Comparison of USPIO-enhanced MRI and magnetically labelled cell tracking for Inflammation detection in ApoE mice

O. M. Sigovan[1], A. Bessaad[1], H. Alsaid[1], G. De Souza[1], C. Corot[2], N. Provost[3], Z. Majd[3], C. Menager[4], N. Nighoghossian[1], S. Nataf[5], and E. Canet-Soulas[1]

[1]CREATIS-LRMN Laboratory, University of Lyon, Lyon, France, [2]Research, Guerbet, Paris, France, [3]Technology Development, Genfit, Lille, France, [4]Laboratoire Liquides Ioniques et Interfaces Chargées, Pierre et Marie Curie University, Paris, France, [5]U842, INSERM, Lyon, France

Introduction

There is a clinical need for a noninvasive method of atherosclerosis assessment. Macrophages play a central role in atherosclerosis and are associated with vulnerable plaques [1]. The objective of the present work was to evaluate two strategies for the MRI detection of atherosclerosis inflammation in Alipoprotein E modified (ApoE) mice.

Materials and Methods

Two groups of ApoE-modified mice, under high fat diet (Western Diet, 0.5% cholic acid and 1.25% de cholesterol), were investigated at 4.7T. After baseline MRI, one group (n=4) received a retro-orbital injection of a dose of 1000 µmolFe/kg, of a rapid pharmacokinetics USPIO (P904, Guerbet Laboratories, Paris, France). The second group (n=5) received an injection of 250 µl containing 10 million magnetically labeled macrophages [2]. All animals were followed for 3 days post contrast administration. At the end of the MR imaging, aortic arch samples were prepared for histological analysis and iron detection by Prussian blue staining.

Cardiac and respiratory gated MRI acquisitions were used for high resolution imaging of one slice, positioned perpendicular to the ascending aorta to visualize the vessel wall. Two spin echo sequences with different T2 weightings were used for lesion detection and USPIO uptake assessment.

Results

Figure 1 shows representative images obtained during the MR follow up. The high in plane resolution (98µm) allowed a clear visualisation of the aortic wall. Direct injection of free USPIO leads to an extended signal loss in the aortic wall (Fig.1A). With labelled macrophages injection, localized regions of signal loss were observed (Fig.1B, white arrows) and were correlated to the presence of iron on histological slices (Fig.1D)

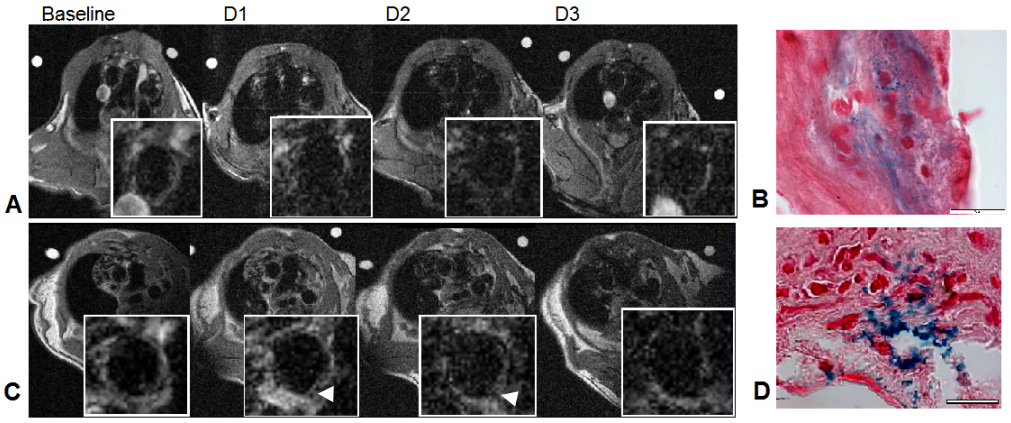

Figure 1. Spin echo images obtained during the MRI follow up for the two strategies: free USPIO injection (A) and magnetically labelled cells (C). The insets represent magnified images of the vessel wall. Corresponding histological slides showing positive Prussian blue staining for iron (B and D, bar=20µm)

Conclusion

The free particle injection strategy allows reliable inflammation detection and has the advantage of being directly applicable in clinics. However, it is not entirely specific to inflammation phenomena at a cellular level, an indirect labeling is performed. The magnetically labeled cell tracking strategy enables a direct view of a specific cellular type, i.e. macrophages. By pushing the MR detection limit, valuable information can be gained on the inflammatory status of atherosclerotic lesions.

References:

1. Ziener, MRM, 2005, 702-706
2. Wilhelm et al., Biomaterials, 2003, 1001-1011