MRI Pulse Sequence Optimization for Molecular Imaging of the Brain Aneurysm Wall

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Target audience: Physicians and researchers that are interested in molecular imaging, contrast agents, and vessel wall MRI.

Purpose: To optimize the imaging parameters to suppress arterial MR signal due to slow non-linear flow while maintaining CNR from surrounding tissue using a realistic vascular replica phantom and test the optimized pulse sequence in an animal model of inflammatory saccular aneurysm.

Fig. 1 Schematic illustration of the motion-sensitized driven-equilibrium pulse sequence

Methods: Optimization of motion-sensitized driven-equilibrium (MSDE) sequence was done in a silicone replica of a rabbit aneurysm (AN) model. The replica was connected to a cardiac pulse duplicator programmed to produce a rabbit specific waveform circulating 60:40 by volume glycerol-water mixture, which mimics the viscosity/relaxivity of blood. To simulate the presence of tissue fat, the replica was embedded in solid oil. Imaging was performed on a 3T whole body MRI scanner using an 8 channel knee coil. MSDE-data was acquired in axial and coronal slices with thickness of 2mm, FOV=120×120×60 mm^3, and in-plane resolution of 0.8×0.8 mm^2 (TR/TE=700/10 ms, FA 70°). The velocity encoded gradient echo imaging parameter (VENC) was optimized to minimize the signal produced by the slow blood flow within the AN. Fat-saturation was implemented using spectral pre-saturation inversion recovery (SPIR) method. To investigate if the optimized sequence was sensitive to paramagnetic contrast agent- induced T1 shortening, a balloon catheter filled with 150 μM GdDTPA was inserted into the AN. Subsequently, MSDE sequence (Fig 1) was tested on a rabbit model with an elastase-induced AN at the origin of the right common carotid artery. MR-imaging was performed with respiratory triggering to minimize motion artifacts. Data acquisition was performed during expiration phase using a multi-2D method at TR=5000 ms determined by the length of the respiratory cycle, with which required T1-weighting for contrast enhancement is no longer achieved. To overcome this, an inversion pulse was added to the sequence as to gain T1-sensitivity by inversion recovery (IR). The IR delay time was determined by minimizing the signal generated by the AN wall as to establish maximal signal difference with respect to post-contrast imaging. The optimized sequence was then applied to a larger cohort of rabbits (n=7) where the naïve aneurysms were imaged before and after the IV injection of MPO-specific contrast agent (bis-5-hydroxytryptamide of DTPAGd, 5HT-DTPAGd, 0.15 mmol/kg)[1]. Two days later, the inflammation in aneurysmal wall was induced by using a local lipopolysaccharide (LPS) injection[2] and the rabbits were re-imaged before and after the 5HT-DTPAGd administration. Signal-to-noise (SNR) change was quantitated in the created aneurysm as well as the contralateral carotid artery.

Fig. 2 Optimization of blood-suppression using MSDE in a vascular replica (A). Blood signal was minimized by changing VENC parameter from 5 cm/s (B), 2 cm/s (C), 1 cm/s (D), 1 cm/s without SPIR (E) – axial slices, with GdDTPA-filled balloon catheter placed in the aneurysm (F, coronal).

Results: Representative results of the *in vitro* study are shown in Fig 2. The vascular replica used for sequence optimization is shown in Fig 2A. In Fig 2B-2E axial slices of MSDE sequence are given with various VENC values with SPIR (Fig 2B-2D), with optimal VENC and without SPIR (Fig. 2E), and a coronal slice of MSDE data with the GdDTPA-filled balloon catheter to confirm T1-weighting (Fig. 2F). Example slices of the MSDE sequence optimization *in vivo* are given in Fig 3; Fig 3A: MSDE (VENC=1cm/s) with respiratory triggering that led to a TR=5000ms, which did not provide sufficient T1-weighting. Fig 3B and Fig 3C show MSDE with triggering and fat-saturation and MSDE with triggering and an inversion pulse, respectively. In Fig 3D MSDE with triggering, fat-saturation and an inversion pulse is given. Here, suppressed signal from aneurysmal blood and minimized signal from the aneurysmal wall are demonstrated, which was achieved with IR delay time of 800 ms. We applied the developed imaging protocol to *in vivo* rabbit aneurysm model. There was a significant increase in SNR (p<0.0001) of the inflamed rabbit aneurysms following 5HT-DTPAGd MPO-specific contrast agent administration as compared to the controls (Fig 4).

Fig. 3 Axial slices of in vivo multi-2D MSDE imaging of rabbit with non-inflamed CCA aneurysm (arrow). MSDE with respiratory triggering (A) and fat saturation (B), triggering and inversion pulse (C) triggering, fat-saturation and inversion pulse (D).

Discussion: It is estimated up to 6% of US population have an intracranial aneurysm (IAs), of which only a small number, 30,000 annually, ruptures with a resultant 50% mortality within 30 days. Despite this high mortality rate, management of patients with unruptured IAs is under debate. Parameters that quantify the likelihood of IA rupture are elusive. Inflammatory changes in the IA wall correlate to rupture[3]. It has been previously shown by us that a myeloperoxidase (MPO) specific MR signal enhancement could be monitored in an animal model of saccular aneurysm inflammation[2]. In order to fully appreciate IA wall and lumen, we investigated the use of black blood (BB) MRI. A commonly used BB sequence is double inversion recovery (DIR), which pre-saturates the blood flowing into the field of view. Although saturation-based sequences are frequently used, they do not completely eliminate complex and/or slow flow blood signal, which is generally the case in IA. Therefore, a MSDE sequence was implemented and optimized. This technique has proven to be more successful in eliminating the signal of blood flow in the carotid artery than DIR while maintaining a higher contrast-to-noise (CNR) of the lumen boundaries[4]. Herein, a motion-sensitized driven-equilibrium BB sequence was optimized to study enhancement of the aneurysm wall following administration of a MPO-specific contrast agent in a model of inflamed saccular aneurysms. Blood signal within the lumen of the aneurysm was sufficiently suppressed in combination with fat-saturation and inversion-pulse specific for aneurysm wall imaging.

Conclusion: Multi-2D MSDE was optimized and implemented for aneurysm wall imaging in a rabbit elastase model. This sequence will contribute in on-going research in the correlation of wall inflammation and intracranial aneurysm instability.

Fig. 4 Change in SNR in the rabbit aneurysm model and control contralateral CCA. *** - p<0.0001)

References: [1] Chen, JW et al. Radiology 2006, 240:473-81; [2] DeLeo III, MJ *et al.* Radiology 2009, 252:696-703 [3] Tulamo, R *et al.* J Neurointervent Surg 2010, 2:12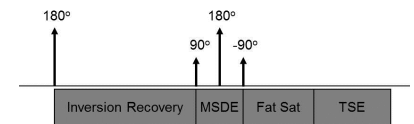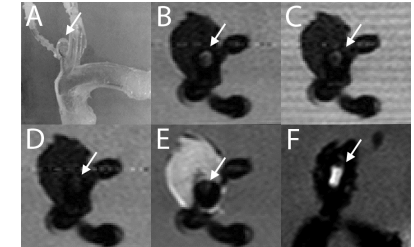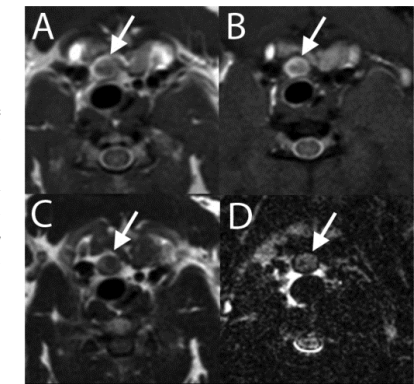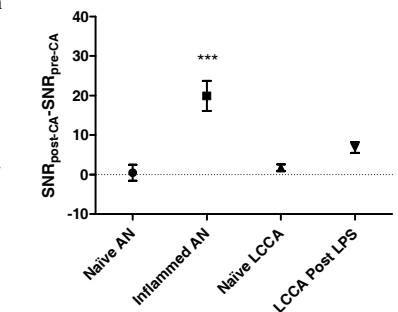0-130 [4] Wang, J *et al. Magn Reson Med.* 2007, 58:973-981