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Magnetic Resonance Diffusion Tensor Imaging Provides New Insights into the Microstructural Alterations in Dilated Cardiomyopathy

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Cardiac MR (CMR) diffusion tensor imaging (DTI) is a promising technique capable of probing the myocardial microstructure by assessing the myofiber orientation[1,2]. New technical developments in CMR DTI in recent years[3–8] have allowed the clinical application of this powerful imaging technique. CMR DTI has been used to study myocardial infarction[9,10] and hypertrophic cardiomyopathy[11,12] in patients, revealing their adverse effects on myocardial microstructure. The article in this issue of *Circulation: Cardiovascular Imaging*, by von Deuster et al[13] describes a new clinical application of CMR DTI.

In this single-center study, von Deuster et al[13] studied dilated cardiomyopathy (DCM) patients using CMR DTI and assessed the change in the myocardial fiber orientation by imaging at two separate time points in the cardiac cycle. DCM is a major cause of heart failure that causes ventricular chamber enlargement, wall thinning and systolic dysfunction. The authors hypothesized that a combination of CMR DTI, myocardial tagging, and biomechanical modeling will shed new insight into the alterations of myocardial microstructure and functional performance (strain) in DCM patients as compared to healthy controls. They measured helix angle transmurality (HAT), and found it was steeper in DCM patients when compared with age-matched controls. Conversely, it was impaired during cardiac contraction in DCM patients, compared to controls. Their developed biomechanical modelling could not explain the steeper HAT in DCM patients, but could support the impaired dynamic reorientation of fibers.

The current study displays the superb and important teamwork between clinicians and scientists that allows this cutting-edge imaging technology into clinical evaluation of cardiovascular diseases, like DCM. Their biomechanical modeling did not support the “steeper” helix angulation, but is a natural extension to collecting functional and

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Disclosures

None.

microstructural CMR data. In addition, the recruitment and scanning of DCM patients are a major accomplishment as many DCM patients having ICD, LVAD, and/or pacemakers.

Although we greatly appreciate the enormous technical challenges that were overcome in completing the study, the choice of CMR DTI technique raises concerns about its accuracy in DCM patients. For example, the dual phase STEAM diffusion CMR technique[14] requires breath-holds to achieve a clinically acceptable scan time since prospective navigator gating has low scan time efficiency[4]. Consequently, each patient underwent 22 breath-holds to achieve the necessary SNR to robustly map myocardial fiber orientations at a single short-axis slice. This is in comparison with the typical 16–20 breath-holds needed for full LV coverage CINE and LGE in a routine clinical CMR exam. Furthermore, the STEAM technique is susceptible to arrhythmia when scanning outside of systole because STEAM diffusion encoding is achieved over two heart beats.

Therefore, STEAM DTI require neighboring heartbeats to be encoded in the exact same position to avoid irreversible motion-induced signal loss. Alternative techniques to address patient comfort and arrhythmia would be motion compensated spin echo diffusion CMR techniques[3,5,7,8] that diffusion encode in a single heart beat allowing for free breathing and more robustness to arrhythmia. Future improvements to the STEAM DTI CMR technique are needed to reduce the burden to patients.

Another technical concern is the estimation of helix angle transmurality (HAT), defined as the slope of the transmural HA course, in DCM patients. DCM patients exhibit thinning of the left ventriclular wall[15,16] making it challenging for diffusion CMR to accurately quantify the HAT with the spatial resolution ($2.5 \times 2.5 \times 8$ mm^3) used in the study. The reported wall thickness for DCM patients used in the study was 9±1 mm and only the inner 80% of the wall was used to calculate the HAT yielding a total of 2–3 pixels at each radial spoke. Further studies are needed to validate if 2–3 pixels is sufficient to yield an accurate estimate of HAT.

A final, and perhaps the most vital consideration is their conclusion that there is a “steeper” diastolic helix angulation in DCM patients than in normal subjects. This finding is not only inconsistent with the biomechanical model used in the study (Fig. 7), but most importantly, it is inconsistent in studies of ex vivo human hearts[17,18], where there is a “flattening” of the helix angulation. Their own strain data support this, as the longitudinal strain is reduced. This diminution of shortening during torsion occurs because the fibers have a more horizontal orientation, as descried by Sallin[19]. We wonder how this fundamental difference between structure and function is resolved, since the steeper helical angulation would enhance, rather than diminish cardiac performance. We look forward to their further studies to provide clarification.

In summary, we commend the authors for adding to the ever growing clinical utility of diffusion CMR. Interfacing myocardial microstructure and its dynamics offers a new exciting perspective to our knowledge, and may extend far beyond studying DCM. Technically, CMR DTI will need to be further improved to reduce the burden of patients. The future holds great promise for using CMR DTI to accurately quantify helix angle

transmurality. A concert of experimental studies is needed in order for this potential to be explored and further validated. We believe that CMR DTI will become a powerful tool to facilitate our understanding of the relationship between myocardial structure and functional performance of the heart and potentially improve diagnosis and treatment of cardiovascular disease.

References

1. Mekkaoui C, Reese TG, Jackowski MP, Bhat H, Sosnovik DE. Diffusion MRI in the heart. NMR Biomed. 2015; doi: 10.1002/nbm.3426
2. Froeling M, Strijkers GJ, Nederveen AJ, Chamuleau SA, Luijten PR. Diffusion Tensor MRI of the Heart – In Vivo Imaging of Myocardial Fiber Architecture. Curr Cardiovasc Imaging Rep. 2014; 7:9276.
3. Nguyen C, Fan Z, Sharif B, He Y, Dharmakumar R, Berman DS, Li D. In vivo three-dimensional high resolution cardiac diffusion-weighted MRI: a motion compensated diffusion-prepared balanced steady-state free precession approach. Magn Reson Med. 2014; 72:1257–1267. [PubMed: 24259113]
4. Nielles-Vallespin S, Mekkaoui C, Gatehouse P, Reese TG, Keegan J, Ferreira PF, Collins S, Speier P, Feiweier T, de Silva R, Jackowski MP, Pennell DJ, Sosnovik DE, Firmin D. In vivo diffusion tensor MRI of the human heart: Reproducibility of breath-hold and navigator-based approaches. Magn Reson Med. 2012; 70:454–465. [PubMed: 23001828]
5. Stoeck CT, Deuster von C, Genet M, Atkinson D, Kozerke S. Second-order motion-compensated spin echo diffusion tensor imaging of the human heart. Magn Reson Med. 2016; 75:1669–76. [PubMed: 26033456]
6. Moulin K, Croisille P, Feiweier T, Delattre BMA, Wei H, Robert B, Beuf O, Viallon M. In vivo free-breathing DTI and IVIM of the whole human heart using a real-time slice-followed SE-EPI navigator-based sequence: A reproducibility study in healthy volunteers. Magn Reson Med. 2015; 76:70–82. [PubMed: 26301785]
7. Aliotta E, Wu HH, Ennis DB. Convex optimized diffusion encoding (CODE) gradient waveforms for minimum echo time and bulk motion-compensated diffusion-weighted MRI. Magn Reson Med. 2016; doi: 10.1002/mrm.26166
8. Nguyen C, Fan Z, Xie Y, Pang J, Speier P, Bi X, Kobashigawa J, Li D. In vivo diffusion-tensor MRI of the human heart on a 3 tesla clinical scanner: An optimized second order (M2) motion compensated diffusion-preparation approach. Magn Reson Med. 2016; doi: 10.1002/mrm.26380
9. Wu M-T, Tseng W-YI, Su M-YM, Liu C-P, Chiou K-R, Wedeen VJ, Reese TG, Yang C-F. Diffusion tensor magnetic resonance imaging mapping the fiber architecture remodeling in human myocardium after infarction: correlation with viability and wall motion. Circulation. 2006; 114:1036–1045. [PubMed: 16940196]
10. Wu MT, Su MYM, Huang YL, Chiou KR, Yang P, Pan HB, Reese TG, Wedeen VJ, Tseng WYI. Sequential Changes of Myocardial Microstructure in Patients Postmyocardial Infarction by Diffusion-Tensor Cardiac MR: Correlation With Left Ventricular Structure and Function. Circulation: Cardiovascular Imaging. 2009; 2:32–40. [PubMed: 19808562]
11. Nguyen C, Lu M, Fan Z, Bi X, Kellman P, Zhao S, Li D. Contrast-free detection of myocardial fibrosis in hypertrophic cardiomyopathy patients with diffusion-weighted cardiovascular magnetic resonance. Journal of Cardiovascular Magnetic Resonance. 2015; 17:107. [PubMed: 26631061]
12. Ferreira PF, Kilner PJ, McGill L-A, Nielles-Vallespin S, Scott AD, Ho SY, McCarthy KP, Haba MM, Ismail TF, Gatehouse PD, de Silva R, Lyon AR, Prasad SK, Firmin DN, Pennell DJ. In vivo cardiovascular magnetic resonance diffusion tensor imaging shows evidence of abnormal myocardial laminar orientations and mobility in hypertrophic cardiomyopathy. Journal of Cardiovascular Magnetic Resonance. 2014; 16:445.
13. Deuster von C, Sammut E, Asner L, Nordsletten D, Lamata P, Stoeck C, Kozerke S, Razavi R. Studying Dynamic Myofibre Aggregate Reorientation in Dilated Cardiomyopathy using in-vivo

Magnetic Resonance Diffusion Tensor Imaging. Circulation: Cardiovascular Imaging. 2016; 9:e005018. [PubMed: 27729361]

14. Stoeck CT, Kalinowska A, Deuster von C, Harmer J, Chan RW, Niemann M, Manka R, Atkinson D, Sosnovik DE, Mekkaoui C, Kozerke S. Dual-phase cardiac diffusion tensor imaging with strain correction. PLoS ONE. 2014; 9:e107159. [PubMed: 25191900]
15. Luk A, Ahn E, Soor GS, Butany J. Dilated cardiomyopathy: a review. J Clin Pathol. 2009; 62:219–225. [PubMed: 19017683]
16. Japp AG, Gulati A, Cook SA, Cowie MR, Prasad SK. The Diagnosis and Evaluation of Dilated Cardiomyopathy. Journal of the American College of Cardiology. 2016; 67:2996–3010. [PubMed: 27339497]
17. MacGowan GA, Shapiro EP, Azhari H, Siu CO, Hees PS, Hutchins GM, Weiss JL, Rademakers FE. Noninvasive measurement of shortening in the fiber and cross-fiber directions in the normal human left ventricle and in idiopathic dilated cardiomyopathy. Circulation. 1997; 96:535–541. [PubMed: 9244222]
18. Buckberg GD, Coghlan HC, Torrent-Guasp F. The structure and function of the helical heart and its buttress wrapping. V. Anatomic and physiologic considerations in the healthy and failing heart. Seminars in Thoracic and Cardiovascular Surgery. 2001; 13:358–385. [PubMed: 11807734]
19. Sallin EA. Fiber orientation and ejection fraction in the human left ventricle. Biophysical Journal. 1969; 9:954–964. [PubMed: 5791550]