Automated scar quantification by CMR: a step in the right direction

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Cardiovascular imaging techniques have advanced our understanding of the pathophysiology of acute and chronic myocardial infarction (MI). Infarct size is intimately related to adverse LV remodeling, heart failure and clinical outcomes (1,2). Rapid, robust, and reproducible quantification of infarct size is therefore desirable in both clinical and research settings. The late gadolinium enhancement (LGE) technique using cardiovascular magnetic resonance is the gold standard method because of its high spatial resolution and excellent contrast (3). The technique uses a chelated gadolinium contrast agent, which acts as an extracellular tracer. This accumulates in areas where cell membranes are not intact (cells destined to die in acute MI) or where there is replacement fibrosis (chronic MI). Gadolinium, which shortens T1, causes the infarct to appear bright (white) on a T1 weighted image (4). Infarction imaged in this way correlates accurately with histological specimens in *ex vivo* animal studies (3,5) and is prognostic in multiple human studies (1). It guides therapy and is used as a surrogate endpoint in many acute infarct trials.

The LGE technique, while the current gold standard, does have limitations in: (I) the fidelity of clinical imaging; (II) the lack of consensus on a definitive post processing method to quantify infarct size from the clinical images obtained (6).

In animal models LGE is able to identify myocardial infarction related fibrosis at near cellular level (7) but clinical imaging in humans is performed with a voxel resolution many hundreds times larger. This loss of fidelity results in partial volume effects mixing bright 'white' infarction with dark 'black' normal myocardium creating literal 'grey' areas. This occurs especially at the boundaries of the infarct, compounding the fact that these areas themselves are composed of a mixture of viable and non viable cardiomyocytes. Not all infarcts are themselves uniformly bright, some appearing patchy 'white-grey-black' or homogenously grey, likely reflecting the same phenomenon. This problem is perhaps most pertinent in the LGE of non-ischaemic scar, such as occurs in hypertrophic cardiomyopathy (HCM). Furthermore, making the image binary (scar or not scar) potentially belies the underlying pathophysiology—for example, most fibrosis is remote from gross segmental scars (conventional infarcts) in end stage ischaemic cardiomyopathy (8); And early-phase contrast enhancement may be able to show the acute area at risk of infarction reflecting non-fibrotic expansion of the interstitial space (9)—yet, this distinction underpins nearly all current post processing techniques. Other, more technically advanced approaches have, disappointingly, not been made widely available for road-testing (10,11). In future, we may be better able to answer these questions, using new T1-mapping sequences to derive the extracellular volume fraction (ECV) of both infarct/non-ischaemic scar and remote/'normal' myocardium (12,13), —an advance which has already shown prognostic value (14).

Investigators including ourselves, have assessed scar quantification methods in humans (15). There is no gold standard to compare the infarct size obtained against and so reproducibility (or, rarely, outcome) has been used as a surrogate. In our previous work, 7 techniques including manual quantification and full width at half maximum (FWHM) methods were compared in acute/chronic MI and HCM. Interestingly, in MI all methods were relatively reproducible (with FWHM optimal) but the LGE area varied significantly with the method used. In HCM where areas of LGE can be more diffuse and difficult to quantify, methods that involve human interaction (manual tracing or methods relying on defining remote myocardium) did not perform well. Removing human interaction with semi-automated methods such as FWHM, will always improve reproducibility but no method is yet fully automated or objective. All methods require human input to remove confounding artefact and noise. Manual tracing of the myocardial borders to exclude blood pool is also required. This is laborious, but more importantly is the largest source of infarct size variability. Automation of myocardial segmentation (epicardium minus endocardium) is therefore likely to be a

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key next step as recently highlighted in the setting of acute MI oedema (16)—further work is much needed.

Lu and colleagues are to be congratulated for taking novel steps in this direction (17). They compared one of the better post processing methods, FWHM, against their newly developed method incorporating: (I) automated epicardial and endocardial border detection using 'free' (otherwise unused) SSFP cine data already obtained in the CMR study; and (II) graph cut algorithms to better delineate the remote myocardium. This new method is attractive since it is quicker, easier and less prone to observer variation—a result confirmed in their paper with an impressive reduction in analysis time from 2-5+ minutes per slice to just less than 1 second and no observer variability (due to the fact the observer is excluded from the process). Their conclusions are sound in that this is an evolution in the field of infarct quantification, and this is an interesting concept. The paper sets the stage for further investigation and opens up new questions to answer, such as: is the technique accurate as well as reproducible? How does this perform on a scan: rescan basis? Can this method cope with phase encoding direction swaps, microvasular obstruction (MVO) and non-ischemic LGE? Is one threshold (resulting in binarisation) good enough? 49% auto segmentation failure rate is too high—can this be improved? What is the effect of higher field strengths/higher resolution? How can this method be implemented practically?

The automated post processing of clinical LGE images advances the field in the right direction, but the quest for new methods must be supported by further planned accuracy and variability testing, with an eye to clinical implementation and distribution for better patient care.

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