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Liver Lesions: Added Value of DWI

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In this presentation, we will review:

1. The added value of DWI for detection of liver lesions compared to other sequences.
2. The added value of DWI for characterization of liver lesions.

Liver lesion detection

- ***Comparison with T2WI***

DWI has been shown to be equal or superior to T2-weighted imaging (T2WI) for liver lesion detection [1-9]. Several studies have compared DWI and T2WI in terms of lesion detection, generally showing improved detection with DWI [1, 5, 8, 9]; or in terms of image quality, showing comparable image quality with DWI using low b values [10, 11]. The improved lesion detection with DWI compared to T2WI relate to improved image contrast using low b values and lack of blurring with SS EPI, compared to T2 FSE or single shot FSE sequences [10]. Black-blood DWI has also been recently proposed as an alternative to T2WI at 3T, giving comparable image quality, improved suppression of fat and blood signals, high contrast-to-noise ratio and SNR [11]. Our experience (in 53 patients with 211 lesions) is similar, also showing that DWI performs better than standard breath-hold T2WI for lesion detection using b value of 50 s/mm^2, with sensitivity of detection of 87.7% vs. 70.1% for all lesions, and 86.4% vs. 62.9% for malignant lesions ($p < 0.001$), respectively for DWI and T2WI [7]. In addition, DWI significantly improved detection of small malignant lesions (< 2 cm) when compared to breath-hold T2WI (78.5% vs. 45.8%, $p < 0.001$).

- ***Comparison with extracellular gadolinium based contrast agents***

A retrospective comparison between DWI and dynamic 3D contrast-enhanced T1WI before and after gadopentetate dimeglumine administration on a population of 51 patients with liver metastases was performed by Hardie et al [12]. Both per-patient and per-lesion analysis did not reveal any significant differences in detection rate, sensitivity and specificity between the two image sets for observer 1 and for pooled data (between 2 observers); however a lower sensitivity was observed with DWI for observer 2 (more experienced than observer 1), with no difference in specificity. In addition, results from the study of Another recent study retrospectively compared a free-breathing DWI sequence (using b 0, 600 and 1000 s/mm^2) to fat suppressed T2WI and dynamic T1WI (using gadopentetate dimeglumine) separately and in combination for the detection of 64 pathologically proven hepatic metastases [13]. In their study, the sensitivity of DWI (84.4%) resulted to be 7.8-26.9% greater than that of T2WI (68.8%) and higher than that of CE T1WI (79.7%) for the detection of metastases. As confirmation of the advantage of combined approach DWI with contrast-enhanced T1WI, results of a study of Kenis et al. [14] revealed a non-significant ($p = 0.09$) difference in diagnostic accuracy between contrast-enhanced T1WI (AUC = 0.89) and DWI (AUC = 0.85), with an substantial improvement by using a combined approach (AUC = 0.93).

There is limited data on the use of DWI for detection of HCC [15-21]. Piana et al [20] which assessed the role of DWI vs. CE T1WI for the detection of HCC (> 10 mm) in a large number of patients (91 patients and 109 HCCs) reported higher sensitivity for DWI compared to CE T1WI for HCC detection. The sensitivity of conventional MR imaging criteria (wash-in/wash-out) for the diagnosis of HCC was 59.6% for both radiologists, compared to 81.7%-72.5% for DWI alone.

Recently, Park et al [22] evaluated the performance of DWI for the detection of HCC in pre-liver transplant patients, compared and combined to contrast-enhanced (CE) T1WI, using liver explant as the standard of reference. They observed generally better performance of CE T1WI (per-lesion sensitivity was significantly higher for CE-set vs. DW-set 59.0% vs. 43.8%). When stratified by lesion size, the difference was significant only for lesions with a size between 1 and 2 cm (42.0% for DW-set vs. 74.0% for CE-set, $p=0.001$). The addition of DWI to CE T1WI improved sensitivity for the more experienced observer.

- ***Comparison with gadoxetic acid***

Bimodal contrast agents with combined dynamic imaging and hepatocyte-specific imaging in one examination can improve accuracy of focal liver lesion detection and characterization, especially for detection of small hepatic metastases and differential diagnosis of hypervascular lesions, compared with extracellular contrast agents [23-27]. At this point, there are few published studies comparing or combining the accuracy of gadoxetic acid-enhanced MRI to DWI for the detection of metastatic liver lesions [28-30]. In the study by Shimada et al [28], there was a better diagnostic performance using gadoxetic acid compared to DWI (AUC: 0.958-0.966 and 0.881-0.906 respectively; p=0.04 for observer 1 and no significant difference for observer 2) for detection of small metastatic lesions (≤ 2 cm), without significant differences in sensitivity and positive predictive values. Compared with previous studies using extra-cellular agents, Shimada et al reported a higher accuracy, likely due to the combination of Gadoxetic acid with 3T.
Lowenthal et al [29], performed at 1.5T, breath-hold DWI was compared to gadoxetic acid-enhanced T1WI. The authors demonstrated superiority of gadoxetic acid (detection rate respectively: 94.4% and 100%, 2 observers) compared to DWI (detection rate: 78.3% and 97.5%) and contrast-enhanced T1WI at the dynamic phase (detection rate: 81.5% and 89.9%). Despite lack of a low b value acquisition (b factors: 0 and 500 s/mm^2) and relatively low in plane resolution (slice thickness 8 mm), subgroup analysis revealed a substantially higher sensitivity for small lesions (≤ 1 cm) and lower accuracy of DWI for the left lobe (7 out of 9 misclassified lesions were located in the left lobe). Both unenhanced and contrast-enhanced image sets resulted in a high diagnostic accuracy (AUC 0.98) without significant differences [29].
Park et al [30] observed a significantly higher accuracy for the combination of gadoxetic acid-enhanced T1WI and DWI for diagnosis of small HCCs (0.952) compared to either technique alone (0.902 for contrast and 0.871 for DWI). Lesion sensitivity was also higher for the combined set (91.1%-93.3%) than in gadoxetic acid set (80.5%-82.1%) or DWI set alone (77.7%-79.9%).

On HBP (hepatobiliary phase) images after administration of gadoxetic acid, there could be minimal signal differences between vessels and small focal lesions, and small hepatic lesions may be missed, and DWI can easily differentiate these small metastases from vessels. On the other hand, artifacts caused by cardiac motion and by magnetic susceptibility artifacts due to the proximity of the lungs, can limit the sensitivity of DWI for the detection of small hepatic lesions at the upper regions of the liver and the left lateral hepatic lobe; while these lesions can be clearly detected on gadoxetic acid -enhanced images.

Studies have suggested the acquisition of DWI after the administration of Gadoxetic acid, by showing minimal or no significant differences in signal intensity and ADC values before and after contrast injection [31-33]. That implies that the acquisition of DWI during the interval between dynamic MRI and hepatobiliary phase can be effective and time-saving, without degrading image quality.

Liver lesion characterization

- ***Role of visual assessment***

Visual assessment of DW images which include higher b values (≥ 500 s/mm^2) can help distinguish between solid and cystic lesions. Whilst simple cysts typically show suppression of high signal intensity at higher b values, T2 shine-through may occasionally be encountered. As a general observation, both benign and malignant solid lesions may demonstrate residual high signal on higher b value images, and would be difficult to characterize by visual assessment of the DWI images alone. Thus, once a cellular hepatic lesion is identified visually, further characterization usually relies on conventional morphologic (with or without contrast enhancement) imaging, supplemented with ADC measurements. Specifically, in malignant lesions, DWI is useful in distinguishing the different components of tumors (cystic/necrotic vs. solid components). On visual inspection of diffusion images alone, false positive identification of malignant disease may result from T2-shine through, partial volume effects from adjacent structures, and cellular benign lesions (e.g. FNH, adenoma and abscess). False negatives may result from metastases arising from mucinous tumors, which can mimic the appearance of a cyst, well-differentiated tumors (e.g. well-differentiated HCC), necrotic lesions (either primarily necrotic or secondary to treatment) and image artifacts which could obscure lesion visualization. In our experience, lesion characterization as benign or malignant was correct in 89% of lesions using DWI with visual assessment [7].

- ***Role of ADC quantification***

ADC quantification requires minimum acceptable SNR at higher b values [34], as well as minimal lesion size of 1.5 to twice the in-plane resolution so to avoid partial volume effect. As a general rule, statistically higher ADC values have been demonstrated for benign lesions compared to malignant lesions, with variable overlap [7, 35-44]**.** The more common benign hepatic lesions, cysts and hemangiomas have significantly higher ADC values compared to normal liver parenchyma or other lesions, including metastatic lesions. Hemangiomas, in particular, have mean ADC values lower than that of cysts, but generally higher than solid focal lesions. In clinical practice, the additional value of DWI in distinguishing cysts and hemangiomas from other lesions is small, as T2WI and CE T1WI sequences easily and reliably are able to diagnose them. However, in cases of contraindication to administration of contrast media, measurements of ADC values can be useful to differentiate between cysts, hemangiomas and solid hepatic lesions. Although cysts and solid lesions are easily distinguishable on ADC map, sometimes metastases and hemangiomas can have similar DWI features. Cystic, mucinous or necrotic metastases may show relatively high ADC values, while occasionally hemangiomas display portions with low ADC values [35, 38, 45]. Conversely, liver metastases originated by neuroendocrine tumors, histopathologically constituted by highly concentrated small round cells, are usually characterized by low ADC values [44]. Among cystic lesions, since diffusion signal depends principally on the degree of viscosity of the fluid, liver abscesses are characterized by hyperintensity on DW images and low ADC, which distinguishes them from cystic or necrotic tumors [46, 47]. For solid benign liver lesions (FNH, adenoma), intermediate ADC values have been reported, with no statistical difference observed with malignant lesions, likely secondary to the high cellularity of these [39, 42, 48]. HCC usually display low ADC values, except when treated and/or necrotic [49]. A large variability in ADC values have been described in the literature for similar type of lesions, due to the lack of standardization of sequence parameters, particularly, in the choice of b values [50, 51]. Therefore, the reported ADC thresholds for lesion characterization can be considered reliable only when applied on imaging studies obtained with similar techniques and b values. It is generally suggested to use at least two b-values (with either a low and a high b value), in order to reliably discriminate malignant and benign focal liver lesions, also allowing reasonable acquisition time of diffusion sequence [39, 43, 52]. In a recent systematic meta-analysis [53] compiling 14 diagnostic studies matching inclusion criteria, eight studies reported a cutoff ADC in the distinction between malignant and benign FLLs, ranging from 1.47–5.5 x 10^3 mm/s^2 (in 6/8 studies the threshold was 1.47-1.6 x 10^3 mm/s^2). Diagnostic performance, expressed by the area under the curve of the summary receiver operator characteristic (SROC) in this meta-analysis was 0.96 (95% CI 0.94–0.98) [53]. The sensitivity ranged from 0.74–1.0 (mean 0.91), while the specificity ranged from 0.77–1.00 (mean 0.93) indicating that DWI could be used as a helpful diagnostic test for diagnosis of malignant hepatic lesions. However, when cysts and hemangiomas are excluded, the specificity decreased substantially suggesting that the ADC cut-off is not as effective in distinguishing malignant lesions from adenomas, FNHs, or abscesses [7, 36, 39, 54, 55].

Conclusion

There is compelling data showing better performance of DWI compared to T2WI for liver lesion detection. In addition, even if more data demonstrating the added value of DWI over contrast-enhanced imaging is needed, the combination of DWI with conventional sequences (including T2WI and contrast enhanced sequences) may potentially improve the diagnostic accuracy of conventional imaging alone for liver lesion detection and characterization.

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