QCT vs. DXA: What's the Score?

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World Health Organisation (WHO) guidelines are widely used for the interpretation of bone mineral density (BMD) results. In addition, WHO patient classification guidelines are now commonly used to interpret BMD results obtained at a variety of skeletal sites. However, it is important to note that patient classification results will vary based on the site measured and the technique used. Because this is sometimes not well known within the community, DXA T-scores thresholds may be inappropriately used to determine classification based on BMD measurement by Quantitative CT (QCT) at the spine. The purpose of this paper is to explain these differences and provide a summary of the current scientific consensus on the effective clinical use of spine QCT in the assessment of osteoporosis.

Introduction

There is a history of debate within the bone densitometry community about how to interpret BMD T-scores at different skeletal sites and using different measurement methods when diagnosing osteoporosis. While at first glance, QCT and DXA spine BMD measurements may appear to serve the same purpose, a deeper investigation reveals each technology produces results that have to be interpreted individually and differently, rather than simply applying the widely adopted parameters outlined by T-scores.

Although T-scores from the WHO guidelines[1] for interpretation of bone density results have been widely used, they do not allow for the variability of bone loss seen at different skeletal sites and when measured by different methods. This anatomical and measurement variability can lead to substantial discordance in patient classification when using the standard T-score classification thresholds[2]. In particular, BMD T-scores at the spine measured by QCT are usually lower than those from PA DXA measurements. However, there are recommended classification thresholds available for the standardised interpretation of spine BMD when measured by QCT.

BMD Measurement by QCT

QCT is a technology that utilises a calibration standard imaged with a patient on a standard CT scanner to allow calibration of grey scale CT image values in terms of bone mineral density. At the hip, QCT is used to produce both areal BMD measurements in g/cm^2 and DXA-equivalent T-scores. However, at the spine, QCT produces a true volumetric analysis of the trabecular bone BMD in g/cm^3 that is interpreted differently than DXA measurements.

Volumetric trabecular BMD measurement can have several advantages over DXA measurements. Since trabecular bone is affected earlier and to a greater degree than cortical bone, QCT is likely to detect low bone mass earlier in the spine than other bone mineral density exams[3]. Added to that, artificially high BMD measurements by DXA due to obesity[4], disc space narrowing or spinal degenerative diseases[5], aortic calcification[6] and osteophytes[7] in patients with arthritis can be avoided.

Classification of Osteoporosis and the use of T-Scores

Diagnoses based on BMD measurements have largely been guided by a report issued by the World Health Organisation (WHO) in 1994[8] about the relationship between certain measurements of bone density and prospective risk of fractures. WHO particularly focused on evaluation of the radius and developed criteria based primarily on the relationship between forearm measurements and prevalent hip fracture in postmenopausal Caucasian females. The findings of the report resulted in the recommendation of using a T-score of -2.5 as diagnostic of osteoporosis. This definition now applies to DXA measurements at the spine, proximal femur and distal third of the forearm.

A T-score indicates by how many standard deviations a measurement is above or below the mean bone mineral density at the site when compared to a young

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normal reference population. In the same report, WHO produced definitions of both osteopenia and severe or established osteoporosis. The WHO classification criteria for T-scores are summarised in Table 1.

Table 1. The WHO classification criteria for T-scores

Classification	T-score
Normal	-1.0 or greater
Low Bone Mass (Osteopenia)	between -1.0 and -2.5
Osteoporosis	-2.5 and below
Severe Osteoporosis (Established Osteoporosis)	-2.5 and below + fragility fracture

In comparison, the US National Osteoporosis Foundation (NOF) guidelines recommend BMD assessments for all women aged 65 years and older, as well as postmenopausal women under the age of 65 years with one or more additional risk factors[9]. Furthermore, NOF recommends therapeutic intervention for those individuals with BMD T-scores below -2.0, or below -1.5 when additional risk factors are present. Because many postmenopausal women have at least a single additional risk factor, the NOF guidelines essentially amount to a therapeutic T-score threshold of -1.5. However, like WHO criteria, the NOF guidelines do not distinguish among different skeletal sites or measurement technologies, although hip BMD measurements are recommended.

The WHO report does acknowledge that individual patients can be classified differently depending on the measurement site, the young adult reference population, and technology used. It is also important to acknowledge that WHO criteria were designed for epidemiologic purposes to compare populations and not for individual diagnosis of osteoporosis.

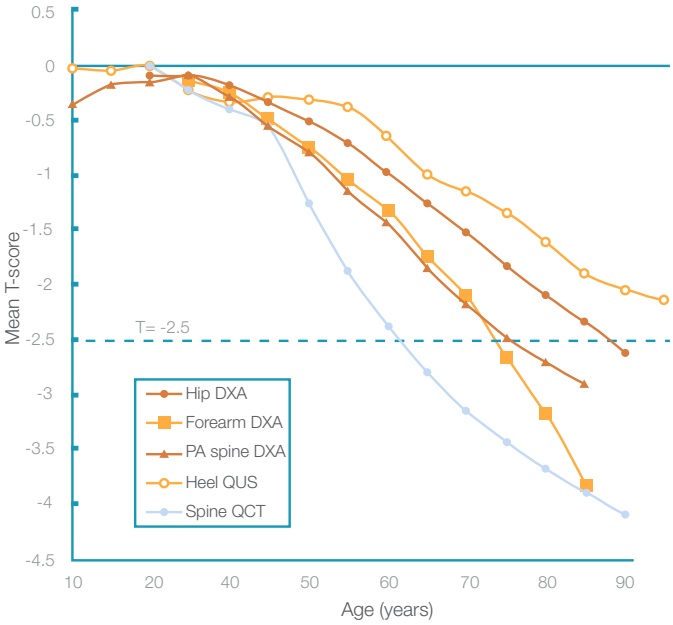
The Trouble with T-Scores

In 2000, the WHO committee issued a position paper updating the previous guidelines[10]. In large part this re-evaluation was done because of the massive confusion caused by the previously-issued recommendations about using a T-score of -2.5 as diagnostic of osteoporosis. With the proliferation of methods for measurement and sites of measurement of BMD or other bone properties, a number of studies were performed comparing these methods, and found that a T-score of -2.5 classified a widely varying percentage of patients as "osteoporotic" depending on the method used and the site measured, see Fig. 1.

Given this disparity, the use of a T-score to "classify" a patient lost its meaning in clinical use. In the same patient population of elderly women, for example, between 19% and 66% of them were classified as "osteoporotic" depending on which skeletal site was measured with the same machine [11].

The update recommended that diagnostic use of T-scores be reserved for use with hip DXA BMD measurement and no other T-scores are used to make a diagnosis of osteoporosis. BMD measurements at sites other than hip can be used to evaluate relative risks for osteoporosis, and in conjunction with other risk factors are used to determine the need for intervention. This is consistent with the use of the WHO FRAX® tool[12] for the calculation of fracture probability over 10 years, which specifies that BMD or T-score should be measured at the femoral neck.

Fig. 1. Age Dependence of T-score results for different densitometry techniques



Clinical use of T-Scores

In their most recent guidelines, WHO state that although the reference standard for the description of osteoporosis is BMD at the femoral neck, other central sites (e.g. lumbar spine, total hip) can be used for diagnosis in clinical practice. However, T-scores should be reserved for diagnostic use in postmenopausal women and men aged 50 years or more.

These recommendations are now in general concordance with recommendations made by the NOF, the International Osteoporosis Foundation and the International Society for Clinical Densitometry (ISCD).

The practical clinical ramifications of these recommendations are that T-scores determined by most BMD methods or at some measurement sites are not to be used for a "diagnosis" of osteoporosis. Only DXA or DXA-equivalent T-scores at the femoral neck or spine should be used for this purpose. However,

clinicians may use BMD values, T-scores, Z-scores, or other parameters related to fracture risk at other skeletal sites in an overall assessment of the patient and in the decision whether or not to institute therapy.

The problem is that although neither QCT nor DXA of the spine were used to develop the WHO guidelines, the T-score had become a convenient means of "classifying" a patient, even though that is not the intent of the WHO guidelines. A T-score measurement at the hip is the best predictor of future hip fracture risk. It is up to the clinician, in consultation with the practitioner making BMD measurements, to determine what information should be used to determine both a diagnosis of osteoporosis and intervention thresholds.

QCT vs PA-DXA Spine T-Scores

Nevertheless, bone densitometry T-scores at the spine remain a very useful measure in the determination of osteoporotic status. One of the most common questions asked by those who use QCT for BMD is why there is often a difference between the spine QCT result and either a previous or subsequent spine PA-DXA result. In most cases, the QCT result was a lower T-score than the DXA result and the concern is that the difference usually means classifying a patient as "osteoporotic" with QCT as opposed to "osteopenia" or even "normal" based on DXA results.

There are four main reasons why spine T-scores by QCT can be different than T-scores by PA-DXA. Three of these are "technical" and one is "physiological" due to age-, hormone-, or treatment-related bone changes. These effects can be additive, which is, if more than one of them is present, one does not dominate but the total effect is the sum of those present, the four reasons are:

1. Physiological effects of menopause and aging

The trabecular bone in the spine changes more rapidly after menopause or oestrogen deficiency than any other region, including total bone in the spine[13]. QCT measures the trabecular bone separately from the total bone. This means that QCT measures a greater rate of bone loss than PA-DXA in the early years after menopause, but then this rate slows down after about age 60-65. In contrast, bone loss measured by DXA in the spine, hip, or forearm occurs more gradually but continues well into the 70s. This means that at any time early after menopause, the spine T-score measured by QCT (or lateral spine DXA) will be more negative than that for PA-DXA of the spine or hip[2], see Table 2.

The ability of QCT to measure purely trabecular bone means that it is a very sensitive method for the detection of early vertebral bone loss. It is likely that the measurement of isolated trabecular bone by QCT is the reason that several studies have shown that in postmenopausal females, QCT of the spine has been found to perform as well as, if not better than, DXA in the prediction of vertebral fractures. This is shown in Fig. 2 (from[14]), in which the data is from a study comparing the sensitivity of QCT, lateral DXA and PA-DXA BMD measurement at the spine in the prediction of a prevalent vertebral fracture.

In this figure, a perfect predictor (correct fracture prediction for every case) would lie on a curve pushed into the top left-hand corner, and a predictor based upon chance such as flipping a coin (50:50 chance of a correct prediction) would lie on a line between bottom left- and top right-hand corners.

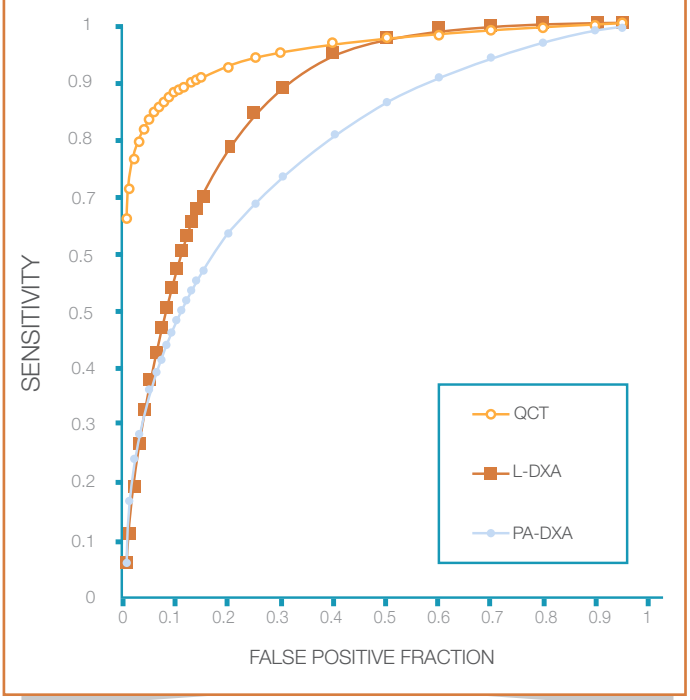
Table 2. Mean T-scores for women as a function of age measured at various sites

	50	60	70	80
QCT Spine	-1.4	-2.5	-3.2	-3.6
Lat-DXA Spine	-1.3	-2.2	-3.4	-5.1
PA-DXA Spine	-0.8	-1.4	-2.1	-2.6
DXA Hip	-0.5	-1.0	-1.5	-1.9
DXA Forearm	-0.8	-1.3	-2.1	-3.5

2. Technical effects of Osteophytes and Aortic Calcification

The structurally important bone in the spine is that of the cortex and trabecular regions of the vertebral body, which together take approximately 85% of the loads in the spine. In younger individuals, the trabecular bone takes about 80% of the load and the cortical shell 20%, while in patients with osteoporosis, the total load bearing capacity of the vertebra is reduced by about

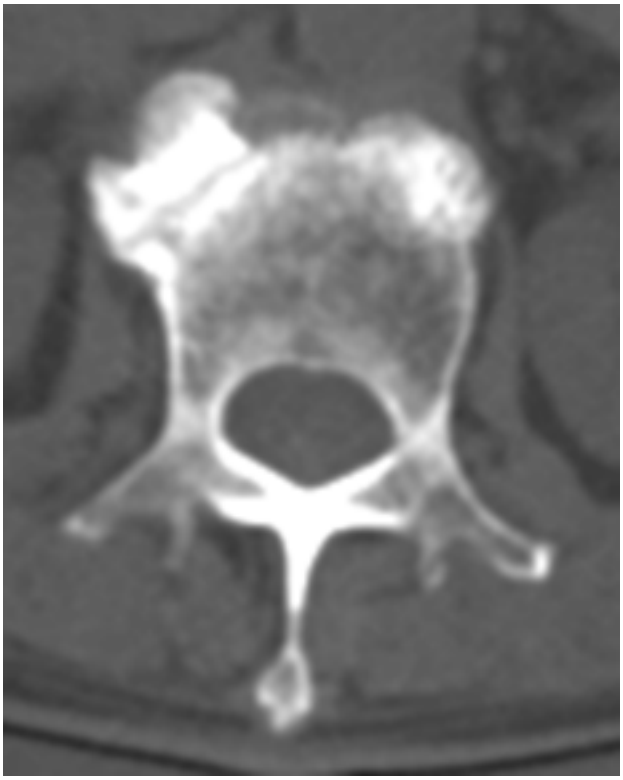
Fig 2. Sensitivty and specificity for prevalent vertebral fracture prediction by BMD measurement using QCT, lateral DXA (L-DXA) and PA-DXA (data from [14])



60-70%, and the ratio is reversed so that the cortex takes about 70% of this remaining load because of the loss of the trabecular bone[15], [16].

In contrast, extra osseous calcification does not contribute to the structural strength of the spine. The two primary components of extra osseous calcification in the older female and male population are osteophytes (see Fig. 3) and osteochondrosis (ligamentous or cartilage calcification) and deposits of calcium in the aorta.

Fig. 3. Osteophytes such as the two here can add a considerable amount of mineral to the DXA signal



When these are present, they can make up anywhere from 5-40% of the total "mineral" in the region of the lumbar spine assessed for BMD by DXA[15]. PA-DXA of the spine estimates the amount of all mineral in the path of the x-ray beam, while QCT estimates only the trabecular bone density within the vertebral body. Several studies have been performed to estimate this effect quantitatively. Table 3 is derived from postmenopausal non-fracture population data with an average age of 62 years[17]. The osteophytes had no significant effect on the measured QCT BMD values in this study.

Other authors have found the presence of various degenerative factors to increase from 35% of postmenopausal women age 55 up to 80% of women at age 70[18]. These authors have recommended that interpretation of PA-DXA spine measurements for women at or above this age range should be complemented by

Table 3. Effect of osteophytes on spine T-score by PA-DXA (from [17])

Osteophyte Grade	0	1	2	3
PA-DXA T-score effect	0	+0.6	+1.1	+2.3

plain film radiographs in order to assess the effect of degenerative changes. Similar recommendations have been made by others, even to the point that for subjects with established OA, assessment of skeletal status by volumetric QCT rather than DXA may be suggested[5].

3. Technical effects due to increased BMI

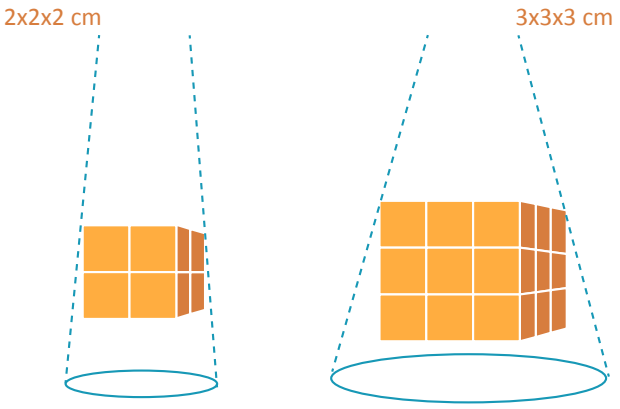
Many studies have shown that increased body mass index, that is, obesity versus normal body habitus, cause PA-DXA spine BMD values to be high. Recent studies have attributed the increased BMD by DXA to errors in the DXA measurement itself and may be due to inhomogeneity of fat distribution[19].

A direct comparison between QCT and DXA[20] showed that for postmenopausal patients classified as clinically obese (Body Mass Index > 27 kg/m^2 as defined by the American Society of Clinical Nutrition), the average T-score by PA-DXA was 1.45 units higher in obese patients than in age and height matched controls, while the QCT T-scores did not differ between the groups. Other researchers have shown similar effects with different systems[21].

4. Technical effects due to bone size

PA-DXA estimates bone mineral content (BMC) in a projected area, then areal BMD is calculated by dividing the BMC by the area. Because the bones in the spine and hip generally scale in 3 dimensions, the "thickness"

Fig. 4. Pitfalls of areal BMD assessment (adapted from Carter et al [22]).



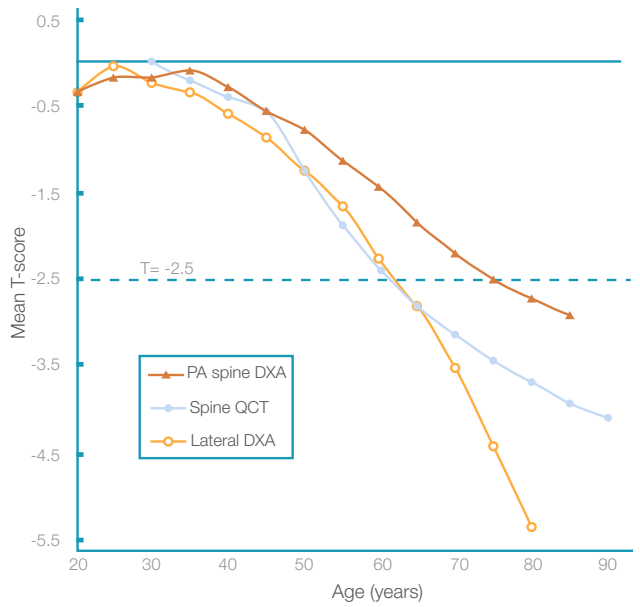
of large bones along the projected measurement is greater than for smaller bones, so the total bone mineral content increases faster than the projected area. This causes PA-DXA BMD estimates to be higher for large-stature patients than for smaller individuals, even if the volumetric BMD is the same, see Fig. 4. With QCT trabecular bone measurement there is no evidence for a relationship across populations of bone size on the BMD result.

Researchers using DXA have tried to estimate and correct for this effect by measuring the spine both from PA and lateral directions and estimating the "volume" of the vertebra, then scaling the BMD value to a "normal" bone size if either tall or petite patients are measured (or children). However, this is not done in clinical practice, and normative data provided with DXA systems does not take into account patient height or estimated bone size in the clinical comparison.

A Word about Lateral DXA

In response to some of the shortcomings of DXA measurement, lateral DXA was originally developed to maximize the amount of trabecular bone and to minimize the amount of cortical bone and extra-vertebral calcification present in the area measurement of vertebral BMD. The lateral projection that resulted was shown to be more sensitive for detection of age-related bone loss than the projection derived from PA-DXA but resulted in poorer precision[23], possibly as a result of patient positioning issues. Because the areal BMD measurement of predominantly trabecular bone using lateral DXA has similarities to QCT spine measurement, the age related decrease of the T-score is significantly larger for lateral DXA and it is comparable to QCT until the age of around 60 (Fig. 5).

Fig. 5. Age Dependence of T-score results for PA-DXA, Lateral DXA and QCT of the spine



To address the reproducibility issues, a lateral DXA scanner with a rotating C-arm was developed that allows the patient to adopt the same supine position for both PA-DXA and lateral DXA[14]. In spite of an increase in precision using this method, lateral DXA is now used primarily for vertebral fracture assessment rather than the measurement of BMD.

QCT vs DXA Interpretation

Although vertebral fractures happen earlier and are twice as common as hip fractures[24], it is the risk of hip fracture that determines diagnostic category by BMD. As we have seen, assigning a WHO diagnostic category based on the QCT spine T-score would probably result in over-estimating a patient's risk of hip fracture.

Table 4. QCT spine BMD classification thresholds

QCT Trabecular Spine BMD Range	Equivalent WHO Diagnostic Category
BMD > 120 mg/cm^3	Normal
80 mg/cm^3 ≤ BMD ≤ 120 mg/cm^3	Osteopenia
BMD < 80 mg/cm^3	Osteoporosis

Instead, patient category definitions are based on actual volumetric BMD thresholds of 120 mg/cm^3 for osteopenia (equivalent to a DXA T-score of -1.0) and 80 mg/cm^3 for osteoporosis (equivalent to a DXA T-score of -2.5)[25], see Table 4.

These categories are derived by selecting thresholds that result in approximately the same fraction of the population being assigned to a specific category based on QCT spine T-score as would assigned based on QCT or DXA hip T-score. Recommended by the American College of Radiology in their "Guideline for the Performance of Quantitative Computed Tomography (QCT) Bone Densitometry"[25], these categories are now widely adopted both in clinical practice and by the major CT scanner manufacturers .

Quantifying QCT

QCT has distinct benefits over DXA in assessing whether a patient is at risk for osteoporosis or whether they are in fact osteoporotic. While QCT was initially secondary to DXA as a means of quick, safe assessment, QCT technology has matured over the last decade to take the lead in the accurate assessment of bone mineral density. The proliferation of densitometry techniques some years ago and consequent confusion over standards of assessment using T-scores has now been largely addressed.

Today in Australia, QCT and DXA are the two methods reimbursed by Medicare[9] for bone density screening exams. The QCT exam is quick at 5-10 minutes and makes use of existing CT imaging resources, making it popular in smaller hospitals and imaging centres with CT scanners that find it uneconomic to run a DXA screening program.

The use of low-dose CT protocols; the avoidance of confounds from osteophytes, DJD and aortic calcification; and the excellent sensitivity of QCT in the detection of early and subtle BMD changes in the spine, have made it an important clinical tool for both routine BMD screening and specialist use in oncology and paediatric rheumatology.

Summary & Conclusions

Modern practices looking for alternative ways to use their CT scanners have adopted QCT to either augment or replace their DXA BMD testing programs. In clinical use it is important to recognise that QCT BMD measurements at the hip produce DXA-equivalent T-scores that may be used in conjunction with the WHO criteria for diagnosis of osteoporosis. These hip T-scores may also be used for fracture risk probability calculation using the WHO FRAX® tool. At the spine, however, DXA and QCT measure different things and the use of QCT T-scores is not appropriate and instead the ACR recommended classification BMD thresholds from Table 4 should be used.

How does QCT Pro™ Measure Up?

The scientists at MindwaysCT have been at the forefront of QCT's technical innovation since their involvement in its invention in the late 1970's. Today, modern QCT technology is the most effective solution for bone densitometry measurement.

MindwaysCT premier product, QCT Pro™, offers both 3D volumetric analysis of BMD in the spine and DXA-equivalent T-scores measurement at the hip. Spine QCT exclusively measures the more metabolically active trabecular bone to demonstrate exceptional sensitivity for the early detection of changes in bone density. This true volumetric QCT analysis gives patients with obesity, scoliosis, degenerative spinal diseases and arthritis a way to access accurate BMD analysis.

At the hip, QCT Pro™ produces the hip T-scores used in the World Health Organisation classification of osteoporosis and in the FRAX® fracture risk tool. QCT does not require the uncomfortable rotation of the hip during imaging because this can be done after image acquisition in software.

Workflow using the streamlined QCT Pro™ interface is simple and efficient and adheres to MindwaysCT"s design philosophy to assist the user but allow them to retain control. QCT Pro™ measurement of BMD in either the spine or hip provides a degree of automation that ensures excellent reproducibility without presenting the user with a "black box" that produces unsupervised results. This produces rapid results and reporting without compromising on quality of analysis.

In addition to producing quality medical devices that are used all over the world, MindwaysCT continues to provide both academic and commercial research with new tools to explore clinical problems associated with osteoporosis, orthopaedics and osteoarthritis. Our QCT systems and software tools are regularly used in pharmaceutical clinical trials and epidemiological studies within these therapeutic areas and MindwaysCT staff are frequently involved in offering expert scientific support. MindwaysCT continues to provide world-class technologies that enable the accurate determination of tissue densities, structures and types through new and innovative application of quantitative CT.

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