

Compensation for bias from unwanted gradient contributions in STEAM diffusion MRI

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Introduction: We propose a simple method to compensate for cross terms produced by imaging gradients in stimulated echo (STEAM) diffusion MRI and demonstrate the necessity for the compensation. STEAM diffusion MRI offers advantages over the spin-echo (PGSE) diffusion MRI when long diffusion times are required, e.g. for axon diameter estimation [1], or T2 is short, e.g. at 7T [2]. However, crusher and slice-select gradients are separated in the STEAM sequence so contribute much more diffusion weighting than in PGSE. These cross terms complicate both data analysis, for ensuring good estimates of diffusion parameters, and experiment design, e.g. to ensure orientationally invariant sampling. Our method addresses both issues. We demonstrate for diffusion tensor (DT) imaging [3] and ActiveAx axon-diameter index mapping [4].

Method: Figure 1 shows the STEAM sequence implemented on a 4.7T Varian small-bore scanner. The crusher and slice-select (butterfly) gradients have gradient vectors $(0, 0, 150)\text{mT/m}$ and $(0, 0, 40)\text{mT/m}$ and durations $\delta_c=1.5\text{ms}$ and $\delta_s=1\text{ms}$, respectively. We optimize STEAM and PGSE ActiveAx protocols, as in [5], for maximum gradient strength 300mT/m . Each protocol consists of three high angular resolution diffusion imaging (HARDI) shells with b -values of $2160, 3151, 9686\text{s/mm}^2$ for PGSE and $2640, 6019, 19599\text{s/mm}^2$ for STEAM. The b -matrix including all cross terms for the STEAM sequence is simple to derive, but we omit the complex expression. However, the butterfly gradients affect both the magnitude and the orientation of the net diffusion weighting and skew evenly distributed sets of HARDI gradient directions towards the slice direction. To compensate we add a component to each diffusion gradient in the negative slice direction to cancel the cross terms. The magnitude of this compensating component is independent of the target gradient direction, but depends on the sequence timing, i.e. TM, δ_D , δ_c , etc. Thus it differs for each HARDI shell, but is the same within each. A simple numerical search provides the compensation for one shell, by maximizing the predicted free-diffusion signal with target b of zero.

We also derive, following [6], the Gaussian phase distribution (GPD) approximation of the signal from restricted diffusion in a cylinder that accounts for all gradients. This extends the minimal model of white matter diffusion in [2], enabling ActiveAx, for STEAM. We acquire data sets from a fixed monkey brain [7] using the PGSE protocol, and the STEAM protocol with and without the compensation.

Experiments and results: We use the $b=6019\text{s/mm}^2$ HARDI shell for DTI using three approximations: A1 ignores the butterfly gradients; A2 adjusts each b -value and effective gradient direction to account for the additional gradients, but ignores cross terms; A3 accounts fully for all gradients and cross terms. In this shell, TM=150ms and the b -value for the crushers alone is 250s/mm^2 (only 10s/mm^2 for PGSE). Figure 2 compares principal direction maps from PGSE with STEAM for each approximation qualitatively. The mean absolute dot product of principal directions weighted by DT linearity [8] quantifies the difference; the PGSE number is the same for the two low b -value PGSE shells. For uncompensated STEAM, ignoring the imaging gradients (A1) introduces severe orientation bias towards the left-right slice direction (the map appears red), because attenuation in that direction is greater than expected. A2 and A3 are better but orientational variance biases towards other directions. The compensated STEAM acquisition reduces bias in orientation and all appear more similar to PGSE, although A1 has visible intensity (FA) differences.

Figure 3 maps the axon diameter index [4] over the mid-sagittal corpus callosum for each data set using ActiveAx. The scales differ (PGSE: red = $0.5\mu\text{m}$; yellow = $3\mu\text{m}$. STEAM: red = $1\mu\text{m}$; yellow = $6\mu\text{m}$), but both PGSE and compensated STEAM show the low-high-low trend, as in [4]. Uncompensated STEAM shows a severely disrupted pattern, accentuated by the callosal fibres pointing along the slice direction. This emphasizes the need to compensate in the acquisition as well as the data analysis.

Discussion: We demonstrate bias in diffusion parameters estimated naively from STEAM diffusion MRI. In particular, accounting for cross terms reduces bias, but compensation for disrupted gradient directions is also important; offsetting the diffusion gradients to compensate for the butterfly gradients is necessary for orientational invariance. Simulations (not shown) suggest the compensation is also necessary on human systems even though the gradients are weaker. The approach we suggest will prove essential for effective diffusion imaging at 7T and above where low T2 makes STEAM advantageous. It also enables orientationally invariant axon diameter estimation with STEAM, which increases sensitivity to larger axons, as the higher index range for the STEAM results in figure 3 reflects. **Acknowledgements:** EU CONNECT consortium; EPSRC EP/E007748.

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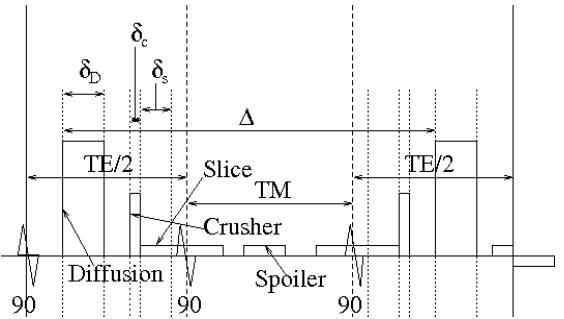


Fig. 1: Schematic of the STEAM diffusion MR sequence.

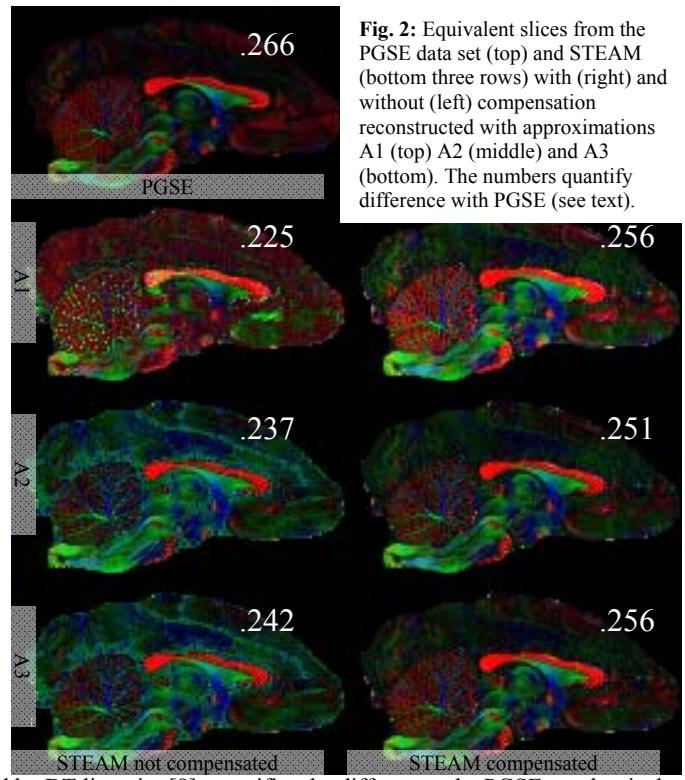


Fig. 2: Equivalent slices from the PGSE data set (top) and STEAM (bottom three rows) with (right) and without (left) compensation reconstructed with approximations A1 (top) A2 (middle) and A3 (bottom). The numbers quantify difference with PGSE (see text).



Fig. 3: ADI maps: PGSE (left); STEAM no comp (middle), and comp (right). The scales differ (PGSE: red = $0.5\mu\text{m}$; yellow = $3\mu\text{m}$. STEAM: red = $1\mu\text{m}$; yellow = $6\mu\text{m}$), but both PGSE and compensated STEAM show the low-high-low trend, as in [4]. Uncompensated STEAM shows a severely disrupted pattern, accentuated by the callosal fibres pointing along the slice direction. This emphasizes the need to compensate in the acquisition as well as the data analysis.