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Bone Densitometry: Current Assessment

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Considerable effort has been expended in the development of methods for quantitatively assessing the skeleton so that osteoporosis can be detected early, its progression and response to therapy carefully monitored, and its risk effectively ascertained. The capability now exists to evaluate the peripheral, central or entire skeleton as well as the trabecular bone or cortical bone envelopes with a high degree of accuracy and precision, and a modest capacity for determining bone strength and predicting fracture risk. Four general methods have been developed that are currently being widely used for non-invasively measuring bone mineral density at various anatomical sites, both in the axial and peripheral skeleton. These methods include single-photon absorptiometry (SPA), dual-photon absorptiometry (DPA), dual X-ray absorptiometry (DXA) and quantitative computed tomography (QCT) (Table 1). While differing in anatomic sites measured and in their estimates of precision, accuracy, and fracture discrimination, all of these methods provide clinically useful measurements of skeletal status and represent major advances in our ability to measure bone non-invasively.

Single-Photon Absorptiometry (SPA)

SPA was the first commercially available technique for the noninvasive measurement of bone mineral density [1]. In SPA, a beam of highly collimated monoenergetic photons from a radionuclide source (typically iodine-125,

Table 1. Comparison of currently used techniques for measuring bone mineral density

	Cortical/trabecular ratio	Precision in vivo (%)	accuracy error (%)	scanning time (min)	Effective dose equivalent (μSv)[a]
Single-photon-aborptiometry					
Distal third radius	95/5	1–2	4-6	10	<1
Ultra distal radius	60/40	1–2	4-6	10	<1
Os calcis	5/95	1–2	4–6	15	<1
Dual-Photon absorptiometry					
Lumbar spine	50/50	2–4	5–10	30	5
Proximal femur	60/40	3–5	5–10	30	3
Total body	80/20	2–3	1–2	40	3
Dual X-ray absorptiometry (pencil beam)					
Lumbar spine					
AP	50/50	1	4–8	5–10	1
Lateral	10/90	2–3	5–10	15–20	3
Proximal femur	60/40	1–2	4–8	5–10	1
Total body	80/20	1	1–2	20	3
Quantitative computed tomography					
Single energy spine	0/100[b]	2–4	5–15	20	50
dual energy spine	0/100[b]	4–6	3–6	25	100

[a] Does not include dose due to localization radiographs such as spine films and computed radiographs. For comparisons, a standard chest radiograph, depending on the technique, has an effective dose equivalent of 100–150μsv

[b] Depends on region of interest. the vertebral core is essentially 100% trabecular bone.

photon energy 27.5 keV) is passed through the measurement site, and the transmitted fraction is detected. The observed attenuation of the radiation beam is a function of the density of the intervening tissues and is used to determine the bone mineral content (BMC, in grams) and areal bone mineral density (BMD, in g/cm^2). The SPA measurement requires a constant soft tissue path length which is achieved by surrounding the measurement site with a known thickness of tissue-equivalent material, typically by immersion in a water bath. This requirement limits the technique to peripheral skeleton measurements, specifically in the ultradistal radius, distal third of the radius and the os calcis.

The most common site of measurement is the distal third of the radius, composed mainly (95%) of cortical bone. For monitoring skeletal response to therapy in individual patients, the distal third of the radius may have limited value; however, the large percentage of trabecular bone in the ultradistal radius (40%) and os calcis (95%) is thought to increase the sensitivity at these sites for detecting early and rapid bone loss. The classic SPA forearm measurement uses only a single pass of the source and detector perpendicular to the limb. For the relatively homogeneous cortical bone of the radial shaft, this single pass provides enough precision for clinical use. When measuring other less uniform and more highly trabecular sites, rectilinear scans are necessary to obtain larger samples and reduce the precision of SPA has been shown to be 1.0%–1.6% at the ultradistal site and 0.9%–1.2% at the distal third site [2,3] with an accuracy of 6%. Precision of the os calcis measurement is reported to be 0.9% in vitro and from 1.0 to 1.5% in vivo [3].

Correlation between the peripheral skeletal BMD measurements in vivo are highest between the two radial sites (r=0.74) and slightly less between the os calcis and the ultradistal radius (r=0.70) and between the os calcis and the distal third (r=0.63) [4]. However, the relatively large standard errors of these SPA correlations preclude the prediction of peripheral bone mass at one site from measurement at another site for individual patients. Prospective studies have shown the value of SPA for predicting appendicular fractures from measurements of the distal third of the radius [5]. Additional prospective data have shown all three SPA measurements to be predictive of future hip [6], vertebral [7] and most appendicular skeletal [8] fractures.

The radiation surface dose due to SPA is of the order of 30–50 μSv. When this surface dose is corrected for body accentuation as well as the type and volume of tissue being irradiated according to protocols established by the International Commission on Radiation Protection, the effective dose equivalent for SPA is less than 1 SV. Adults in the United States receive on average 3000 Sv each year from radiation, two thirds of which comes from natural radioactive decay within the body. Thus a single SPA examination represents the equivalent an additional of 0.03% of effective dose equivalent above the yearly average. For comparison, a dental bitewing X-ray study has an additional effective dose equivalent of approximately 2%, a chest X-ray about 4%, and a mammogram about 25% above the average annual effective dose equivalent.

Dual-Photon Absorptiometry (DPA)

While peripheral measurements of bone mineral density using SPA are relatively simple to perform, measurements of the axial skeleton are more difficult due to variations in tissue thickness. DPA eliminates the need for a constant soft-tissue-equivalent path length by scanning the patient with two photon energies, typically from a gadolinium-153 radioisotope source with effective photon energies of 44 and 100 keV. At these photon energies the differences in the mass attenuation coefficients for bone and soft tissue allow the separation of the bone and soft tissue components [9]. In this way, a DPA scanner can measure the BMC (in units of grams) of bone and soft tissue along the length of the incident radiation beam. Using a point source and a rectilinear scanning procedure, the bone area can be estimated by multiplying the number of pixels representing the scanned body by the pixel area to determine the areal BMD (in g/cm^2).

DPA is typically used to measure the bone mineral density of the lumbar spine, proximal femur, and total body. Long-term precision of spinal BMD measurement in vivo is between 1.4% [10] and 3.7% [2] with an accuracy of 5%–10%. Precision at the hip is comparable to that at the spine (between 3% and 5%) with similar accuracy. Precision of total body mineral in vivo from DPA has been reported as 2.4% with an accuracy of 1.5% [11]. Long-term precision error of DPA is affected by an aging isotope source and may be much greater in some scanners [12]. Spinal DPA measurements show modest correlations with SPA measurements of the ultradistal radius (r=0.74) but with a standard error of the estimate ranging from 10% to 20%, precluding accurate predictions of axial BMD based on peripheral measurements for individual patients [12]. Significant correlations have also been found between DPA measurements of excised vertebral specimens and ultimate compressive strength determined by compression testing (r=0.86) [13].

Comparison of SPA of the forearm and DPA of the lumbar spine during early menopause has shown larger deductions in spinal than in radial bone mineral density [2]. Based on cross-sectional data, DPA spinal measurements have been shown to be more effective than SPA measures of the radius for detecting osteoporosis when defined by the presence or absence of spinal fracture [14]. Limited prospective data relating DPA measurements to fracture incidence exist; available data show equivalent results for spinal DPA compared with radial and calcaneal SPA measurements in predicting both spinal and appendicular fractures [12,15].

Surface doses for DPA range from 30 to 50 Sv, with an effective dose equivalent for the spine scan of approximately 5 Sv (0.2% of natural yearly radiation) and 3 Sv for the hip scan (0.1% of natural yearly radiation).

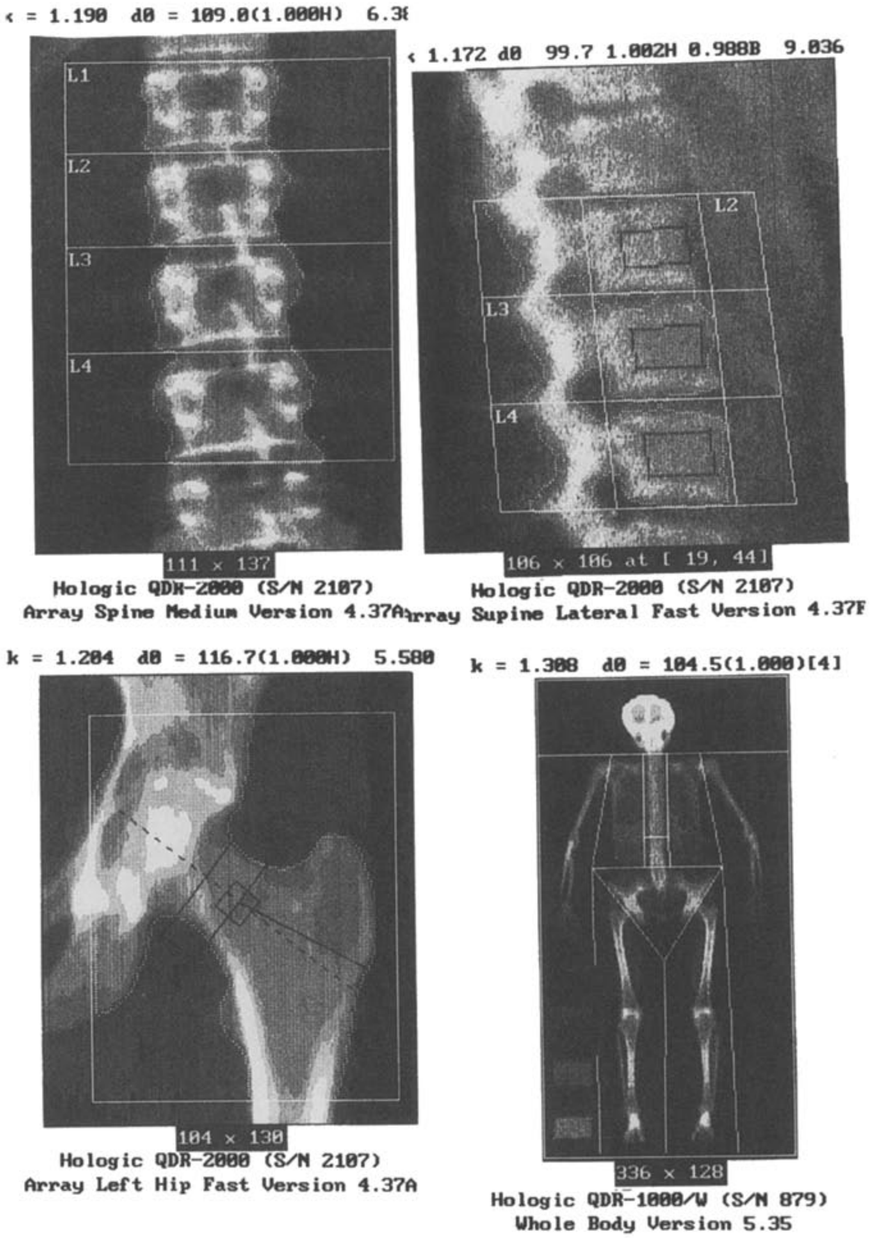

Fig. 1. DXA is currently widely used to measure areal bone mineral density of the AP spine, lateral spine, hip and total body.

Dual X-ray Absorptiometry (DXA)

Researchers have found that the radiation spectrum of gadolinium-153 can be simulated using a highly stable X-ray tube and either k-edge filtration or rapid switching of the tube supply voltage. The X-ray tube is capable of producing a higher radiation flux than the isotope source, allowing for increased precision and reduced scan times. Due to the advantages of an X-ray tube over the decaying isotope source, all previous DPA manufacturers have switched to producing DXA scanners. Several acronyms have been suggested to describe these X-ray-based dual-energy scanners; however DXA is preferred as the most generic yet technically accurate item [16].

As with DPA, DXA systems are used to measure the BMD of the lumbar spine, hip, and total body (Fig. 1). In vitro spinal BMD precision is better than 0.5% while the in vivo BMD precision is 1% or better at the spine and between 1% and 2% at the femur [17–19]. The high level of DXA precision in vivo has greatly enhanced the ability to monitor bone density changes longitudinally in individual patients. Several studies have confirmed the high correlation between DPA and DXA measurements in vivo, with correlation coefficients exceeding 0.95 in most cases

[17–20]. The accuracy of the DXA instruments is approximately 4%–8%, comparable to DPA but with slight improvements due to enhanced edge detection algorithms and analysis software. Substantial differences exist between the absolute measurements among different manufacturers due to calibration and software procedures, resulting in variations of up to 20% in some patients [21]. Currently no absolute standard exists for calibration of DXA instruments. A standard calibration phantom for both DXA and QCT has been suggested [22] which has tentatively been accepted by the various DXA manufacturers.

Most DXA scanners are also capable of measuring mineral density of the total body, the forearm, and the lumbar vertebral bodies in lateral projection. Lateral DXA allows the evaluation of the highly trabecular vertebral body without major influence of the primarily compact posterior elements, aortic calcifications, osteophytes, or other abnormalities encountered in the conventional anterior-posterior (AP) scan field. In the lateral decubitus position, the measurement of L1 and L2 is affected by overlying ribs, while L4 is frequently obscured by the iliac crest. Precision error is also increased to roughly 2%–3%, yet early research indicated that the lateral BMD value may provide a greater sensitivity for detecting vertebral bone loss than the standard AP scan [23,24]. Current advances are designed to allow lateral scanning in the supine position using a rotating gantry with an array of radiation detectors and a fan beam source [25,26].

Limited prospective data to date [27,28] have shown at least comparable fracture risk prediction with DXA relative to SPA for fractures in general, while for hip fracture specifically, DXA measurement of the hip is significantly better than any of the SPA methods.

Surface doses for DXA are diminished relative to DPA through the use of a highly stable X-ray tube; estimates range from 10 to 30 μSv. The effective dose equivalent for the AP spine scan as well as the hip scan is approximately 1 Sv (0.03% of natural yearly radiation) and approximately 5 μSv for the lateral spine scan (0.2% of natural yearly radiation). As with SPA and DPA, these doses are well below those associated with other typical diagnostic X-ray studies – up to a factor of 100 less than a dental X-ray examination.

Quantitative Computed Tomography (QCT)

QCT is unique in that it is the only noninvasive measurement of bone mineral to measure a true three-dimensional density as opposed to the areal density of the previously mentioned techniques (Fig. 2). The cross-sectional images allow the isolation of the purely trabecular bone of the

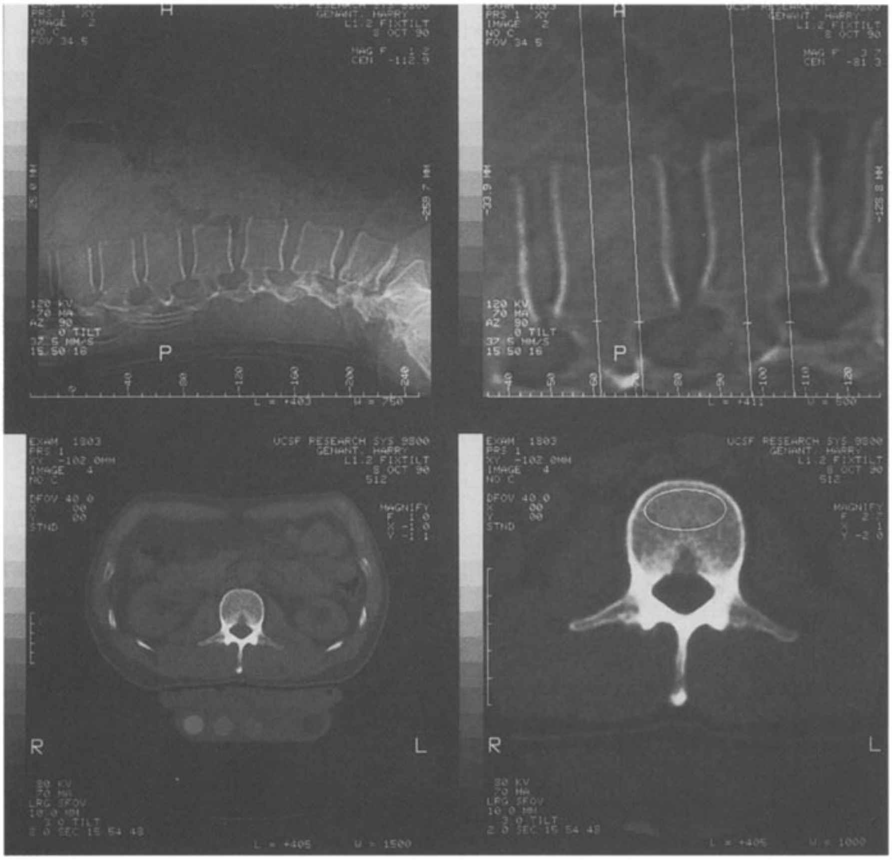

Fig. 2. QCT is widely used to measure volumetric bone mineral density of purely trabecular bone of the lumbar vertebral bodies.

vertebral body, which is a more sensitive site for detecting bone loss than the more cortical measurement sites [14,29]. QCT can be performed on most commercial CT scanners using a calibration standard to correct for scanner drift. In the standard protocol a computed radiograph is used to localise the midplane of two to four lumbar vertebral bodies. A single 8–10 mm slice is obtained through the center of each vertebra and the average CT number of the anterior trabecular vertebral bone is determined. Based on a linear regression of the CT numbers from the calibration standard containing mineral equivalents of known density, the vertebral CT value is converted to a physical density in the same units as the calibration standards.

The first calibration standards contained liquid solutions of dipotassium hydrogen phosphate and were scanned simultaneously underneath the patient [30]. Recently, several manufacturers have developed more stable solid calibration standards based on calcium hydroxyapatite in comparable concentrations [31,32]. Others have designed nonsimultaneous calibration systems that approximate human anatomy using inserts of varying density which must be scanned immediately after the patient. As with DXA, no absolute standards exist fro QCT measurements, making direct comparison between measurements obtained using different calibration systems and/or different scanners difficult [33].

QCT is capable of measuring trabecular, cortical or integral (trabecular plus cortical) bone at any site, centrally or peripherally. Most QCT is limited to the lumbar spine, with some work being done at the radius and tibia [34,35] and at the proximal femur [36,37]. The clinical precision error of the spinal QCT density measurement is between 2% and 4% [38], but can be reduced through careful patient positioning and automated image evaluation algorithms [39]. The accuracy of QCT is affected by variable fat content in the vertebral body, such that the absolute trabecular density is substantially underestimated with residual errors of 10%–15% [40]. Through the use of dual-energy techniques the underestimation of vertebral density can be reduced; however, discrimination between normal and osteoporotic patients is not significantly improved [39,41, 42] since the presence of intravertebral fat may enhance fracture discrimination. Furthermore, dual-energy QCT reduces precision and increases radiation exposure, both by a factor of two, and as a result is not recommended for most clinical applications. The average annual age-related bone loss in normal women from youth to old age is similar when measured with single-energy QCT (1.14% per year) and dual-energy QCT (1.03% per year) [42] and is significantly larger than average normal age-related losses measured by DPA (0.62% per year) [43] and DXA (0.54% per year) [44].

Good correlations between spinal QCT and DPA (r=0.83–0.87) as well as QCT and DXA (r=0.85) have been reported among healthy adults [18,41], but the correlation between QCT and DXA or DPA is diminished for patients with osteoporotic fractures (r=0.53–0.58) [41,44] for both technical and anatomical reasons. In vitro studies have shown significant correlations between vertebral fracture loads and QCT trabecular mineral density [45]. QCT has also been found to be a useful tool for estimating strength in vivo at the spine [46] and at the femoral neck [37]. QCT has been compared to DXA, DPA and SPA in its ability to separate normal and osteoporotic patients based on cross-sectional data. In general, the best sensitivity and specificity for discriminating spinal osteoporotics from normals is provided by QCT, followed by DXA and DPA and finally SPA [14,38,41,47]. For discriminating appendicular fractures, however, data from one study have shown that SPA measurements of the radius are superior to QCT measurements of the spine [47]. Prospective longitudinal studies have not yet been reported establishing the ability of QCT to predict spinal or appendicular fractures.

When properly performed using low-dose protocols, the surface dose for single-energy QCT is approximately 2000 μSv with an effective dose equivalent to 50 μSv (not including the dose from the computed radiograph used for slice localization). Thus a single-energy QCT examination is equivalent to roughly 2% of the annual natural background radiation dose, or about the same effective dose equivalent as a dental X-ray. Dual-energy QCT required twice the number of scans which doubles the effective dose equivalent to roughly 100 μSv per examination, or 4% of the annual radiation dose (equivalent to a chest X-ray).

Conclusions

Noninvasive measurements of bone mineral density allow the assessment of skeletal integrity, both centrally and peripherally, with high precision and accuracy and with relatively low radiation dose. When estimating skeletal status, it may be important to measure bone mineral density at more than one site to assess differential skeletal responses related to disease or therapy and to assess differential fracture risk. Due to technical differences between the various methods of bone mineral measurement, the quantitative results are typically expressed with differing calibration standards, such that direct comparisons must be carefully made.

SPA measurements have been shown in several prospective studies to aid in the assessment of osteoporotic fracture risk. Limited data to date have shown spinal DPA to be at least comparable to peripheral SPA for fracture risk assessment, and current research with DXA indicates promising results for the X-ray-based bone densitometers. DXA has seen rapid growth in recent years, with current scanners able to measure the spine, hip, forearm and total body bone mineral density with a speed and precision previously unattainable with the isotope-based DPA systems. Longitudinal studies have shown QCT to be highly sensitive for detecting early and rapid bone loss and cross-sectional studies have shown QCT's capacity for separating normal and osteoporotic patient populations, though prospective studies are needed to confirm the latter result. QCT has the disadvantage of higher cost and radiation dose compared with the other methods currently in use, but it is the only noninvasive modality able preferentially to measure trabecular, cortical, or integral bone density at any skeletal site. All of the techniques in current clinical use, specifically SPA, DPA, DXA and QCT, represent major advances for the noninvasive measurement of bone mineral density at radiation doses significantly less than those due to yearly exposure from normal background radiation.

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