

Direct detection of postinfarction myocardial fibrosis with ultrashort TE (UTE) MRI

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Background - In myocardial infarction, the assessment of myocardial injury after ischemia is an important predictive parameter for clinical outcome. The standard non-invasive technique currently used for assessment of myocardial viability is delayed contrast enhancement¹, which allows for the detection of both necrosis and excessive collagen deposition (fibrosis) of the myocardium.

As gadolinium uptake in the interstitial space is non-specific, delayed enhancement cannot discriminate between different forms of tissue damage within the heart. Therefore, to date there is a growing demand to a non-invasive technique that can be used for the direct detection of fibrosis due to remodeling in diseased human hearts. The aim of this study is to investigate the potential of ultrashort TE MRI to generate endogenous contrast from cardiac fibrosis after infarction.

Methods - Myocardial infarction was created in 11 Lewis rats by ligating the left anterior descending artery. As a control, 6 rats underwent sham-surgery. Six weeks after surgery, rats were anaesthetized and the heart was extirpated for *ex vivo* analysis. The heart was placed in a plastic tube filled with foblin, to provide magnetic susceptibility matching between tissue and the surroundings. Imaging was performed on a 7 Tesla MRI scanner (Philips Healthcare, Cleveland, USA), using a home built quadrature transmit and receive coil with a circular shaped element of 5 cm in diameter and a stripline element of 6 cm length. Balanced fast field echo images (TR/TE 8.3/4.2 ms, flip angle 5 deg) were acquired for anatomical reference with histology. 3D gradient echo (UTE GRE) images with radial sampling (TR/TE 14/0.15 ms, flip angle 20 deg) were acquired to detect short T_2 components. The 3D GRE was repeated with a TE of 6 ms. All images were acquired with FOV 30 x 30 x 30 mm³, and acquired isotropic resolution of 0.35 mm. The 3D GRE images with TE=6 ms were subtracted from the UTE GRE images with TE=0.15 ms to suppress tissues with long T_2 . On the subtracted images, intensity of the healthy myocardium was measured and the mean + 2x SD was considered as UTE target signal. The UTE target signal area/total myocardial area ratio was determined on three levels of each heart. After imaging, hearts were fixed in formalin and embedded in paraffin. Hearts were cut in slices of 4µm thickness and stained with 0.1% Picosirius red to show presence of collagen in the myocardium. The area of collagen in the myocardium and total area of the myocardium were determined by using ImageJ software and the collagen-rich area/total myocardial area ratio was determined.

Results & Discussion - In subtracted images of infarcted hearts, UTE signal in the infarcted area clearly differs from the signal in healthy myocardium of the same heart (Fig 1), whereas in subtracted images of sham hearts hardly any difference in signal is detected. The MRI ratio and the histological ratio of collagen-rich area/total myocardial area are positively correlated (Fig 2; $r^2=0.78$; initial results, based on four hearts). In a pilot study, one heart was stained for iron to exclude that the target signal was caused by iron in the tissue (e.g. due to blood compounds). In this heart no iron staining was observed.

Conclusions - Here we show for the first time that the use of ultrashort TE MRI technology can be used for the direct detection of post-infarction collagen formation. This technique to detect fibrosis in a non-invasive way might be of great value in stratification of patients.

References:

1. Pennell DJ, Sechtem UP, Higgins CB, Manning WJ, Pohost GM, Rademakers FE, *et al.* Clinical indications for cardiovascular magnetic resonance (CMR): Consensus Panel report. *J Cardiovasc Magn Reson.* 2004;6(4):727-65.

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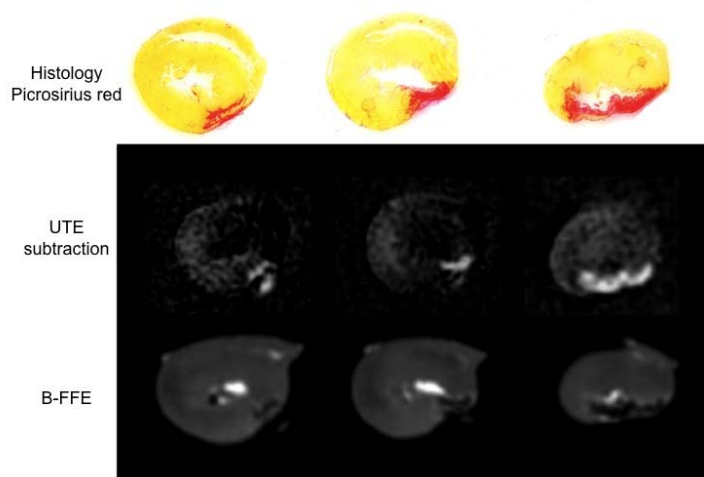


Figure 1. Transversal sections of three levels of an infarcted heart. Upper part: histological data, red=collagen; yellow=healthy myocardium. Middle part: subtracted images of corresponding sections. Bottom part: corresponding balanced fast field echo (B-FFE) images.

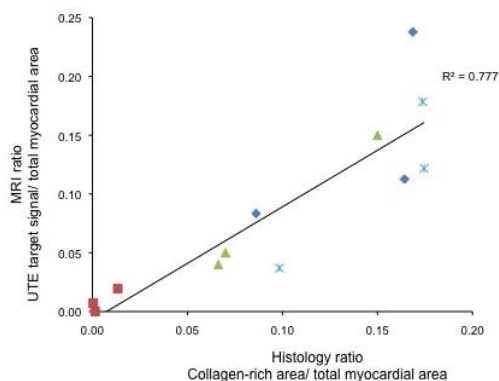


Figure 2. Correlation between MRI and histology regarding the ratio of the collagen-rich area and total myocardial area. Heart 1, 3, and 4=infarcted heart, heart 2=control. $R^2=0.78$.