Cardiac Magnetic Resonance Stress and Rest Perfusion with T1 Mapping: Is It Ready to Assess for Ischaemic Heart Disease?

The high diagnostic accuracy of cardiac magnetic resonance (CMR) stress and rest perfusion for the assessment of ischaemic heart disease is well established[1]. However, this requires gadolinium based contrast agent injection which carries a small risk of anaphylaxis and needs to be used with caution in the context of renal impairment[2]. Furthermore, there is still the unknown significance of gadolinium retention and deposition in the brain[2].
T1 mapping is a CMR sequence/ technique which allows the objective measurement of the myocardial T1 values[3]. These myocardial T1 values can be altered by changes in the myocardial tissue composition (eg. an increase in myocardial fibrosis, iron deposition, or water). For stress and rest T1 mapping, the alteration in blood flow and therefore water content results in changes in the T1 values which allows inference of satisfactory or reduced myocardial perfusion to diagnose obstructive coronary artery disease (CAD) or infarcted myocardial tissue. In the first proof of concept paper on stress and rest T1 mapping assessment of ischaemic heart disease [IHD] published in 2014[4], the authors demonstrated that during pharmacological stress there are detectable changes in the native myocardial T1 values due to coronary vascular recruitment and that normal myocardium could be differentiated from ischaemic and infarcted myocardial segments. In this first study, the Shortened Modified Look-Locker Inversion Recovery sequence (ShMOLLI) for T1 mapping was utilised and adenosine was the stress agent. In normal practice, other stress agents maybe utilised such as regadenoson, adenosine triphosphate, dipyridamole or dobutamine. Furthermore, there are different T1 mapping sequences available for use. The most common being the Modified Look-Locker Inversion Recovery sequence (MOLLI). Therefore, in order for this technique to be clinically translatable further work needed to be done to determine that this technique could be replicated with different T1 mapping sequences and different stress agents.
In this issue of the International Journal of Cardiology, Burrage et al[5] have worked to establish the use of stress and rest T1 mapping with regadenoson whilst utilising the same ShMOLLI sequence utilised in the first study. A previous study by Bohnen et al[6], had already established that stress and rest T1 mapping with regadenoson was feasible, but the MOLLI sequence at that time was used and normal volunteers were not included as part of the study. This contributed to the already published studies showing that adenosine[7] and exercise[8] stress and rest T1 mapping was feasible in differentiating normal, ischaemic and infarcted myocardium. Burrage et al's study adds further data to the feasibility of stress and rest T1 mapping in IHD assessment (see table 1 for list of other stress and rest T1 mapping studies for assessment of IHD).

Based on the studies published a picture is emerging which shows that normal myocardium tends to have a percentage increase in T1 values of ≥4% regardless of pharmacological stress agent or exercise[7-9] whereas ischaemic myocardium and infarcted myocardium showed minimal change in native T1 values of between -2 to +2%. The feature which separates ischaemic and infarcted myocardium is the resting native T1 values which is higher in the infarcted myocardium.

Full clinical translation though requires some major hurdles to be tackled. Firstly, there needs to be standardisation of T1 mapping sequences. Of the studies published so far ShMOLLI and MOLLI are the only sequences to be utilised. ShMOLLI has the potential advantage in stress and rest perfusion imaging due to its shorter acquisition preventing higher heart rates altering the native T1 values compared to MOLLI which has a longer acquisition. MOLLI is more easily available and as a result more commonly utilised in many centres. Furthermore, ShMOLLI is vendor specific at this point in time and thus not available to sites willing to use the sequence. T1 mapping also has the issue of variable normal values across different sites/ scanners and significantly different T1 values at 1.5T and 3T. Efforts are being made, including by the authors of this issue[10], to establish standardised normal values across multiple sites that can be adopted by new CMR sites or new CMR scanners. This will reduce the requirement of sites to establish their own normal ranges[3]. As of the current clinical landscape, T1 mapping utilisation is confined to CMR scanning units with significant expertise and experience.

A second area for development is the contouring of the stress and rest T1 maps without the perfusion images and late gadolinium enhancement (LGE) images for reference. The accuracy of these measurements need to be established against coronary angiography fractional flow reserve which is the current gold standard to identify obstructive CAD. One way to overcome this hurdle maybe to have T1 maps with a suitable colour spectrum allowing visual identification of suitable areas for contouring. This will need to be adapted to each scanner as the reference ranges will be slightly different until standardisation of T1 maps can be established.

Lastly, motion artefact during stress needs to be correctly handled to help ensure reliable and accurate T1 maps. This needs to be established before stress and rest T1 mapping can be fully utilised.

Nonetheless, stress and rest T1 mapping is an exciting avenue which if further developed can help birth a new clinical tool for obstructive CAD assessment without the need for contrast.

Table 1. Studies of Stress and Rest T1 Mapping for Assessment of Ischaemic Heart Disease

Studies	Year of Publication	Number of Subjects	Reference Standard	Stress Agent/ Exercise	T1 Mapping Sequence	Normal Myocardium T1 change (%)	Ischaemic Myocardium T1 Change (%)	Infarcted Myocardium T1 Change (%)
Liu, et al.	2016	20 Normal Controls; 10 CAD Patients	Catheter coronary angiography, CMR stress perfusion, LGE	Adenosine	ShMOLLI	3.9±0.6 (patient); 6.2±0.5 (Normal Control)	0.2±0.8	0.2±1.5
Bohnen, et al	2019	100 patients	CMR stress Perfusion and LGE images	Regadenoson	MOLLI 5s(3s)3s	4.72 (CI 3.90 to 5.54)	-2.65 (CI -3.84 to -1.46)	-1.72 (CI 3.90 to 5.54)
Nakamori, et al	2020	28 healthy subjects; 14 CAD patients	SPECT and catheter coronary angiogrpahy	Exercise (Supine bicycle ergometer)	Slice interleaved T1 Mapping	Median 4.9 [IQR 3.7 to 6.3]	0.72	0.12
Yimcharoen, et al	2020	181	CMR stress Perfusion and LGE images	Adenosine	MOLLI 5b(3b)3b	4.79± 3.14	1.38±3.02	1.55±5.25
Burrage, et al	2021	10 Healthy controls;	CMR stress Perfusion	Regadenoson	ShMOLLI	Median 4.3 [IQR 3.1 to 6.3];	0.5±1.6	Median -0.8 [IQR -1.9 to 0.5]

		25 CAD patients	and LGE images			8.2±0.8 (Healthy controls)		

Reference Standard refers to method of confirming ischaemia or infarct.
T1 Change presented as mean ± standard deviation, mean and confidence interval or median and interquartile range.
CAD = Coronary Artery Disease; CI = Confidence interval; CMR = Cardiac Magnetic Resonance; IQR = Interquartile range; LGE = Late Gadolinium Enhancement; MOLLI = Modified Look-Locker Inversion Recovery; ShMOLLI = Shortened Modified Look-Locker Inversion Recovery

References:

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