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In Vivo Cardiac Diffusion imaging without motion-compensation leads to unreasonably high diffusivity

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LIST OF ABBREVIATIONS:

Diffusion-weighted imaging - DWI
Apparent diffusion coefficient – ADC
Mean diffusivity – MD
Diffusion tensor imaging - (DTI)
Intra-voxel incoherent motion (IVIM)

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In tissue, water molecules move due to large physiological bulk motion, perfusion, or diffusion effects. Diffusion-weighted imaging (DWI) is a technique that aims to use motion-encoding gradient waveforms to sensitize the MR signal to the diffusion of water molecules. The diffusivity of water molecules is temperature driven and restricted and/or hindered by the tissue microstructure. At a normal body temperature of 37°C in a non-restricted environment, the diffusion coefficient of water is about $2.9 \times 10^{-3} \text{mm}^2/\text{s}$, which is thus the physical upper limit of the observable diffusion coefficients in tissue[1]. Across diffusion models, several parameters may represent the diffusivity of water molecules in the extra- and intra-cellular tissue compartments, including the apparent diffusion coefficient (*ADC*), the mean diffusivity (*MD*) for the diffusion tensor imaging (DTI) model, or *D* (also called *D_{slow}*) for the Intra-voxel incoherent motion (IVIM) model; all are subject to the theoretical limit of $2.9 \times 10^{-3} \text{mm}^2/\text{s}$.

The principal challenge of performing DWI accurately in the heart is to separate the motion of water molecules due to diffusion from that resulting from cardiac deformation. Traditional diffusion-encoding waveforms used in stationary tissues, such as the brain, are sensitive to cardiac motion and may lead to unwanted DWI signal attenuation and hence calculated diffusivities artifactually high (even $>2.9 \times 10^{-3} \text{mm}^2/\text{s}$). Recently, advanced diffusion encoding strategies have been proposed, such as the STEAM approach[2] or motion-compensated diffusion encoding gradient waveforms [3], which reduce the impact of cardiac deformation. These motion compensation strategies have largely contributed to the development of cardiac DWI. As of today, more than 50 cardiac DWI studies using ADC, IVIM, or DTI models on healthy and pathologic cases have been published. As shown in Figure 1, none of the studies employing motion-compensation strategies have ever reported a diffusivity parameter above the theoretical limit.

However, the implementation of IVIM in the heart remains particularly challenging. Spinner et al.[4] have demonstrated that motion-compensated waveforms may alter the perfusion sensitivity of cardiac DWI used in the IVIM model. For this reason, STEAM sequences or retrospective motion compensation strategies may be preferred for IVIM. Nonetheless, it is evident that cardiac IVIM acquired without motion compensation strategies will result in corrupted images and erroneous results.

We, therefore, note with some concern that several recent cardiac DWI studies using the IVIM model have reported diffusivities clearly above $2.9 \times 10^{-3} \text{mm}^2/\text{s}$: three research articles published in *JMRI*: Laissy et al. 2013[5] ($ADC=6-9.2 \times 10^{-3} \text{mm}^2/\text{s}$), Mou et al. 2017[6] ($D_{slow}=3.04-3.37 \times 10^{-3} \text{mm}^2/\text{s}$), Xiang et al. 2022[7] ($D=4.30-4.75 \times 10^{-3} \text{mm}^2/\text{s}$); one observational study published in *Medicine*: Xiang et al. 2018[8] ($D=1.7-3.5 \times 10^{-3} \text{mm}^2/\text{s}$); one case report published in *Frontiers in Cardiovascular Medicine*: Li et al. 2022[9] ($D_{slow}=2.25-3.5 \times 10^{-3} \text{mm}^2/\text{s}$); and one ISMRM conference proceeding by Lan et al. 2018[10] ($D_{slow}=3.77-3.84 \times 10^{-3} \text{mm}^2/\text{s}$). Some of these studies have been already the subject of a previous letter attributing these high diffusivities to cardiac motion[1]. It is worth noting that none of these studies used motion-compensation strategies. In addition, the cardiac DWI images shown in these studies all display remarkable signal loss in the myocardium, or even an absent myocardium[5–10]. To the best of our knowledge, these high diffusivity values can only be attributed to motion-corrupted DWI signals and shouldn't be considered a reliable report of cardiac diffusivity and thus not an accurate reflection of underlying tissue microstructure.

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