Quantitative Dynamic Contrast Enhanced MRI in Acute ST-Elevated Myocardial Infarction: Blood Flow, Microvascular Permeability and Interstitial Volume in Infarct and Peri-Infarct Edema

David A Broadbent[1,2], Ananth Kidambi[2], Sven Plein[2], and David L Buckley[1,2]

[1]*Division of Medical Physics, University of Leeds, Leeds, West Yorkshire, United Kingdom,* [2]*Multidisciplinary Cardiovascular Research Centre, University of Leeds, Leeds, West Yorkshire, United Kingdom*

Target Audience: Clinicians and scientists with an interest in myocardial blood flow

Background: Following a period of ischemia and subsequent therapeutic reperfusion, cardiomyocyte necrosis extends from the subendocardium of the occluded territory and can be accompanied by other pathologies including edema and microvascular obstruction (MVO) [1]. Consequently in acute reperfused myocardial infarction (MI) myocardial tissue exists in several distinct states. Due to differences in microvascular, cellular and interstitial space characteristics these exhibit differing contrast agent uptake characteristics.

Gadolinium based contrast enhanced MRI is an established tool for post-MI assessment which exploits these differences in uptake to identify regions of reversible and irreversible damage. Abnormal early and late enhancement patterns in acute MI have been shown to have value in predicting recovery [2,3], and high-temporal resolution dynamic contrast enhanced (DCE) MRI can identify regions without restored perfusion ("no-reflow") [4]. Quantitative analysis of DCE data also allows measurement of physiological parameters such as myocardial blood flow (MBF) [4] and has been performed in sub-acute MI (2-3 weeks post-MI) [6]. We have shown in healthy volunteers that use of a distributed parameter (DP) tracer kinetic model allows estimation of additional parameters including microvascular permeability-surface area product (PS), first pass extraction fraction (E) and blood and interstitial volume fractions (v_b and v_e) [7]. In this study we applied these methods in acute ST-elevation MI (STEMI) following reperfusion by primary percutaneous coronary intervention.

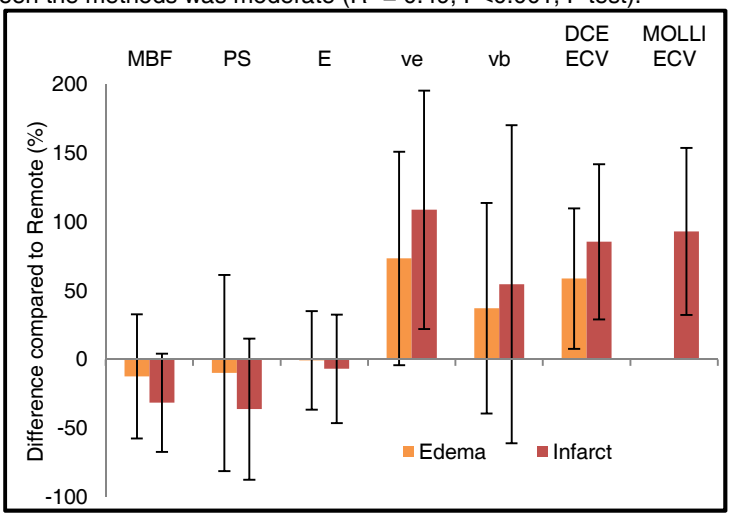
Methods: The study was approved by the local ethics committee and 40 subjects gave written informed consent. Scanning was performed on a Philips 3T Achieva TX system with a 32-channel cardiac phased array receiver coil and data were acquired as part of a comprehensive CMR exam (including cine MRI, T_2 weighted imaging (T2w), myocardial tagging, DCE-MRI, early and late gadolinium enhanced imaging (EGE & LGE) and T_1 mapping) within 3 days of reperfusion therapy for patients presenting with STEMI. Blood samples were taken for hematocrit measurement. DCE data were acquired (saturation recovery gradient echo, TR/TE/TS = 2.8/0.9/100 ms, FA = 15°, SENSE factor 2, voxel size = 2.7x2.7x10 mm, FOV: body habitus dependent) at rest for 3 short-axis slices with temporal sampling equal to the subjects' heart rates. An initial 210 phases were acquired during which a dual-bolus of 0.01/0.1mmol/kg Gd-DO3A-butrol was administered. MOLLI [8] T_1 maps were acquired pre- and at 10 & 15 minutes post-contrast. Additional 21 phase DCE series were acquired approximately 6 & 12 minutes post-contrast. Regions of remote myocardium, infarct (excluding MVO) and peri-infarct edema were identified using T2w and LGE images and contours transferred to DCE data (with manual motion correction).

DCE signal-time courses were converted to ΔR_1 through estimation of S_0 and saturation pulse efficiency based on native and 10-minute post-contrast T_1 and signal intensity (SI). 10-minute post-contrast SI was estimated by fitting a bi-exponential function to the arterial input function tail. Model fitting was performed for the main bolus administration using the DP model with Laplace domain fitting [9], as previously reported [7]. Total extracellular volume fraction (ECV) was also estimated by equilibrium contrast CMR [10] using T_1 and hematocrit data (infarct and remote myocardium only).

Results: Modelling was successful in 86% of regions (similar success rate to rest studies in volunteers [7]), with greater success in pathological (88%) than remote (79%) regions. Absolute results are presented in the table and differences relative to remote myocardium in the figure. ECV by contrast equilibrium CMR showed a similar relative increase compared to remote myocardium (88%), but absolute results were systematically higher and correlation between the methods was moderate (R^2 = 0.49, P<0.001; F test).

		Mean (std. dev.)		
		Remote	Edema	Infarct
DCE	MBF (ml/min/100ml)	118(57)	100(85)*	77(45)**/^
	PS (ml/min/100ml)	50(30)	31(23)*	27(17)**
	E (%)	53(14)	48(13)	47(13)**
	v_e (%)	17(5)	26(11)**	35(14)**/^^
	v_b (%)	11(6)	14(8)	15(8)*
	ECV (%)	23(6)	34(11)**	43(14)**/^^
MOLLI	ECV (%)	29(6)	-	56(16)**

*Paired t-test P *<0.05/**<0.01 vs remote, ^<0.05/^^<0.01 vs edema*



Discussion and Conclusions: The previously demonstrated application of DP modeling in healthy volunteers has been extended to include analysis of myocardium in several pathological states with elevated ECV and reduced MBF. Despite reduced region of interest sizes and MBF (both leading to poorer contrast-to-noise) fitting was successful in the majority of cases. In the previous work it was hypothesized that some fitting failures may be due to the DP model being over-parameterized in cases with flow-limited perfusion. The increased success rate with the DP model in pathological tissue with lower first-pass extraction fraction observed in this work further supports this hypothesis.

The findings of lower MBF and higher ECV in infarct compared to remote myocardium are similar to results in DCE MRI of sub-acute myocardial infarction [6]. Significant differences are also observed between peri-infarct edema and remote myocardium which are compatible with current understanding of the physiology of acute MI and reperfusion injury.

References: [1] N. Ahmed, et al. (2013). Heart Lung Circ 22(4):243-255. [2] W. J. Rogers, et al. (1999). Circulation 99(6):744-750. [3] B. L. Gerber, et al. (2002). Circulation 106(9):1083-1089. [4] B. L. Gerber, et al. (2008). JCMR 10(1):18+. [5] M. Jerosch-Herold (2010). JCMR 12(1):57+. [6] E. Hopp, et al. (2013). Acta Radiologica 54(4):401-411. [7] D.A. Broadbent, et al. (2013). MRM 70(6):1591-1597. [8] D. R. Messroghli, et al. (2004). MRM 52(1):141-146. [9] A. Garpebring, et al. (2009). IEEE Trans Med Imaging 28(9):1375-1383. [10] E. Schelbert, et al. (2011). JCMR 13(1):16+.