Combining diffusion-weighted MR imaging with Gd-EOB-DTPA enhanced MR imaging improves the detection of colorectal liver metastases

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Introduction:
In patients with colorectal cancer, accurate assessment of the size, location and segmental distribution of liver metastases on a per-lesion basis is critical for treatment planning. Diffusion-weighted MR imaging (DW-MRI) has a high sensitivity and specificity for liver metastasis detection [1-3]. Combining DW-MRI with T1-weighted imaging after liver specific contrast medium Magalofadipir trifosodium (MnDP) administration, improved the diagnostic accuracy compared with either technique alone [2]. Gadolinium-ethoxybenzyl-DTPA (Gd-EOB-DTPA; Primovist®) is a relatively new hepatocyte selective MR contrast medium that is useful for detecting smaller (< 1 cm) liver metastases [4]. Delayed T1-weighted Imaging at 20 – 60 minutes after contrast demonstrates metastases as hypointense lesions against the avidly enhancing liver parenchyma. However, the value of combining DW-MRI with Gd-EOB-DTPA enhanced MR imaging for detecting colorectal liver metastases has not been established.

Purpose: The purpose of this study was to compare the diagnostic accuracy of Gd-EOB-DTPA enhanced MRI, DW-MRI and the combination of both techniques for the detection of hepatic metastases in patients with colorectal cancer.

Materials and Methods
23 patients with colorectal cancer have been evaluated so far in this on-going study. Inclusion criteria: (a) histopathological proven colorectal cancer, (b) suspected liver metastases on imaging (CT/ultrasound/MRI/18FDG-PET) and (c) patients deemed suitable for neoadjuvant chemotherapy prior to surgery or minimally invasive therapies. MR imaging was performed on a 1.5T system (Siemens’ Avanto, Erlangen, Germany). Imaging sequences: Pre-contrast Breath-hold T1W in/oppose phase gradient-echo; fat-suppressed respiratory triggered T2W turbo-spin echo; T2W HASTE and free breathing single-shot echo-planar DW-MRI (TR =4500 ms, TE = 60 ms, NEX = 4, partition thickness = 6 mm, GRAPPA factor = 2) with 6 b-values (0, 50, 100, 250, 500 and 750 s/mm²). Post-contrast 3D-VIBE (TR/TE = 5.1/2.7 ms) in arterial, portovenous and interstitial phases of liver enhancement; and at one hour (delayed) after contrast. Image analysis: Images were reviewed by two expert radiologists (> 10 years experience) in consensus blinded to clinical information. Three image sets were independently assessed at least one week apart: Gd-EOB-DTPA set; Unenhanced T1/T2-weighted and delayed post Gd-EOB-DTPA T1W 3D-VIBE images; DW-MRI set: Unenhanced T1/T2-weighted and DW-MRI images; and Combined set: Unenhanced T1/T2 weighted, delayed post Gd-EOB-DTPA T1W 3D-VIBE images and DW-MRI images. Each lesion detected on each image set was scored on a 5-point scale: Score of 5 represented a definite metastasis and 1 definitely not a metastasis. Follow-up imaging (n = 20) and/or histopathology following surgery (n = 3) were used as the gold standard. On follow-up imaging, a lesion was regarded as a metastases if: (a) it was not previously visible on imaging, (b) showed 20% increase or decrease in size on chemotherapy and/ or (3) showed avid 18FDG tracer uptake on PET imaging. Statistical analysis: Receiver operating characteristics (ROC) curve analysis was performed to determine the areas under the curve (Az) for each image set and comparison made using the variance z-test. A p-value of < 0.05 was considered statistically significant.

Results:
By gold-standard tests, there were 158 metastases and 39 benign lesions (36 cysts, 1 focal nodular hyperplasia, 3 post radiofrequency ablation defects). The mean size of metastases was 2.3 cm (range: 0.3 – 12 cm). Using the combined image set resulted in the highest diagnostic accuracy (Az = 0.97; 95% CI = 0.94 – 0.99) compared with DW-MRI image set (Az = 0.95; 95% CI = 0.91 – 0.98) or the Gd-EOB-DTPA image set (Az = 0.90; 95% CI = 0.85 – 0.95) (Figure 1). Combining DW-MRI with Gd-EOB-DTPA enhanced imaging significantly improved metastatic detection compared with Gd-EOB-DTPA enhanced imaging (p < 0.01, z-test), and a trend towards improving detection compared with DW-MRI (p = 0.053, z-test). Compared with Gd-EOB-DTPA enhanced imaging, DW-MRI had a significantly higher diagnostic accuracy (p = 0.03, z-test). Using the Gd-EOB-DTPA enhanced image set, 17 metastases were missed, but all were < 1 cm in diameter (mean 0.6 cm) mimicking small intra-hepatic vasculature (Figure 2) or lying in periphery of liver. Using the DW-MRI image set, 14 metastases < 1 cm in diameter (mean 0.7 cm) were missed due to partial volume effects, signal suppression on higher (> 500 s/mm²) b-value image and artifacts. Only 2 metastases < 1 cm in diameter were not visualized on the combined image set.

Discussion:
Metastases appear as high signal intensity lesions of restricted diffusion on higher b-value DW-MRI images. However, DW-MRI is sensitive to a range of artefacts, which can obscure lesion visualization. Using hepatocyte selective contrast medium (e.g. Gd-EOB-DTPA), metastases appear as hypointense non-enhancing foci on delayed imaging. However, intra-hepatic vessels are also hypointense in the hepatic phase of enhancement and small metastases may be mistaken for blood vessels. Combining DW-MRI with Gd-EOB-DTPA enhanced imaging can minimize the disadvantages of each technique and improve lesion detection. DW-MRI enables metastases to be distinguished from intra-hepatic vasculature, while the anatomical detail of Gd-EOB-DTPA enhanced imaging is advantageous for assessing regions (e.g. sub-cardiac) prone to DW-MRI artefacts.

Conclusions:
The combination of DW-MRI with Gd-EOB-DTPA enhanced T1W imaging resulted in the highest diagnostic accuracy for the detection of colorectal liver metastases compared with either technique on its own.

Clinical Implication: Imaging combining DW-MRI with hepatocyte selective contrast media may be optimum in defining the burden and distribution of colorectal hepatic metastases to inform management strategies.

References:

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