Post-processing of diffusion-weighted MR data lowers the accuracy of the weighted linear least squares estimator

Jelle Veraart[1] and Jan Sijbers[1]
[1]*Vision Lab, University of Antwerp, Antwerp, Belgium*

TARGET AUDIENCE: Scientists working in the field of diffusion MRI. **PURPOSE:** During the last decade, many approaches have been proposed for improving the estimation of diffusion measures. These techniques have already shown an increase in accuracy based on theoretical considerations, such as incorporating prior knowledge of the data distribution, which is often assumed to be Rician[1]. Opposite to the wealth of *advanced* diffusion parameter estimators, the weighted linear least squares (WLLS) estimator stands out by its simplicity and elegance. First, the WLLS estimators have a global closed-form solution. Therefore, unlike iterative nonlinear strategies, the linear estimators are computationally efficient. Second, the linear estimators are in general very accurate in the estimation of parameters of log-linear models such as diffusion tensor imaging (DTI) and diffusion kurtosis imaging (DKI), especially compared to the nonlinear least squares (NLS) estimator. If the SNR exceeds two, the linear estimators are even unbiased due to the zero expectation of the error term in the log-Rician framework[2,3]. Third, the high accuracy is not at the expense of the ease of use. Indeed, the linear estimators don't require the knowledge of the noise parameters. Unfortunately, the noise parameter is very difficult to estimate because of its spatial variability in case of parallel imaging. Therefore, a lack of need for the noise parameter is often the deciding factor to prefer WLLS to (asymptotically) unbiased estimators such as the maximum likelihood (ML) estimators or the recently proposed conditional least squares (CLS) estimator. The increased accuracy of diffusion metric estimators such as WLLS, ML, and CLS is typically observed in well-defined simulations, where the assumptions regarding properties of the data distribution are known to be valid. In practice, however, correcting for subject motion and geometric eddy current deformations alters the data distribution tremendously such that it can no longer be expressed in a closed form. The image processing steps that precede the model fitting will render several assumptions on the data distribution invalid, potentially nullifying the benefit of applying more advanced diffusion estimators. In this work, we will show the effect of data interpolation on the performance of three least squares estimator: WLLS, NLS, and CLS. By doing so, we will show that for an accurate estimation of diffusion parameters, the prior knowledge of the noise parameter is a must. **METHODS:** Consider a Rice distributed diffusion-weighted signal $\tilde{S}$, which can be modeled by DTI or DKI as $\tilde{S} = \exp(\boldsymbol{B}_n\boldsymbol{\beta}_0) + \varepsilon$ or $w_n \ln \tilde{S} = w_n \boldsymbol{B}_n \boldsymbol{\beta}_0 + \varepsilon^*$ with $\boldsymbol{B}_n$ the n$^{\text{th}}$ row of the model-specific b-matrix $\boldsymbol{B}$, $\boldsymbol{\beta}_0$ the noise-free diffusion parameter vector, w_n the n$^{\text{th}}$ element of the diagonal weight matrix $\boldsymbol{W}$ and ε and ε^* the respective error terms. Despite the models being equivalent, their parameters are estimated with different estimation strategies: NLS, WLLS estimator, respectively. A least squares estimator will only be unbiased if the expectation value of the error terms is zero. For NLS this conditional is only (approximately) met if SNR of the diffusion-weighted signals exceeds 10, whereas the WLLS is unbiased if the SNR exceeds two. To nullify the systematic error of the NLS, one can replace the model prediction – $\exp(\boldsymbol{B}_n\boldsymbol{\beta})$ – in the object function by its expectation value, given the Rician nature of the data. The estimation procedure based on the minimization of a (weighted) sum of squared deviations about the expectations is called the CLS estimator. The respective error terms are zero for all SNR and, as such, the CLS will show higher accuracy then WLLS if SNR<2. Unfortunately, the expectation value can only be computed if the noise parameter is known. The expectation value of the errors is shown in Fig1(a). In a simulation experiment, we consider $\tilde{S}_m$, being the weighted sum of 25 samples of the same Rician distribution, instead of $\tilde{S}$ to study the effect of interpolation in an homogeneous region on the accuracy of the estimator. The weights did correspond to the weights of a Gaussian smoothing filter (5x5) with different widths, i.e. standard deviation: 0, 0.25, 0.5, 0.75, and 1.

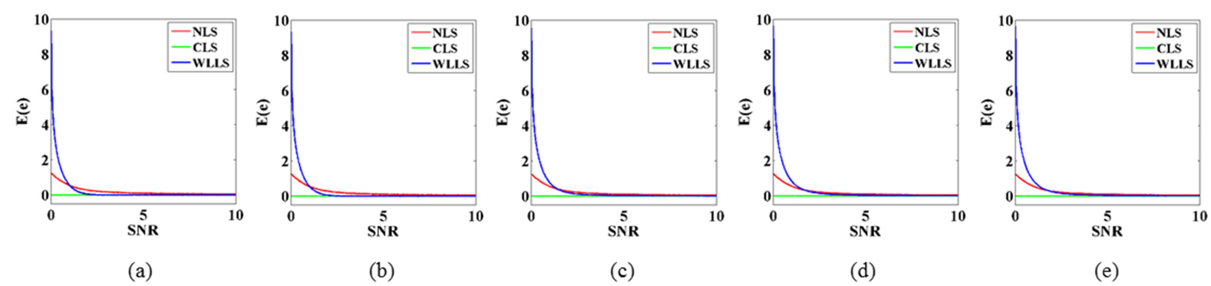

Fig. 2: Expectation value of the error term as a function of the SNR, given different filter widths (0, 0.25, 0.5, 075, and 1, respectively)

RESULTS: First, due to the linearity of the expectation value operator, weighted averaging prior to model fitting will not affect the accuracy of the nonlinear least squares estimator (CLS and NLS). Indeed, the expectation value of the error terms is independent of the filter width (green and red curves in Fig 1). Next, the accuracy of the WLLS depends on the interpolation kernel as the expectation value of the error terms increases with filter width. Indeed, by increasing the filter width, the accuracy of the WLLS will drop, despite its favorable theoretical properties. We can see that the minimal SNR for unbiasedness, i.e. expectation value of the error is zero, increases up to a level of 6 (blue curves in Fig 1). The drop in accuracy of the WLLS in the estimation of the mean diffusivity (MD) can also be observed in a whole brain simulation experiment (Fig. 2). We evaluated the accuracy of NLS, WLLS, and CLS in terms of MD. The experiments, based on simulated Rician distributed whole brain diffusion-weighted data, was done before (*uncorrected*) and after (*corrected*) performing a half-pixel shift in both in-plane directions to mimic an interpolation effect, similar to the one that occurs when performing motion/eddy current distortion prior to model fitting. WLLS and CLS are accurate in the absence of magnitude processing of the data prior to tensor fit, whereas NLS shows the well-known underestimation of MD. After data correction, WLLS shows a similar bias whereas CLS remains accurate. **DISCUSSION/CONCLUSION:** For clinically relevant SNR values, the WLLS is theoretically expected to be as accurate as the CLS and ML estimators in the estimation of DTI/DKI model parameters. However, one must bear in mind that the improved accuracy, compared to ordinary NLS, vanishes if magnitude operations are applied prior to model fitting. Because of the changing data distribution, the mathematical reasoning of Salvador et al.[3] no longer holds. After magnitude operations, which are generally included in the diffusion MRI processing pipeline, the CLS is the only unbiased estimator in high SNR or homogeneous regions. Unfortunately, the prior knowledge of the noise parameter is a must.

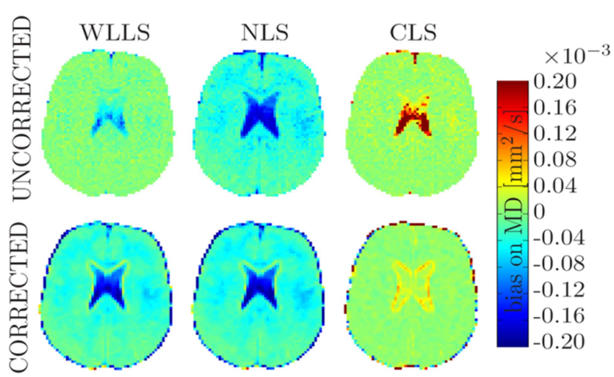

Fig. 1: The DTI-estimators' biases on MD ([mm2/s]) were shown. Results were shown without and with data resampling before model fitting in the top and bottom row, respectively.

REFERENCES: [1]Veraart et al. (2012) MRM in press, [2]Veraart et al. (2013) NeuroImage 8:335-346, [3]Salvador et al. (2005) HBM 24 144-155