Off-resonance positive contrast flow imaging using extraneous paramagnetic biomarker-induced spin labeling

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INTRODUCTION: Various positive contrast techniques have been proposed for MRI, including those which are targeted to visualize areas affected by magnetic field disturbances or short relaxation times as a result of paramagnetic objects or iron oxide (FeO) based contrast agents [1,2,3]. By exploiting the frequency dispersion of protons residing in the dipolar field generated by magnetic susceptibility, positive contrast MRI can be performed after the administration and in vivo distribution of Gd or FeO contrast agents, as has been shown in off-resonance MR lymphography and angiography applications [4,5,6]. In this study, off resonance imaging was used to explore the generation of positive contrast by extraneous paramagnetic biomarkers, specifically for the dynamic labeling of moving protons.

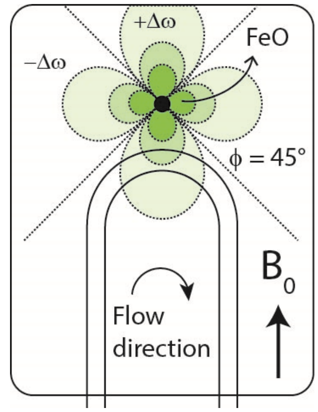

Fig. 1. Schematic representation of the agarose gel flow phantom. Isofrequency lines of the FeO loaded cylinder induced susceptibility field are indicated. In cylindrical structures Δω is zero at a 45° angle with respect to the main magnetic field.

METHODS: A flow phantom was designed containing a solidified agar solution in a 1:25 weight ratio with tap water. A 1 mL syringe filled with a highly concentrated FeO solution (5 mg/mL FeO) and rubber tubing was inserted before final solidification of the agar. The tube was positioned in the positive lobe of the magnetic susceptibility field (+ΔB) induced by the FeO cylinder (Fig 1). A water flow was generated using a water pump located outside of the magnet room with a flow ranging from 1 to 10 mL/s. All measurements were performed on a 3.0 T clinical MRI scanner (MAGNETOM Prisma, Siemens AG, Erlangen, Germany). An on-resonant saturation pulse (bandwidth 50 Hz, radio frequency (RF) excitation angle 90°) with variable delay times (100 ms to 2 s) was applied prior to each acquired k-space segment of a 2D GRE imaging sequence. Parameters: TR/TEs 6.0/3.3 ms, FOV (250 x 172 mm^2), matrix 128x128, slice thickness 2 mm, RF excitation angle 10°, and a receiver bandwidth of 1000 Hz/pixel. Data was acquired using a body array RF coil and and image analysis performed in ImageJ to determine the velocity of the moving contrast front, by calculating the subtraction and difference images of data where the flow was switched on and/or off.

RESULTS AND DISCUSSION: Off resonance imaging using an on-resonant saturation pulse clearly allowed visualization of the magnetic field distortions of the FeO loaded cylinder (Fig 1B). Protons in the vicinity of the FeO cylinder resonate at a different frequency and were not affected by the saturation pulse. Conversely, protons outside of the FeO sensitive area are saturated and their signals effectively nulled at the start of the imaging sequence. Increasing the delay times after the saturation pulse, labeled spins gave rise to progressively hyper intense regions further downstream (Fig 2). The average velocity of this moving contrast front was consistent with that of the water, ~2cm/s. Since images were acquired with constant RF excitation angles, images with a longer delay time (>1s) demonstrated progressive effects of increased background magnetization recovery at the onset of the imaging sequence when compared to those acquired with shorter delay times. The dependence of the off-resonance spin labeling mechanism on the delay times and flip angle of the saturation pulse was not investigated but will be subject to further studies.

CONCLUSION: A new source of exogenous contrast was demonstrated that is not dependent on contrast agent injection. The duration of the effect and the range of spin labeling is T1 dependent and the length of the vessel seen depends on several parameters, including flow velocity, background T1, and imaging parameters. Different delay times of the saturation pulse leads to a wider range of spin labeling, and positive contrast in further downstream areas, allowing for the visualization of flow around paramagnetic objects, such as stents, or the application of less motion sensitive positive contrast MRA.

REF: [1] Stuber *et al*., MRM 58:1072-1077(2007) [2] Seppenwoolde *et al*., MRM 50:784-790(2003) [3] Seevinck *et al.*, MRM 65:146-156 (2011) [4] Gitsioudis *et al.,* JMRI 38:836-844 (2013) [5] Korosoglou *et al.,* Radiology 249:501-509 (2008) [6] Edelman *et al*., MRM 57:475-484 (2007)

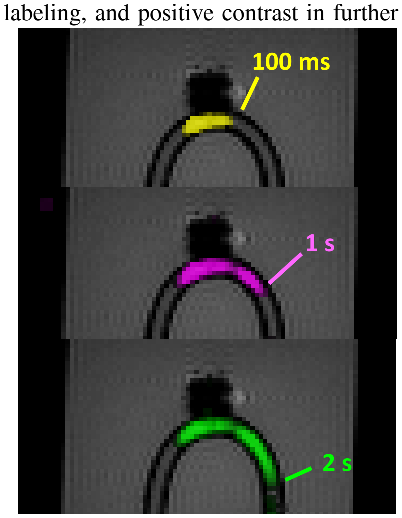

Fig. 2. GRE image (identical to Fig 2A) overlain with positive contrast images that were obtained with 3 different delay times (100 ms, 1 s, 2 s) between the saturation pulse and the imaging sequence. A progressively increasing area of spin labeling is achieved with increasing delay times.

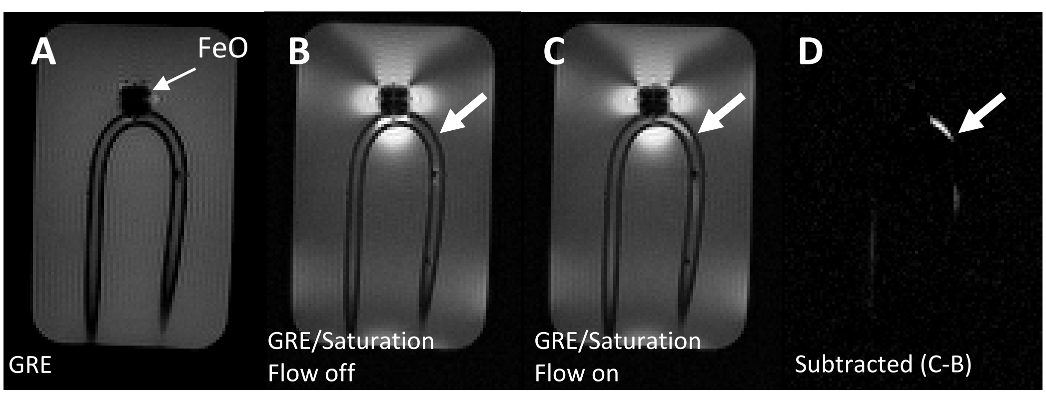

Fig. 3. GRE MRI images acquired of the flow phantom without the on resonant saturation pulse (A) and with the on resonant saturation pulse, using an imaging delay of 1 s (B and C). With the water flow turned on (C), moving protons in the vicinity of the FeO loaded cylinder are positively labeled using on-resonance saturation, indicated by white arrows (B and C), are more clearly visualized in the subtracted image (D).