Early versus Advanced Atherosclerotic Plaque in vivo Detection by Gadofluorine M-Enhanced Magnetic Resonance Imaging

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Introduction: Detection of subclinical atherosclerosis such as early lesions could improve diagnostic and guidance of therapy. Growth of atherosclerotic plaques is accompanied by neovascularization from vasa vasorum microvessels extending through the media into the base of the plaque.[1] Our group has recently reported the use of Gadofluorine M-enhanced MRI for detection of lipid-rich atherosclerotic plaques.[2] A possible mechanism of plaque enhancement is the penetration of the contrast agent through the adventitia due to increased vasa vasorum feeding the plaque neovasculature. We sought to evaluate in an experimental animal model of atherosclerosis the use of Gadofluorine M for (1) the assessment of early atherosclerotic lesions and (2) to test the hypothesis than enhancement is related to neovascularization from vasa vasorum.

Material and Methods: Atherosclerotic plaques were induced in the abdominal aorta of 12 New Zealand White (NZW) rabbits by balloon injury and hypercholesterolemic diet (HC). They were subsequently divided in 2 groups. The first group (Early) was fed HC for 2 months (n=6) and the second group (Advanced) was fed HC for 8 months (n=6). Six age- and sex- matched animals were used as control (no HC). MRI was performed in a 1.5 T MR system (Siemens) before, and 24 hours after Gadofluorine M (Schering AG) injection (50 µmol/kg; i.v). A T1-weighted segmented gradient-echo sequence was used with an inversion recovery (IR) prepulse and a diffusion (DIFF) based flow suppression prepulse. DIFF prepulse consisted of 3 rectangular radio frequency pulses separated by DIFF gradients as previously reported[2]. The sequence parameters were as follow: TR/TE=300/4 ms; flip angle=20°; BW=±230Hz/pixel; Nex=16; slice thickness=2.5mm; FOV=12cm; matrix 256 x 256; number of segments = 15. Histopathological analysis was performed after Masson's trichrome elastin stain (CME) for atherosclerotic plaque classification. Immunohistochemistry for vasa vasorum microvessels staining was performed using CD34 endothelial cell antibody (at 1:30 dilution). An experienced pathologist, blinded to the MR findings, performed the microvessels quantification in early and advanced atherosclerotic lesions by planimetry.

Results: Gadofluorine M-enhancement MRI was successful in both Early and Advanced lesions (**Figure1**). Contrast-to-noise ratio (CNR) was significantly higher in Advanced group compared to early group ($P<0.01$). No enhancement was seen in control animals. Modified AHA classification revealed type II and III plaque in early group, and type IV, Va and Vc plaque in Advanced group ($P<0.001$). Density of vasa vasorum in advanced lesions was significantly higher compared to early lesions ($P<0.042$). A good correlation ($R=0.60$; $P<0.001$) was found between plaque enhancement (CNR) in MR images and presence of neovessels (vasa vasorum) within the corresponding histopathologic lesions (**Figure2**).

Conclusions:

We demonstrated the successful use of Gadofluorine M-enhanced MRI for early atherosclerotic plaque detection. Early lesions could be differentiated from advanced plaque according to CNR values after Gadofluorine M injection. A good correlation was found between plaque enhancement in MRI and density of vasa vasorum feeding the plaque, suggesting that plaque enhancement is dependent of neovessels density.

References:

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2. Sirol M et al. Lipid-Rich Atherosclerotic Plaques Detected by Gadofluorine M-Enhanced In Vivo Magnetic Resonance Imaging. Circulation.2004;109:2890-2896.

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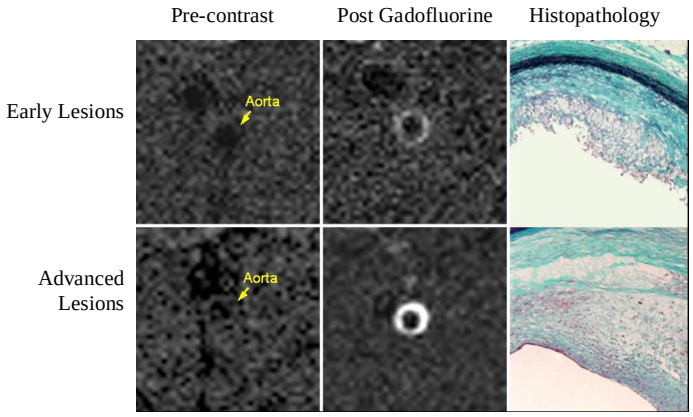

Figure 1

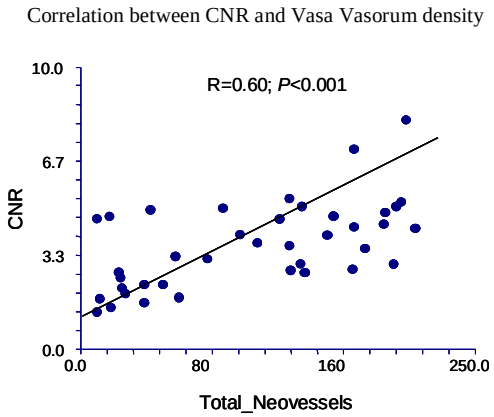

Figure 2