MRI Assessment of Trabecular and Cortical Bone Structure and Strength

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Bone is a living tissue with an extra-cellular matrix consisting of predominantly mineralized collagen fibers. This nanostructural organization confers to bone its unique compressive and tensile strength necessary for fulfilling its various functions, including locomotion and weight bearing. On a structural level the tissue is organized into compact and trabecular (also referred to as cortical and cancellous, respectively) bone. The long bones of the extremities consist largely of compact bone except for the portion near the joints where a thin cortical shell encases a 3D network of interconnected plates and struts, embedded in bone marrow, an arrangement characteristic of trabecular bone. The axial skeleton (trunk, rib cage and pelvis) has a similar architecture.

Bone remodels, which implies a dynamic equilibrium between bone formation by osteoblasts and bone resorption by osteoclasts. In this manner bone responds to changes in loading conditions or hormonal signaling. While near peak bone mass resorption and formation balance each other, at advancing age and depletion of gonadal steroids, resorption prevails over formation. Treatment with corticosteroids for inflammatory conditions also entail bone loss, which is due primarily to suppressed formation.

Most osteoporotic fractures occur at skeletal locations of predominantly trabecular bone, i.e. the wrist, vertebrae and proximal femur, even though a portion of the strength is also conferred by cortical bone (in particular, the femoral neck, site of the most traumatic fractures).

Currently, x-ray based techniques, notably dual-energy X-ray absorptiometry (DXA) and quantitative computed tomography (QCT) are being used as modalities for assessment of fracture risk. Both provide a measurement of bone mineral density (BMD) measured in g/cm^2 (DXA) or g/cm^3 (QCT). BMD is usually expressed in terms of standard deviations from peak density achieved in early adulthood (T-score). T = ±1 is considered normal, -2.5 < T < -1 classifies a subject as osteopenic (low bone density), and T < 2.5 as osteoporotic (1).

Unfortunately, BMD is a poor predictor of fracture risk, in that about half the subjects with osteoporotic fractures have either normal BMD or are osteopenic only (2). This situation has spurred the search for other causes predisposing people to elevated fracture risk, leading to the concept of *bone quality* as an additional measure of bone fragility (3,4). Among the various contributors to bone quality, architecture at the macro- and microstructural level is a key contributor.

MRI is uniquely suited for assessing bone architecture. Since bone is ordinarily invisible in MR images as a result of the extremely short life-times (T_2) of the protons (tightly bound water and collagen), its structure can be inferred from the signal of the surrounding soft tissues, i.e. bone marrow. Technical advances during the past decade now allow images to be obtained from the trabecular network, from which faithful 3D models of the architecture can be obtained (5). Signal-to-noise ratio (SNR) achievable with advanced RF receive coil arrays at 3 Tesla field strength now allow voxel sizes of $4x10^{-6}$ to $8x10^{-6}$ mm^3 to be achieved in about 10 minutes total scan time, at least at the distal extremities (distal radius and tibia). Among the technical requirements to be met, prevention of, and correction for, involuntary subject motion, is key to a successful examination (5,6). Other technical capabilities critical in drug intervention studies designed to assess treatment effectiveness, are means for image registration, ensuring analysis of precisely the same image

volume between baseline and repeat studies (7). Lastly, algorithms are needed for accurate segmentation of the images given the limited partial resolution and the presence of image intensity shading due to homogenous reception profiles of the receive coils (8) (9).

Once a 3D model of the trabecular and cortical bone is obtained, two possible approaches can be pursued. The first entails analysis of the network in terms of parameters of scale (e.g. bone volume fraction, trabecular thickness), topology (e.g. differentiation of plates from rods and their interconnections) and orientation. Bone is intrinsically structurally anisotropic, with trabeculae following either major stress lines, or being oriented perpendicular to these (Wolff's Law (10)). These parameters (or their combinations) may serve as surrogates for bone strength (11). Alternatively, strength can be assessed more directly by resorting to computational biomechanics (since in vivo the bone cannot be subjected to mechanical stress testing). One approach, called "finite-element analysis" (FEA) converts the voxel array into a set of finite elements. Subsequently, the structure is subjected to simulated loading. Solving of the large number of simultaneous equations yields the strain distribution and parameters such as stiffness and failure load (12). Since a typical analysis volume comprises millions of voxels (and thus finite elements) FEA is computationally demanding. It is shown that with high-end multi-core desktops computers and improvements in algorithms these tasks can now be accomplished in minutes and thus have become clinically practical (13).

Examples from the author's laboratory of both approaches (structure analysis vs. simulated mechanical testing) will be provided. The data show that MRI assessed structure and FEA assessed mechanical parameters can provide information complementary to BMD. Of particular interest are doing intervention trials involving treatment with antiresorptives (i.e. drugs that prevent abnormal bone resorption such as in postmenopausal osteoporosis) involving estradiol supplementation (14) or synthetic osteoclast inhibitors of the bisphosphonate class. While estrogen loss following menopause is the primary cause of osteoporosis in older women, men also are affected, e.g. in cases of testosterone deficiency (15).

In summary, high-resolution MRI of bone structure and mechanics has shown considerable potential as a means to assess fracture risk and as a modality to evaluate the effects of intervention. Translation to the clinic is further facilitated by the very large installed base of MRI systems (>10,000 units in the United States alone) and by the modality's noninvasive nature.

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