Diffusion-Weighted Imaging of the Liver
Techniques and Applications

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KEYWORDS

• Diffusion • Liver MRI • Apparent diffusion coefficient • Liver lesion detection • Liver lesion characterization • IVIM • Cirrhosis • Echo planar imaging

KEY POINTS

- Diffusion-weighted imaging (DWI) is based on differences in the mobility of water protons in tissues. Single-shot echo planar DWI sequences are most commonly used in liver imaging.
- DWI is generally more sensitive than fast-spin-echo fat-suppressed T2-weighted imaging for liver lesion detection. The combination of DWI and contrast-enhanced T1-weighted imaging is most sensitive for the detection of malignant liver lesions.
- Apparent diffusion coefficient (ADC) quantification can be used to characterize liver lesions as cystic/necrotic or solid. However, ADC alone is insufficient for lesion characterization.
- ADC has potential value in the evaluation of tumor treatment response, with changes in ADC preceding changes in lesion size.
- ADC quantification and intravoxel incoherent motion DWI have diagnostic value in the noninvasive detection of liver fibrosis and cirrhosis.

INTRODUCTION

Diffusion-weighted imaging (DWI) is a magnetic resonance (MR) imaging technique that reports on the physical process of microscopic thermal motion of water molecules in biologic tissues.[1,2] The differences in the mobility of water protons create image contrast, which is influenced by the interaction of water molecules with cellular membranes, macromolecules, degree of cellular density, and the size of the extracellular extravascular space.[3] DWI is increasingly being used in liver MR imaging given the recent technologic advances and improvements in image quality, including the introduction of echo planar imaging (EPI), parallel imaging, multichannel coils, and high amplitude gradients.

Accurate lesion detection and characterization are essential for treatment planning for patients with primary or secondary liver tumors, especially in selecting patients who may undergo liver resection or locoregional or systemic therapies.[4,5] DWI can be used for focal liver lesion detection and characterization, for the assessment of tumor response, and for the evaluation of diffuse liver disease.[3] This sequence is easily incorporated into routine clinical protocols, especially given that DWI is a noncontrast technique and may be performed either before or after contrast administration. DWI can be acquired rapidly within a breath hold, and it provides

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both qualitative and quantitative information as an adjunct to conventional sequences. Quantification of apparent diffusion coefficient (ADC) has enabled differentiation of solid cellular lesions from cystic or necrotic lesions.[6] ADC quantification has also demonstrated promising results for predicting tumor response to therapy.[7,8] The purpose of this article is to review the basic principles of DWI, discuss protocol optimization, summarize the performance of DWI compared with conventional sequences, discuss the role of DWI in the evaluation of treatment response, and examine the potential role of DWI in the assessment of liver fibrosis.

DWI TECHNIQUE

Concepts

Principles of molecular diffusion

Diffusion describes random molecular motion occurring in tissues as a result of thermally activated translations of atoms and molecules. The resulting motion can be described as a stochastic process, with a gaussian probability distribution given as follows:

$$P(r,\ t) \sim e^{-r^2/4Dt} \qquad \mathbf{1}$$

where D is the diffusion coefficient and r is the distance traveled by the diffusing molecule during time (t)

D depends on the species undergoing diffusion and on the medium in which diffusion occurs. For water self-diffusion at 37°C, $D = 3.0\ mm^2/s$.[9] Larger molecules tend to undergo slower diffusion resulting in lower D, as is also the case of diffusion in fluids of higher viscosity. The gaussian distribution in Equation 1 describes free diffusion of molecules in an infinite medium. An important variation of this concept is restricted diffusion whereby molecular motion is restrained within hard boundaries. Restricted diffusion, which is common in tissues, generally leads to lower D and nongaussian distributions.

DWI physics

Nuclear MR offers a novel way to measure diffusion, via the application of magnetic field gradients. If such gradients are deployed in pulses of opposed polarity (using a gradient or spin-echo sequence), moving spins undergo dephasing while static spins show a null phase at the echo time. By considering the effect of a stochastic diffusion process on the magnetic signal, one can derive the signal attenuation resulting from the application of pulsed gradients in a spin-echo experiment[10]:

$$S = S_0 e^{-bD}$$

with S_0 the signal in the absence of gradient and b a function of the applied gradient

$$b = (\gamma G \delta)^2 \left(\Delta - \frac{\delta}{3}\right)$$

with γ the spin gyromagnetic ratio, G and δ the gradient strength and length, and Δ the time separating the gradient pair.

The factor b, called *b value*, determines the strength of the diffusion weighting. The diffusion gradients can be inserted in an imaging experiment as a preparation module in order to provide additional contrast to the MR imaging signal and to estimate molecular diffusion in different organs and tissues.

Quantification of diffusion properties in tissues

In its simplest form, the diffusion experiment involves acquiring 2 sets of images, one at low or zero b value and another at high b value, to derive a voxelwise diffusion coefficient. Because multiple tissues and compartments may be present in a single voxel, the derived coefficient is referred to as an ADC that reflects a sum of exponential decays rather than a single, pure diffusion constant. In addition to the ADC, which assumes monoexponential decay of diffusion signal, there are models that account for the more complex properties of tissues:

- Flowing blood contributes to diffusion signal and leads to measureable effects on the diffusion decay. The intravoxel incoherent motion (IVIM) approach[11] integrates these effects in a biexponential model whereby a faster decaying exponential, reflecting perfusion effects at low b values, can be separated from slower exponential decay reflecting true water diffusion. This approach is especially appropriate in highly perfused organs, such as the liver.[12–18]
- Because of restricted diffusion in tissues, the gaussian model of Equation 1 is not valid anymore, and diffusion weighting has a less trivial form. A successful approach has been diffusion kurtosis imaging (DKI) that evaluates restricted diffusion by analyzing the nongaussian diffusion distribution, using an additional constant derived from acquisitions at a higher b value.[19] Recently, DKI has been investigated in liver explant studies, whereby results have been correlated with hepatocellular carcinoma (HCC) tumor cellularity.[20]
- Biologic tissues can be anisotropic and, therefore, so can diffusion decay. The ADC measured using different diffusion gradient directions may differ in an anisotropic sample; therefore, diffusion tensor imaging[21] (DTI) has been proposed in order to extract direction-specific information using at least 6