Current State of Bone Densitometry for Osteoporosis[1]

Harry K. Genant, MD

■ INTRODUCTION

Osteoporosis is one of the most devastating disorders associated with aging. The disease is characterized by decreased bone mineral density (BMD) and microarchitectural deterioration in bone tissue, resulting in an increased risk of fracture. Studies have shown large (5%–20%) annual losses in spinal trabecular BMD in women undergoing surgical or natural menopause (1–3). Each year, over 1.5 million Americans sustain fractures related to osteoporosis at a cost exceeding $13 billion (4).

Osteoporosis-related fractures result in significant morbidity and mortality. As BMD assessment techniques have progressed from simple radiography to more sensitive methods, the quality of BMD measurements has improved substantially. With advances in noninvasive detection techniques, osteoporosis can now be detected early and a course of treatment established. The availability of reliable BMD assessment techniques also makes it possible to monitor response to therapy. Furthermore, the capability now exists to evaluate any part of the skeleton with a high degree of precision and accuracy, thereby making it possible to assess bone strength reliably and predict fracture risk.

This article discusses current imaging techniques for BMD assessment, including single x-ray absorptiometry (SXA), dual x-ray absorptiometry (DXA), quantitative computed tomography (CT), and quantitative ultrasound (US). The article discusses the procedural aspects as well as the advantages and limitations of each technique.

■ CURRENT IMAGING TECHNIQUES

Older methods of assessing BMD include conventional radiography and single- and dual-photon absorptiometry. In recent years, these methods have largely been replaced by more sensitive techniques that allow site-specific BMD assessments for suspected fracture risk.

• Conventional Radiography

Conventional radiography is not sufficiently sensitive for the early diagnosis of osteoporosis. Bone loss can be detected with conventional radiography only when such loss exceeds 30%–50% (5), and in most cases, osteoporosis can be detected only after a fracture has occurred, making conventional radiography a poor tool for monitoring treatment.

• Single X-ray Absorptiometry

SXA has succeeded single-photon absorptiometry and is used for quantitative BMD assessment of the peripheral skeleton (eg, distal or ultradistal radius, calcaneus). Because SXA is an area projectional technique, separate measurements of trabecular and cortical bone are not possible (6). SXA has been used successfully in the diagnosis of osteoporosis with reasonable precision and low radiation dose. In the past several years, small portable DXA systems have begun to replace SXA systems.

Abbreviations: BMD = bone mineral density, DXA = dual x-ray absorptiometry, SXA = single x-ray absorptiometry

Index terms: Bones, absorptiometry, 30.12171, 40.12171 • Bones, CT, 30.1211, 40.1211 • Bones, US, 30.1298, 40.1298 • Osteoporosis, 30.56, 40.56

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[1]From the Department of Radiology, University of California, 505 Parnassus Ave, Suite M392, San Francisco, CA 94143-0628. From the Plenary Session, Friday Imaging Symposium: Advances in Women's Imaging, at the 1997 RSNA scientific assembly. Received February 9, 1998; revision requested March 6 and received March 23; accepted March 23. **Address reprint requests to** the author.

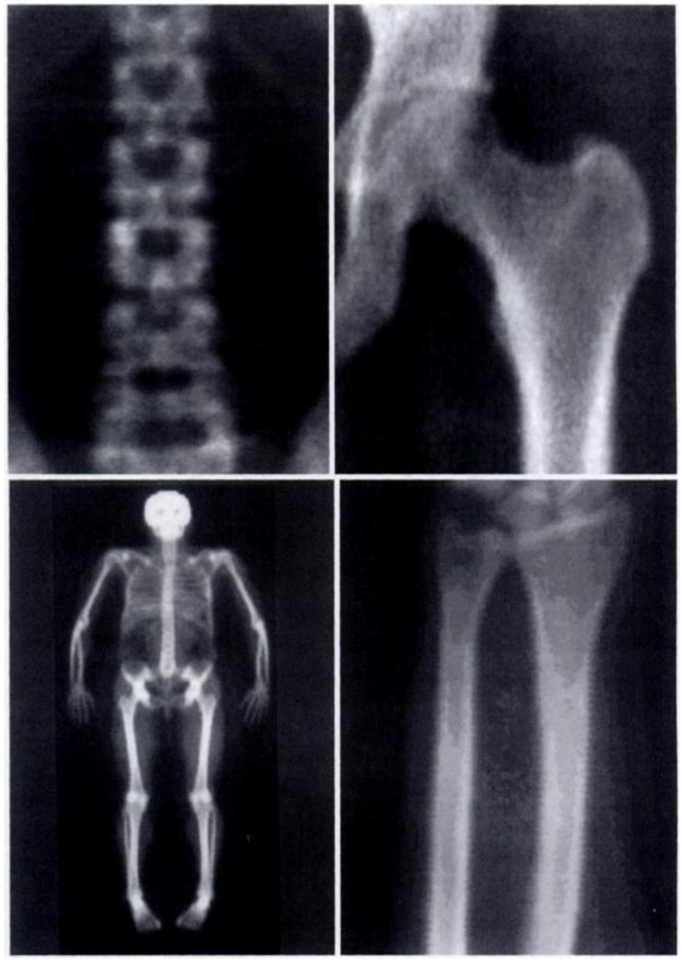


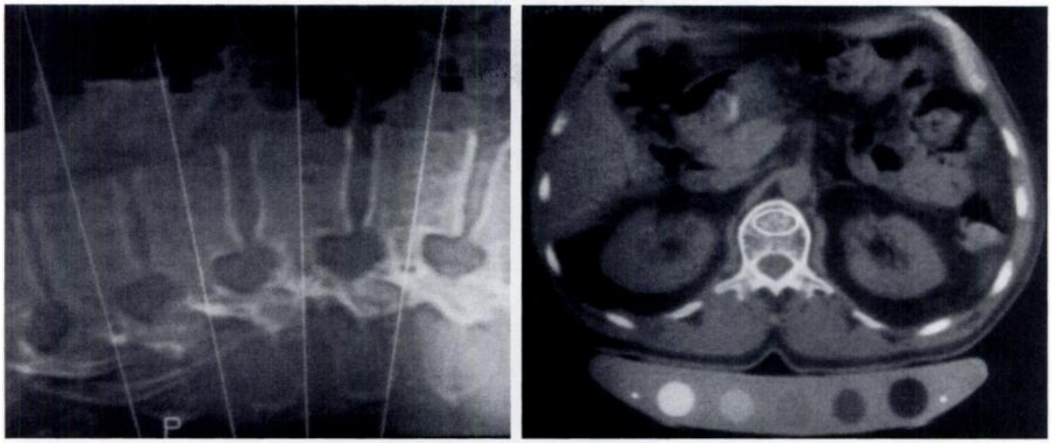
Figure 1. DXA images show the lumbar spine (upper left), hip (upper right), whole body (lower left), and forearm (lower right), the anatomic sites where DXA is typically applied. (Reprinted, with permission, from reference 12.)

• Dual X-ray Absorptiometry

Because single-energy measurements cannot be obtained at sites with variable soft-tissue thickness and composition (eg, axial skeleton, hip), dual-energy techniques were introduced. Generally, beams having two distinct energy levels are either produced by the x-ray generator or filtered from an x-ray spectrum (6). The x-ray tube can produce a higher radiation flux than earlier techniques (eg, dual-photon absorptiometry) that made use of a radioisotope source, allowing greater precision and reduced scan times (6–8). DXA is used to measure the BMD of the lumbar spine, hip, whole body, and forearm (7,9–11) (Fig 1).

The sophisticated software of all DXA units allows the physician to identify regions having different combinations of trabecular and cortical bone, such as the femoral neck and trochanter, and the high resolution of DXA scanners allows clear depiction of anatomic details. When used to assess the BMD of the lumbar spine, the scanning beam is usually parallel to the vertebral end plates. In the lateral projections, this allows reasonably clear definition of vertebral dimensions for morphometric analysis. This application of DXA is sometimes called morphometric x-ray absorptiometry (6).

DXA has replaced dual-photon absorptiometry as the most widely used technique for BMD assessment in clinical practice in the United States (8). There are nearly 10,000 DXA systems worldwide.



a. b.

Figure 2. Evaluation of trabecular bone density with quantitative CT. **(a)** Lateral scout view provides a rapid and simple means of defining the midplane of four vertebral bodies. *P* = posterior. **(b)** A single CT scan (8–10-mm section thickness) is obtained at each level, and the classic oval region of interest is placed anteriorly in the middle of the vertebral body of three or four consecutive lumbar vertebrae. This region of interest contains purely trabecular bone. For reference, regions of interest are also placed in the compartments of the calibration standards that contain distinct solution of mineral equivalents. (Reprinted, with permission, from reference 12.)

• Quantitative CT

Quantitative CT can be used to determine the true volumetric density (in milligrams per cubic centimeter) of trabecular or cortical bone in three dimensions at any skeletal site. However, because trabecular bone has high responsiveness and is important for vertebral strength, quantitative CT has been used primarily to determine trabecular bone density in the vertebral centrum. In this application, quantitative CT has been used to assess vertebral fracture risk, measure age-related bone loss, and follow up osteoporosis and other metabolic bone diseases. The validity of quantitative CT for the measurement of cancellous vertebral bone is widely accepted, and this modality is used at over 4,000 centers worldwide.

Generally, spinal quantitative CT is performed with standard clinical CT scanners and makes use of an external bone mineral reference phantom to calibrate the CT attenuation measurements to bone-equivalent values. This technique also makes use of special software to place regions of interest inside the vertebral body.

In a typical quantitative CT scan, the calibration phantom is placed under the patient's back and scanned simultaneously with the spine. Normally, a lateral scout view is obtained first to determine the midlevels of the lumbar vertebrae being scanned (usually L1–L3), and each vertebra is subsequently imaged with a 1-cm section thickness and with the gantry angled appropriately (Fig 1). After the data have been acquired, the reconstructed image is analyzed with software that places a region of interest in the central trabecular bone or cortical rim of the vertebral body. The average attenuation observed in the region of interest is determined by using an equation to plot a regression line between the known densities and attenuation measurements of the calibration phantom channels. The calibrated BMD values for the individual vertebrae are averaged, and this average value is compared with values in a population-specific normative database adjusted for the patient's age and the type of scanner used (Fig 2). Despite the use of calibration, however, there are differences among CT scanners, so that longitudinal measurements should be obtained with the same scanner.

Good correlation between spinal quantitative CT and DXA has been reported among healthy adult patients, although correlation is diminished somewhat for patients with osteoporotic fractures because of technical and anatomic considerations (7,13). The ability to selectively assess the metabolically active and structurally important trabecular bone in the vertebral centrum with quantitative CT allows excellent discrimination of patients with vertebral fracture and reliable measurement of BMD loss, generally with better sensitivity than with DXA (6,8).

New research involving quantitative CT includes high-resolution and microstructural CT techniques (6) (Fig 3). Both techniques provide the microstructural analysis needed for improved assessment of bone strength and prediction of fracture risk. The spatial resolution of standard CT scanners (typically <0.5 mm) is generally inadequate for highly accurate cortical measurements and analysis of discrete trabecular morphologic parameters. These issues are being addressed through research with microstructural CT techniques.

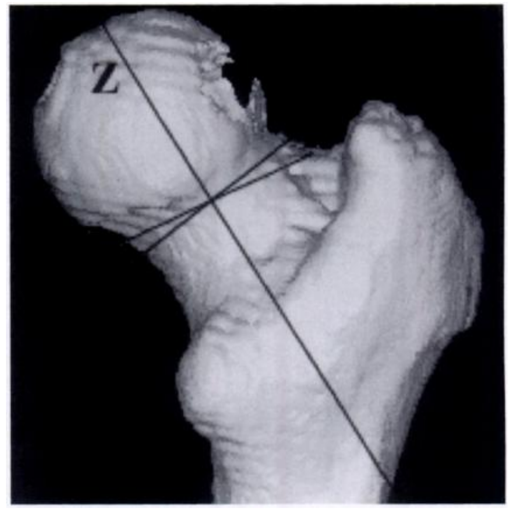


Figure 3. Three-dimensional reconstructed image of the proximal femur obtained with quantitative CT in a patient with osteoporosis secondary to paraplegia. The proximal femur was encompassed with 3-mm contiguous sections, and segmentation was achieved by mapping the bone surface with a contour-tracking algorithm. (Reprinted, with permission, from reference 3.)

• Peripheral Quantitative CT

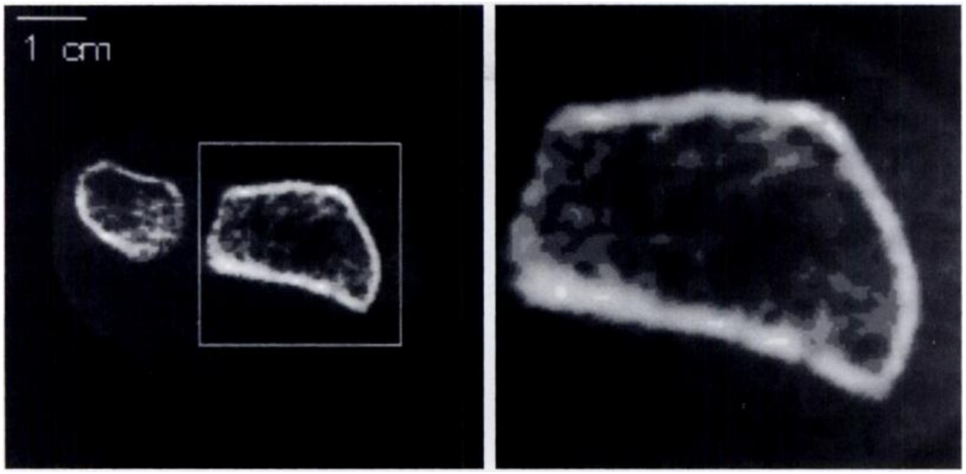
As the name implies, peripheral quantitative CT is used to obtain BMD measurements in the peripheral skeleton (principally the distal radius). Peripheral quantitative CT makes use of special-purpose scanners with x-ray sources to obtain a true volumetric density measurement of bone without superimposition of other tissues. Exact three-dimensional localization of target volumes is possible with peripheral quantitative CT (6,7) (Fig 4). Modern peripheral quantitative CT scanners incorporate a multisection data acquisition capability that covers a larger volume of bone than does the commonly used single-section technique. The measurement of multiple sections is potentially more representative of changes in the distal radius and therefore may reflect the bone status of an individual more accurately. If studies that make use of the multisection peripheral quantitative CT technique are successful, they may encourage more extensive use of this already promising technique (6).

Ease of use and the capability of assessing trabecular and cortical bone compartments separately make peripheral quantitative CT an attractive alternative to projectional techniques such as DXA (14). In addition, measurements obtained with peripheral quantitative CT provide reasonable precision and accuracy (7,10). There are about 1,000 systems in use worldwide.

• Quantitative US

Quantitative US measurements include attenuation, velocity, and a derived parameter, "stiffness." The attenuation and velocity of a sound wave passing through bone are related to the biomechanical properties, geometry, and density of the bone; the more complex the structure, the greater the attenuation and velocity. Normal bone demonstrates higher attenuation and is associated with greater sound velocity than osteoporotic bone. Stiffness does not reflect a biomechanical property of bone; rather, it is an algorithm derived from the attenuation and velocity of the sound wave (8).

Quantification of bone density and structure can be achieved by analyzing the attenuation or velocity of US in bone. This procedure is currently being investigated in the United States and is portable, relatively inexpensive, extremely easy to use, and does not involve exposing patients or personnel to ionizing radiation. Investigational measurements of sound wave velocity and attenuation have been obtained at various easily accessible anatomic sites, including the tibia, radius, and patella (5).



a. b.

Figure 4. Declination of cortical and central trabecular bone in the forearm. **(a)** Peripheral cross-sectional quantitative CT scan obtained at the level that represents 4% of the ulnar length from the distal radial end plate shows the area of interest (box). **(b)** Magnified view of the area of interest shows the bone declination to greater advantage. (Reprinted, with permission, from reference 12.)

Preliminary clinical results with these investigational measurements have been promising, prompting further investigation and commercial development (15).

More than a dozen types of quantitative US devices are commercially available. However, none has been cleared by the Food and Drug Administration for clinical use (although approval is currently pending); consequently, most quantitative US devices currently being used for BMD assessment in the United States are located at research centers. Quantitative US enjoys wider distribution in Europe and Asia, with a global distribution of about 3,000 systems.

■ CONCLUSIONS

Monitoring the course of osteoporosis or therapy is a major clinical application of bone densitometry. Some clinical leaders believe osteoporosis should not be treated without monitoring the progress of therapy with densitometry (14,16–18).

In the past, the techniques used to assess BMD were imprecise and could not be used to measure changes in BMD accurately in individual patients. Today, the most widely used techniques—SXA, DXA, and quantitative CT—have errors in precision of 0.5%–2% (6). To achieve this degree of precision, strict quality control measures and careful technical monitoring are necessary (17). Of the three techniques, DXA and SXA are the most precise, whereas quantitative CT is the most sensitive (16,19). Quantitative CT is less accurate than DXA, but because it can help detect alterations in purely trabecular bone, it may be the most useful of the three methods in the diagnosis of spinal osteoporosis (13,20). However, because of the higher radiation dose and longer scan times associated with quantitative CT, clinical application of this technique has not been as widespread as that of DXA. With regard to determining longitudinal changes in BMD and monitoring the response to therapy, DXA is characterized by a high degree of precision, moderate sensitivity, and a reasonably low radiation dose. Generally, measurements obtained with either spinal DXA or quantitative CT are preferred for serial assessment of disease progression or therapeutic response. In their present state, the various methods of measuring BMD for diagnostic purposes appear to be complementary rather than competitive (9).

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