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Application of quantitative computed tomography for assessment of trabecular bone mineral density, microarchitecture and mechanical property

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ABSTRACT

Osteoporosis is a common metabolic bone disease, causing increased skeletal fragility characterized by a low bone mass and trabecular microarchitectural deterioration. Assessment of the bone mineral density (BMD) is the primary determinant of skeletal fragility. Computed tomography (CT)-based trabecular microarchitectural and mechanical assessments are important methods to evaluate the skeletal strength. In this review, we focus the feasibility of QCT BMD measurement using a calibration phantom or phantomless. The application of QCT could extend the bone mineral density assessment to all patients who underwent a heart, lung, whole-body, and as well as all routine clinical implications of CT scan.

1. Introduction

Fragility fracture is a common public health problem with a high mortality, morbidity and cost. Osteoporosis significantly related to bone fragility and consequent fracture. Therefore, the diagnosis and monitoring of osteoporosis with BMD measurement are strongly associated with bone health. BMD explains about 70–75% of the variance in strength [1,2]. The World Health Organization (WHO) proposed guidelines for the diagnosis of osteoporosis based on BMD measurement by using dual X-ray absorptiometry (DXA) in 1994 [3]. Since then, DXA has been widely used for the epidemiological studies, clinical research and treatment strategies of osteoporosis [4,5]. Lumbar QCT had been employed in the 1980s [6], is also recommended as an acceptable method in the diagnosing osteoporosis by the WHO. A certain number of new technologies have been developed for assessing bone mineral density until now, including peripheral QCT (pQCT) [7], μCT (microCT) [8], magnetic resonance imaging (MRI) [9,10] and quantitative ultrasound (QUS) [11]. Compared to DXA, QCT offers superior sensitivity in diagnosing osteoporosis, monitoring the bone density changes, and evaluating the bone trabecular microarchitectural and mechanical property simultaneously, but still considered a supplemental method due to its high radiation [12]. Two-dimensional QCT BMD measurement of the spine tended to show a lower precision, which lead to limited employment [13]. In the U.S., there are over 12,000 multidetector CT (MDCT) scanners [14]. CT scanning is widely used in diagnosis and prognosis for lung cancer, cardiac disease, as well as abdominal and pelvic disease. With the high resolution MDCT images, clinicians can obtain important information of BMD, trabecular microarchitectural and mechanical property, as an additional utility to clinical applications. The aims of the review are to evaluate: 1. Method and feasibility of QCT in BMD assessment with the use of phantom or phantomless calibration, 2. The ability of QCT to diagnose the osteoporosis and to monitor the aging-, disease- and medicine-related BMD changes, 3. Feasibility in the trabecular microarchitectural and mechanical assessment using current MDCT images.

2. Method of QCT bone mineral density measurement

2.1. QCT technique in the lumbar spine

Hounsfield unit (CTHU)-based QCT technique has been utilized over the last three decades [3,6]. Lumbar QCT was the only method initially [6]. With this technique, the CT image was obtained using routine scan parameters in the lumbar spine with a calibration phantom under the patient's back. Lower radiation dose protocol was used in most studies, such as 80kVp/140 mAs or 140 kVp/80 mAs with 5 mm image thickness or greater [6,15]. The calibration phantom technique has two functions, translating the CTHU to the bone units (mg/mm^3) and calibrating CTHU within location, patients and scanners made by many manufacturers. The calibration standard was originally designed by Cann et al [6] (Mindway, South San Francisco, CA, USA). Subsequently, two standard phantoms were also used commonly, developed by the

Abbreviations: MDCT, Multi-row detector CT; CACs, Coronary artery calcium scan; QCT, Quantitative CT; BMD, Bone mineral density; CTHU, CT hounsfeild unit.

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Image analysis, (Columbia, KY, USA) [16] and Siemens Medical System [17] (Erlangen, Germany). Those phantoms consist of a water-equivalent solid resin matrix and rods filled by a calcium material with varying concentration. The calcium material usually includes a dipotassium hydrogen phosphate or calcium hydroxyapatite (CaHA). The concentrations of the calcium material in rods are equivalent to 200, 100, 50, 0 mg/mm^3 and larger than 200 mg/mm^3 or close the density of fatty tissue [6,16]. The lumbar trabecular bone and the phantom rods at the center area (L1–L4, or L1–L3) can be segmented semi-automatically by a computer system. The trabecular BMD, as well as the T and Z score can be calculated automatically by using the conversion equations and their standard references developed by the manufacturers. Those references included mean values and standard deviation in the younger group and every age group (most from 20 to 85 years) of men and women.

To date, manufacturers have not developed a uniform standard reference for calculating the T score with CT. Theoretically, T-scores derived by QCT should not be used to assign a diagnostic category, as it may differ from that of DXA [18]. Nonetheless, the standard of osteoporosis based on T score by DXA was used in most QCT studies [19–22]. The American College of Radiology (ACR) has published guidelines for the performance of QCT in lumbar spine in 2008 and amended in 2014. Based on the guidelines, volumetric trabecular BMD values from 120 to 80 mg/cm^3 were defined as osteopenic and below 80 mg/cm^3 as osteoporosis [18]. This definition was suggested to assigned as a diagnostic criteria approximately equivalent to WHO diagnostic categories with a hip DXA. In an analysis of osteoporosis diagnosis in 2028 lumbar QCT data [23], the number of individuals detected with osteoporosis (<80 mg/cm^3, and T<-2.5) was 74 and 379 in 1011 women, 74 and 191 in 1017 men by ACR and Image analysis programs respectively. The result demonstrated a significant difference in the reference value for the diagnosis of osteoporosis between ACR and Image analysis methods. Therefore, validating and establishing a uniform standard reference is an important work for future BMD assessment.

2.2. Thoracic vertebral QCT with a routine heart scan (Fig. 1)

Osteoporosis and coronary atherosclerosis have been recognized as co-existing conditions with aging, and both may share common etiologies and pathogenesis [24,25]. They are independent risk factors for bone fracture and cardiovascular disease, consequently, resulting in significant medical and financial cost each year. In the United States alone, osteoporosis affects more than 25 million men and women, 1 in 2 women and 1 in 5 men aged 50 and above during their lifetimes [26]; meanwhile coronary artery calcium burden (CAC), as a specific marker of atherosclerosis was noted in 50–70% in men and 35–45% in women older than 45 years in multi-ethnic populations [27]. The diagnosis of osteoporosis and coronary atherosclerosis is important in the prevention, prediction and management of bone fracture and coronary artery disease. In women, menopause is associated with increased bone loss and deleterious changes in the physiological bone structure. BMD examination was recommended as a screening to determine skeletal status in men aged 65 years or older [28]. Women who have experienced menopause and men who have the risk of fracture before the age of 65 must also be considered for BMD screening [28,29]. In general, there is a growing consensus that subjects aged ≥50 years should be evaluated for osteoporosis [30].

Compared to the CAC CT scan, QCT has not been used extensively as a common technique for bone mineral measurement due to its high radiation (3.5 mSv) [31] and cost. If the thoracic trabecular BMD can be measured from the same cardiac CT image with only one mSv radiation, it should potentially cover most populations recommended for BMD screening. Furthermore, the deformity at mid-lower thoracic spine can be evaluated simultaneously, which is a common anatomic site of fracture (most fractures present in T7, T12 and L1) [32]. The validated studies have demonstrated that the EKG-gated heart CT scans with a calibration phantom can be used to assess the thoracic vertebrae BMD using the lumbar QCT technique [21,33,34]. The reference value for the standardization of the T and Z score in the thoracic vertebrae BMD had been developed [21].

In current CAC scanning protocols, three thoracic spines can be evaluated in all studies at least. Since the variation exists within individual spinal BMD [35], fixing the levels is an important issue for decreasing the precision error of BMD assessment. The continuous three thoracic spines (3 T) beginning from the level of the left coronary artery are commonly used to assess the trabecular BMD on CAC scanning [21,36]. A similar segmenting and calculating method with the lumbar spine is used in the thoracic QCT (shown in Fig. 1).

A significant association (0.85–0.99) between the thoracic and lumbar trabecular mineral density exists, which is confirmed by previous studies [21,33,34]. Based on this result, the thoracic BMD can translate to the lumbar equivalent values, and get the T score using the lumbar reference value. The formulas for translating the BMD value measured by thoracic QCT to the equivalent value with Lumbar QCT is: Lumbar BMD=0.8401×thoracic BMD+0.62 in female, and =0.8139×thoracic BMD+11.8 (mg/CM^3) in male, derived from the study data [21,23].

2.3. Phantomless assessment of the thoracic vertebral BMD using a routine heart scan

The clinical role of coronary calcium assessment by CT scan has undergone significant endorsement over the past 30 years [37]. The CT image from gated heart scans provide an opportunity to assess the CAC, and also thoracic BMD. As such, most of these studies were done without phantoms present. A phantomless thoracic BMD measurement would be a great advance in clinical practice. To date, three methods were used for the phantomless BMD measurement at spine: 1) Using an individual body tissue as a calibration reference, such as the paraspinal fat and psoas [38,39]; 2) Using a modified calibration factor (calibration curve) [40,41]; 3) Using the CTHU directly [42]. Although the standardization of CTHU was done by individual manufacturers, and the calibration procedure was performed before the row data reconstruction, a significant variation between scanners still exists [36,43]. The stabilization of CTHU can be influenced by numerous factors, including the scanner's model, scan algorithm parameters [44], patient's body size [35] and many other factors, which needs to be corrected before any quantitative assessment. Moreover, the attenuation

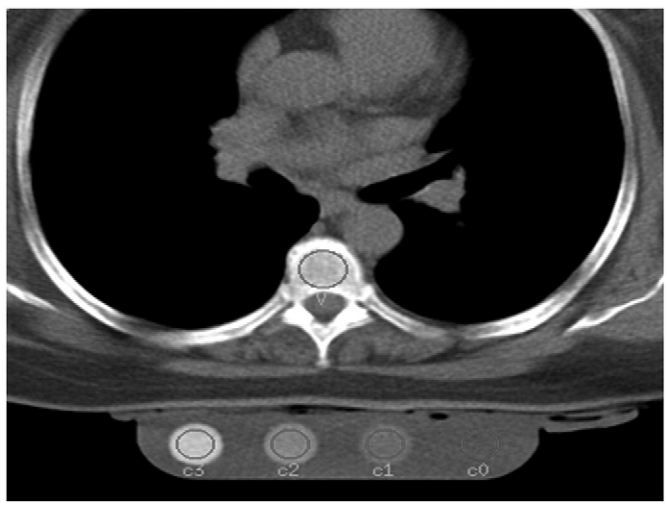

Fig. 1. The thoracic and lumbar BMD measurement by QCT. The bone mineral densities (mg/cm^3) in the three thoracic spines (from left main coronary artery level) were measured using the QCT technique. After selecting the spine slice, the cursor was located at the center of a spine or phantom rods automatically. The trabecular bone mineral densities (mg/cm^3) of 10 mm in thickness were displayed and recorded by computer. T scores were calculated using the reference values derived by the manufactory.