Introduction

Quantitative Computed Tomography (QCT) is a well recognised technique for the measurement of bone mineral density (BMD) in the lumbar spine and forearm. This technique is the only BMD measurement method to provide, firstly, a true volumetric measurement of bone density in mg/cm$^3$ and secondly, a separate measurement of trabecular and cortical bone density. The latter is due to the difference in computer tomography (CT) attenuation values, expressed in Hounsfield Units (HU), of trabecular and cortical bone. This enables the outer cortical rim with a higher attenuation value to be clearly separated from the inner lower attenuated trabecular bone on the cross-sectional CT image. Trabecular bone has a higher turnover than cortical bone due to its greater surface area and this makes QCT a very useful technique to monitor bone turnover and the efficacy of treatment. QCT measurements have been used to assess vertebral fracture risk and has been found to be a superior technique against other BMD measurement methods for assessing age-related bone loss, discriminating fracture and diagnostic classification. Recent developments in CT, such as spiral, has allowed three-dimensional (3-D) volumetric BMD analysis of the proximal femur and the investigation of trabecular structure is now possible with high resolution CT scanning together with texture analysis.
Spinal QCT Measurement

Technique

Spinal QCT measurements are performed on standard clinical CT scanners with the assistance of specially designed QCT software packages making it readily available around the world. This technique consists of a measurement of trabecular BMD in a number of consecutive vertebrae, usually between T12 to L4. The patient is scanned lying supine on a QCT bone mineral density calibration phantom. From a lateral scanogram or scoutview of the lumbar spine (Fig 1), the mid plane of the relevant vertebral bodies are selected.

Figure 1
Lateral scanogram of the lumbar spine used to localise the position of the mid-vertebral slices (L2-4) for the QCT scans. The automated software has been used.

Using a low kV technique, single 8-10 mm slices are taken through the selected vertebrae (Fig 2a). The scanner gantry is angled for each vertebral slice so that slice plane bisects the vertebral body in the midplane and is parallel to the end plates. In the case of a fractured vertebra, a slightly narrower slice thickness (eg 5 mm) may be required so that the end plates are not included. With their inclusion the BMD will be artificially raised and in the case of a marked reduction in vertebral height, the vertebra should be excluded from the measurement.

For the BMD calculation, a region of interest (ROI) is positioned either manually or with the aid of specially designed QCT software within the trabecular portion of the vertebral body. This region may encompass all the trabecular bone or be oval, circular or ‘pacman’ in shape dependant upon the technique chosen. The BMD is then calculated by converting the CT attenuation value of the trabecular ROI (where air = -1000 HU, water = 0 HU and cortical bone = up to +1000 HU) into bone mineral equivalent using the ROI’s representing bone and water within the calibration phantom. The vertebral densities are averaged to
provide a mean BMD for the patient under examination. The result can then be plotted against a normal age and sex-matched range for the population (Fig 2b). Spinal QCT normative data ranges are available for both adults\textsuperscript{11} and children\textsuperscript{12}. The cortical rim of each vertebral body can also be defined and a cortical BMD calculated as well as an integral BMD (cortical and trabecular BMD) for the patient.

Figure 2b

With the low kV QCT technique (80 kV), the effective dose of radiation to the patient is 60 μSv. The examination time is approximately 10-15 minutes depending upon the technique and software used. The in vivo precision and accuracy of this technique is 2-4% and 4-15% respectively\textsuperscript{7}. Short and long-term QCT precision together with examination time has been improved by the use of specially designed software that automatically selects the mid slice level from the lateral scoutview, defines the ROI’s on the axial slices, calculates the BMD level and plots the result on a graph showing the normal range\textsuperscript{7}. This software also helps to reduce operator induced variations that may affect the precision of the technique when it is performed manually. Software is now available from a number of companies (Image Analysis Inc; USA and Mindways Software Inc; USA) enabling off line evaluation of QCT data thus reducing CT machine time and increasing patient throughput.

Spinal QCT Calibration Phantoms
The use of a calibration phantom provides a consistent bone equivalent standard and compensates for any alteration in CT attenuation values. The latter can be caused by changes in beam hardening due to the different sizes and shapes of patients under examination and the variation in scanner stability due to scanner external current alterations. Any alteration in attenuation values is not relevant to the normal clinical CT image but has major importance when the scan attenuation information is to be used to quantify absolute values and change such as in QCT measurements.

A variety of calibration phantoms have been developed. The first was a liquid calibration phantom developed by the pioneers of QCT measurements, Cann and Genant at the University of California, San Francisco\textsuperscript{1}. The phantom is made of plexiglass and contains a number of liquid insets representing water, fat and three different concentrations of dipotassium hydrogen phosphate (K$_2$HPO$_4$) representing three levels of bone mineral equivalent (50, 100 and 200 mg/cm$^3$). This phantom has been used in many centres around
the world, but its long-term stability was found to be limited and therefore solid state phantoms are now in general use (Fig 2a). They contain a solid water equivalent compound together with calcium hydroxyapatite for the bone equivalent.

Advantages of QCT Technique
QCT provides a measurement of the metabolically more active trabecular bone where as Dual Energy X-ray Absorptiometry (DXA) produces a measurement of the less active integral bone making QCT measurements more sensitive to change. Postero-anterior DXA measurements of the lumbar spine may be artfactually increased because of the presence of extraneous calcification (eg aortic) and degenerative disease in the field of interest. In QCT, this problem is not encountered because of the axial slice and the selected ROI making the measurement more accurate. The presence of lumbar fractures may also increase the DXA measurement and this can be avoided by the QCT midplane slice which does not include the sclerotic endplates in the measurement. With centres who have access to CT scanners, the cost of a QCT measurement can be considerably less than DXA scan because the purchase of the QCT software is considerably less than the capital outlay for DXA equipment together with extra staff and the cost of a new examination room.

Peripheral QCT (pQCT) Measurement Technique
Peripheral QCT (pQCT) measurements are performed on specially designed small gantry CT scanners using a translate-rotate movement with a multi-detector head (Fig 3). As with spinal QCT, a separate measurement of cortical and trabecular bone is obtained but in peripheral regions of the body such as the forearm, femur, tibia and in the mandible. Measurements of BMD and bone mineral content (BMC) together with an axial crosssectional area of the bones concerned can be calculated. The original scanners used an I-125 source but the current pQCT commercial scanners (Stratec Electronic GmbH, Germany and Scanco Medical, Switzerland) use an X-ray source. There are now over a 1,000 pQCT scanners in use, mainly within Europe. The majority of the systems are in clinical use but a small number using multi-slice, ultra-high resolution, high precision techniques can be found in research settings.

In clinical pQCT scanners, a single axial CT slice, 2.5 mm in thickness, is taken through the distal radius and ulna at the level which represents 4% of the ulnar length from its distal end(Fig 4). Like the spinal QCT technique, a scout view is used to position the axial scan plane. Examination time is short and the effective equivalent dose of radiation to the patient is 6 μSv. On follow-up scans, the software automatically repositions the axial slice plane to the same level as the baseline scan improving precision. The software automatically defines the cortical and trabecular ROI's within the radius and the BMD is calculated using
threshold algorithms and iterative contour detection methods. Normative European data is available for forearm pQCT measurements and the Stratec machines are calibrated against the European Forearm Phantom. The in-vivo precision (CV%) for pQCT of the forearm is 0.5-2.1% with in-vitro accuracy of around 2%.

Figure 4
pQCT images of the forearm, showing the reference scanogram on the right and the axial slice of the radius. The patient’s total density and trabecular density are printed on separate graphs of the BMD versus age. The normative data range is shown on the graph.

Cross-Calibration of QCT and pQCT Scanners
The European Spine Phantom (ESP) and the European Forearm Phantom (EFP) were developed with funding from the EEC for the COMAC-BME project. The ESP phantom provides cross-calibration between QCT and DXA equipment for spinal BMD measurements and the EFP is used for forearm measurement cross-calibration between pQCT and peripheral DXA (pDXA) equipment. The composition of these phantoms together with their use will be discussed in the later section of this report dealing with ‘Quality Assurance of Bone Densitometers’.

Future Developments in QCT Measurements
Volumetric QCT
With the development of split-ring technology, low kV spiral CT allows volumetric scans of the lumbar spine and hip. Reformatted axial slices using any slice thickness (normally 4–10 mm) and 3-D images can be produced from these volumetric data sets (Mindways Software Inc, USA). In the spine, more representative mid plane slices may be created so that vertebral endplates can be excluded from the measurement. Using Mindways software, bone mineral density measurements of the proximal hip can be produced from reformatted CT images. The regions are very similar to those measured by DXA i.e. the femoral neck, Ward’s triangle, trochanter and total hip and the results can be normalised to the NHANES hip database. Volumetric bone density measurements in mg/cm³ of the cortical and trabecular components of the hip can also be expressed. QCT measurements of the hip have not been generally performed in the past because of the high radiation dose to the patient and the hip’s complex architecture. With low dose volumetric scanning and this specially designed software, the viability of examining this region of the skeleton may change in the future.
High Resolution QCT

Micro structural analysis of trabecular bone may assist in the prediction of future fracture risk and high resolution QCT provides information on the bony architecture of the region of interest. This technique requires thin slice high resolution computer tomography together with complicated processing techniques. Currently this work is only being performed in the research setting on bone specimens and the peripheral skeleton but it provides important information on bone structure and strength but could possibly be extended to the clinical setting.

Summary

QCT bone density measurements of the lumbar spine can be performed on standard clinical CT scanners with the assistance of specialist software and pQCT measurements on specially designed small bore CT scanners. The measurements are accurate and precise using a comparatively low dose of radiation in comparison with a diagnostic CT procedure. A volumetric measurement is provided separately of trabecular and cortical BMD. The former being the most sensitive to metabolic and age related changes. In the spine and especially in the older population, QCT may provide a more accurate BMD measurement than DXA because it avoids the effects of degenerative disease and extraneous calcification.

References