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## **T<sub>1</sub> Mapping for Assessment of Myocardial Injury and Microvascular Obstruction at One Week Post Myocardial Infarction**

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**Abstract**

**Objectives:** To compare 3T T<sub>1</sub> mapping to conventional T<sub>2</sub>-weighted (T<sub>2</sub>W) imaging for delineating myocardial oedema one week after ST-elevation myocardial infarction (STEMI), and to explore the confounding effects of microvascular obstruction (MVO) on each technique.

**Methods:** T<sub>2</sub>W spectral attenuated inversion recovery and native T<sub>1</sub> mapping were applied in 10 healthy volunteers and 62 STEMI patients, and late gadolinium enhancement was included for infarct localisation at 1 week and at 6 months post-STEMI. Segmental T<sub>1</sub> values and T<sub>2</sub>W signal intensity ratios were calculated; oedema volumes and salvage indices were determined in patients using image thresholding—a receiver operator characteristic (ROC) derived T<sub>1</sub> threshold, and a 2SD T<sub>2</sub>W threshold; and the results were compared between patients with/without MVO (n=35/27).

**Results:** Native T<sub>1</sub> mapping delineated oedema with significantly better discriminatory power than T<sub>2</sub>W—as indicated by ROC analysis (area-under-the-curve, AUC = 0.89 vs 0.83, p=0.009; and sensitivity/specificity= 83/83% vs 73/73%). The optimal ROC threshold derived for T<sub>1</sub> mapping was 1241 ms, which gave significantly larger oedema volumes than 2SD T<sub>2</sub>W (p=0.006); with this threshold, patients with and without MVO showed similar oedema volumes, but patients with MVO had significantly poorer salvage indices (p<0.05) than those without. Neither method was significantly affected by MVO, the volume of which was seen to increase exponentially with infarct size.

**Conclusions:** Native T<sub>1</sub> mapping at 3T can delineate oedema one week post-STEMI, showing larger oedema volumes and better discriminatory power than T<sub>2</sub>W imaging, and it is suitable

for quantitative thresholding. Both techniques are robust against MVO-related magnetic susceptibility.

**Keywords:** acute myocardial infarction; magnetic resonance imaging; myocardium at risk; myocardial oedema; microvascular obstruction;  $T_1$  mapping.

## Introduction

Quantitative  $T_1$  mapping has recently emerged as a powerful tool for myocardial tissue characterisation,[1] and previous work has already illustrated its utility for delineating myocardial oedema in acute myocardial infarction (AMI),[2, 3] and acute stress-induced cardiomyopathy patients.[4, 5] We have seen that, in the first 24 hours after acute myocardial injury, native  $T_1$  mapping assessment of oedema appears to be at least as good as that of  $T_2$ -weighted ( $T_2W$ ) short tau inversion recovery imaging,[3] which is the current standard for oedema assessment with cardiovascular magnetic resonance (CMR). However, it is still unknown whether  $T_1$  mapping's strengths are maintained beyond 24 hours after AMI, as—despite promising initial studies with  $T_1$ -weighted imaging at 1.5T—it has not yet been studied at this time point.[6]

A significant shortcoming of  $T_2W$ -based studies to date is that they identify oedema qualitatively, using reference regions in remote myocardium. Such regions are presumed to contain healthy tissue, a questionable assumption in patient populations—where risk factors can lead to subtle myocardial changes.[7] In contrast, native  $T_1$  mapping's primary strength is its quantitative nature, which obviates the need for a reference region and allows for powerful parametric thresholding.[4] Such benefits advocate the use of  $T_1$  mapping for detecting oedematous myocardium; however, this up-and-coming method may yet be confounded by microvascular obstruction (MVO), a phenomenon that is frequently seen after AMI.[8] Indeed, MVO has already been reported to hinder  $T_2W$  oedema detection,[9, 10] being associated with paramagnetic species—deoxygenated haemoglobin and elemental iron—that introduce  $T_2$ -shortening susceptibility gradients and decrease signal intensity in the  $T_2W$ -detected oedema region.[11, 12] MVO's effects have already been reported in quantitative  $T_2$  mapping studies, where affected regions were indistinguishable from normal myocardium on

T<sub>2</sub> maps.[13] Clearly this phenomenon poses problems for CMR oedema quantification, and its potential repercussions for T<sub>1</sub> mapping warrant immediate investigation.[14]

The primary purpose of this prospective study is to determine how native 3T T<sub>1</sub> mapping and T<sub>2</sub>- weighted (T<sub>2</sub>W) imaging compare for delineating myocardial oedema, both segmentally and volumetrically, one week after ST-elevation myocardial infarction (STEMI). The volumetric analysis includes an exploration of suitable pixel thresholding approaches for each of the two methods, with comparisons against a typical two-standard-deviation technique. Furthermore, features of MVO are investigated, including its effect on T<sub>1</sub> relaxation times and T<sub>2</sub>W signal intensity ratios.

## **Materials and Methods**

### *Patients and Healthy Volunteers*

Sixty two patients with first acute ST-segment elevation myocardial infarction (STEMI) were consecutively recruited at [REDACTED FOR PEER REVIEW] from September 2011 to April 2013 as part of the [REDACTED FOR PEER REVIEW] clinical trial.[15] All patients had TIMI 0/1 flow at the time of diagnostic angiography and underwent primary percutaneous coronary intervention (PCI) within 12 hours of the onset of chest pain. They were scanned one week after myocardial infarction (MI) and again six months later, provided that no further revascularisation procedures occurred in the interim. Furthermore, to establish the normal range of myocardial T<sub>1</sub> values and T<sub>2</sub>W signal intensity ratios, ten age-matched healthy volunteers were recruited: six males, no past medical history, no medication, and median heart rate (range) = 65 (50-75) bpm. All participants gave informed consent, and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as

reflected in a priori approval by [REDACTED FOR PEER REVIEW] human research committee.

### *Cardiac Magnetic Resonance Imaging*

CMR was performed using a 3 tesla MRI system (Achieva 3.0T TX, Philips Healthcare, Best, Netherlands) with a six-channel cardiac phased-array coil and radiofrequency shimming. T<sub>2</sub>W spectral attenuated inversion recovery (SPAIR) was applied as a short-axis stack, with repetition time (TR)/ echo time (TE) = 1600/80 ms, in-plane resolution 1.8 mm × 2.2 mm, slice thickness/gap = 10/0 mm.[16] A corresponding stack of modified Look-Locker inversion recovery (MOLLI) T<sub>1</sub> mapping images was acquired with: a 3b(3b)3b(3b)5b scheme; balanced steady-state free-precession readout; 35° flip angle; TR/TE = 2.7/1.1 ms; in-plane resolution 1.7 mm × 2.1 mm; slice thickness = 10 mm; sensitivity encoding factor = 2; and cardiac triggering to end diastole. This protocol conformed to the guidelines stipulated in the Society for Cardiovascular Magnetic Resonance T<sub>1</sub> mapping position statement.[17]

For infarct localisation in STEMI patients, short-axis late gadolinium enhancement (LGE) images were acquired using spoiled gradient echo inversion recovery (25° flip angle; TR/TE = 6.1/3.0 ms; in-plane resolution 1.8 mm × 2.2 mm; slice thickness/gap = 8/2 mm) within a 10-20 minute window after contrast administration (0.1 mmol kg<sup>-1</sup> gadolinium diethylenetriaminepentacetate, Gadovist; Bayer, Leverkusen, Germany). Infarct size was determined from both the acute scan and the six- month follow-up in order to account for the remodelling process.

*Image Analysis*

$T_1$  maps were generated from MOLLI source images using in-house software (IDL, Excelis, Boulder, CO, USA) and controlled for artefacts with the aid of chi-square error maps. They were then prepared for segmental analysis, whereby the multi-slice  $T_1$  data were pooled into basal, mid-cavity, and apical sets, and were segmented according to the American Heart Association 17-segment model,[18] omitting the apical cap and including MVO, where present. Individual  $T_1$  values were calculated for the remaining 16 segments, and a blood pool threshold—measured in normal volunteers as the mean left ventricular blood pool  $T_1$  minus 2SD—was used to exclude pixels contaminated by blood contributions. Consistent with  $T_1$  mapping,  $T_2$ -weighted images were segmented and examined for artefacts, and reference regions of interest (ROIs) were drawn in pectoral muscle for calculation of signal intensity ratios.[19]

Infarcted (LGE+) segments were identified on LGE images by an experienced cardiologist (five years' experience) as regions with signal intensity greater than the mean signal intensity in remote myocardium (diametrically opposite the STEMI area) plus 5SD.[20] Given that early and late gadolinium enhancement show similar sensitivity and specificity for detecting MVO,[10] LGE images were selected for MVO identification. Thus LGE+ segments were subdivided according to whether or not they contained MVO (MVO+ or MVO-, respectively), which was identified as subendocardial or mid-wall hypoenhancement within gadolinium-enhanced myocardium.[21] The total MVO volume was expressed as a percentage of the myocardial volume.



### *Inter- and Intra-Observer Reproducibility*

To compare the inter- and intra-observer reproducibility of T<sub>1</sub> mapping and T<sub>2</sub>W-SPAIR, segmental measurements were repeated in five patients and five volunteers and re-measured by a second independent and blinded observer (three years' experience) in those same participants.

### *T<sub>1</sub> Mapping versus T<sub>2</sub>W-SPAIR: Performance for Detecting At-Risk Myocardium*

ROC analysis was performed to assess the discriminatory power of T<sub>1</sub> mapping and T<sub>2</sub>W-SPAIR in the entire patient cohort, as well in MVO+/MVO- patient subgroups. LGE was considered a surrogate of acute myocardial injury, given that endocardial surface area LGE is accepted as a method for measuring area at risk.[22] Therefore, acute (one week post STEMI) LGE+ segments were used as the oedema-positive test state, as previously described,[3] and normal segments from healthy volunteers were used as the oedema-negative test state. All T<sub>1</sub> map and T<sub>2</sub>W-SPAIR segments were categorised as LGE+ or LGE-, and were only included if they were artefact-free in both T<sub>1</sub> maps and T<sub>2</sub>W-SPAIR images. ROC thresholds were chosen for equal sensitivity and specificity.

### *Volume of Myocardium at Risk: T<sub>1</sub> Mapping versus T<sub>2</sub>W-SPAIR*

For T<sub>2</sub>W-SPAIR volumetric analysis, pixels with signal intensities 2SD higher than the mean signal intensity of remote myocardium were considered oedematous,[23] and oedema volume was expressed as a percentage of the total myocardial volume. For T<sub>1</sub> mapping, two methods were used to measure the oedema volume: 1) a 2SD threshold, equivalent to that described for T<sub>2</sub>W-SPAIR; 2) a pre-set threshold, where pixels were considered oedematous

if their  $T_1$  values fell between the ROC-derived threshold and the mean blood pool  $T_1$  minus 2SD. The pre-set threshold also included a window to accommodate haemorrhagic  $T_1$  values (500-1025 ms), which would otherwise be excluded from the oedema volume, in order to mitigate any bias in the volume calculation. Infarct size was measured on acute and six-month LGE images using a 5SD threshold, and was used to calculate salvage index as follows: (oedema volume  $\times$  infarct size) = oedema volume.

### *Statistical Analysis*

Intra-method comparisons were made in SPSS (IBM, Armonk, NY, USA) using analysis of variance, and significant inter-group differences were verified using two-tailed independent *t*-tests or Mann-Whitney U tests. In ROC analysis, area-under-the-curve (AUC) values were compared according to Hanley and McNeil.[24] Finally, inter- and intra-observer reproducibility were evaluated using Bland-Altman analysis and intra-class correlation coefficients (ICC).

## **Results**

### *Patient Demographics*

Patient characteristics, risk factors, culprit arteries and CMR characteristics are presented in Table 1. MVO+ patients had significantly larger raw and indexed left ventricular volumes, (end-systolic  $p=0.003$ , end-diastolic  $p=0.03$ , indexed end-systolic  $p=0.001$ , indexed end-diastolic  $p=0.01$ ), reduced left ventricular ejection fractions ( $p<0.001$ ), and higher 12 hour Troponin I levels compared to the MVO- group ( $p=0.001$ ). There was no significant

difference in the time from the onset of chest pain to percutaneous intervention between the MVO- and MVO+ groups.

### *Imaging Results*

Representative images from this study are shown in Figure 1. From a total of 1152 segments, 382 were discarded from T<sub>2</sub>W-SPAIR image analysis (5.3 per participant, on average) as a result of coil-sensitivity-related signal dropout, which occurred mainly in infero-lateral segments. A total of 174 T<sub>1</sub> map segments were discarded (2.4 per participant, on average): mostly anterior and infero-lateral segments affected by off-resonance artefact near the coronary veins. The T<sub>1</sub> of normal myocardium in healthy volunteers was seen to be significantly shorter ( $p < 0.001$ ) than the T<sub>1</sub> of the segments most remote from infarction in patients, with mean (SD) T<sub>1</sub> values of 1192 (30) ms versus 1215 (39) ms, respectively. The mean (SD) blood pool T<sub>1</sub> measured in healthy volunteers was 1774 (46) ms, and thus an upper pixel threshold of 1682 ms (mean blood pool T<sub>1</sub> minus 2SD) was chosen to exclude blood pool contamination from myocardial T<sub>1</sub> measurements.

### *Performance for Detecting At-Risk Myocardium and Effect of MVO*

Figure 2 shows ROC analyses, grouped by imaging sequence. For the whole patient group, the AUC for T<sub>1</sub> mapping was significantly greater than that of T<sub>2</sub>W-SPAIR (0.89 versus 0.83,  $p = 0.009$ ), and the calculated oedema threshold T<sub>1</sub> was 1241 ms (sensitivity and specificity of 83%). For T<sub>2</sub>W-SPAIR, ROC analysis gave a sensitivity and specificity of 73%.

Examining MVO- and MVO+ patient groups: in MVO- patients, T<sub>1</sub> mapping had significantly better discriminatory power than T<sub>2</sub>W-SPAIR, with an AUC of 0.93 versus 0.81, ( $p = 0.004$ ); in MVO+ patients, there was no significant difference between the two

techniques, with ROC analysis giving an AUC of 0.88 for T<sub>1</sub> mapping versus an AUC of 0.84 for T<sub>2</sub>W-SPAIR, (p=0.11). The oedema threshold T<sub>1</sub> values calculated from these data were 1243 ms (sensitivity and specificity 86%) in the absence of MVO and 1238 ms (sensitivity and specificity 82%) in the presence of MVO. Given the similarity of these values, the 1241 ms threshold derived from the complete dataset was adopted for volumetric analysis.

#### *Volume of Myocardium at Risk: T<sub>1</sub> Mapping versus T<sub>2</sub>W-SPAIR*

Myocardial oedema volumes and salvage indices derived in all patients using each of the three methods are shown in Table 2. The oedema volume measured with T<sub>1</sub> mapping-ROC was significantly larger than that measured with T<sub>2</sub>W-SPAIR 2SD in the entire group (p=0.006) and in the MVO- group (p=0.02), whereas in the MVO+ group no significant difference was seen. With the two T<sub>1</sub> mapping approaches (2SD and ROC) MVO- and MVO+ patients showed similar oedema volumes; however, T<sub>2</sub>W-SPAIR showed larger oedema volume measurements in the MVO+ group compared to the MVO- group (p<0.05). Measurements of myocardial salvage index did not differ significantly whether infarct size was measured from acute or follow-up LGE scans. However, with both T<sub>1</sub> mapping thresholds, salvage index was significantly greater in the MVO- group compared to the MVO+ group (p<0.05 for both).

Figure 3 shows examples of oedema highlighted by each of the three threshold methods. The areas delimited by each technique were similar; however, the T<sub>1</sub> mapping ROC threshold highlighted a region of abnormal myocardium extending farther towards the lateral wall than that shown by the T<sub>2</sub>W 2SD approach. This region may be curtailed in the T<sub>2</sub>W 2SD map as a consequence of subtle signal loss in the source images that is not detectable by

eye. Of the three approaches, the  $T_1$  mapping 2SD gave the most conservative estimate of oedema volume in the example shown.

#### *Microvascular Obstruction Characterisation*

Figure 4 demonstrates that, in our study cohort, there is an exponential relationship between MVO extent and infarct size, with a strong, significant positive correlation between the two (Spearman's  $\rho = 0.73$ ,  $p \ll 0.001$ ). Infarcts larger than 35% of the left ventricular myocardium tended to demonstrate large areas of MVO, whereas smaller infarcts tended to contain MVO no more than 5% of the total myocardial volume. Furthermore, three MVO+ patients exhibited the very low  $T_1$  values associated with haemorrhage. In these patients, direct measurement of  $T_1$  in haemorrhagic segments gave a median (range)  $T_1 = 785$  (524-1025) ms.

#### *Inter- and Intra-Observer Reproducibility Results*

For segmental  $T_1$  mapping and  $T_2W$ -SPAIR, inter-observer and intra-observer bias and limits of agreement were similar, with no statistically significant differences. ICCs were 0.91 for  $T_1$  mapping and 0.84 for  $T_2W$ -SPAIR.

## **Discussion**

The main findings of this work are as follows: I) 3T native  $T_1$  mapping identifies oedematous myocardium one week post-acute-STEMI and has a better discriminatory performance than  $T_2W$ -SPAIR; II) when using an optimised, ROC-derived threshold,  $T_1$  mapping detects significantly larger oedema volumes than 2SD  $T_2W$ -SPAIR, whereas with a

2SD threshold,  $T_1$  mapping yields similar oedema volumes to 2SD  $T_2$ W SPAIR; III) in general, the presence of MVO does not significantly affect the performance of  $T_1$  mapping or  $T_2$ W-SPAIR for identifying oedematous myocardium one week post STEMI; and (IV), typically, MVO is only found in medium-to-large MIs and its extent increases exponentially with infarct size.

Myocardial salvage is an important predictor of mortality in patients with AMI,[25] but to date there is no gold standard for measuring myocardial oedema in vivo in humans. Several oedema imaging methods exist—single-photon emission computed tomography,[26]  $T_2$ W CMR,[19] LGE endocardial surface area,[27]  $T_1$  mapping CMR,[3, 4, 23] and  $T_2$  mapping CMR[13, 23]—but this study represents the first application of  $T_1$  mapping with a quantitative ROC-threshold optimised to a STEMI population. The precedent for such an approach was set by Ferreira et al.[28], in a recent study on myocarditis. This study showed that—with an appropriate  $T_1$  threshold— $T_1$  mapping detects a significantly larger oedema volume than  $T_2$ W imaging. In the current work we show similar findings in myocardial infarction patients; namely, the extent of oedema identified by our optimised ROC threshold method, one week post-MI, is significantly larger than that measured by  $T_2$ W-SPAIR, except in MVO+ patients where the difference is not statistically significant. This builds on the pre-clinical findings of O h-Ici et al.[29] and Ugander et al.[23], who have already demonstrated that  $T_1$  mapping can identify the area-at-risk, and the region so measured shows excellent correlation with microspheres. In the context of human studies, our work provides an interesting counterpoint to the findings of Dall'Armellina et al.[3] who noted that  $T_1$  mapping and  $T_2$ W-SPAIR detected similar oedema volumes in STEMI patients 24 hours post-MI. The differences may lie in the way oedema was measured; indeed, when we employed the simple

2SD  $T_1$  threshold used by Dall'Armellina et al. at 1.5 T, our findings were consistent with theirs.

In our patient cohort, we observed that remote myocardial segments—diametrically opposite the infarction—had significantly increased native  $T_1$  values compared to segments in age-matched healthy volunteers. There are two possible explanations for this important finding. First, in AMI the entire myocardium may suffer mild inflammation. Indeed, this hypothesis was put forward by other investigators who showed that ultra-small superparamagnetic particles of iron oxide are retained in segments very remote from the infarct.[27] Second, the  $T_1$  may have been abnormal in these patients prior to myocardial infarction, due to discrete microscopic fibrosis caused by comorbidities such as diabetes, hypertension or hypercholesterolemia.[30, 31] In order to establish which hypothesis is correct, our findings would have to be validated through histology. Given that our proposed ROC-derived threshold is free from any assumptions regarding remote myocardium, we believe it is more appropriate than  $T_2W$  imaging for delimiting myocardial oedema in vivo.

More than half of the patients included in this study exhibited MVO—demonstrating differentially worse cardiac remodelling and significantly higher levels of cardiac biomarkers than those that did not. They also showed comparable oedema volumes but lower salvage indices than MVO- patients, confirming the significance of MVO as an adverse prognostic marker in STEMI.[32] We included MVO in our  $T_1$  mapping and  $T_2W$  SPAIR ROIs to establish its effect on the discriminatory power of these techniques. In patients with MVO, we observed that both methods are subtly—not significantly—influenced by haemorrhage, with some haemorrhagic pixels showing  $T_1$  values similar to those of normal myocardium, and much lower in some extreme examples, which also showed reduced  $T_2W$  signal intensity

ratios. Despite this,  $T_1$  mapping was superior to  $T_2W$ -SPAIR for detecting oedema, both overall and in the subgroup of patients without MVO.  $T_1$  mapping was also less prone to artefact than  $T_2W$ -SPAIR, and its ICC was larger—though not significantly so.

### *Study Limitations*

Due to time constraints,  $T_2^*$  mapping was not applied in this work, thus haemorrhage and MVO were both identified using LGE images alone. Furthermore, improvements have been made to the MOLLI  $T_1$  mapping pulse sequence since the beginning of the study, resulting in higher signal-to-noise, reduced artefact, shorter breath-holds and minimal  $T_1$  heart-rate dependence—further increasing clinical utility. Our fixed  $T_1$  threshold value may differ slightly for other  $T_1$  mapping sequences, but this is to be expected due to different manufacturer setups, hardware and other factors. Further studies are required to determine appropriate  $T_1$  mapping ROC thresholds on other platforms.

Given that this is a clinical study, histology would not have been a viable means of validating our technique; however, we and others have previously shown that  $T_1$  mapping reflects oedema in other acute pathologies in man.[4, 5] Human studies such as this are very important, as the immediate post-infarct stage represents a dynamic post-reperfusion healing process that differs between man and animal models.

In conclusion,  $T_1$  mapping at 3T robustly detects myocardial oedema one week post-AMI. Compared to standard  $T_2W$  imaging, it shows superior discriminatory power and similar reproducibility, it can be applied with a receiver operator characteristic threshold—rendering it independent of assumptions about the remote myocardium—and it describes



larger volumes of oedema. Neither  $T_1$  mapping nor  $T_2W$  imaging were significantly affected by microvascular obstruction.

### **Conflict of Interest**

David M. Higgins is an employee of Philips Healthcare. All other authors have no further conflicts of interest to declare.

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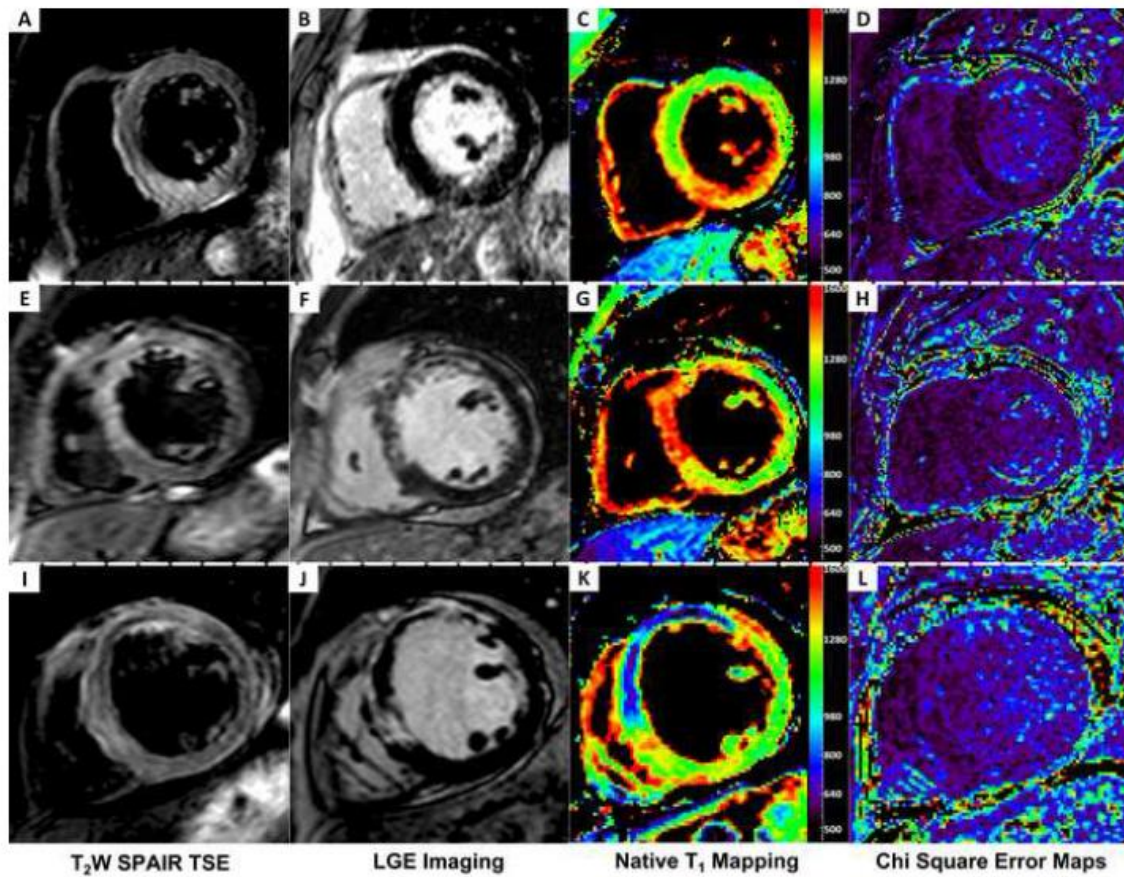
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## Figure Captions

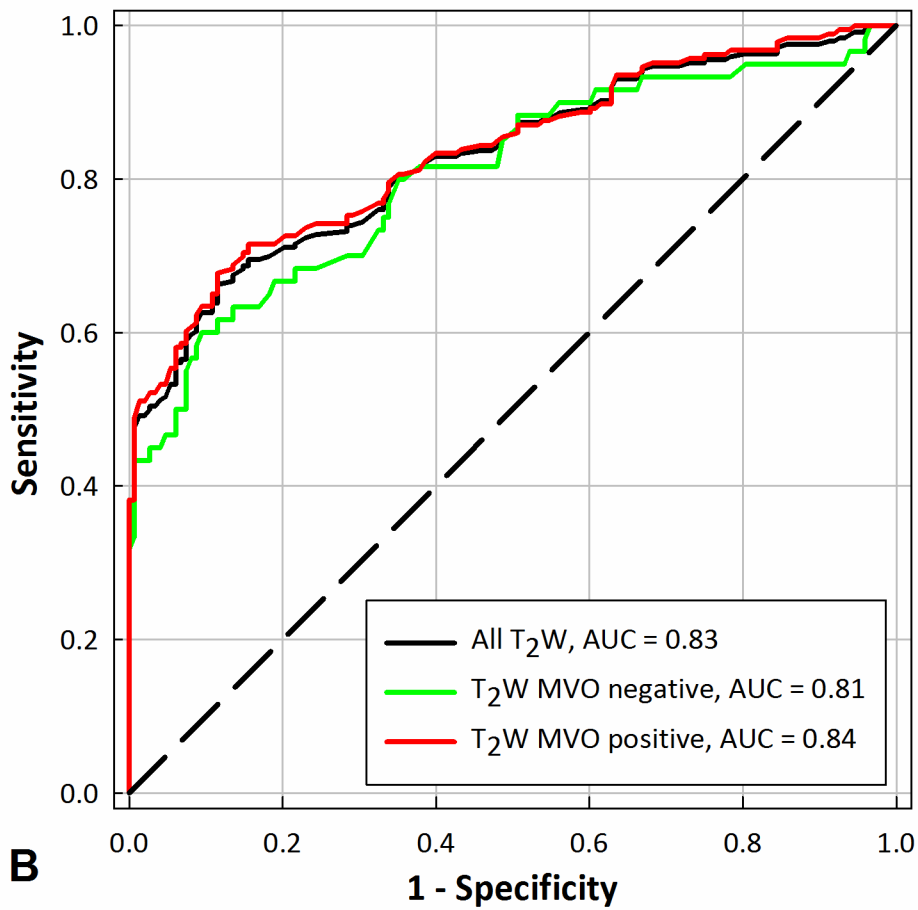
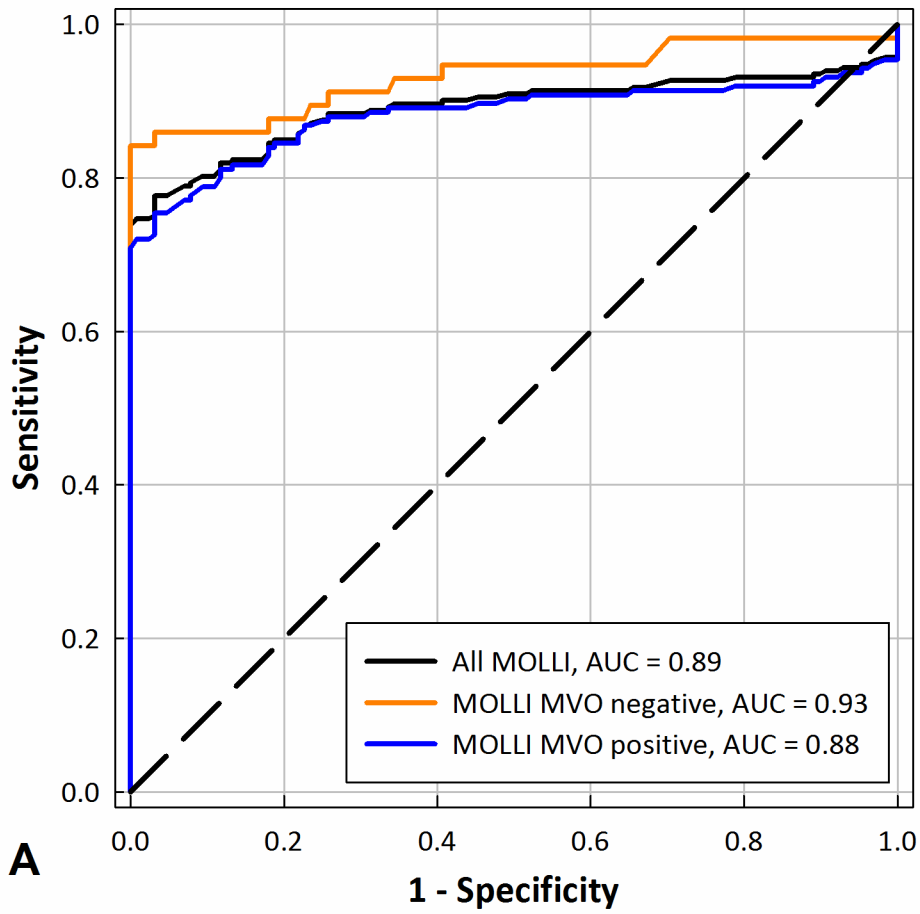
**Figure 1:** Representative short-axis CMR images—from a patient with no microvascular obstruction (MVO)(A-D), a small amount of MVO (E-H) and a large, confluent area of MVO (I-L). The top row shows an inferior myocardial infarction (infarct size 3% of total myocardium), middle and bottom rows are anteroseptal myocardial infarctions (infarct sizes 33% and 57% respectively). T<sub>2</sub>-weighted spectral attenuated inversion recovery turbo spin echo (T<sub>2</sub>W-SPAIR TSE) images were acquired with repetition time (TR) = 1600 ms and echo time (TE) = 80 ms. Acute late gadolinium enhancement (LGE) images were acquired with a 25° flip angle, TR/TE = 6.1/3.0 ms, and an inversion time chosen to optimise myocardial nulling. T<sub>1</sub> maps and chi-square maps were generated from T<sub>1</sub> mapping source images, which were acquired with a 3b(3b)3b(3b)5b sampling scheme, 35° flip angle, and TR/TE = 2.7/1.1

ms. The  $T_1$  map colour scale was chosen to highlight myocardium.

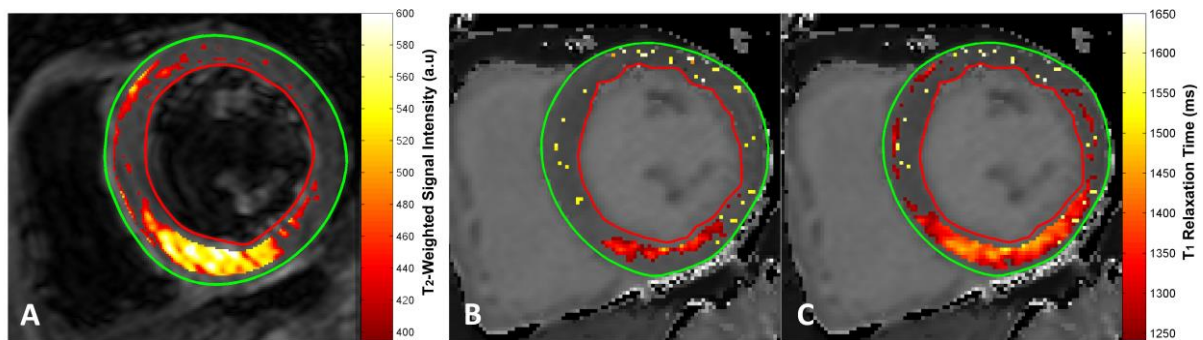


**Figure 2:** Receiver operator characteristic (ROC) curves—demonstrating the discriminatory power of  $T_1$  mapping (A) and  $T_2$ -weighted spectral attenuated inversion recovery ( $T_2$ W-SPAIR)(B) for identifying myocardial oedema. Each of the plots are subdivided into microvascular obstruction (MVO)+ and MVO- patient groups. No statistically significant differences were seen between the MVO+/- groups with either method, but  $T_1$  mapping gave a significantly larger area-under-the-curve (AUC) than  $T_2$ W-SPAIR.

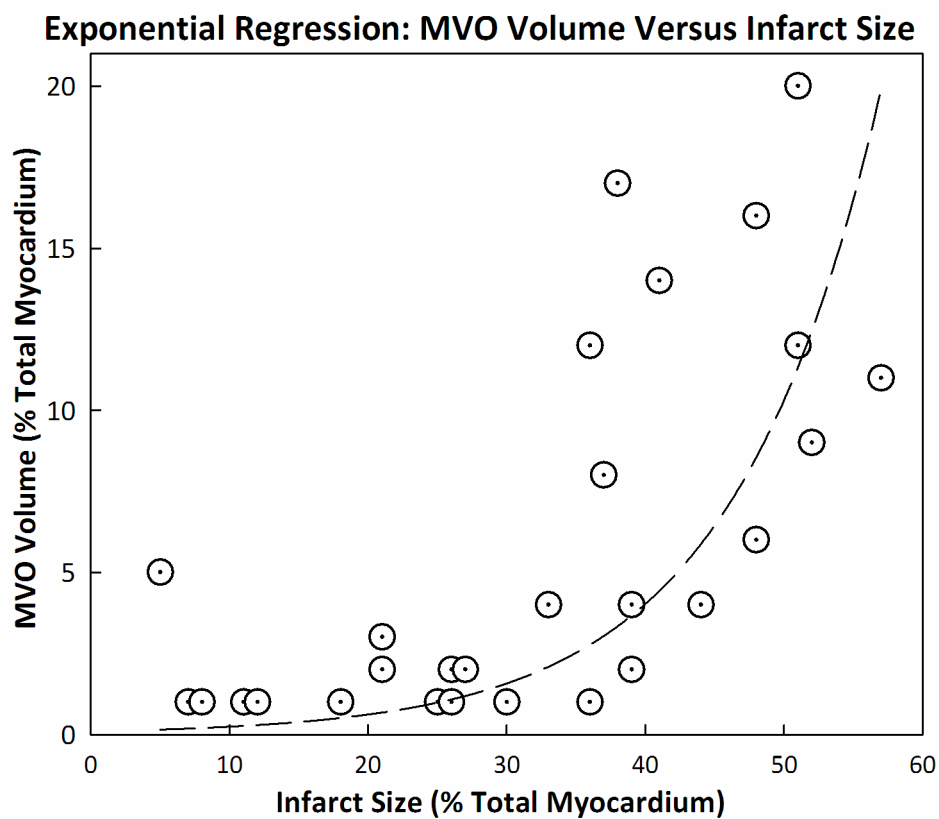




**Figure 3:** Basal short-axis images with visual thresholds—(A) a T<sub>2</sub>-weighted spectral attenuated inversion recovery (T<sub>2</sub>W-SPAIR) image with a 2SD threshold, (B) a T<sub>1</sub> map with a 2SD threshold, (C) a T<sub>1</sub> map with a receiver operator characteristic (ROC)-derived threshold. Highlighted regions (delimiting elevated signal intensity or T<sub>1</sub> values) are visible in the inferior part of the myocardium, corresponding to late gadolinium enhancement. Green and red lines denote epicardial and endocardial borders, respectively.



**Figure 4:** Plot showing the extent of microvascular obstruction (MVO) versus infarct size, as measured by late gadolinium enhancement (LGE) imaging - both are measured as a percentage of the total myocardium. Very large volumes of MVO (>5%) can be seen in larger infarcts (>35% of total myocardium). An exponential regression line indicates the tendency for MVO size to increase with infarct size.



<b>Table 1. General and CMR Patient Characteristics</b>	<b>All Patients (n=62)</b>	<b>MVO- (n=27)</b>	<b>MVO+ (n=35)</b>
Age [Median (range) yrs]	59 (29-88)	60 (46-83)	58 (29-88)

<b>Male gender</b> [%]	46 (74%)	18 (67%)	28 (80%)
<b>BSA</b> [Median (range) m <sup>2</sup> ]	1.96 (1.48-2.35)	1.95 (1.48-2.22)	1.99 (1.53-2.35)
<b>Heart Rate</b> [Median (range) bpm]	65 (50-85)	62 (53-70)*	68 (50-85)*
<b>Risk Factors [n (%)]</b>			
-Diabetes Mellitus	5 (8%)	1 (4%)	4 (11%)
-Smoking	24 (39%)	10 (37%)	14 (40%)
-Hypertension	11 (18%)	3 (11%)	8 (23%)
-Hypercholesterolemia	27 (24%)	8 (30%)	9 (26%)
-Prior Angina	1 (2%)	1 (4%)	0 (0%)
<b>Troponin I (12 Hr)</b> [Median (range) ng/ml]	64 (2-461)	43 (2-155)*	97 (16-461)*
<b>Time Onset C/P to PCI</b> [Median (range) hrs]	2.7 (0.8-12.0)	3.3 (0.8-12.0)	4.1 (1.1-8.2)
<b>Time PCI to CMR</b> [Days]	7	7	7
<b>Culprit Artery</b>			
-LAD	25 (40%)	4 (15%)	21 (60%)
-LCX	3 (5%)	0 (0%)	3 (9%)
-RCA	34 (55%)	23 (85 %)	11 (31%)
<b>LVEDV</b> [Mean (SD) ml]	164 (37)	146 (30)*	179 (37)*
<b>LVESV</b> [Mean (SD) ml]	84 (33)	65 (21)*	100 (32)*
<b>EF</b> [Mean (SD) %]	50 (10)	57 (7)*	45 (9)*
<b>LVM</b> [Mean (SD) ml]	147 (45)	130 (42)	161 (44)
<b>Indexed LVEDV</b> [Mean (SD) ml]	84 (17)	76 (11)*	90 (18)*
<b>Indexed LVESV</b> [Mean (SD) ml]	43 (16)	33 (9)*	51 (16)*
<b>LVM Index</b> [Mean (SD) g/m <sup>2</sup> ]	75 (20)	67 (18)	81 (19)

**Table 1. Patient characteristics** - \* denotes a statistically significant difference between MVO+ and MVO- groups ( $p < 0.05$ ), with specific p-values shown in the text. BSA = body surface area, C/P = chest-pain, CMR = cardiovascular magnetic resonance, EF = ejection fraction, LVEDV = left ventricular end-diastolic volume, LVESV = left ventricular end-systolic volume, LVM = left ventricular mass, PCI = percutaneous coronary intervention, RCA.

<b>Table 2. Myocardium at Risk and Salvage Index</b>	<b>All Patients</b>	<b>MVO-</b>	<b>MVO+</b>
<b>Oedema Volume (%)</b>			
-T <sub>2</sub> W-SPAIR 2SD	40 (16)	28 (11)†	48 (13)†
-T <sub>1</sub> Mapping 2SD	37 (9)	37 (12)	38 (7)*
-T <sub>1</sub> Mapping ROC	55 (7)*	57 (7)*	53 (8)
<b>Salvage Index</b>			
-1 Week: T <sub>2</sub> W-SPAIR 2SD	0.66 (0.23)	0.75 (0.17)	0.59 (0.25)
-1 Week: T <sub>1</sub> Mapping 2SD	0.59 (0.35)	0.84 (0.09)†	0.42 (0.36)†
-1 Week: T <sub>1</sub> Mapping ROC	0.73 (0.22)	0.89 (0.08)*†	0.63 (0.22)†
-6 Months: T <sub>2</sub> W-SPAIR 2SD	0.56 (0.25)	0.69 (0.29)	0.51 (0.22)
-6 Months: T <sub>1</sub> Mapping 2SD	0.51 (0.30)	0.76 (0.19)†	0.39 (0.30)†
-6 Months: T <sub>1</sub> Mapping ROC	0.67 (0.21)	0.85 (0.12)*†	0.59 (0.21)†

**Table 2.** Myocardial oedema volume and salvage index measured using T<sub>2</sub>W-SPAIR and T<sub>1</sub> mapping - Data are presented as mean (SD). \* denotes a statistically significant difference between T<sub>1</sub> mapping with a two standard deviation (2SD) or receiver operator characteristic (ROC) threshold and T<sub>2</sub>-weighted spectral attenuated inversion recovery (T<sub>2</sub>W-SPAIR); † denotes a statistically significant difference between microvascular-obstruction-positive (MVO+) and microvascular-obstruction-negative (MVO-) groups (p values in the text). No significant difference was seen between salvage index measurements made using infarct size at one week and infarct size at six months.

