Radiological diagnostic progress in skeletal diseases

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Summary

High-resolution bone imaging has made tremendous progress in the recent past. Both imaging modalities, computed tomography as well as MR imaging, have improved image quality. New developments such as HR-pQCT now make it possible to acquire *in vivo* images at peripheral sites with isotropic voxel size in a very short time. Further enhancements in the MR field have made it possible to image more central body sites such as the proximal femur with very high spatial resolution. New analysis methods can obtain direct estimates of biomechanical properties and important information related to bone's topology, as well as parameters of scale and orientation. These accomplishments will be essential in the noninvasive assessment of osteoporosis and fracture risk, will provide insight into the mechanisms behind bone loss, and will increasingly play a role as a tool for assessing treatment efficacy.

KEY WORDS: osteoporosis; High Resolution Computed Tomography; High Resolution Magnetic Resonance Imaging.

Introduction

Osteoporosis is the most common metabolic bone disease. It is characterized by reduced bone mass, altered bone architecture and the clinical consequence of easy fracture with little or no trauma (low trauma fractures). The relationship between Bone Mineral Density (BMD) and bone fragility lead to the advent of techniques to quantitatively as well as qualitatively assess bone density with accuracy and reproducibility in order to diagnose osteoporosis, predict fracture disk, determine therapeutic intervention and monitor response to therapy (1,2,3).
The aim of this brief review was to illustrate the recent advances in bone densitometry using High Resolution Computed Tomography (HR-CT) and HR Magnetic Resonance Imaging (HR-MRI) in the diagnosis of metabolic bone diseases.

High Resolution Computed Tomography (HR-CT)

During the last years Quantitative Computed Tomography (QCT) has been used, as established technique for measuring BMD, in the axial spine and appendicular skeleton (forearm and tibia) (4).
Axial QCT has been employed in the assessment of vertebral fracture risk measuring trabecular bone in the center of vertebral body.
On the other hand, peripheral QCT (pQCT) of radius and tibia has been performed to evaluate trabecular and cortical bone components, bone geometry, muscle mass and muscle/bone relationships.
Furthermore, clinical practice evidenced several limitations of both axial and peripheral QCT, like the high level of dependence on the operator, the complexity and numerosity of parameters obtained (especially for pQCT) and, in particular, the lack of assessment of hip, one of the most common and clinically relevant fracture site.
With the advent of Multi-Detector CT (MDCT) systems and high-performance computer workstations, the powerful applications of helical CT scanning and 3D-image analysis have been applied to the spine and the hip, leading to volumetric QCT (vQCT) and High Resolution CT (HR-CT).
Compared to the conventional technique, vQCT grants a shorter scan time (30 seconds), minimal positioning requirements and, above all, volume acquisition.
The analysis of vertebrae and hip performed with vQCT provides a wide assessment range from volumetric BMD (measured with automated elliptical regions of interest - ROI), true geometry properties and macro-structural features to finite element modeling of the strength of bone based on reconstruction of cross sections and volumes of femoral neck or vertebral tissue and material properties mapped from CT image values (5,6).
On the other hand, application of standard whole-body MDCT for high-resolution imaging of trabecular and cortical bone microarchitecture has been conducted to obtain a more specific quantification of trabecular structure (7).
Using computerized image analysis, HR-CT provides the assessment of amount of bone area and volume, mean trabecular thickness, number of connections, trabecular direction and fractal dimension (complexity / connectivity) (8,9).
MDCT is available in lots of diagnostic imaging departments, so a dedicated scanner is not required. This technique allows the study of more central regions of the skeleton which are common sites of osteoporotic fracture like spine and hip, improving the prediction of fracture risk and monitoring therapy.
Nevertheless, the use of MDCT in the study of bone architecture is limited because the spatial resolution is above the trabecular dimensions and the imaging of individual trabeculae is subjected to significant partial volume effects (10).
Also the application in clinical routine or studies is not suitable, because HR-CT needs a considerably higher radiation dose to obtain an adequate spatial resolution, compared with standard techniques for measuring BMD like DXA.
Over the few years, with the aim of avoiding this limitations, it has been created a specific high resolution extremity imaging system dedicated to trabecular-scale imaging *in vivo* (XtremeCT, Scanco Medical AG, Bruttisellen, Swizterland) (Figure 1).
The image analysis and postprocessing is based on a semiautomated contouring and segmentation process. Densitometric,

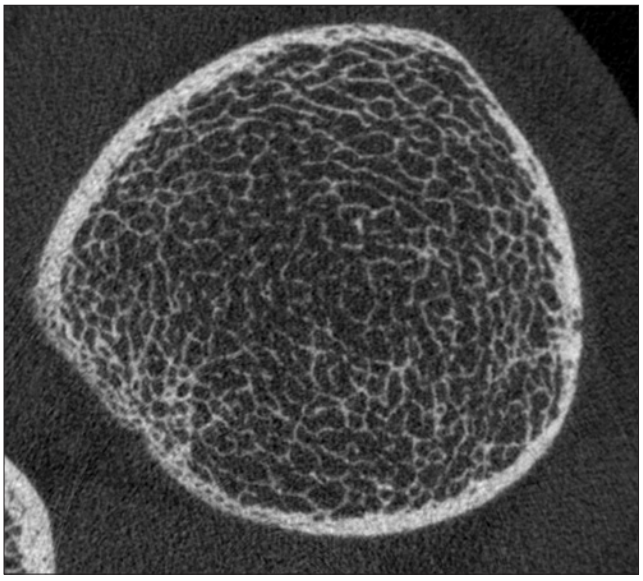

Figure 1 - *In vivo* 3D-CT: 82 mm isotropic 3D resolution allows to image the three-dimensional trabecular network in normal human forearm. Courtesy SCANCO Medical AG.

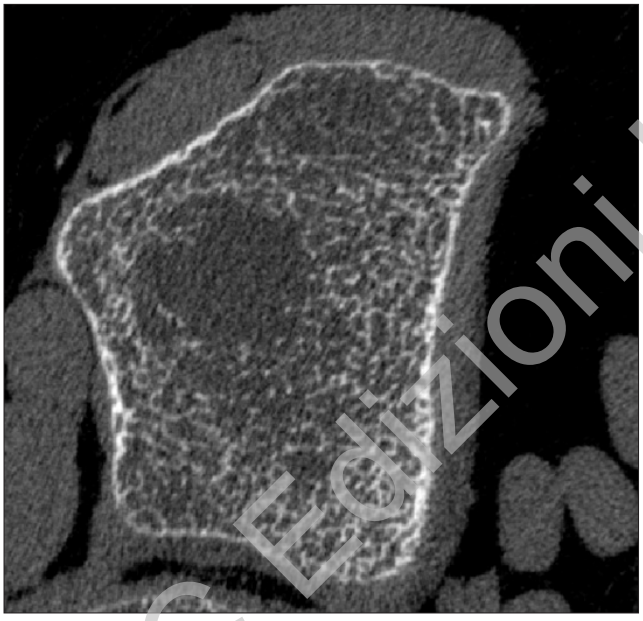

Figure 2 - *In vivo* 3D-CT: 82 mm isotropic 3D resolution allows to image the three-dimensional trabecular network in osteoporotic human forearm. Courtesy SCANCO Medical AG

morphometric, and biomechanical analyses are performed by using a standard protocol provided by the manufacturer based on the reconstructed images (Figure 2).
The High-Resolution pQCT, compared with standard MDCT, has a significantly higher Signal-Noise-Rate (SNR) and spatial resolution (11); even the radiation dose is lower and does not involve critical, radiosensitive organs because tomographic scan region is distal radius or tibia (12,13).
On the contrary there are also several disadvantages to this technology: first of all, the lack of assessment of bone quality in the lumbar spine or hip; as mentioned before, these are common sites for osteoporotic fragility fractures and have a huge financial and social impact on life of patients.
In addition, the necessity of an expensive dedicated device limits the diffusion to major research institutes.
All the data obtained represent BMD, bone micro-architecture, geometry and composition; those elements reflect, in a wider sense, the concept of stability (14,15).
Bone strength assessment, in fact, leads to fracture risk prediction and allows an improved identification of individuals at risk and indications for a better management of osteoporosis (16).

HR-MRI

Over the past few years (17,18), study of osteoporosis and other metabolic bone diseases with MRI have become an emerging area due to technological progress and new quantitative approaches in the study of bone structure in addition to BMD which have granted (19-22) an important upgrade in fracture discrimination (23).
Bone structure analysis with MRI needs to differentiate trabecular from cortical bone, by using different criteria for measurement and analysis.

Trabecular bone

Trabecular bone can be evaluated using certain MR sequences in which the influence of trabecular matrix over bone marrow signal is especially pronounced. In the gradient-echo (GRE) sequences, the difference of signal between trabecular matrix and adjacent marrow causes a more rapid MR signal decay, which can be measured by transverse relaxation time T2* (Figure 3). Several studies demonstrated that T2* correlates with trabecular bone density and T2* is shorter in normal trabecular bone than osteoporotic bone tissue (24-26). Even bone marrow T2* reflects the orientation of the trabeculae and, consequently, bone strength (27). All these features make MRI useful in evaluating the quality of spongy bone not only identifying occult fractures, but also in the prediction of fracture risk (28).
With regard to this, high-field quantitative MRI has been used to obtain high-resolution images, considering that the diameter of the trabeculae is in the order of 100–150 µm (29-31).
In the last years, gradient-echo sequences (GRE) denominated fully balanced steady-state free precession (bSSFP) have revealed an optimal field of application for the study of trabecular bone microarchitecture (32).
Although high-field MRI (3T) has a better SNR and consequently higher spatial resolution, it is more sensitive to signal loss. The introduction of fully balanced steady-state spin-echo sequence (bSSSE) have provided the best SNR at high field MRI and have demonstrated more accurate measurements of the microarchitecture of trabecular bone (33).
Analysis of MRI images starts with definition of trabecular bone ROI; after the correction of coil sensitivity, bone marrow segmentation and other structural parameters are calculated.
The analysis of trabecular bone ROI ends with the obtainment of bone volume fraction (BVF), which is one of the most important parameter extracted by HR-MRI (Figure 4).
Guglielmi et al. (34) choose the calcaneus tuberosity as the preferred site for studies because heel bone is at 95% composed of spongy bone.
Quantitative HR-MRI analysis demonstrated higher sensitivity in quantifying changes in trabecular bone structure and quality compared to DXA.

Cortical bone

Cortical bone analysis especially involves hip joint and femural neck. HR-MRI can be even useful in the detection intracapsular hip frac-

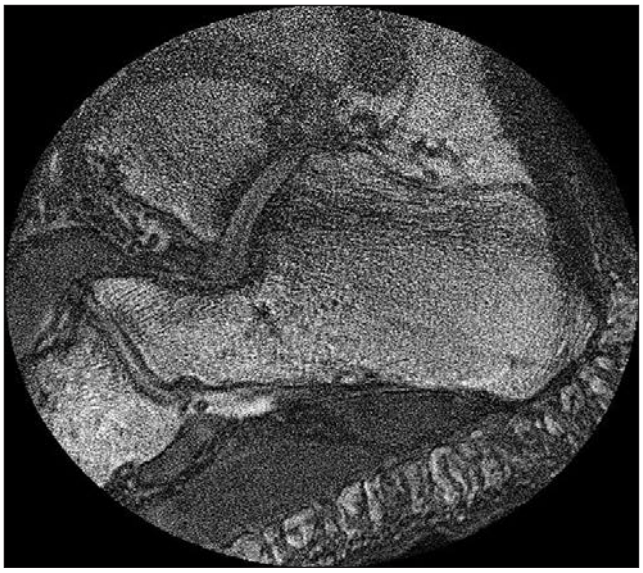

Figure 3 - 3D Radial Gradient-Echo (1.5 T); TE = 2.9 ms; TR = 23.0 ms; Acq. matrix = 512 x 512 ; FOV = 100 mm; Image resolution = 195 µmm; Slice thickness = 0.7 mm; NSA = 2; Synergy Flex-S coil.

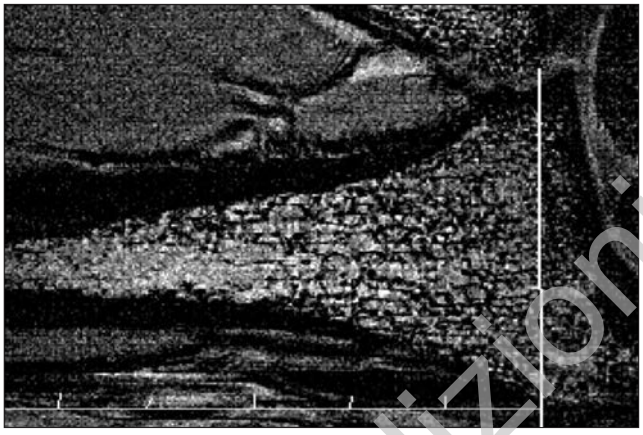

Figure 4 - High Resolution MR image of coronal distal radius (156x156x500 µm). Non-osteoporotic 40 year old. The figure illustrates the bone fraction in the radius as one moves from the joint line into the shaft.

tures, which could be unreported with conventional techniques (35). 3D analysis of cortical architecture in this deep sites is quite complicated and even the double oblique angle between neck and axes requires special approaches.

Goldenstein et al. (36) analyzed intracortical porosity and found different types of fluid contained in cortical bone pores.

In recent studies, a new approach for cortical bone analysis has been introduced: microscopic pores of haversian lacunocanalicular systems and collagen included in mineral matrix of cortical bone contain a certain amount of water. As the hydratation of bone tissue is strictly correlated with its strength and stability properties, modification of water percentage by volume in cortical bone could be associated with modification of its porosity and a reduction of its viscoelastic features. Although micropores are too small to be directly detected by one voxel, quantification of cortical bone water using MRI could indirectly provide a quantification of cortical bone pores.

Techawiboonwong et al. (37, 38) used a Ultra Short Echo Times (UTE) sequences to detect water protons decay signal and to obtain bone water quantification in sheep and human cadaveric specimens.

Analysis followed a semiautomatic definition of inner and outer cortical contours adjusted by the operator, obtaining cortical volume and thickness parameters.

Conclusions

Bone quality has been an emerging concept in the area of osteoporosis. Trabecular bone as well as cortical bone microarchitecture, bone geometry and associated marrow changes in osteoporosis can be probed using CT and MRI. Thus, CT and MRI techniques has the potential to provide a complete whole-organ assessment of skeletal status in osteoporosis and further developments in this imaging modality and research studies are clearly warranted especially in predicting fracture risk and in the evaluation of treatment in osteoporotic patients.

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