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Low b-Value Diffusion-Weighted Cardiac Magnetic Resonance Imaging:

Initial Results in Humans Using an Optimal Time-Window Imaging Approach

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Abstract

Objectives—Diffusion-weighted imaging (DWI) using low b-values permits imaging of intravoxel incoherent motion in tissues. However, low b-value DWI of the human heart has been considered too challenging because of additional signal loss due to physiological motion, which reduces both signal intensity and the signal-to-noise ratio (SNR). We address these signal loss concerns by analyzing cardiac motion during a heartbeat to determine the time-window during which cardiac bulk motion is minimal. Using this information to optimize the acquisition of DWI data and combining it with a dedicated image processing approach has enabled us to develop a novel low b-value diffusion-weighted cardiac magnetic resonance imaging approach, which significantly reduces intravoxel incoherent motion measurement bias introduced by motion.

Materials and Methods—Simulations from displacement encoded motion data sets permitted the delineation of an optimal time-window with minimal cardiac motion. A number of single-shot repetitions of low b-value DWI cardiac magnetic resonance imaging data were acquired during this time-window under free-breathing conditions with bulk physiological motion corrected for by using nonrigid registration. Principal component analysis (PCA) was performed on the registered images to improve the SNR, and temporal maximum intensity projection (TMIP) was applied to recover signal intensity from time-fluctuant motion-induced signal loss. This PCATMIP method was validated with experimental data, and its benefits were evaluated in volunteers before being applied to patients.

Results—Optimal time-window cardiac DWI in combination with PCATMIP postprocessing yielded significant benefits for signal recovery, contrast-to-noise ratio, and SNR in the presence of bulk motion for both numerical simulations and human volunteer studies. Analysis of mean apparent diffusion coefficient (ADC) maps showed homogeneous values among volunteers and good reproducibility between free-breathing and breath-hold acquisitions. The PCATMIP DWI approach also indicated its potential utility by detecting ADC variations in acute myocardial infarction patients.

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We chose to shift the PCA computation details into an appendix attached as to avoid burdening the leading thread and allow the interested reader to understand the mathematical details as well as to enable the reproduction of the method. The document is in Word format with a corresponding figure named figure A.

Conclusions—Studying cardiac motion may provide an appropriate strategy for minimizing the impact of bulk motion on cardiac DWI. Applying PCATMIP image processing improves low b-value DWI and enables reliable analysis of ADC in the myocardium. The use of a limited number of repetitions in a free-breathing mode also enables easier application in clinical conditions.

Keywords

diffusion-weighted cardiac MRI (DWI); motion sensitivity; PCA; temporal MIP; CMR; IVIM

MR diffusion-weighted imaging (DWI) using low b-values ($<300 \text{ s/mm}^2$) permits imaging of intravoxel incoherent motion (IVIM), which combines diffusion of water molecules and microcirculation in capillaries.¹ Low b-value DWI was performed in a previous cardiac study to demonstrate the capability of DWI to reveal microcirculation velocity, anisotropy, and volume² when bulk motion can be fully controlled.

Diffusion imaging is widely used in routine brain imaging because of its ability to highlight ischemic regions during the early hours of an ischemic event³ when brain tissue might still be salvageable and long before conventional magnetic resonance imaging (MRI) becomes abnormal.^{4–6} However, because DWI phase-sensitive contrast is highly sensitive to physiological motion,^{7,8} its application to in vivo cardiac studies is problematic.^{9–11} The inherent challenge of DW-cardiac MRI is to robustly differentiate the capillary microflow within a beating organ from the combination of respiratory and cardiac motion, which are both several orders of magnitude larger than in the (almost) stationary brain. On the flip side of this tremendous challenge is the potentially broad scope of clinical utility: from the characterization of ischemic injury¹² to understand the myocardial remodeling process.¹¹

Besides revealing the state of the parenchyma and changes induced by pathology or treatment, IVIM may also provide macroscopic information about the muscle, including architectural structure and potential alterations. The use of IVIM for assessing the microcirculation is of significant interest due to its key role in the healing myocardium and postischemic remodeling.¹³ To access IVIM changes in patients by using a reproducible protocol would help to clarify the healing processes after myocardial ischemia and the underlying relationship between cardiac dysfunction and structure.

The purpose of this work was to propose and evaluate an innovative approach combining a specific acquisition method with a dedicated image postprocessing technique for improving the reliability of IVIM estimation using low b-value apparent diffusion coefficient (ADC) values for in vivo cardiac DWI.

MATERIALS AND METHODS

Determining an Optimal Time-Window for DWI Acquisition

Cardiac MR techniques sensitive to phase variations^{14,15} are usually affected by cardiac longitudinal motion, which leads to additional signal loss and distortion. To analyze the impact of cardiac motion on diffusion-weighted signal loss, a numerical simulation of signal loss¹⁵ was performed using in vivo cardiac longitudinal motion measured with motion tracking MRI (displacement-encoding using stimulated echoes [DENSE])¹⁶ using 30 milliseconds time resolution. The initial condition for the simulation was homogeneous (ADC, $D = 5 \times 10^{-3} \text{ mm}^2/\text{s}$), low b-value (50 and 100 s/mm^2) DW images acquired from an eddy-currents compensated, twice-refocused, spin-echo echo-planar imaging (EPI) sequence.¹⁴ DENSE data from a human volunteer were used as cardiac motion input for the simulation of signal loss from slice contraction and intravoxel phase dispersion due to displacement along the diffusion encoding direction.¹⁵ The optimal time-window for

triggering further DWI acquisitions was defined as the longest duration over which the maximal intensity maintained stability (within the 10th upper percentile). DWI acquisitions corresponding to simulation were performed on the same volunteer to confirm this optimal time window.

Volunteer and Patient Enrollment

The study enrolled 7 volunteers (2 females and 5 males, ages 25–44, heart rate [HR] 61–85 bpm) and 7 patients (3 females and 4 males, ages 21–56, HR 57–85 bpm) admitted for acute ST-elevation myocardial infarction (AMI), with total occlusion of a coronary artery. Percutaneous coronary intervention was performed to obtain a final thrombolysis in myocardial infarction (TIMI)-3 flow in the culprit artery territory. Cardiac MR imaging was performed 2 to 4 days postreperfusion. All subjects gave informed consent to the institutional review board-approved study protocol.

Acquisition Strategy and MRI Protocol

Our strategy for coping with intensity fluctuations arising due to motion was to acquire multiple DWI images for a given slice position with incremental trigger delays. Trigger increments were defined as 10 milliseconds so that multiple repetitions fit within the time-windows of minimal motion as calculated from the cine data acquired. This strategy of sliding temporal window acquisitions covering the entire optimal time-window was intended to capture the moment when motion-induced signal loss was at a minimum, ie, when the attenuation caused by motion was minimized.

Experiments were conducted using a 1.5-T clinical scanner (MAGNETOM Avanto, Siemens, Erlangen, Germany) with a maximum gradient strength of 40 mT/m and a maximum slew rate of 200 mT/m/s. DWI was performed with a single-shot, twice-refocused spin-echo EPI sequence available on the clinical scanner.¹⁴ Because DWI usually requires a minimum of 4 images (1 image for $b = 0$ and 3 for the 3 orthogonal diffusion-encoding directions for each nonzero b -value) with a repetition time of at least 2 to 3 seconds, and signal-to-noise ratio (SNR) demand impose a minimum of 10 repetitions, the scan duration is not conducive to breath-hold scanning. Hence, all scans were performed under free-breathing (FB) conditions. The following acquisition parameters were used: imaging matrix of 160×128 with isotropic in-plane resolution of $2.6 \times 2.6 \text{ mm}^2$ and slice thickness of 6 mm, echo-train duration of 70 milliseconds, parallel imaging acceleration with a rate of 2 using Generalized autocalibrating partially parallel acquisitions,¹⁷ echo time (TE) of 51 milliseconds, diffusion-weighting b -values of 0, 50 and 100 s/mm^2 and 3 orthogonal diffusion encoding directions for each nonzero b -value. Acquisitions were electrocardiograph-triggered at every 2 or 3 heart beats depending on the subject's HR to ensure that repetition time (TR) ≥ 2 seconds. The trigger was set within the optimal diastolic time-window defined by an initial observation of targeted slice relaxation in CINE-MR images. An initial dummy scan was used to reach a steady state. Two midventricular slices were acquired in each volunteer.

Additionally, for contrast investigation in the infarct area in post-AMI patients, edema-enhanced T_2 -weighted images were acquired with a short inversion time (TI) inversion-recovery turbo-spin-echo dark blood sequence with TE = 47 milliseconds, TR equal to 2 heartbeats (~ 2 seconds), TI = 170 milliseconds, a resolution of $1.5 \times 1.5 \times 8 \text{ mm}^3$, and a matrix of 256×208 . Subsequent to T2W and DWI image acquisition, early- and delayed hyperenhanced (DHE) images were acquired at 3 and 10 minutes after injection of 0.2 mmol/kg gadolinium (DOTAREM, Guerbet, France) using an inversion-recovery spoiled gradient-echo 3D segmented sequence with TE = 1.36 milliseconds, TR = 4.17 milliseconds, TI = 400 milliseconds, parallel imaging acceleration with a rate of 2 using Generalized

autocalibrating partially parallel acquisitions,¹⁷ 5 mm slices, a field of view of 300×400 mm² and an acquisition matrix of 256×142 pixels.

Image Processing Workflow

Data sets for each diffusion-weighting ($b = 0, 50$ and 100 s/mm²) and diffusion-encoding orthogonal direction (x, y, z) contained 10 images acquired at equally spaced time points (ie, 10 milliseconds shifted in our volunteers) within the optimal diastolic window. Because all of the images were acquired under FB conditions, the images were first registered with a nonrigid registration algorithm.^{18,19} At each pixel location, we identified 1 of the 10 repetitions providing the highest intensity value. By assigning the highest intensity to that pixel in a reconstructed DW image and repeating this procedure for every pixel, the resulting image was a DW image with minimal signal loss due to motion. This process is called temporal maximum intensity projection (TMIP), where the repetitions represent the “time” axis. However, a major drawback of the TMIP process is that the SNR level of the reconstructed image remains the same as that for a single repetition, and so the image quality does not benefit from multiple repetitions.

To obtain the SNR potential of multiple acquisitions, we performed a block-wise spatiotemporal filtering prior to TMIP. This filtering²⁰ (mentioned in the Appendix, online only, available at: <http://links.lww.com/RLI/A47>) was based on a principal component analysis (PCA)²¹ of the 10 repetitions. PCA was applied on a 15×15 pixels boxcar sliding over each diffusion-weighted image. A pixel-wise TMIP operation was subsequently performed on these filtered images for each diffusion-weighting and gradient direction:

$$I_{PCATMIP}(x, y) = (\text{MIP along repetition } i) [I_{PCA}(i, x, y)] \quad (1)$$

These PCATMIP images sets were then used to calculate the ADC in the 3 orthogonal directions by linear regression of the $\log(I_{PCATMIP})$ versus b plots. The mean ADC was defined as the mean value over the 3 directions:

$$ADC_m = (ADC_{xx} + ADC_{yy} + ADC_{zz}) / 3 \quad (2)$$

Comparison Between Images Averaging, TMIP, and PCATMIP

Signal intensity (SI) and image quality (SNR) benefits of TMIP and PCATMIP processing for data acquired in the presence of motion were evaluated against pixel-wise averaging (AVG) in a numerical simulation. Low b -value DW images were simulated for a homogeneous $D = 5 \times 10^{-3}$ mm²/s slice with and without motion-related signal loss using 3D displacement fields obtained from a DENSE¹⁶ acquisition on a healthy volunteer. Displacement fields were acquired during the optimal diastolic time-window. Rician noise was then added to the motion-induced data sets to obtain a noise-level equivalent to experimental observations. Eventually, the AVG, TMIP, and PCATMIP methods were applied to simulated data sets and compared with the initial data (ie, data without Rician noise) on their DW SI images, SNR, contrast-to-noise ratio (CNR), and ADC estimation.

At each b -value, the DW image SNR was evaluated as follows:

$$SNR = \frac{\langle I \rangle_{LV}}{Noise} \quad (3)$$

where “ $\langle I \rangle_{LV}$ ” denotes the “mean” over the left ventricular wall and “Noise” was measured by the standard deviation (SD) of pixel intensities in a signal-void region of the DW image. Phase-array coils correction²² was applied to the SNR values.

Image CNR was evaluated as:

$$CNR = \frac{\langle I \rangle_{LV} - \langle I \rangle_{blood}}{Noise} \quad (4)$$

where $\langle I \rangle_{blood}$ denotes the mean intensity measured in the blood pool.

Mean ADC values ($\langle ADC_m \rangle$) for the myocardium were computed using Eq. (2) and compared for each method.

For quantitative analysis, the diffusion trace-weighted image (T-DWI) for a diffusion weighting b was defined as the geometrical mean of the DW intensity over the 3 orthogonal directions:

$$T - DWI(b) = \sqrt[3]{DWI_{b,XX} \cdot DWI_{b,YY} \cdot DWI_{b,ZZ}} \quad (5)$$

Repeatability of ADC_m Measurements

To assess the repeatability of mean ADC measurements, the same slice scan was repeated 5 times (with 10 repetitions each scan).

To assess the effects of breathing motion, in 1 volunteer, we acquired 2 separate FB scans and a breath-hold (BH) scan for the same slice prescription (10 time-shifted repetitions each scan).

To assess the effect of cardiac motion on the slice position definition, we repeated the same scan for 3 short axis slices (apical, midventricular, and basal views) and 2 long-axis slices (2- and 4-chamber views) in 1 volunteer.

For each study, the endo- and epicardial borders of the left ventricular (LV) wall were manually drawn, and the regional assessment of the LV wall was performed by segmenting it into several sectors following the American Heart Association standards.²³

DWI Measurements in AMI Patients

In post-AMI patients, trace-DWI (T-DWI) and ADC_m maps were obtained for each processing method in a mid-LV short-axis slice that was located within the ischemia-reperfusion injury zone. Using T₂-weighted and postgadolinium-enhanced images, following 3 regions were defined for each patient: infarct, microvascular obstruction (MVO), and remote regions. The mean values were retrieved in manually drawn regions of interest in each compartment.

Statistical Analysis

DW-image SI, SNR, and CNR differences among image-processing methods and b-values were compared using 2-way repeated analysis of variance (ANOVA) with Greenhouse-Geisser sphericity correction when required and post hoc Scheffé procedure.

ADC_m values obtained with the different methods (AVG, TMIP, PCATMIP) in volunteers, those obtained with, and without BH as well as mean ADC values measured in regions

(infarct, MVO, and remote) on PCATMIP maps in AMI patients were assessed for differences using an 1-factor repeated measures ANOVA.

All statistical analysis was performed using Stata 11 (College Station, TX) statistical software. A $P < 0.05$ was considered as statistically significant.

RESULTS

Optimal Time-Window Considering the Influence of Motion on DWI Intensity

Figure 1 shows the SI as a function of cardiac phase for $b = 100 \text{ s/mm}^2$. Simulated motion-induced signal loss tends to be minimal in several short duration time-windows in end- and middiastole and in a longer time-window of about 80 milliseconds in end-diastole. Experimental DWI data from the volunteer tend to confirm the existence of the shorter systolic window and the longer window in end-diastole (Fig. 1, gray). It showed that the decrease in motion-related intensity was only absent in the optimal diastolic window and a window of less than 50 milliseconds during endsystole.

Theoretical Comparison Between Images AVG, TMIP, and PCATMIP Effectiveness for Processing Cardiac DWI Data

Results from the processing of simulated cardiac DW images (with cardiac motion measured from a DENSE acquisition) showed that TMIP and PCATMIP processing can reduce the impact of cardiac motion (Fig. 2, top). Figure 2 reveals a heterogeneous pattern of signal loss due to motion throughout the myocardium because motion and torsion are indeed spatially and temporally inhomogeneously distributed.²⁴ This finding yielded an inhomogeneous ADC_m map when adequate postprocessing was not performed. TMIP offered a reduction of motion-induced signal loss and minimized the ADC estimation error ($0.1 \times 10^{-3} \text{ mm}^2/\text{s}$) as well as PCATMIP ($0.3 \times 10^{-3} \text{ mm}^2/\text{s}$) compared with AVG ($1.1 \times 10^{-3} \text{ mm}^2/\text{s}$). Homogeneity of ADC maps was also recovered ($SD = 2\%$ for TMIP and 6% for PCATMIP), which is critical for accurately separating compartments with pathology-related modified diffusion. PCATMIP also yields DWI images with improved SNR (21.7 compared with 10.2 for TMIP) and improved CNR (27.9 compared with 14.5 for TMIP) (Fig. 2). PCATMIP processing of low b -value DWI significantly reduced captured myocardium motion and retrieves initial ADC information with a limited quantitative bias (6%).

In Vivo Comparison Between Images AVG, TMIP, and PCATMIP in Volunteers

The top section of Figure 3 shows a volunteer's trace-DW images from raw images of 10 repetitions for $b = 100 \text{ s/mm}^2$ in the mid-LV short axis slice. These were acquired in the diastolic time-window during FB. The intensity fluctuation was clearly visible with SI changes related to residual motion and illustrates the previously observed sensitivity of the DW images to physiological motion.

The bottom section of Figure 3 summarizes the results of 3 postprocessing techniques applied to this data set. Direct AVG of the 10 images reduced noise but resulted in signal loss due to motion; TMIP was able to minimize the intensity drop but resulted in a high level of speckle-like noise; PCATMIP resulted in low image noise similar to AVG and like TMIP, a reduction in signal loss. In this example, the PCATMIP method was clearly the best option.

Figure 4A summarizes the increase in SI attributed to a reduction of motion-induced signal loss by the TMIP and PCATMIP methods when compared with simple AVG. The TMIP procedure significantly increased myocardial intensity compared with AVG: $51\% \pm 38\%$ and $72\% \pm 48\%$ for $b = 50$ and 100 s/mm^2 , respectively ($P < 0.001$). The PCATMIP

procedure also yielded $24\% \pm 30\%$ and $35\% \pm 31\%$ increase at $b = 50$ and 100 s/mm^2 , respectively ($P < 0.001$). Benefits for both the approaches appeared to increase for higher b -values ($P < 0.001$). Although TMIP gave systematically higher signal intensities than PCATMIP, this method was associated with a high level of noise as shown in Figures 4B and C. Figure 4B summarizes the SNR in TMIP and PCATMIP relative to AVG. For nonzero diffusion weighting, TMIP resulted in significantly lower SNRs of $-31\% \pm 17\%$ and $-26\% \pm 21\%$ for $b = 50$ and 100 s/mm^2 , respectively ($P < 0.001$). In contrast, PCATMIP yielded $7\% \pm 20\%$ and $11\% \pm 20\%$ increases in SNRs for $b = 50$ and 100 s/mm^2 , respectively ($P = 0.005$ and 0.003). Figure 5C shows that TMIP decreased CNRs ($-82\% \pm 16\%$, $-28\% \pm 15\%$, and $-27\% \pm 26\%$ for $b = 0, 50$, and 100 s/mm^2 with $P < 0.001$, $P < 0.001$, and $P = 0.008$, respectively) relative to AVG, while PCATMIP achieved CNRs similar to AVG ($-13\% \pm 12\%$, $-6\% \pm 24\%$, and $+11\% \pm 45\%$ for $b = 0, 50$, and 100 s/mm^2 with $P = 0.005, 0.7$, and 0.9 , respectively).

Figure 5 shows the mean ADC values $\langle ADC_m \rangle$ obtained using the 3 methods and illustrates the impact of minimizing motion-related signal loss. With AVG, the signal loss increased with diffusion weighting and resulted in artificially elevated ADC_m values due to motion. Both TMIP and PCATMIP yielded systematic lower mean ADC values than AVG (17% and 7%, respectively) in myocardium. The TMIP values were approximately 13.7% lower than the PCATMIP values ($P = 0.047$). The in vivo results for each method were very similar to simulation results (Fig. 3) and confirmed the potential of PCATMIP to reduce motion-induced DWI signal loss in situ.

Reproducibility of Mean Diffusivity Measurements and the Effect of Breathing

The SD of the mean ADC across 5 repetitions of the same scan when processed with PCATMIP ranges as $1.2 \pm 0.6 \times 10^{-3} \text{ mm}^2/\text{s}$ ($16\% \pm 8\%$ of mean ADC values across repetitions), whereas the AVG of each scan yields an SD range of $2.1 \pm 1.0 \times 10^{-3} \text{ mm}^2/\text{s}$ (Fig. 6A).

The myocardial mean ADC values from 2 FB examinations and 1 BH examination were very stable (Fig. 6B: $\langle ADC_m(\text{FB1}) \rangle 7.4$, $\langle ADC_m(\text{FB2}) \rangle 6.5$, and $\langle ADC_m(\text{BH}) \rangle 7.1 \times 10^{-3} \text{ mm}^2/\text{s}$). These were acquired from a single volunteer at about the same slice position and were both processed using the PCATMIP procedure. Single-factor repeated measures ANOVA showed that there was no significant difference between the results of the 2 FB scans and the BH scan ($P = 0.36$).

Segmentation results (Fig. 6C) of the 3 short-axis slices (apical, midventricular, and basal) and 2 long-axis slices (4-chamber and 2-chamber) acquired in the same volunteer showed no significant ($P = 0.9$) impact of slice position on ADC estimation, although mean ADC increased closer to the apex ($\langle ADC_m \rangle 9.9 \times 10^{-3} \text{ mm}^2/\text{s}$) than to the base ($\langle ADC_m \rangle 9.2 \times 10^{-3} \text{ mm}^2/\text{s}$).

DWI Measurements in AMI Patients

Figure 7 shows DWI (T-DWI and ADC_m maps), T2w, and DHE images from a mid-LV slice in one of the patients. PCATMIP makes the anatomic delineation of the myocardium features relatively easy as it provided high intensity compared with AVG and reduced noise compared with TMIP. A hyperintense area can be clearly delineated in the PCATMIP-processed Trace-DWI (Fig. 7, top right), which matched the location of the injured myocardium (T2w and DHE).

The mean ADC maps concurred with the T-DWI observations. While AVG led to an overestimation of ADC_m values, the TMIP ADC_m map suffered from artifacts due to the high noise level. PCATMIP yields the ADC_m map with a better contrast and lower noise

level. Among all scanned patients, the PCATMIP ADC map revealed significantly lower ADC values in the culprit artery territory ($6.9 \pm 1.7 \times 10^{-3} \text{ mm}^2/\text{s}$, $P < 0.001$) and even lower ADC values in the MVO area ($4.5 \pm 1.7 \times 10^{-3} \text{ mm}^2/\text{s}$) than in the remote regions ($8.3 \pm 0.6 \times 10^{-3} \text{ mm}^2/\text{s}$, $P < 0.001$). Low ADC value regions were consistent with the location and extent of the hyper SI within the myocardium in the early-hyperenhanced and DHE images. The MVO location observed in early DHE demonstrated with the lowest mean ADC values ($< 6 \times 10^{-3} \text{ mm}^2/\text{s}$).

DISCUSSION

In this work, we developed an optimal time window-based acquisition strategy in combination with dedicated image processing for applying low-b-value DWI to cardiac MRI. While a variety of approaches^{9,10} have been proposed for studying cardiac diffusion, these have used dedicated MRI sequences to compensate for physiological motion. However, our approach differs because it uses DW-MRI sequences available on the clinical scanners and acquires data over multiple repetitions during an optimal time-window in the cardiac cycle. This optimal time-window is determined by performing numerical simulation on a longitudinal motion cardiac dataset. Due to the durability of the motion-reduced phase, the time-window in diastole is preferred over that in systole for the DWI acquisition. Remaining motion-induced signal loss can be compensated for by processing multiple time-shifted repetitions with a pixel-wise TMIP.

The basic concept of TMIP also accounts for additional asynchronous contractile motion as the minimum signal loss can occur at different times in the cardiac cycle for different cardiac segments. However, because TMIP assigns the pixel values of individual repetitions to the final result, noise spikes can easily be highlighted and may lead to an overestimation of the image intensity and high noise levels. To minimize sensitivity to noise, our approach uses PCA of local temporal modes to minimize random noise from the physiological fluctuations before performing the TMIP procedure. The potential of PCATMIP is demonstrated by the fact that it reduces the effect of physiological motion (subsequent to registration of bulk motion) to a level where the impact of myocardium infarction on ADC estimation is higher than that of bulk motion (Fig. 7). The results of cardiac DWI of patients are promising and reveal very small intersubject SDs.

The mean ADC values obtained in volunteers revealed the difference between IVIM effects at low b-values from molecular diffusion at high b-values, but the approach could evolve to the full IVIM model²⁵ with higher b-values. Our results concurred with an earlier study in canine hearts,² which showed that ADC measurements at low b-value may not correspond with high b-value ex vivo ADCs ($ADC_m < 10^{-3} \text{ mm}^2/\text{s}$) because microcirculation dominates in capillaries and gave much higher ADCs values. However, the same study proved that structural information from low b-value IVIM imaging in the heart matched the spatial information provided by ex vivo DWI. Molecular diffusion and coronary microperfusion are difficult to differentiate with low b-value DWI contrary to approaches used in brain imaging.^{3,5,6} Unfortunately, there exists no gold standard for evaluating the information obtained through DWI in the heart in vivo. For all of these reasons, cardiac low b-value IVIM imaging holds as much interest in the diagnosis of cardiac diseases as pure DWI does for brain lesions. Accessing the velocity of micro flows or their direction might help in understanding pathophysiological processes.

Recent data²⁶ obtained with state-of-the-art commercial pulse sequences in humans have demonstrated that DW EPI sequences, when feasible in patients, might be sensitive to increased water content. Therefore, these sequences would be alternative to standard short TI inversion-recovery T2-weighted sequences for detecting high signal regions of the

myocardium in patients with recent myocardial infarctions. Our experience was that the reproducibility with these sequences was poor in patients, which limited the capability of low b-value DWI characterization. In addition, postischemic irreversible (necrotic) or reversible (stunned myocardium) regional dysfunction in the culprit artery vascular bed intrinsically biases DWI by reducing signal loss from motion that may in turn be inappropriately interpreted as regions showing reduced ADC. By utilizing a state-of-the-art clinical DWI sequence over an optimized time-window in diastole and combining it with a novel image processing strategy, we have developed an approach for minimizing the bias introduced by physiological motion or regional dysfunction on DWI in the human heart.

Limitations

A single-shot double-refocused DWI sequence was used in this study to minimize the eddy-current effects. However, this limited the maximum diffusion-weighting b parameter for cardiac DWI to low values ($<150 \text{ s/mm}^2$). On the other hand, our choice of restricting b-values to a maximum of 100 s/mm^2 can be justified from the need to propose a method to image cardiac diffusion that is robust and can be reproduced even in the presence of large physiological motion, such as for severely ill patients.

Note that the proposed optimized time-window acquisition in combination with PCATMIP processing was not restricted to the DWI sequence used and can be implemented with any sequence kernel. Also, while dedicated MRI sequences, such as those using non-Cartesian acquisitions, might be explored to enable acquisitions at higher b-values, these could increase the sensitivity of the acquisition to other MRI parameters, such as magnetic field inhomogeneities.

Due to the limitation of the parallel imaging reconstruction software on the scanner, only the absolute image intensity was available without any phase information. This led to relatively high noise sensitivity. In comparison, additional simulations have shown that with magnitude and phase data of the same noise level, the optimal threshold Et (mentioned in the Appendix, online only, available at: <http://links.lww.com/RLI/A47>) would be 10 times lower.²⁰ This finding indicates that PCATMIP can tolerate higher noise levels with complex data and obtain better SNR in the processed results given the same input SNR.

CONCLUSION

Physiological motion introduces a bias in cardiac DWI, which can be reduced by acquiring data during an appropriate diastolic time-window. However, dedicated postprocessing is required to obtain reliable and reproducible DWI parametric maps. Combining PCA and TMIP allows us to reduce motion-induced DWI bias and improves the feasibility of cardiac DWI. Overall, the proposed approach is promising for in vivo exploration of IVIM within cardiac muscle. Low b-value DWI potentially provides a new contrast mechanism for investigating the combined effects of microcirculation and diffusion in the myocardium. Our results suggest that cardiac DWI holds potential in a clinical context using low b-values and an appropriate acquisition strategy. Further studies are required to investigate the full potential of this approach for characterizing cardiac diseases.

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FIGURE 1.

Quantification of longitudinal cardiac motion and associated DWI signal loss in mid-LV short-axis slices of a healthy volunteer. Experimental slice contraction data over the cardiac cycle (right scale) were used to estimate DWI signal loss by simulation for $b = 100 \text{ s/mm}^2$. Simulations were performed for the same slice thickness of 6 mm as actual DWI experiments. Panel (left scale) shows simulated versus measured signal level over the cardiac cycle for $b = 100 \text{ s/mm}^2$. The simulation shows that signal loss is minimal in only a few phases of the cycle (gray areas). The optimal time-window occurs during diastole and lasts for about 80 milliseconds. Experimental results support this finding except in mid-diastole, where the signal intensity appears more stable than predicted.

FIGURE 2.

Theoretical impact of the image processing approach on DWI simulated with volunteer's physiological motion. TOP: trace-DW images (T-DWI) ($b = 100 \text{ s/mm}^2$): reference, motion + noise-induced data, AVG, TMIP, and PCATMIP results. BOTTOM: mean ADC (ADC_m) estimation maps corresponding to each data set. Simulation sampling was limited by DENSE resolution ($3.5 \times 3.5 \text{ mm}^2$). Values are the mean (SD).

FIGURE 3.

Top: Free-breathing trace DW-images for $b = 100 \text{ s/mm}^2$ from 10 repetitions acquired at different time points within the optimal diastolic window in a volunteer. The intensity fluctuation is apparent. Bottom: Processed DW-images using the following 3 methods: AVG, direct TMIP, and PCATMIP. All image intensities are graphed identically.

FIGURE 4.

Signal intensity (SI) (A), signal-to-noise ratio (SNR) (B), and contrast-to-noise ratio (CNR) (C) showing the benefits of TMIP and PCATMIP relative to AVG in volunteers. SI benefits are defined as the ratio of mean SI values of DW images over the LV wall: $R_{SI_{method}}(b) = \langle SI_{method}(b) \rangle / \langle SI_{AVG}(b) \rangle$. SNR benefits are defined as the ratio of SNR values of DW images: $R_{SNR_{method}}(b) = \langle SNR_{method}(b) \rangle / \langle SNR_{AVG}(b) \rangle$. CNR benefits are defined as the ratio of CNR values of DW images: $R_{CNR_{method}}(b) = \langle CNR_{method}(b) \rangle / \langle CNR_{AVG}(b) \rangle$. Data are the mean $\pm$ SD * $P < 0.05$.

FIGURE 5.

Mean apparent diffusion coefficient (ADC_m) values using the 3 processing methods in the volunteers. Overall, there was no statistically significant difference among methods ($P=0.29$). Both TMIP and PCATMIP yielded systematically lower values than AVG (-17% and -7% , respectively). The values from PCATMIP were higher than TMIP. The error bars represent the standard deviations in data sets.

FIGURE 6.

A, Repeatability results among 5 identical scans of the same slice. Mean ADC standard deviation ranges $1.2 \pm 0.6 \times 10^{-3} \text{ mm}^2/\text{s}$ compared with $8.4 \pm 3.0 \times 10^{-3} \text{ mm}^2/\text{s}$ for mean values. B, Breathing motion mean ADC values did not vary significantly ($P = 0.36$) between the same scan performed during free-breathing (FB1, FB2) or breath-holding (BH). C, Measurements at different locations of the heart on the same volunteer using short-axis (base, mid, apex) and long-axis (2 and 4 chambers) slices showed increased the mean ADC between the base ($\langle ADC_m \rangle = 9.2 \times 10^{-3} \text{ mm}^2/\text{s}$) and the apex ($\langle ADC_m \rangle = 9.9 \times 10^{-3} \text{ mm}^2/\text{s}$).

FIGURE 7.

Short-axis images obtained in a patient with inferior segment acute myocardial infarction (AMI) with microvascular obstruction (MVO). Top: T2-weighted image (STIR) and a postgadolinium IR-GRE delayed enhancement (at 10 minutes, DHE) image. ADC_m distribution in the myocardium for PCATMIPDWI; Middle: Trace diffusion-weighted images (T-DWI) ($b = 100 \text{ s/mm}^2$) for each processing method; Bottom: Mean apparent diffusion coefficient (ADC_m) maps.