Panel Session: Bone Mass, Bone Loss Measurement

Technical Aspects and Clinical Interpretation of Bone Mineral Measurements

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Synopsis

Four procedures—single photon absorptiometry, dual photon absorptiometry, dual energy radiography, and quantitative computed tomography—allow nontraumatic measurement of bone mineral, with high accuracy and precision, under conditions generally encountered in patient care situations. By using these procedures, almost any part of the skeleton is accessible to such measurements. Total bone is measured by the absorptiometry procedures, trabecular bone by quantitative computed tomography. Several commercial instruments are available for each technique. For clinical use, if decisions are being made based on measurements in a given patient, preferred measurement sites are the spine (for Type I osteoporosis) and hip (for Type II osteoporosis). The newly introduced dual energy x-ray absorptiometry (DEXA) procedure allows measurements of the spine and hip with the highest precision and accuracy, the lowest radiation dose, and the shortest scanning time.

WHILE THE CONTROVERSY still continues as to whether screening healthy women to predict fractures later in life is indicated, bone mineral measurements have gained importance in the diagnosis and management of patients with osteoporosis and metabolic bone disease. Several specific indications have been established. The measurements are used to give information on fracture risk for a specific skeletal site, and, when used under well-defined conditions, can be used to estimate the rate of bone loss. The latter use is indicated for monitoring treatment effects, and identifying rapid bone loss.

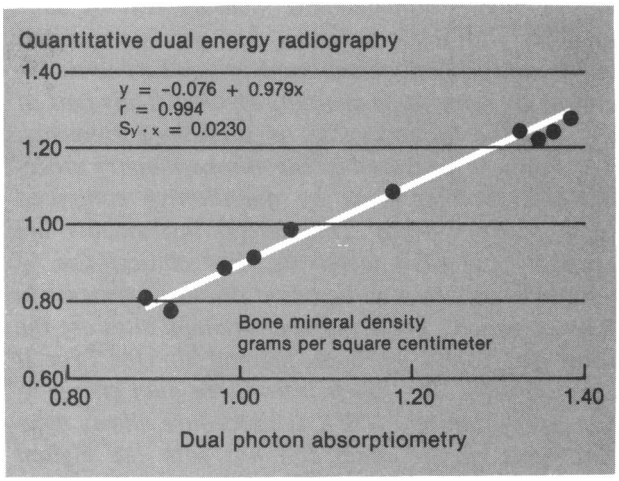
A number of methods for nontraumatic estimation of bone mineral have been described in the last 20 years (*1-3*). Only a few procedures need to be considered as potentially useful for clinical practice. Their performance characteristics have been studied and described, and they are acceptable to the patient, generally available, and relatively inexpensive. For measurement of integral bone (that is, compact and trabecular bone), there are four methods: single photon absorptiometry (SPA), with the radius and calcaneus being the sites of greatest interest; dual photon absorptiometry (DPA) with spine, hips, and total skeletal mineral (calcium) measurements; and dual energy x-ray absorptiometry (DEXA), a new procedure designed as a technical improvement of DPA. For measuring trabecular bone, quantitative computed tomography (QCT) can be used for axial bone; it is less readily adapted for measurements on appendicular bone or hip.

Of these four methods, SPA has been available for more than 20 years and has been reviewed extensively (*1, 2*). All methods are based on the principle of x-ray transmission. The first three techniques involve rectilinear scanning of the body, or portions of it; QCT is an adaptation of routine computed tomography for organ imaging (*3*). The clinically attractive DPA and DER procedures will be discussed in more detail.

Dual Photon Absorptiometry

In DPA, the spine, hips, or the entire patient is scanned with a dual energy photon beam, generally from gadolinium-153 (40 and 100 kilovolts, half-life 250 days). Two absorption curves are obtained, from which bone mineral is calculated. The results are expressed in grams per square centimeter (g per cm^2), or bone mass per cm^2 area scanned. Several commercial instruments are available; quality control recommendations and contraindications have been defined (*4*). Measurements can be performed with a precision of 2-3 percent (coefficient of variation (CV)) for spine, 3-5 percent for femur neck and trochanter, and 6-8 percent for Ward's triangle. The method has

Comparison of bone mineral density measured in the lumbar spine (L2-L4) made with a dual photon absorptiometry instrument (DPA, Lunar, Inc.), and an instrument based on dual energy radiography (Hologic, Inc.)



a similar accuracy of 6–8 percent when tested on ashed bones, and is relatively insensitive to variation in body composition. Extremes in body thickness (obesity, children) require special considerations (*4*).

Dual Energy X-ray Absorptiometry (DEXA)

DEXA is a new method that is similar to DPA in concept and performance, but it is based on dual energy x-rays rather than on an isotope source. The use of x-rays results in a stable incident radiation intensity (no decay, as with an isotope source); a smaller beam results in bone mineral images of higher resolution, and, most importantly, precision is better, about 1.0 percent (CV) for the spine. The data output and display are similar to those from a DPA instrument. When results from DPA and DEXA instruments are compared, they are highly correlated over the entire range of bone mineral content seen in patients ($r = 0.99$) (fig. 1). Bone mineral density measurements by DEXA are 6–12 percent lower due in part to a more accurate assessment of bone area. As in DPA, the position of the bone in the radiation beam is critical, and patient thickness influences the data (*5*). These problems are well known from DPA, and can be corrected for.

A more detailed comparison among the four procedures is shown in table 1.

Clinical Use of Bone Mineral Measurement

Bone mass measurements in clinical practice are potentially useful for two different approaches: (*a*) as regional bone mineral measurements for fracture risk assessments, and (*b*) for repeated bone mineral measurements, which can be used to estimate the integrated rate of bone loss over periods of 1–2 years. Bone mineral measurements should not be used for the diagnosis of existing fractures; for this, radiography is the best procedure.

The use of bone mineral measurements for fracture risk assessment is based on the well-documented relationship between bone mass (ash weight) and compressive strength (*6*). For this, one needs instruments of high accuracy. Measurement results are site-specific. In postmenopausal osteoporosis (Type I), measurements should be performed on the spine; for senile osteoporosis (Type II), on the hip. Many studies have shown that bone loss at specific skeletal sites cannot be predicted from measurements at remote sites. Although bone loss correlates well in all bones throughout the skeleton, the 95 percent confidence interval for predicting bone mineral content of the spine by radius measurements on a given patient would exceed 20 percent. This is true for all sites on the radius, regardless of the trabecular bone content.

The relationship between bone mineral at a given skeletal site and nontraumatic fracture at that site is more complex than was initially expected. Although bone mineral is important, it is not the only factor responsible for fracture. Melton and co-workers (*7*) and others have shown that the decreasing bone mineral that occurs with age is a major factor in fractures, and have enumerated factors that must be considered in fracture risk prediction. In the absence of severe trauma, fractures do not occur until bone mineral is more than two standard deviations below that of young adults. This results in a fracture threshold of 1.0 g per cm^2 for both femur and spine, which is based on absolute bone mineral values and is independent of age, sex, and probably also of race. With a further decrease in bone mineral, fracture prevalence in the spine and, less markedly, fracture incidence in the hip, increase. The nonlinear increase of fracture risk with a linear decrease in bone mineral reflects the presence of other factors in fracturing.

Similar results are obtained from bone mineral measurements of trabecular bone in the spine by QCT. Some studies (*3*) have shown a marginal improvement in fracture risk prediction when trabecular bone was measured. The magnitude of this difference is not large enough to affect the clinical usefulness of either DER or QCT in clinical practice at this time. However, it is important to note that bone loss is about three times the rate in physiological trabecular bone (QCT) than in integral bone (DPA).

Measurement of bone mineral, by any procedure,

Table 1. Comparison of four techniques: single photon absorptiometry (SPA), dual photon absorptiometry (DPA), dual energy x-ray absorptiometry (DEXA), and quantitative computed tomography (QCT) for bone mineral measurements

Parameter	*SPA*	*DPA*	*DEXA*	*QCT*
Source	^{125}I	^{153}Gd	X-ray	X-ray
Energy (kilovolts)	30	40, 100	70, 140	80
Bone site	Extremities	Spine, hip, total skeleton	Spine, hip, total skeleton	Spine, hip,
Bone type	Cortical, integral	Integral	Integral	Trabecular, (cortical, integral)
Precision (CV), percent	1-2	1.5-3	0.5-1.5	4-8
Radiation (mrad per scan)	15	< 5	< 5	200-400
Time per scan (minutes)	20 (radius)	35 (spine)	6 (spine)	20 (spine)
Cost ($ per scan)	50-100 (radius)	100-300 (spine)	100-200 (spine)	200-400 (spine)
Instrument cost ($)	25,000	40-60,000	70,000	25,000 (QCT upgrade)

is controversial as a risk assessment in healthy women for early detection of those whose bones may fracture later in life. However, measurements in the axial skeleton have been found useful in the following applications:

1. Scanning for osteoporosis in patients with multiple historical risk factors for osteoporosis;
2. Making therapeutic decisions for individuals with a disease or drug known to cause osteoporosis;
3. Establishing the diagnosis of osteoporosis in women whose radiograph shows only radiolucency, or minimal vertebrae deformities; and
4. Deciding whether to begin estrogen treatment in women at menopause.

With experience in using these measurements in clinical practice, this list will probably be expanded.

Measurement of Rate of Bone Loss

The normal rate of bone loss in the spine is small. When expressed as a percentage of basal bone mineral per year in g per cm^2, normal rates in women are < 1 percent per year in young adults, and 3-6 percent per year in women for a few years around the menopause. Patients with accelerated bone loss may be expected to show a loss of 4-8 percent per year. Even higher rates of loss are seen in patients with metabolic bone disease. Values of 4-8 percent per year have been reported for women with osteoporosis. With sodium fluoride treatment, a rate of bone mass increase of about 5-10 percent per year is noted; in patients with liver disease and after liver transplants, a loss of 5-15 percent per year can be observed. Clinicians are interested in the rate of change so that they can monitor the effect of treatment on bone mass and on the rate of loss. This would allow the separation of responders from nonresponders, and would, in turn, allow the identification of fast bone losers, presumably the subjects with a high risk of fracture.

The accuracy of rate of change of bone mass depends upon the amplitude of change and the precision of the instrument. To obtain reliable measurements, instrument, patient, and data analysis factors must be considered. Everything else being optimal, precision of the standard DPA instruments varies with the bone mineral being measured. Values range from about 3 percent (CV) for a bone mineral content of 0.6 g per cm^2, to about 1.2 percent (CV) for a bone mineral content of 1.5 g per cm^2.

For analysis, the bone mineral data are plotted against time, and a linear regression model is used to calculate the width of the 95 percent confidence interval. Typical data are summarized in table 2. A review of table 2 allows selection of optimal scan number and time interval for a given instrument precision to achieve the desired sensitivity of measurement.

If a woman with a bone mineral of 1 g per cm^2 has a reported loss of 4 percent based on two scans performed over a 2-year period, measured with an instrument which has 2.4 percent precision, there is a 95 percent chance that her true change in bone mineral was between a gain of 2 percent per year and a loss of 10 percent per year. This wide confidence interval is of limited clinical use.

Table 2. Comparison of precision of DPA and DEXA instruments

Interval	Measurement frequency	95 Percent Confidence Interval[1] DPA	DEXA
6 months	2	26	14
	3	14	6
	4	8	4
1 year	2	14	6
	3	6	4
	4	4	2
2 years	2	6	3.4
	3	4	1.6
	4	2	1.0

[1]Precision: DPA 2.4 percent CV; DEXA 1.2 percent CV. Confidence interval expressed as percent of 1.0 g per cm² mineral density.

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If the same measurement could be made with a DEXA instrument having a precision of 1.2 percent, then there is a 95 percent chance that the true change in bone mineral would be a loss between 0.6 and 7.4 percent per year. If a loss exceeding this should be found in a patient receiving estrogen or sodium fluoride treatment, it would suggest treatment failure. If four measurements were carried out with DEXA (two at the baseline, two at 2 years), there would be a 95 percent chance that the true change was a loss between 3 and 5 percent per year. This is clinically useful information. More frequent measurements, and a longer time between scans, shorten the confidence interval.

The debate over usefulness of bone mineral measurements for screening continues. One should not, however, overlook the meaningful clinical information in diagnosis and management of osteoporosis, and diseases or conditions associated with bone loss that can be obtained with bone mineral measurements. The rate of loss has been difficult to estimate in the past within usefully short intervals, but with DEXA more confidence can be placed in these measurements, and the time interval can be shortened to more meaningful limits. The new DEXA-based fast scans should allow reduction in cost of the test to the patient, better accuracy and precision, and improved use for rate of loss measurements, and fracture risk predictions in the hip.

Definition of specific regions of interest, and improvements in how to select them in the hip, have made this site more attractive for prediction of hip fracture risk in clinical practice. More insights are to be expected within the near future. Many bone clinics in this country have successfully used bone mineral measurements for years as part of the diagnostic and management approach to patients with osteopenia-associated bone disease. Consumers who choose to have a bone mineral measurement, without interpretation by a physician who is familiar with their health condition, risk getting little more than a number with a high chance for misinterpretation due to the complexity of diagnosing osteopenia and its causes.

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