In vivo ultra short TE (UTE) MRI of mouse myocardial infarction

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Introduction

Fibrosis is an important hallmark of various cardiac pathologies. The excessive accumulation of extracellular matrix (ECM) proteins, such as collagen, plays a pivotal role in the progression of cardiac pathology towards heart failure (HF)[1]. Late gadolinium enhancement MRI can be used to detect fibrosis associated with ischemic and non-ischemic heart disease[2]. However, the accumulation of Gd-DTPA is rather nonspecific. Ultra short TE (UTE) MRI has the potential to detect protons with very high transverse relaxation rates (low T_2 relaxation time), including those associated with fibrotic tissue and specifically collagen[3]. Therefore, UTE MRI may provide a more specific detection of myocardial fibrosis.

The **aim** of this study was to demonstrate *in vivo* visualization of fibrotic tissue in infarcted mouse myocardium by UTE cardiovascular MRI.

Methods

UTE sequence design: A 9.4T small animal MRI scanner was used equipped with a 72-mm-diameter quadrature transmit coil and a 4 element phased-array receive coil. The 3D UTE sequence consisted of a non slice-selective RF block-pulse (α=5°, 20 µs, BW=64 kHz), followed by a 3D radial readout. The echo time (TE) was either TE=21µs (short-TE) or TE=4ms (long-TE). Other sequence parameters were: TR=8.4 ms, NSA=1, FOV=3x3x3 cm^3 and matrix size=128x128x128. To account for eddy-current induced errors, actual k-space trajectories and gradient timing were measured and optimized using a glass sphere phantom filled with an aqueous solution of 1 g/l $CuSO_4$[4].

Mouse model: Myocardial infarction was induced in C57BL/6 mice (♂, age 11 weeks, n = 6) by means of permanent occlusion of the left coronary artery. The animals were allowed to recover for 1 week. Healthy littermates were used as control. During MRI mice were anesthetized with isoflurane.

In vivo MRI: The readout of the 3D UTE sequence was triggered immediately after ECG R-wave detection. Respiratory gating was applied to prevent motion artifacts. To limit the acquisition time to about 14-16 min (depending on the mouse heart rate), 3 k-lines were measured after every R-wave and the acquisition matrix was undersampled by a factor 3. A blood-saturation slice in a short-axis orientation positioned above the left ventricle (LV) base provided improved contrast between blood and myocardium. UTE images with long-TE were subtracted from images with short-TE to obtain ΔUTE images highlighting myocardial tissue with high transversal relaxation rates in the infarct area. To confirm infarct location, a late gadolinium enhancement scan was performed at the end of the MRI session using 0.5 mmol/kg Gd-DTPA and a retrospectively gated cine FLASH sequence[5].

Histology: Immediately after MRI, mice were euthanized, their hearts were excised and used for *ex vivo* 3D UTE MRI measurements. Finally, hearts were embedded in paraffin, cut in 5-µm-thick sections and stained with Picrosirius Red to confirm the excessive presence of collagen in the infarct area.

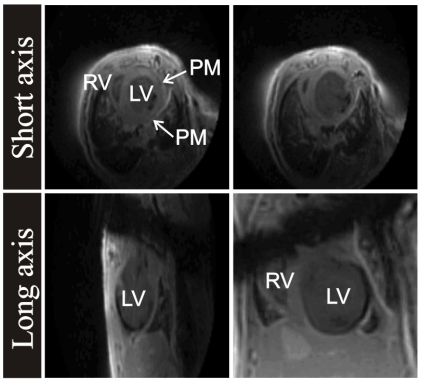

Fig. 1. *Two short-axis and long-axis UTE images (TE=21µs) of a mouse heart with an infarct. Indicated are the right ventricle (RV), left ventricle (LV) and the papillary muscles (PM). A dark saturation slice is visible in the two long-axis images.*

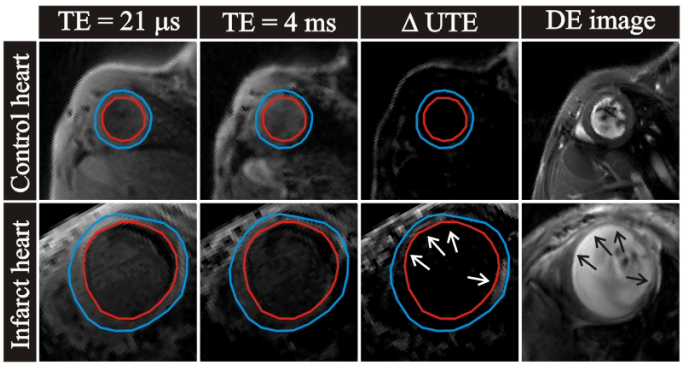

Fig. 2. *Example of an in vivo short-axis cross-section of a healthy heart (top row) and a heart with an infarct (bottom row) obtained with the 3D UTE sequence (TE = 21 µs, TE = 4 ms, ΔUTE difference image). The corresponding delayed enhancement (DE) scans are shown in the right column.*

Results and Discussion

Fig. 1 shows UTE images of an infarcted mouse heart. The right ventricle, LV, papillary muscles and infarct area could be clearly distinguished as well as the anatomy of the ribs. The dark bands resulted from the saturation slice to suppress blood signal in the LV lumen. Typical examples of *in vivo* short-TE and long-TE UTE images of a healthy heart and a heart with an infarct are presented in **Fig. 2**. The short-TE and long-TE images were registered before calculation of the difference images. ΔUTE images clearly revealed signal in the infarct area, which was confirmed to correspond to the infarct area by late gadolinium enhanced MRI. No such contrast was observed for the healthy heart. The presence of collagen in the infarcts was established using Picrosirius Red staining (**Fig. 3**). Collagen in the apex and free wall of the infarcted heart corresponded well to contrast observed in *ex vivo* ΔUTE images. Very little collagen was found in these regions in the healthy heart in accordance with absence of ΔUTE contrast.

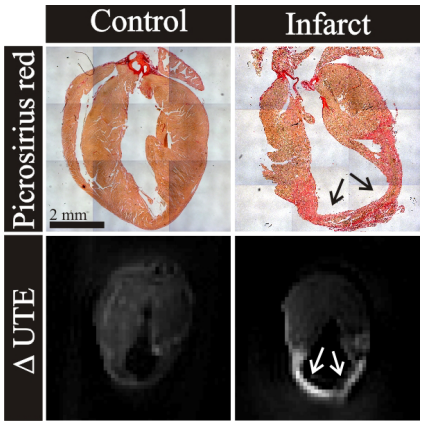

Fig. 3. *Examples of ex vivo long-axis cross-sections stained with Picrosirius Red (top row) and the corresponding ΔUTE difference images (bottom row) for a healthy heart (left) and a heart with an infarct (right).*

Conclusion

In this study a method is presented for 3D UTE imaging of the *in vivo* mouse heart. Clear contrast between remote and infarct myocardium was observed in UTE difference images, likely caused by the presence of significant amounts of collagen in the infarct resulting in short tissue T_2 relaxation times. Histology confirmed that the infarct area contained significant amounts of collagen.

Future research will focus on the application of this method to study the role of fibrosis in other mouse models of cardiac disease.

Acknowledgement

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References

1) Creemers *et al.* Cardiovasc Res, **2011** (98), p265. 2) Jackson *et al.* Clin Radiol, **2007** (62), p395. 3) de Jong *et al.* J Moll Cell Cardiol, **2011** (51), p974. 4) Duyn *et al.* J Magn Reson, **1998** (132), p150. 5) Coolen *et al.* MRM, **2010** (64), p1658.