Analysis of Systematic Errors on Estimated Parameters in q-Space MRI

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Introduction: There is hope that q-space MRI will allow probing the micro-structure (1). However, on clinical scanners the effects of the finite duration of the diffusion encoding gradients become very important when interpreting the data. Today, parameters characterizing the probability density distribution (PDF) are estimated without taking these effects into account.
We have investigated the effects of the gradients on the basis of a simple model: one dimensional restricted diffusion between planar boundaries. In this case the MR-signal can be calculated exactly. Different reconstruction schemes of the PDF were considered and three characterizing parameters were analyzed: return-to-origin probability (RTO), standard deviation and kurtosis. It turns out that large systematic errors will result depending on the gradient timings.

Methods: In the short-gradient-pulse approximation, the MR signal is the Fourier transform of the averaged propagator:

$$S(q) = \int P(Z,\Delta)\exp(i2\pi qZ)dZ \qquad [1]$$

Here, the q-space coordinate is given by $q = \gamma g \delta$ with g the amplitude of the diffusion encoding gradients, δ the duration of one lobe and Δ the time separation between the onsets of the two lobes in the spin echo sequence. The averaged propagator represents the probability P the spins have diffused a distance Z in a time Δ. For restricted diffusion between reflecting planar boundaries (distance a), the averaged propagator becomes:

$$P(\rho,\mu) = 1-|\rho| + \sum_{n=1}^{\infty}\exp\left(-\pi^2 n^2 \mu\right)\left[\left(1-|\rho|\right)\cos(n\pi|\rho|) - \frac{\sin(n\pi|\rho|)}{n\pi}\right] \qquad [2]$$

with $\rho = Z/a$ and $\mu = D\Delta/a^2$ (diffusion coefficient D). By decomposing a finite duration gradient waveform into a sequence of impulses and using multiple propagators, the MR signal can be expressed exactly into matrix form (2).
The MR-signal $S(\theta)$ ($\theta = qa$) was calculated for different values of μ and $\varepsilon = \delta/\Delta$. Fourier reconstruction leads to the classical estimated PDF $P_F(\rho)$. A correction proposed in ref. (3) leaded to $P_L(\rho) = \eta P_F(\rho/\eta)$ with $\eta = \sqrt{(1-\varepsilon/3)/(1+\varepsilon)}$. The RTO-probability $P(\rho=0)$, standard deviation σ and kurtosis k were estimated. Another possible reconstruction is by using a Gram-Charlier expansion until fourth order (4):

$$P_{GC}(\rho) = \frac{\exp\left(-\rho^2/2\sigma^2\right)}{\sqrt{2\pi}\sigma}\left[1 + \frac{k}{4!}Her_4\left(\frac{\rho}{\sigma}\right)\right] \qquad [3]$$

This is equivalent to a 4-th order cumulant expansion of the MR-signal and is in fact valid until 5-th order because the skewness is zero in our case.
The relative error $R_X = (X - X_c)/X_c$ (with X the estimated parameter and X_c the correct one based on eq.[2]) was determined in each case. Finally $A\,P(\rho,\mu)$ (see eq.[2]) was fitted to the Fourier reconstructed PDF (fitted parameters A and μ) to check if an effective (normalized) diffusion time μ_{fit} could be introduced.

Results and conclusions: Figure 1 shows the correct PDF (averaged propagator from eq.[1]) for $\mu = 1$ and three reconstructed ones as described above ($\varepsilon = 0.5$). It can be seen that direct Fourier reconstruction overestimates the height and underestimates the width of the PDF. The correction proposed in ref. (3) improves this partially. By visual inspection, the Gram-Charlier expansion leads to the best approximation. For direct Fourier reconstruction, the relative error for the standard deviation can be as large as -60% for $(\mu,\varepsilon) \in [0,1]$ (see Fig.2). For the RTO-probability, the error can be even 130% (see Fig.3). Kurtosis leads to even more dramatic errors (400% at small $\mu \approx 0.1$ down to 10% around $\mu \approx 0.2$ and up to 60% at $\mu = 1$).
The Lori-correction doesn't improve the standard deviation and kurtosis (this could be expected because the used transformation does not change the moments of the PDF). However, it does improve the RTO (maximum error 40%). The Gram-Charlier expansion leads to visual better estimations but the relative errors on the parameters have comparable order of magnitude as for the other reconstructions. The fitted surface $\mu_{fit}(\mu,\varepsilon)$ was not smooth but contained steep transitions suggesting that the data cannot be interpreted in terms of an averaged propagator with effective diffusion time.
In conclusion, estimated PDF's and their related parameters in q-space imaging contain significant systematic errors when performed on clinical systems. Unfortunately, these errors cannot be quantified in practice because the correct diffusion model is still unknown.

References:
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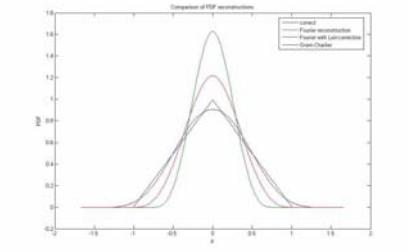

Fig.1: Comparison of PDF-reconstructions.

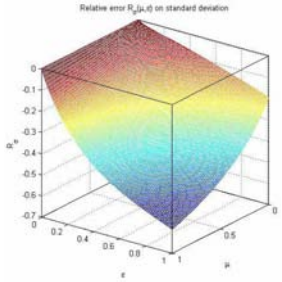

Fig.2: Effect of gradients on standard deviation.

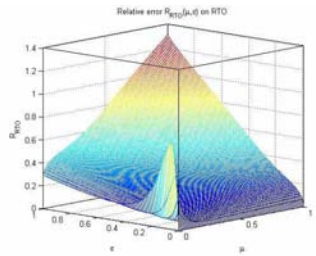

Fig.3: Effect of gradients on RTO-probability.