Reply to Letter from Di Marco et al.

We thank Dr Di Marco et al. for their letter. We agree that contrast enhanced Multidetector Computed Tomography (MDCT) is excellent for non-invasively defining myocardial structure for electroanatomical map integration to determine, for example, the impact of epicardial fat. [1]

Myocardial tissue characterisation by imaging, CT and magnetic resonance imaging (MRI), provides insights into underlying activated disease pathways for focal fat and focal fibrosis in arrhythmogenic right ventricular cardiomyopathy (ARVC). How do they compare and how can they synergise?

Contraindications to MRI include presence of implanted devices and it has lower resolution than CT, but new approaches are emerging. Third generation late gadolinium enhancement (LGE) techniques with motion correction are superior, whilst dark blood techniques[2] visualize scar at lower thresholds. MRI in the presence of pacemakers and defibrillators is far safer than previously appreciated[3, 4] and now routine in our centre. Device related metal artefacts can now be removed with new approaches. [5] For focal fibrosis, particularly non-ischemic scar, MRI remains superior to CT mainly because although gadolinium chelates and iodinated contrast agents have identical kinetics and volumes of distribution, at clinically used doses, gadolinium chelates alter MRI signal-to-noise ratio far more than iodinated agents on CT. For fat, no exogenous contrast agent is used in MRI. CT is improving fast, particularly with iterative reconstruction and has emerging utility in this domain. The CT study by Berte et al.[6] showed apparent fat by CT but used a hybrid approach with exogenous contrast, so hypoattenuation is clearer but may represent fat and/or hypoperfused fibrosis.

Two decades of ARVC MRI have taught important lessons for imaging studies. The normal RV is complex. Hypokinesis adjacent to the moderator band insertion can be overcalled. Intra-myocardial fat and fibrosis can be hard to differentiate from epicardial fat in the thin walled RV, [7] so were therefore downgraded as biomarkers in the 2010 ARVC taskforce criteria. We recommend that all RV tissue characterisation studies (CT or MRI) use latest generation hardware/sequences/approaches, have mandatory control groups, ideally use genotyped subjects, use at least 2 readers blinded to disease status, and always illustrate publications with RV normal and abnormal findings so quality and interpretation can be judged.

Unfortunately, in our study, no patients underwent MDCT. By MRI, we found no RV wall motion abnormalities without RV LGE, but we may have been cautious calling both (specificity prioritised over sensitivity). Pathophysiologically, we suspect true RV ARVC dysfunction is caused by myocyte loss and replacement by fat/fibrosis rather than myocyte dysfunction, but we need to know more – the cellular mechanism: is it infiltration or metaplasia and why ? What is the signalling leading from desmosomal abnormalities to potential myocyte metaplasia? How does this relate to macroscopic findings, including the less common left ventricular (LV) ones such as apparent mild LV hypertrophy and small voltages?
We thank Dr Di Marco et al. for highlighting this and are keen to see more careful work on ARVC myocardial phenotype development using multiple techniques, hopefully leading to better treatments and outcomes for our patients.

References

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