Quantitative Computed Tomography

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KEYWORDS

• Computed tomography • Osteoporosis • Bone density
• Bone geometry • Bone strength

Osteoporosis is one of the major public health problems facing the elderly population,[1] and hip fractures are the most serious manifestation of osteoporosis, affecting over 250,000 elderly in the United States annually and resulting in a 20% mortality rate and substantial loss of quality of life.[2] The number of osteoporotic fractures is expected to increase as the population ages, resulting both from age-related changes in skeletal material properties and geometry that adversely affect bone strength, and from age-related increases in the risk of falling. Thus, with increasing age, decreased skeletal strength is combined with an increased probability of falls and other events that increase the risk of pathologic loads on bone.

Bone strength is a function of skeletal geometry and of material properties, elastic modulus, and material strength, at each point, as they vary throughout the structure.[3] Image-based methods operate in the clinical setting as surrogate measures for bone strength. Image-based methods range from dual x-ray absorptiometry (DXA), which measures the mass and areal bone mineral density (BMD) of large volumes of bone tissue, to DXA-based hip structure analysis, which derives simple geometric measurements from DXA images.[4] Quantitative computed tomography (QCT) methods range from compartmental measures of trabecular and cortical bone mineral density, to simple measures of bone geometry and structure, and ultimately to QCT-based finite element modeling,[3,5–12] which uses voxel-based estimates of material properties across the bone structure to directly calculate whole bone strength and stiffness.

Until relatively recently, x-ray-based imaging has been principally employed for density measurement. Areal BMDs by DXA is the most widely employed clinical surrogate for bone strength. In DXA studies, a one SD reduction in femoral BMD compared with age-matched normal BMD resulted in an approximately threefold increase in fracture risk, depending on the femoral subregion assessed.[7,8] Additionally, geometric measurements, such as hip axis length or increased trochanteric width,[9,10] have also been related to hip fracture risk. QCT, on the other hand, provides measurements of cortical and trabecular volumetric BMD (vBMD).[11] Epidemiologic studies have documented that individual subregions based on trabecular and cortical compartments are independent predictors of hip fracture,[12] and clinical trials have shown that the cortical and trabecular compartments demonstrate differential responses to pharmacologic interventions in osteoporosis.[13] Although BMD measures, whether by DXA or QCT, have strong associations with incident and prevalent fracture, they are poor fracture predictors on an individual basis. Many individuals with high BMD sustain fractures, and many with low BMD do not. Further, changes in BMD do not appear to account for the large changes in fracture risk associated with pharmacologic interventions. Over time, these findings and others have led to the investigation of other skeletal factors not captured in BMD measurements, including measures of bone macroarchitecture, such as bone shape and size, and microarchitecture related to the microstructure of trabecular and cortical bone.

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This article focuses on volumetric QCT (vQCT) imaging, both for measures of BMD and for more novel measures that take into account the ability of QCT to quantify the distribution of BMD within skeletal envelopes as it relates to bone strength. In addition to bone strength estimates, vQCT has also been shown to provide measures of muscle size and composition that also relate to risk of fracture through their ability to take into account nonskeletal risk factors such as muscle weakness and falls. Whereas other techniques have evolved, such as MR imaging, or high-resolution peripheral QCT and micro-CT, which can examine the detailed trabecular and cortical microarchitecture of peripheral skeletal sites, these topics will not be discussed here.

QCT: IMAGE ACQUISITION

CT is a three-dimensional (3D) radiographic absorptiometric measurement that provides the distribution of linear attenuation coefficient in a thin cross section of tissue. **Fig. 1** depicts the geometry of a CT measurement. The cross section of the object being scanned is contained within a fan of x-rays defined between the edges of the detector array and a x-ray point source. The x-ray attenuation of the patient is measured along ray-paths corresponding to the lines defined between individual detector elements and the x-ray source. Along the length of the scanning system, the x-ray beam is shaped to radiate a relatively thin "slice" of tissue, ranging from 0.5mm to 10 mm in the case of clinical scanners. The fan of x-rays circumscribes a circular field of view, which is itself contained within a square image matrix that typically consists of two-dimensional arrays of square pixel elements, or "pixels." Because the image represents a cross section of tissue, the picture elements are effectively volume elements, or "voxels." The voxel dimensions depend on the number of elements in the matrix and the size of the field of view. They may thus be adjusted depending on the size of the organ being imaged. Depending on the type of scanner, the voxel dimensions range from the hundreds of microns to roughly 1 mm "in plane" and up to several millimeters in slice thickness. The CT image is acquired when the x-ray source and detector rotate around the patient, and the absorption is continuously measured for each detector element. Through a full acquisition, in which the detector may rotate from 180° to 360°, each voxel is intersected by several ray-paths. The x-ray absorption measurements taken at the different angles are recorded in a computer and combined in a process known as filtered back-projection to calculate the linear attenuation coefficient at each voxel. In the resulting CT image, the voxel values are based on the linear attenuation coefficients. Because these linear attenuation coefficients depend on the effective x-ray energy (which varies between CT scanner models and different peak kilovoltage [kVp] settings of the same scanner), a simple scale, known as the Hounsfield scale, is used to standardize them. The gray-scale value of each voxel is represented as a Hounsfield unit (HU), which is defined as the difference of the linear attenuation coefficient of a given voxel from that of water, divided by the linear attenuation coefficient of water. The HU scale is a linear scale in which air has a value of −1000, water 0, muscle 30, with bone typically ranging from 300 to 3000 units.

The value of the HU for a given voxel depends on several technical factors related primarily to the size of the voxel and the spatial resolution of the imaging system, but also on the linearity of the attenuation coefficient measurements. First, if the sizes of the structures in the tissue are

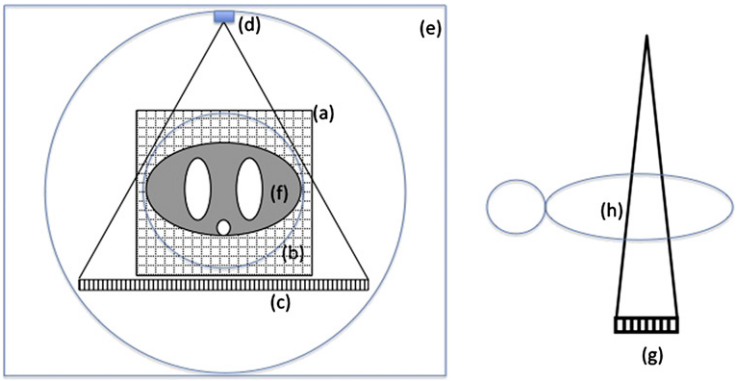

Fig. 1. Simplified A multidetector CT system. Frontal view: (a) image matrix, (b) reconstruction circle, (c) detector array, (d) x-ray source (vertex of fan encompassing edges of detector array and reconstruction circle), (e) CT gantry, (f) transverse view of patient including lung and spine, (g) side view of detector array showing multiple detector rows, and (h) side view of patient.