Contrast-Enhanced High Resolution MRI of atherosclerotic plaque in Watanabe rabbits

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Introduction
There is a growing field of investigation dealing with plaque identification and characterization before plaque rupture or lumen obstruction. In this scope, intravascular agent like MS325 (Angiomark®) or USPIO (Sinerem®) have been used as vascular wall marker to highlight vessel wall abnormalities. In this concept, due to its size and shape, P792 is a Rapid Clearance Blood Pool Agent (RCBPA), which is a marker of the intravascular space except in case of endothelium damage.

The present study was designed to get an insight into atherosclerosis process on high resolution MR images of aorta with atherosclerotic lesions in heterozygous Watanabe rabbits, using two agents USPIO and P792.

Material & Methods
MR experiments were performed on a 1.5 Tesla (Vision, Siemens) using a transmit-receive head coil.

Three old heritable hyperlipidemic rabbits (19 to 24 months) were used and two were fed a lipid-rich diet. For each animal, several MRI examinations on thoracic aorta were done, as follows:

First, 3DTOF (TR/TE=25/11ms, 0.3x0.3x2mm3) and T1 SE (TR/TE=450/14ms, 0.2x0.2x3mm3) and T2 TSE (TR/TE=2000/45ms, 0.5x0.5x3mm3) sequences were performed. Five days after injection of USPIO (dose of 1mMol Fe/kg), contrast-enhanced 3DMRA (TR/TE=4.6/1.8ms, 0.7x0.7x1mm3) was done. And 15 days after, 3DMRA was acquired using P792 at a dose of 0.016mMol/kg. And T1 SE sequence was performed before and 15 minutes after the injection.

For histopathologic analysis, transversal slices of the aorta were cut in the corresponding imaged regions with haematoxylin, eosin (HE), Oil Red O (for lipids), Orceine (for elastin), and Von Kosa (for calcification) staining.

Arterial lumen and wall definition were compared before and after injection of contrast agent. Quantitative SNR measurements of lumen and artery wall were conducted on each T1 MR images of the different rabbits, and enhancement evaluated as follows [\((\text{SNR}_{\text{after}} - \text{SNR}_{\text{before}})/\text{SNR}_{\text{before}}\)\%].

Results
Before injection of contrast agent, atherosclerotic lesions of the thoracic aorta were detected only in the diet-fed rabbit, showing heterogeneity and concentric thickening of the wall on T1 weighted images. The arterial wall in rabbits without diet was difficult to distinguish since the wall was thin (less than 1mm), weakly injured and hidden by the surrounding fat tissues.

Five days after USPIO injection, the arterial wall signal intensity decreased (-12.3±30.4%) on T1 weighted images (figure 1). This signal intensity decrease varied upon location along the aorta. On MRA images, susceptibility artifacts in the vessel wall appeared in the arterial lumen edges. In diet-fed rabbits, T1 weighted images, after the injection of P792, showed enhancement of the arterial wall (32.3±13.7%) and lumen was better defined than before (figure 2). No such enhancement was observed in rabbits with normal diet. As shown by histology, composition and structure of lesions varied along the thoracic aorta as also observed by MRI.

Conclusion
Normal Watanabe rabbits develop thin lesions compared to cholesterol-diet rabbits, as previously found by MRI and confirmed by histology. Thus, in diet-fed rabbits, signal intensity of atherosclerotic wall was considerably increased after P792 injection. This feature facilitated arterial lumen and wall observation contrary to the signal decrease observed with USPIO. In addition, this agent may improve differentiation from normal to atherosclerotic wall as observed between normal and diet-fed rabbits. Furthermore, it may indicate the permeability or neovascularization of arterial wall, which is linked to inflammatory activity. Previous studies have shown the uptake of USPIO contrast agent by macrophages present in atherosclerotic plaques, which appeared as susceptibility artifact on MR angiography. Toward this end, dynamic contrast-enhanced MR imaging is necessary to develop new tools to understand the mechanisms involved in atherosclerotic disease.

References