Imaging inflammation in abdominal aortic aneurysms with MRI

C. Gray[1], TJ. MacGillivray[1], JMJ. Richards[2], SI. Semple[1], JP. Langrish[2], M. Williams[2], M. Dweck[2], W. Wallace[3], G. Mckillop[4], RTA. Chalmers[5], OJ. Garden[6], DE. Newby[2]

(1) Clinical Research Imaging Centre, University of Edinburgh; (2) Centre for Cardiovascular Science, University of Edinburgh; (3) Department of Pathology, Royal Infirmary of Edinburgh; (4) Department of Radiology, Royal Infirmary of Edinburgh; (5) Department of Surgery, Royal Infirmary of Edinburgh; (6) Centre of Clinical and Surgical Sciences (Surgery), University of Edinburgh

Lay Summary

Ruptured abdominal aortic aneurysm has a mortality rate greater than 90%. Accurate assessment of risk of rupture would allow correct identification of those patients who would benefit from preventative surgery. Existing methods are reliant solely upon measuring the maximum diameter of the aneurysm from scans and do not take into account the biology of the disease.

Aneurysm tissue is characterised by excessive medial neovascularisation, inflammation and irreversible remodelling of the extracellular matrix weakening the vessel wall. These pathological processes do not affect the aorta uniformly but are focal in nature. Such biological *hotspots* are thought to be regions of the wall at increased risk of expansion and rupture, and therefore represent potential imaging targets. The aim of this study was to investigate the use of Magnetic Resonance Imaging with specialized particles that not only gather in inflammatory areas but also show up dark in the scans. This allows *hotspots* to be identified. Based on encouraging early results it is hoped that in the near future that this type of Magnetic Resonance Imaging might improve the assessment of patients for risk of rupture.

Background

Abdominal aortic aneurysm (AAA) disease is characterised by focal *hotspots* of neovascularisation, inflammation and proteolysis. These *hotspots* represent areas of AAAs at risk of expansion and rupture[1-3]. We have used Magnetic Resonance Imaging (MRI) scanning with ultrasmall superparamagnetic particles of iron oxide (USPIO) to detect areas of cellular (macrophage) inflammation.

Methods

Patients (n=29) with asymptomatic AAA (>4 cm in diameter) were imaged in a 3T MRI scanner before and 24 h after administration of USPIO. Multi-echo, gradient-echo T2*-weighted and TSE T2-weighted sequences were acquired. Images were registered, and custom written software calculated a mean per cent change in T2* value (ΔT2*) from a multi-voxel grid and presented on a colour map.

Results

USPIO administration resulted in differential changes in T2* value within the AAA. A change in T2* value in the peri-luminal thrombus was seen in the majority of patients. In addition, some patients had focal areas of USPIO uptake elsewhere within the AAA, consistent with inflammatory hotspots and aneurysm instability. The T2* value of skeletal muscle (control) was unchanged. Histological analysis of operative tissue samples from AAA wall showed USPIO co-localising with macrophages.

Discussion and Conclusions

We have demonstrated for the first time non-invasive, in vivo detection of macrophages and inflammation in AAA using MRI and USPIO. This represents a promising, highly relevant approach to the detection of AAA inflammation and the prediction of disease progression and rupture. In a wider context, this technique could be applied to non-invasive imaging of inflammatory processes in other parts of the body.

Figure 1: Siemens Magnetom Verio 3T Whole-Body MRI Scanner located in the Clinical Research Imaging Centre, Edinburgh.

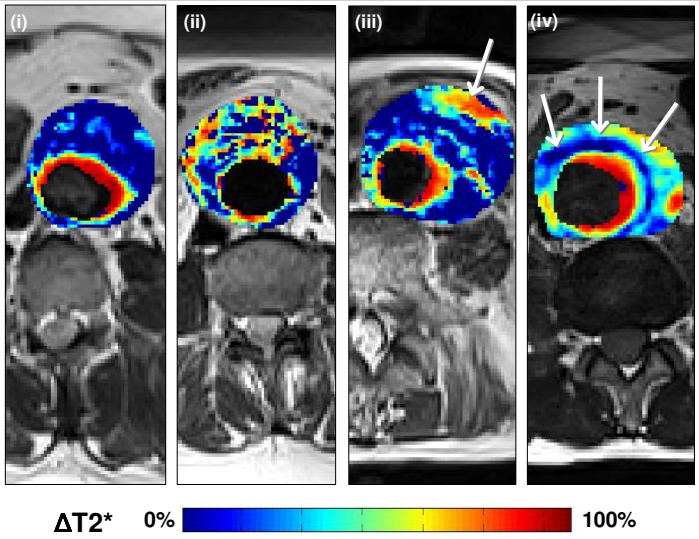

Figure 2: Figures i-iii are colour maps of representative slices for patients classified into three groups showing distinctive patterns of USPIO uptake:

Fig i) USPIO uptake in the peri-luminal region (group 1)

Fig ii) Patchy uptake throughout the thrombus, no hotspot (group 2)

Fig iii) Discrete hotspot (arrow) which involves the wall of the AAA and is distinct from the peri-luminal region (group 3). This patient subsequently died suddenly from a presumed ruptured AAA.

Fig iv) Patient with an inflammatory aneurysm (ESR>100 mm/hr), a specific subtype of AAA characterized by a thickened aortic wall, and inflammation/fibrosis extending beyond the aorta into surrounding tissues. This produced a unique ΔT2* pattern with intense USPIO uptake extending beyond the wall (arrows) of the AAA .

References

1. Choke, E. et al. Abdominal aortic aneurysm rupture is associated with increased medial neovascularization and overexpression of proangiogenic cytokines. Arterioscler Thromb Vasc Biol 26, 2077-82 (2006).
2. Thompson, M.M., Jones, L., Nasim, A., Sayers, R.D. & Bell, P.R. Angiogenesis in abdominal aortic aneurysms. Eur J Vasc Endovasc Surg 11, 464-9 (1996).
3. Wilson, W.R. et al. Matrix metalloproteinase-8 and -9 are increased at the site of abdominal aortic aneurysm rupture. Circulation 113, 438-45 (2006).

Acknowledgments

This study was made possible through the clinical research infrastructure that exists in Edinburgh. This included **nursing assistance** and **sample-processing** from the Edinburgh **Wellcome Trust Clinical Research Facility**, and 3T MRI scanning in **Clinical Research Imaging Centre** with comprehensive **physics** and **image analysis support**.

clinical research facility EDINBURGH
THE UNIVERSITY OF EDINBURGH
SC005336
British Heart Foundation
SINAPSE
NHS Lothian
clinical research imaging centre EDINBURGH