# Magnetic Resonance Imaging of Bone Marrow

Xiaojuan Li, PhD
Associate Professor, Musculoskeletal Quantitative Imaging Research Group
Dept. of Radiology and Biomedical Imaging, University of California, San Francisco, USA

## Bone Marrow Anatomy and Function

Following skin, bone and muscle, bone marrow is the fourth largest organ of human body. The primary function of bone marrow is hematopoietic, providing the optimal supply of circulating platelets, white and red blood cells (WBC and RBC). The normal bone marrow has three primary components: (1) an osseous component consisting of cancellous or trabecular bone; (2) a cellular component including hematopoietic, fat, and reticulum cells; (3) a supporting system consisting of vascular, neural, and lymphatic elements. Bone marrow can be classified into red or yellow marrow. The red marrow contains approximately 35-40% water, 40-45% fat, and 15% protein, which is hematopoietically active and produces RBCs, WBCs, and platelet precursors. The yellow or hematopoietically inactive marrow contains approximately 15% water, 80% fat, and 5% protein. During skeletal maturation, red marrow is converted to fatty marrow. The different compositions between these two types of marrow account for their different appearance in MR images. Other techniques for imaging bone marrow include radiographs, computerized tomography (CT), positron emission tomography (PET), and bone scintigraphy. Alterations in marrow signal occur in a variety of disorders including marrow reconversion, infiltration (benign or malignant), myeloid depletion, myelofibrosis, edema, ischemia and osteoporosis.

## Conventional MRI Techniques of Bone Marrow

The standard MRI protocol for bone marrow includes T1-weight spin-echo images; fat-saturated T2-weighted fast spin-echo images; and short Tau inversion recovery (STIR) images. Increased fat content within yellow marrow results in significant shortening of the T1 relaxation time compared to red marrow. On T1 weighted images the yellow marrow has higher signal intensity than red marrow. Both benign and malignant disorders of bone marrow have long T1 values, resulting in decreased signal intensity. On fat-saturated T2-weighted or STIR images, hematopoietic red marrow shows intermediate signal intensity similar to that of muscle, whereas fatty yellow marrow shows a signal intensity lower than that of muscle. Most marrow pathology exhibits relatively high signal intensity in fat-saturated T2-weighted or STIR images than that of red and yellow marrow. The drawbacks of STIR images include relatively low SNR and long acquisition time, while fast STIR imaging techniques have been developed. The diagnostic efficacy of fat-saturated T2-weighted images will depend on adequate fat suppression.

## Contrast Enhanced MRI of Bone Marrow

Contrast agents, including gadolinium-based T1 contrast agents (the most commonly used), as well as the T2 or T2* agents such as super paramagnetic iron oxides (SPIO) or ultraasmall SPIO (USPIO), have been used to provide better contrast of marrow lesions. Increased signal intensity in T1-weighted images is observed within the bone marrow of healthy individuals, especially in red marrow, after gadolinium administration because of bone vascularity. The enhancement of normal marrow is greatest in young patients and those with lower marrow fat content, and decreased significantly with aging and pathologies such as osteoporosis. Studies also reported altered marrow perfusion in osteoarthritis and avascular necrosis, featuring longer contrast retaining time in the marrow. Strong enhancement in both routine and dynamic contrast studies are usually seen in different pathological processes, including infection, inflammation, and tumor, and thus is a nonspecific finding. Perfusion parameters can be calculated using dynamic contrast enhanced (DCE) MRI with data acquired at multiple time points, either empirically or using pharmacokinetic models. Other non-contrast imaging techniques have been developed for

quantifying perfusion, including arterial spin labeling (ASL) and intravoxel incoherent motion. However, the applications of these techniques in bone marrow are challenging due to low SNR and susceptibility difference between trabecular bone and marrow. T2 and T2* agents are still under investigation for their clinical utility. The different enhancement patterns seen with iron oxides may help in detecting marrow lesions and distinguishing red marrow from neoplastic marrow by providing high marrow-to-tumor contrast.

## Diffusion-weighted MRI of Bone Marrow

Diffusion MRI measures Brownian motion of water molecules in tissues, which provides a non-invasive method for evaluating microscopic cellular structures. Diffusion-weighted MRI is increasingly being used to assess bone marrow disorders. Some studies reported decreased apparent diffusion coefficient (ADC) in marrow tumors, probably due to the increased tumor cell density and membranes. On the other hand, infiltration of normal bone marrow by tumor cells also appears to increases ADC values, which may be explained by the displacement of adiposity and increased vascularity. More studies are needed to explore the diagnostic value of using DWI as an objective marker for evaluating malignant marrow disease. DWI has been also used in distinguishing benign osteoporotic and malignant vertebral compression fractures, with the former showing hypointense or isointense, and the latter showing hyperintense. The hypothesis is that the molecular diffusion of water is substantially increased in osteoporotic fractures because of bone-marrow edema and the disruption of the trabecular structure; while in malignant vertebral compression fractures, the diffusion is partially restricted due to the high cellularity of tumor tissue. In non-fracture osteoporosis subjects, however, lower ADC was observed, which was explained by the increase of adiposity in the marrow. Obviously, the pathophysiological background of diffusion properties in marrow is not yet fully understood. In addition, ADC values of different studies are not always comparable due to varying measurement setups, which should be optimized and standardized in the future.

## Proton MR Spectroscopy of Bone Marrow

Proton MRS provides a non-invasive method for quantifying biochemical or metabolic changes in tissues based on chemical shift effect. In bone marrow, MRS can evaluate the changes of water and lipids quantitatively at molecular level. Water resonance at 4.65 ppm and lipid resonance (methylene group $(CH_2)_n$ ) at 1.3 ppm are the dominant signals in bone marrow. Other lipid resonances can be also detected. In particular, olefinic, double bond -CH=CH- protons at 5.31 ppm, has been used to calculate the unsaturation index using *in vivo* MRS. Thus, MRS provides markers not only for fat content (normally calculated as water to fat ratio), but also for the fatty acid composition, which can be clinically significant. Both point resolved spectroscopy (PRESS) and stimulated echo acquisition (STEAM) techniques have been used for MRS acquisition. More advanced spectral techniques, such as 2D correlation spectroscopy (COSY) and total correlation spectroscopy (TOCSY), are being developed in order to quantify the fatty acid composition more reliably. High field and ultra high field provide the advantages of high SNR as well as wider spectral dispersion. The spectral pattern of the marrow depends on location and marrow composition (red vs. yellow marrow). Presence of trabecular bone results in a higher linewidth of the marrow spectra. The relationship between fat and bone is a topic of intense research with increasing appreciation that the marrow fat depot is dynamically linked to bone, affecting both bone quantity and quality. MRS measured marrow fat contents increased significantly with aging and in subjects with low bone mineral density (BMD).  More interestingly, studies suggested that lower unsaturation levels or higher saturation levels of vertebral marrow are associated with higher risk of vertebral fractures, independent of BMD. Thus, marrow fat content and composition have the great potential to be useful non-invasive imaging markers for predicting fractures and for treatment monitoring of osteoporosis.

In summary, MRI provides information related to morphologic and functional changes of bone marrow and is a powerful non-invasive modality of investigating bone marrow disorders.