# Maximum likelihood analysis provides accurate ADC estimates from diffusion-weighted prostate images acquired with multichannel coils

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## Introduction

Diffusion-weighted MR imaging (DW MRI) is commonly performed to determine the apparent diffusion coefficient (ADC) of body tissues. Since DW images are reconstructed as magnitude images, they are contaminated with Rician noise [1, 2], which depends on the signal amplitude and the number of receiver channels N [3]. For a single receiver channel, it has been shown that the signal distortion caused by Rician noise leads to bias in ADC estimates [4, 5]. For multiple receiver channels, this noise-related bias is expected to be higher, as it was shown for T2 measurements with phased arrays [6]. We study the influence of Rician noise in DW images acquired with multichannel receivers on ADC values calculated using three methods: the noise-corrected maximum likelihood estimation (MLE) [7] and the uncorrected nonlinear least-squares fitting (NLSQ) and log-linear fitting (LL). We explore the accuracy and precision of these methods for a range of ADC and varying number of receiver channels using simulations and phantom and in vivo imaging of human prostate.

**Simulations:** All analyses were performed in Matlab (Mathworks; Natick, MA). Rician probability density for multichannel receivers [3] was incorporated into MLE; NLSQ and LL fitting was done without noise correction. Monte Carlo simulations (3000 trials) were performed with ideal data simulated using monoexponential model  $S(b)=S_0exp(-b\cdotADC)$  for  $b=0-1600 \text{ s/mm}^2$  in steps of  $\Delta b=100 \text{ s/mm}^2$ . This signal was assumed to be real and contribute equally to each of N receiver channels, N=1-32. Gaussian noise with zero mean and standard deviation  $\sigma$  was added to both real and imaginary signal components in each channel. Signal-to-noise ratio (SNR) was varied by adjusting  $\sigma$ . The same SNR for different N was achieved by scaling  $\sigma$  as  $\sqrt{N}$  [6]. Simulations were first performed for a fixed ADC=1.0·10<sup>-3</sup> mm<sup>2</sup>/s and SNR=2-50. Another set of simulations was performed for SNR=10 and ADC=(0.2-2.0)·10<sup>-3</sup> mm<sup>2</sup>/s. **Phantom imaging:** A uniform copper sulfate solution phantom was imaged on a 3T whole-body unit (Signa HDx; GE, Milwakee, WI) with single shot spin echo echo-planar imaging sequence (TR/TE=3500/93.3 ms; matrix, 128x128 acquired, 256x256 interpolated; slice/gap, 3/3 mm; 17 uniformly spaced b-values 0 to 1000 s/mm<sup>2</sup>). Endorectal coil (Medrad; Indianola, PA) (1 channel) combined with torso phased array (7 channels) was used for signal reception. To vary SNR, images were acquired at two different fields of view (FOV), FOV<sub>1</sub>=16x16 cm<sup>2</sup> (1.25x1.25x3 mm<sup>3</sup> voxel) and FOV<sub>2</sub>=32x32 cm<sup>2</sup> (2.5x2.5x3 mm<sup>3</sup> voxel). The noise parameter was determined as  $\sigma = \frac{1}{\sqrt{2N}} \overline{s^2}$ , where  $\overline{s^2}$  is the mean square intensity

across voxels in an empty ROI [3]. ADC voxel maps were calculated by all three methods. **In vivo imaging:** After providing informed consent, a 59-year-old patient was imaged at 3T with the same coils and sequence (TR/TE=3500/104.9 ms; FOV, 16x16 cm<sup>2</sup>; slice/gap, 3/3 mm; matrix, 96x96 acquired, 256x256 interpolated; b=0-1600 s/mm<sup>2</sup>,  $\Delta b=100$  s/mm<sup>2</sup>). The noise parameter  $\sigma$  was determined as described above from an ROI in the center of endorectal coil. ADC voxel maps were calculated by each method.

## Results

**Simulations:** NLSQ and LL progressively underestimate ADC as SNR decreases, while MLE is accurate within 10% for N=8 at SNR=5 and is bias-free at higher SNR (Fig. 1). However, MLE is less precise than NLSQ and LL up to SNR=10. MLE appears to be accurate across the entire range of ADC or N (Fig. 2a). NLSQ and LL underestimate higher ADCs more strongly than lower ones and this effect is exacerbated at higher N (Fig. 2b,c). Phantom imaging: As expected, for FOV<sub>2</sub>, ADC<sub>NLSQ</sub> and ADC<sub>MLE</sub> are equivalent (Pearson R=1.0, mean difference= $1.12 \cdot 10^6$  mm<sup>2</sup>/s), while for FOV<sub>1</sub> ADC<sub>NLSQ</sub><ADC<sub>MLE</sub>, especially at fitted ADC> $2.5 \cdot 10^3$  mm<sup>2</sup>/s. ADC<sub>LL</sub> shows large scatter vs ADC<sub>MLE</sub> at both FOVs. All methods provided similar average ADC across the phantom ( $2.2 \cdot 10^3$  mm<sup>2</sup>/s). In vivo imaging: ADC maps showed a region of low ADC in transition zone (Fig. 3). The mean ADC in an ROI drawn in this region from MLE/NLSQ/LL analyses was ( $0.58/0.58/0.58/0.58/0.70/0.58/0.10^3$  mm<sup>2</sup>/s, respectively. An ROI drawn in an adjacent area with higher ADC was (1.43/1.35/1.28) $\cdot 10^3$  mm<sup>2</sup>/s and the ADC difference between the two ROIs was ( $0.85/0.78/0.70/0.10^3$  mm<sup>2</sup>/s. As predicted by simulations, MLE yielded higher ADC estimates and higher ADC contrast between ROIs than NLSQ or LL.



**Fig. 1:** Mean ADC (symbols) and standard deviation of ADC (one-way error bar) for N=8 receivers. True ADC is 1.0·10<sup>-3</sup> mm<sup>2</sup>/s (dashed line).



Fig. 2: Ratio of calculated to true ADC for a range of ADC and number of receiver channels N. MLE provides accurate estimates across the entire range, while NLSQ and LL progressively underestimate ADC at higher values of ADC and N.



**Fig. 3:** Prostate ADC maps. The color bar is in units of mm<sup>2</sup>/s. ROIs in low (1) and high (2) ADC areas are shown on MLE map (a). MLE provides higher ADC difference between these ROIs than NLSQ and LL, but yields unrealistic ADCs in areas of artifacts, such as in the region adjacent to the endorectal coil.

#### References

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#### •\* Discussion

MLE provides more accurate ADC estimates across a range of ADC and N than NLSQ and LL, although it is less precise at SNR<10. NLSQ and LL progressively underestimate ADC for lower SNR and higher N. Higher ADCs are underestimated more strongly than lower ones. This variable negative bias reduces the contrast between high and low ADC areas, which is often used to discriminate cancer (low ADC) from benign tissue (high ADC). This effect is more strongly pronounced in tissues with higher ADC, such as prostate. Accounting for noise-related bias is important in studies where SNR is low or varies across the image, such as in images acquired with endorectal coil, and when images are acquired with phased arrays, especially for coils with higher number of receiver channels.

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