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LETTERS TO THE EDITOR

3D CMR Mapping of Metabolism by Hyperpolarized 13C-Pyruvate in Ischemia–Reperfusion

The objective of this study was to evaluate the capability and accuracy of cardiac magnetic resonance with hyperpolarized [1-13C]-pyruvate using the fast 3-dimensional (3D) pulse sequence to detect the presence and regional distribution of transient cardiac metabolic changes in a pig model of ischemia–reperfusion.

In 7 male pigs, a pneumatic coronary occluder was placed around the left anterior descending coronary artery. [1-13C]-pyruvate polarization was performed using dynamic nuclear polarization as previously described (1). Injections were performed at rest, during coronary occlusion, and during reperfusion. A 3D IDEAL spiral sequence was used at 3-T cardiac magnetic resonance (2). Metabolite signal was evaluated in 120 myocardial sectors. The metabolic activity mismatch (MAM) between 2 segmental variation maps was defined as $100(S_{ai}-S_{bi})/(S_{ai}+S_{bi})/2$, where S_{ai} and S_{bi} are the relative values of the signal of metabolite in the segment "i" in condition "a" and "b".

The MAM of lactate and bicarbonate of the ischemic segments (middle and apical anteroseptal and anterior segments) was significantly different from that of the remote regions. In reperfusion, a significant inhomogeneity of MAM of bicarbonate ($p < 0.001$) was found, whereas no significant difference was found for lactate. Figure 1 shows a different distribution for lactate (-21 ± 6 vs. 3 ± 5, $p < 0.001$) or bicarbonate metabolic activity (-29 ± 7 vs. 33 ± 6, $p < 0.0001$) in the left ventricular segments involved in the ischemic process than in the remote segments. In reperfusion, lactate signal increased (20 ± 10 vs. -7 ± 5, $p = 0.007$) and bicarbonate decreased (-38 ± 12 vs. 36 ± 11, $p < 0.0001$) in the involved segments.

We evaluated cardiac metabolism in vivo during ischemia and acute reperfusion with a whole-heart acquisition using volume coils and high spatial resolution acquisition. Neither of these requirements was met by previously described methods. The main finding of the current study was that spatial resolution obtained using a 3D IDEAL spiral chemical shift imaging pulse sequence was high enough to provide 3D information on acute changes in pyruvate and metabolites in left ventricular myocardium using the conventional regional segmentation.

The IDEAL spiral chemical shift imaging pulse sequence allows the complete 3D dataset of information to be obtained simultaneously for each metabolite, with optimal signal-to-noise ratio and short acquisition time. This might be relevant for the application of hyperpolarized [1-13C]-pyruvate in humans, allowing complete acquisition during 1 breath-hold, increasing the signal-to-noise ratio and minimizing the effect of the main limitation of this technique, which is the fast signal decay of hyperpolarized substrates.

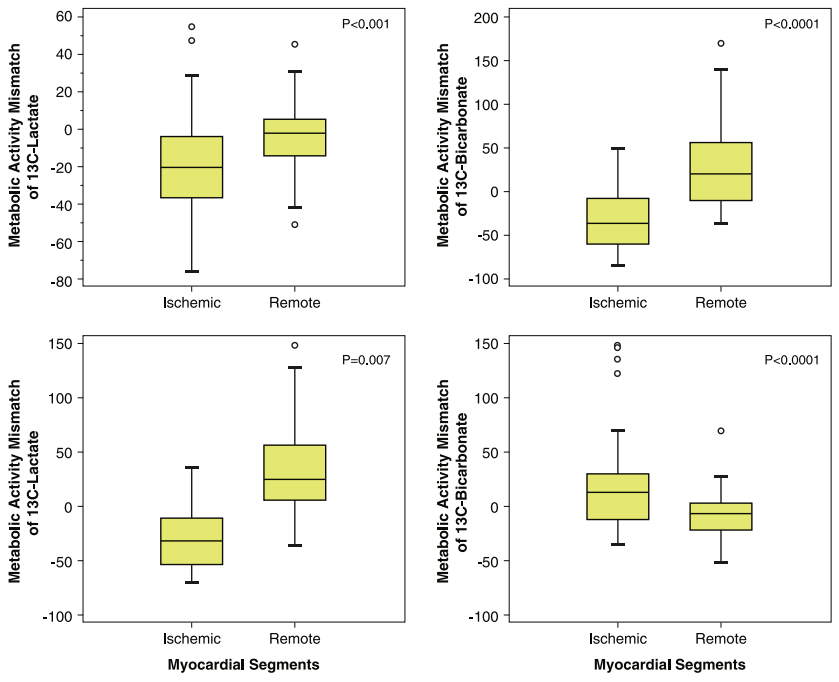

Figure 1. Metabolic Changes in Ischemia and Reperfusion

Box-and-whiskers plots show metabolic changes during occlusion **(Top)** and reperfusion **(Bottom)**.

Giovanni Donato Aquaro, MD,* Francesca Frijia, MSc, Vincenzo Positano, MSc, Luca Menichetti, PhD, Maria Filomena Santarelli, PhD, Jan Henrik Ardenkjaer-Larsen, PhD, Florian Wiesinger, PhD, Vincenzo Lionetti, MD, PhD, Simone Lorenzo Romano, MD, Giacomo Bianchi, MD, Danilo Neglia, MD, Giulio Giovannetti, MD, Rolf F. Schulte, PhD, Fabio Anastasio Recchia, MD, PhD, Luigi Landini, PhD, Massimo Lombardi, MD

*Fondazione G. Monasterio CNR-Regione Toscana, Via G. Moruzzi, 1, 56124, Pisa, Italy. *E-mail: aquaro@ftgm.it*

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Understanding the Asymmetrical Vena Contracta Area

The Difficult Relationship Between 2D and 3D Measurements

We read with great interest the paper by Hyodo et al. (1) and the accompanying editorial by Little (2). We would like to provide a few additional details for presenting a more comprehensive view to the development of the concept of the 3-dimensional (3D) vena contracta area (VCA) of a mitral regurgitant jet over the past years. Khanna et al. (3) deserve to be mentioned as the first to describe direct planimetry of the VCA in a real-time 3D dataset. In 2008, our group (4) validated the basic concept of the asymmetrical VCA by a systematic analysis of the relationship between 2D vena contracta width (VCW) and 3D VCA in dependence of the asymmetry of the VCA in both organic and functional mitral regurgitation (MR). This work revealed the systematic underestimation of asymmetrical VCAs by 2-dimensional (2D) VCW measurements being typically found in functional MR. Based on these results, we determined a larger cutoff value of 0.6 cm^2 for 3D VCA compared with 0.4 cm^2 for 2D-derived effective regurgitant orifice area (EROA) and accordingly 0.8 cm for mean VCW (4- and 2-chamber views) instead of 4-chamber–based VCW of 0.7 cm for severe MR for all etiologies including functional MR. Later in the year 2008, Little et al. (5) provided a thorough in vitro and in vivo validation of the accuracy of 3D VCA measurements against independent methods. In 2009, Yosefy et al. (6) further validated the superiority of 3D VCA measurements compared with 2D VCA measurements in both central and eccentric jets. In 2011, Zeng et al. (7) also examined the asymmetry of the VCA and proposed a cutoff value of 0.41 cm^2 for differentiation of moderate from severe MR that can be applied in all etiologies and orifice shapes. After all these investigations and a growing understanding and acceptance of the asymmetry of the 3D VCA, a new cutoff value that can be clinically applied is urgently needed. But why are the 2 cutoff values—the 0.6 cm^2 by Kahlert et al. (4) and the 0.41 cm^2 by Zeng et al. (7)—so different and which might be closer to the truth?

Kahlert et al. (4) derived their 3D cutoff value of 0.6 cm^2 by extrapolating symmetrical 2D EROAs to asymmetrical 3D VCAs, thus correcting the previous cutoff value for the underestimation by 2D methods, whereas Zeng et al. (7) derived their 3D VCA cutoff value of 0.41 cm^2 from conventional MR grading based on an integration of 2D methods, including 2D proximal isovelocity surface area, 2D VCW, and 2D jet area, which is important to understand why the 0.41 cm^2 value was so much closer to the previously proposed 2D cutoff values of 0.4 cm^2 for organic MR and 0.2 cm^2 for functional MR.

Understanding the 3D VCA means to acknowledge its asymmetry and to understand the limitations of 2D estimates of the VCA including VCW and EROA by PISA. As a consequence, further clinical studies are needed to define new cutoff values for 3D VCA based on independent parameters of MR severity and clinical progress.

Thomas Buck, MD,* Björn Plicht, MD, Philipp Kahlert, MD, Raimund Erbel, MD

*West German Heart Center Essen, Department of Cardiology, University Hospital Essen, University Duisburg-Essen, Hufelandstrasse 55, 45122 Essen, Germany. *E-mail: thomas.buck@uk-essen.de*

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