in vivo and ex vivo multimodal characterisation of human carotid artery atherosclerosis plaques.

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Introduction:

Plaque ulceration, thrombosis and intraplaque haemorrhage are the main causes of stroke and clinical symptoms of atherosclerosis [1,2]. In addition to the degree of luminal narrowing, characterisation of the plaque composition and ultrastructure is important for the assessment of stroke risk. *Ex vivo* MR microimaging at very high magnetic field allows for detailed assessment of the plaques components. Furthermore, *in vivo* MR images can easily be correlated to histological analysis based on ex vivo high spatial resolution images. In this multimodal study, *ex vivo* plaque contrast and relaxation characteristics were analysed based on high spatial resolution images and compared to in vivo MRI and CT images.

Material and methods:

Patients and samples preparation: The selected patients (n=8) showed mixed irregular calcified soft plaques with > 70 % stenoses on both CT angiogram and carotid Doppler ultrasound. They underwent an eversion carotid endarterectomy with feathering of the ICA distal plaque. The used plaques were 1-3.5 cm long and 0.5-1.4 cm wide. They were fixed in formalin following removal.

In vivo MRI: Patients were scanned on a 3T Philips scanner using a 16 channel cardiovascular array coil. For the carotid imaging, the applied sequences were: 3D Time Of Flight angiography (140 slices, Spat.Res.=0.7x1.2x1mm); pre- and post-contrast T_1 weighted spin echo (TE/TR=27/604ms, 16 slices, Spat.Res.=1x0.9x3mm); T_2 weighted TSE (TE/TR=80/3000ms, 21 slices, Spat.Res.=0.6x0.7x3mm) with fat saturation; and contrast-enhanced MR angiography (150 slices, Spat.Res.=0.6x0.6x1mm).

Ex vivo MRI: Data were acquired on a 9.4 T Agilent scanner (Agilent Technologies, Santa Clara, CA, USA) using a transmit/receive volume coil (Ø = 33 mm, made by Rapid Biomedical). Before the scanning, the plaques were immersed in fomblin to avoid any susceptibility artefacts. Manual shimming was performed after positioning of the plaques based on low spatial resolution pilot images. The high spatial resolution T_1 and T_2 weighted images (T_{1W} and T_{2W}) were acquired using 3D fast spin echo sequences. The T_2^* weighted images ($T_2^*{}_W$) were acquired using 3D multi gradient echo sequence. The spatial resolution of the acquired images was 100x100x100 μm^3 (FOV=51.2x12.8x12.8 mm3, Matrix=512x128x128). The readout encoding was applied along the longest dimension of the plaques. For the comparison with the in vivo images, the ex vivo images were reorientated to be displayed as axial images. The acquisition parameters were: (a) for the T_{1W} images, $TE/TE_{eff}/TR$ = 8.3/8.3/500 ms, ETL=2, NEX=4; (b) for the T_{2W} images, $TE/TE_{eff}/TR$ = 15/15/2000 ms, ETL=2, NEX=1; and (c) for the $T_2^*{}_W$, TR=100 ms, TE=2.9/9.4/15.9/22.4/28.9 ms, NEX=8. The data were fitted using a Matlab program developed in-house.

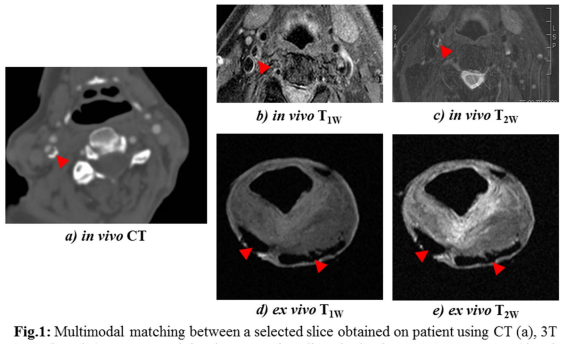

Fig.1: Multimodal matching between a selected slice obtained on patient using CT (a), 3T MRI (b and c) scanners and the closest ex vivo slice obtained at 9.4T MRI scanner (d and

Results:

Fig 1 is a representative case showing one selected slice of an ex vivo plaque image. These images were obtained using 3D multi-GE T_2*W (Fig 1.a), 3D SE T_1W (Fig 1.b), 3D SE T_2W (Fig 1.c) sequences. Fig 1.d shows the results of the T_2* mapping based on multi-TE images. The very restricted lumen is indicated by blue arrows. Fig 2 shows the multimodal matching between the selected slice obtained on patient at 3T and CT scanners and the closest ex vivo slice obtained at 9.4T. *Ex vivo* T2* values were lower than 30ms. The range of T2* values within the bright regions on both T1W and T2W images was 20-30 ms. The dark regions (indicated by red arrows on Fig2) on MR images correspond to the calcified regions which are bright on CT images. The areas of T2 hyperintensity (long T2 and T2*) close to the lumen represent fibrous and myxomatous plaque components.

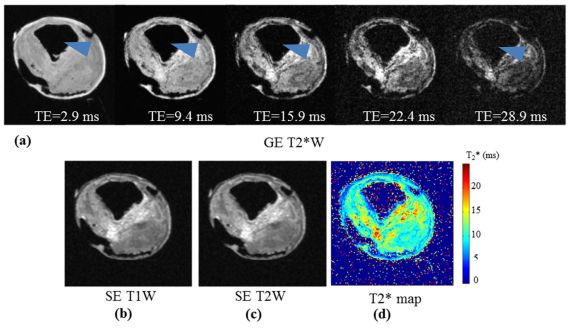

Fig2: Ex vivo plaque images of one selected slice obtained with different sequences. a) 3D multi-GE images. b) 3D SE T_{1W} images obtained at T_{eff} = 20 ms. c) 3D SE T_{2W} images obtained at T_{eff} = 8.9 ms. d) T_2* mapping based on multi-GE images.

Discussion:

Plaque morphology was assessed using complementary in vivo and ex vivo imaging approaches , allowing detailed assessment of intra-plaque haemorrhage (short T1) , calcification, dark regions on the MRI due to the very short T_2 (red arrows), and fibrous and myxomatous components (bright regions on MR images (long T2 and T2*). Compared to the *in vivo* images, more structure can be distinguished on *ex vivo* high spatial resolution images.

Conclusion and Perspectives:

This multimodal imaging study performed on in vivo and ex vivo plaques allows a comprehensive assessment of the plaque ultrastructure. Ex vivo studies are useful to optimise parameters for in vivo clinical scanning and provide quantitative parameters of plaque components helping the identification of patients with high stroke risk. This preliminary study was designed to compare native contrast imaging between in vivo and ex vivo scanning of atherosclerotic plaques. Further studies based on targeted contrast agents [4] might provide increased specificity, and might serve as a basis for translation of these agents into the clinics.

References: [1] Sharma Magn. Reson. Med. Sci. 2002 ; [2] Altaf et al. Radiology 2011; [3] van Engelen et al. Phys. Med. Biol. 2012 ; [4] Phinikaridou Circulation 2012.