BONE DENSITOMETRY:

Understand It Before You Apply It

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A measurement of bone mineral density is the single most valuable risk factor available to predict osteoporosis. Various methods for BMD measurement are available, and many studies have been done by researchers in the field to compare their diagnostic sensitivities. The most accurate method for diagnosis of vertebral-fracture osteoporosis is QCT, with accuracy of 75–80%, lateral DXA of the spine is 60–70%, AP DXA of the spine is 50–65%, and peripheral BMD measures of the radius, hands or heel are in the range of 40–60% (1–5). The new methodology of quantitative ultrasound (QUS) for bone assessment does not measure bone density per se but may provide information about bone microarchitecture which may be an independent predictor of fracture. Prediction of increased risk for hip fractures or other non-spinal osteoporotic fractures is also possible from bone density measurements, although factors such as bone geometry and falls are also involved in the etiology of these fractures (6–10). There are many factors which influence the strength of bone and its susceptibility to fracture, but few are major predictors of fracture *independent* of bone mass or density. The previous clinical definition classified a patient with low bone mass in the presence of a minimally-traumatic fracture as osteoporotic. Unfortunately, this meant that a patient was not osteoporotic the day before the fracture and was diagnosed with osteoporosis as a consequence of the fracture. Recently a committee of the World Health Organization has defined osteoporosis as the condition where bone mineral density is 2.5 standard deviations below the young normal peak of bone mass, and this definition is being adopted by most of the health care providers in their classification of reimbursible bone density procedures. All bone density measurements have associated with them a value known as the "fracture threshold"—when the bone density falls below this value the patient's risk of fracture goes up significantly. For most techniques, this fracture threshold corresponds roughly to 2.5 SD below the young normal peak bone mass, and thus validates this definition of osteoporosis. While there is great debate about which bone density method is superior overall and much continuing research on the etiology of osteoporosis and fractures, there is no debate about the *clinical* value of bone densitometry and its use to classify patients as being at increased risk of fracture.

Peripheral Bone Densitometry

Measurements of peripheral bone mass, size, density, or other parameters have been done since the early 1960s, and thus have a great body of clinical data to help interpret the results. Their advantages are that they are generally rapid, simple to use, and inexpensive, requiring less sophisticated equipment than central measurements (excluding the research tool of peripheral quantitative computed tomography). Radiogrammetry of the metacarpals, single photon absorptiometry (SPA/SXA) of the forearm or heel, radiographic absorptiometry of the phalanges and ultrasound of the patella, heel, phalanges, and tibia have all been used at one time or another. All except ultrasound (not FDA approved yet) come under the new HCFA reimbursement code **G0062**, "peripheral skeletal bone mineral density study" with 0.22 Work, 0.82 Practice Expense, and 0.07 Malpractice RVUs.

The primary disadvantage of peripheral skeletal measurements is that they all measure bone which is relatively slow-turnover, and thus changes slowly in response to hormonal imbalance or therapy. This is true not only of "cortical" bone in the peripheral skeleton, but also of "trabecular" sites, because bone marrow in the peripheral skeleton is almost all fat and has limited ability to recruit osteoclasts from the marrow. This physiological property of peripheral bone means that no matter how *accurately* one can measure the amount of bone, it is very difficult to use one of these measurements to follow therapy in the patient. Even methods that have very high *precision* for the quantity measured do not do well in following therapy in *individual patients* because the rule of thumb is that the difference between two measurements must be about 3 times the measurement precision for one to believe that it is a real change in the bone and not just statistical error. For following *groups* of patients, as is done in clinical research studies, the larger the number of individuals in the group, the less the error in the average change so that these measurements can be used successfully in such population studies.

Because of their simplicity and relatively low cost, peripheral bone measurements are best used for a single point measurement in a patient, to determine their bone mass relative to some "normal" population or some "risk threshold" value. However, if the patient is going to be treated, a measurement at a more central site (spine or hip) is the procedure of choice because these can be used both for diagnosis and followup.

Central Bone Densitometry

Bone mineral densitometry of the central skeleton (spine and femur) is an established technique for the diagnosis of osteoporosis and the monitoring of treatment. Currently, two methods are used routinely for measurement of bone mineral density (BMD) of the central sksleton, dual energy x-ray absorptiometry (DXA) and quantitative computed tomography (QCT). Both of these methods are well established and they or their predecessors have been in clinical use since the early 1980s. DXA is used clinically to measure the spine and proximal femur, while QCT is used for spinal measurements, although proximal femur measurements have been done in research studies. DXA is a two-dimensional projection x-ray technique. Conventional QCT uses several isolated 1 cm thick transaxial images from which spinal trabecular BMD measurements are made, but this method cannot be used successfully to measure the proximal femur. 3DQCT uses a volumetric data set to obtain BMD data of the spine or of the proximal femur in three dimensions. These 3D data can be projected back into two dimensions to simulate the projection x-ray data obtained by DXA. The HCFA "central skeletal bone mineral density study" code **G0063** covers "spine, pelvis" with 0.30 Work, 3.07 Practice Expense, and 0.21 Malpractice RVUs. Old CPT codes 76070 (QCT) and 76075 (DXA) have been combined under the new code **G0063**.

QCT has been used clinically for the diagnosis and monitoring of osteoporosis since 1981, at about the same time dual photon absorptiometry was introduced. During the early to mid 1980s both methods had their advocates and detractors, being promoted by competing communities (radiology using QCT versus internal medicine, endocrinology and rheumatology using DPA), and to a large extent the same situation pertains today. However, the changing healthcare environment along with changing technology for both QCT and DXA is serving to break down some of these barriers. QCT has gone from a hospital-based modality with limited access to a widespread method in use at many imaging centers, utilizing scanner time more available now that MRI is well established and duplicate CT and MRI scanning is no longer being reimbursed. In addition, almost all new CT scanners have helical scanning capabilities, allowing fast acquisition of 3D volumetric data sets for 3D QCT studies. Ubiquitous networking hardware and software allows CT scanner images to be transferred out of the CT scanner suite to a remote location for analysis, meaning that a "high-use" referring physician could do his/her own analysis of 3D QCT exams where the radiologist is not trained in the interpretation of bone densitometry. DPA has evolved from a relatively inexpensive technology sited in physicians' offices to an x-ray based technique more often than not placed in a hospital setting, often in radiology departments. QCT has often been faulted for being "high radiation dose," but some of the new imaging DXA densitometers now deliver a dose within a factor of 2 of the QCT exam, with both doses being well below that used for mammography or simple lateral spine films (12–14). The politics of QCT versus DXA is still being fought, with the "bone" physicians claiming that only they can interpret the bone densitometry reports correctly, while the radiologists say that because x-ray images are used in both QCT and DXA the techniques should be under their control (15).

The cost of a QCT system added on to a CT scanner is $5,000–$30,000, depending on the type of analysis and marketing factors. The low-end QCT systems sold for $5,000 do not have the high diagnostic accuracy or reproducibility of the other systems, and provide information similar to peripheral skeletal densitometry. There are fundamental differences in how commercial QCT systems operate, and the lack of standardization has left QCT as a "poor relative" to DXA in the eyes of the bone densitometry community. However, 3D QCT has been cited as the future direction for QCT by leaders in the bone densitometry community (16).

Quality Control and Precision

The fundamental limitations for both QCT and DXA in their use in *individual patients* has been the relatively reduced precision of measurement in the clinical setting compared to the numbers quoted by the manufacturers or published from research sites. As an example, in a recent publication (17) researchers tried to test the hypothesis that a measurement of spine or hip BMD by DXA early after menopause could be used to predict later bone loss. The study used 3 measurements per patient, with a mean separation of almost 2 years (22 months) between pairs. Precision in the spine was 1.0% and in the femoral neck 1.7%. While there were significant changes in both spine and hip for early and late periods for the *group*, the authors could not predict *individual* changes ("fast" *versus* "slow" losers). Unfortunately, given the average rate of change of 1.4%/year in both spine and femoral neck, 48% of the spine paired comparisons and 74% of the hip comparisons were statistically "no change," so the hypothesis could not be tested adequately (Figure 1).

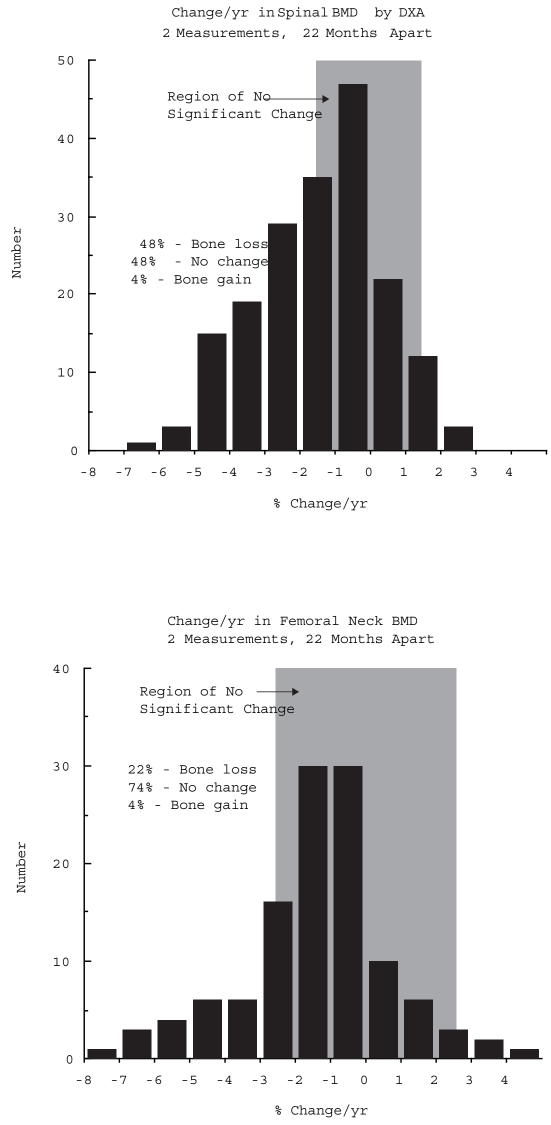

Figure 1

Results such as this argue that even “central” measurement techniques may not be sensitive enough to follow therapy easily, or that yearly measurements should be done to improve presision.

Spinal trabecular bone by QCT has been shown to change about 2–3 times as fast as an integral measurement by DXA, so that for the same precision QCT should show changes in about one-third to one-half the time. Conventional QCT, using single scans through 3–4 vertebrae, has a reproducibility as good as 1.7% in research studies (18). In clinical practice, however, QCT has often been done so poorly, with no quality control or standardization, that the precision is often a factor of 2–3 worse, or 4–5%. This negates the inherent advantage of QCT over DXA based on more rapid trabecular bone change. However, 3D QCT, when done with appropriate quality control, has a precision for spinal trabecular bone of 0.7% (19–21). The major advantage of 3D QCT over conventional methods is that patient positioning errors, artifacts in the images from bowel gas or increased image noise from gantry angulation are eliminated. In addition, the known advantages of QCT over DXA for elimination of inaccuracies due to extravertebral calcification, scoliosis, and mild compressions are even more so with 3D QCT because slice thickness and region of interest can be modified retrospectively.

Accuracy of QCT has often been questioned as well, but again this has to do in large part to the lack of standardization and quality control provided by the QCT vendors. Cross calibrations of different QCT patient calibration phantoms (original liquid K_2HPO_4 and various solid hydroxyapatite–plastic water designs) give widely varying results. For some reason, all the solid designs are inaccurate when compared to the solid European Spine Phantom, while K_2HPO_4 gives accurate results (Figure 2).

With appropriate standardization and calibration, 3D QCT can be done with a reproducibility of 1% or better even in the clinical setting, so that the inherent advantages of QCT over DXA should finally be realized in the use of bone densitometry measurements in individual patients.

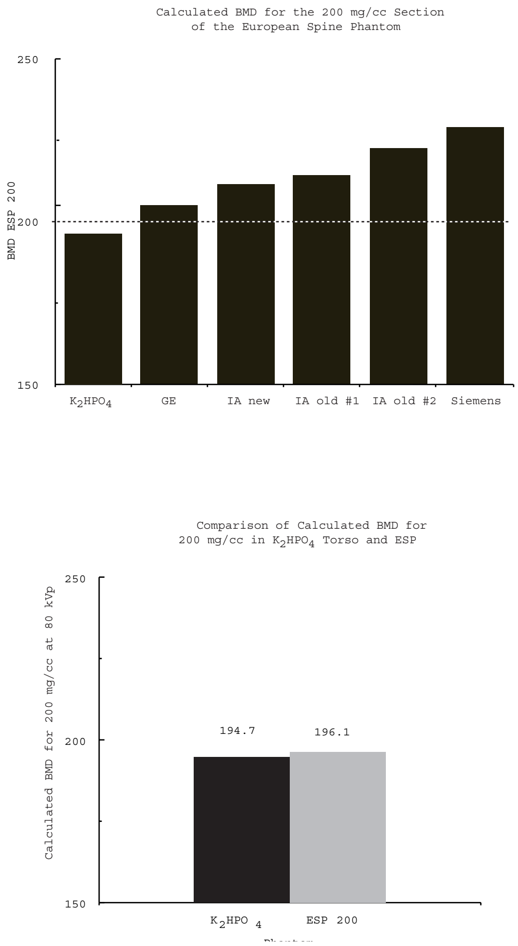

Figure 2

References

1. Guglielmi G, Grimston SK, Fischer KC, Pacifici R. Osteoporosis: diagnosis with lateral and posteroanterior dual x-ray absorptiometry compared with quantitative CT. Radiology 1994; 192: 845–850.

2. Jergas M, Grampp S, Lang P, Engelke K, Godfredsen N, Lu Y, Gluer C-C, Genant HK. Measurements of bone density at the axial skeleton: a comparative analysis of quantitative computed tomography and dual x-ray absorptiometry. J Bone Min Res 1994; 9: S406.

3. Faulkner K. Measurement of axial and peripheral bone mass by QCT. National Osteoporosis Foundation; Bone mass measurement in osteoporosis and other diseases, November 1995.

4. Lafferty FW, Rowland DY. The superiority of spinal supine lateral QDR and QCT over spinal AP-QDR in detecting vertebral compression fractures. J Bone Min Res 1994; 9: S274.

5. Yu W, Gluer C-C, Grampp S, Jergas M, Fuerst T, Wu CY, Lu Y, Fan B, Genant HK. Spinal bone mineral assessment in postmenopausal women: a comparison between dual x-ray absorptiometry and quantitative computed tomography. Osteoporosis Int 1995; 5: 433–439.

6. Cummings SR, Black DM, Nevitt MC, et al. Appendicular bone density and age predict hip fractures in women. JAMA 1990; 263: 665–668.

7. Cummings SR, Black DM, Nevitt MC, et al. Bone density at various sites for prediction of hip fractures. Lancet 1993; 341: 72–75.

8. Wasnich RD, Ross PD, Heilbrun LK, et al. Prediction of postmenopausal fracture risk with use of bone mineral measurements. Am J Obstet Gynecol 1985; 153: 745–751.

9. Hui SL, Slemenda CW, Johnston CC, et al. Baseline measurement of bone mass predicts fracture in white women. Ann Intern Med 1989; 11: 355–361.

10. Hayes WC, Piazza SJ, Zysset PK. Biomechanics of fracture risk prediction of the hip and spine by quantitative computed tomography. Radiol Clin North Amer 1991; 29: 1–18.

11. Sartoris DJ. Coding and reimbursement issues for dual energy x-ray absorptiometry. AJR 1994; 163: 137–139.

12. Cann CE. A rational approach to radiation exposure in bone densitometry. Radiology 1987; 165(P):184.

13. Kalender WA. Effective dose values in bone mineral measurements by photon absorptiometry and computed tomography. Osteoporosis Int 1992; 2: 82–87.

14. Blake GM, Pastel R, Lewis MK, Batchelor S, Potts E, Smith IG, Fogelman I. New generation DXA scanners increase radiation dose to patients and staff. J Bone Min Res 1996; 11: S157.

15. Genant HK, Faulkner KG, Feurst T, Gluer C-C. Controversies in the diagnosis of osteoporosis. Radiology 1996; 201(P): 28.

16. Lenchik L, Sartoris DJ. Current concepts in osteoporosis. AJR 1997; 168: 905–911.

17. Pouilles JM, Tremollieres F, Ribot C. Variability of vertebral and femoral postmenopausal bone loss: a longitudinal study. Osteoporosis Int 1996; 6: 320–324.

18. Rosenthal DI, Gannot MA, Wyshak G, Slovik DM, Doppelt SH, Neer RM. Quantitative computed tomography for spinal density measurement. Factors affecting precision. Invest Radiol 1985; 20: 306–310.

19. Cann CE, Genant HK. Precise measurement of vertebral mineral content using computed tomography. J Comput Assist Tomogr 1980; 4: 493–500.

20. Cann CE, Henzl M, Burry K, Andreyko J, Hanson F, Adamson GD, Trobough G, Heinrichs L, Stewart G. Reversible bone loss is produced by the GnRH agonist Nafarelin. in Cohn DV, Martin TJ, Meunier PJ (eds): Calcium Regulation and Bone Metabolism: Basic and Clinical Aspects, Vol. 9. Elsevier Science Publishers, New York, 1987, p 123–127.

21. Cavanaugh DJ, Cann CE. Brisk walking does not stop bone loss in postmenopausal women. Bone 1988; 9: 201-204.