

Department of Radiology

In Vivo Molecular Enzyme-Specific MR Imaging of Active Inflammation in a Pilot Animal Model of Carotid Artery Aneurysm

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Background: Half of all patients who suffer aneurysmal subarachnoid hemorrhage die within the first 30 days. Recent evidence implicates acute local intramural inflammation in intracranial aneurysm instability and rupture.

Objectives: The purpose of this pilot study was to demonstrate the feasibility of using a myeloperoxidase (MPO)-specific paramagnetic MR contrast agent to identify active inflammation in an animal model of carotid artery aneurysm not yet described in the literature.

Methods: All animal experiments were approved by our Institutional Animal Care and Use Committee. Elastase-induced saccular aneurysms were created at the root of the right common carotid artery in New Zealand white rabbits (n=16). Intramural and perivascular injection of *E. coli* lipopolysaccharide (LPS) was delivered via endovascular approach to induce aneurysm inflammation. Following intra-arterial injection of 0.1mmol/kg di-5-HT-GdDTPA, animals were subjected to 3T MRI. Intramural presence of MPO in LPS-injected aneurysms was confirmed immunohistologically. Active MPO activity was verified by measuring the spectrophotometric oxidation of guaiacol.

Results: Endovascular injection of LPS resulted in inflammatory cell infiltration into the aneurysm wall and there was a difference of expression of active MPO compared to control aneurysms (20.3 ngMPO/mg tissue versus 0.12 ngMPO/mg tissue, $p<0.002$). 3T MR imaging of inflamed aneurysms demonstrated a difference in enhancement ratio compared to control aneurysms (1.55 ± 0.05 for LPS versus 1.16 ± 0.10 for control, $p<0.02$).

Conclusion: This pilot study establishes the feasibility of an animal model of saccular aneurysm inflammation that can be visualized with clinical field strength MRI using the enzyme-sensitive MR contrast agent di-5-hydroxytryptamide of GdDTPA, a paramagnetic MPO substrate that specifically enhances MR signal.