Detection and Characterization of Focal Liver Lesions using Respiratory-Triggered Diffusion-Weighted MR Imaging (DWI)

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Diffusion-weighted MR imaging (DWI), theoretically described as far back as the 1950s and 1960s by Carr/Purcell and Stejskal/Tanner [1, 2], has become an established method in neuroradiology since the introduction of the intravoxel incoherent motion technique by Le Bihan and coworkers in 1988 [3]. Due to a number of technical challenges, the use of DWI was initially confined to the brain with its low incidence of movement artifacts and the high homogeneity and signal-to-noise ratio (SNR) of brain tissue. Physiological motion artifacts (e.g. motility of the bowel, cardiac pulsation, respiratory motions) and the heterogeneous composition of many extracranial organs had precluded the application of DWI in body imaging until a series of technologic advances such as the development of echo-planar imaging (EPI), high-gradient amplitudes, multichannel coils and parallel imaging techniques enabled the acquisition of high quality diffusion-weighted images of the body. Over the last few years, DWI has become increasingly used in extracranial organs to detect and characterize tumors for the functional evaluation of different organs and for response evaluation in oncology (for review see [4, 5]).

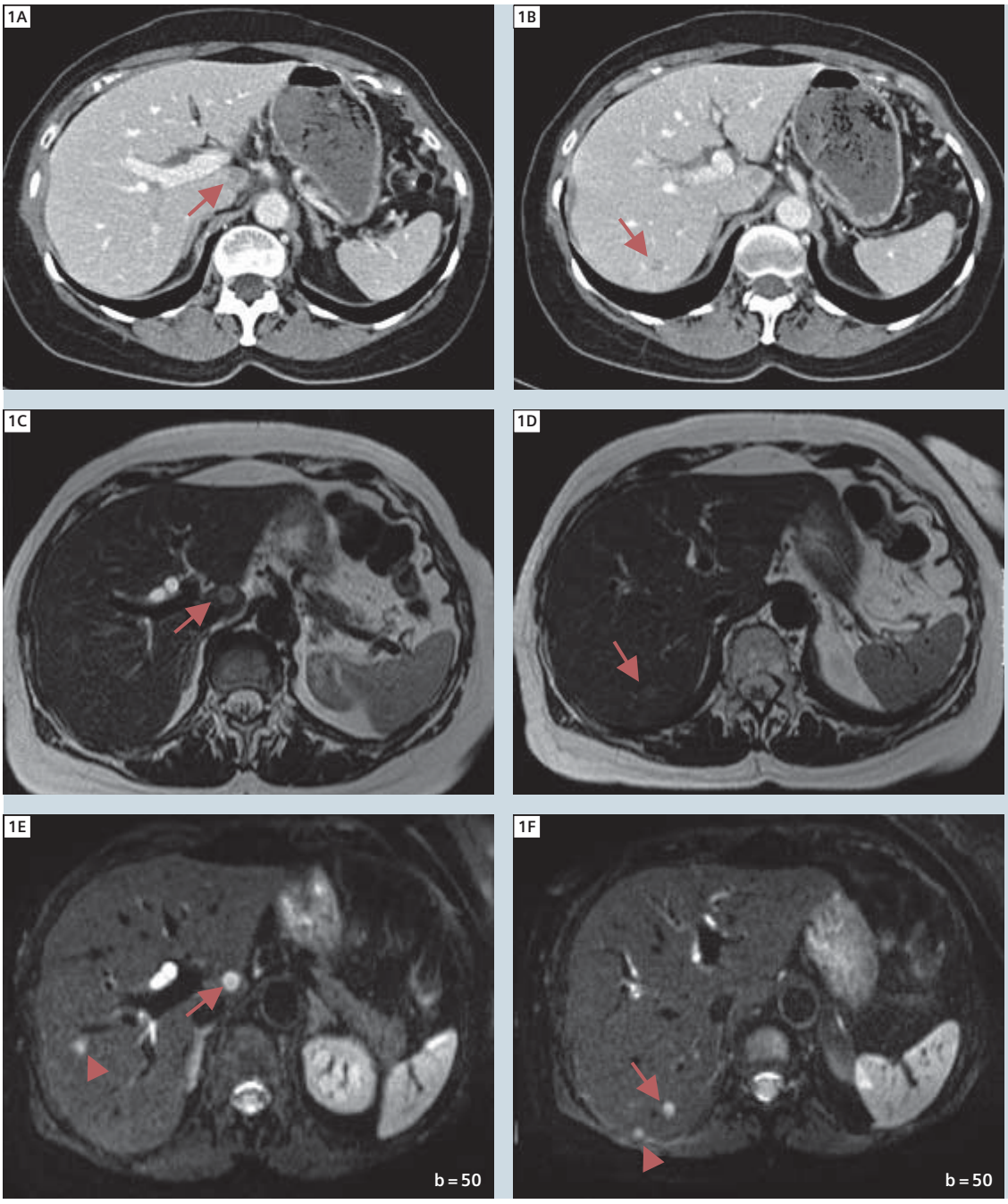
The term 'diffusion' defines the random thermally induced motion of water molecules in biologic tissues ('Brownian motion'). The addition of motion probing gradient (MPG) pulses to MR sequences allows quantifying the combined effects of capillary perfusion ('pseudodiffusion') and diffusion in vivo by means of the apparent diffusion coefficient (ADC). For DWI, diffusion gradients are applied before and after the 180°-pulse of a single-shot spin-echo echoplanar imaging (SSEPI) sequence, for example. The b-value represents the diffusion factor [s/mm^2] and represents amplitude and duration of the diffusion gradients. The ADC [mm^2/s] describes the slope of the curve of signal intensity vs. b-value, and is calculated using the following formula: $ADC = (\ln SI_1/SI_2)/(b_2-b_1)$ where b_1 and b_2 are motion-probing gradient factors (diffusion factors) of sequences S_1 and S_2, and SI_1 and SI_2 are signal intensities in these sequences.

Liver DWI protocol used in our institution [6]

At the Department of Radiology of the Technical University of Munich we use a SSEPI sequence at a 1.5T scanner (MAGNETOM Avanto) for DWI. MR imaging is performed with two six-channel body phased array coils anterior and two spine clusters (three channels each) posterior. As image quality of respiratory-triggered sequences has been shown to be superior to breath-hold sequences, we obtain diffusion-weighted images applying respiratory-triggering using prospective acquisition correction (PACE). A single-shot EPI readout is preceded by a diffusion-sensitizing block consisting of two 180° radiofrequency pulses and four motion probing gradient (MPG) pulses in order to reduce the influence of eddy currents compared to the conventional Stejskal-Tanner preparation. The technical parameters are as follows: echo time: 69 ms; echo train length: 58; echo spacing: 0.69; receiver bandwidth: 1,736 Hz/pixel; spectral fat saturation; field of view: 263 × 350 mm; matrix: 144 × 192; number of signal averages: 3; section thickness: 5 mm; intersection gap: 0.5 mm; 30–45 transverse sections acquired; ≈ 4–6 min acquisition time, b-values of 50, 300 and 600 s/mm^2. Integrated parallel imaging techniques (iPAT) by means of generalized autocalibrating partially parallel acquisitions (GRAPPA) with a twofold acceleration factor is used to shorten the echo train length.

Detection of focal liver lesions using DWI

Over the last few years several studies have investigated the use of DWI in the detection of focal liver lesions (FLL). DWI was superior to T2-weighted sequences [7–10] and to superparamagnetic iron oxide (SPIO)-enhanced MR imaging in the detection of focal liver lesions [11]. The detection of small FLLs in particular seems to be significantly improved by DWI [7, 9, 10] (Fig. 1). High SNRs and high lesion-to-liver signal intensity ratios are seen especially at low b values alleviating the depiction of focal liver lesions. In addition, the 'black blood effect' of diffusion-weighted images makes it easier to distinguish small FLLs from hepatic vessels. Furthermore, DWI seems to improve the perceptibility of FLLs, especially of hepatocellular car-

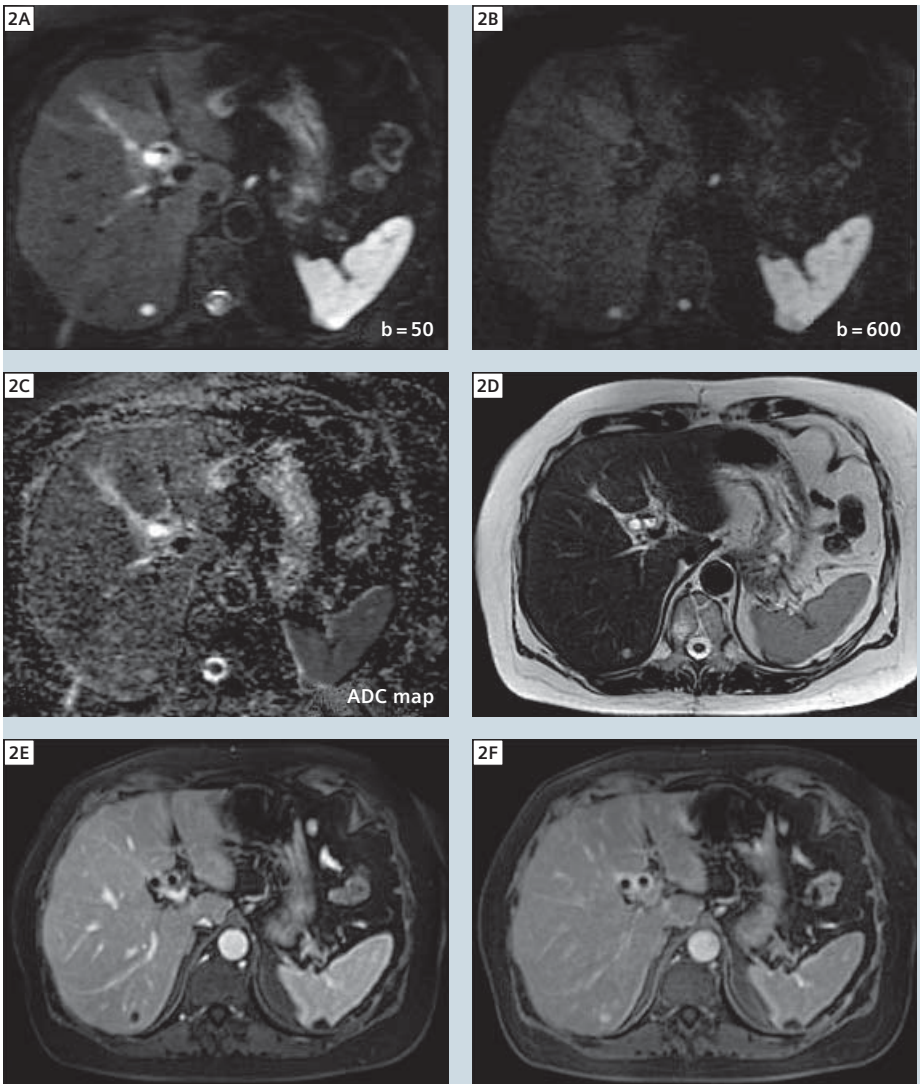


1 Detection of focal liver lesions using DWI. Multi-slice CT (MSCT, A, B), T2-weighted TSE (C, D) and diffusion-weighted SSEPI MR images (E, F) of a patient with breast cancer. On MSCT and T2-weighted MR images one liver metastasis can be seen on each image (arrows). However, on diffusion-weighted images on each slice an additional metastasis can be identified that cannot be seen on MSCT and T2-weighted MR images (arrowheads).

cinomas (HCCs) in patients with liver cirrhosis as that the heterogeneity and increased signal intensity of the cirrhotic liver parenchyma as a result of nodular regeneration, fibrosis, and scarring appears to be less pronounced on DWI compared to T2-weighted images [7]. However, in one study DWI was inferior to Manganese dipyridoxyl-diphosphate (MnDPDP)-enhanced MRI in the detection of FLLs [12] and the potential benefit of DWI in association or compared with conventional gadolinium-enhanced liver MR imaging remains to be investigated [7].

Characterization of focal liver lesions using DWI

Differences in cellularity between benign and malignant liver lesions resulting in different diffusion properties of water protons within these lesions are reflected by different ADC values measured by DWI. Typically, benign liver lesions like cysts or hemangiomas that are hypocellular compared to liver parenchyma allow relatively unhindered diffusion of water protons resulting in high ADC values (e.g. ~ 2 × 10–3 mm^2/s in hemangiomas, ~ 3 × 10–3 mm^2/s in cysts) compared to low ADC values in commonly hypercellular malignant liver lesions such as metastases or HCCs (e.g. 1.1 – 1.3 × 10–3 mm^2/s in HCCs and 1.1 – 1.4 × 10–3 mm^2/s in metastases) where diffusion of water protons is

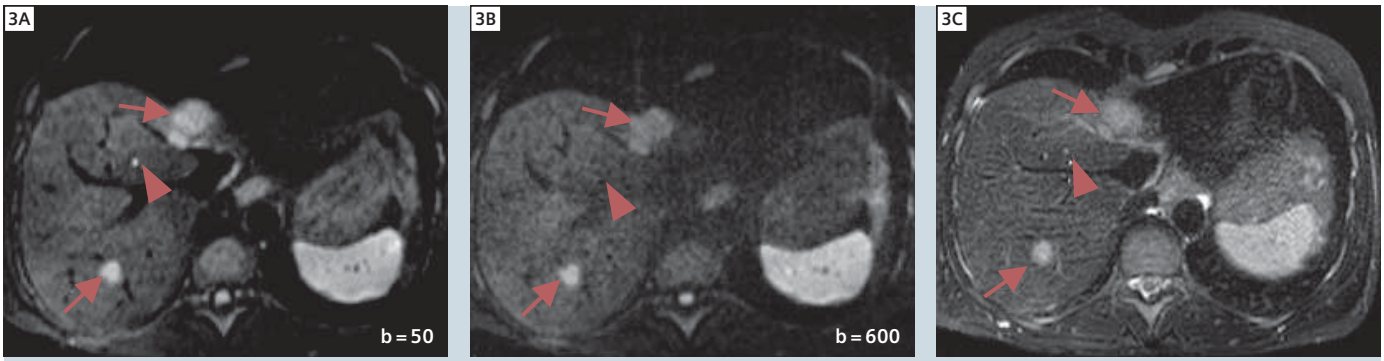


2 Characterization of focal liver lesions by DWI. Diffusion-weighted SSEPI (A–C), T2-weighted TSE (D) and Gd-enhanced T1-weighted MR images (3D Volume Interpolated Breathhold Examination [VIBE] with fat saturation, E, F) in a patient with pancreatic cancer. A small focal liver lesion in segment 7 is hyperintense on the b-50 image (A), shows signal loss at a high b-value (B) and thus, a moderately high ADC value (1.96 × 10–3 mm^2/s, c) typically seen in hemangiomas. The lesion is hyperintense on the T2-weighted image (D) and shows centripetal enhancement on dynamic post-contrast images (E, F), features typical for hemangiomas.

more restricted [6] (Figs. 2, 3). Thus, several studies have identified significantly lower ADC values in malignant compared to benign FLLs [6, 7, 13]. A feasible threshold ADC for differentiating benign from malignant FLLs would be 1.5 – 1.7 × 10–3 mm^2/s [6]. As in the brain, secondary to highly viscous pus containing proteinaceous fluid and necrotic cells, hepatic abscesses show extremely low ADC values in most cases and therefore are an exception to this rule [14, 15]. However, the differentiation between benign solid FLLs like focal nodular hyperplasia (FNHs) and adenomas from malignant lesions often is impossible by DWI as there is considerable overlap of ADC values between both groups. Furthermore, although mean ADC values of hemangiomas and metastases are significantly different, characterizing a single liver lesion by means of the ADC value prospectively can be difficult. Thus, in our opinion, DWI should be used as a complementary method in the characterization of FLLs.

DWI for response evaluation of treated liver tumors

The value of DWI in the detection and prediction of tumor response to chemotherapy, radiation therapy, or other modalities is increasingly studied. Effective anticancer treatment results in lysis of tumor cells, loss of cell membrane integrity, increased extracellular space, and, consequently, an increase in water diffusion reflected by a rising ADC value [5]. Promising animal studies report a significant rise in ADC values in patients with HCC who respond to transcatheter arterial chemoembolization [16]. In addition, amongst patients with colorectal hepatic metastases, an increase in ADC was observed in those with at least a partial response to treatment, while no ADC increase was observed in non-responders [17]. Furthermore, in the same study, metastases with low baseline ADC values have been shown to respond better to chemotherapy than tumors that exhibit high pre-treatment ADC values [17]. One possible explanation is that tumors with high pre-treatment ADC values are likely to be more necrotic than those with low values. Necrotic tumors frequently are hypoxic, acidotic, and poorly perfused, leading to diminished sensitivity to chemotherapy and to radiation therapy [5].



3 Characterization of focal liver lesions by DWI. Diffusion-weighted SSEPI (A, B) and fat-saturated T2-weighted TSE MR images (C) in a patient with rectal cancer. Two metastases (arrows) are hyperintense both on the b-50 (A) and b-600 image (B) resulting in low ADC values (1.18 and 1.27 × 10–3 mm²/s, respectively) typically seen in malignant liver lesions. A small cyst (arrowhead) is hyperintense on the b-50 image (A) but shows considerable signal loss on the b-600 image (B) resulting in a high ADC value (2.79 × 10–3 mm²/s). Note that on the T2-weighted image the small cyst can hardly be differentiated from a small metastasis (C).

Conclusion

In summary, DWI is a valuable tool in the detection of FLLs, especially with regard to small lesions. In the characterization of FLLs, DWI is of use as an additional, complementary method being interpreted in conjunction with other MR sequences. Finally, DWI seems to have great potential in the response evaluation of treated liver tumors: This has to be investigated in further studies.

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