Axial CT in the diagnosis of osteoporosis

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Summary

Quantitative computed tomography (QCT) is an established technique for measuring bone mineral density (BMD) in the axial spine and appendicular skeleton (forearm, tibia). It provides cross-sectional images, so that it is uniquely able to provide separate estimates of trabecular and cortical bone BMD as well as a true volumetric mineral density in grams per cubic centimeter. However, because of the high responsiveness of spinal trabecular bone and its importance for vertebral strength, it has been principally employed to determine trabecular BMD in the vertebral body. QCT has been used for assessment of vertebral fracture risk, measurement of age-related bone loss, and follow-up of osteoporosis and other metabolic bone diseases. QCT has a better sensitivity to predict vertebral fracture than projectional methods like DXA, due to its ability to isolate and measure trabecular bone in the center of vertebral body. This mini-review deals with the current capabilities of axial QCT and the recent technical developments, including volumetric acquisition.

KEY WORDS: Bone Mineral Density (BMD), spinal quantitative computed tomography (QCT), volumetric QCT.

QCT is a X-ray absorptiometric technique such as SXA, and DXA (Single and Dual X-ray Absorptiometry), but it is different from these methods of measurement because it provides separate estimates of trabecular and cortical bone BMD as a true volumetric mineral density in mg/cm^3. It measures high-turnover trabecular bone in consecutive vertebrae of the spine (usually two to four vertebrae out of T12 to L4), using commercial CT scanners and a bone mineral reference standard to calibrate each scan. Beginning from an initial lateral localized image and using a low-dose technique with the gantry angled parallel to the vertebral end plate, single 8 to 10 mm-thick sections are obtained through the midplane of each of these vertebrae (Fig. 1). A region of interest (ROI) is manually positioned in the anterior portion of trabecular bone of the vertebral body for analysis (1-3). It is possible to automate the sagittal location of midvertebral slices and the axial placement of ROIs to improve precision and reduce acquisition and analysis time. A software automatically
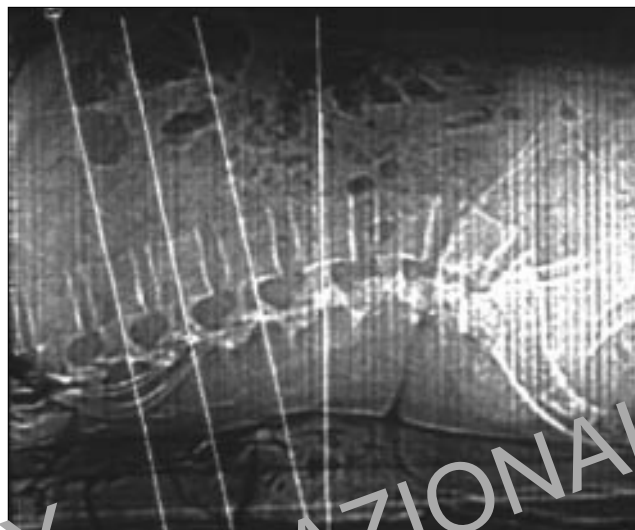

Figure 1 - Lateral scout view of the lumbar spine used to determine vertebral levels for axial locals.

locates the vertebral body, maps its outer edges, and employs anatomic landmarks, such as the spinous process and spinal canal and it calculates in this way size and location of the ROIs. Either trabecular, cortical, or integral (cortical and trabecular) bone ROIs are defined by these systems. The basivertebral vein and sclerotic foci such as bone islands have to be excluded. Hounsfield units (HU) (also known as CT number) are used to measure the CT density of the selected area of interest within a slice through a vertebral body. Then, comparing the CT number of the trabecular bone to that of the compartments of the calibration standard, it is possible to achieve a conversion to mg/cm^3. The calculated densities for the vertebrae are averaged and compared to those of a normal population (4). Normative data are gender-and race-specific (5).

Women have a different bone density curve over age than men. This difference is based on an accelerated bone loss in women soon after the onset of menopause, superimposing the normal physiologic bone loss that occurs in both men and women in aging. Moreover, absolute normal bone density values are race-dependent. Some studies show that black-race has higher bone density values than white-race (both in men and women) (6).

At present solid hydroxyapatite or calcium carbonate are used as calibration materials (Fig. 2). They are quite different from the first used liquid calibration reference phantoms. Infact, these last contained varying concentrations of bipotassium hydrogen phosphate (K_2HPO_4), with the drawback of limited long-term stability of the solutions. In this way scanning was difficult and inaccurate: air bubbles developed in the solution because of the transpiration of fluid from the solution into the plexiglas shell of the phantom.

A study of the spine with QCT takes about 30 minutes. The skin radiation dose is generally 100 to 300 mrem. Actually, only a
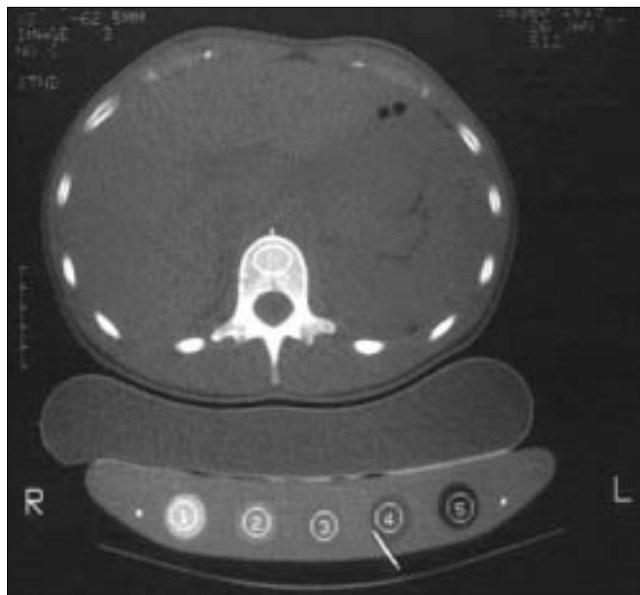
Figure 2 - Axial slice, 10 mm thick, through L2 vertebral body, showing the bone equivalent calibration phantom positioned under the patient and an elliptical ROI in the vertebral trabecular bone. The solid reference phantom is based on calcium carbonate, which enables any whole body CT scanner to perform accurate and reliable bone mineral density measurements.

small portion of marrow is irradiated during a QCT study of the spine, so that the effective dose or whole-body equivalent dose is generally in the range of only 3 mrem (30 μSv) (7). The localizer scan that precedes the actual QCT study will add an additional 3 mrem to the effective dose. These values are quite acceptable compared to a natural background radiation of approximately 20 mrem per month.

QCT can be performed in single-energy (SEQCT) or dual-energy (DEQCT) modes. These two techniques differ in accuracy, precision, and radiation. Variable marrow fat composition in the vertebrae, accuracy of the calibration standard and beam hardening errors and scatter, among other factors, contribute to the accuracy of SEQCT for spinal bone mineral determination. Marrow fat is the principal source of error, because it causes SEQCT measurements to underestimate bone mineral density (BMD) and overestimate BMD loss. Marrow fat increases with age producing an increasingly large error in the accuracy of spine QCT measurements in older patients. The presence of marrow fat results in an underestimation of bone density in the young of about 20 mg/cm^3 and as much as 30 mg/cm^3 in the elderly, so that QCT has an accuracy from 5 to 15%, depending on the percentage of marrow fat and the age of the patient (8). However it is possible to use a simple correction procedure that takes this into account reducing the BMD accuracy errors to levels that are small compared with the biological variation. Additionally, we can also reduce the errors caused by marrow fat by using a kVp setting that minimizes the fat sensitivity for a particular scanner. DEQCT too improves accuracy, but this approach incurs poorer *in vivo* precision and higher radiation dose, so that it is recommended only for research studies that require higher accuracy.

The precision error of 2 to 4% coefficient of variation (CV) and the accuracy errors of 5 to 15% CV reported *in vivo* for spinal QCT are generally higher than those observed for posteroanterior (PA) DXA of the spine and comparable with those of lateral DXA. It has an excellent ability to predict vertebral fracture and

to serially measure bone loss, generally with better sensitivity than projectional methods such as DXA because it selectively assesses the metabolically active and structurally trabecular bone in the center of the vertebral body. The postmenopausal trabecular bone loss measured by QCT is 2 to 3 times greater than the integral bone loss measured by DXA (9-18). It has been shown that low bone density increases fracture risk. Both biomechanical *in vitro* studies and clinical *in vivo* studies comparing patients with and without osteoporotic fractures show that there is a convincing risk gradient: the lower the bone density the higher the risk of bone fracture (19).

Some studies have examined BMD decrements between normal subjects and those with vertebral fractures. These studies showed that the decrement as measured by spinal QCT is significantly higher than that observed by PA-DXA and that QCT usually allows a superior vertebral fracture discrimination. Moreover, QCT shows a comparatively good sensitivity for measurement of age-related bone loss following menopause, because the metabolic rate in the vertebral trabecular bone is substantially greater than that of the surrounding cortical bone. In a cross-sectional study of 108 postmenopausal women Guglielmi et al. measured overall bone loss rates of 1.96%/year with QCT, compared with 0.97%/year and 0.45%/year for lateral DXA and PA-DXA, respectively (20). In a retrospective study Yu et al. found that spinal trabecular BMD assessed by QCT showed a larger decrement in age-matched populations, with and without vertebral fracture, than did DXA, in either the PA or lateral projection, and they also found that low spinal trabecular BMD confers higher relative risk for vertebral fracture (odds ratio 3.6) than did lateral or PA-DXA (odds ratio respectively 2.00 and 1.54) (21). In addition to its biomechanical importance, spinal trabecular bone has a high metabolic activity and this is evident in the relative rates of bone loss measured by DXA and QCT (22). Most of the studies comparing spinal QCT and DXA BMD measurements between subjects with vertebral fractures and age-matched controls have found that spinal trabecular BMD demonstrates larger percentage decrements in those with no fracture, and confers higher risks for vertebral fractures, even if a published European multicenter study found comparable results for the two techniques (23).

While the use of standard QCT has been based on two-dimensional characterization of vertebral trabecular bone, three-dimensional, or volumetric QCT, are new techniques that allow to improve spinal measurements and to extend QCT assessments to the proximal femur. They encompass the entire object of interest with stacked slices, or spiral CT scans, and can use anatomic landmarks to automatically generate relevant projections. Volumetric QCT can not only determine BMD of the entire bone or subregion, such as a vertebral body or femoral neck, it can also provide separate analysis of the trabecular or cortical components. Because a true and highly accurate volumetric rendering is provided, important geometrical and biomechanically relevant assessments can be derived, such as cross-sectional moment of inertia and finite element analysis (24-27).

A lateral scout view covering T11-L5 is first employed to delineate the lumbar spine vertebral levels. To relate the CT measurements to BMD, patients are scanned simultaneously with a bone mineral reference phantom containing calibration objects with equivalent densities to those of calcium hydroxyapatite. A computer program can identify and analyze the calibration objects of bone mineral reference phantom and it is used to derive calibration equations relating the CT numbers to BMD for each section. Three-dimensional ROIs are based on combining the boundaries of the vertebral body. The anatomic coordinate system is defined interactively. Three volumetric ROIs encompassing trabecular, cortical, and integral bone are defined on the central 70% of the vertebral body, based on the user deter-
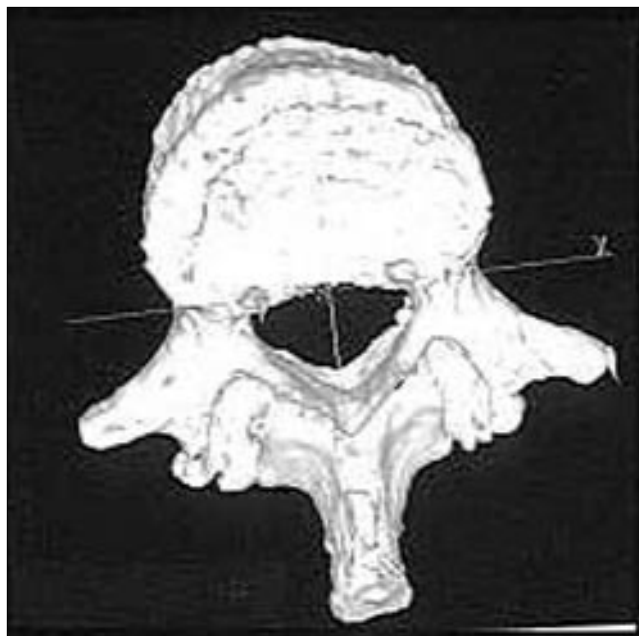
Figure 3 - Volumetric QCT 3D reconstruction showing the entire vertebral body.

mined vertebral midplane and end plate location. The volumetric ROIs are determined by stacking ROIs delineated on each of these slices. Using spiral CT scanning, it is possible to acquire volumetric QCT scans of the L1-L2 vertebral bodies in 30 to 40 seconds (Fig. 3). Because the volume of interest is determined three-dimensionally in software, patient positioning is of lesser concern than with conventional two-dimensional QCT or with DXA. The shorter scanning time may result in greater economic feasibility for QCT spinal trabecular BMD measurements, not only because they would require less time but also because the advent of spiral CT scanning has made more time available on CT scanners, due to shortening of other diagnostic scanning procedure (24, 28-32).

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