In vivo MRI and MRA assessment of patency in a novel model of vascular remodelling using patent aortic grafts

K. K. Cheung[1,2], A. R. Thompson[3], H. Hafez[4], A. M. Taylor[5], R. J. Ordidge[1], S. E. Humphries[3], and M. F. Lythgoe[2]

[1]Department of Medical Physics & Bioengineering, University College London (UCL), London, United Kingdom, [2]Centre for Advanced Biomedical Imaging, Institute of Child Health and Department of Medicine, UCL, London, United Kingdom, [3]Centre for Cardiovascular Genetics, British Heart Foundation Laboratories, Royal Free & University College London Medical School, London, United Kingdom, [4]Department of Vascular Surgery, St Richards Hospital, Chichester, West Sussex, United Kingdom, [5]Centre for Cardiovascular MR, UCL Institute of Child Health, UCL, London, United Kingdom

Introduction

Fibulin-5 (fbln-5) is an extracellular matrix protein that is central to elastic fibre maturation and vessel development[1,2]. The roles of fbln-5 in vascular remodelling have been characterised in a model of carotid ligation in the fbln-5$^{-/-}$ mice[3]; however, this approach is somewhat limited in reflecting the pathogenic environment of vascular remodelling, as there is total lack of flow at the site of lesion. To date, no similar studies have been conducted using patent vessels. We have devised a novel model using an existing carotid graft technique to investigate the role of fbln-5 in vascular remodelling of a patent vessel. As continued graft patency is essential to this model, we evaluated the accuracy of MRI and MRA as non-invasive methods for determining graft patency *in vivo*.

Methods

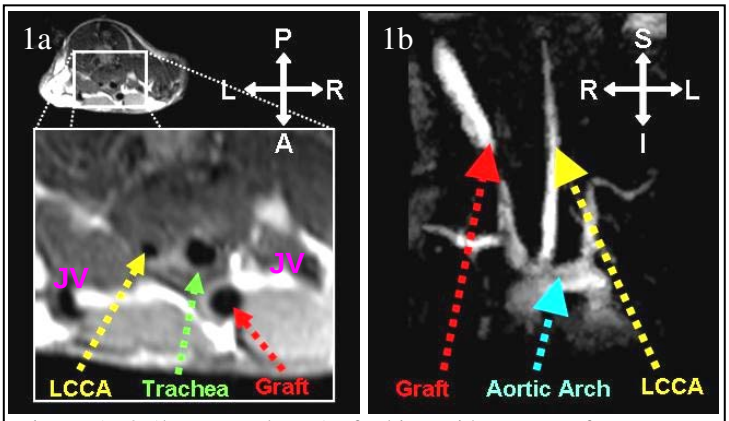
Surgery: Wild-type and fbln-5$^{-/-}$ mice (n=11) were anaesthetised and underwent surgery where allogous aortic grafts were placed in the right carotid circulation using a well-described cuff technique[4].

MRI & MRA evaluation: Animals were scanned between 2-4 weeks after surgery to assess graft patency. All scans were performed using a 2.35T SMIS system. A 2DFT spin-echo sequence was used to utilise the time-of-flight (TOF) effect, where fast-flowing blood appears as signal void. 30 transverse slices of the neck region were acquired. (TR=800ms; TE=28ms; FOV=30×30mm^2; matrix size=256×256, slice thickness=1mm; slice separation=0.5mm, 6 averages). 3D-TOF-MRA of the same region was also performed. (TR=100ms, TE=12ms, FOV=30^2×25mm^3; matrix size=128^2×96, α=70°)

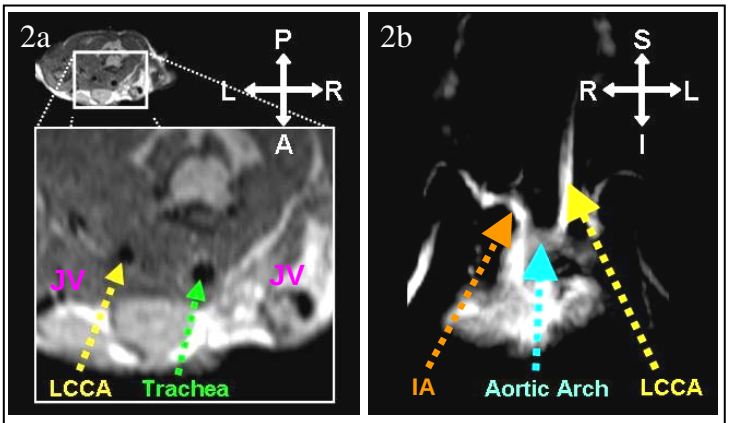
Validation of patency: After MRI and MRA evaluation, vessel grafts were explored by surgery. Patency was assessed by visual inspection as indicated by pulsatile blood flow through the graft.

Results

Figures 1a and 1b are representative MRI and MRA images, showing a well-defined, dilated graft on the right as compared to the left common carotid artery (shown in red and yellow arrows respectively). The signal void in the MRI image and the clear signal in the MRA at the expected location of the graft suggest that the graft is patent. In contrast, no graft-like structure could be identified in Figure 2a. Furthermore, MRA demonstrated absence of signal at the expected location of the graft (Figure 2b), thus suggestive of a blocked graft. By adopting this assessment protocol, we correctly identified all patent (n=8) and non-patent (n=3) grafts in this study.



Figures 1a & 1b: MRI and MRA of subject with patent graft. (LCCA= left common carotid artery; JV= jugular veins)



Figures 2a & 2b: MRI and MRA of subject with non-patent graft. Note the absence of graft-like structure on MRI, and absence of signal distal to the innominate artery (IA) on MRA.

Conclusion

We have demonstrated the potential role of MRI and MRA as a highly-accurate method for assessing vascular graft patency *in vivo* in a novel fbln-5$^{-/-}$ mouse model of vascular remodelling. As the state of patency is fundamental to this model, the non-invasive and robust nature of MRI and MRA offers an excellent alternative to traditional assessment through repeated invasive surgery, thus improving survival and reducing animal usage. In future studies, we also aim to characterise the evolution of morphological and functional changes of the graft as a result of vascular remodelling by multi-parametric MRI.

References

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