Selective depiction of holmium-loaded microspheres (HoMS) using susceptibility gradient mapping (SGM): initial experience in animal models

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Introduction- Internal radiation therapy with radioactive holmium-loaded microspheres (HoMS) is a promising treatment option for both unresectable liver metastases and hepatocellular carcinoma. In previous animal studies on internal radiation therapy of hepatic malignancies, MR imaging was shown to be the modality of choice for guiding the administration, planning and follow-up. In particular, T_2*-weighted MR images and T_2* maps were used to visualize and quantify the distribution of HoMS in the liver[1,2]. However, the inhomogeneous signal of liver tissue as well as the presence of macroscopic field inhomogeneities introduced due to air-tissue interfaces often complicates selective identification of HoMS depositions. In this work, we investigate the role of susceptibility gradient mapping (SGM) for the selective visualization of HoMS with positive contrast while avoiding the above complications. We illustrate the influence of the echo time and study the use of directional information of SGM as applied to ex vivo data from rabbit livers and in vivo data from pig livers.

Methods- *Susceptibility gradient mapping* SG maps were calculated as described by Dahnke et al.[3]. SG maps represent the local echo shift (m) in a certain direction induced by a local magnetic field gradient (G^{susc}) during the echo time TE ($m \propto G^{susc}TE$). By varying TE, the sensitivity of SGM can be controlled. The parameter m was determined for each direction (x,y and z) and combined into 2D and/or 3D SG maps according to $m_{x,y} = \sqrt{(m_x^2 + m_y^2)}$ and $m_{x,y,z} = \sqrt{(m_x^2 + m_y^2 + m_z^2)}$. This is demonstrated using a phantom containing an air-filled cylinder in agarose gel. *Data acquisition* Phantom experiment. A 3D GE with TR/TE/flip = 8.2/3.8/10°, FOV = 128x128x64, scan matrix (SM) = 128x128x64 and WFS = 0.5 was applied to an agarose gel phantom with a glass cylinder ($d\chi$=10.3ppm) positioned perpendicular to B_0 on a 3T system (Achieva, Philips Healthcare). Ex vivo experiments. Up to 40mg of highly-loaded HoMS were administered in steps of 10mg into the hepatic artery of an excised rabbit liver[4]. After each administration multi-gradient echo acquisition were performed using multi-slice imaging with $TR/TE_1/\Delta TE/flip$ = 500/1.36/1.11/50°, 3 echoes, FOV = 128x128x44mm, SM = 128x128x11 on a 3T system. In vivo pig experiments. After MR-guided catheterization of the hepatic artery, 600 mg of HoMS were administered to the liver of a healthy pig. MRI was performed on a 1.5T system (Achieva, Philips Healthcare) using a 3D multi-gradient echo sequence with $TR/TE_1/\Delta TE/flip$ = 25/2.2/1.4/25°, 15 echoes. FOV = 320x256x136mm, SM = 208x149x68 applying breathhold.

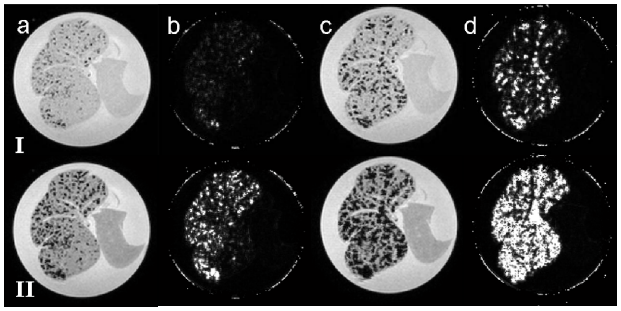

Figure 1. T_2^*-w images (a,c) and SGM's (b,d) of 1st (I) and 3rd (II) echo of rabbit liver with 10mg (a,b) and 40mg (c,d) of HoMS.

Results- SGM successfully depicted the distribution of HoMS in the ex vivo rabbit liver (Fig. 1) with positive contrast (PC). For the small tracer dose (10 mg) an increased echo time resulted in an increased conspicuity of the HoMS. The distribution of PC as displayed by SGM was similar to the signal voids observed in T2*-w images. For a higher accumulated dose (40mg) a short echo time turned out to be favorable in order to keep the depiction of HoMS more local. Directional SG maps of the agarose phantom (Fig. 2) showed specific echo shift patterns due to an anisotropic gradient distribution (G_x,G_y,G_z) induced by the air cylinder perpendicular to the B_0 field. It clearly demonstrated that by selecting the z-direction in which no field disortions are expected outside a cylinder, the large x and y susceptibility gradients were successfully discarded, leading to an absence of PC in the SGM of the z-direction. This phenomenon was exploited in the in vivo pig experiments to separate macroscopic field inhomogeneities from local ones. The distribution of HoMS was clearly depicted in the pig liver. Similar distributions were shown by 2D SGM (Fig. 3b) and T2*-w images (Fig. 3a) as presented by the overlay in blue in Fig. 3c. However, the presence of air in the abdomen and in the lungs introduced field inhomogeneities which resulted in PC in abdomen and lungs and showed that SGM cannot distinguish between different origins of the susceptibility effect. When comparing SGM to the R2* map (Fig. 3d), a similar pattern of PC and high R_2* was observed in the liver (red outline). However, the R_2* map showed high values close to the tissue-air interface due to anisotropic macroscopic field inhomogeneities caused by the air in the lungs (Fig. 3d, white arrows). The 2D SG discarded these macroscopic field inhomogeneities in the feet-head direction and thereby avoiding the depiction of PC due to these macroscopic field effects while maintaining the depiction of isotropic field variations due to HoMS as shown in Fig. 3b and c.

An observation that needs further investigation is the depiction of water-fat interfaces by SGM. This is shown in Fig. 3.I b and c, stressed by the red arrows for an image acquired with an out-of-phase echo time (TE=2.3ms @ 1.5T). This enhancement was not observed in Fig. 3II, which was acquired at an echo time (TE=5.0ms) close to in-phase, suggesting that either the phase effects or the partial volume effects due to tissue-fat interfaces may lead to PC in SGM.

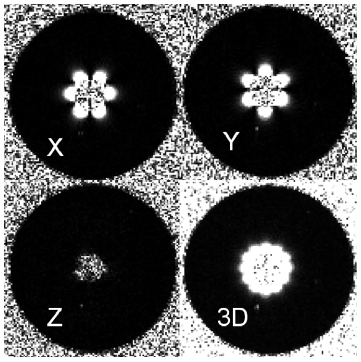

Figure 2. SGM of X,Y and Z direction and 3D of an air cylinder in agarose.

Discussion & Conclusion- SGM allows detailed qualitative depiction of HoMS in liver tissue in ex vivo and in vivo animal models. Longer echo times can be chosen to increase PC due to an increase of the underlying echo shift. This echo time dependency may be used to optimize PC in areas with different concentrations of contrast agent, i.e. longer echo times for low concentrations and shorter for higher concentrations. Signal voids due to T_2 or absence of protons can be distinguished from voids due to T_2*. Although SGM is not sensitive to the origin of the induced echo shift, directional information (i.e. 1D and 2D SG maps) can be used to exclude some macroscopic shifts along certain directions. This allows discriminating between T_2* effects induced by paramagnetic substances (local $d\chi$) and macroscopic field inhomogeneities, which tend to create anisotropic susceptibility gradients.

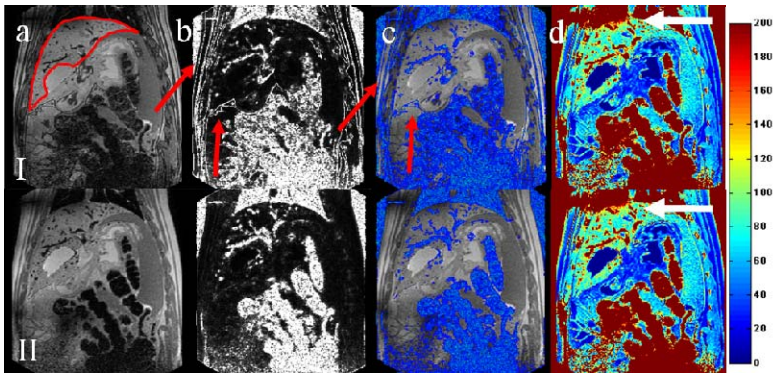

Figure 3. T_2^*-w images (a), 2D SGM's (b) and SGM's overlaid on T_2^*-w images of 1st (I) and 3rd (II) echo and R_2* maps of a pig liver with 600 mg of HoMS administered.

[1] Seppenwoolde JH, MRM 2005, 53:767-784
[2] Nijsen JF, Radiology 2004; 231(2):491-499
[3] Dahnke H, MRM 2008, MRM 2008, 60:595-603
[4] Seevinck PR, ISMRM 2008: #274