Characterization and Early detection of liver metastasis by fMRI

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Background/ Aims:

The liver is very commonly involved in metastatic disease. Liver metastases are the major cause of death of colorectal carcinoma patients. Since liver function tests in patients with liver metastases tend to be insensitive and non-specific, the disease is diagnosed at late stages. Thus, imaging plays a vital role in the early diagnosis which is critical for treatment by resection. One of the key pathologic factors for differential diagnosis between liver tumors and dysplastic nodules is the vascular supply to the lesion. We recently developed a new MRI method that enables us to follow liver perfusion and hemodynamics by enrichment with different inhaled gases (CO_2, and O_2). This method facilitates the monitoring of arterial vs. portal blood flow distribution[1,2]. In the present study, we aim to characterize the early vascularization events in metastatic liver tumor development using fMRI.

Methods:

MRI: Experiments were preformed on a 4.7T Bruker Biospec spectrometer using a bird cage coil. Hepatic volumetric assessment is acquired by serial coronal and axial T_1W SE images (TR/TE=250/18ms). Tumor assessment was done using T_2W fast SE images (TR/TE= 2000/40 ms). Changes in hepatic hemodynamics were evaluated from GE images acquired during breathing of air, air-CO_2 (5% CO_2), and carbogen (95% oxygen; 5% CO2) as described[1]. Eight images were acquired at each gas mixture (slice thickness=1mm; TR/TE=100/10ms; FOV=3cm; in plane resolution =117µm). The change induced by O_2 signifies tissue perfusion. The change generated by CO_2 corresponds to the distribution of blood nourishment to the liver as described previously[2]. Data analysis was performed using home written IDL software. CO_2 reactivity and O_2 maps are given as the percentage of change of signal intensity (SI).

Animals: Murine colon carcinoma CT-26 cells (10^4) were injected intrasplenically to BALB/C mice to generate liver metastases, and the spleen was removed 5min later. In this model, 1-4 metastatic nodules are formed between 13-15 days after cell inoculation. Images, were acquired every 2-3 days, beginning 6 days following cell inoculation (n=18). Animals were sacrificed, and livers were taken for histology.

Results and Discussion

As we have shown previously, in healthy livers the %change of SI due to CO_2 reactivity was negative (-32±6%), while the %change due to O_2 was positive (72±13%). Results from CO_2 and O_2 reactivity clearly highlighted tumors from healthy liver tissue (Fig 1). During tumor progression the %change of SI due to CO_2 became less negative and mean values were -14±5.6% ($p<0.001$). Moreover, the %change of SI due to O_2 in tumors had reduced and mean values were 28±18% ($p<0.001$). These results suggest that in metastatic nodules there is a higher arterial/portal blood flow ratio along with a decrease in vascularity.

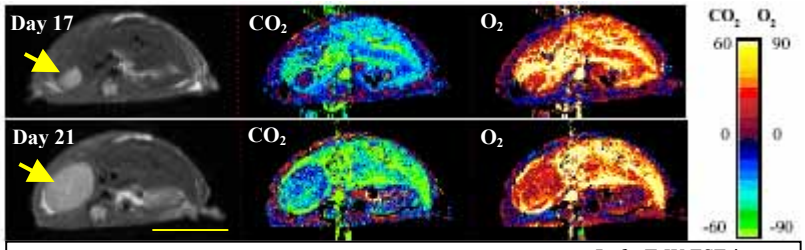

Fig.1: Metastatic liver tumor growth and vascular characterization. Left- T_2W FSE images of liver acquired 17 days (top) and 21 days (bottom) following cell inoculation (arrows-tumors); Maps of %change in SI due to CO_2 (Centre) and O_2 (Right); scale bar Bar=1cm.

In this colon metastatic model, tumors were detected in T_2W FSE images only 13 days following cell injection. The smallest lesion visible was of 1mm in diameter. Using our inhalation approach, we detected areas with SI change 2-4 days earlier (Fig 2). Furthermore, these SI changes due to CO_2 and O_2 reinforced our decision regarding suspected lesions. These results are in accordance with the literature that in liver tumors, there is loss of portal tracts and development of new arterial vessels. Pathological findings correlated well with the MRI images with respect to both tumor size and location.

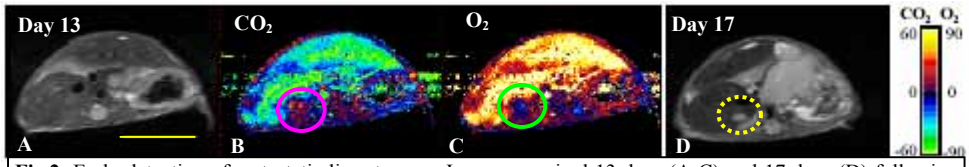

Fig.2: Early detection of metastatic liver tumors. Images acquired 13 days (A-C) and 17 days (D) following cell inoculation; (A, D) T_2W FSE images; (B) CO_2 and (C) O_2 maps of %change in SI. Areas with SI change (circled area in B, C) were detected 4 days earlier than in T_2W image; (D, yellow circle). Bar=1cm.

In summary, results from these experiments will broaden our knowledge regarding vascular development in liver tumors. This fMRI method provides a non-invasive tool for better and earlier diagnosis of liver tumors and would hopefully assist in tumor differentiation.

References: 1. Abramovitch R., Dafni H., Smouha E., Benjamin L., and Neeman M. **Cancer Research** 59: 5012-6, 1999.
2. Harel H, Gross E, Spira G, Matot I, Galun E, Vlodavsky I, Abramovitch R; [2004] abstract no. 357, ISMRM.