Self-gated dynamic contrast enhanced (DCE) MRI with compressed sensing acceleration to quantify permeability in the aortic root of atherosclerotic mice

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TARGET AUDIENCE: Investigators interested in the in vivo quantification of atherosclerotic plaque permeability using non-invasive MRI.

PURPOSE: High-risk atherosclerotic plaques are characterized by increased endothelial permeability due to inflammation[1]. DCE-MRI (dynamic contrast enhanced magnetic resonance imaging) has previously been applied in atherosclerotic patients[2] and rabbits[3-4] to quantify plaque permeability. Nevertheless, the relationship between endothelial permeability and specific genetic, cellular and molecular pathways in the atherosclerotic cascade remains to be investigated. The inflamed atherosclerotic plaque in the aortic root of the mouse presents an ideal model to study this relationship,since genetic, molecular and cellular assays are well established in mice. However, DCE-MRI in the aortic root of mice is challenging, due to the small dimensions, rapid blood flow through the valves, and high heart rate. The **aim** of this study was therefore to develop a robust DCE-MRI protocol to investigate endothelial permeability in the mouse aortic root.

METHODS: A novel self-gated fast low angle shot (FLASH) sequence was applied to overcome the described challenges in DCE-MRI of the mouse aortic root[5-6]. Unlike conventional cardiac and/or respiratory triggered techniques, this sequence acquires MR data continuously and asynchronously with the periodic cardiac and respiratory motion(**Fig 1A, green bars**). After the acquisition, self-gated data are binned into complete MR images that correspond to different cardiac phases (**Fig 1A, gray dashed lines**), and temporal frames. Binning is accomplished based on the signal of a navigator echo (**Fig 1B**), positioned over the left ventricle (**Fig 1C, white dashed box**). The number of reconstructed cardiac phases and temporal frames can be chosen arbitrarily, although it is limited by the total amount of data acquired.To maximize the number of reconstructed cardiac phases and temporal frames, we have combined self-gated DCE-MRI with prospective **compressed sensing under-sampling[7-8].** For this strategy, we used a weighted sampling strategy, which acquires the center of k-space more often than the rest of the lines in a Gaussian distribution scheme. Using this acquisition, ApoE -/- atherosclerotic mice (n=6, 7 months on Western Diet) were imaged on a 7T pre-clinical MR scanner using a 35 mm volume coil for signal reception. After scout imaging to locate the aortic root (**Fig 1C**),self-gated DCE-MRI was acquired continuously for 30 minutes. After the first 3 minutes, 0.3 mmol/Kg of Gd-DTPA was injected through the tail vein. Imaging parameters are detailed in **Table 1**. Using off-line software written in Matlab, self-gated DCE-MRI was reconstructed using compressed sensing (**Fig 2**), using spatial and temporal total variation (TV) as sparsifying transforms[7]. 15 cardiac phases and 10 temporal dynamic frames were reconstructed, for a total of 150 images.For each reconstruction, a region of interest (ROI) encompassing the aortic root was selected in one cardiac frame, and propagated throughout the 10 dynamic frames to extract theenhancement curves. MR signal was converted to contrast agent concentration using a linearity assumption.

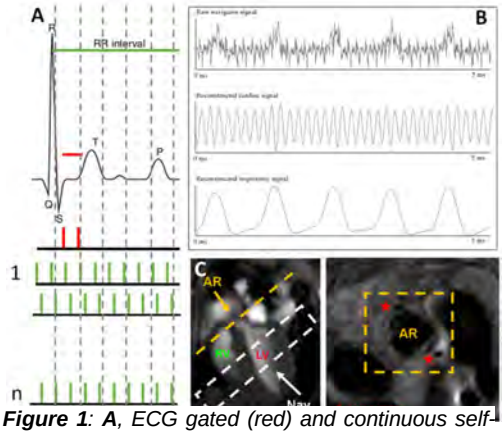

***Figure 1**: **A**, ECG gated (red) and continuous self-gated acquisitions (green). Gray dashed lines, bins for cardiac phases. **B**, raw navigator signal (upper), sorted into cardiac (middle) and respiratory (bottom) signal.**C, left panel:** long axis, 2-chambers view of the heart, showing the left (LV) and right (RV) ventricles, the aortic root (AR, yellow dashed box), and the navigator on the LV (Nav, white dashed box). **C, right panel:** axial image (2D T1W SE ECG triggered) of the AR (yellow dashed box) corresponding to the slice shown in the left panel. Red stars, coronary arteries.*

Table 1	Intragate DCE
Repetition time (TR), ms	9.5
Echo time (TE), ms	2
Flip angle (FA)	10
Spatial resolution, μm²	100 x 100
Slice thickness, mm	1 mm
Field of view (FOV), mm²	2.56 x 2.56
Matrix size	256 x 256
Number of slices	1
Number of frames	15 and higher
Time resolution, min	3 and lower
Total acquisition time, min	~30

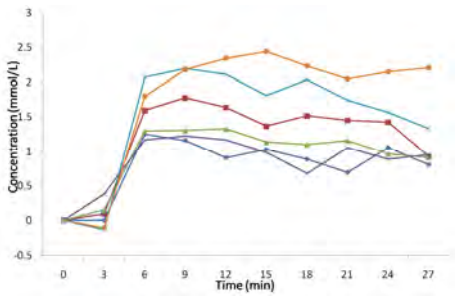

***Figure 3**: ROI contrast agent concentration curves from the aortic root of different mice (selected cardiac phase).*

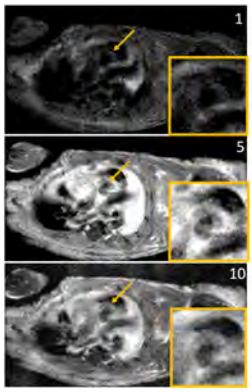

***Figure 2**: Compressed sensing reconstruction of self-gated DCE-MRI of the aortic root. Orange arrow and zoomed-in inserts, aortic root. Numbers indicate temporal frames. The same cardiac phase was depicted.*

RESULTS: We were able to successfully reconstruct 15 cardiac phases and 10 dynamic frames from all acquisitions. For each acquisition, at least one cardiac phase that would clearly show the vessel wall of the aortic root could be identified. **Fig 2** shows an example of such a cardiac phase: three temporal frames are depicted. Signal enhancement can be clearly seen in temporal frames 5 and 10, acquired after contrast agent injection, with respect to temporal dynamic 1, acquired before contrast injection. This pattern of temporal enhancement was found to be consistent across all animals. This is exemplified in **Fig 3**, where ROI concentration curves from each animal (and from one cardiac phase) are represented.

DISCUSSION and CONCLUSIONS: Our results demonstrate the feasibility of self-gated DCE-MRI of the mouse aortic root with prospective compressed sensing acceleration. The continuous, stochastic nature of the self-gated acquisition intrinsically allows reconstructing an arbitrary number of phases during the cardiac cycle, and an arbitrary number of frames during the dynamic acquisition. Here, we reconstruct 15 cardiac phases, and 10 temporal dynamic frames. We foresee that additional optimization of the k-space sampling scheme or of the image reconstruction algorithms may allow accelerating this acquisition even further, to improve the accuracy of permeability quantification in the mouse aortic root. We are currently implementing these approaches to facilitate the extraction of quantitative permeability indices, such as K^{trans}. These measures will be correlated with genetic, molecular and cellular assays in the root, and will serve as read-outs of plaque progression or regression after anti-atherosclerotic therapy. **REFERENCES:**1. Virmani et al, J Am Coll Cardiol 2006; 2.Kerwin WS et al Circulation 2003;3. Chen H Magn Reson Med 2012; 4.Calcagno C et al ATVB 2008; 5.Coolen BF et al Magn Reson Med 2013; 6.Den Adel B et al PLoS One 2013; 7.Motaal AG et al NMR in biomedicine 2012; 8.Lustig M et al Magn Reson Med 2007.