

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

D-M. Koh<sup>1</sup>, T. Wallace<sup>1</sup>, E. Scurr<sup>1</sup>, D. J. Collins<sup>1,2</sup>, and A. Riddell<sup>1</sup>

<sup>1</sup>Department of Radiology, Royal Marsden Hospital, Sutton, Surrey, United Kingdom, <sup>2</sup>CR UK Clinical Magnetic Resonance Research Group, Institute of Cancer Research, Sutton, Surrey, United Kingdom

## 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 Magafodipir trisodium (MnDPDP) 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/<sup>18</sup>FDG-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/mm<sup>2</sup>). **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 <sup>18</sup>FDG 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/mm<sup>2</sup>) 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:

[1] Nasu K et al. Radiology 2000; [2] Koh DM et al. Eur Radiol 2008; [3] Ichikawa T et al. AJR 1998; [4] Hammerstingl R et al. Eur Radiol 2008

## Acknowledgements:

This work was supported by Cancer Research UK grant number C1060/A5117 and also NHS funding to the NIHR Biomedical Research Centre.

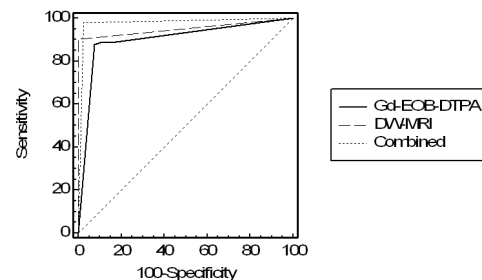


Figure 1. Receiver operating characteristic curves showing diagnostic performance of Gd-EOB-DTPA, DW-MRI and combined image sets

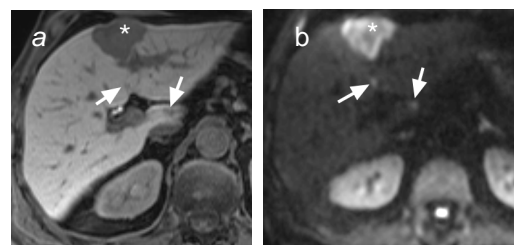


Figure 2. (a) T1W post Gd-EOB-DTPA and (b) b = 750 s/mm<sup>2</sup> DW-MRI images showing a large metastasis (\*) in left lobe of liver. Note two < 1 cm metastases (arrows) visible on DW-MRI but overlooked on contrast enhanced image.