


## Motion-Induced Signal Loss in In Vivo Cardiac Diffusion-Weighted Imaging

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To the Editor:

In vivo cardiac diffusion-weighted imaging (DWI) has experienced a renaissance over the past several years. A key to its revival has been advances in magnetic resonance imaging (MRI) hardware technology and pulse sequences, including the continuous development of cardiac motion compensation strategies. Although none of these methods are currently available as commercial products, exciting pilot clinical studies hint that this method may become a new cardiovascular magnetic resonance (CMR) clinical tool in the near future.

The choice of imaging sequence and imaging parameters inevitably affects the measured diffusion indices.<sup>1–3</sup> However, the self-diffusivity of free water ( $2.92 \times 10^{-3} \text{ mm}^2/\text{s}$  at  $35^\circ\text{C}$ ),<sup>4</sup> which is independent of the measurement sequence, provides a temperature-dependent physical upper limit for in vivo water diffusion. In soft tissues, microstructural diffusive barriers result in a reduced measured diffusivity. By using monopolar/motion-compensated gradient waveforms, measured diffusivities as low as  $0.94\text{--}1.52 \times 10^{-3} \text{ mm}^2/\text{s}$  /  $1.26\text{--}1.66 \times 10^{-3} \text{ mm}^2/\text{s}$  have been reported in blood at  $37^\circ\text{C}$ .<sup>5</sup>

In the 2013 article by Laissy et al,<sup>6</sup> 2017 article by Mou et al,<sup>7</sup> the 2018 article by Xiang et al,<sup>8</sup> and the 2018 ISMRM conference proceeding by Lan et al,<sup>9</sup> diffusivities of  $6.32\text{--}8.95 \times 10^{-3} \text{ mm}^2/\text{s}$ ,  $3.04\text{--}3.38 \times 10^{-3} \text{ mm}^2/\text{s}$ ,  $1.7\text{--}3.5 \times 10^{-3} \text{ mm}^2/\text{s}$  and  $3.77\text{--}3.84 \times 10^{-3} \text{ mm}^2/\text{s}$ , respectively, have been reported for myocardium, which clearly exceed the upper limit defined by free water diffusion, and hence cannot be interpreted as measures of self-diffusion in cardiac tissue. We note that none of these studies report using any method to compensate for bulk motion and strain of the myocardium during diffusion encoding. Conventional DWI with spin-echo echo planar imaging (EPI) (even with ECG-gating) is artifact-prone and known to be ineffective in addressing the types and ranges of motion encountered in the in vivo heart, resulting in dephasing of the spins and apparent signal attenuation.

Mou et al<sup>7</sup> realized the large discrepancy with previously reported values and speculated that the excessively high diffusivities are related to the absence of parallel imaging, differences between SE and STEAM imaging, field strength, and even differences in ethnicity. While all these attributes may have an effect on the measurement results, the authors failed to identify the more obvious contribution of motion-induced signal attenuation, despite the hint in the study results: Mou et al<sup>7</sup> provide a clear correlation of their success rate of diastolic imaging to the subject's heart rate (the higher the heart rate the shorter the diastolic quiescent period and hence the lower the success rate). Furthermore, the authors report that at b-values above  $300 \text{ s/mm}^2$  "remarkable signal loss of the myocardium or even an

absent myocardium" was found. A b-value of  $300 \text{ s/mm}^2$  is not considered excessively high and other studies have used larger b-values without suffering from signal loss (eg, Scott et al<sup>10</sup>:  $b_{\text{max}} = 750 \text{ s/mm}^2$  for STEAM or von Deuster et al<sup>1</sup>:  $b_{\text{max}} = 450 \text{ s/mm}^2$  for SE).

Diffusion metrics such as the apparent diffusion coefficient and the mean diffusivity have the potential to become clinically relevant biomarkers and methodological improvements continue to develop. The Society for Cardiovascular Magnetic Resonance Cardiac Diffusion Special Interest Group (<https://scmr.org/members/group.aspx?code=Diffusion>) is a potential resource for investigators interested in this topic. As the field advances, it is imperative and our collective responsibility to limit methodological inaccuracies, to correctly ascribe MRI signal changes to the correct underlying mechanism, and to mitigate misleading interpretations.

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**Level of Evidence: 5**

**Technical Efficacy Stage: 2**