Macroscopic meets microscopic: the use of Multi Acquisition Variable Resonance Image Combination (MAVRIC) for detection of microscopic objects by means of off-resonance excitation

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Introduction: Positive contrast by means of off-resonance excitation can be used to visualize objects that have a susceptibility that differs from their surroundings. The concept is based on the fact that spins that reside in the vicinity of these objects have a resonance frequency that differs from the on-resonance frequency $f_0=B_0 \cdot \gamma/2\pi$ with B_0 the main magnetic field and γ the gyromagnetic ratio. Positive contrast mechanisms have the advantage that objects of clinical interest can be separated from signal voids. The mechanism has been shown to be effective for e.g. iron-labeled cells [1], gadolinium [2, 3] and Holmium-166 loaded microspheres [4].
The major drawbacks of acquiring a single off-resonance image, like is done in [1], [2] and [3], are the lack of anatomic context and the partial excitation of the frequency spectrum induced by the microscopic disturbers. In many cases, the objects of interest induce positive and negative field offsets that lead to a much broader frequency spectrum than can be covered by a single Radio Frequency (RF) pulse, leaving a potential source of signal unused. By exciting and detecting the entire range of off-resonance frequencies, the sensitivity and therefore the potential to detect objects of interest would increase. Furthermore, for accurate quantitative measurements, all off-resonance frequencies should be included to be able to relate the amount of off-resonance signal to the amount of microscopic objects.
To overcome the drawbacks mentioned above, we investigated the feasibility of using an MRI sequence, called Multi Acquisition Variable Resonance Image Combination (MAVRIC), to visualize microscopic objects. MAVRIC was developed for imaging near metallic implants [5]. Since metallic implants induce large field deviations, protons in the vicinity of these implants have a Larmor frequency that is not covered by the RF excitation bandwidth, which leads to signal voids. MAVRIC solves this problem by using multiple acquisitions with discrete offsets in RF transmission and reception frequency within the framework of a single 3D spin echo sequence. Combining data from the multiple acquisitions results in one image which covers a broad frequency range. In this work we will show that MAVRIC can be used for detection of microscopic field disturbers, for the special case of Holmium-166 loaded microspheres. It will be demonstrated that, using MAVRIC, the whole range of off-resonance frequencies induced by the microspheres can be covered and that positive contrast can be generated while anatomical reference information is preserved.

Materials and methods: Phantom: An agarose gel series (2% by weight) containing HoMS concentrations ranging from 0 to 8 mg/ml was made in 25-ml tubes. $MnCl_2$ was added to the native gel to decrease the baseline T_1 in order to reduce T_1-weighting. The Holmium content of the microspheres was 18.7% by weight resulting in a volume susceptibility of 880ppm [6]. Ex-vivo rabbit liver: An excised rabbit liver was cannulated and after extensive flushing using $MnCl_2$ doped saline, HoMS were administered selectively to one liver lobe. After administration, the liver was flushed again and stored in doped saline. Experiments: MAVRIC images were acquired using a 1.5T whole body scanner (Philips Healthcare, Best, The Netherlands). A 3D non-selective spin echo sequence was applied using 7 discrete transmission and reception frequencies. For the phantom experiment the tubes were placed parallel to the main magnetic field. An RF excitation and refocusing bandwidth of 600Hz was used with discrete center frequency offsets of 0, -200, +200, -400, +400, -600, +600Hz. Further imaging parameters included: FOV: 128x128x100mm^3, scan matrix: 64x64x10, TR/TE: 300/15ms. The ex-vivo rabbit liver was imaged using a RF excitation and refocusing bandwidth of 850Hz with discrete center frequency offsets of 0, -400, +400, -800, +800, -1200, +1200Hz. To decrease the total scan time, a turbo spin echo sequence was used with a turbo factor of 40, resulting in a scan time of 8m40s. Imaging parameters included: FOV: 128x128x111mm^3, scan matrix: 128x128x37, TR/TE: 600/40ms.

Results: In Figure 1, MAVRIC images of the phantom setup are shown for seven discrete frequency offsets. The central image is the on-resonance image in which all samples are clearly visible. For increasing concentrations of HoMS the signal intensity decreases. This is caused by two effects: a) protons are not excited because they are off-resonance and b) diffusion induced T_2-decay which has been shown to occur in HoMS containing systems [7]. Shifting the excitation frequency clearly leads to signal and contrast changes although caution should be exercised with the interpretation of signal changes between the shown images since they are scaled differently for visualization. For a frequency shift of +400Hz, samples with higher concentrations show the highest signal intensity. For a shift of +600Hz, the lowest concentrations do not show any signal at all. For negative frequency shifts, signal behavior is somewhat different but similar effects are visible. For a shift of -400Hz, signal has disappeared for the lowest concentration whereas for -600Hz, no signal is received at all, indicating asymmetric behavior around f_0. Figure 2 shows MAVRIC images of the ex-vivo rabbit liver where similar effects are observed. Whereas the central image shows the on-resonance liver tissue and the surrounding saline, this signal disappears for higher frequency off-sets, while hyper-intense voxels appear at locations where HoMS are present.

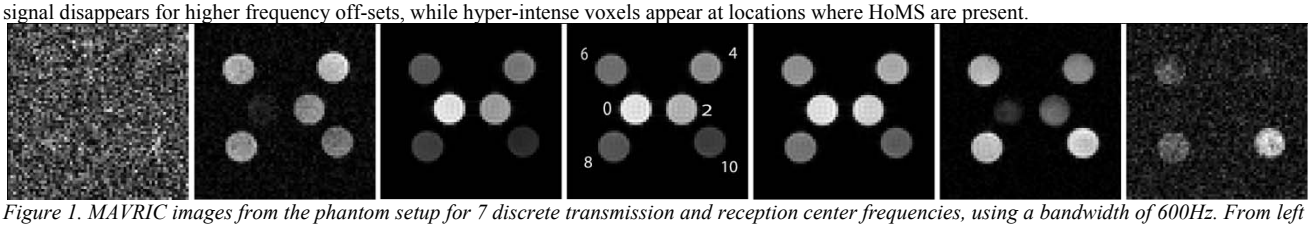

Figure 1. MAVRIC images from the phantom setup for 7 discrete transmission and reception center frequencies, using a bandwidth of 600Hz. From left to right: -600Hz, -400Hz, -200Hz, 0Hz (f0), +200Hz, +400Hz, +600Hz. Images are scaled differently for visualization. Concentrations of HoMS are indicated in the central image in mg/ml.

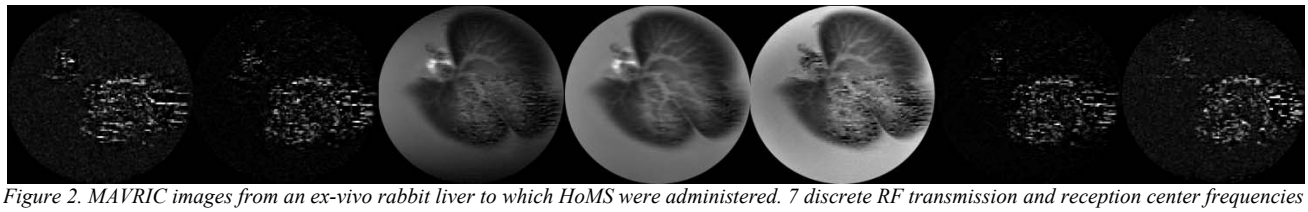

Figure 2. MAVRIC images from an ex-vivo rabbit liver to which HoMS were administered. 7 discrete RF transmission and reception center frequencies were used with a bandwidth of 850Hz. From left to right: -1200Hz, -800Hz, -400Hz, 0Hz (f0), +400Hz, +800Hz, +1200Hz. Images are scaled differently for visualization.

Discussion and conclusions: It was shown that MAVRIC, an MRI technique developed for imaging near metallic implants, can be used for detection of microscopic field disturbers by means of off-resonance excitation. MAVRIC offers the opportunity to cover the whole range of off-resonance frequencies, necessary for accurate detection of the disturbers, within one 3D spin echo sequence. By combining the off-resonance images, positive contrast images with increased sensitivity can be generated and used for more accurate quantitative measurements. In addition, the on-resonance image, needed for anatomical reference, is preserved. The method was demonstrated for the special case of HoMS, but can also be applied to iron-labeled cells or other objects that have a susceptibility that differs from their surroundings. Finally, the proposed methodology could be used to investigate requirements concerning RF excitation bandwidth and frequency for imaging objects of interest in certain studies.

References [1] CH Cunningham et al. Magn Res Med 2005; 53:999 [2] RR Edelman et al. Magn Res Med 2007; 57:475 [3] E Vonken et al. Magn Res Med 2009; 62:314 [4] GH van de Maat et al. Proc Int Soc Magn Res Med 2010; 18 [5] KM Koch et al. Magn Res Med 2009; 61:381 [6] PR Seevinck et al. Magn Res Med 2008; 60:1466 [7] GH van de Maat et al. Proc Int Soc Magn Res Med 2009; 17:4468