MRI ASSESSMENT OF ENDOTHELIAL DAMAGE AND ANGIOGENESIS IN PORCINE CORONARY ARTERIES USING GADOFOSVESET

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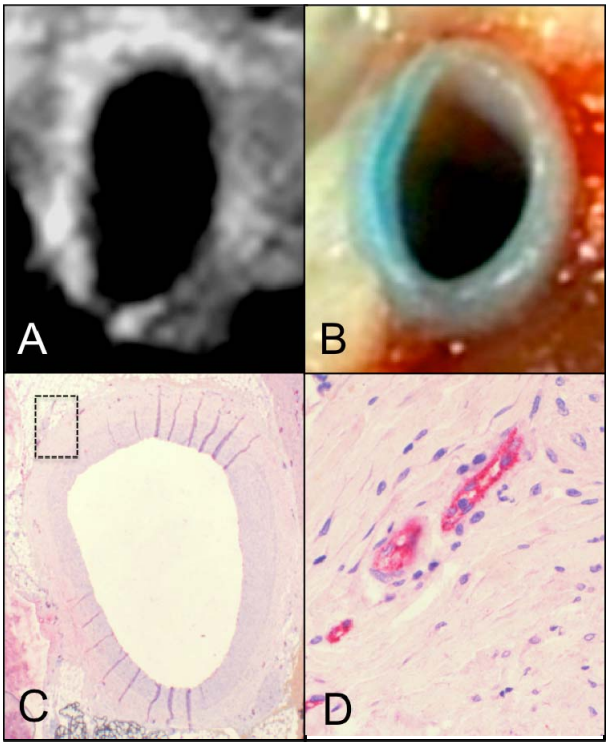
Introduction: Endothelial damage and angiogenesis are essential in atherosclerotic plaque development and destabilization (1). Macromolecules in the blood may extravasate into the vessel wall through leaky neovessels or damaged endothelium. Gadofosveset is an MRI contrast agent that binds reversibly to albumin and may enter damaged tissue such as the atherosclerotic vessel wall together with albumin (2,3). We sought to examine whether contrast enhanced MRI using gadofosveset would enable the detection of endothelial damage and neovessels in balloon injured porcine coronary arteries.

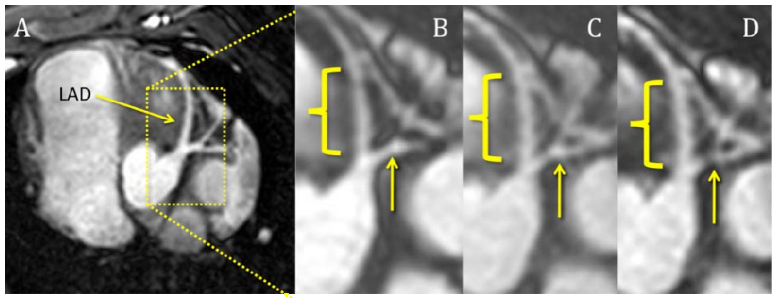
Methods: Ten pigs underwent balloon injury of the left anterior descending coronary artery (LAD) to induce endothelial damage and angiogenesis. After balloon injury, in-vivo and ex-vivo T1-weighted coronary MRI was performed after intravenous injection of gadofosveset. The ex-vivo MR images were matched with corresponding histological sections and correlated to endothelial damage and angiogenesis.

Results: Ex-vivo coronary vessel wall MRI contrast enhancement was in agreement with extravasated Evans blue as a marker of endothelial damage with a kappa value of 0.64 ($p<0.001$) (Figure 1)). Sixty minutes post contrast, MRI showed contrast enhancement of the injured LAD as compared to the non-injured circumflex artery that served as control with a significant increase in the diameter of the artery (30±19 % versus 4±8%; P=0.01) (Figure 2)). There was a linear correlation between coronary MRI contrast-enhancement and microvessel density ($r=0.78$, $p<0.001$) (Figure 3).

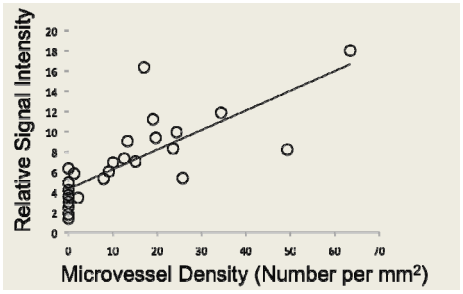
Conclusion: Contrast enhanced coronary MRI using gadofosveset is a promising approach for the non-invasive detection of endothelial damage and angiogenesis in the coronary artery wall



Figur 1: Ex vivo T1-weighted MR images of a balloon damage porcine coronary artery 2 hours after injection of gadofosveset (A). Photo of the corresponding segment demonstrating extravasation of Evansblue into the arterial wall (B). Histological identification of microvessels (positive for von Willebrandfactor[C,D]). Note the strong MR signal located to the arterial wall after injection of gadofosveset corresponding to the area with uptake of Evans blue and to neovessel-rich areas in the histological section (D).



Figur 2: Coronary bright-blood MR-angiography (A). T1-weighted inversion-recovery at 5 min (B) 15 min (C), and 20 min (D) after intravenous administration of gadofosveset.Notice that the diameter of the balloon damage LAD segment increases over time and develops a characteristic ripple pattern.Balloon damage=({), control vessel CX= (arrow).



Figur 3: Comparison of plaque enhancement by MRI and wall microvessel density by histology (number per mm2). $r=0.78$, $p<0.001$. regression line are automatically drawn.

(1) Naghavi M, Libby P, Falk E et al. From vulnerable plaque to vulnerable patient: a call for new definitions and risk assessment strategies: Part I. *Circulation* 2003;7;108(14):1664-72. **(2)** Goyen M, Shamsi K, Schoenberg SO. Vasovist-enhanced MR angiography. *Eur Radiol* 2006;16 Suppl 2:B9-14. **(3)** Caravan P, Ellison JJ, McMurry TJ, Lauffer RB. Gadolinium(III) Chelates as MRI Contrast Agents: Structure, Dynamics, and Applications. *Chem Rev* 1999;8;99(9):2293-352.