

Sophisticated Imaging Technology in the Assessment of Osteoporosis Risk

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1. Introduction

Osteoporosis is a common disease characterized by low bone mass and microstructural deterioration of bone tissue, with an increased fracture risk. With an aging population, osteoporosis and its related fractures have become an increasingly important health and socioeconomic issue. The aim of osteoporosis screening and treatment is to prevent bone fracture. A fracture occurs when the external force applied to a bone exceeds its strength. The ability of a bone to resist fracture depends on its amount, spatial distribution, and intrinsic properties. Sophisticated bone imaging techniques, as new modalities, improve the potential for non-invasive study of bone anatomy, physiology and pathophysiology. The objective of bone imaging in osteoporosis is to minimize fracture occurrence by identifying the osteoporotic process at an early stage, differentiate distinctive patterns of bone loss, predict fracture risk accurately and monitor treatment response precisely. Non-invasive imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI), provide structural information, beyond bone mineral density (BMD). Non-invasive or non-destructive imaging techniques can provide important structural information about the local and systemic skeletal status and about the propensity to fracture. These advanced imaging techniques provide information about bone beyond standard bone mineral densitometry. In this chapter, we will discuss recent progress in bone imaging in a range from the macro- to micro-structures in order to investigate the structural basis of the skeletal fragility underlying osteoporosis.

2. Bone mineral density measurement

In bone fragility assessment, BMD is the main parameter to quantify because of its relationship to bone strength and prediction fracture risk. In the past two decades bone densitometry has been performed with direct methods such as dual X-ray absorptiometry (DXA) and quantitative computed tomography (QCT), which also evaluates bone structural

characteristics. The most commonly used quantitative imaging measure in osteoporosis is the areal BMD assessed by DXA. The assessment of bone macro- and micro-architecture by using more sensitive three-dimensional (3D) methods is important to determine certain aspects of bone structure and quality. Research has especially focused on the assessment of compartmental BMD and bone microstructure, since it has become technologically possible to obtain relatively high resolution volumetric images of bone *in vivo*.

2.1 Dual X-ray absorptiometry

Bone mineral density (BMD) measurement by dual X-ray absorptiometry (DXA) has been available for clinical use since 1987. It provides a quantitative assessment of mineralized bone mass at the axial and appendicular skeleton *in vivo*. This technique is currently the most readily available surrogate marker of bone strength and fracture risk. DXA measures the attenuation of photons of two different energies during radiation transmission. Bone mineral content (BMC, g) and areal BMD (g/cm^2) of a region of interest are obtained. As low areal BMD is a strong risk factor for fractures, this technique provides the basis for the World Health Organization (WHO)'s guidelines for diagnosis of osteoporosis. DXA is limited in that it measures only areal BMD two-dimensionally. DXA is also limited in that it does not distinguish cortical and trabecular bone. Furthermore, measurements are subject to artefacts due to degenerative changes such as osteophytes and aortic calcification. Recommendations from the International Society for Clinical Densitometry regarding DXA examination for all ages have been updated. Although DXA is the gold standard for clinical assessment of fracture risk, its shortcomings are increasingly being recognized. Individual fracture risk has recently been standardized using the WHO Fracture Risk Assessment tool (FRAX), which was released in 2009 (Kanis et al., 2009). FRAX combines BMD from DXA with other well-known major risk factors for osteoporosis, such as age, sex and a parental history of hip fracture, to provide a 10-year risk of hip and other major fractures. Although it is not an ideal system, FRAX represents an important initiative in allowing clinicians to individualize fracture risk based on DXA examination and other factors.

2.2 Quantitative computed tomography (QCT)

In quantitative computed tomography (QCT), the X-ray source and detector rotate in synchronised fashion around the subject. Algorithms are used to reconstruct the attenuation data into 3D images. Use of a bone mineral or hydroxyapatite phantom allows calibration of the data, providing a measurement of bone density that is independent of bone size. Compared with DXA, one advantage of QCT is the capacity for separate analysis of the cortical and trabecular BMD. QCT also provides real bone density per bone volume (mg/cm^3). Recently, 3D volume data from the scanning of an entire bone, such as a vertebral body or proximal femur, can be reconstructed to adjust the exact selected region for several serial images in a longitudinal study, which enables monitoring of successive changes with very good precision. QCT-based bone measurements have been used to evaluate age-, sex- and ethnic-related differences in vertebral and femoral geometry and density, providing insights into the development of skeletal fragility.

2.2.1 Volumetric BMD assessment by QCT

CT image is a two step process of initial scan acquisition and then tomographic image reconstruction by a mathematical process of calculating from acquired raw data. All clinical

CT scanners are calibrated to the X-ray attenuation to the water, resulting in CT numbers, measured in Hounsfield Units (HU). To transform HU into bone mineral equivalents (mg/cm^3) an appropriate bone mineral phantom is included in the scan field. QCT is the unique modality that measures the real bone density in a determinate volume (mg/cm^3) without the overlapping of others tissues. QCT differs from DXA as it can allow a selective assessment of both trabecular and cortical bone. Trabecular BMD obtained by QCT shows a more rapid age dependent decrement than that measured by DXA. Single Energy QCT is normally used for clinical setting, though BMD estimation can be altered by quantity of fat tissue, which substitutes the red marrow in elderly people. This effect produces an increasing error of evaluation with the increase of elderly patients. Even if Dual Energy QCT improves the accuracy, nevertheless it uses higher radiation dose and longer scanning times without increasing QCT sensibility in discriminating between healthy and osteoporotic subjects. Over the last decade, technical developments in CT, including multi-detector CT (MDCT) have resulted in images of volumes of tissue being acquired very rapidly, and this has had an impact on QCT in that 3D volume images can be acquired rapidly. Such 3D volumetric QCT enables analysis of the hip, the important site of osteoporotic fracture, which was not feasible with 2D single slices.

2.2.2 Vertebral trabecular QCT assessment

The trabecular BMD, particularly in the vertebra, is metabolically more active and may therefore serve as an early indicator of osteoporosis treatment effect. Vertebral trabecular BMD was demonstrated to have a significant correlation with vertebral fracture. Worldwide, the number of subjects in thoracic and abdominal CT examinations has increased dramatically over the last two decades (McCollough et al., 2009). Several recent studies have shown how it is possible to obtain meaningful QCT BMD values from subjects undergoing thoraco-abdominal CT examinations without the use of a calibration phantom. Such BMD values have a high correlation with BMD values obtained from QCT. These studies demonstrate that it is technically feasible to obtain reasonably accurate BMD values in subjects undergoing thoracic or abdominal CT examinations for other reasons. It is very useful for subjects as it will allow predictions of vertebral fractures without additional radiation exposure (Lenchik et al., 2004). The analysis of BMD at different vertebral levels is necessary because most osteoporotic vertebral fractures are located in the thoracolumbar spine between T4 and L1, with the segments between T7 and L1 most affected (Wasnich, 1996). Osteoporotic fractures of the cervical spine are considered uncommon. The etiology of the striking segmental differences for osteoporotic vertebral fractures is not well explained. Recently we measured the trabecular BMD of thoracic and lumbar vertebrae from 1,031 subjects who had undergone MDCT examination (Hayashi et al., 2011). The vertebral trabecular BMD of both men and women tended to gradually decrease from Th1 to L3 in all age categories (Fig. 1). In relation to vertebral level, L3 had the lowest trabecular BMD among the thoracic and lumbar vertebrae. The correlation of the trabecular BMD among thoracic and lumbar vertebrae was also studied. On the whole, we found that the further the vertebrae were from each other, the weaker were their correlations of the trabecular BMD, and vice versa. 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 L3 BMD in CT images from abdominal organ examinations, the estimated accuracy of T12 ($r=0.92$) would be better than that of T7 ($r=0.79$) because T12 is nearer to L3

than T7 (Hayashi et al., 2011). That is to say, it may be appropriate to use an arbitrary vertebra as a first approximation for assessing vertebrae which are in the area of predilection for the fracture. If the BMD of one vertebra is known, the BMD of other vertebrae may be estimated using our knowledge of BMD correlations.

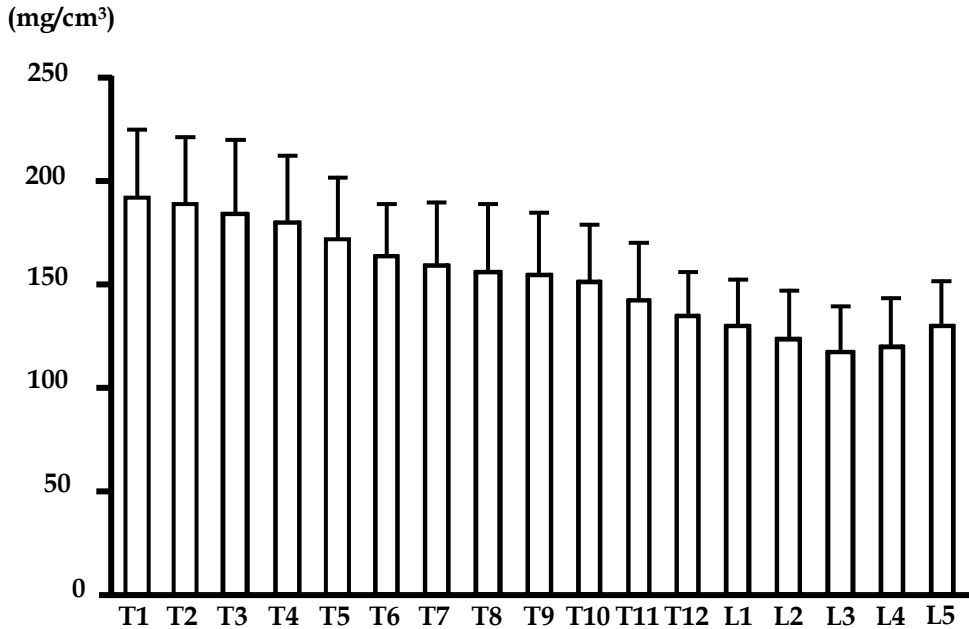


Fig. 1. The trabecular BMD of the thoracic and lumbar vertebrae. The BMD tends to decrease from the first thoracic to third lumbar vertebra (Hayashi et al., 2011)

3. Bone quality assessment

As BMD explains only part of the variation seen in bone strength and only some of the observed reduction in fracture risk that occurs with treatment, recent developments have focused more on measuring bone structure and quality of both cortical and trabecular bone rather than bone mass alone. This is done with the knowledge that a measure encompassing bone quality and structure along with bone mass will provide a better prediction of fracture risk than bone mass alone.

3.1 Conventional X-rays

Conventional radiography is a low-cost, readily available technique with high spatial resolution capable of providing fine bone detail, especially for appendicular skeleton such as the distal forearm and phalanges. It is widely available method, provides a good tissue contrast and has the potential to reflect bone microstructure. Conventional radiography is the first and most important method to identify fractures. The distal radius fractures are almost always identified by standard radiographs, while hip and especially spine fractures may have a difficult detection with important significance in their management, prognosis and therapy.

A more accurate evaluation of lateral chest radiographs routinely executed could lead to the detection of a major number of vertebral fractures and earlier diagnosis of osteoporosis. Although it is ideally suited for use in large population studies, the limitation of radiography is that as a projection imaging technique, it cannot consistently visualize individual trabecula and it depends heavily on the depth of tissues under investigation. Despite these limitations, the trabecular bone properties could be described by texture analysis. Good correlations were found between direct, 3D measures of trabecular architecture and a multiple parameter model, based on 2D texture parameters, such as fractal, statistical and anisotropy measures (Guggenbuhl et al., 2006). With increasing sophistication of structural analysis techniques and an improving ability to acquire high-resolution radiographic detail, interest remains in developing radiography to more precisely evaluate trabecular bone microstructure.

3.2 Multi-detector computed tomography (MDCT)

Computed tomography (CT) is a 3D X-ray imaging technique, which provides positive contrast of mineralized tissues. The image formation process begins with the acquisition of serial radiographic projections over a range of angular positions around the object of interest. The cross-sectional field of view is then reconstructed using established computational techniques. Similar to simple radiography, the reconstructed image intensity values represent the local X-ray attenuation. A material property related to the electron density. Several classes of CT devices are presently used for high-resolution imaging of trabecular and cortical bone microstructure. The multi-detector CT (MDCT) is a clinical CT technique, which is available in most diagnostic imaging departments and thus a dedicated scanner is not required. Since its inception, the number of detector rows on clinical CT units has increased from 4 to the current clinical standard of 64 rows, although 320-row MDCT systems are also commercially available. As expected, MDCT fared less well with trabecular thickness and number because the spatial resolution of all MDCT systems (250–300 μm) remains larger than the trabecular thickness of 50 to 200 μm (Issever et al., 2010). Nevertheless, structural parameters by MDCT provide a better discriminator of change than DXA. It has been shown that trabecular bone parameters obtained with MDCT correlate with those determined in contact radiographs from histological bone sections and micro-CT (Link et al., 2003). The advantage of MDCT technique is that more central regions of the skeleton such as the spine and proximal femur can be visualized. However, in order to achieve adequate spatial resolution and image quality the required radiation exposure is substantial, which offsets the technique's applicability in clinical routine and scientific studies. High-resolution CT scanning is associated with considerably higher radiation dose compared with standard techniques for measuring BMD. Using clinical imaging in more central regions of the skeleton such as spine and femur, it is still noted that the trabecular bone architecture visualized with MDCT is more a texture of the trabecular bone than a true visualization of the individual trabecular structure.

3.3 Peripheral quantitative CT and high-resolution peripheral quantitative CT

The peripheral QCT (pQCT) with a resolution comparable to that of MDCT has been available since 1990 to examine the peripheral skeleton. pQCT confers a smaller effective radiation dose and is particularly useful for studying cortical bone changes in metabolic bone disorders because the distal radius contains more cortical bone than the vertebral body. As pQCT units use low-power X-ray tubes, these examinations are slow, with a

tendency toward motion artifact. With this limitation in mind, the feasibility of using clinical CT scanners with a dedicated forearm phantom as an alternative to pQCT has been investigated. The cortical and trabecular BMD, and bone geometrical parameters, such as marrow and cortical cross-sectional area, cortical thickness, periosteal and endosteal circumference, biomechanical parameters can be obtained, like cross-sectional moment of inertia, which is a measure of bending strength, polar moment of inertia, indicating bone strength in torsion and stress strain index (SSI). A non-invasive bone strength marker as SSI measured by pQCT, could be significantly correlated with a biomechanical bone strength index, as maximum load at bone failure, assessed by three-point bending test. pQCT can non-invasively determine bone mechanical properties by assessing parameters with accepted prognostic value on bone strength (Kokoroghiannis, et al., 2009). Bridging the clinical need for an imaging modality with lower radiation dose and better spatial resolution is the high-resolution pQCT (HR-pQCT). This can measure trabecular and cortical bone density and bone microstructure with an isotropic voxel of about 80 μ m. This technique has excellent precision for both density and structure measurements (Dalzell et al., 2009). In 2005, the first published clinical study assessing HR-pQCT found that postmenopausal women had lower BMD, trabecular number and cortical thickness compared with premenopausal women at the distal radius and tibia, although spine and hip BMD was similar. HR-pQCT is a useful modality for assessing changes in cortical and trabecular bone, with a precision of about 2% to 5% (Boutroy et al., 2005). The main limitation of HR-pQCT is that it requires a dedicated scanner, is confined to examination of distal forearm and leg, has some difficulty with registration in the Z plane and should take into consideration the expected difference among individuals of short or long radial or tibial length.

3.4 Micro-CT (μ CT)

The earlier conventional tool for assessing trabecular bone architecture was histomorphometry from bone biopsies, which produces a two-dimensional representation of tissue structure, while bone structure is three-dimensional. In recent years, it has progressively been imposed the direct 3D analysis of biopsy specimens imaged by micro-CT (μ CT). The most common application of this technology has been the in vitro quantitation of osteoporotic change in trabecular bone architecture. The μ CT system has been demonstrated to be the first device able to non-destructively reveal the "real" trabecular architecture and is an X-ray-based technique that provides 3D images of very high spatial resolution below 8 μ m. Since μ CT allows the depiction of individual trabecula and enables the full characterization of the trabecular network, many investigators have used it to study the trabecular network at different skeletal sites, in direct relation to biomechanical properties or as a "gold standard" for evaluating other techniques, although most of the μ CT are limited to ex vivo investigations. Microarchitectural 3D data elaborated by specific software consents to evaluate many metric and non-metric bone structural parameters, such as the bone volume (BV), tissue volume (TV), bone volume fraction (BV/TV), trabecular thickness (Tb.Th), trabecular number (Tb.N), trabecular separation (Tb.Sp), structure model index (SMI), connectivity degree (Conn.D) and degree of anisotropy (DA).

3.4.1 Hamster bone μ CT assessment

Age-related bone loss, which is poorly characterized, is a major underlying cause of osteoporotic fractures in the elderly. In order to identify the morphological feature of age-related bone loss, we investigated sex and site (tibia, femur and vertebra) dependence of

bone microstructure in aging hamsters from 3 to 24 months of age using μ CT (Chen et al., 2008a). In the proximal tibia and distal femur, the trabecular BV/TV, Tb.N, Tb.Th and BMD increased to a maximum at 6 or 12 months and then declined progressively from 12 to 24 months of age (Fig. 2). Tb.Sp, trabecular bone pattern factor (Tb.Pf) and SMI increased with age. As compared with male hamsters, BV/TV and Tb.N were significantly lower in females at 18 and 24 months of age. Age-related decrease of BV/TV in the vertebral body was less than that of the femoral and tibial metaphyses. In the mid-femoral diaphysis, cortical bone area remained constant from 3 to 24 months of age. Cortical thickness decreased from 12 to 24 months and cortical BMD declined significantly from 18 to 24 months of age. These findings indicate that skeletal site and sex differences exist in hamster bone structure. Age-related bone changes in hamsters resemble those in humans. Hamsters may be a useful animal model to study at least some aspects of bone loss during human aging.

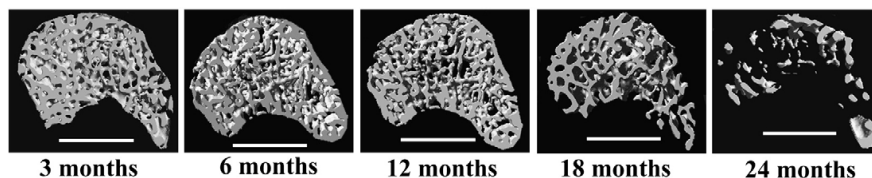


Fig. 2. Three-dimensional images of the proximal tibial metaphysis in female hamsters at 3, 6, 12, 18 and 24 months of age. Trabecular bone volume is highest at 6 and 12 months of age, and declined at 18 and 24 months of age. Scale bar=1.0mm (Chen et al., 2008a)

3.4.2 Osteoporosis model mouse (SAMP6) bone μ CT assessment

The senescence-accelerated mouse P6 (SAMP6) is a model of senile osteoporosis, which possesses many features of senile osteoporosis in humans. So far, little is known about the systemic bone microstructural changes that occur at multiple skeletal sites. Recently, we investigated site dependence of bone microstructure and BMD in SAMP6 and the normal control mouse (SAMR1) using quantitative μ CT and imaging analysis software (Chen et al., 2009). As compared with SAMR1, the most prominent change in SAMP6 was the reduction of vertebral trabecular BV/TV (Fig. 3) and BMD. Moderate decrease of trabecular bone loss was observed in the proximal tibia and distal femur. Increased bone marrow area and periosteal perimeter were investigated, although the cortical area and cortical thickness had no marked changes in the mid-tibial and mid-femoral cortical bones. These results indicate that bone microstructural properties in SAMP6 are remarkably heterogeneous throughout the skeleton, which is analogous to changes that occur in human bones. These findings further validate the relevance of SAMP6 as a model of senile osteoporosis.

3.4.3 Human vertebral trabecular bone μ CT assessment

The vertebral trabecular bone has a complex 3D microstructure, with inhomogeneous morphology. A thorough understanding of regional variations in the microstructural properties is crucial for evaluating age- and gender-related bone loss of the vertebra, and may help to gain more insight into the mechanism of the vertebral osteoporosis and the related fracture risks. Fifty-six fourth lumbar vertebral bodies from 28 women and men (57-98 years of age) cadaver donors were studied. Both women and men were divided into 3 age groups, middle-aged, old age and elderly groups. Five cubic specimens were prepared from

anterosuperior, anteroinferior, central, posterosuperior and posteroinferior regions at sagittal section (Chen et al., 2008b). Bone specimens were examined by μ CT and scanning electron microscope. The results showed that BV/TV, Tb.N and Conn.D decreased, while SMI increased significantly between middle-aged and old age groups, and between old age and elderly groups. As compared with women, men had higher Tb.N in the old age group, and higher Conn.D in the middle-aged and old age groups. The central and anterosuperior regions had lower BV/TV and Conn.D than their corresponding posteroinferior region (Fig. 4). Increased resorbing surfaces, perforated or disconnected trabeculae and microcallus formations were found with aging. Vertebral trabeculae are microstructurally heterogeneous. Decreases in BV/TV and Conn.D with age are similar in women and men. Significant differences between women and men are observed at some microstructural parameters. Age-related vertebral trabecular bone loss may be caused by increased activity of resorption. These findings illustrate potential mechanisms underlying vertebral fractures.

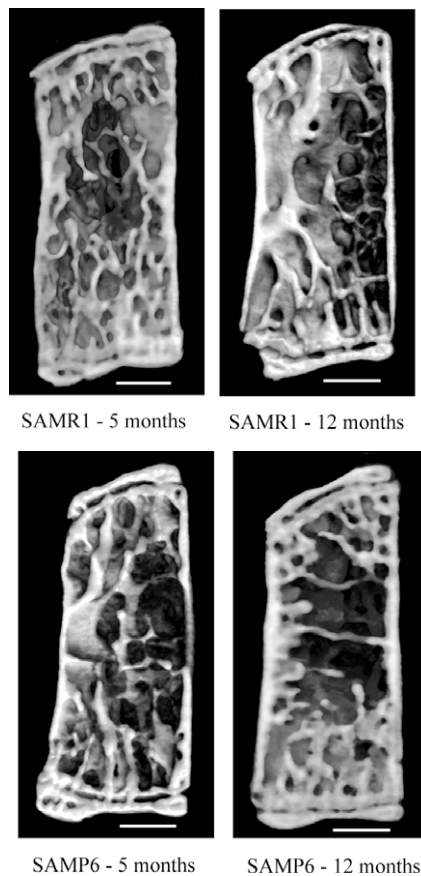


Fig. 3. Micro-CT images representative the fourth lumbar vertebral body in SAMP6 and SAMR1 mice at 5 and 12 months of age. Compared with SAMR1, the trabecular bone is reduced in SAMP6 both at 5 and 12 months of age. Scale bar=0.5mm (Chen et al., 2009)

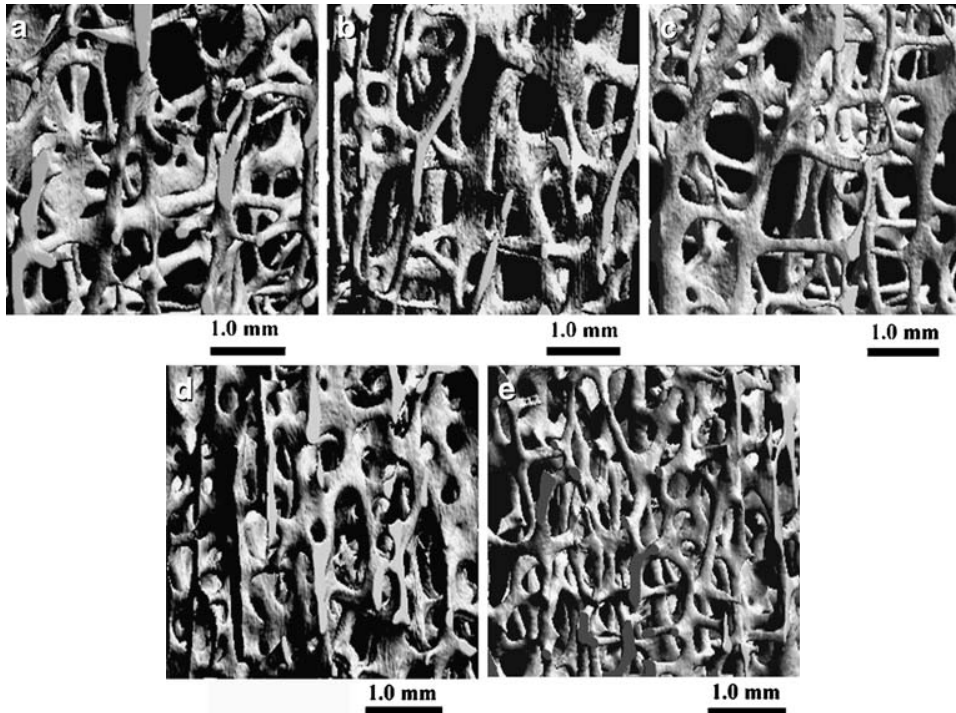


Fig. 4. Three-dimensional micro-CT image in different regions of the vertebral body from a woman aged 78 years: anterosuperior (a), anteroinferior (b), central (c), posterosuperior (d) and posteroinferior (e) regions. The trabecular bone is higher in the posterosuperior and posteroinferior regions than that of the central and anterosuperior regions (Chen et al., 2008b)

3.4.4 Human femoral neck μ CT assessment

Femoral neck fracture, which is one of the most common outcomes of age-related and postmenopausal osteoporosis, is a significant cause of morbidity and mortality worldwide. Femoral neck fracture is attributed to both cortical and trabecular bone loss. The relative contribution of femoral neck cortical and trabecular bone to whole bone strength is unclear. We identified 3D microstructural changes of both cortical and trabecular bone simultaneously in human femoral neck from 57 to 98 years of age (Chen et al., 2010). The findings demonstrate that cortical thickness (Ct.Th) decreased by 10-15%, cortical porosity (Ca.V/TV) almost doubled between the middle-aged and elderly groups (Fig. 5).

The trabecular BV/TV declined by around 20% between the middle-aged and elderly groups. The most obvious age-related change in the femoral neck is the increase of Ca.V/TV. The decrease of BV/TV with age is more noticeable than that of Ct.Th. There was a significant inverse correlation between Ca.V/TV and BV/TV for both women and men. As compared with women, men had higher Ct.Th and BV/TV and lower Ca.V/TV. These findings may serve as reference for ethnic comparison with age and gender and may help to gain more insight into femoral neck fracture risk.

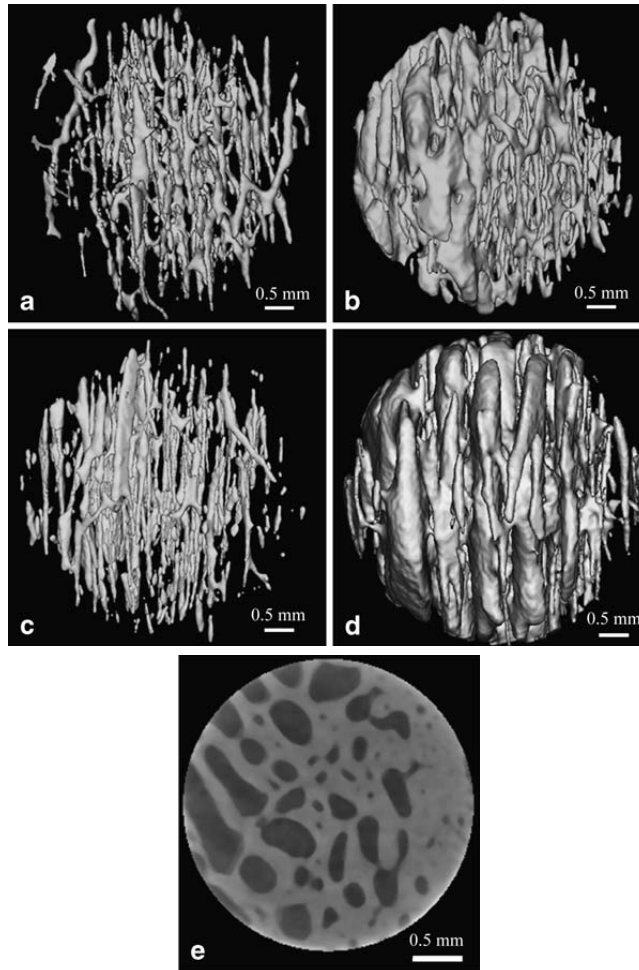


Fig. 5. Three-dimensional reconstructed images of the canal networks in the inferior femoral neck cortex from a man aged 62 years (a), a man aged 92 years (b), a woman aged 62 years (c) and a woman aged 92 years (d). There are more enlarged canals in the 92-year-old woman than that of the 62-year-old man. Representative two-dimensional micro-CT image of the femoral neck cortex from a woman aged 92 years (e) is shown. Periosteal surface faces right for all specimens (Chen et al., 2010)

3.4.5 Human proximal tibia μ CT assessment

The analyses of local trabecular microstructure have been mainly performed in regions most susceptible to fractures, such as spine, proximal femur and radius. Studies of the proximal tibia also have an important clinical significance, as it is fractured in aging patients, specifically those suffering from osteoporosis. The proximal tibia, with its rich trabecular network, can be used as a donor site for bone grafting and it is the most easily accessible site for quantification of BMD and bone microstructure. The trabecular bone specimens from the medial

compartment of the proximal tibial metaphyses were examined with μ CT and scanning electron microscopy (Chen et al., 2011). It was shown that from 57 to 98 years of age, the trabecular BV/TV decreased by 6-7% and the trabecular BMD declined around 4% per decade at the proximal tibia. Figure 6 shows the typical 3D reconstructions of trabecular bone of the middle-aged and elderly groups for both women and men. The trabecular Tb.Th decreased between the middle-aged and elderly groups similarly in women and men. However, Tb.N decreased by 13% between the middle-aged and elderly groups in women and nearly doubled that in men. As compared with women, men had higher BV/TV and lower Tb.Sp in the old age and elderly groups, and higher Tb.N and Conn.D in the elderly group. Increased trabecular resorbing surfaces, perforated or disconnected trabeculae and microcallus formations were observed with age. These findings indicate that both BMD and BV/TV decreased at the proximal tibia with age similarly for women and men, but significant differences between women and men were observed for some microstructural parameters.

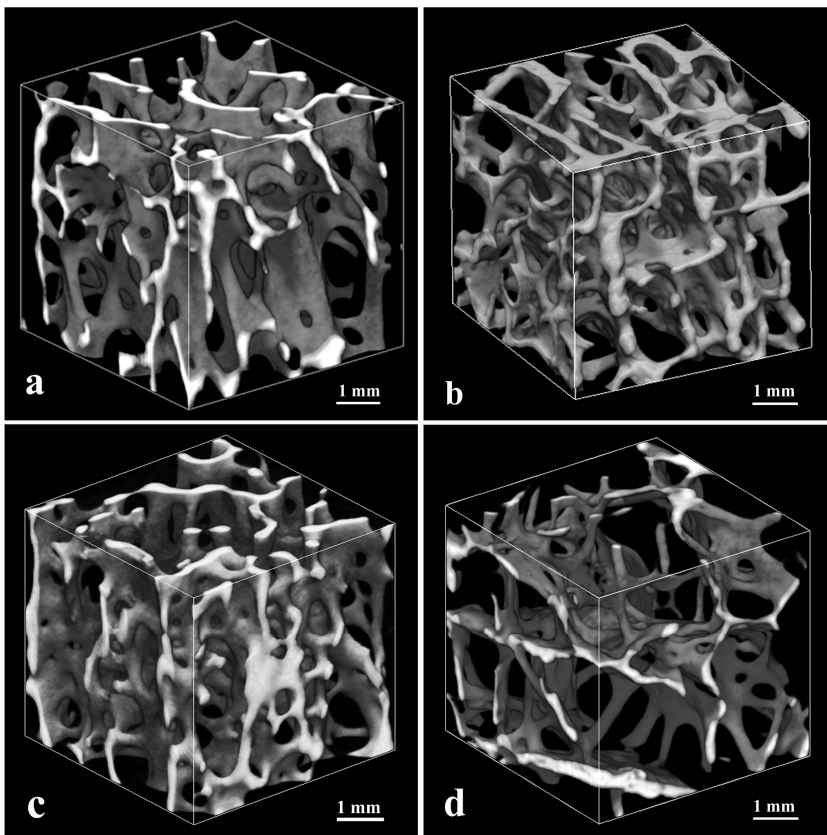


Fig. 6. Three-dimensional reconstructed images of trabecular microstructure at proximal tibia from a man aged 62 years (a), a man aged 92 years (b), a woman aged 62 years (c) and a woman aged 92 years (d). The trabecular bone volume fraction is highest in man aged 62 years and lowest in woman aged 92 years (Chen et al., 2011)

3.5 Magnetic resonance imaging (MRI)

Magnetic resonance imaging (MRI) is a non-ionizing method that uses a strong magnetic field in combination with specialized sequences of radio-frequency pulses to generate high-resolution 3D images of cortical and trabecular bone *in vivo*. Therefore, it is well suitable for assessing bone structure clinically (Link, 2010). With technical advances in MRI, such as optimized coil design, fast gradients, high gradients and high field strength, MRI scanners provide an *in vivo* spatial resolution close to the diameter of a single trabecula. MRI signal of trabecular bone itself is not visualized and trabeculae appear as a signal void, surrounded by high-intensity fatty bone marrows. As a result, the bone structure is assessed indirectly via measurements of the surrounding marrow and other soft tissues. Advances in the past decade have focused on image acquisition and analysis techniques to overcome inherent obstacles in MR imaging of bone. With the advent of parallel imaging, motion correlation techniques and new sequences, the limits of spatial resolution and scan time can be further overcome. This non-ionizing, 3D imaging technique is a very attractive tool to analyze trabecular bone structure, investigating bone structure and metabolism in osteoporosis or osteoarthritis. Various studies have been undertaken to optimize image acquisition and post processing, and to calibrate and validate measurements of the trabecular architecture. However, methods can be technically challenging to achieve and optimize.

4. Conclusion

Bone fragility, composite description of bone's biomechanical properties, is directly related to bone's susceptibility to fracture and is inversely related to bone's fracture resistance. As fractures compromise the quality of life and shorten life expectancy, the sophisticated bone imaging modalities play an important role in clearly and accurately identifying the presence and features of fragility fractures. The analysis of bone mass and bone microstructure is an exciting field in the assessment of osteoporotic risk. With the recent advances in MRI and CT, including the introduction of clinical μ CT, imaging of true bone structure is becoming more feasible. These non-invasive sophisticated imaging techniques help us to gain more insight into the potential mechanism of metabolic bone diseases, particularly osteoporosis. However, further research is required for improvements in reproducibility, standardization and clinical application of these methods. New technological advances may further refine the imaging of osteoporotic bone and assessment of fracture risk. Recently various computer-aided diagnosis systems were developed for assessment of osteoporosis risks. The dental clinics took numerous panoramic radiographs for examining dental diseases worldwide. Several investigators demonstrated significant associations between mandibular cortical indices on panoramic radiographs and BMD of the skeleton generally, such as the spine and femur, biochemical markers of bone turnover and risk of osteoporotic fractures (Taguchi, 2010). So the computer-aided diagnosis system, based on digital panoramic radiography, may offer a new triage screening for osteoporosis risk in the near future.

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