**In vivo cardiac diffusion tensor imaging: Selecting a b-value and acquiring the reference data**

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**Target audience:** Physicists and clinicians with an interest in the cardiac microstructure.

**Purpose:** To investigate the influence of the diffusion weighting (the b-value) on in vivo cardiac diffusion tensor imaging (cDTI). This includes the diffusion weighting of the main diffusion weighted and reference images (referred to as bref) and the effect of the orientation of the diffusion weighting in the reference data.

**Method:** cDTI was performed in 10 healthy subjects (7 male, age 23-57, Siemens Skyra) using the stimulated echo single shot EPI sequence with monopolar diffusion encoding, described previously1,2. GRAPPA parallel imaging and a reduced phase field of view (zonal excitation) were used to accelerate the acquisition. A single short axis slice in the mid-ventricle was imaged at a resolution of 2.8x2.8x8mm^3. One average was acquired per breath hold and 8 averages were obtained. Each average consisted of 6 diffusion directions at b=50,150,350,550,750,950 mm^2/s and a reference image, where the effective diffusion weighting was b=15 mm^2/s. In-house software2 written in MATLAB (The Mathworks, Natick MA) was used for processing. Pixel wise diffusion tensors were calculated using each b-value with b=15 mm^2/s and then also using all b-values less than the current b-value as bref (e.g. b=750 vs. bref=15,50,150,350,550mm^2/s). Mean diffusivity (MD), fractional anisotropy (FA) and helical angle (HA) maps were derived in each case. To investigate the way the reference data is acquired, this was repeated using all averages and references (ALL), all averages of the first diffusion direction (1DIR) and 1 average of each direction as a reference (1AV). For each subject the average diffusion weighted signal (geometric mean over all directions) at each b-value was calculated in the left ventricle for comparison with the standard model of mono-exponential decay (\(S = A \exp[-bD]\), where S is signal, and D is the diffusivity).

**Discussion:** When the bref is low, measured MD is augmented by another process with a high apparent diffusivity (D_2), which is thought to be microvascular perfusion. Previous work in diffusion weighted imaging of the heart has also demonstrated a bi-exponential signal decay with b-value1, but this is the first in vivo work in cDTI to consider this effect. Here bref ≥ 150 mm^2/s resulted in sufficient suppression of the microvascular perfusion in the measured diffusion tensor. Typically in cDTI the reference data is acquired with diffusion weighting along a single direction (i.e. the 1DIR case here), but using reference data acquired with diffusion weighting in 6 directions results in more stable values of MD and FA. Using 1 average of each direction (1AV) for the reference data produces similar results to using all 8 averages of all directions (ALL), without increasing the amount of data required. Most previous studies have used b-values around 350 mm^2/s1,2,4,5, but increasing the b-value used in cDTI results in more uniform MD and FA, presumably due to an increase in the signal to noise ratio of the calculated diffusion tensor. In this work, b=750 and bref=150 mm^2/s, appeared to be optimal and MD was closest to the diffusion component (D_1) in a bi-exponential model fitted to data from all 10 subjects.

**Conclusion:** Parameter maps obtained from in vivo cDTI data can be improved by using higher b-values than in previous studies. The contribution of microvascular perfusion to the measured diffusion tensor can be reduced by applying diffusion weighting to the reference data, the direction of which should change between averages.


**Results:** Figure 1 shows the signal loss in the left ventricle with b-value. A bi-exponential fit (fitted to b<1000 mm^2/s to avoid the noise floor), with diffusion (D_1) and microvascular perfusion (D_2) components more closely matches the data than the standard mono-exponential model (R^2=0.994 vs. 0.987). By b=150 mm^2/s, D_2 contributes approximately only 1% of the signal. Figure 2 plots mean MD and FA for: (A and B) b=750 s mm^{-2} with increasing reference b-value for all three correction methods; and (C and D) for all possible pairs of b-values using the ALL reference method. Using the 1DIR method of correction, MD rapidly deviates from the D_1 value obtained in figure 1 and FA steadily increases. However, using the 1AV method, MD remains close to D_1. FA shows only a small increase and both measures closely match those obtained with the ALL method, which should be more reliable. From parts C and D, with increasing bref the MD reduces and FA increases. With larger main b-values, maps are less noisy and there is less variation between subjects. MD is closest to D_1 with b=750 vs. bref=150mm^2/s. Figure 3 shows example cDTI parameter maps calculated using 4 pairs of b-values (using the ALL method of correction in the right hand data).