Cone of Uncertainty Assessment in Cardiac Diffusion Tensor Imaging: A Comparison between Spin Echo and Stimulated Echo Sequences

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TARGET AUDIENCE – Scientists working in cardiac diffusion tensor imaging

PURPOSE – Cardiac diffusion tensor imaging (DTI) has emerged as an important tool for characterizing myocardial fiber structure to better understand cardiac functionality and to diagnose and follow up diseases. Traditionally, stimulated echo (STE) diffusion sequence is used for cardiac DTI since it allows synchronizing the two diffusion encoding gradient lobes to the same point in successive cardiac cycles, which can reduce the inherent motion-induced signal attenuation (1,2). However, this synchronizing scheme and the resulting long mixing time and diffusion time (~ 1 R-R interval) have several undesirable effects. Firstly, the long mixing time further reduces the signal-to-noise ratio (SNR) in an already SNR-starved sequence as STE. Secondly, the long diffusion time makes the sequence more sensitive to strain (3). Lastly, diffusion time and therefore b-value varies during the acquisition if the subject has irregular heart rate. Recently, together with the advancement of gradient systems, motion-insensitive spin echo (SE) diffusion sequences were proposed as alternatives to cardiac DTI (4,5). Since SE and STE measure diffusion at very different diffusion time, the question is whether the two types of acquisitions give different estimation in diffusion-related properties in the heart. In this work, we investigate how the difference in derived diffusion parameters from SE and STE experiments, if exists, affects the estimation of myocardial fiber organization through the assessment of the cone of uncertainty (COU) of the major eigenvector of the diffusion tensor.

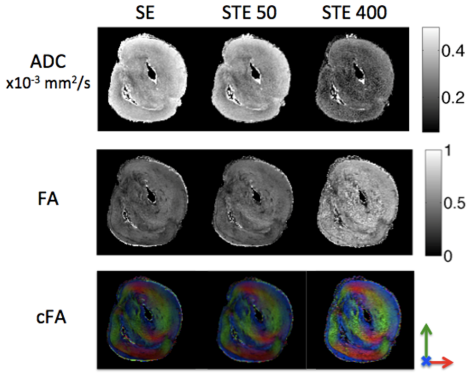

***Fig. 1** – Estimated diffusion parameter maps.*

METHODS – *MR measurement*: To eliminate the confounding effects of motion, the experiments were performed on an ex-vivo cow heart. The heart was obtained from a certified commercial slaughterhouse several hours after slaughtering. For both SE and STE, diffusion encoding was done with b = 1500 s/mm^2, thirty diffusion encoding directions, and one b = 0. Other common parameters are as follows: TE/TR = 71/3000 ms, FOV = 20 cm, slice thickness = 5 mm, 5 slices at 20 mm spacing, matrix size = 128 x 128, 8-shot EPI readout trajectory, echo spacing = 880 us, partial Fourier encoding with 24 over-scan lines. For SE, the effective diffusion time was ~ 36 ms. For STE, two diffusion times were measured: 50 ms and 400 ms. To match SNR between different acquisitions, the number of repetitions were 1, 4, and 6 for SE, STE with 50 ms diffusion time, and STE with 400 ms diffusion time, respectively. For STE acquisition, the effects of crushers and slice-selective gradients were compensated by scaling the diffusion gradient appropriately without affecting their crusher capability. B-matrices for each diffusion direction were computed by integrating the gradient waveforms and used in diffusion parameter estimation. All data were acquired on a 3 T MR750w GE scanner using a 16-channel flexible receiver array.

Cone of uncertainty estimation: Diffusion tensor was estimated using an in-house program. Elliptical 95% confidence COU was analytically constructed based on the error propagation method proposed by Koay et al. (6,7). To isolate the effects of the derived diffusion parameters, the same SNR was assumed for SE and STE acquisitions when constructing COU. For simplicity, the angles of deviation of the principle axes of the elliptical COU (deviation angles) were compared across acquisitions.

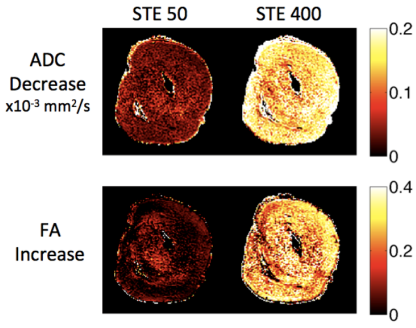

***Fig. 2** – Change of STE-estimated diffusion parameters as compared to SE. ADC Decrease = (ADC_{SE} - ADC_{STE}). FA Increase = (FA_{STE} - FA_{SE}).*

RESULTS – The STE sequence was first verified through a series of diffusion-weighted experiments on a water phantom at different diffusion times from 40 ms to 800 ms. The estimated ADC was 2.11±0.04 x10^{-3} mm^2/s, which is in good agreement with SE measurements (2.16±0.02 x10^{-3} mm^2/s). Fig. 1 shows the estimated ADC, FA, color-coded FA (cFA) maps from a short axis slice of the cow heart using SE, STE with 50 ms diffusion time (STE 50), and STE with 400 ms diffusion time (STE 400) acquisitions. The range of obtained ADC and FA falls within the range of a previous study (8). As the diffusion time increases from 36 ms (SE) to 50 ms (STE 50) to 400 ms (STE 400), a decrease in ADC and an increase in FA can be observed (Fig. 2). At the same SNR, these changes in ADC and FA lead to changes in the elliptical 95% confidence COU of the primary eigenvector of the diffusion tensor as shown in Fig. 3. Deviation angles θ_1 and θ_2 of an elliptical COU are illustrated on the left of Fig. 3. Constructed maps of θ_1 and θ_2 from estimated diffusion maps and average SNR of ~ 30 are presented on the right of Fig. 3. Comparing SE and STE 400, maximum decreases of 5 degree and 2 degree were detected for θ_1 and θ_2, respectively, implying a marginally more reliable estimation of the primary diffusion direction from STE 400 data.

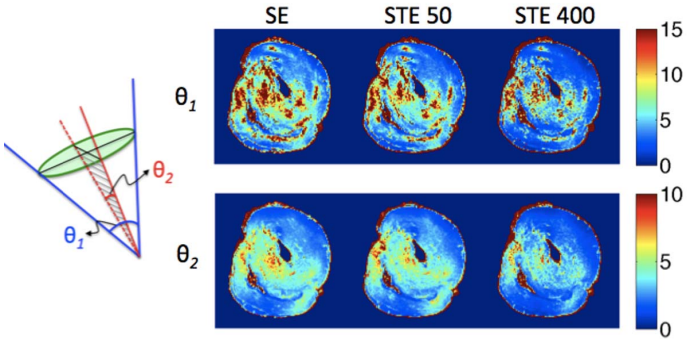

***Fig. 3** – Angles of deviation of the principle axes of the cone of uncertainty (θ_1 and θ_2). Left: definition of θ_1 and θ_2; right: maps of θ_1 and θ_2 (in degree) derived from different acquisitions.*

DISCUSSION & CONCLUSION – It has been shown previously in ex vivo cow heart using STE that an increase in diffusion time leads to a decrease in estimated ADC and an increase in estimated FA (8). Therefore, the observed discrepancy in estimated diffusion maps from the short diffusion-time SE and the long diffusion-time STE acquisitions in this study is expected. However, it is not clear how this discrepancy affects the estimation of myocardial fiber organization. Many methods exist to construct fiber organization from diffusion-weighted data, the most widely used of which is following the primary eigenvector of the diffusion tensor. At long diffusion time, the larger effect of restriction effectively "reduces diffusivity," leading to a noisier estimation of the diffusion tensor (Fig. 1). As a result the uncertainty of the primary eigenvector of the diffusion tensor increases, hence larger COU or equivalently, larger θ_1 and θ_2. In anisotropic regions, measurements at longer diffusion time result in larger FA values or better distinction of the primary eigenvector and hence smaller COU or equivalently, smaller θ_1 and θ_2. The analytical construction of COU used in this study considers both conflicting effects simultaneously. While the changes in ADC and FA are significant (Fig. 2), the obtained COUs suggest that only a marginally more reliable myocardial fiber organization can be estimated from STE 400 data than SE (Fig. 3). It is difficult to extrapolate the finding of the current study to in vivo experiments due to changes in diffusivity as well as experiment conditions. However, this study serves as a proof of potential discrepancies between SE and STE diffusion experiments that needs considering before replacing/interchanging one method with another.

References: [1] Edelman, MRM 32:423, 1994, [2] Nielles-Vallespin, MRM doi: 10.1002/mrm.24488, [3] Reese, JMRB 112:253, 1996, [4] Gamper, MRM 57:331, 2007, [5] Stoeck, ISMRM 21:480, 2012, [6] Koay, IEEE TMI 26:1017, 2007, [7] Koay, IEEE TMI 27:834, 2008, [8] Kim, MRM 54:1387, 2005.