

Appropriate use of QCT

Kenneth G. Faulkner PH.D., Chief Scientist, GE Lunar



Fig. 1: CT Scanner

Introduction

Before the advent of dual x-ray absorptiometry (DXA), several researchers reported using computed tomography (CT) scanners to obtain bone density measurements. This technique is called quantitative CT (QCT) to differentiate it from imaging CT. QCT is the only noninvasive three-dimensional bone mass measurement technique available. QCT reports a volumetric density (in mg/cm³) as opposed to the area density (in grams/cm²) from other techniques. Initially, QCT was performed without any special equipment (other than the CT system) by measuring the average CT number of the vertebral body. However, more advanced procedures were developed to improve the accuracy and precision of the measurement.

QCT is used clinically to measure the bone density of the spine. It has the advantage of measuring the central bone of the vertebral body, which is a more sensitive site for detecting bone mineral changes than most other skeletal sites. QCT can be performed on most commercial CT systems with the

addition of a bone mineral standard for calibration of the CT measurement (Figure 2). Several different types of calibration systems are commercially available from CT manufacturers and third party vendors.

In the standard QCT protocol, three to four lumbar vertebral bodies are measured using a single 8-10 mm slice through the center of each vertebra. The calibration standard must also be measured, either at the same time or immediately after the patient is scanned. Low-dose settings are used to reduce radiation exposure well below a standard CT examination, but still well above other types of bone density measurements (such as DXA). From the CT images, the average attenuation of the vertebral body bone is determined as well as the attenuation of the calibration standard. Using the known density of each of the standards and the measured CT values of the bone mineral standard, the vertebral CT value is converted to a physical density.

While most QCT studies are limited to the lumbar spine, specialized QCT systems (called peripheral QCT, or pQCT) have been introduced for measuring the forearm. This technique offers the advantages of measuring the volumetric density of the forearm, as well as providing measures of trabecular, cortical, and integral (trabecular plus cortical) bone. However, these scanners are limited to the forearm and can cost as much as full table DXA devices capable of density

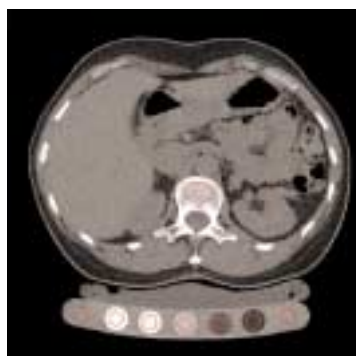


Fig. 2: QCT EXam

SCIENCE
— in bone densitometry



GE Medical Systems
LUNAR

gemedicalsystems.com

measurements at multiple skeletal sites. When properly performed, QCT can be a useful clinical tool. The measurement of a purely trabecular bone sample may have some advantages for the diagnosis of osteoporosis, assessing fracture risk, and monitoring bone changes. Each of these uses of QCT is described.

Diagnosis of Osteoporosis and Assessing Fracture Risk

The primary reason for measuring BMD is to diagnose osteoporosis and assess fracture risk. Unfortunately, there have been relatively few published prospective studies regarding the use of QCT measurements for predicting fracture. The vast majority of prospective studies have been with DXA. For predicting hip fracture, it is generally agreed that a direct femoral measurement is the best choice. Currently DXA is the only clinically available method for femoral measurements, though QCT protocols are in development. For vertebral fracture prediction, spinal QCT may have some advantage, though this remains to be proven. In particular, QCT may offer some advantage in elderly subjects to avoid the degenerative changes typically seen at the spine. On the other hand, it is conceivable that the ability of DXA to measure both cortical and trabecular bone provides some advantage for predicting fracture compared to QCT. Bone strength is influenced by both cortical and trabecular bone, so that measurement of both components might provide an advantage. In the absence of a comparative prospective study between the two techniques, the answer remains unknown.

Case-control comparisons between DXA and QCT have shown both techniques to have the ability to separate fractured subjects from controls. Often QCT is shown to provide better discrimination of vertebral fracture subjects from controls than DXA of the spine, likely due to its ability to exclude osteophytes, facet joint degeneration, and end plate deformities.

In clinical practice, the evaluation of BMD is not usually related directly to fracture risk. Instead, the measured BMD is compared to an established reference range in order to make a diagnosis of osteoporosis. This is most often done using the T-score, defined as the number of standard deviations the measured BMD lies from the young normal value. In 1994, an advisory panel of the World Health Organization (WHO) defined osteoporosis as a bone density T-score at least 2.5 standard deviations below the young

adult normal value (a T-score of -2.5 or less). At the time this definition was proposed, the only published prospective data relating BMD to fracture risk were for peripheral density measurements (predominantly forearm measurements). Spine and hip data were available, but only from cross sectional studies that compared BMD to fracture prevalence. The WHO panel reviewed the available literature, comparing the prevalence of low BMD at central and peripheral sites, with the risk for fracture in women 50 years of age and older. Based on this review, an epidemiological definition of osteoporosis as a T-score of -2.5 was proposed.

Almost a decade later, this same diagnostic definition is still in use. Yet since the original WHO report, published studies have confirmed that T-score values can vary significantly between skeletal sites and measurement techniques. Yet the $T = -2.5$ criterion is used for many different BMD techniques. This is despite the fact that it was based primarily upon the relationship between forearm measurements and prevalent hip fracture in postmenopausal Caucasian females. It is reasonable to expect that a T-score threshold of -2.5 may be inappropriate for different skeletal sites and measurement techniques.

Fig. 3: Age-related decline in T-scores for various BMD measurements.

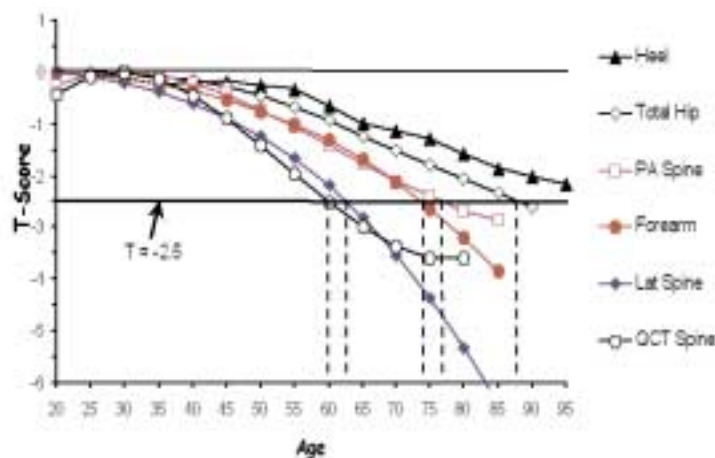


Figure 3 shows a comparison of the age-related decline in T-scores with different BMD measurements. The central skeleton, particularly the spine, shows the largest T-score decline with age. However, there is considerable variation in the T-scores at different skeletal sites. The normative data crosses the -2.5 SD level at age 60 with QCT compared to age 77 for DXA spine measurements. At age 60, the prevalence of osteoporosis using the WHO definition is 50% using QCT compared to 14% with spinal DXA. Based on results shown in Figure 3, it is apparent

that this discrepancy is particularly large for QCT, resulting in T-scores that are significantly lower than other BMD techniques.

Table 1: Average BMD values for DXA and QCT.

Table 1: Average BMD values for DXA and QCT http://courses.washington.edu/bonephys/qct.html				
Age	DXA		QCT	
	sBMD (mg/cm ²)	T-score	BMD (mg/cm ³)	T-score
25	955	0	166	0
35	945	-0.08	162	-0.21
45	920	-0.28	151	-0.79
55	876	-0.64	119	-2.47
65	809	-1.19	103	-3.32
75	740	-1.75	83	-4.37

Table 1 compares the T-scores from DXA and QCT based on published reference populations. It is clear from this comparison that QCT T-scores will be 2 to 3 times lower than DXA T-scores at the spine. This is predominantly due to differences in the normal data from which the T-scores are derived, resulting in a smaller relative standard deviation for QCT compared to DXA. This alone will cause the DXA T-scores to disagree with QCT T-scores. For example, if a technique has a standard deviation of 10%, a T-score of -2.5 would indicate the measurement is 25% below young adult. However, if the standard deviation were only 5%, the same T-score of -2.5 would only be 12.5% below the young adult value. Differences in the standard deviation between two techniques will automatically produce differences in the T-scores, even at the same BMD. For this reason, it is now acknowledged that a single T-score criterion cannot be universally applied to all BMD measurements. Specifically, use of the WHO guidelines with QCT will result in an overestimation of osteoporosis and fracture risk.

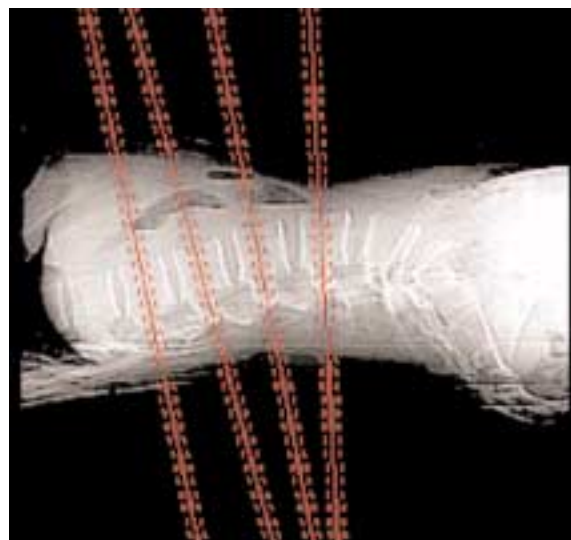
Monitoring Changes in BMD

Studies have shown that QCT is a more sensitive measure of age related bone loss and response to therapy than DXA. QCT shows 2 to 3 times the change in BMD seen with DXA, either due to aging or response to therapy. Yet, QCT is typically less precise than DXA. Precision errors with QCT are reported to be 2 to 3 times as great as for DXA, due to difficulties in patient positioning, consistent slice location (Figure 4), system

stability, and consistent region of interest placement. Thus the increased sensitivity of QCT is offset by the increased precision error of the technique, resulting in no significant advantage for monitoring changes. However, when QCT is carefully performed, these precision errors can be reduced, particularly with volume acquisition techniques and automated analysis software.

As with DXA, it is essential to use proper quality control when monitoring changes with QCT. As CT instruments are designed for imaging and not quantitative assessments, it is essential that the stability of the system be monitored on a frequent basis. Acquisition protocols (tube voltage and current) must be consistent from exam to exam. Daily quality control measures must be maintained to guard against drifts in either the x-ray tube or detectors that might

Figure 4: QCT slice location.



influence the BMD result. All QCT manufacturers provide tools for monitoring system performance that should be followed to ensure consistent results.

An additional consideration with repeated use of QCT is radiation dose. Compared to most radiological exams, QCT has a very low dose, on the order of a mammogram. Yet compared to DXA, a single QCT exam has an effective dose equivalent of 50 to 100 times that of a DXA exam. Improperly performed exams (using imaging protocols rather than BMD protocols) can increase this dose by another factor of 10. As with all radiological examinations, QCT should be performed only at appropriate intervals to avoid excess or unnecessary exposure. As with

DXA, exams every 1-2 years are appropriate to evaluate BMD changes either in response to aging or anti-resorptive therapy.

Other Considerations

In addition to the clinical and technical considerations, there are a few practical issues regarding the use of QCT. Foremost is the need for a CT scanner. This limits the use of the technique to radiology facilities with the proper equipment and available scanner time. Often obtaining scanner time can be the most significant hurdle to performing QCT. Daily quality assurance procedures require 15 minutes each day to monitor the QCT system. The exam itself takes from 15-30 minutes to perform, including time for patient preparation and scan acquisition. With competing pressures for scanner time in many radiology departments, it can be difficult to find time to schedule bone density patients. Current reimbursements for QCT are the same as for DXA (approximately \$140), which is below the levels for most other CT examinations.

If scanner time is available, QCT can be performed on most commercial CT units. QCT calibration and systems can be obtained from several manufacturers. They include a special calibration phantom, a quality control phantom to monitor system stability, and analysis software. Cost ranges from \$15,000 to \$25,000. In addition to the calibration system, it is also essential to have a CT technologist properly trained in QCT procedures. This training should include the essentials of CT system quality control, proper scan acquisition (including proper mAs and kVp settings to obtain accurate QCT results), and scan analysis. This will help to ensure that QCT exams are done safely and accurately for all patients.

References

- 1). Cann CE, Genant HK 1980 Precise measurement of vertebral mineral content using computed tomography. *J Comput Assist Tomogr* 4:493-500.
- 2). Genant HK, Cann CE, Ettinger B, Gorday GS 1982 Quantitative computed tomography of vertebral spongiosa: a sensitive method for detecting early bone loss after oophorectomy. *Ann Intern Med* 97:699-705.
- 3). Steiger P, Block J, Steiger S, Heuck AF, Friedlander A, Ettinger B, Harris ST, Gluer CC, Genant HK 1990 Spinal bone mineral density measured with quantitative CT: Effect of region of interest, vertebral level, and technique. *Radiology* 175:537-543.
- 4). Kalender WA 1992 Effective dose values in bone mineral measurements by photon absorptiometry and computed tomography. *Osteoporos Int* 2:82-87.
- 5). Ruegsegger P, Dambacher MA, Ruegsegger MS, Fischer JA 1984 Bone loss in perimenopausal and postmenopausal women. *J Bone Joint Surg* 66A:1015-1023.
- 6). Hangartner TN, Overton TR 1982 Quantitative assessment of bone density with a special purpose computed tomography scanner. *J Comp Assist Tomogr* 6:1156-1162.
- 7). Cann CE 1988 Quantitative CT for determination of bone mineral density: a review. *Radiology* 166:509-522.
- 8). Cann CE 1987 Quantitative CT applications: comparison of current scanners. *Radiology* 162:257-261.
- 9). Block JE, Smith R, Gluer CC, Steiger P, Ettinger B, Genant HK 1989 Models of spinal trabecular bone loss as determined by quantitative computed tomography. *J Bone Miner Res* 4(2):249-257.
- 10). Looker AC, Wahner HW, Dunn WL, Calvo MS, Harris TB, Heyse SP, Johnston CC Jr, Lindsay R 1998 Updated data on proximal femur bone mineral levels of US adults. *Osteoporos Int* 8(5):468-489.
- 11). Faulkner KG, von Stetten E, Miller P 1999 Discordance in patient classification using T-scores. *J Clin Densitometry* 2(3):343-350.
- 12). Faulkner KG, Gluer CC, Grampp S, Genant HK 1993 Cross calibration of liquid and solid QCT calibration standards: corrections to the UCSF normative data. *Osteoporosis Int* 3(1):36-42.
- 13). Guglielmi G, Grimston SK, Fisher KC, Pacifici R 1994 Osteoporosis: diagnosis with lateral and posteroanterior dual x-ray absorptiometry compared with quantitative CT. *Radiology* 192:845-850.
- 14). Pacifici R, Rupich R, Griffin M, Chines A, Susman N, Avioli L 1990 Dual energy radiography versus quantitative computer tomography for the diagnosis of osteoporosis. *J Clin Endocrinol Metab* 7(3):705-710.
- 15). Faulkner KG, Cann CE, Hasegawa BH 1990 The effect of bone distribution on vertebral strength: Assessment with patient-specific non-linear finite element analysis. *Radiology* 179:669-674.
- 16). Faulkner KG 1998 Bone densitometry: Choosing the proper skeletal site to measure. *J Clinical Densitometry* 1(3):279-285.

