

3D dynamic contrast enhanced (DCE) MRI of atherosclerotic plaques: image quality, temporal stability and ex vivo validation in a rabbit model

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Target audience: Researchers interested in novel methods to improve the quantification of atherosclerotic plaques permeability and vulnerability.

Purpose: Abundant, permeable microvasculature is a hallmark of atherosclerotic plaques at high risk of causing acute cardiovascular events¹, and can be quantified using non-invasive 2D dynamic contrast enhanced (DCE) MRI². However, 2D DCE-MRI can typically quantify plaque perfusion only at a few locations in a vascular bed. This limitation impacts our ability to extensively assess plaque vulnerability, and its changes after intervention. Here, we evaluate and validate a 3D DCE-MRI method with extensive spatial coverage, to improve the quantification of plaque microvasculature/permeability in the entire abdominal aorta of atherosclerotic rabbits.

Table 1	3D TFE	3D TSE	2D DIR
Orientation	Sagittal	Sagittal	Axial
XY resolution	0.5 ² mm ²	0.4 ² mm ²	0.54 ² mm ²
Slice thickness	0.6 mm	0.6 mm	3 mm
SENSE factor	2	1	2
N of slices	20	20	5
Time res	32s	36s	26s

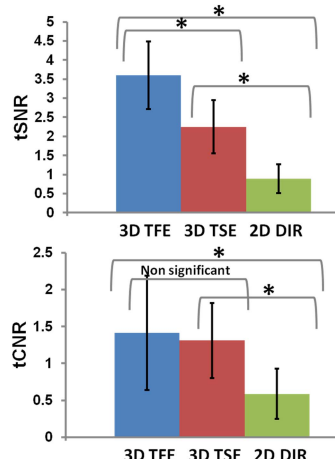


Figure 1: Upper panel, tSNR. Lower panel, tCNR.

Methods: Atherosclerosis was induced in 5 New Zealand White (NZW) rabbits by a combination of high fat diet and double balloon injury of the abdominal aorta². Three normal rabbits were used as non-atherosclerotic controls. Animals were imaged 3 times with DCE-MRI on a 3T clinical MR scanner (Philips Achieva), using a knee coil, with the following sequences: 1) 3D T1W turbo field echo (TFE) with T2 preparation for blood suppression³; 2) 3D T1W turbo spin echo (TSE)⁴; 3) validated 2D double inversion recovery (DIR) T1W TSE², used as gold standard (Table 1). Regions-of-interest (ROIs) encompassing the aortic vessel wall were drawn on all 5 axial slices for 2D DIR, and on all reformatted axial slices in the abdominal aorta for 3D sequences. To compare image quality among different sequences, ROI curves were analyzed by calculating the temporal signal to noise ratio (tSNR) and vessel wall/lumen temporal contrast to noise ratio (tCNR), normalized by slice thickness and by the square root of the acquisition time per frame³. After conversion to concentration, the area under the concentration versus time curve (AUC) was calculated. AUC is a non-model based parameter and a validated measure of plaque microvasculature/permeability in rabbits². After the last imaging session, rabbits were injected with Evans Blue (EB), an albumin binding dye commonly used to quantify vascular permeability ex vivo⁵. Thirty minutes after injection, rabbits were euthanized and the abdominal aortas excised and

imaged with near infra red fluorescence (NIRF). Ex vivo permeability was quantified as EB fluorescent radiant efficiency by NIRF imaging.

Results and discussion: tSNR was significantly higher in 3D TFE DCE-MRI compared to 3D TSE and 2D DIR TSE, while tCNR was not significantly different between 3D sequences (but significantly different from 2D DIR TSE, Figure 1). This indicates a higher temporal stability of ROI curves derived from 3D TFE and comparable image quality between 3D TFE and TSE in terms of vessel wall/lumen delineation. AUC from both 3D TFE and TSE was significantly

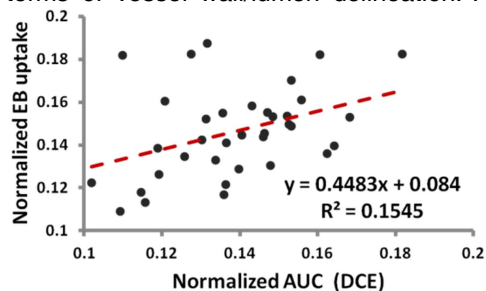


Figure 3: AUC from 3D TFE DCE-MRI correlates with ex vivo EB permeability.

different between atherosclerotic and control animals ($p < 0.05$), as validated by ex vivo EB NIRF ($p < 0.05$, Figure 2). Lastly we found that in vivo permeability quantified as AUC from 3D TFE was significantly correlated with ex vivo permeability by EB NIRF (Figure 3, $R^2 = 0.15$, $p < 0.05$) in atherosclerotic rabbits. The correlation with 3D TSE was instead weaker, and non significant ($R^2 = 0.06$, $p < 0.16$).

Conclusion: Among the 3D sequences tested, DCE-MRI with TFE shows higher tSNR (temporal stability), and a significant correlation with plaque permeability quantified by ex vivo EB fluorescence. We are working on substantiating these preliminary results, and on optimizing 3D TFE DCE-MRI to improve the quantification of plaque microvasculature/permeability by measuring truly quantitative permeability parameters (K^{trans}) using kinetic modeling. This work was supported by NIH/NHLBI R01 HL071021

References: 1. Virmani R, J Am Coll Cardiol, 2006; 2. Calcagno C, Arterioscl Thromb Vasc Biol, 2008; 3. Balu N, Magn Reson Med, 2011; 4. Fan Z, J Magn Reson Imaging, 2010; 5. Greish K, Methods Mol Biol, 2010

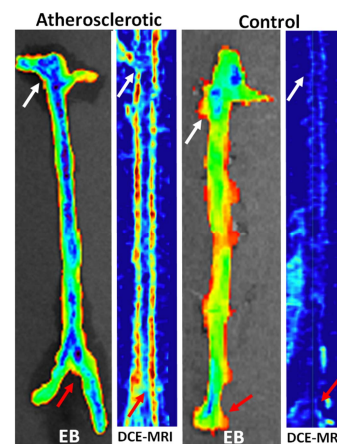


Figure 2: AUC from 3D TFE DCE-MRI is significantly different between atherosclerotic and control animals (hot colors, high AUC), and correlates with EB uptake (blue color, high uptake). White arrows, renal arteries. Red arrows, iliac bifurcation.