Validation of atherosclerotic plaque composition and structure at 7T and 3T MRI

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Background

Stroke is the third leading cause of death and the single largest cause of disability in the UK [1]. Eighty percent of strokes are ischaemic stroke, and approximately 25-50% of these are caused by carotid atherosclerosis [2]. While carotid endarterectomy (CEA) is a useful procedure to reduce the risk of stroke in patients with moderate or severe stenosis, 70% of symptomatic patients with severe stenosis remain stroke-free over the next 5 years with medical therapy alone [3]. Others with lesser grade stenosis may progress more rapidly to stroke, due to underlying active atherosclerotic plaque. Outcomes from CEA could be improved by targeting treatment at high-risk subgroups and not simply relying on the degree of stenotic measurement [4].

The aim of this project is to validate non-invasive in-vivo (3T) and ex-vivo (7T) MRI with histopathological examination to assess atherosclerotic plaque composition.

Methods: Thirty three endarterectomy cross sections, from 14 patients, were studied. The datasets consisted of in-vivo 3T MRI, ex-vivo 7T MRI and histopathology.

In-vivo: Imaging was carried out using a 3T MRI GE Signa Excite HD and a 4–channel surface coil. The imaging protocol was: Time-of-Flight (TOF) MR angiogram (MRA) of carotid bifurcations (TR/TE/Flip Angle/slice thickness: =16.52ms/3.848ms/80°/3mm, 89 slices), axial 2D FSE (fast spin echo) double inversion recovery (DIR; TI: 1550ms, fat sat), peripheral cardiac gating: T1-W (TR/TE:722-1034ms/7-12ms), PD-W(TR/TE:1411-2857ms/8-21ms) & T2-W (TR/TE:1237-2105ms/57-62ms, depending on heart rate) +/-T1-W post gadolinium. 3-5 slices (2-2.5mm), FoV: 140mm^2, 512^2 matrix.

Ex-vivo: CEA specimens were immediately fixed following surgical removal in 10% formaldehyde. They were rehydrated in sterile phosphate buffer saline (PBS), at room temperature for 24 hours prior to scanning and then placed in a de-gassed Fomblin-filled syringe along with a phantom (1g/l $MgCl_2$) for imaging. The MRI system used was a 7T Bruker Biospin Biospec 70/30 MRI (35mm Bruker birdcage). The protocol included: T1-W FLASH (TR/TE/flip angle: 40ms/2.315 ms/30˚/matrix: 280x170x170/FOV: 2.8x1.7x1.7 cm^3), T2-W multi slice multi echo (MSME)(TR/TE: 1200ms/8.018ms/ matrix 155x94x94/ FOV: 2.8x1.7x1.7cm^3). Diffusion-weighted imaging: stimulated echo (TR/TE: 750ms/13ms, δ: 2.2 ms, b-values: 0 & 750 s/mm^2, along 3 directions. Resolution: 100 μm^3, scan time ~ 38 hours.

Histology: Following ex-vivo MR, the specimen was divided into approximately 5 sections, each embedded en bloc in paraffin wax. 4 μm thick sections were taken from each section and stained with haematoxylin & eosin (H&E) and Miller's elastin/van Gieson (EVG).

Data analysis was carried out using Analyze (AnalyzeDirect, Inc.) for co-registrations, and a semiautomated method was programmed in Matlab (MatLabWorks, Inc.) for image segmentation. MRI signal from the different image-weightings were normalised to the sternocleidomastoid muscle [5] in the case of the in-vivo results while in ex-vivo was relative to the external phantom added.

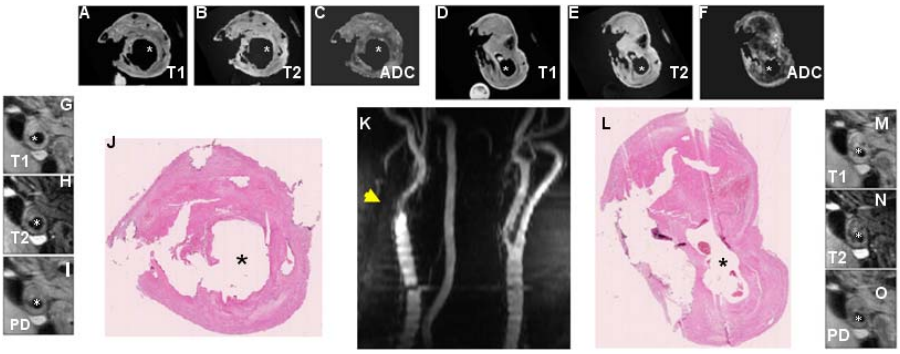

Figure. Multicontrast weighted images (T1-w, T2-w, PD-w and ADC) of vulnerable plaque at the common and the bifurcation were obtained in vivo (G-I and M-O) and ex vivo (A-F). Asterisks indicate the lumen. Histological images stained with haematoxylin & eosin digitised (J and L). Head arrow indicates the plaque location.

Results and Conclusions: 3T/7T MRI and histology measurement showed no significant differences, except for 7T LR/NC (Lipid Rich/Necrotic Core) without haemorrhage and haemorrhage, but combined LR/NC with haemorrhage presented non significant difference in the average area per plaque by a paired t-test. The results showed good correlation between MRI and histopathology measurements, although haemorrhage (r = 0.26, p = 0.437) at 3T MR was poorly correlated with histology; calcification (r = 0.4, p = 0.22) and LR/NC without Haemorrhage (r = 0.4, p = 0.23) at 7T showed less good correlations with histology. This study provides evidences that 3T/7T MRI techniques might help to determine atherosclerotic plaque composition by comparing with the composition defined by histology. A combination of different MRI techniques might help to improve haemorrhage identification.

References: 1. National Audit Office. Department of Health. Reducing Brain Damage: Faster access to better stroke care 2005. www.nao.org.uk. 2. Adams HP, Bendixen BH, Kapelle LJ, Biller J, Love BB, Gordon DL, et al. Stroke 1993; 24(1):35e41. 3. Dennis MS, Bamford JM, Sandercock PA, Warlow CP. *Stroke* 1989; 20: 1494–99. 4. Markus HS, King A, Shipley M, et al. Lancet Neurol 2010;4422(10):70120-4. 5. Saam T, Ferguson MS, Yarnykh VL, Takaya N, Xu D, Polissar NL, Hatsukami TS, Yuan C. Arterioscler. Tromb. Vasc. Biol, 2005, 25:234-239.