IN VIVO DETECTION OF MYOCARDIAL FIBROSIS USING NATIVE T1P AND T2* MAPPING IN AN ANIMAL MODEL OF CHRONIC MYOCARDIAL INFARCTION

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Purpose: To perform both T_{2*}- and $T_{1\rho}$-mapping *in vivo* in a porcine animal model of chronic myocardial infarction (MI), and correlate with *in vivo* gold standard LGE and *ex vivo* histology.

Background

In cardiac regenerative medicine, assessment of infarct scar area becomes more important, both for treatment planning as for follow up after therapy[1]. Gold standard for imaging myocardial fibrosis is MRI with late gadolinium enhancement (LGE) which indirectly measures the infarct area. Direct detection of myocardial fibrosis could be beneficial and provide additional information for planning and follow up of treatment.

Recently it was shown in a small animal model that Ultrashort Echo Time imaging (UTE) and T_{2*} mapping show a significant lower T_{2*} in the infarct area[2,3]. A decrease in T_{2*} was associated in a recent study with regional iron deposition due to intramyocardial hemorrhage[4]. Another promising method for native assessment of MI is $T_{1\rho}$-mapping. Studies in animal models of chronic MI showed the first *in vivo* evidence that myocardial fibrosis can be detected with $T_{1\rho}$-mapping [5,6].

Methods

In vivo MRI was performed in 16 anesthesized pigs (79.8 ± 5.8 kg), 8 weeks after 90 minutes left anterior descending artery (LAD). Scans were performed on a clinical 3 T scanner (Achieva TX, Philips Healthcare) with a 32-channel receive coil.

$T_{1\rho}$-mapping was performed using a 3D, T_1-prepared, multi-shot gradient echo sequence. Five images with different spin-lock preparation times with an amplitude of 500 Hz were acquired (SL = 1, 10, 20, 30, 40 ms). Bandwidth/pixel = 287 Hz, TE/TR = 2.6/5.3 ms, resolution = 1.5 x 1.5 mm, slice thickness = 6 mm, FOV = 336x336 mm^2, flip angle = 8 degrees, 8 TFE shots, NSA =2, R-R = 2 beats.

T_{2*}-mapping was performed using a gradient echo sequence, with 10 echoes: Bandwidth/pixel = 1560 Hz, TE1 = 1.56 ms, ΔTE = 0.9 ms, TR = 1000 ms, resolution = 1.5 x 1.5 mm, slice thickness = 6 mm, FOV = 336x336 mm^2, flip angle = 90 degrees, NSA = 1.

LGE MRI was performed 15 minutes after injection of 0.2 ml/kg gadobutrol (Gadovist, Bayer Healthcare. LGE imaging parameters were: TI = 200-250 ms, TE/TR = 1.5/4.7 ms, resolution = 1.5 x 1.5 mm^2, slice thickness = 6 mm, FOV = 300x300 mm^2, flip angle = 25 degrees, 63 TFE shots).

After scanning the pigs were sacrificed for triphenyltetrazolium chloride (TTC) staining of serial sectioned slices and Perls' Prussians blue staining (PPB) of remote and infarct areas for detection of iron. $T_{1\rho}$ and T_{2*} maps were calculated by pixelwise fitting of a mono-exponential decay function in Matlab (Mathworks).

Results

$T_{1\rho}$ relaxation time was significantly higher in the infarct region(57 ± 11 ms), compared to healthy remote myocardium (37 ± 4 ms) ($p<0.0001$). T_{2*} was found significantly lower in the infarct region (17 ± 5 ms), compared to the remote area (24 ± 7 ms) ($p<0.002$). The areas with a higher $T_{1\rho}$ and lower T_{2*} closely corresponded with the matched LGE images and TTC staining results (fig. 1). Perls' Prussian blue staining showed an abundance of iron in the infarct area compared to remote myocardium.

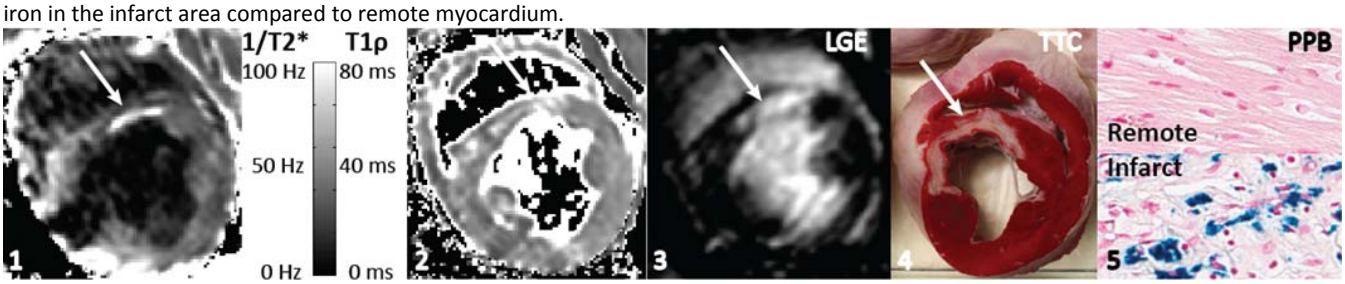

Figure 1: Representative (1) *in vivo* $1/T_{2*}$ map, (2) $T_{1\rho}$ map, (3) LGE image, (4) *ex vivo* TTC staining and (5) iron staining

Discussion

Previous studies hypothesized that myocardial scar could be detected by T_{2*} mapping because of field inhomogeneities induced by collagen and/or the short T_2 of water that is weakly bound to the collagen molecules. In this study we observe abundant iron deposition in the infarct region, and therefore the chronic changes in T_{2*} signal intensity could relate to post-reperfusion intramyocardial hemorrhage. It is known that $T_{1\rho}$ decreases with increasing iron concentrations[7]. Since we observe an increase of $T_{1\rho}$ in the infarct, another contrast mechanism outweighs this negative effect, resulting in a higher $T_{1\rho}$. $T_{1\rho}$ was proven to be sensitive to changes in macromolecular content, and therefore the higher $T_{1\rho}$ in MI tissue could relate to changes in tissue composition.

Conclusion

In this study the first time a direct comparison between T_{2*} and $T_{1\rho}$ changes in chronic MI is made. A significantly lower T_{2*} and significantly higher $T_{1\rho}$ relaxation time is found in the infarct area. The decrease in T_{2*} could be explained by an abundance of iron in the infarct tissue, caused by intramyocardial hemorrhage. $T_{1\rho}$-mapping *in vivo* is most promising for non-contrast enhanced detection of myocardial fibrosis.

References: [1]Jadcxyk, T et al. *Br. J. Pharmacol (2012)* [2]*De Jong, S. et al. JMCC(2011)* [3]*Aguor, E. et al. , MAGMA (2012)* [4]*Kali, A. et al. Circulation (2013),* [5]*Witschey, W.R. et al. JCMR.(2012)* [6]*Musthafa, H. et al. MRM(2012)* [7]Moonen, R. P. M. et al. *Proc. Int. Soc. Magn. Reson. Med.(2013)*