Delineation of ischemically injured myocardium on T1 weighted MRI after intravenous injection of SHU555A

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Introduction

In contrast to extracellular contrast media, iron-containing blood-pool contrast media have been shown to allow stable delineation of ischemically injured myocardium over a prolonged period of time (up to 90 min) [1]. SHU 555 A is a superparamagnetic iron oxide (SPIO), coated with carboxydextran. The hydrodynamic diameter of particles ranges between 40 and 65 nm. The particle size the relaxivity of the particles. SHU 555 A has a r1 of 7.2 L(mmol x sec) and r2 of 82 L(mmol x sec) measured at 1.5 T and 37° C in blood. The relaxivity ratio (r2/r1) of 11.4 suggests a predominantly T2/T2*-shortening effect of the contrast medium. However, this value is an average over the contributions of the different fractions of particles. Due to the range of the particle size, non-uniform features of particles with different sizes must be expected. The smaller-particle fraction stays longer in the blood, compared to larger particles [2]. Owing to their smaller size, these particles have a higher r1 relaxivity than large particles. SHU 555 A has previously been shown to increase portal venous signal by 237% on T1-weighted images after intravenous injection and has been successfully used for magnetic resonance angiography [2]. The purpose of this study was to determine whether ischemically injured myocardium can be delineated at MRI after intravenous administration of the SPIO (small particle of iron oxide) SHU555A.

Methods

In 7 pigs reperfused myocardial infarction was induced by occluding the left anterior coronary artery for 45 minutes using a balloon-catheter. Two hours after reperfusion MRI was started at a 1.5 T closed bore system (Intera, Philips, Best, The Netherlands). MR imaging was started with the acquisition of segmented ECG-gated, steady state free precession (SSFP) images (also known as balanced FFE = balanced fast field echo or True-FISP = fast imaging in steady state precession) in the two chamber, four chamber and short axis view (TR/TE, flip angle, slice thickness 8 mm). From the stack of 8-10 short axis slices covering the entire left ventricle from the apex to the base, a slice showing regional impairment of systolic myocardial thickening was selected. At this slice position, an inversion recovery sequence for measuring the regional T1-values was carried out. For this purpose, the sequence, initially introduced by Look and Locker, was employed with the following parameters: field of view of 320 mm, TR/TE = 3000/3.5ms, flip angle of 10°, EPI factor 3 and a 128 × 128 matrix, resulting in an isotropic 2.5 mm in-plane resolution. Signals were not averaged. After an initial 180° pulse, triggered to the R-wave, 100 images were acquired with an interval of 36 ms between consecutive images. SHU 555 A (Resovist, Schering, Berlin, Germany) was intravenously applied at a dose of 0.16 mmol Fe/10 kg bodyweight. The Look-Locker sequence was carried out 3 and 15 min after intravenous injection of SHU 555 A and then after time intervals of 30 min for 3 hours. Post-mortem, hearts were excised and stained with 2,3,5-triphenyltetrazolium chloride (TTC), to delineate the infarct.

Results

Prior to the injection of SHU555A the T1 value of ischemically injured myocardium was 875 ± 61 ms, while the T1 value of remote myocardium was 787 ± 31 ms (p=n.s.). After intravenous injection of SHU 555 A the T1 value of ischemically injured myocardium gradually decreased (Fig 1), while the T1 value of remote myocardium only slowly decreased. Analysis of variance results showed a significant difference of regional T1 for remote and infarcted myocardium ($F=6.2$, $df = 4, 30$, $p< 0.001$). The T1 value of ischemically injured myocardium was significantly lower than that of remote myocardium starting 60 min after the intravenous injection of SHU 555 A (paired t-test, $p < 0.05$) (Fig 1). The T1 values were 588 ± 54 ms for ischemically injured and 759 ± 22 ms for remote myocardium, 3 hours after intravenous injection of SHU 555 A ($p < 0.05$). The size of ischemically injured myocardium remained constant over the last 2 hours of the observation period on the MR images (Fig.2). Compared to TTC staining size of infarction was overestimated by 5.1 ± 1.6 % on MRI.

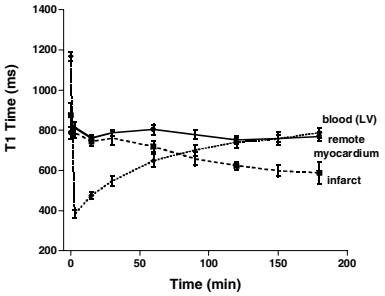

Figure 1: The plot demonstrates changes in T1 values of infarcted and remote myocardium and left ventricular (LV) blood after intravenous injection of 0.16 mmol/10kg bodyweight SHU 555 A over the observation period of 3 hours.

Discussion

SHU555A has the potential for delineating the spatial extent of ischemically injured myocardium stably over a time period of at least two hours. This contrast medium may be useful as a marker for MR guided interventions. However, the long time necessary for obtaining a significant decrease in T1 of ischemically injured myocardium is a clear disadvantaged.

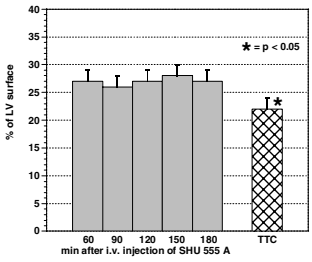

Figure 2: Size of the ischemically injured myocardium, compared to the size of the infarct as measured at TTC. There was no significant change of the size of the hyperenhance area during imaging.

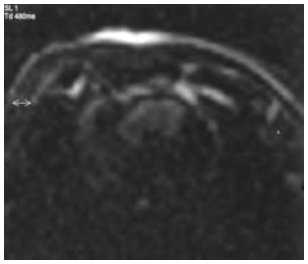

Figure 3: Selected image from the Look-Locker sequence acquired with inversion times of 408 ms. The ischemically injured myocardium is hyperintense compared to remote myocardium.

1. Krombach GA et al. Radiology. 225:479-486 (2002)
2. Allkemper T et al. Radiology 223:432-438 (2002)