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The Radiologic Assessment of Osteoporosis

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Abstract: Non-invasive radiologic assessment of bone mineral density continues to play an important role in diagnosing, treating, and studying osteoporosis. Complications of osteoporosis result in major morbidity, health care expenditures, and mortality. Concomitant with a growing elderly population, these complications will become increasingly important.

Traditional techniques for assessing bone mineral density include single-photon absorptiometry (SPA), dual-photon absorptiometry (DPA), single- or dual-energy quantitative computed tomography (QCT), single-energy X-ray absorptiometry (SXA), and dual-energy X-ray absorptiometry (DEXA, DXA). Potential new techniques that may prove useful in determining either bone mineral density or bone micro-structural integrity include ultrasound (US) and magnetic resonance imaging (MRI). The advantages and disadvantages of each technique will be discussed, with an emphasis on DEXA.

Introduction

Osteoporosis is a disease characterized by low bone mass and abnormal bone microarchitecture [29, 30] affecting about 30% of post-menopausal women, with as many as 54% more at risk [28, 59]. Osteoporotic complications result in major morbidity, health care expenditures, and mortality.

The clinical utility of non-invasive radiologic assessment of bone mineral density (BMD) has been well established in diagnosing, studying, and assessing treatment in patients with osteoporosis [59]. Recently, six points of international consensus have been achieved [37, 59]:

1. "Bone-mass measurements predict a patient's future risk of fracture." This

relationship is as strong as hypercholesterolemia and heart disease [27] or hypertension and stroke [57]. The only objective and direct measure of bone mass is bone densitometry.

2. "Osteoporosis can be diagnosed on the basis of bone-mass measurements even in the absence of prevalent fractures." Previously, the diagnosis of osteoporosis was made on the basis of an insufficiency fracture. According to the World Health Organization [59], osteoporosis can now be diagnosed in white women who have bone mineral density more than 2.5 SD below the mean for young adult control women, a BMD found in 95% of women with osteoporotic fractures [28,35]. (Reference standards, well established for white women, are less well established for non-white women; in any event, white women are at higher risk for developing osteoporosis than non-white women.) In addition, a diagnosis of osteopenia is made with a BMD 1.0--2.5 SD below the same mean. Identification of this less-affected group is important because fracture risk increases 1.5--2.5 times for every SD below the mean [5,27,35,43,45].
3. "Bone-mass measurements provide information that can affect the management of patients." Patients with estrogen deficiency, radiographic osteopenia, asymptomatic primary hyperparathyroidism, and long-term glucocorticoid therapy are most likely to benefit.
4. "The choice of the appropriate measurement site(s) for the assessment of bone mass or fracture risk may vary depending on the specific circumstances of the patient." Measurements from different sites are concordant in 85% of cases [6,42], and several studies suggest that many skeletal sites are equally successful in predicting future fracture risk [27,43,49]. However, direct bone densitometry measurements of the hip may be superior to other sites for predicting fracture in the hip [5,23]. Therefore, if risk of fracture at a particular site is a clinical concern, it is best to measure that site directly, if possible.
5. "The choice of the appropriate technique for bone-mass measurements in any given clinical circumstance should be based on an understanding of the strength and limitations of the different techniques," and is further discussed below. Table 1 provides an overview.
6. "Bone-mass data should be accompanied by a clinical interpretation." A narrative report should accompany the computer-generated data to help guide the primary care physician with clinical decision-making.

Table 1. Comparison of several techniques for bone mineral density measurements*

Technique	Site	Precision error (%)	Accuracy error (%)	Effective dose equivalent (μSv)
SPA/SXA	Radius/calcaneus	1--2	4--6	<1
DPA	AP spine	2--5	4--6	5
DXA	AP spine	1--2	3--9	<1
QCT	Single energy	2--4	5--15	50
	Dual energy	4--8	3--6	100

SPA, single photon absorptiometry; SXA, single X-ray absorptiometry; DPA, dual photon absorptiometry; DXA, dual X-ray absorptiometry; QCT, quantitative computed tomography.

*Adapted from Guglielmi [24].

Techniques for Assessing Bone Mineral Density

Traditional techniques for assessing bone mineral density include plain film radiography, single-photon absorptiometry (SPA), dual-photon absorptiometry (DPA), single- and dual-energy quantitative computed tomography (QCT), single-energy X-ray absorptiometry (SXA), and dual-energy X-ray absorptiometry (DEXA or DXA [17, 60]). New applications of ultrasound (US) and magnetic resonance imaging (MRI) may prove useful in determining either bone mineral density or bone micro-structural integrity. The advantages and disadvantages of each technique will be discussed.

Two major considerations of any technique are the precision and the accuracy. Precision assesses the reproducibility of the results, usually as a coefficient of variation (CV), often expressed as a percent of the measured value, mathematically described as follows:

$$CV = (SD / X_c) \times 100,$$

where SD is the standard deviation of the between test variance and X_c is the combined mean of successive test results. Accuracy assesses the ability of the measurement to correctly reflect the true bone mineral density value. Other considerations include radiation dose, scanning time, potential artifacts, cost, maintenance, and patient comfort.

Generally, bone mineral density measurements are not performed more frequently than yearly, because changes are usually not detectable with more frequent testing. Exceptions include states of rapid bone changes, such as with corticosteroid use or estrogen responding patients. Observed changes should be at least 2.8 times the coefficient of variation to be considered a real effect [4,56]. Ideally, patients should be examined longitudinally with the same machine, and continuing quality assurance is an integral part of maintaining instrument precision.

Quality assurance (QA) is essential for all bone densitometry techniques. Proper QA can improve precision, accuracy, and longitudinal comparisons. Important QA procedures have been described related to personnel, patient data, longitudinal monitoring, cross-calibration between different scanners, and phantom data [19,40,44].

Plain film radiography

In the appendicular skeleton, plain film radiography can readily identify fractures. In addition to the qualitative assessment of bone mineral density, many semi-quantitative indices have been developed to assess BMD, eg., trabecular quantification (Singh [50]) or combined cortical thickness quantification (Garn [13]). However, at least 20% of bone mineral content needs to be lost before osteopenia is radiographically visible [1], and therefore, the sensitivity and reproducibility of plain film techniques have been poor.

In the spine, the effects of osteoporosis may manifest as bi-concave central compression fractures, anterior wedge compression fractures, symmetric transverse compression fractures, and increasing kyphosis. However, the primary clinical goal is prevention of fractures, rather than their identification.

SPA

The first commercially available technique for bone densitometry was SPA [2]. A transmission scan is performed, typically with 200 mCi iodine-125 (27.5 keV; half-life = 60 days). However, the radioisotope needs periodic replacement, usually about every 6 months.

Precision error is 1--2% [12,38] and accuracy is 4--6% [39]. The surface dose is 30--50 μSv with an effective dose equivalent of less than 1 μSv [16]. Scan time is 5--10 minutes.

SPA is limited to the appendicular skeleton, and gives a combined measure of cortical and trabecular bone. Because a water bath is required to compensate for soft tissues, the radius and calcaneus are most commonly measured.

SXA

SXA is similar to SPA except that an X-ray source is used instead of the transmission radioisotope source. As a result, long-term stability and cost effectiveness may be improved.

Precision is improved to 0.8--1.2% in the calcaneus [21]. Accuracy and radiation dose are similar to SPA.

DPA

In 1966, Reed showed that adding a second photon beam of a different energy allowed compensation for soft tissue [41]. This dismissed the water bath requirement and allowed measurement of the spine and hip. A dual transmission scan is usually performed with gadolinium-153 (44 and 100 keV; half-life = 240 days).

Precision is 2--5% with an accuracy is 4--6%. The effective dose of about 5 μSv [48]. Scan time is slow, usually 20--40 minutes.

DEXA

In 1970, Krokowski capitalized on the same principles as DPA but used X-rays with two different energies instead of radioisotope photons with two different energies [31]. Different manufacturers used different techniques to generate these dual X-ray energies. Hologic (Waltham, MA) uses rapid switching between 70 kVp and 140 kVp. Lunar (Madison, WI) operates at 76 kVp, uses a cerium K-edge filter, and uses energies of 38 keV and 70 keV. Norland (Fort Atkinson, WI) operates at 100 kVp, uses a samarium filter, and uses energies of 46.8 keV and 80 keV [55].

Precision error for the AP lumbar spine is 1--2% and accuracy is 3--9% [20,26] with an equivalent dose of less than 1 μSv [16]. Scan time is 2--10 minutes. Compared with DPA, DEXA is faster (because photon flux is 10--1000 times greater), has better precision, has higher resolution, and finer collimation (1.5 mm vs. 5--8 mm), which improves artifact detection, and has decreased source renewal requirements. Hence, DEXA has essentially replaced DPA.

The most common sites measured are the lumbar spine (AP and lateral), proximal femur, total body, forearm, and calcaneus. The frontal spine may be susceptible to artifacts including aortic calcifications, facet joint arthrosis, or osteophytes. The lateral spine measurement is less precise because of patient positioning [47,51], although recent C-arm improvements may improve lateral lumbar spine precision to 1.0--1.2% [7,52].

Data can be obtained as bone mineral content (BMC) in g/cm or areal bone mineral density (BMD) in g/cm^2 . Relatively low resolution images are also generated, as shown in Figures 1A, B, and C for the normal AP lumbar spine, femoral neck, and total body. Figure 1D demonstrates a markedly abnormal AP spine with scoliosis that complicates the interpretation. In the future, image resolution may be improved with morphometric X-ray absorptiometry (MXA), such that the need for correlative plain films may be eliminated

[53]. Individual patient data is then plotted and compared with normative data based on age, sex, and measurement site, as shown in Figure 2.


 Figure 1

Fig. 1. Images from dual energy X-ray absorptiometry (Lunar DPX; Madison, WI): **A** demonstrates a normal antero-posterior (AP) lumbar spine; **B** demonstrates a normal AP femoral neck; and **C** demonstrates a normal AP total body scan. **D** demonstrates a markedly abnormal AP lumbar spine with scoliosis.


 Figure 2

Fig. 2. Individual patient data plotted with normative data based on age, sex, and measurement site (Lunar DPX; Madison, WI). **A** and **B** are for the lumbar spine for female and male patients, respectively. **C** and **D** are for the femoral neck for female and male patients, respectively.

QCT

In 1976, Ruegsegger and colleagues described appendicular QCT [46]; in 1982, Genant and colleagues analyzed cross-sectional axial images through vertebral bodies with region of interest comparisons with known reference standards [15].

Precision is 1--4% and accuracy is 4--15% [3,14] with an effective dose of about 60 μ Sv. Examination time is about 10--15 minutes. The major advantage of QCT is the ability to measure cortical and trabecular bone densities separately. However, reference standard stability and interchangeability can be problematic [11,18,22,54].

Recent advances may have specific applications. High resolution QCT (HRQCT) can examine trabecular structure to a resolution of 0.15 mm [8,9]. Volumetric QCT (vQCT) may assist volume localization and assess geometry [32]. Micro-CT seems promising for in vitro work [32]. Finite element analysis mathematically relates bone distribution to its strength [10,25].

QUS

Broadband ultrasound attenuation (BUA) and speed of sound (SOS) have been measured in vitro and in vivo [33,36]. At present, these techniques require further investigation. However, they offer the potential of an independent assessment of fracture risk without ionizing radiation.

QMR

Ionizing radiation techniques (eg., plain films, CT) are excellent for imaging bony structures. In contrast, magnetic resonance imaging has evaluated soft tissue structures to great advantage. Recent advances in gradient strength, imaging sequences, and post-processing techniques have allowed the study of trabecular structure in bone by exploiting differences in magnetic susceptibility between trabeculae and marrow [34,42,58]. However, these techniques are not yet currently practical clinically, in part because of low signal-to-noise, which limits resolution and results in motion artifacts from relatively long imaging times.

Discussion

Given the current state of the art, DXA (DEXA) is the preferred technique for bone mineral density assessment [37,59]. The technique is precise (reproducible), accurate, fast, and low in radiation dose to the patient. A typical examination consists of an evaluation of the lumbar spine and femoral neck. If a single site is desired, especially in younger patients or to assess therapy, the lumbar spine alone might be chosen, as the precision is better in the lumbar spine than in the femoral neck. However, extensive degenerative disease or vascular calcification may complicate the interpretation of lumbar spine measurements. Likewise, orthopaedic hardware in the hip or elsewhere may make a particular site less desirable. DXA is not available at all institutions, and in those circumstances, DPA is probably the best alternative. For peripheral sites, SPA or SPX could be obtained.

When and how patients should be treated is a personal decision between the patient and physician, and it is not the purpose of this paper to address these complex issues. Clinical risk factors need to be assessed, and patient preferences for possible therapeutic options will be important. Nevertheless, the bone mineral density measurement offers not only an objective baseline, but also an objective measure of bone maintenance, disease progression, or disease improvement.

Four clinical situations have been clearly identified in which bone mineral density information could affect clinical management: estrogen deficiency, osteopenia on plain radiography, asymptomatic primary hyperparathyroidism, and long-term glucocorticoid therapy [37,59]. Who else should be included in screening is still open to debate. For example, patients with historical (e.g., strong family history), physical, or laboratory risk factors might be considered for early screening.

It would also seem prudent that any patient undergoing treatment for osteoporosis receive serial bone densitometry measurements. Although no absolute time interval has been established, many recommend annual screening, although in some instances, shorter or longer time intervals may be appropriate [37,59]. Although not proven, it has been suggested that serial measurements may help improve patient compliance [37,59].

Finally, serial bone densitometry measurements will continue to play an important role in clinical trials of therapeutic interventions by providing an objective measure of bone density.

Summary

State-of-the-art bone densitometry techniques are precise and accurate, and they predict future fracture risk. These techniques include SPA, DPA, QCT, SXA, and increasingly DEXA.

Potential new techniques that may prove useful in determining either bone mineral

density or bone micro-structural integrity include QUS and QMR, although these new techniques are not yet ready for clinical practice.

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