Journal of Cardiovascular Magnetic Resonance

Poster presentation

Open Access

A new approach for noninvasive assessment of chronic cardiac allograft rejection in rat by cellular cardiac MRI

Qing Ye*, Yijen L Wu, lesley M Foley, T Kevin Hitchens, Danielle Eytan and Chien Ho

Address: Pittsburgh NMR center for biomedical research, Pittsburgh, PA, USA
* Corresponding author

from 13th Annual SCMR Scientific Sessions
Phoenix, AZ, USA. 21-24 January 2010

Published: 21 January 2010

Journal of Cardiovascular Magnetic Resonance 2010, **12**(Suppl 1):P255 doi:10.1186/1532-429X-12-S1-P255

This abstract is available from: http://jcmr-online.com/content/12/S1/P255

Introduction

Long-term cardiac transplant survival rates can be improved only if patients undergo proper monitoring and treatment after transplantation. Repetitive endomyocardial biopsy, the gold standard for monitoring rejection status, is not only invasive but is also prone to sampling errors because of the limited size and location of graft tissue available. We have developed cellular and functional MRI techniques as a non-invasive method to detect and stage acute cardiac allograft rejection. Our recent studies indicate that macrophages can be detected by MRI in our rat model of CCAR. Therefore, we seek to develop CCMRI for non-invasive evaluation of CCAR.

Purpose

The aim of this study was to investigate the feasibility of using cellular cardiac MRI (CCMRI) for the non-invasive assessment of chronic cardiac allograft rejection (CCAR) in real time using a rat model.

Methods

An abdominal heterotopic working heart rat model was used in this study. Immune cells (mainly macrophages) were *in-situ* labeled by direct i.v. injection of micrometer-sized paramagnetic iron oxide (MPIO) particles one day prior to initial *in-vivo* MRI. EKG- and respiratory-gated CCMRI were used to longitudinally monitor the accumulation of MPIO-labeled macrophages in the graft at 4.7 Tesla for up to 120 days. Grafts were then harvested and fixed for high-resolution 3D magnetic resonance microscopy (MRM) at 11.7 Tesla. Fluorescence microscopy for dragon-green co-labeled MPIO and pathology were used to verify the *in-vivo* CCMRI and MRM results.

Results

The status of CCAR can be assessed longitudinally by monitoring macrophage infiltration associated with CCAR by CCMRI with a single MPIO injection (Fig. 1A-C). Labeled macrophages appeared as dark spots on T_2*-weighted images and the location and distribution of labeled macrophages can be easily mapped with high-resolution 3D-MRM (Fig. 1D-F). Co-registered MRM and fluorescence micrographs confirm that these dark spots are caused by the MPIO particles (Fig. 1G). The number of dark spots correlates with the severity of chronic rejection (Fig. 2A&2B and 2E&2F). Pathology of the corresponding tissue sections confirmed the result (mild rejection: Figs. 2C&2D, severe rejection: Figs. 2G&2H).

Conclusion

Macrophage infiltration to the heart graft experiencing CCAR can be serially monitored by MRI following a single i.v. injection of MPIO. Furthermore, the observed increase in MPIO-labeled macrophages correlates with the severity of CCAR and this method provides a non-invasive, real-time and whole-heart assessment of rejection. This study demonstrates the feasibility of non-invasive assessment of CCAR which has great potential in clinical applications.

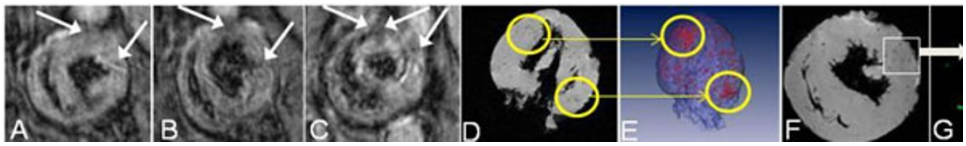

Figure 1
T_2* - weighted *in vivo* CCMR at 4.7 Tesla show monitored macrophages infiltration associated with CCAR progression on Post-operative days 14, 77, and 96 (A-C) respectively). The MPIO-labeled macrophage infiltration foci, appear as dark spots of hypointensity (arros) are confirmed with *ex vivo* high-resolution 3D MRM at 11.7 T (D, F), 3D rendering provides a whole-heart perspective of rejection and reaveals that macrophage infiltration during CCAR is heterogeneous. Fluorescence in microscopy confirms that thes dark spots are caused by MPIO-labeled macrophages (G, dragon green fluorescence).

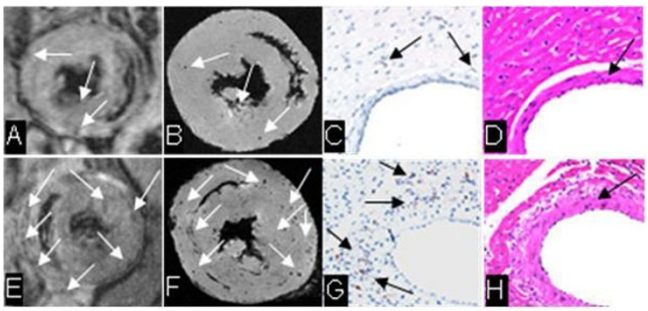

Figure 2
Top row shows images from allograft with mild CCAR (A-D), the bottom row shows images of an allograft with severe CCAR (E-H). A few spots of hypointensity can be seen in T_2* weighted *in vivo* CCMRI (A) resulting from labeled macrophage infiltration in different regions of the allograft experiecnin mild rejection. There are a larger number of dark spots detected in the severly rejecting allograft (E). These dark spots were confirmed by MRM at 11.7 T (B and F). The corresponding tissue sections stating with anti-rat EDI antibody (C and G) were used to confirm macrophage infiltration. The H&£ staining indicated a mild rejecting allograft graft (D) has less CCAR dchanges. The more concentrated macrophage accumulated in the encdocardium, adventititta, and severe intimal thickening in the severly rejecting allograft.