Asymptomatic patients harbouring vulnerable carotid plaques can be identified by USPIO enhanced multi-sequence MRI

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Purpose: Recently, ultrasmall superparamagnetic iron oxide (USPIO) enhanced MRI has been validated to identify inflamed plaques in symptomatic patients. The ability to identify vulnerable, inflamed plaques in asymptomatic patients would improve the selection of patients for definitive therapy prior to plaque rupture and subsequent ischemic stroke. We set out to determine whether vulnerable carotid plaques could be identified in asymptomatic patients using histological criteria to validate the in vivo findings of multi-sequence USPIO enhanced MRI.

Methods and Materials: In vivo MR imaging of 8 patients was performed on a 1.5T whole body system using a dedicated 4 channel phased-array coil. The following 2D, ECG-gated, blood suppressed, fast spin echo (FSE) pulse sequences were used with a voxel size of 0.4x0.4x3mm: T_1W fat saturated (TR/TE: 1*RR/ 7.8ms, pixel size:), Intermediate T_2W fat saturated (TR/TE: 2*RR/46ms), T_2W (TR/TE: 2*RR/99.8ms), STIR (TR/TE: 2*RR/46) In addition two 2D blood suppressed T_2*W spiral sequences (TR/TE: 1*RR/5.6 & 15ms) were used with an effective voxel size: 0.42x0.42x3mm. The USPIO contrast agent Sinerem® (Guerbet, Roissy, France) was given by i.v. infusion and the carotid arteries re-imaged 24-36hours post infusion using theT_1W and T_2*W sequences. Retrieved specimens were stained to identify fibrous cap, lipid core, iron and macrophage content. Previously validated MR criteria were used to identify plaque components and USPIO particles on MRI. Excised plaques were classified as inflamed if there were a large number of macrophages present; inflammation on MR images was classified by the presence of an USPIO particle induced signal drop. The sensitivity and specificity of USPIO enhanced MRI for identifying inflamed plaques was determined.

Results: Data from 2 patients was excluded due to poor quality of images or histological preparation. Thereafter there were 25 matched MR and histological slices for comparison. Histologically, there were 13 inflamed plaque sections in 3 patients. Double immunostaining and electron microscopy confirmed co-localization of USPIO particles within macrophages. USPIO caused a drop in signal intensity on post-infusion T2*W images (Fig 1). USPIO enhanced multi-sequence MR had a sensitivity of 77% and specificity of 72% for identifying inflamed plaques.

Conclusion: Multi-sequence USPIO enhanced MRI was able to identify inflamed plaques with high macrophage content in asymptomatic patients. This technique has the potential to identify vulnerable plaques prior to rupture, thus allowing early intervention to be instituted.

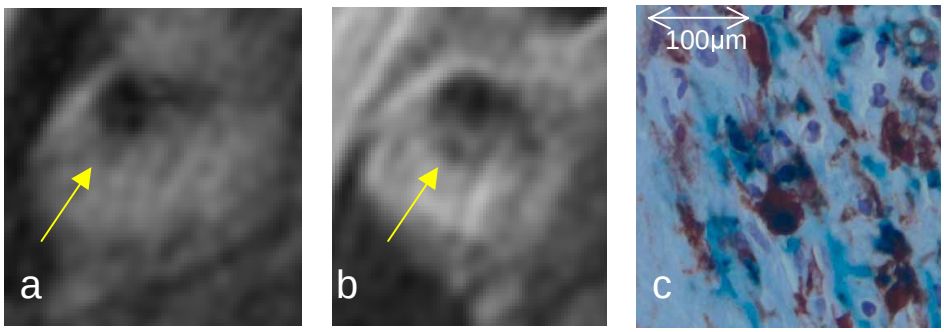

Fig 1. T2*W images (a) Pre- and (b) post USPIO infusion, showing area of USPIO induce signal drop (arrow); (c) Mac 387/Perls double stain showing co-localization of USPIO with macrophages.