"Squashing Peanuts and Smashing Pumpkins": How Noise Distorts Diffusion-Weighted MR Data

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INTRODUCTION: New diffusion-weighted imaging (DWI) methods, including high *b*, high *q* and high angular resolution sampling techniques (e.g. **1-4**), attempt to extract information about non-Gaussian diffusion in tissue that is not provided by low *b*-value ($b \approx 1000$ s mm^{-2}) DW or diffusion tensor imaging. Additionally, DWI data with higher spatial resolution is being acquired to resolve fine anatomical structures, e.g. white matter fasciculi for tractography applications. Increasing diffusion weighting or resolution reduces the signal-to-noise ratio (SNR), resulting in some DWI signals being close to the rectified noise floor (**5**). Here we report several newly identified artifacts that can be explained by considering how the noise floor affects the peanut-shaped angular apparent diffusion coefficient (ADC) profile. These include an orientationally-dependent deviation from a Gaussian distribution of the ADC, an *underestimation* of diffusion anisotropy, an artifactual negative correlation between mean diffusivity and diffusion anisotropy estimates, increased gray/ white matter contrast at high *b*-values and elevated anisotropy in acute ischemia. We show how all these artifacts can be understood in terms of the peanut-shaped angular ADC profile and propose a strategy for remedying the problem. These artifacts do not manifest themselves in the typical *b*-value range at which DTI is currently performed ($b \approx 1000$ s mm^{-2}).

METHODS: Monte Carlo (MC) simulations were performed in both 2D and 3D to investigate the effect of the noise floor on diffusion-derived parameters. For simulated tensors with a given trace and fractional anisotropy (*FA*), noise free DW signals were obtained over a large number of sampling orientations for $b = 0$ and $b_{\max}$, (a "two-point" approach). Noise was then added to both signals in quadrature and the ADC for that orientation recomputed. This was repeated 500 times for each orientation and the mean ADC was used to reconstruct the noisy angular ADC profile, from which the noisy tensor and its trace and *FA* were derived. These experiments were repeated for a range of *FA*s, b_{max} values and SNRs. We also simulated experiments in which DW data were collected at multiple *b*-values between $b = 0$ and $b_{\max}$ and compared various ADC estimation procedures including weighted and un-weighted linear regression, non-linear regression and a new non-linear method in which a noise-parameter was included in the fitting. The robustness of this method is improved if a number of signals are collected at sufficiently high *b*-values such that only the noise floor is sampled. To this end, and to avoid lengthening acquisition times, we propose that data could be sampled in lower *b*-value images in a region outside the brain and equated with the signals that would be observed at extremely high *b*-values ($b > 40{,}000$ s/mm^2). This was simulated in the MC simulations, by obtaining estimates of the rectified signal in the absence of any true signal.

RESULTS: Increasing $b_{\max}$ in the two-point method causes the noisy ADC profile to deviate from the idealized peanut shape. The peanut gets increasingly 'squashed' along the long axis (Fig. 1) as $b_{\max}$ increases. This effect also becomes more pronounced as anisotropy increases since, for a given Trace, the ADC along the long axis increases. This brings the DW-signal closer to the rectified noise floor, leading to an underestimation of the ADC. Furthermore, for a given *FA*, as the Trace increases, the diffusivity along all axes increases – resulting in increased squashing of the peanut – and hence reduced anisotropy, which leads to an artifactual negative correlation between estimated Trace and noise-free *FA*. Conversely, when the peanut is already squashed, a reduction in mean diffusivity will lead to an increase in the estimated anisotropy. Fig. 2 shows the results of using the different fitting methods with multiple *b*-value data. Weighted linear regression produces a profile that is peanut shaped, however it does not follow the form of the idealized peanut and still leads to underestimated Trace and *FA*. Non-linear fitting greatly ameliorates the problem, providing estimates of Trace and *FA* that are close to their noise-free values, but the ADC profile is still squashed. The proposed new approach of including a noise-parameter in the estimation resulted in ADC profiles that matched the noise-free profiles most accurately. Increasing the number of *b*-values (between $b = 0$ and b_{mzx}) and the number of measurements associated with extremely high *b*-values reduced the deviation between the fitted and noise-free profiles.

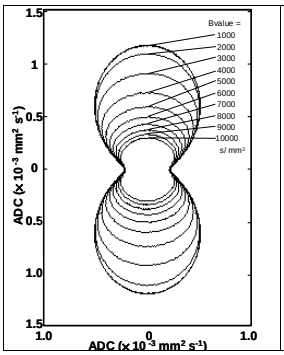

Figure 1. Demonstration of the 'squashing' of the peanut shaped ADC profile with increasing *b*-value that is seen with the 'two-point' fitting approach. These profiles were obtained assuming a fractional anisotropy (*FA*) of 0.9, mean diffusivity of 0.7×10^{-3} mm^{2}s^{-1} and an SNR of 20:1.

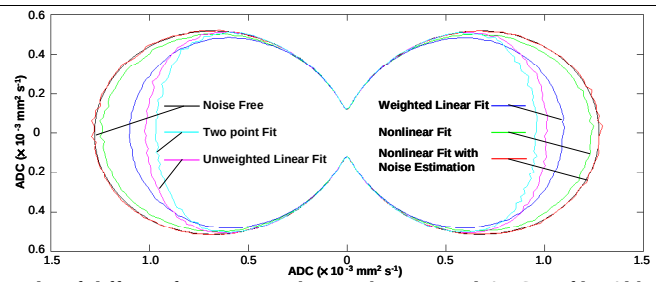

Figure 2. Results of different fitting approaches on the estimated ADC profile. Although non-linear fitting of multi-point data yields good results, the most accurate profile is obtained when using the proposed strategy of including a noise parameter in the estimation process.

DISCUSSION: In high *b*-value / low SNR data, the rectified noise floor leads to underestimation of both Trace and *FA*. Furthermore, it introduces an artifactual negative correlation between Trace and *FA* that are generally assumed to be statistically independent quantities. The correlation also means that a reduction in ADC (e.g. in acute ischemia) can produce an apparent increase in tissue anisotropy in high *b*-value / low SNR data.

Several groups have attempted to characterize non-Gaussian diffusion by examining the angular ADC profile obtained at high *b*-values. For a single fiber population, the idealized ADC profile is the peanut shape that can be described by the 0th and 2nd-order spherical harmonics. Some groups have interpreted the need to use higher order harmonics to describe the ADC profile as an indication of non-Gaussian diffusion behavior caused by increased tissue complexity (**3,4**). However, as seen here, the ADC profile can deviate from the idealized profile solely as a result of the noise floor. Our finding that these artifacts can be effectively removed by collecting multiple *b*-value data and adopting a non-linear fitting approach has consequences for the design of future studies that aim to characterize non-Gaussian diffusion from high *b*-value data. We note, however, that this fitting strategy is only appropriate for model-based approaches and is obviously not appropriate for model-free approaches (e.g. **1**), which will nevertheless be affected by the noise-floor in the same manner. Finally, we note that in this study, we only report results for single fiber populations whose ADC profiles can be described by the peanut shape. However, the same artifacts manifest themselves with multiple fiber populations that at low *b*-values, have an ADC profile that is more akin to a 'pumpkin' (**2**), hence the title of this work.

REFERENCES: 1. Wedeen VJ *et al*. Proc ISMRM 2000, p82**; 2.** Frank LR. *Magn Reson Med* 2001; 45: 935-939. **3.** Frank LR *Magn Reson Med* 2002; 47: 1083-1089; **4.**Alexander DC *et al.* Proc ISMRM 2002, p1158. **5.** Dietrich O *et al. Magn Reson Med* 2001; 45: 448-453.