

MSK MRI Symposium II: Quantitative MR imaging in musculoskeletal field: where are we?

SY28-1

## **T2, T2\*, uTE**

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T2 relaxation times relate to the rate of transverse magnetization decay, caused by the loss of phase coherence induced by a preceding radiofrequency pulse. T2 relaxation times are primarily dependent on water and collagen content of the extracellular matrix as well as the orientation of the collagen fibers. The T2 relaxation time is measured by fitting signal measured in T2-weighted images acquired with different echo times (TE) to a mono- or multi-exponential decay curve. T2 measurements showed significant variation, which was explained by different sensitivity of each sequence to system imperfections including stimulated echoes, off resonance signals and eddy currents. Different fitting methods will also introduce bias to T2 quantification.

T2\* mapping is a technique similar to T2 mapping, but with shorter scan times, as gradient-echo signals are used for T2\*-weighted images and spin-echo signals for T2 imaging are not required. T2\* imaging allows high image spatial resolution and isotropic three-dimensional (3D) evaluation in clinically practical scan times. T2\* mapping has several limitations including higher sensitivity to susceptibility artifacts and magic angle effects.

T2\* mapping can also be used with ultrashort TE (UTE) sequences allowing evaluation of the deep calcified cartilage layer. UTE sequences allow to image tissue components with very short T2 of a few milliseconds or less, which is of particular significance in the deep, calcified layer of the cartilage and the menisci. In the calcified zone close to the bone–cartilage interface, the T2 relaxation times can be 10 ms or less. This region forms an important interface between cartilage and bone as it attaches the cartilage to the bone and transmits forces between cartilage and bone. This layer may, therefore, have an important role in the early cartilage degeneration and UTE imaging may allow to better characterize this region and the associated abnormalities. While ultrashort TE (UTE) sequences have great promise to explore the osteochondral junction, current clinical application is still limited due to spatial resolution and signal-to-noise ratio (SNR).

**Keywords :** quantitative

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## Dynamic contrast enhanced (DCE) MR image

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### DCE-MRI

Perfusion imaging technique

Provide noninvasive imaging biomarkers of tumor biological response to antiangiogenic and vascular targeting agents in a number of clinical trials.

An imaging technique that can measure the density, integrity and leakiness of tissue vasculature

Performed with fast (usually volumetric) gradient echo sequences, repeated several times after IV contrast agent administration

Temporal resolution; depends on the need for spatial resolution & field-of-view (FOV) coverage

### Data acquisition

A region of interest (ROI) is selected → MR images are collected before, during and after a contrast agent (CA) administration  
Each image acquired corresponds to one time point & each pixel in each image results its own time course → analyzed with a mathematical model

Model parameters; blood flow (perfusion), vessel wall permeability, vessel surface area, extracellular extravascular volume fraction

Quantitative DCE-MRI data acquisition require three measurements

a map of the native T1 values before contrast administration

acquisitions of T1WIs following CA introduction at a reasonably high temporal resolution to be able to characterize the kinetics of the CA entry and exit into tissue

a method to estimate the time rate of change of the concentration of the CA in the blood plasma, the so-called arterial input function (AIF).

### DCE-MRI data analysis

employed Tofts model

Creation of time-intensity curves from a ROI

At the first pass, tissue microvascularization and perfusion account for any early enhancement → capillary permeability and enhancement of the interstitial space account for the plateau, washout, or postarterial increase in enhancement.

Observation of the pattern of enhancement over time on a time-intensity curve provides insight into the vascular pharmacokinetics of a lesion that can be assessed qualitatively (characterization of the enhancement pattern) or quantitatively (calculation of various pharmacokinetic parameters such as the mean arterial slope or the time to peak enhancement)

example) distinguishing patterns of enhancement; mainly by assessing the first-pass kinetics

Pharmacokinetic modeling to quantifying lesion blood flow, microvasculature, capillary permeability

; fractional volume of the extracellular extravascular space ( $V_e$ )

; the transfer constant characterizing extravasation of gadolinium containing agents from the plasma ( $K_{trans}$ )

; the transfer constant characterizing reflux of gadopentetate dimeglumine from the extravascular extracellular compartment into the plasma compartment ( $K_{ep} = K_{trans} / V_e$ )

### Musculoskeletal application

Bone and soft tissue tumors

; differentiation of benign & malignant tumors

; recurrence

; tumor heterogeneity

; bone marrow tumors

Changes in the parameters obtained by DCE-MRI; assess longitudinal changes within a tumor, treatment response

; monitoring preoperative chemotherapy or radiotherapy of malignancies

Predict event-free survival in multiple myeloma

Inflammatory rheumatoid disease

**Limitations**

Relatively cumbersome, requires postprocessing time

Variables represent composites of physiologic processes rather than absolute measurements of flow or capillary permeability ; the values of DCE-MRI variables are strongly affected by the definition of the tumor ROI (recommendation; 3D-ROI covering the entire tumor).

Pharmacokinetic models overestimate  $K_{trans}$  and underestimate the blood plasma volume fraction.

Considerable variations in measurement reproducibility reduce the confidence limits for individual measurements in a clinical setting.

Validation of DCE-MRI variables against histologic and serum biomarkers of angiogenesis is incomplete.

**Keywords :** Magnetic resonance, Dynamic contrast enhancement, Tumors

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## Diffusion-weighted imaging in musculoskeletal system

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Diffusion-weighted imaging (DWI) measures the Brownian motion of water at a microscopic level and provides quantitative information concerning the microscopic movements of water at the cellular level. Since DWI was applied for early detection of the stroke, the application of DWI is gradually expanding beyond the brain. In the musculoskeletal system, the relative value of DWI in addition to or as alternatives to conventional MR sequences has been widely researched. In this lecture, the basic principle and recent advancement of the DWI will be briefly reviewed. Then clinical application of DWI in tumor and inflammatory diseases will be discussed.

### Basic principle

The movement of water molecules in tissue is limited by cellular and subcellular microstructures. Diffusion-weighted image (DWI) is capable of measuring the water diffusivity by the application of diffusion sensitizing gradients, which probe the motion of water molecule. Signal loss on DWI is proportional to both the motion of water molecules and the diffusion gradient strength. Actually, the signal loss is exponential as the strength and duration of diffusion gradients increase. This signal attenuation is quantified as the apparent diffusion coefficient (ADC). The ADC value is defined as the slope of the logarithmic decrease in signal intensity between two or more b-values.

### Recent advancement in diffusion metrics

The signal decay of tissues with increasing b-value demonstrates bi-exponential behavior. Therefore, ADC calculated from images with low b-values is generally larger than that obtained from higher b values. The initial exponent caused by signal decay in intravascular water component is referred to as fast diffusion or pseudodiffusion. Whereas, the second component caused by extravascular and extracellular water component is referred to as slow diffusion or true diffusion. Perfusion fraction, and ADC of pseudodiffusion and true diffusion can be calculated by building a hypothetical bi-exponential model. Parametric DWI using this model is called intravoxel incoherent motion (IVIM). As b-value is increased over 1000 s/mm<sup>2</sup>, the ADC gradually decreases. This phenomenon reflects the hindrance of diffusion by heterogeneous tissue elements. Diffusion kurtosis imaging (DKI) is a measure of the heterogeneity of the diffusion environment consisting of various types of cells and their membranes. The structural heterogeneity at subcellular level causes the diffusion displacement probability distribution to deviate substantially from a Gaussian form. The degree of the deviation is quantified with the mean, radial and axial kurtosis.

### Oncologic application of DWI

Restricted water diffusion is observed in malignant tumors and has been attributed to the increased cellularity that restricts water motion. As such, DWI is a measure of cellularity or cellular integrity. Detection of the malignancy is enhanced with DWI of high b-value, where the signal from the malignant cells persist while background signal from normal tissues is suppressed. In addition, DWI can also be used for the characterization of vertebral fractures, discrimination of soft tissue masses as benign or malignancy. Most of all, DWI can be an effective early marker of response for chemotherapy.

### Clinical application of DWI in inflammatory lesions

DWI also can provide the significant information on soft tissue infection. Pus in soft tissue infection exhibits low ADC probably due to the combined effect of inflammatory cells, proteins, cellular debris and bacteria, and bound water molecules to macromolecules. Therefore, DWI also helps detect infectious bursitis, tenosynovitis or septic arthritis by demonstrating restricted diffusion due to the viscous nature of the fluid/pus. DWI is also useful in differentiation of degenerative marrow change and spondylitis based on the observation that mean ADC value in infectious bone marrow was significantly higher than that in normal and degenerative marrow.

**Keywords :** Diffusion-weighted imaging, Musculoskeletal, Oncology, Infection

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## Fat quantification

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Vertebral bone marrow imaging is important for oncologic patient because spine is one of the most common site for metastasis(1, 2).As bone marrow infiltrative process tend to replace the normal fatty marrow lowering fat content, fat quantification is an important issue to diagnose bone metastasis in oncologic patient. Single-voxel magnetic resonance (MR) spectroscopy has been the gold standard technique for accurate quantification of fat content in localized regions of the vertebral bodies (3-6). However, MR spectroscopy remains largely a research tool because it is technically demanding, time-consuming, subject to sampling errors associated with low spatial resolution, and spatially heterogeneous distribution of bone marrow fat content (6-8). In routine clinical practice, conventional MR imaging is usually first used for bone marrow assessment, because malignant bone marrow infiltrative pathology has a lower signal intensity relative to adjacent nondegenerative intervertebral disc on T1-weighted image (T1WI) indicating decreased fat content within the bone marrow (9-12). However, difficulty in qualitative interpretation of MR imaging frequently arises when patient has heterogeneous bone marrow signal intensity including focal red marrow hyperplasia, endplate degeneration or benign vertebral fracture. To overcome qualitative assessment of bone marrow fat content, many studies have investigated to quantify the fatty marrow to facilitate distinction between malignant and benign processes. Semiquantitative assessment with chemical shift imaging, which consists of two dimensional dual-echo in-phase and opposed-phase gradient-echo images, allows detection of fat in abnormal marrow lesions and thus may be predictive of whether it is likely caused by neoplastic or nonneoplastic lesions (13-15). However, it is well known that there are so many confounding factors in calculation of fat or water signal by chemical shift MR imaging, including main magnetic field inhomogeneity effects, the presence of multiple peaks in the fat spectrum, T2\* effects, T1 effects, eddy current effects, and the presence of susceptibility-induced fat resonance shifts (6, 8, 16, 17). With recent technical achievements, various chemical shift-based water-fat separation methods, e.g. DIXON methods, have been used to provide robust separation of water and fat by correcting such confounding factors (6, 16, 18-21, 22, 23). Fat-signal fraction estimated from these methods is expected to improve the diagnostic performance of chemical shift MR imaging in differentiation of benign from malignant lesions. Measurement of the fat-signal fraction (FF) derived from Dixon method with correction of T2\* confounding effects could be a powerful noninvasive tool for the quantitative analysis of bone marrow invasion.

**Keywords :** Dixon method, Bone marrow, Quantification