Heim, Hahn, Auer:

# Diffusion Tensor Imaging: on the assessment of data quality - a preliminary bootstrap analysis

Sonderforschungsbereich 386, Paper 356 (2003)

Online unter: http://epub.ub.uni-muenchen.de/

# Diffusion Tensor Imaging: on the assessment of data quality – a preliminary bootstrap analysis

S. Heim[1], K. Hahn[2], D. P. Auer[1]

[1]Max-Planck-Institute of Psychiatry, Munich, Research Group NMR

[2]Gesellschaft für Strahlenforschung (GSF), Neuherberg, Institute of Biomathematics and Biometry

08/2003

## Abstract

In the field of nuclear magnetic resonance imaging, diffusion tensor imaging (DTI) has proven an important method for the characterisation of ultrastructural tissue properties. Yet various technical and biological sources of signal uncertainty may prolong into variables derived from diffusion weighted images and thus compromise data validity and reliability. To gain an objective quality rating of real raw data we aimed at implementing the previously described bootstrap methodology (Efron, 1979) and investigating its sensitivity to a selection of extraneous influencing factors.

We applied the bootstrap method on real DTI data volumes of six volunteers which were varied by different acquisition conditions, smoothing and artificial noising. In addition a clinical sample group of 46 Multiple Sclerosis patients and 24 healthy controls was investigated. The response variables (RV) extracted from the histogram of the confidence intervals of fractional anisotropy were mean width, peak position and height.

The addition of noising showed a significant effect when exceeding about 130% of the original background noise. The application of an edge-preserving smoothing algorithm resulted in an inverse alteration of the RV. Subject motion was also clearly depicted whereas its prevention by use of a vacuum device only resulted in a marginal improvement. We also observed a marked gender-specific effect in a sample of 24 healthy control subjects the causes of which remained unclear. In contrary to this, the mere effect of a different signal intensity distribution due to illness (Multiple Sclerosis) did not alter the response variables. In conclusion bootstrap procedure could be proved to be a highly sensitive, however unspecific method in order to assess DTI data quality.

**Keywords:** bootstrap, DTI, data quality, reliability

Corresponding author:

PD Dr. Dorothee P. Auer

Kraepelinstraße 10 • 80804 Munich, Germany

Phone: +49-89-30622-293 • Fax: +49-89-30622-520 • E-mail: auer@mpipsykl.mpg.de

## BACKGROUND

Diffusion tensor imaging (DTI) is prone to numerous detrimental sources of artefacts which impair the reliability and validity of obtained data (Basser et al., 2002). Hereby, thermal noise, eddy currents, susceptibility artefacts, rigid body motion, physiological pulsation flow and further hardware issues as gradient miscalibration comprise the main components of the resulting overall noise.

While considerable research has focussed on the analysis and modelling of some of the perturbing factors (Skare et al., 2000; Anderson, 2001; Bastin et al., 1998) and the development of respective correction methods (Dietrich et al., 2001; Andersson, 2002; Parker et al., 2000), relatively few effort has been spent on estimating the residual error in real data.

A major problem following out of this is the uncontrolled prolongation into derived parameters (Skare et al., 2000; Pajevic et al., 2003) causing both random and systematic errors. In practical terms this particularly affects the reliability of results from fiber tractography (Lori et al., 2002; Jones, 2003), anisotropy estimates and in more general, any inferences from group comparisons which are enhanced by identically distributed data quality.

Therefore objective measures which indicate the data quality of an individual dataset are urgently needed. So far, several attempts have been made to determine the uncertainty in DTI data by specific metrics as for example the motion artefact index (Virta et al., 1999). However, the signal-to-noise ratio (SNR) is the most commonly used measure of data quality but may be criticised for a number of reasons: First, no unequivocal definition for the calculation of SNR exists which aggravates a universal comparison of SNR-related findings. In addition, the SNR is highly dependent on details of the NMR diffusion sequence and encoding scheme (e.g. *b*-values, number of acquisition repeats) (Anderson, 2001). A further drawback is the yet unknown sensitivity of SNR to motion artefacts which play a role in clinical trials.

We introduce a new approach to assess uncertainty of measured signals using a non-parametric bootstrap analysis (Efron, 1979). In this study, we aimed at implementing the bootstrap method in a research NMR environment in order to objectively characterize the quality of DTI data. Subsequently we investigated the sensitivity of the bootstrap method to several factors which frequently impair data quality in a clinical setting. First, we addressed the issue of background noise and artificially augmented the overall noise level by defined portions of the given original background noise. Contrary to this manipulation we explored the effect of an edge-preserving smoothing postprocessing step which can be expected to reduce background noise. Second, the influence of subject motion was studied by both provoking motion and preventing motion using a vacuum device. Third, we explored the impact of biological variables as gender and disease effects.

## Materials and methods

### Data acquisition and processing

Diffusion tensor images (DTI) were acquired on a clinical 1.5 T scanner (Signa Echospeed, General Electric, Medical Systems, Milwaukee, WI) using a spin echo echo-planar sequence with TR/TE = 4200/120 ms and 6 non-collinear gradient directions with a *b*-value of 880 or 0 s/mm$^2$. The acquisition consisted of a $128 \times 128$ image matrix with $24 \times 24$ cm$^2$ FOV giving $1.875 \times 1.875$ mm$^2$ in-plane resolution. A total of 24 slices of 3 mm thickness, 1 mm gap, were obtained with three or two repetitions for $b = 880$ and 0 s/mm$^2$ respectively. The effective diffusion tensor was calculated with (Papadakis et al., 1999) from which the fractional anisotropy (FA) (Basser et al., 1996) index was determined using in-house routines written in IDL (Research Systems, Incorporated (RSI) of Boulder, Colorado). Whole brain masks were produced semi-automatically applying a region growing algorithm and manual corrections where needed. This way, background and extracerebral tissue was cut-off. Brain white matter (WM) was then automatedly segmented using empirically derived thresholds as proposed by (Cercignani et al., 2001): A mean diffusivity threshold of $D \le 1.8 \times 10^{-3}$ mm$^2$/s effectively cuts off cerebrospinal fluid and a fractional anisotropy (FA) threshold of FA > 0.2 excludes grey matter.

### Bootstrap Method

The bootstrap method (Efron, 1979; 1994) as a non-parametric technique is predestined for analysing variables of partly or entirely unknown distribution such as FA in low SNR voxels (Pierpaoli et al., 1996; Skare et al., 2000, Pajevic et al., 2003). The application of the bootstrap procedure yields *N* sub- or resamples of a given dataset by drawing with replacement and, thus, provides various parameters describing the statistical properties of a measure of interest.

Fig. 1 depicts the bootstrap scheme that matches our clinical acquisition design. The $b_{ij}$ labels the *j*th measurement belonging to the *i*th gradient direction. In order to maintain the original structure of two unweighted ($b_{0j}, j = 1,2$) and three times six weighted ($b_{ij}$, $i = 1,\ldots,6$, $j = 1,2,3$) images, the resampling is subjected to the seven subsets represented by the rows. The order within each row need not to be considered due to the subsequent regression analysis for tensor calculation. Hence there are $\binom{n_i + k_i - 1}{k_i}$ possible combinations per gradient direction $i = 1,\ldots,6$, where $n_i$ designates the number of repeats and $k_i$ the number of drawings, here $n_i = k_i = 3$. Multiplication with the combinations from the unweighted case ($n_0 = k_0 = 2$) yields a total of $3 \cdot 10^6$ possible new datasets. Evidently, the reliability of the bootstrap method depends on the number $N$ of resamples and the number $n_i$ of equivalent observations.

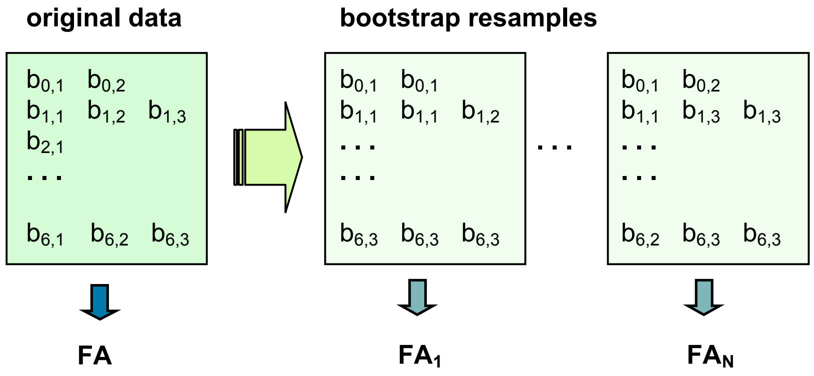


**Fig. 1:** Graphical illustration of the bootstrap method adapted to the present data acquisition scheme.

For the purpose of inferring the overall uncertainty contained in a single dataset, $N = 100$ resamples were generated yielding a voxelwise FA distribution from which the width of the 95% confidence interval (CI) is extracted as key feature. This first information of voxelwise reliability is then comprised in a histogram whose mean, peak position and height provide variables of the individual dataset quality. To allow direct interindividual shape comparison each histogram is normalised to the corresponding size of the identified WM.

The greater the variation of the two or three different comparable measurements, the more strikingly the bootstrap resamples may differ from each other. Hence, histogram-metrics are expected to reflect noise in general and, in particular, the aspect of between-scan motion.

In this paper, the bootstrap method was applied to study three aspects thought to directly or indirectly affect data quality: noise (adding noise, smoothing regimen (Hahn et al., 2003)), motion (experimentally enhanced (voluntary) motion or reduced (vacuum cushion)), and clinico-epidemiologic data (gender, disease).

NOISING

The mean signal-to-noise ratio (SNR) of a certain $b$-value image is defined as in (Bastin et al., 1998; Parker et al., 2000) by

$$\mathrm{SNR}_b = \frac{\overline{S_{\text{brain}}}}{\sigma}, \qquad (1)$$

where the mean magnitude signal $S$ within brain, calculated over the $n_i, i = 0,\ldots 6$, available repetitions for a given $b$-value, determines the nominator. The denominator describes the Gaussian noise which is estimated in accordance with (Gudbjartsson et al., 1995):

$$\sigma = \frac{\sigma_{\text{background}}}{0.66}\sqrt{\frac{1}{n}}. \qquad (2)$$

Background area covered four bars positioned far enough from both skull and image margin in order to avoid contamination due to artefacts. Modification with the factor 0.66 accounts for Rayleigh distribution while multiplication with $\sqrt{1/n}$ adjusts to repeated measurements.

For the purpose of investigating the effect of thermal noise, the six datasets recorded under normal condition are supplementarily adulterated. Artificial noise was simulated from a $N\left(0, \alpha \cdot \sigma_0^2\right)$ with $\sigma_0$ being estimate of the present underlying Gaussian noise (cf. eq. (2)). Following (Parker et al., 2000) the generated noise is added to the magnitude signals, whereby resulting negative intensities are set to zero. This operation leads to small deviations from the intended percentual increase of $\alpha \cdot 100\%$. The resulting noise degrees and averaged SNRs are listed in Table 1.

**Table 1:** Percentual noise increment and their corresponding SNRs

| effective percentual increase of noise | 0% | 10% | 20% | 30% | 40% |
|---|---|---|---|---|---|
| mean SNR ± std.dev. | 18.33 ± 4.89 | 16.68 ± 4.45 | 15.50 ± 4.14 | 14.23 ± 3.80 | 13.28 ± 3.54 |

**SMOOTHING**

Noise was reduced in two steps. First, the magnitude signals of one row in a bootstrap resample box, see Fig. 1, were voxelwise averaged. Then a filter chain (Hahn et al., 2003) was applied to this averaged magnitude signal to perform additional spatial smoothing. To conserve the inherent discontinuities in DTI data the filter is nonlinear, see Parker et al. (2000) and Hahn et al. (2003) for more details.

### MOTION EXPERIMENTS

For a small experimental study 6 volunteers (3 males, 3 females, age in years: $26.8 \pm 2.9$) were investigated under three different conditions: First, according to the imaging scheme described above, a volume of a total of 20 image datasets was acquired using a vacuum device in order to minimize head motion. Then, each subject was instructed to lie as still as possible in the scanner with standard fixation but no vacuum cushion identical to the clinical setting. Finally, a third DTI acquisition was recorded while the subject was asked to yawn, chew, shake or nod the head, in order to induce voluntarily typical motion in x, y, and z direction. The different DTI experiments were collected within one scanning session in order to reduce the diffusion variability conditioned by the current amount of water molecules in the brain or other scanner dependent instabilities.

### DISEASE STUDY GROUP

In clinical neuroscience, DTI is currently mainly applied to detect disease-specific alterations based on formal group comparisons of DTI derived voxelwise, regional, tissue specific or global variables. The validity of the deployed statistics, however, relies on the assumption that both groups yield comparable data quality which remains largely untested. Therefore, we were interested to test whether the bootstrap resampling would allow to detect potential non-specific disease effects on DTI variables. To this end, DTI data from an on-going clinical study comparing patients with Multiple Sclerosis (MS) and healthy control subjects were analysed for intergroup comparability.

## RESULTS AND DISCUSSION

### EFFECT OF NOISING

With the aim of simulating pseudo-realistic data of different noise levels, Gaussian distributed thermal noise was superimposed on the original baseline data (see noising description above). The maximal increment was chosen to reflect the spread of usual noise derived from a control group ($N$ = 24), i. e. mean regular noise plus twice the standard deviation. As Fig. 2 demonstrates, increasing noise is associated with a right shift and larger dispersion, namely lower accuracy of determining local, regional and global FA.

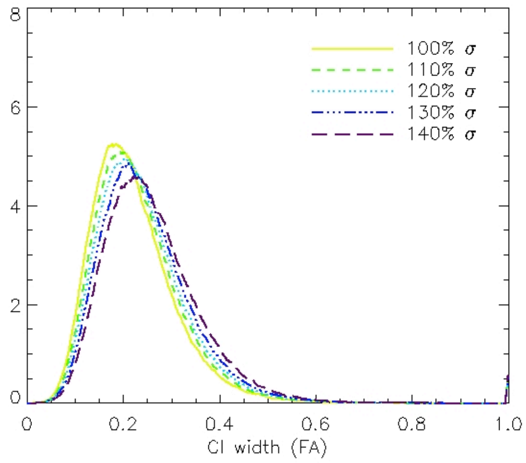


**Fig. 2:** Averaged histograms for various degrees of additional noising.

From a multivariate repeated measurement analysis with mean CI width, peak position and height as response variables, we can infer a significant influence of the general noise degree contained in an image volume (Wilks-Lambda, p-value = 0.001). Simple contrasts to the baseline, zero noised dataset allow a more precise conclusion: Noise resulted only in a significant effect when the level equals or exceeds 30%. Table 2 gives the corresponding p-values for the three depending variables.

**Table 2:** P-values of simple contrasts to baseline image for the three response variables.

| | | percentual increase of noise | | | |
|---|---|---|---|---|---|
| | | 10% | 20% | 30% | 40% |
| p-values of simple contrasts to 0% noised data | peak position | 0.821 | 0.243 | **0.027** | **0.010** |
| | peak height | 0.861 | 0.309 | 0.118 | **0.042** |
| | mean CI width | 0.923 | 0.543 | 0.190 | **0.049** |

## EFFECT OF SMOOTHING

In general edge preserving smoothing leads to amelioration in data with acceptable quality. Direct comparison of the unprocessed and processed, normally acquired data exposes a distinct improvement in the latter case (small left shift, less dispersion; Fig. 3 (a)). Similar results are achieved after the edge preserving smoothing of the datasets gained under the use of a vacuum cushion (Fig. 3 (b)), which is discussed in the ensuing section. Low-quality data, however, does not improve substantially. This is likewise apparent in Fig. 3 (b), where datasets containing strong motion artefacts remain hardly affected (minor deviation of dotted line compared to long-dashed). Since the motion experiment suggests a rather equivalent data quality with or without a vacuum cushion, the effect of postprocessing smoothing is further thoroughly studied relative to ‚normal‘ acquisition.

The corresponding graphic (Fig. 3 (a)) also depicts the artificially corrupted case (40% noise increment); all histograms are averaged over the six probands.

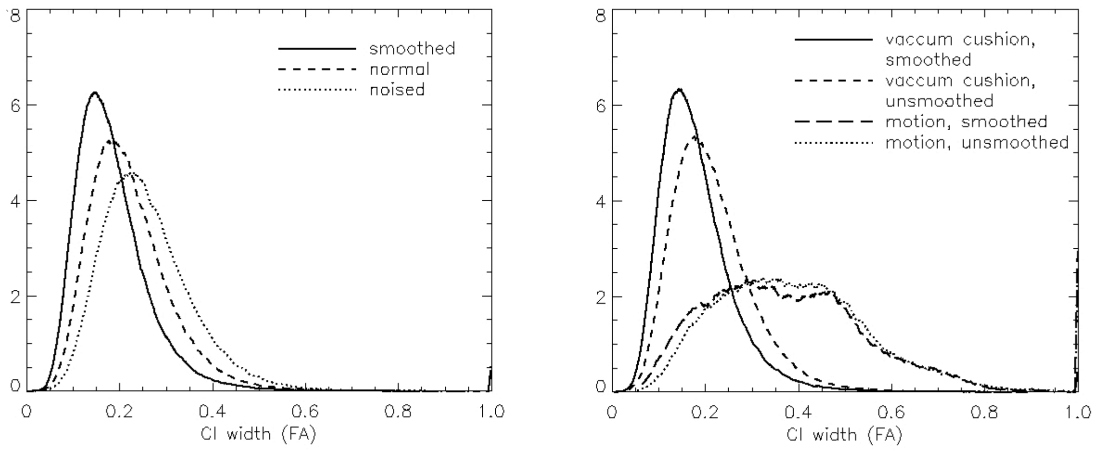


**Fig. 3:** Averaged histograms representing the effect of smoothing and noising compared to the unchanged original case (a). (b) illustrates the effect of smoothing when using a vacuum cushion or demanding for explicit motion.

A multivariate repeated measurement analysis verifies the visual finding of a distinctive improvement due to the application of edge preserving smoothing (overall p-value $< 0.0001$). Simple contrasts of the smoothing or noising level to normal give p-values 0.001 (peak position), 0.001 (peak height), $< 0.0001$ (mean width), and 0.01, 0.042, 0.049, respectively.

## EFFECT OF MOTION

Motion suppression is a general topic in MRI acquisition and using a vacuum cushion during the recording is thought to improve data quality by reducing involuntary motion. In order to analyse the effect of a vacuum cushion and of intentionally enhanced motion (chewing, nodding, shaking) on DTI data quality as assessed by the bootstrap technique, we conducted a small volunteer study.

From the graphical display (Fig. 4) emerges an evident effect of additional movements on data quality, thus making any further quantification dispensable in this regard. In contrast, the potential influence of the vacuum cushion is of major interest in particular with respect to necessary changes in the clinical protocol. Referring to this, data quality appears minimally improved (see left shift of solid line compared to dashed). We therefore applied a multivariate repeated measurement model with mean CI width, peak position and height as response variables and ‚vacuum cushion' versus ‚normal' acquisition as factor levels, thereby avoiding confounding with the dominant impact of explicit head motion. The resulting p-value of 0.422 indicates a fairly even data quality for both conditions. Univariate p-values from paired t-tests assume 0.1 (mean CI width), 0.1 (peak height) and 0.06 (peak position), respectively. Even though no statistically significant difference turned out for the use of the vacuum cushion, one has to account for the limited statistical power of this experiment. Thus, a minor positive effect of the vacuum cushion may go undetected.

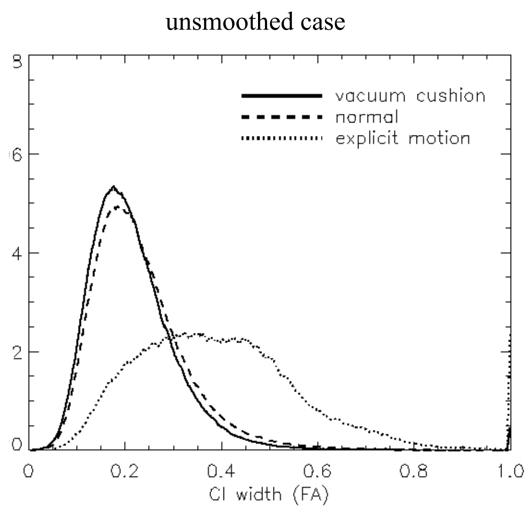


**Fig. 4:** Averaged histograms, basing on unsmoothed datasets, from three different data acquisition conditions.

## EFFECT OF GENDER AND DISEASE

A subsequent gender-specific comparison of the smoothed, normal and noised datasets (Fig. 5) reveals a striking gap between gender, though results based on subsample sizes of $N = 3$ merit careful interpretation.

The suggested difference in gender manifests, for instance, in the coincidence of the ‚normal' histogram from the males with the ‚noised' histogram from the females where the degree of noise was enhanced by 40%. This leads to the question whether the originally prevailing noise level was much lower in female than in male datasets. Consulting the

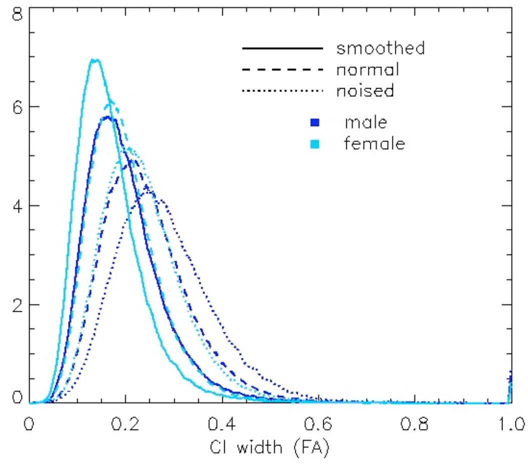


**Fig. 5:** Averaged histograms representing the effect of smoothing and noising compared to the unchanged original case, separated for sex.

common measure of image quality, no difference of SNR could be detected between genders. In fact, a supplementary inspection of $N = 24$ controls (10 males, 14 females) corroborates the finding of a gender dependent image quality as assessed by bootstrap approach (MANOVA, p-value < 0.0001). This subject matter is of enormous relevance for gender not being uniformly distributed in most diseases, e.g. MS.

However, a generalisation of a possible gender effect requires further investigation, in particular a seriously enlarged sample size. Beyond, the restriction of the WM compartment to a selected area such as the corpus callosum seems advisable due to varying head size of men and women. For this reason, the recorded slices cover different regions, i.e. tissues, up to now. As an appreciated side effect of the restriction the computational effort would reduce considerably.

Lastly, we applied the bootstrap method to test group comparability in order to determine whether the disease produces unspecific reduction of data quality. For this purpose, the already mentioned 24 controls and another 46 Multiple Sclerosis (MS) patients showing severe WM lesions were studied (Auer et al., 2003). When consequently restricting to females, no difference in image quality can be inferred between the two study groups (14 controls, 28 MS patients; MANCOVA, age as covariate, p-value = 0.278).Thus one benefit of the bootstrap method consists in the detection of potential confounds from mere data quality difference, prior to performing intergroup comparison.

## METHODOLOGICAL ISSUES AND LIMITATIONS

As obvious from Monte Carlo simulations, the application of bootstrap method leads to varying dispersion of voxelwise FA depending on (a) the seed of the random number generator, (b) the size of the pool from which subsamples are drawn with replacement and (c) the number of generated subsamples itself. Whereas (a) is basically increasing the offline computational effort, the size of the total sample pool (b) and the number of sampled subsets (c) can only be increased by acquiring more repeat scans and, thus, inevitably extending the total scanning time. This, however, is limited in a clinical setting. Yet the repeated application of bootstrap on the same dataset gave similar results, thus assuring the reliability of the method. The reproducibility in terms of a test-retest study could be satisfactorily ascertained and was investigated as well as within-scanner variability of FA (Pfefferbaum et al., 2003).

Concerning the motion experiment, the instructed simulation of motion mirrors realistic motion only roughly. The fact of instructing for moving inherently leads to overreaction, that is almost permanent motion in contrast to a naturally arising amount. Apart from heavily head wobbling, yet mere frequent eye movements as well as strong breathing, as linked with common bronchial infection, may results in markedly increased inhomogeneity of the image data. In general, the term ‚motion‘ comprises several confounding factors which cannot be isolated by such a simple experimental setting.

Regarding the use of a vacuum device, this preliminary study does not justify a general recommendation, in particular when weighing against the related drawbacks. First, there is no guarantee of vacuum sealing. Additional fixation of the patients heads is time consuming and thus increases the medical treatment expenses. Also, there is added discomfort in all patients and those who suffer abnormal anxiety may unnecessarily be stressed which, in turn, can lead to a breakup of the scanning process. On the other hand, the small sample size in our volunteer study and the fact that only young healthy volunteers were included, calls for further investigation of the subject including older and diseases subjects.

## OUTLOOK

In order to supplement the principal group comparability referring to data quality, the consideration of the disease effect will be expanded to further indispositions (Alzheimer disease, Mild Cognitive Impairment). The possible causes of the observed gender effect warrants further investigation. This includes the inspection of a sufficiently large sample, preferably homogeneous in age, and the restriction of the WM compartment. Beyond, more sophisticated simulations of movement are planned. Above all, the extension of the bootstrap technique to the recently developed fiber tracking algorithm (Gössl et al., 2002) promises to provide confidence regions for fiber tracts in the near future.

## CONCLUSION

Implementation of the bootstrap procedure results in automated quantitative assessment of data quality. Beyond, this approach turns out to be highly sensitive. Quality impairment due to gross errors, such as faulty acquisition evolved from technical issues or crude motion during the scanning time, is successfully identified. Gradual noise corruption of the magnitude signal is directly linked to increasing mean width of the confidence intervals for FA in white matter voxels. On the other hand, the application of bootstrap method proved the potential of a nonlinear smoothing technique to recover image quality. Sensitivity to biological effects, e.g. gender, could be preliminarily determined. On the other hand, bootstrap method does not allow to infer the underlying cause of a change in shape and derived measures, respectively.

## ACKNOWLEDGEMENTS

The authors thank Rosa Hemauer, Reinhold Borschke and Elke Schreiter for performing the data acquisition, Uwe Wolff for preparing the whole brain masks and especially Philipp Sämann for helpful discussion and general support. We gratefully acknowledge financial support from the SFB386 „Statistical Analysis of Discrete Structures“, sponsored by the German Science Foundation (DFG).

## REFERENCES


Anderson AW. Theoretical Analysis of the Effects of Noise on Diffusion Tensor Imaging. MRM 2001;46:1174-1188

Andersson JLR, Skare S. A Model-Based Method for Retrospective Correction of Geometric Distortions in Diffusion-Weighted EPI. NeuroImage 2002;16:177-199

Auer DP, Schubert MI, Gottschalk M, Pütz B, Weber F. Evaluation of Diffusion Tensor Imaging derived Disease Markers for Multiple Sclerosis: EDSS and the MSFC. Proceedings ISMRM 2003;11:2087

Bastin ME, Armitage PA, Marshall I. A Theoretical Study of the Effect of Experimental Noise on the Measurement of Anisotropy in Diffusion Imaging. MRI 1998;16:773-85

Basser PJ, Pierpaoli C. Microstructural and Physiological Features of Tissues Elucidated by Quantitative-Diffusion-Tensor MRI. JMR 1996;111:209-19

Basser PJ, Jones DK. Diffusion-Tensor MRI: Theory, Experimental Design and Data Analysis – a Technical Review. NMR Biomed 2002; 15:456-467

Cercignani M, Bozzali M, Iannucci G et al. Magnetization Transfer and Mean Diffusivity of Normal Appearing White and Grey Matter from Patients with MS. J Neurol Neurosurg Psychiatry 2001;70:311-7.

Dietrich O, Heiland S, Sartor K. Noise Correction for the Exact Determination of Apparent Diffusion Coefficients at Low SNR. MRM 2001;45:448-453

Efron B. Bootstrap Methods: Another Look at the Jackknife. Ann Statist 1979;7:1-16

Efron B, Tibshirani, RJ. An Introduction to the Bootstrap. Boca Raton, FL: CRC Press´1994

Gössl C, Fahrmeir L, Pütz B, Auer LM, Auer DP. Fiber Tracking from DTI Using Linear State Space Models: Detectability of the Pyramidal Tract. NeuroImage 2002;16:378-88

Gudbjartsson H, Patz S. The Rician Distribution of Noisy MRI Data. MRM 1995;34:910-14

Hahn K, Prigarin S, Pütz B. Spatial Smoothing for Diffusion Tensor Imaging with Low SNR. Discussion Paper 358, SFB 386, 2003, Ludwig-Maximilians-Universität München

Jones DK. Determining and Visualizing Uncertainty in Estimates of Fiber Orientation from Diffusion Tensor MRI. MRM 2003;49:7-12

Lori NF, Akbudak E, Shimony JS, Cull TS, Snyder AZ, Guillory RK, Conturo TE. Diffusion Tensor Fiber Tracking of Human Brain Connectivity: Acquisition Methods, Reliability Analysis and Biological Results. NMR Biomed 2002;15:493-515

Pajevic S, Basser PJ. Parametric and Non-Parametric Statistical Analysis of DT-MRI Data. JMR 2003;161:1-14

Papadakis NG, Xing D, Huang, ChLH., Hall LD, Carpenter TA. A Comparative Study of Acquisition Schemes for Diffusion Tensor Imaging Using MRI. JMR 1999;137:67-82

Parker GJM, Schnabel JA, Symms MR, Werring DJ, Barker GJ. Nonlinear Smoothing for the Reduction of Systematic and Random Errors in Diffusion Tensor Imaging. JMRI 2000;11:702-10

Pfefferbaum A, Adalsteinsson E, Sullivan EV. Reliability of Brain Diffusion Tensor Imaging. Proceedings ISMRM 2003;11:248

Pierpaoli C, Basser PJ. Toward a Quantitative Assessment of Diffusion Anisotropy. MRM 1996;36:893-906

Skare S, Li TQ, Nordell B, Ingvar M. Noise Considerations in the Determination of Diffusion Tensor Anisotropy. MRI 2000;18:659-69

Virta A, Barnett A, Pierpaoli C. Visualizing and Characterizing White Matter Fiber Structure and Architecture in the Human Pyramidal Tract Using Diffusion Tensor MRI. MRI 1999;17:1121-1133