(1) Clinical Significance

Bone strength governs fracture risk and reflects the integration of two main features: bone mass or density and bone quality. Bone mineral density (BMD) is expressed as grams of mineral per area or volume and in any given individual is determined by peak bone mass and amount of bone loss. Bone quality refers to trabecular bone architecture, turnover, damage accumulation (e.g., microfractures), cortical bone thickness, macro-architecture, osteon density, for both trabecular and cortical bone – mineralization, and other factors such as cell viability and osteocyte density as previously defined by the NIH Consensus Development Panel in 2001 (1).

Among these bone quality parameters trabecular and cortical bone architecture are most accessible with non-invasive imaging techniques and multiple studies have shown that architecture gives additional information to BMD in assessing bone strength and discriminating patients with and without osteoporotic fractures (2-13). Today it is widely recognized that bone structure assessment improves our knowledge of the pathophysiology of osteoporosis, may improve fracture prediction and may give us more information on therapeutic effects of osteoporosis specific medications on bone. Recently also MR based measures of bone marrow function, such as spectroscopy and perfusion have been introduced to study bone metabolism (14-16).

(2) Background

With technical advances in radiological techniques a number of high-resolution tomographic techniques such as high-resolution magnetic resonance imaging (MRI), computed tomography (CT), and micro computed tomography have emerged, which are
attractive for analyzing bone structure. Studies have validated both CT- and MRI-based structure measures comparing them with contact radiography, bone histomorphometry and microCT as standards of reference (17-20). It has also been found that in vitro structure measures predict biomechanically determined fracture load (7, 21-23).

Imaging trabecular and cortical bone architecture, however, it should be kept in mind that the diameter of bone trabeculae ranges in size between approximately 0.05 – 0.20 mm. Maximum in plane spatial resolutions of clinical MRI is in the range of 0.15 mm² and minimum slice thicknesses is around 0.5 mm. This means that visualization of bone architecture in vivo is challenging and a substantial amount of partial volume effects have to be considered. Cortical thickness and other geometric measurements are technically less challenging, however, the assessment of cortical porosity again requires maximum spatial resolution.

In addition to structure measurements a number of studies have focused on using bone marrow spectroscopy and perfusion to better assess the function of the bone marrow, which is an integral component of bone and also responsible for its stability (14-16).

(3) Imaging of Trabecular Bone Structure

With the advent of phased array coils, parallel imaging and improved software and hardware including 3T imaging, it has been possible to push the frontiers of magnetic resonance imaging concerning spatial resolution. The three-dimensional imaging capability, along with the fact that MR is a non-ionizing modality, makes it very attractive as a tool for imaging bone structure, in particular in scientific studies focusing on osteoporosis, osteoarthritis and pathology of bone metabolism.

A number of calibration and validation studies (both in vitro and in vivo) have been undertaken in which MR-derived measures of structure were compared with measures derived from other modalities, such as histology, micro-CT, BMD, and with biomechanical parameters; in addition these measures were used to differentiate patients with and without osteoporotic fractures (6, 8, 9, 24-27). Most of the in vivo studies focused on imaging of the distal radius, the calcaneus and the distal tibia as these sites have a large number of trabeculae and the distal radius is a typical site for osteoporotic
fractures. Also these sites are easily accessible with localized surface (detection) coils and subjects are able to tolerate immobilization for the period required for high-resolution imaging. Figure 1 shows high resolution MR images depicting the trabecular bone architecture at the distal radius and the distal tibia in an early postmenopausal subject. High resolution imaging at the spine to visualize trabecular bone architecture is severely limited by size of the trabeculae, hematopoietic bone marrow, which obscures trabeculae and motion artifacts due to breathing.

**Fig. 1:** Axial MR images of the distal radius (a) and the distal tibia (b) obtained at 3.0T using a Steady-State-Free-Precession (SSFP) sequence visualizing trabecular bone architecture.

The processing of high resolution MR images generally consists of several stages and Newitt *et al.* (28) have shown that each stage needs to be standardized and normalized in order to ensure a high degree of reproducibility. In particular, these authors describe a standardized analysis system with considerable reduction of human interaction. The efficiency of this system was evaluated in terms of reproducibility (2-4%) and has been successfully applied in several cross-sectional and early longitudinal studies.

One of the early longitudinal studies showed that salmon calcitonin nasal spray had therapeutic benefit compared with placebo in maintaining trabecular microarchitecture at multiple skeletal sites and supported the use of MRI technology for assessment of trabecular microarchitecture in clinical research trials (29). Another
longitudinal study in hypogonadal men suggested the possibility that testosterone replacement improves trabecular architecture (30).

Using MRI at higher field strength (3.0T) visualization of trabecular bone architecture can be substantially improved as demonstrated in a recent study by Phan et al (19). These investigators showed in an in vitro study that MR imaging at 3.0 T provided a better measure of the trabecular bone structure than did MR imaging at 1.5 T using microCT measures as a standard of reference. Clearly with the proliferation of high field systems, and further research in the area of imaging trabecular bone structure application of these techniques will be more feasible.

Recently Krug et al. investigated the potential of 7 Tesla MRI in visualizing bone architecture and found signal-to-noise (SNR) benefit and great potential for bone imaging at 7 Tesla compared to 3 Tesla imaging (31). These investigators also optimized 3 Tesla MR imaging for proximal femur trabecular bone architecture thus moving these analyses to more central body parts that are frequently affected by osteoporotic fractures (32).

**Fig. 2:** MR images of distal tibia using a SSFP sequence at 7 (a) and 3 (b) Tesla, image quality at 7T is superior to this at 3T.

![Distal Tibia Images](image)

(4) **Imaging of Cortical Bone Structure**

Previous studies also focused on cortical bone imaging to study predominantly geometric parameters (33, 34). Sievanen et al. found that thin cortical bone at the narrowest location
of the femoral neck could be delineated precisely and accurately with a standard clinical 1.5 T MRI device, they concluded that MRI provided a feasible tool for the assessment of mechanically important cortical bone at the femoral neck and may be of clinical utility in assessing hip fragility (33). Another approach has been to use ultrashort TE (UTE) pulse sequences to characterize cortical bone (35); Reichert et al. found that signal can be detected from normal and abnormal cortical bone with UTE pulse sequences, and this can be used to measure its T(1) and T(2)* as well as to quantify contrast enhancement. As imaging spatial resolution is improved MRI may also be used to study the porosity of cortical bone, which so far has been fairly limited. However, the significance of these findings is not completely understood and future research will have to study cortical porosity, developing structural parameters to quantify them and to understand clinical implications.

(5) Imaging of Bone Function
Recently dynamic contrast-enhanced MR imaging and MR spectroscopy have been proposed to study bone marrow composition and function as increase in bone marrow fat has been associated with osteoporosis and increased fracture risk (14-16). Griffith et al. found in 110 post-menopausal subjects that a decrease in vertebral marrow maximum enhancement and enhancement slope as well as an increase in marrow fat content measured with spectroscopy were associated with lower BMD (15). Similar results were presented by Shen et al. (16).

(6) Conclusion
Advanced MRI techniques are available that provide insights in the structure and function of trabecular and cortical bone in vivo, thus providing to some extent a “virtual bone biopsy”. The potential of including these methodologies in the study of bone metabolism holds tremendous promise for the identification of high fracture risk patients, management of osteoporosis longitudinally and for assessment of therapeutic efficacy.
References:


resolution peripheral quantitative computed tomography ex vivo and in vivo. Osteoporos Int.


Pre-Test questions for registrants

1. Which statement is correct?
   A: 3T MR imaging cannot be used to image trabecular bone structure because of the increased susceptibility effects.
   B: Parallel imaging is particularly beneficial if used with quadrature coils.
   C: In vivo trabecular bone structure imaging is subjected to substantial partial volume effects.
   D: The spine is a particularly attractive site for bone structure imaging.
   E: Ultrashort TE imaging is used to decrease signal of the cortical bone.

2. Which statement is not correct?
   A: At 3T trabeculae are amplified due to increased susceptibility effects.
   B: Trabecular bone structure parameters have been shown to contribute to BMD in assessing biomechanical strength of bone and in better differentiating subjects with and without osteoporotic fractures.
   C: Bone marrow spectroscopy can be used to assess bone marrow fat content, which is a parameter that contributes to bone fragility.
   D: The most important parameter in assessing bone quality is BMD.
   E: The long-term precision of bone structure parameters determined in MR images is generally inferior to that of BMD measured by DXA.