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Quantitative computed tomography

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ABSTRACT

Quantitative computed tomography (QCT) was introduced in the mid 1970s. The technique is most commonly applied to 2D slices in the lumbar spine to measure trabecular bone mineral density (BMD; mg/cm^3). Although not as widely utilized as dual-energy X-ray absortiometry (DXA) QCT has some advantages when studying the skeleton (separate measures of cortical and trabecular BMD; measurement of volumetric, as opposed to 'areal' DXA-BMDa, so not size dependent; geometric and structural parameters obtained which contribute to bone strength). A limitation is that the World Health Organisation (WHO) definition of osteoporosis in terms of bone densitometry (*T* score −2.5 or below using DXA) is not applicable. QCT can be performed on conventional body CT scanners, or at peripheral sites (radius, tibia) using smaller, less expensive dedicated peripheral CT scanners (pQCT). Although the ionising radiation dose of spinal QCT is higher than for DXA, the dose compares favorably with those of other radiographic procedures (spinal radiographs) performed in patients suspected of having osteoporosis. The radiation dose from peripheral QCT scanners is negligible. Technical developments in CT (spiral multi-detector CT; improved spatial resolution) allow rapid acquisition of 3D volume images which enable QCT to be applied to the clinically important site of the proximal femur, more sophisticated analysis of cortical and trabecular bone, the imaging of trabecular structure and the application of finite element analysis (FEA). Such research studies contribute importantly to the understanding of bone growth and development, the effect of disease and treatment on the skeleton and the biomechanics of bone strength and fracture.

1. Introduction

Osteoporosis is defined as 'a skeletal disease, characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture' [1]. This has driven the requirement for accurate and precise quantitative methods of skeleton assessment. The early methods that were developed involved measurement of radiographic cortical morphometry, usually of the second metacarpal of the non-dominant hand (metacarpal index) [2] and single- and dual-energy photon absortiometry (SPA and DPA) using radionuclide sources [3]. In the latter the scanning time was long (15 min or more per site scanned) and there was decay of the radionuclide which had to be regularly replaced. In the late 1980s the radionuclide source was replaced with a low dose X-ray source resulting in dual-energy X-ray absorptiometry (DXA) scanners, which provide fast scanning (now less than 1 min per site), improved spatial resolution and which can be applied to central and peripheral skeletal sites [4,5].

However, in the decade before this computed tomography (CT) was introduced, initially for head scanning in 1973 [6], and a few years later whole body CT scanners were available [7]. Soon after this the quantitative capability of CT (QCT) was applied to the skeleton [8,9]. Subsequently QCT was applied for quantitative assessment of the skeleton in disease [10,11], but with the introduction of DXA, with its lower ionising radiation doses and wide use in epidemiological and pharmaceutical studies, the use of QCT diminished. However, in recent years, with technical developments in CT and the recognition of the advantages of CT over DXA (separate measures of cortical and trabecular BMD, information on bone morphometry from which biomechanical parameters can be extracted) the use of CT and QCT in musculoskeletal research studies is increasing [12].

1.1. Principles and technical aspects

CT utilizes X-rays and provides an image which is based on the linear X-ray absorption coefficients of the tissues through which it passes. All clinical body CT scanners are similarly calibrated to the X-ray attenuation of water, resulting in CT numbers, measured in Hounsfield Units (HU), in relation to water being 0HU. Areas of high atomic number materials, such as bone, absorb more X-rays, have a high HU number and appear white on the image. Generation of the

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CT image is a two step process of initial scan data acquisition and then tomographic reconstruction by a mathematical process of calculating the image from the acquired data. The operator can select a variety of parameters to acquire and reconstruct the image which impact on image quality and radiation exposure [13]. To transform HU into bone mineral equivalents (mg/cm^3) an appropriate bone mineral phantom is included in the scan field.

Original CT scanners gathered the information of a slice through the body using a rotate/translate scan mode; slice width was 10 mm and each section took 20 s to acquire. In early CT scanners QCT was applied to the lumbar spine (usually 3–4 vertebrae between T12 and L4) using single two-dimensional (2D) 8–10 mm slices through the middle of each vertebral body. The region of interest (ROI) measured was either an oval or PacMan shape in the trabecular bone [14–16]; there was found to be good agreement between such measures [17]. Over the last decade technical developments in CT, including complete and multiple rings of detectors and spiral rotation of the X-ray tube (spiral multi-detector computed tomography: MDCT) have resulted in images of volumes of tissue being acquired very rapidly (e.g. thorax and abdomen in 20 s) [18]. This has had an impact on QCT in that 3D volume images of tissue can be acquired rapidly and from which either single slice 2D (ROI) or volumetric (VOI) analyses can be made. Such 3D volumetric QCT enables analysis of the hip, a clinically important site of fracture, which was not feasible with 2D single slices due to poor precision. Scan times for MSCT are typically below 10 s for the lumbar spine or the proximal femur. With the introduction of spiral MDCT there is a trend to scan two complete vertebrae between T12 and L3 to minimize radiation exposure, and the acquisition slice width is narrower at 1–3 mm, which improves spatial resolution. There has been interest in using CT images to determine trabecular bone structure; however, ionising radiation dose constrains such applications in central skeletal sites.

Dedicated peripheral CT scanners to measure BMD and bone morphology in the radius and tibia [9,19,20] are smaller, more mobile and less expensive that whole body CT scanners (Stratec Medizintechnik, Pforzheim, Germany). More recently dedicated high resolution pQCT scanners have been developed to image trabecular structure in peripheral skeletal sites in humans (Xtreme CT, Scanco Medical, Zurich, Switzerland) and microCT in animals and bone specimens (SkyScan 1072, Aartselaar, Belgium). In these scanners the operator has fewer choices for changing the acquisition and reconstruction parameter settings than with whole body CT scanners. Peripheral skeletal sites can also be scanned on whole body CT scanners, so the term pQCT applies equally to the study of peripheral skeletal sites, whether acquired on dedicated peripheral BMD scanners or general whole body CT scanners.

1.1.1. Phantoms

With whole body CT scanners a calibration phantom is required to be scanned with the patient, to convert HU into bone mineral units. These calibration phantoms contain various concentrations of material with similar X-ray attenuation characteristics to bone. From the regression of attenuation and concentration of the calibration substance, the attenuation measured in the trabecular bone can be converted from HU to bone mineral equivalents in mg/cm^3 (g/l). Originally these were fluid calibration phantoms (K_2HPO_4), but because of leakage or transpiration of fluid from the solutions into the Perspex of the phantom, air bubbles developed in the solutions making scanning difficult or inaccurate. Consequently, calibration phantoms using solid materials (hydroxyapatite) were developed and are now used with specific analysis software packages (e.g. Mindways Software Inc., Austin, Texas USA; Image Analysis, Inc. Columbia, Kentucky USA; Siemens, Erlangen, Germany). The results from different types of calibration phantoms are not interchangeable, unless a cross-calibration calculation can be made. Phantoms

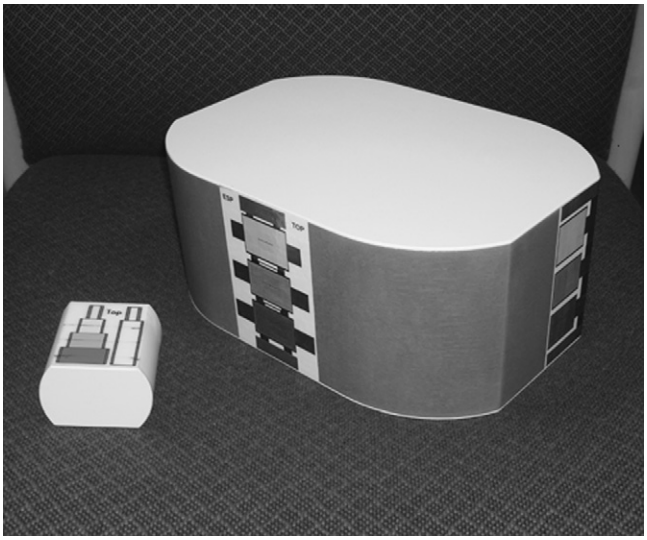

Fig. 1. Phantoms: for cross-calibrating between scanners and for quality assurance testing in CT the European Forearm phantom (left; reference [22]) is used for pQCT sites and the European Spine phantom (right; reference [21]) is used for spinal QCT.

that have been developed for the such cross calibration and Quality Assurance (QA) testing of CT parameters on different manufacturers' scanners are the European Spine phantom (ESP) [21] (Fig. 1) for general purpose scanners and the European Forearm phantom (EFP) [22,23] (Fig. 1) (QRM GmbH, Dorfstrasse 4, Moehrendorf, Germany) for dedicated pQCT scanners. In longitudinal studies the same reference phantom must be used.

1.1.2. Radiation doses

As the original 2D QCT of the spine did not require the same image quality as did CT performed for imaging, a low dose technique could be used (e.g. 80 kVp, 70 mA and 2 s scan time) [24,25] (Table 1). QCT of the lumbar spine with a dose of approximately 90 μSv EDE is higher than that associated with DXA (1–6 μSv) but compares favorably with other X-ray based investigations which are performed in patients suspected of having osteoporosis (e.g. spinal radiographs 700–2000 μSv) [25] and with the annual natural background radiation does (2.4–20 mSv per annum, depending on geographic location [26,27] (Table 1). In spiral MDCT scanners, auto-modulation techniques are used to significantly reduce radiation exposure by optimally adapting the X-ray tube current to the individual subject and anatomical site being scanned [28,29].

1.1.3. Spatial resolution and partial volume effect

In the study of differential effects of age related changes and pharmaceutical effects on BMD, bone geometry and strength parameters both the cortical and trabecular compartments are relevant. However, accurate segmentation and analysis of cortical bone and trabeculae requires adequate spatial resolution in the image obtained [20]. Spatial resolution of CT depends on slice width, pixel size, noise and modulation transfer function (MTF) [30]. However, often spatial resolution is incorrectly given as being synonymous with pixel size, which will overestimate spatial resolution as pixel size is usually smaller that true spatial resolution. Trabecular thickness ranges from 60 to 150 μm and separation between trabeculae from 300 to 1000 μm [31]. In central skeletal sites radiation doses limit the spatial resolution which can be achieved which is between 160 and 300 μm. Although individual trabeculae are not being resolved information can still be extracted about trabecular structure and orientation from texture analysis of 2D or 3D images and demonstrate change with therapy (teriparatide) [32]. In the peripheral sites it is feasible to obtain images of higher spatial resolution