# Lipid-Rich Atherosclerotic Plaque Detection In Vivo Using Gadofluorine and MRI

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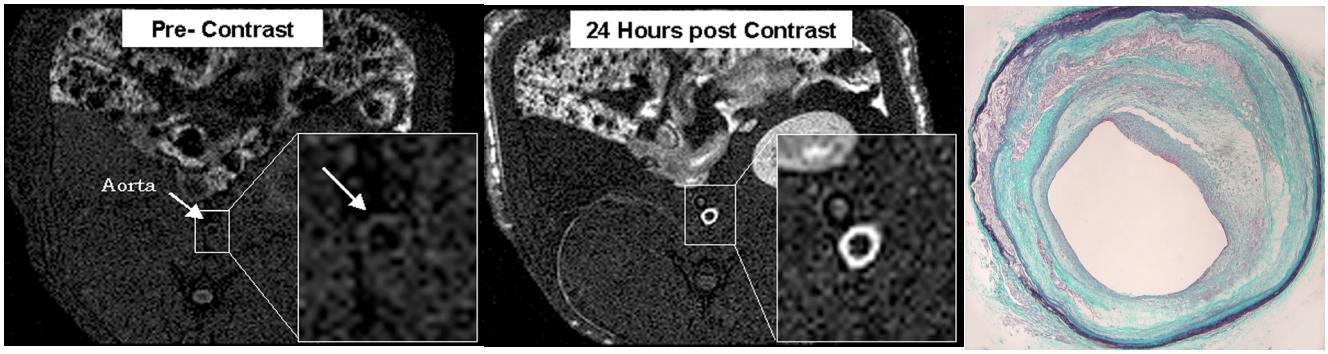
**Introduction**: High spatial resolution and multicontrast MRI have been shown to be capable of characterizing atherosclerotic plaque. However, current imaging techniques are restricted to relatively superficial vascular structures. To address this issue, Gadofluorine has been shown to potentially improve plaque detection using contrast-enhanced MRI.[1] Gadofluorine is a macrocyclic gadolinium based contrast agent, with high relaxivity, long-plasma half-life, water solubility, and lipophilicity compared to Gd-DTPA. Since Gadofluorine has a higher relaxivity (R1) compared to Gd-DTPA, the T1 of the blood immediately post injection, is very short. This leads to a high signal in the arterial lumen that cannot be suppressed using previously used MR methods (e.g. single or multiple inversion recovery preparatory pulses). The aims of our study were: 1) to optimize MR plaque imaging methods using Gadofluorine; and 2) to evaluate the ability of Gadofluorine to detect lipid rich (LR) plaques.

**Material and Methods**: Atherosclerotic plaques were induced by balloon injury and hypercholesterolemic diet in the abdominal aorta of 16 New Zealand White (NZW) rabbits. Eight "normal" rabbits were used as control. MRI was performed in a 1.5 T MR system (Siemens) before (PRE), and after injection (POST) of 50 µmol/kg Gadofluorine (i.v). Different time points were evaluated after injection: PRE, immediately POST, 1-hour and 24 hours POST. Two T1-weighted segmented gradient echo (TFL) MR sequences were optimized for: 1) blood flow suppression (black blood); and 2) plaque enhancement POST. Black blood imaging was performed using TFL with either: a) an inversion recovery (IR) prepulse or b) a diffusion (DIFF) based flow suppression prepulse. DIFF prepulse consisted of 3 rectangular radio frequency pulses separated by DIFF gradients. To enhance vessel wall delineation POST, the surrounding tissue was suppressed by using either IR prepulse or the combination of IR and DIFF prepulse (IR-DIFF). 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 analyses using hematoxylin and eosin (H&E) stain and Masson's trichrome elastin stain (CME) were performed.

**Results**: Using IR-DIFF sequence, either at 1hour or 24hours POST, a pronounced plaque enhancement occurred within the aorta ($p<0.01$ and $p<0.001$ respectively). In contrast, at 1hour POST, using IR-TFL the vessel wall was not delineated due to poor flow suppression, as indicated by contrast-to-noise ratio (CNR): 13.0 ± 7.7 (IR-DIFF-TFL) vs. –19.8 ± 8.3 (IR-TFL) ($p<0.005$). The negative CNR value with IR was due to the high signal intensity (SI) of the aortic lumen (very short blood T1) compared to the SI from the adjacent aortic wall. At 24 hours POST, CNR was higher using IR-DIFF-TFL vs. IR-TFL, but the difference did not reach statistical significance (respectively 15.2 ± 5.9 vs. 11.4 ± 8.9; $p=0.052$). Histological analysis showed different features of the plaque, such as lipid rich (LR) areas, collagen content or fibrous cap thickness. Although the pattern of enhancement was circumferential in all transverse aortic MR images analyzed, measurement of SI and CNR was higher in the LR quadrants compared to non-LR quadrants as shown by histology ($p<0.05$; $p<0.001$, respectively). A strong correlation ($r^2 = 0.87$; $p<0.001$) was found between CNR at 24 hours POST and the LR areas, suggesting a high affinity of Gadofluorine for lipid components.




**Conclusion**:

Our study demonstrates that Gadofluorine facilitates and improves plaque detection in NZW atherosclerotic rabbits compared to conventional contrast-enhanced and non-contrast-enhanced MRI. The development of a new T1-weighted sequence (IR-DIFF) that allows in vivo detection of atherosclerotic plaque within the first hour after Gadofluorine injection is very useful. The strong correlation between lipid rich areas as shown by histology and CNR in matched MR images suggests a high affinity of Gadofluorine for lipid-rich regions of the plaque. Gadofluorine-enhanced MR imaging may be helpful in the detection of atherosclerotic plaque burden and components and the assessment of the efficacy of anti-atherogenic therapies.

**Reference**

1. Barkhausen J, Ebert W, Heyer C, Debatin JF, Weinmann H-J. Detection of Atherosclerotic Plaque With Gadofluorine-Enhanced Magnetic Resonance Imaging. *Circulation*. 2003;108:605-609.

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