Positive Enhancement of Microvascular Obstruction in Reperfused Acute Myocardial Infarction Using T1 Prep Look-Locker Sequence: a Short Time-course Study

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Introduction: Delayed contrast-enhanced MRI (DE-MRI) has been widely used for the determination of myocardial viability and can delineate accurately the extent of myocardial infarction as a positive contrast. However, negative contrast can result from microvascular obstruction (MO) that occurs in 30%-40% of patients post acute myocardial infarction (AMI) and is a strong unfavorable predictor for short and/or long-term clinical outcome in these patients [1,2]. A noninvasive MRI technique with positive enhancement of MO will improve the identification of MO, and thus would have value in MRI evaluation in patients with AMI after revascularization procedures. This study investigates a modified T1 prep Look-Locker sequence before and during a Gd-DTPA infusion for the positive enhancement of MO in a porcine model of reperfused AMI developed by percutaneous balloon occlusion and demonstrates the early time course of MO.

Materials and Methods: Reperfused AMI model: In twelve Yorkshire pigs (22-28 kg) a reperfused AMI was produced using a 90-minute percutaneous balloon occlusion of the left anterior descending artery (LAD) distal to the second septal branch followed by 150 minutes reperfusion under an x-ray C-arm system (OEC 9800, GE Healthcare). Amiodarone (150 mg bolus) and lidocaine (2 mg/min infusion) were used to reduce the risk of severe arrhythmia throughout the course of experiments.

MRI techniques: All MRI studies were performed on a GE 1.5T Signa Excite system (GE Healthcare, Milwaukee). All pigs underwent a baseline MRI study including a steady-state free precession (SSFP) functional study and the T1 Prep technique. The T1 Prep technique uses a modified Look-Locker pulse sequence [3] acquiring a set of eight spiral images, corresponding to the differences between signals in a train of 15-deg excitations at intervals of 120 ms, obtained with and without a preceding inversion at the same cardiac phase. The signal difference isolates the T1 contribution from the approach to steady state in the small-tip train, so that longer T1 values yield bright signal at later points (effectively longer TI). After the intervention, SSFP and T1 Prep pulse sequences were repeated in the same location. First pass myocardial perfusion (FPMP) was obtained immediately after a Gd-DTPA bolus injection (0.2mmol/kg) followed by a continuous intravenous drip of Gd-DTPA at a rate of 0.004 mmol/kg/min. DE-MRI (IR-prepared FGRE) was performed 30-45 minutes post Gd-DTPA injection and T1 Prep was applied 45-60 minutes post Gd-DTPA injection (steady state). SSFP LV function, FPMP and DE-MRI analysis were conducted on a GE Advantage workstation using Mass Plus software (Medis, Netherlands). T1 change was calculated from the MO, hyperenhanced regions in DE-MRI (DHE), control segments and LV with the following formula: [(T1 at baseline - T1 at steady state post Gd-DTPA)/T1 at baseline] using manually drawn regions-of-interest and custom or commercial fitting algorithms (Xcinema, Stanford; Functool 2, GE Healthcare). Paired t-tests were used for the testing of statistical significance of T1 reductions between MO, DHE, control segments, and LV. MO areas were measured on T1 Prep and DE-MRI images in the same location and were compared using a paired t-test.

Six of twelve pigs were survived for one week to repeat the MR examination using the same protocol described above to characterize the early time course of MO. All pigs were sacrificed for TTC staining and histology.

Results: MO was defined as the persistent hypoenhanced area in the infarcted myocardium observed on FPMP and DE-MRI (Fig. 1a). In the modified T1 prep Look-Locker pulse sequence during the steady-state Gd-DTPA infusion, MO was identified as bright regions in later T1 prep difference images while the surrounding DHE regions appeared dark (Fig.1b-c). MO was seen in ten of twelve pigs post reperfused AMI just after the intervention. In four pigs the MO size was greater than 50% of total AMI volume (52%, 53%, 60% and 67%). In the other six pigs MO size was less than 40% of AMI volume (6%, 13%, 19%, 23%, 24% and 39%). Fig.1d shows the typical signals from MO, DHE, and control regions in T1 prep difference images across the small tip train (effectively, varying TI). In the six pigs that were survived for one week and had MO identified on the previous MRI scan, no MO was observed on DE-MRI and T1 prep difference images in the follow-up MRI (Fig.1e-f). MO areas calculated from the DE-MRI (1.30±0.78 cm^2) and T1 prep difference images (1.36±0.83 cm^2) in the same location were comparable with a trend toward greater area in the T1 prep difference images although no statistical significance was reached (Fig 2, p=0.1, paired t-test). T1 change with Gd-DTPA in MO regions (30.3±22.9%) was smaller compared to measurements from the control segments (39.8 ±7.3%, p=0.16), DHE regions (78.1±14.2%, p<0.0001) and LV (84.2±9.8%, p=0.0001) using a paired t-test. Pre-contrast T1 values across the myocardial segments were the same. All pigs had an AMI confirmed by TTC staining and histology (Fig.1g).

Discussion and Conclusion: The concept of microvascular obstruction (MO) or the "no-reflow" phenomenon in the infarcted myocardium was proposed decades ago using a canine model [4]. The incidence and extent of early MO has been proven to be a strong predictor of negative LV remodeling, LV systolic dysfunction and worse clinical outcome [1,2,5]. Furthermore, long-term persistent MO predicts worse scar thinning and infarction expansion [6]. DE-MRI is a sensitive method to demonstrate MO as a hypoenhanced region within AMI [2]. However, the extent of MO might be underestimated or small MO could be missed due to the extremely high signal intensity from the infarcted myocardium. In this study, MO at early stages of reperfused AMI was identified as bright areas on images from a modified T1 prep Look-Locker sequence post-contrast and was shown to be resolved in a one-week follow-up study using the same MRI technique. Although MO areas calculated from the DE-MRI and T1 prep image in the same location were comparable with no statistical significance reached, a trend was noticed toward greater area in the T1 prep difference images. Positive enhancement may yield greater specificity since it can identify even partial volumes of MO. Quantitative analysis with theT1 prep MRI technique may also facilitate more accurate evaluation of longitudinal changes reflecting Gd-DTPA distribution volume in MO relative to both control and DHE regions. In conclusion, we have developed a modified T1 prep Look-Locker pulse sequence for positive enhancement of MO in a porcine model of reperfused AMI, which may have value in MRI evaluation of patients with AMI after revascularization procedures.

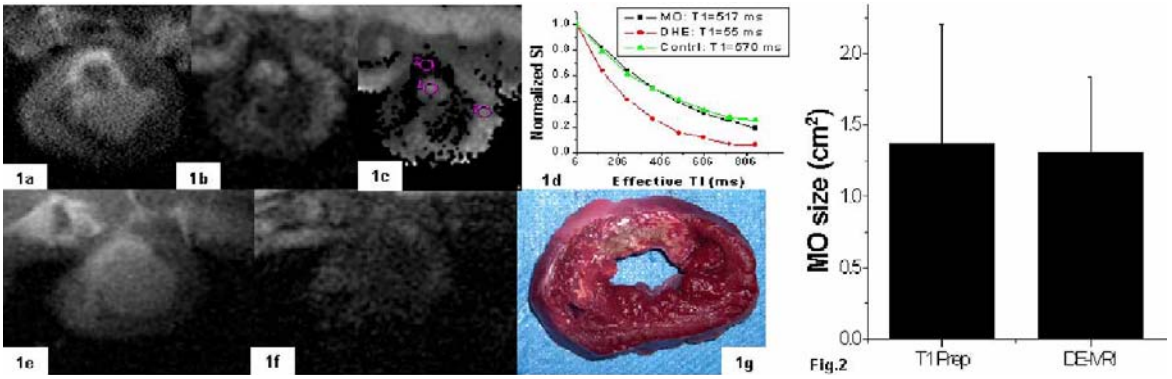

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Fig.1 & Fig. 2: 1a. DE-MRI at day 0: MO as hypo-enhanced region (TI=250 ms). **1b**. A T1 prep image at day 0 (post-Gd, TI=606 ms): MO as a positively enhanced area. **1c.** T1 map (gray scale proportional to T1) at day 0: ROI 1:MO, ROI 2: DHE, ROI 3: control region. **1d**. Normalized SI difference with and without inversion vs effective TI at day 0. **1e-f** (DE-MRI and T1 prep image) at day 7 -- no MO was observed. **1g**.TTC staining. **Fig.2:** comparison of MO size from T1 prep and DE-MRI measurement.