R_2*-ρ Imaging on Rat Allograft Cardiac Transplantation with Acute Rejection: A Preliminary Study

F-C. Yeh[1], Y. L. Wu[2], Q. Ye[2], T. K. Hitchens[2], and C. Ho[2]
[1]Department of Biomedical Engineering, Carnegie Mellon University, Pittsburgh, PA, United States, [2]Pittsburgh NMR Center for Biomedical Research, Department of Biological Sciences, Carnegie Mellon University, Pittsburgh, PA

Introduction:
Cellular imaging of the immune response by MRI has been used to reveal the existence of particular cells in the tissue, which has several important applications in biomedical research. One important application is the detection of the rejection severity in cardiac allograft transplantation. Non-invasive methods using ultra-small superparamagnetic iron oxide (USPIO) and micrometer-sized superparamagnetic iron oxide (MPIO) particles on T_2*-weighted images have been shown to be sensitive to acute and chronic rejection [1][2][3]. Using this approach of labeling macrophages by iron oxide particle, the rejection tissue can be visible in areas with decreased signal intensity on T_2*-weighted images. However, the exact measurement of the rejection level requires accurate quantification of the iron particles, and the signal decreases on T_2*-weighted image is not linearly related to the iron concentration, making it hard to perform quantification and to specify the severity of the rejection. To improve the quantification, R_2* value has been shown to linearly correlated with the iron concentration, but it is well known that R_2* is vulnerable to susceptibility artifact, and thus it only offers a non-specific quantification of the iron particles. In this study, we propose a new imaging modality called R_2*-ρ, which is obtained by multiplying the R_2* value by the spin density (ρ) to reduce the susceptibility artifact. To accurately estimate the R_2* value and the spin density, a more accurate R_2* estimation model was used to carry out the parameter estimation [4]. The proposed method is applied to acute cardiac rejection on rat allograft model, and both pre-contrast and post-USPIO images were acquired to perform a comparison and to evaluate the performance of the proposed method.

Methods:
MRI:
The in-vivo MRI scan was conducted on a Bruker AVANCE AV1 4.7 T scanner (Bruker, Billerica MA). A 5.5-cm hand-built surface coil was used for spin excitation and signal detection. The T_2*-weighted images were acquired with both ECG and respiratory gating. TR=the respiration cycle (~1 sec), TE=4.5, 7.5, 10, 13 ms. FOV=4 cm, slice thickness=1.5 mm In-plane resolution=156 μm.
Rat allograft model:
The rat allograft model follows our previous study [1], using Inbred male Dark-Agouti (DA; RT^{av}) and Brown Norway (BN; RT^{n}) rats. Heart-lung transplantation was conducted, and the MRI images were acquired on post-operation day (POD) 6. USPIO particles were injected through a femoral venous catheter to label macrophage *in vivo*. Both pre-contrast and post-USPIO images were acquired for comparison.
R_2*-ρ calculation
The R_2* model that we used is as follows [4]:

$$S(TE) = \rho \cdot (1-\xi) \cdot \exp(-R_2^* \cdot (t_C - TE))$$

To estimate the R2* value, we first calculate $S(TE_1)/S(TE_2)$, which is equal to $\exp(-R_2^* \cdot (TE_1 - TE_2))$. Each combination of two different TE values can result in an estimation of a R_2* value. Since we have 4 TE samples, a total of 6 R_2* samples can be generated. We choose the median among these 6 samples to be the final R_2* estimation. The spin density is then estimated by using the known R_2* value and assume $(1-\xi) \approx 1$ and $t_C << TE$.
The R_2*-ρ is then calculated by multiplying the estimated R_2* value with the spin density.

Results and Discussion:
The R_2* images of the pre-contrast and post-USPIO condition are shown in Fig. 1. A prominent noise pattern can be observed in the image background and also the air-tissue interface, which hinders accurate interpretation of the cell accumulation. Although the increase of the R_2* is also observed in the rejected tissues, it still lack of specificity and thus not suitable for rigorous inspection. The R_2*-ρ images of both the pre-contrast and post-USPIO are shown in Fig. 2. The increase intensity can be observed in the site of cell accumulation, and the unwanted artifact is greatly reduced in both the pre-contrast and post-USPIO image, thereby offering a more specific inspection modality that is feasible for clinical usage. The future works include investigating the effect of tissue motions in different imaging TE, using an independent spin density estimation to give a more robust result, and comparing with the conventional R_2* fitting approaches to confirm the accuracy of the method and evaluate its application in iron particle quantification.

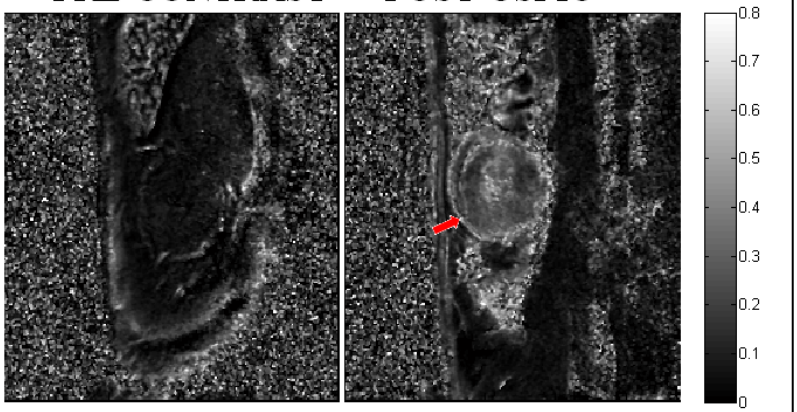

Figure 1. The R_2* mapping of post-USPIO injection (left) and pre-contrast (right) in short axis view of the graft heart. Although the increased R_2* value in the graft heart can be observed on the post-USPIO image, the prominent noise pattern in the air-tissue interface and in the image background affect the identification of iron-labeled macrophages.

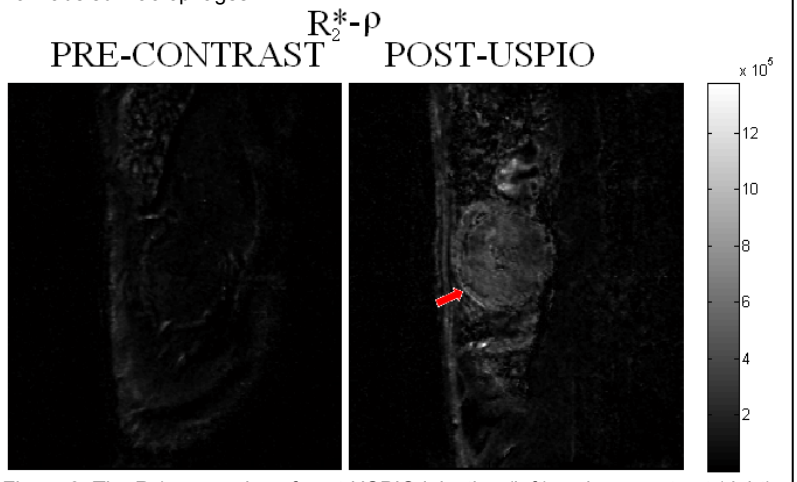

Figure 2. The R_2*-ρ mapping of post-USPIO injection (left) and pre-contrast (right) in short axis view of the graft heart. Note that the noise is greatly suppressed by introducing the spin density. The cell accumulation site of the graft heart (arrow) is readily visible in the post-USPIO image. The resulting image offers a more specific identification of the labeled macrophages.

References: [1]Wu, YL et al. PNAS 2006, 103, 1852-1857. [2]Ye, Q et al. Circulation 2008, 118, 149-156. [3]Wu, YL et al. JACC Cardiovasc Imaging 2009, 2, 731-741. [4]Yablonskiy, D.A. et al. MRM 1994, 32, 749-763