Assessment of tumour oxygenation in hepatocellular carcinoma with BOLD MRI at 3T: preliminary results

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Introduction

In normal liver tissue oxygenation and arterial blood flow is autoregulated, with the liver receiving a dual blood supply from the portal vein and hepatic artery. It is well established that in chronic liver disease the development of hepatic fibrosis and ultimately cirrhosis is accompanied by increased relative arterial blood flow. In addition, many liver tumours, including hepatocellular carcinoma (HCC), derive their blood supply almost exclusively from hepatic arterial input.

Blood Oxygen Level Dependent (BOLD) MRI is a non-invasive technique widely used for fMRI in the brain that can detect R2* signal changes in tissues that occur in response to changes in blood flow and tissue deoxyhaemoglobin concentration. Technical challenges such as respiratory motion and susceptibility artefacts have limited its application outside the brain. In addition, stimuli to alter blood flow and tissue oxygenation have proven difficult to achieve and early work increasing hepatic blood flow using Carbogen (95% O_2, 5% CO_2) in animals is not well tolerated by patients. Previous work suggests that BOLD MRI is possible with a low degree of variability using a simple oxygen challenge technique [1,2] with several studies demonstrating similar changes in R2* in animal models of HCC following oxygen challenge [3,4]. The aim of this study is to investigate whether there are significant differences in BOLD effect between normal liver, cirrhotic liver and primary liver tumours (HCC) at 3 Tesla using the challenge of breathing an increased oxygen concentration compared with normal room air.

Methods

Eight healthy volunteers (6 male, 1 female, mean age 37 years) with no history of hepatobiliary or cardiovascular disease and not receiving any regular medication were recruited. Nine patients (all male, mean age 69 years) with hepatocellular carcinoma in a cirrhotic liver were recruited. Background liver disease was confirmed by histopathological analysis of previous liver biopsies (Table 1). All volunteers and patients fasted for 8 hours prior to their study. Imaging was performed using a whole body 3T MRI system (Signa HDx, GE Healthcare, Milwaukee, USA) with an 8 channel cardiac receive coil before and after inhalation of pure oxygen. A multi-echo fast gradient echo sequence was used - TE:2.3/6.9/11.5-43.7ms, TR:46ms, Flip:15°, Matrix:192x96, ASSET:2, BW:62.5KHz, FOV: 35cm (80%), slice thickness:8mm. Five sagittal slices were prescribed in the mid liver through the tumour location. An initial breath-held dataset was acquired breathing room air. Oxygen was subsequently delivered at 10L/min via facial mask and another breath-held (BH) dataset acquired after 8 minutes. R2* maps were generated for the pre and post data sets using purpose designed software. Using Image J (NIH, Bethesda, Maryland, USA) regions of interest (ROIs) were placed over the liver, excluding major blood vessels, and the mean R2* value and standard deviation of background parenchyma measured. Measurement of R2* values in the tumour was performed using the same technique.

Results

Eight HCCs were evaluated in total (mean size 4 cm ± 2.1 cm, range 1.8-7.5 cm). One patient had hepatic iron accumulation secondary to haemochromatosis; marked signal loss precluded successful analysis in this case. There was no significant change in R2* values in the livers of healthy volunteers pre and post O2 (p=0.945, see Figure 1). In patients' tumors a consistent fall in R2* value was demonstrated following O_2, which suggests an impaired auto-regulatory response to increased O_2 levels (p=0.004, see Figs.1, 2). One extreme outlier was observed and review of the image data demonstrated that the small tumour in a sub-diaphragmatic region was close to an area of lung which created substantial susceptibility artefacts and distortion. In the background parenchyma of patients' livers a fall in R2* following O_2 was also observed in all but one case. This difference was not statistically significant (p=0.074), however, the result is likely confounded by the relatively small sample size.

Patient	Background liver	Tumour
1	Non-alcoholic steatohepatitis (NASH) cirrhosis	6.5 cm HCC, segment 4
2	Cirrhosis (α1-antitrypsin deficiency)	7.5 cm HCC, segment 7
3	Non-alcoholic steatohepatitis (NASH) cirrhosis	2.5 cm HCC, segment 4
4	Alcohol-related cirrhosis	1.8 cm HCC, segment 2
5	Chronic hepatitis, fibrosis (Hep C +ve)	1.5 cm HCC, segment 1
6	Cirrhosis (Hep B +ve)	4.5 cm HCC, segment 6
7	Alcohol-related cirrhosis	3.6 cm HCC, segment 8
8	Cirrhosis (α1-antitrypsin deficiency)	3.9 cm HCC, segment 8

Table 1. Patient background liver and tumour details

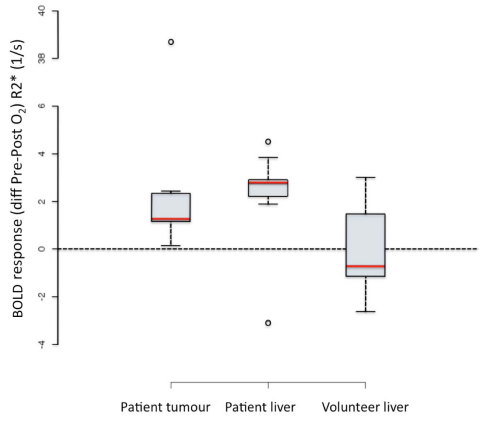

Fig.1. Pre/Post O_2 challenge R2* change in HCC, diseased background liver and healthy volunteers

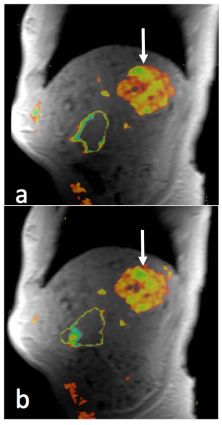

Fig.2. T2* maps pre (a) and post (b) O_2 challenge in Pt 2 demonstrating subtle increase in T2* (decrease in R2*) in a right lobe HCC

Conclusion

As expected no significant difference in BOLD response was observed in healthy livers following oxygen challenge in keeping with normal effective autoregulation. Changes in R2* following oxygen challenge were observed in both the HCCs and diseased background livers of patients, reflecting reduced tumour and cirrhotic liver deoxyhaemoglobin levels following the oxygen challenge consistent with dysregulation of arterial blood flow. Further work is required to investigate whether or not this strategy would provide either an effective method detecting HCC in a cirrhotic liver or whether the relative arterialization and BOLD response might help further characterize HCC lesions and their response to treatment.

References

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