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Robust estimator framework in diffusion tensor imaging

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Abstract

Diffusion of water molecules in the human brain tissue has strong similarities with diffusion in porous media. It is affected by different factors such as restrictions and compartmentalization, interaction with membrane walls, strong anisotropy imposed by cellular microstructure, etc. However, multiple artefacts abound in *in vivo* measurements either from subject motions, such as cardiac pulsation, bulk head motion, respiratory motion, and involuntary tics and tremor, or hardware related problems, such as table vibrations, etc. All these artefacts can substantially degrade the resulting images and render post-processing diffusion analysis difficult or even impossible. In order to overcome these problems, we have developed a robust and efficient approach based on the least trimmed squares algorithm that works well with severely degraded datasets with low signal-to-noise ratio. This approach has been compared with other diffusion imaging post-processing algorithms using simulations and *in vivo* experiments. We demonstrate that the least trimmed squares algorithm can be easily adopted for multiple non-Gaussian diffusion models such as the biexponential model. The developed approach is shown to exhibit a high efficiency and accuracy and can, in principle, be exploited in other diffusion studies where artefact/outlier suppression is demanded.

Keywords: diffusion tensor imaging, robust estimator, human brain imaging

Introduction

Diffusion tensor imaging (DTI) is a powerful non-invasive medical technique allowing one to probe the microstructure of human brain tissue on the micrometre scale [1,2]. Geometrical properties of the biological tissue [3,4] such as preferable fibre orientation can easily be visualised by the diffusion tensor reconstructed from diffusion-weighted signal attenuation curves. In turn, DTI provides multiple additional characteristics of the tissue based on the rotational invariants of the diffusion tensor such as fractional anisotropy (FA), mean diffusivity (MD), radial/axial diffusivity, Westin's metrics, etc. [3-7]. Diffusion scalar metrics are an important source of biomarkers which are intensively exploited in many clinical studies and help one to diagnose different diseases such as acute stroke, tumours,

neurodegenerative/aging related changes in white matter of the human brain, Alzheimer's disease, Parkinson's disease and many others [8-10]. However, the efficacy and reliability of diagnosis with DTI are strongly dependent on the workflow, experimental settings (shimming, pulse sequence, gradient encoding schemes, etc) and post-processing algorithms (motion/eddy current/EPI corrections, noise correction, fitting algorithm, etc) [11,12].

In vivo, the measurement of diffusion signal attenuation can be distorted by multiple artefacts caused by bulk head motion, cardiac pulsation, respiratory motion and other effects such as neurological motion disorders with tics and tremor. Hardware imperfections, such as table vibrations caused by switching of magnetic gradient fields, are an additional source of artefacts. As a consequence, the measured dataset can be corrupted and can exhibit large signal drop-outs, also known as outliers. In turn, diffusion tensor evaluation becomes unstable and frequently leads to erroneous values. During the last decade, many different approaches have been introduced [13-15] in order to exclude artefacts from the diffusion signal attenuation and to improve the accuracy of tensor estimation. These proposed algorithms, such as RESTORE [13], least median squares or least trimmed squares (LTS) [14] and PATCH [15], are well conditioned, either in the case of high signal-to-noise ratio (SNR) or when a redundant dataset is measured. These approaches exploit different estimators from robust statistics. The robust statistics produce the estimators that are insensitive to significant deviations from the model assumption and incorporates the properties of the classic statistics. The most simple and scholastic example is a median. Indeed, slight deviations in the original dataset only weakly influence the median estimation.

At the same time magnetic resonance images tend to be influenced by various random factors usually referred to as "noise" as well. The complexity of modern methods for fast imaging with multiple-coils for parallel imaging reception and reconstruction, sophisticated gradient coils, the local field inhomogeneities and human tissue singularities related to physiological artefacts allow one to hypothesize that the noise distribution over the image is spatially dependent and demands special algorithms for a appropriate noise treatment [16-18]. It is noteworthy that conventional noise correction approaches, such as background estimation or histogram algorithm (see ref. [17] for details), operate into the frame where noise is the same for the whole image. However, the noise correction becomes crucial in the case of the non-Gaussian diffusion models where low SNR is a result of using high diffusion weightings. In particular, the biexponential model [18,19] suffers from the problems related to the noise/outlier artefacts due to very low SNR where signal decay is comparable to the noise. In this paper we present the robust post-processing framework which allows one to overcome these problems with outliers/noise and to produce reliable diffusion tensor estimations. The developed framework can be easily adapted to many different models of diffusion such as the biexponential model, for example.

Methods and Materials

Outlier detection and correction

The typical fitting algorithm applied to fit the signal attenuation curve is the least squares approach (LSQ). In the case of the conventional monoexponential fitting function when the signal attenuation can be approximated by Gaussian diffusion, it can be expressed as follows:

$$f_{\mathrm{LSQ}}(d) = \|S - S_0 \exp(-\mathbf{B}\, d)\|^2, \tag{1}$$

where $\|\cdot\|$ denotes the vector norm, S is the vector consisting of measured signal, S_0 is the signal amplitude in the absence of diffusion weightings, $\mathbf{B}$ is the b-matrix $N\times 6$ (N is a number of diffusion gradients) consisting of gradient unit vectors, $[g_x, g_y, g_z]$, and appropriate b-values in each row as $b\cdot[g_x^2, 2g_xg_y, 2g_xg_y, g_y^2, 2g_yg_z, g_z^2]$, d is a vector representation of the diffusion tensor $\mathbf{D}$ in form $[D_{xx}, D_{xy}, D_{xz}, D_{yy}, D_{yz}, D_{zz}]$. The diffusion tensor $\mathbf{D}$ has only six independent elements due to symmetry reasons [9,14]. The classical

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least squares method exploits the sum of squared residuals. However, any deviation of the measured signal S_i from a hypothesis leads to substantial deviations in the fitting parameters, d, even with the large number of encoding gradients N. In order to improve the estimation one can apply the robust estimator, for example the least trimmed squares approach. As a result, one obtains a robust estimator with a high resistance to contamination of the raw datasets by outliers. The amount of outliers can reach up to 50% of the dataset. In this case, the following minimization function is evaluated:

$$f_{\mathrm{LTS}}(d) = \sum^{h}_{i=1} [r_i^2], \tag{2}$$

where residuals r_i are arranged in such a way that $r_1<r_2<\ldots<r_N$ and h is a truncation factor from the range $[N/2+1, N]$. In the case of the biexponential model the residuals are estimated using two diffusion tensors as follows:

$$f_{\mathrm{BiLS}}(d_{\mathrm{fast}}, d_{\mathrm{slow}}) = \|S - S_0 \{ f_a \exp(-\mathbf{B}\, d_{\mathrm{fast}}) - (1-f_a) \exp(-\mathbf{B}\, d_{\mathrm{slow}}) \}\|^2, \tag{3}$$

where d_{fast} and d_{slow} are the fast and slow components of the diffusion tensor, respectively, f_a is the relative fraction of the fast component. In the case of the biexponential model the robust least trimmed squares approach keeps the same procedure as is in Eq. (2), excepting using the residuals from Eq. (3).

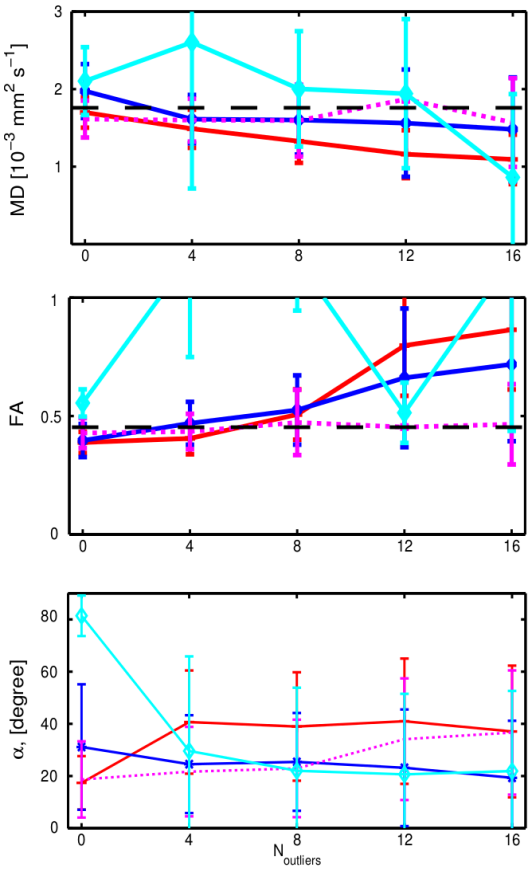

Figure 1. Results of a comparison between different algorithms of statistically simulated diffusion tensor estimations (300 trials). LSQ is marked by red, RESTORE – blue, PATCH – cyan, and LTS – magenta. Black lines correspond to the true values of MD and FA.

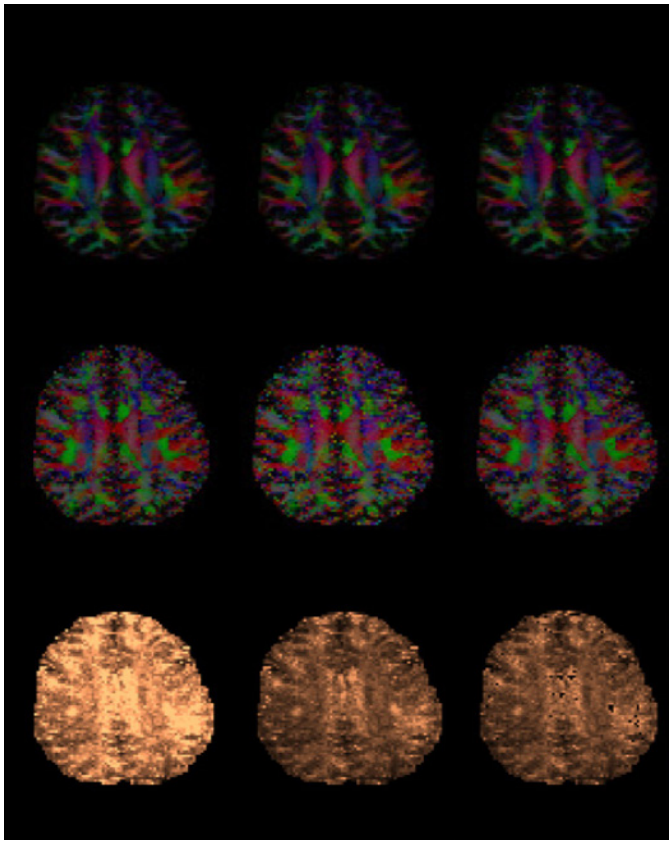

Figure 2. FA maps obtained for biexponential model of diffusion. From left to right: the columns refer to the method of LSQ, RESTORE and LTS. The rows correspond to the fast (top) and slow (middle) components of the biexponential model, and error maps (bottom).

Noise correction

The noise correction scheme is described in detail in Ref. [17]. The robust estimator in the noise correction algorithm is the median absolute deviation (MAD) and is assessed in each voxel. This estimator is very simple and computationally easy to implement, i.e. does not produce time-consuming evaluations. Note that for high diffusion weightings the noise cannot be considered as the Gaussian but should be described by the Rician distribution [17]. For this purpose we applied the correction function, depending on SNR, to the standard deviation obtained from MAD [17].

Experimental

In vivo diffusion brain experiments were carried out with a whole-body 3T Siemens MAGNETOM Tim Trio scanner (Siemens Medical Systems, Erlangen, Germany). A body coil was used for RF transmit and the manufacturer supplied 12-element phased array coil for signal receive. The gradient system provided a maximal gradient strength of 40 mT/m. Diffusion-weighted images were acquired using a bipolar gradient, twice refocused double spin-echo echo-planar imaging pulse sequence provided by Siemens Medical System. We used fifteen *b*-values [0,200,400,600,800,1000,1500,2000,2500,3000, 3500,4000,5000,6000,7000] s mm^{-2} and six non-collinear directions of the diffusion encoding gradients. The voxel size was 2×2×2 mm^3 and data matrix = 88×128, FOV = 256 mm, and the partial Fourier sampling factor was 5/8. The echo time, TE = 113 ms and the repetition time, TR = 1000 ms. Acquisitions were repeated 32 times for two slices. Each repetition takes 1.4 min. For demonstration purposes, we studied a 27-year old healthy male volunteer after providing a written, informed consent. The study was performed in accordance with the ethical approval from the local ethics committee.

Results

In order to illustrate the typical problems of post-processing procedures we performed simulations. The signal attenuation of the *a priori* known diffusion tensor was simulated for 30 diffusion directions and corrupted by the Rician noise (SNR = 10). The results are presented in Figure 1: we see how different algorithms ameliorate the diffusion tensor estimation. In the simulation we used a known diffusion tensor with the following parameters: eigenvalues are [1.1; 1.5; 3.0] × 10^{-3} mm^2 s^{-1}, MD = 1.87 × 10^{-3} mm^2 s^{-1}, FA = 0.4915, the main eigenvector of the diffusion tensor is directed along **Z** axis, with the random Rician noise and different number of outliers with random amplitudes from the range [0, 1.5]. The parameters of the diffusion tensor (namely, MD, FA, and angular deviation from original direction of diffusion tensor) have been estimated using the LSQ (red), RESTORE (blue), PATCH (cyan) and LTS (magenta) algorithms.

In Figure 2 we present the results of estimations of the biexponential diffusion model for *in vivo* experiments. In the first step, we used the BURST noise correction algorithm [17] for the measured dataset. After that, we applied three algorithms, namely, LSQ (first column), RESTORE (second column) and LTS (third column) in order to produce FA maps for the given slice. The colour coded FA maps for the fast and slow diffusion tensors and the resulting error maps are presented in Fig. 2.

Discussion and Conclusion

In this manuscript we address potential problems that arise in an estimation of typical diffusion scalar metrics in *in vivo* experiments. We compared the different post-processing approaches in order to find the most efficient and accurate method. In the simulation we see that not all robust approaches are equal in the resulting estimations, particularly, the PATCH algorithm exhibits the problem in the estimation of the main eigenvector orientation. The low SNR (in our case, about 10) typical for clinical studies introduces additional problems in the estimations of all algorithms and produces notable variations

of scalar metrics. As a result, based on the simulations, the LTS algorithm was selected as the best estimator of FA, MD and angular deviation. In practice, the accurate estimation of the main eigenvector is especially important for further tractography due to a reduced uncertainty in fibre tracking evaluation. At the same time, precision of evaluated diffusion tensors in the biexponential model has a great impact on the slow component of diffusion tensors. The slow diffusion tensor is a source of additional microstructure information of human brain tissue [19]. Thus, the LTS algorithm has demonstrated its potential in accurate estimations of diffusion scalar metrics in more sophisticated non-Gaussian diffusion models.

The developed algorithm exhibits a sufficient computational speed, numerical stability and precision, and it is rather insensitive to the presence of outliers at low SNR. These features should allow one to implement the LTS approach as an important tool in the optimisation of data treatment from DTI protocols with conventional and high diffusion weightings.

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