A New Method to Visualize Vessels. Off-Resonance Angiography.

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Introduction:

Contrast agent enhanced magnetic resonance angiography (CE-MRA) is a technique with widely accepted cardiovascular applications. Currently, CE-MRA techniques are based upon the T_1-shortening of blood caused by MRA contrast agents. Here we introduce a new concept in CE-MRA using Inversion Recovery with ON-resonant water suppression (IRON)[1]. The positive contrast created by this method is based upon shifts in the Larmor frequencies caused by the exposure of superparamagnetic particles to a static magnetic field. With this approach, IRON produces positive contrast within the vessel lumen and simultaneously suppresses signal from on-resonant protons and fat contained in the surrounding stationary tissue.

Materials and Methods:

In vivo experiments were performed in 11 rabbits which received a single intravenous bolus administration of 80µmol Fe/kg (n=6) or 250µmol Fe/kg (n=5) of monocrystalline iron oxide nanoparticle MION-47[2]. MRA from all animals were acquired at baseline and 5-30 minutes, 2 hours, 1 day and 3 days after MION-47 injection. Imaging was performed using a clinical Philips 3T Achieva system (Philips Medical Systems, Best, NL). For conventional T_1-weighted MRA a 3D gradient-echo imaging sequence was applied (field-of-view of 200x100mm, matrix of 400x200, TR/TE of 25/2.7ms, α of 20°). For IRON MRA (off-resonance angiography), an on-resonant IRON pre-pulse with a bandwidth of 100Hz and an excitation angle of 100° was added to the fat suppressed 3D segmented k-space gradient-echo imaging sequence (field-of-view of 140x112mm, matrix of 288x220, TR/TE of 3.9/1.54ms, α of 15°). On both conventional and IRON MRA, the contrast-to-noise ratio between the aortic blood-pool and the surrounding tissue was quantified.

Results:

After injection of 250µmol Fe/kg MION-47 the lumen of aorta was signal attenuated on T_1-weighted MRA compared to baseline (Figures 1b and 1f). The signal in the vessel lumen increased after 1 day (1c and 1g) and returned to baseline 3 days after MION-47 injection (1d and 1h). Using IRON, the stationary background tissue was homogenously suppressed both in the abdomen and in the thorax of the rabbits at baseline (Figure 2a and 2e). After MION-47 injection (250µmol Fe/kg) the aortic lumen had high signal intensity while the surrounding tissue continued to be signal-suppressed, supporting excellent vascular contrast (2b and 2f). Vascular enhancement persisted up to 24 hours after injection (2c and 2g).

Contrast-to-noise ratio (CNR) measurements in the abdominal aorta of the rabbits agreed with the visual findings. Thus, after injection of the high dose of 250mmol/kg (n=5), CNR decreased on T_1-weighted MRA (-9.7±2.0 versus 12.2±5.1 at baseline, *$p<0.001$) but increased markedly on IRON MRA (58.7±12.9 versus 0.3±2.1 at baseline, $p<0.001$). CNR remained high using IRON up to 24 hours after the injection (61.9±12.4 at 2 hours and 76.2±15.9 after 1 day, ¶$p<0.001$ versus baseline), (Figure 3a). Similarly, after injection of 80µmol Fe/kg MION-47 (n=6), CNR decreased on conventional T_1-weighted MRA (9.0±2.5 versus 16.8±4.1 at baseline, *$p<0.05$) but increased strongly using IRON (76.7±8.9 versus 1.1±0.4 at baseline, ¶$p<0.001$) and remained high up to 24 hours (78.6±8.9 after 2 hours and 43.0±5.6 after 1 day, ¶$p<0.001$ versus baseline for both), (Figure 3b).

Conclusion:

This is the first study that exploits off-resonance rather than T_1-shortening or in-flow for generating contrast between the intravascular lumen blood-pool and the surrounding tissue *in vivo*. In combination with IRON imaging, the administration of MION-47 resulted in a strong increase in CNR between the vessel lumen and the surrounding tissue. CNR remained unchanged after 2 hours and persisted up to 24 hours after a single intravenous bolus administration of MION-47. Thus, IRON in combination with magnetic nanoparticles as a contrast agent may allow high resolution imaging of vascular pathologies because of the very high CNR and the longevity of the contrast agent.

References:

[1] Stuber et al, ISMRM, 2005.

[2] Weissleder et al, Radiology, 1994;191:225-30

Figure 1: *Using conventional T_1-weighted MRA, administration of 250µmol Fe/kg MION-47 caused signal void in the abdominal (f) and in the thoracic aorta (b) compared to baseline (a, e). These effects resolved 1-3 days after injection (c-d and g-h).*

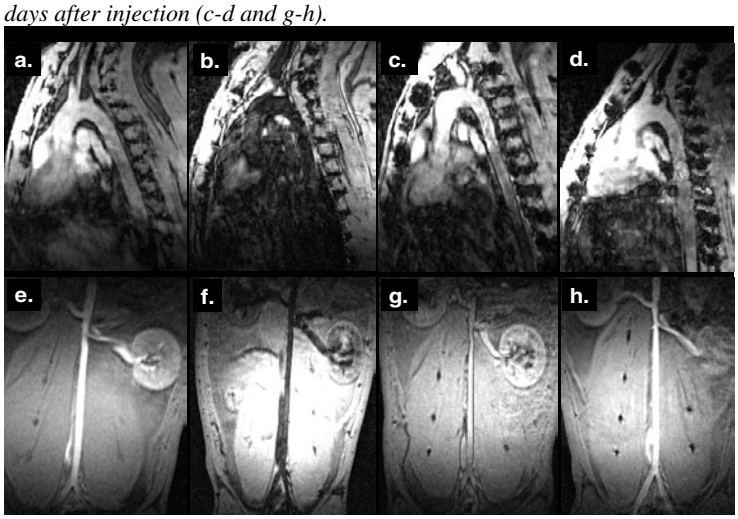

Figure 2: *Using IRON (=off-resonance MRA), abdominal and thoracic tissue was homogenously suppressed at baseline (a, e). After injection of 250µmol Fe/kg MION-47 strong intravascular enhancement was present (b, f), which remained present up to 24 hours after the injection (c, g).*

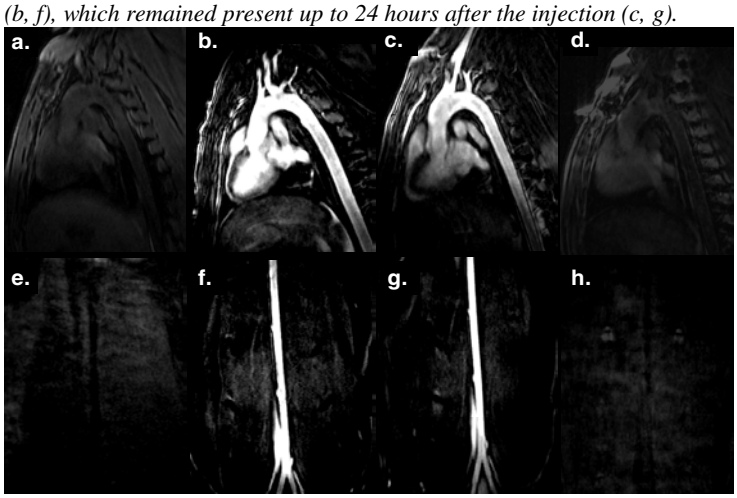

Figure 3: *Contrast-to-noise ratios confirm visual findings and demonstrate a strong increase in contrast on IRON-MRA at both high (left) and low (right) doses of MION-47.*