Diffusion and Perfusion MR Imaging of the Prostate

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MR imaging plays an important role in the initial detection, localization, and staging of prostate cancer and the assessment of posttreatment changes in prostate cancer. In the near future, more image-guided techniques will become available, permitting precise biopsies and targeted focal treatment. Accurate and detailed information on tumor localization and size is needed to perform these image-guided interventions and therapies optimally. This article focuses on the role of diffusion-weighted MR imaging (DWI) and dynamic contrast-enhanced (DCE) MR imaging (or perfusion-weighted MR imaging) of the prostate. Background aspects and the clinical usefulness of DWI and DCE MR imaging for assessment of prostate cancer are reviewed.

DIFFUSION WEIGHTED IMAGING

Diffusion and Prostate Cancer

Water molecules exhibit random motion in tissue, related to temperature (Brownian effect).[1] DWI can quantify this water motion in an indirect manner.[2,3] The DWI pulse sequence labels hydrogen nuclei in space, of which most is water molecules at any moment, and determines the length of the path that water molecules travel over a short period of time. DWI estimates the mean distance traveled by all hydrogen nuclei in every voxel of imaged tissue. The greater this mean distance the more self-diffusion of water molecules has occurred in a certain time interval.[4] The degree of restriction to water diffusion in biologic tissue is inversely correlated to tissue cellularity and the integrity of cell membranes. Free motion of water molecules is more restricted in tissues with a high cellular density. The sensitivity of the DWI sequence to water motion can be varied by changing the gradient amplitude, expressed as the b-value. By performing DWI using different b-values, quantitative analysis can be made to determine the apparent diffusion coefficient (ADC).

In a volume of pure water this self-diffusion is equal in all directions, hence isotropic, and not restricted by any barrier. Because diffusion in tissue is limited by cellular structures, to establish a reliable estimate of this mean distance traveled by hydrogen nuclei, DWI is acquired in at least three different orthogonal directions for each b-value.[4,5] This phenomenon of varying restriction of self-diffusion along different axes is called "anisotropy" and can also be used for tissue characterization. As in linear aligned tissue this anisotropy is more pronounced because there is one direction that contributes most to the DWI. Diffusion tensor imaging is a specific technique that

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quantifies the level of anisotropy in tissue, expressed in a fractional anisotropy value. This is low in imaged tissue without substantial anisotropy and is higher in imaged tissue in which the larger part of diffusion takes place in one direction.[5,6] Diffusion tensor imaging can be used in addition to DWI to determine the structural organization of tissue along which diffusion takes place.

DWI typically has T2- and diffusion-weighted characteristics. The intensity of the signal on the diffusion-weighted image represents a combination of signal from the T2 relaxation and the dephasing caused by water motion in the presence of the diffusion gradients. At low b-values there is greater contribution from the T2 signal, and at higher b-values contrast is determined more by relative diffusion.[7] When a diffusion image is bright because of high T2 signal rather than restricted diffusion, it is known as ''T2 shine-through'' effect. ADC maps should be obtained with at least two b-values to correct for the T2 shine-through effect, typically a low b-value, between 0 and 50 s/mm^2, and a high b-value. Tissue microperfusion can contaminate the signal attenuation in DWI acquisition, which could be decreased by using an additional low b-value greater than 0 (eg, b = 50 s/mm^2) and a high b-value.

To minimize the influence of bulk motion as a distorting factor and minimizing T2 shine-through, typically a TE as short as possible is chosen. Typical sequence parameters for the prostate (as used in the authors' institution) include TR 2600 milliseconds; TE 91 milliseconds; and b-values of 0, 50, 500, 800 s/mm^2 in three orthogonal directions with parallel imaging (**Table 1**).

Diffusion-Weighted MR Imaging Characteristics of Prostate Tissue

DWI was initially used for the early detection of cerebral ischemia.[8] The evolution of DWI characteristics in cerebral ischemia over time has classically been attributed to the extracellular to intracellular distribution of hydrogen nuclei caused by different types of edema.[9] It has been postulated that extracellular water molecules have a far higher range of self-diffusion because they are not bound within membranes or by other cellular structures.[10,11] When this is translated to prostate tissue, which is predominantly glandular tissue, the predominant contribution of the extracellular component is from tubular structures and their fluid content, whereas the intracellular component is determined by the epithelial and stromal cells. Fractional anisotropy is determined along the axis of the tubular structures of normal prostate tissue. A prerequisite for the correct interpretation of diffusion and ADC images relies on good knowledge of the diffusion characteristics of the different anatomic zones of the prostate and of benign prostatic conditions compared with prostate cancer.[12]

The normal prostatic gland is rich in tubular structures. This allows for abundant self-diffusion of water molecules within their contents and provides high ADC values. In most cases, the peripheral zone can be easily discriminated from the central gland on DWI, because it displays relative higher ADC values.[13–15] The exact background of this phenomenon remains unclear, because the exact ratio of extracellular to intracellular components for the different anatomic zones of the prostate has not yet been described. The central gland by observation consists of more compact smooth muscle and sparser glandular elements than the peripheral zone, however, leading to lower extracellular to intracellular fluid ratio.[16] Furthermore, an age-related increase of T2 signal intensity of the peripheral zone compared with the central gland has been observed,[17] and an age-related increase in ADC values in both central gland and peripheral zone has been observed,[15] which are most likely caused by atrophy in the prostate leading to reduced cell volume and enlarged glandular ducts.

Benign prostatic hyperplasia (BPH) gives rise to nodular adenomas in the transition zone and with time these compress the central zone to form a pseudocapsule, occupying the complete central gland. The peripheral zone is usually not affected by BPH and retains its own histologic characteristics. BPH is defined by hyperplasia of all cells that constitute the central gland, with glandular, muscular, and fibrous compartments more or less evenly involved. This nodular hyperplasia gives rise to inhomogeneous diffusion patterns and because tubular structures often remain in place, the increased cellular density of hyperplasia, which is far less predominant than in prostate carcinoma, might explain the observed reduction in ADC levels of the central gland on DWI, because of decreased ratio of extracellular to intracellular volume. Because BPH has inhomogeneous diffusion characteristics, however, an increase in ADC also has been observed.[18]

Prostatitis almost uniquely originates in the peripheral zone. With respect to MR imaging, chronic prostatitis is of far more importance than the acute prostatitis counterpart because it is asymptomatic in many cases or its symptoms might mimic BPH, often associated with elevated prostate-specific antigen levels, raising the suspicion of prostate cancer. Histologically, chronic prostatitis is characterized by extracellular edema surrounding the involved prostatic cells with concomitant