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tissue (2). If this experimental work focuses precisely on infarct sizing, the reader is left with several open questions.

On observation of the different figures from this article (Figures 3 and 6), there is a 50% reduction of infarct size by ce-CMR, whereas there is a 26% increase in myocardial salvage and a 30% reduction in extracellular volume by pathology in the infarcted myocardium and adjacent areas between day 0 and day 7. In this rapid series of myocardial tissue changes, it is hard for the reader to understand that the same changes do not occur in the myocardial area at risk as determined by edema imaging by the same T2-weighted (T2w) CMR at 6 h and set as reference by the authors. Besides, the area at risk assessment by T2w CMR has been challenged significantly in recent reports (3–5). Because of the massive swelling in the true area at risk within the first hours after reperfusion (2), it is also very likely that at the acute timing chosen by the authors (6 h), CMR-measured area at risk was equally overestimated. Why then was there no pathological determination of the true area at risk according to the same protocol that was applied for infarct size? This would probably have put to rest all these debates, along with providing a real assessment of myocardial salvage at the same time.

Considering the high variability of myocardial salvage assessment shown in this experimental setting, do the authors think this challenges the findings of numerous clinical trials in which myocardial salvage by CMR was set as the principal endpoint?

One of the explanations for this rapid resorption of infarct size between day 0 and 7 proposed by the authors is the partial volume effect, with the original notion of "archipelago-like" progression of infarction. With spatial resolution of 0.5 mm at best, this would be difficult to assess. Besides, if these archipelagos of infarction truly existed, they would not disappear in time, and one would assume they would be seen on pathology.

How is ex-vivo T2w imaging to assess the area at risk affected by a myocardium saturated with gadolinium in the infarcted area?

Altogether, the take-home message from this work is that myocardial tissue in the infarcted area and its surroundings undergoes numerous complex and rapid changes that will affect any imaging method until the final fibrotic scar is constituted around 30 days after reperfusion. Considering this, we agree with the authors that timing of imaging is critical when assessing myocardial infarction with ce-CMR.

Mathieu Schaaf, MD, MSc
Nathan Mewton, MD, PhD*
Borja Ibanez, MD, PhD

*Hopital Cardiologique Louis Pradel
Centre d'Investigation Clinique
INSERM 1407
28 avenue du Doyen Lepine
Lyon, Rhone 69677
France
E-mail: nathan.mewton@chu-lyon.fr

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THE AUTHORS REPLY:

We thank Dr. Schaaf and colleagues for their interest in our work (1). The responses to their questions are as follows:

Dr. Schaaf and colleagues comment on why changes in the myocardium at risk (MaR) do not occur during the first week, in parallel with infarct size and extracellular volume (ECV). Independent of MaR, we demonstrated that infarct size by late gadolinium enhancement cardiac magnetic resonance (CMR) is larger acutely than on day 7 compared with histopathology using triphenyltetrazolium chloride staining, and this results in different salvage acutely and on day 7 (1). However, when salvage is determined with triphenyltetrazolium chloride as the infarct reference and MaR from T2-weighted (T2w) CMR, the results are similar at both time points (1). Thus, an overestimation of MaR in the acute phase is unlikely. Furthermore, T2w CMR has been validated against myocardial single-photon emission computed tomography

(SPECT) (2,3), and the extent of edema was unchanged 1 week after infarction in patients (3). Nordlund et al. (4) recently showed that MaR is stable over the first week, which does not support a bimodal pattern of edema after infarction in humans. The same study (4) also demonstrated that T2w CMR is sequence dependent, which could explain variations seen between vendors.

We acknowledge that histopathological determination of MaR using microspheres would have facilitated a comparison to previous studies. However, this was not part of the study design.

Dr. Schaaf and colleagues comment on the variability of salvage in our study (1) and whether this challenges the findings of trials in which salvage was used as an endpoint. We only studied salvage at days 0 and 7; how salvage varies when CMR is performed at interim time points needs investigation.

Dr. Schaaf and colleagues remark on the "archipelago-like" progression of infarction as an explanation for the rapid resorption of infarct size. We agree that the most likely explanation for the overestimation acutely is edema in MaR close to the infarct zone that resorbs over 1 week, but we cannot rule out other pathophysiological explanations.

Finally, Dr. Schaaf and colleagues inquire how ex vivo T2w imaging is affected by gadolinium. Experimentally, ex vivo T2w imaging with and without gadolinium agrees with SPECT for determination of MaR (2).

In summary, we again stress that timing of infarct imaging using late gadolinium enhancement CMR is important.

Robert Jablonowski, MD, PhD
Henrik Engblom, MD, PhD
Mikael Kanski, MD, PhD
David Nordlund, MD
Sasha Koul, MD, PhD
Jesper van der Pals, MD, PhD
Elisabet Englund, MD, PhD
Einar Heiberg, PhD
David Erlinge, MD, PhD
Marcus Carlsson, MD, PhD
Håkan Arheden, MD, PhD*

*Department of Clinical Physiology
Skåne University Hospital in Lund
SE-221 85 Lund, Sweden
E-mail: hakan.arheden@med.lu.se

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Please note: Dr. Arheden is a shareholder in Imacor. Drs. Engblom, Heiberg, Carlsson, and Arheden have been part-time employees for Imacor. Dr. Heiberg has reported that he is the founder of Medviso AB.

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3D Echocardiography and Level III Training

Echocardiography is the most widely used diagnostic imaging modality in cardiology. It is invaluable in the assessment of cardiac structure and function and as such it is a mandatory part of cardiology fellowship training. In most instances, the general cardiologist on entering the workforce is prepared for independent interpretation of echocardiograms. This is designated by the guidelines for training (COCATS) as level II (1). The education of level III echocardiographers, however, is more extensive because these trainees must possess the tools to direct echocardiography laboratories, teach future trainees, and advance the field with research and innovation.

The most recent training guidelines, COCATS 4, were published by the American College of Cardiology in 2015. COCATS 4 briefly and unclearly outlines knowledge on 3-dimensional (3D) echocardiography as a prerequisite for the level III echocardiographer (1). However, widespread incorporation of 3D echocardiography beyond academic or large training institutions is often viewed as challenging or unnecessary. We strongly believe that ensuring competency in 3D echocardiography during level III training will enhance the skills of new echocardiographers and improve the use and comfort level with 3D echocardiography in the community. We further believe that this is the opportune time to draw attention to this issue in advance of the anticipated advanced training statements in echocardiography (1).

The literature strongly supports the role for 3D echocardiography. The current 2015 American Society of Echocardiography/European Association of Cardiovascular Imaging chamber quantification guidelines recommend that when possible laboratories