Magnetic resonance imaging of inflammation in abdominal aortic aneurysms using USPIO

J. M. Richards[1], S. I. Semple[2], C. Gray[2], W. Wallace[3], R. T. Chalmers[4], O. J. Garden[5], G. McKillop[6], and D. E. Newby[1]

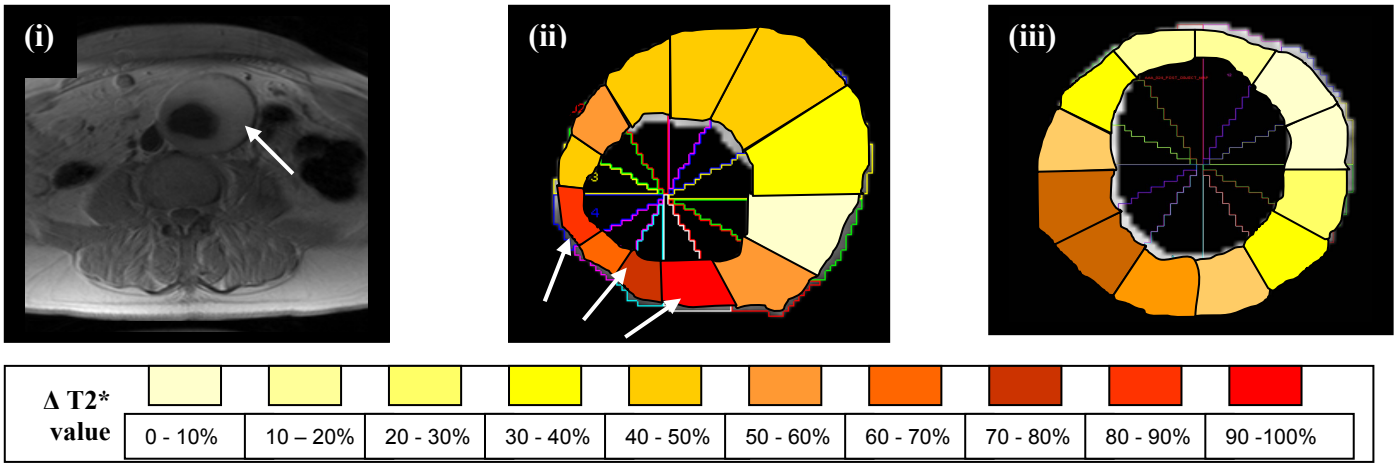
[1]Centre of Cardiovascular Science, University of Edinburgh, Edinburgh, United Kingdom, [2]Clinical Research Imaging Centre, University of Edinburgh, Edinburgh, United Kingdom, [3]Department of Pathology, NHS Lothian, Edinburgh, United Kingdom, [4]Vascular Surgical Service, NHS Lothian, Edinburgh, United Kingdom, [5]Clinical and Surgical Sciences (Surgery), University of Edinburgh, Edinburgh, United Kingdom, [6]Department of Radiology, NHS Lothian, Edinburgh, United Kingdom

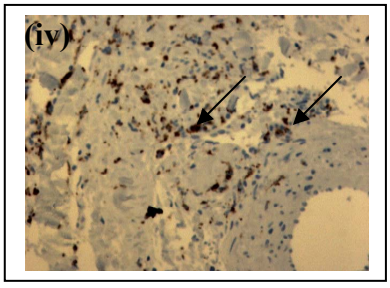
Introduction: Ruptured abdominal aortic aneurysm (AAA) has a mortality rate in excess of 90%. Accurate assessment of risk of rupture would allow correct identification of those patients who would benefit from preventative surgery. Existing methods are reliant solely upon the maximum diameter of the aneurysm and do not take into account the biology of the disease[1]. Aneurysm tissue is characterised by excessive medial neovascularisation, inflammation and irreversible remodelling of the extracellular matrix weakening the vessel wall[2,3,4]. 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. Sinerem is an MRI contrast agent which contains ultrasmall superparamagnetic particles of iron oxide (USPIOs) which, when given intravenously, are engulfed by inflammatory cells (monocytes/macrophages) and result in dropout of signal in the target site on T2*-weighted imaging. The aim of this study was to investigate the use of Magnetic Resonance Imaging and USPIOs to identify inflammatory hotspots in the wall of AAA.

Method: Patients (N=9) with AAA (>5.5cm in diameter) who were scheduled for aneurysm surgery were scanned before and 48 hours after administration of 2.6mg/kg Sinerem (Guerbet, France). A 1.5T Avanto MRI scanner (Siemens Erlangen, Germany) with a standard body matrix coil was used to acquire T2*-weighted gradient-echo sequences (TE 4.8ms and 14.3ms). Images were analysed using the programme Analyze (Mayo Clinic). A region of interest representing the aortic wall was further subdivided into 12 segments. The mean T2* value was calculated for each segment from signal intensity values at the two echo-times. This was performed pre- and post-contrast allowing the % change in T2* value to be determined for each segment.

At the time of surgery a sample of the anterior aortic sac was obtained, fixed in formalin and stained for CD68 (macrophage marker) and Iron (Perl's iron stain).

Results: Changes in T2* value were demonstrated following the administration of Sinerem. Consistent with the concept of biological hotspots, variation in the extent of the change in T2* value was seen in different AAA segments in the same patient (fig ii and iii). Segments with a greater change in T2* value, which might represent hotspots, were clustered together, giving biological plausibility to these observations. These hotspots, where present, tended to be located posteriorly which is consistent with the clinical observation that the majority of aneurysms rupture posteriorly. Histological analysis demonstrated the presence of macrophages (Fig iv) and iron deposition (Fig v) in adjacent sections of AAA sac.





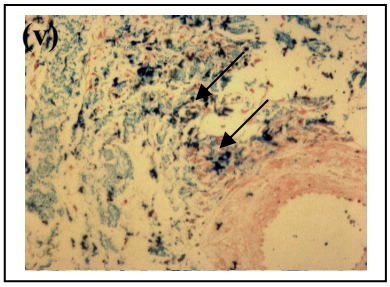


Figure Legend

Fig i: T2*-weighted (TE 4.8ms) axial slice through the body of the aneurysm (centre, arrow)
Fig ii: Diagram showing change in T2* value (see colour scale) following adminstration of Sinerem. Dark colours show a potential hotspot of inflammation (arrows) in the posterior wall of the aneurysm which may indicate a potential rupture site.
Fig iii: Diagram showing change in T2* value following administration of Sinerem in a second patient. No hotspot is seen suggesting that this aneurysm may be stable with a lower risk of rupture.
Fig iv: Immunohistochemical staining (CD68) of a sample of aortic wall demonstrating the presence of macrophages (brown, arrows) within the aortic wall.
Fig v: Perl's iron stain demonstrating the presence of iron (blue, arrows) within the aortic wall.

Conclusion:

1. A change in T2* value was observed following the administration of Sinerem. Regional variation in different parts of the aneurysm sac is consistent with the concept of biological hotspots, and also with the probable location (posterior) of these hotspots.
2. The presence of iron nanoparticles and inflammatory cells within the aneurysm sac was confirmed by histological examination of operative tissue samples.
3. The initial results from this pilot study demonstrate the potential for USPIO contrast agents to be used in the assessment of AAA.
4. Potential weaknesses of this pilot acquisition are the use of only two echo times to calculate the T2* value, and the resolution of the T2*-weighted gradient-echo sequences which makes discrimination of the aortic wall from the intra-luminal thrombus challenging Further data will be collected at 3T where the T2* effect of iron nanoparticles is more significant and better resolution is achievable. A multiecho sequence will be used to improve T2* fitting and reproducibility validation of T2* calculation will be performed.

References

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