporosis, estimation of fracture risk and monitoring of patients undergoing treatment. Additional features of DXA include measurement of BMD at multiple skeletal sites, vertebral fracture assessment and body composition assessment, including fat mass and lean soft tissue mass of the whole body and the segments. This book contains reviews and original studies about DXA and its different uses in clinical practice (diagnosis of osteoporosis, monitoring of BMD measurement) and in medical research in several situations (e.g. assessment of morphological asymmetry in athletes, estimation of resting energy expenditure, assessment of vertebral strength and vertebral fracture risk, or study of dry bones such as the ulna).

How to reference

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Kazuhiro Imai (2012). Ex Vivo and In Vivo Assessment of Vertebral Strength and Vertebral Fracture Risk Assessed by Dual Energy X-Ray Absorptiometry, Dual Energy X-Ray Absorptiometry, Prof. Abdelah El Maghraoui (Ed.), ISBN: 978-953-307-877-9, InTech, Available from: http://www.intechopen.com/books/dual-energy-x-ray-absorptiometry/ex-vivo-and-in-vivo-assessment-of-vertebral-strength-and-vertebral-fracture-risk-assessed-by-dual-en

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