Optimizing Accuracy and Precision in High Resolution Diffusion Tensor Imaging of the Ex Vivo Rat Heart

P. W. Hales[1], R. Burton[2], C. Bollensdorff[2], and J. E. Schneider[1]
[1]Cardiovascular Medicine, Oxford University, Oxford, Oxon, United Kingdom, [2]Physiology, Anatomy & Genetics, Oxford University, Oxford, Oxon, United Kingdom

Introduction

Diffusion Tensor Imaging (DTI) is a powerful tool for the determination of myo-fibre architecture in the heart. To determine the diffusion tensor, diffusion gradients must be applied in at least six non-co-linear sampling directions; however it has been shown that increasing the number of unique diffusion gradient directions (n_g), as well as increasing the signal to noise ratio (SNR), allows for more robust tensor determination [1]. This in turn increases the accuracy of anisotropy indices and eigenvector orientation derived from the diffusion tensor. As the primary eigenvector ($\boldsymbol{v}_1$) is aligned locally with the bulk orientation of myocytes [2], this will lead to more accurate modelling of the structure and electrophysiology of the heart. Further to the theoretical factors that determine the accuracy of tensor determination, inter-scan factors, such as gradient performance and sample stability, will affect the reproducibility (or precision) of the DTI data; if this limits the accuracy of experiments, the choice of gradient sampling scheme may be irrelevant. In this study, we examined how both accuracy and precision of high resolution (203 μm isotropic) ex vivo cardiac DTI data is affected by the choice of diffusion gradient sampling scheme, and SNR. We also investigated how reduced encoding (RE) using the approximate generalized series reconstruction technique [3] can affect the accuracy and precision of DTI data.

Methods

A heart was excised from a Sprague Dowley rat, fixed with Karnovsky's solution, and embedded in agarose gel inside a 28 mm diameter glass NMR tube (details of protocol in [4]). DTI data were acquired using a Varian 9.4 T (400 MHz) MR system (Varian Inc, Palo Alto, CA). A birdcage coil with an inner diameter of 28mm (Rapid Biomedical, Wurzburg, Germany) was used to transmit/receive the NMR signals. A diffusion weighted fast spin echo pulse sequence was used to collect 3D data at 203 μm resolution (b = 711 s/mm^2). Experiment 1 involved repeated measurements using the 6 and 10 direction diffusion gradient schemes described in [1], with number of averages (NSA) varied from 1 to 3 in order to vary SNR from 150 to 450 in the myocardium (total scan time = 62.6 h). Precision was defined as the mean angle (θ_p) by which the voxel-wise orientation of $\boldsymbol{v}_1$ varied between repetitions of identical scans, for a given value of n_g and SNR. For experiment 2 the n_g=30 scheme described in [1] was used, and SNR was varied by using 1 to 3 averages (total scan time = 53 h). Sub-samples were extracted from these data, corresponding to n_g of 6, 10, and 15 directions [5]. The dataset with n_g=30 and NSA=3 was taken as the 'gold standard', and the mean angle (θ_a) by which the voxel-wise orientation of $\boldsymbol{v}_1$ differed in subsequent datasets, with n_g<30 and/or NSA<3, was used to quantify changes in accuracy. Reduced encoding using the approximate GS method was then applied to all data during post-processing, using RE factors (i.e. percentage of data replacement in all diffusion weighted (DW) images from the un-weighted image) of 0 to 75 %. This was used to simulate the increase in signal averaging that could be achieved in the same scan time if reduced encoding is used. The corresponding changes in θ_p and θ_a were modelled using the empirically derived relationships from the experiments 1 and 2. The additional error introduced to the accuracy of $\boldsymbol{v}_1$ (θ_{RE}), caused by the replacement of original data in the DW images, was calculated based on comparisons to equivalent datasets with RE=0.

Results

Fig 1a shows the mean value of precision (θ_p) is shown as a function of SNR for n_g=6 and n_g=10. Precision improved with increasing SNR in both cases, and was proportional to SNR$^{-0.96}$ using n_g=6, and SNR$^{-0.71}$ using n_g=10. Fig 1b shows the effect of n_g on accuracy, based on comparisons to the 'gold standard' dataset: θ_a decreases with increasing SNR (α SNR$^{-0.74}$, SNR$^{-0.80}$, SNR$^{-0.83}$ for n_g= 6,10,15 respectively) and increasing n_g. Fig 1c shows the modelled effect that RE has on both precision and accuracy, for n_g=6, when the scan time that is saved during RE acquisition of DW images is used to increase signal averaging. Increasing RE allows for higher SNR, which improves precision, however it also introduces a new error (θ_{RE}) into the DTI data: provided $\theta_{RE} + \theta_a$ is below the precision of the experiment it will not effect the results, and the optimal RE factor (RE$_{opt}$) is where $\theta_p = \theta_{RE} + \theta_a$. For n_g=6, RE$_{opt}$ = 27 %, and for n_g=10, RE$_{opt}$ = 23 %. In both cases, reduced encoding at RE$_{opt}$ decreased the overall error in the orientation of $\boldsymbol{v}_1$ (compared to RE=0): by 12.6 % for n_g=6 and 8.5 % for n_g=10.

Conclusion

The variation of θ_p with SNR when n_g=6, shown in Fig 1a, shows good agreement with the analysis of the 'cone of uncertainty' in a typical white matter voxel in the brain, described in [6]. However, our results show that this relationship changes significantly in myocardium when n_g=10. We have also demonstrated that the use of optimized reduced encoding can reduce the overall error in the orientation in $\boldsymbol{v}_1$ for n_g of 6 and 10, without increasing scan time. The 12.6 % increase in accuracy shown in Fig 1c may have a significant impact on the methodology described in [4], in which cardiac DTI data (obtained using n_g=6) are incorporated into 3D computer models in order to investigate the electrophysiological behaviour of individual hearts. Future work will explore this further, and develop the relationship between accuracy and precision in cardiac DTI over an increased range of diffusion encoding directions and SNR levels.

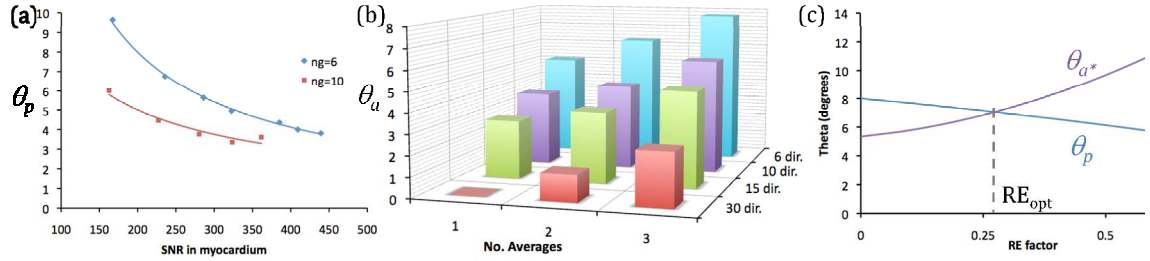

Fig. 1 The effect of SNR and number of diffusion gradients on the error in $\boldsymbol{v}_1$, due to (a) precision (θ_p), and (b) accuracy (θ_a) in the ex vivo rat heart. (c) Modelled changes in precision, and overall accuracy ($\theta_{a*}=\theta_a+\theta_{RE}$), as a function of RE factor. The optimum RE factor is where $\theta_p = \theta_{a*}$.

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References

[1] Jones, D.K. *MRM*, 42:515-524 (1999)
[2] Holmes, A.A et al. *MRM*, 44:157-161 (2000)
[3] Liang, Z.P. et al. *IEEE Trans. Med. Imag.* 13:(4)677-685 (1994)
[4] Plank et al. *Philos Transact A Math Phys Eng Sci* 2009; **367**: 2257-2292
[5] Landman, B.A. et al. *NeuroImage* 36: 1123-1138 (2007)
[6] Jeong, H-K. et a. *MRM*, 60:1408-1421 (2008)