# Testing the variability of Diffusion Spectrum Imaging (DSI): Inter- and intra-site comparison on "identical" 3T scanners

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## Introduction

Multi-center neuroimaging studies have more power than smaller ones to conduct sophisticated studies of basic neuroanatomy and clinical disorders. One important confound of combining images obtained from different scanners is the potential for scanner effects to introduce systematic error, thus making the interpretation of results difficult. Differences in diffusion imaging measurements due to scanner-dependent inaccuracies may either mimic or obscure true changes. In the context of multicentric Swiss project on brain connectivity in patients with epilepsy, we used DSI (Diffusion Spectrum Imaging) [1] acquired on different scanners to address the limitation of DTI (Diffusion Tensor Imaging) where imaging of multiple fiber orientation in a single voxel is not possible. Since DSI is a very recent development of MRI there is no information on inter- and intra-site reproducibility, while concerning the DTI there are very few studies on a 3T scanner and even less on cross center reliability measures [2].

## Method and material

Six healthy volunteers underwent DSI (2.2x2.2x3 mm; 44 slices; 257 directions; b-max 6400), T1-weighted MPRAGE and T2-weighted images, each one scanned once on each scanner and twice on one of them (3T Trio a Tim System, Siemens, Erlangen, Germany) using a 32-channel head helmet coil and matched acquisition sequences. A written informed consent was obtained from each subject before the acquisition. Three different standard analysis techniques were used to assess the reliability of our measurements:

- *Tract-based:* 70 cortical and 8 subcortical regions with anatomical landmarks were mapped from MPRAGEs image using Freesurfer 5.0 software [3]. Then some areas of interest were grouped together to create seven pairs of regions (ROIs) which are connected by some important fiber-bundles relevant to this study (Uncinate Fasciculus, Corpus Callosum body, Corpus callosum Splenium, Thalamocortical fibers, Fornix, Fronto-occipital fasciculus, Arcuate Fasciculus). After coregistering the ROIs to the diffusion image space using a nonlinear registration tool of FSL [4], the DTK [5] was used for the reconstruction of the ODF (Orientation Density Function). Tractography was performed in the white matter areas using an in-house streamline-based algorithm adapted to work with DSI data. Next, the Apparent Diffusion Coefficient (ADC) and the Fractional Anisotropy (FA) maps were obtained by fitting the tensor from DSI data choosing the lowest shells (33 directions), while the GFA (Generalized Fractional Anisotropy) [6] was directly computed from the ODFs. Finally, we performed our analysis using CV (Coefficient of Variation, standard deviation along all the subjects for every scanning session over the mean) and the ICC (Intra-class Correlation Coefficient, the correlation between two scanning session: site A and site B, site B and site B second scan) [7] on the mean value along the selected tracks of the three scalar maps, FA, ADC and GFA respectively.
- *Region-based:* Every FA, ADC and GFA map for each subject was registered to the MNI space where 3 regions of interest were drawn (Corpus Callosum Splenium(CCS), Corticalspinal Tract(CST), Uncinate Fascicle(UF)) by an expert neurologist. The measurements for the analysis of CV and ICC in this case, were the mean GFA (FA, ADC) for each ROI.
- *Whole brain Voxel-based*: We also explored the voxel-based analysis by performing a whole brain analysis meaning that for each voxel value (GFA, FA and ADC) the ICC and CV where calculated over all subjects.

## Results and discussions

As we can see from the table, the values of CV are all below 10% (values in green) for the regional voxel-wise analysis and almost all for the Tract-based analysis, which is desirable for biological variables related to imaging [8]. Values of ICC above 0.7 are considered as measures of high reproducibility [8]. From the table we can clearly see that for some big tracts such as the Fronto-occipital fasciculus (FOF) and Arcuate Fasciculus (AF) the ICC is high, but the contrary for smaller ones namely the fornix. For the regional based analysis, the ICC is high for all the three regions using the GFA measurements, but low for ADC in the inter-site comparison. This can be due to the fact that the FA and ADC were reconstructed by fitting a tensor from DSI data, and not directly measured from the ODFs. However, the intra-site comparison gives a slightly higher ICC over some fiber-bundles and regions, but the difference is not big enough comparing to the variance between the subjects. Moreover, visual inspection of the whole brain images showed very low variances between the sites. In figure 1 we illustrate this with the CV of GFA measures on the two different sites (A and B), we can see here that the CV is especially low in the white matter which is important for our study.

## Conclusion

By using three different methodologies we have shown that the regional based analysis shows a better reproducibility. This could be explained by the fact that the regions chosen where concentrated to areas with high anisotropy, while the Tract-based analysis is more sensitive to the instability of the fiber-tracking algorithm (especially for smaller tracts). GFA measurements performed better compared to the measurements from the fitted tensor; this is very likely due to the b-value used even at lowest shells in DSI acquisitions. The observed inter-scanner differences illustrate that nominal identical scanners gives a slightly different results compared to the intra-scan. However, given the fact that the overall variation in our study is very low, our findings support the feasibility of cross-site pooling of DSI data from identical scanners.

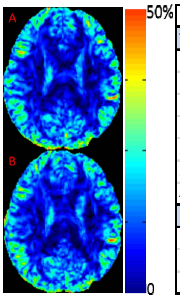


***Figure 1**: Whole brain voxel based analysis of the CV from GFA along all the subjects on site A and site B, same low variance in the white matter.*

***Table**: Tract based analysis on 7 tracts and regional based analysis on 3 regions, where the green values are considered measures of high reproducibility*

| | ICC INTER | | | ICC INTRA | | | CV site A | | | CV site B | | | CV site B second | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Tracks** | ***GFA*** | ***FA*** | ***ADC*** | ***GFA*** | ***FA*** | ***ADC*** | ***GFA*** | ***FA*** | ***ADC*** | ***GFA*** | ***FA*** | ***ADC*** | ***GFA*** | ***FA*** | ***ADC*** |
| *UF* | 0,78 | 0,88 | 0,65 | 0,44 | 0,73 | 0,72 | 0,12 | 0,11 | 0,05 | 0,14 | 0,12 | 0,08 | 0,09 | 0,07 | 0,05 |
| *CCB* | 0,62 | 0,41 | 0,12 | 0,79 | 0,77 | 0,37 | 0,06 | 0,08 | 0,03 | 0,06 | 0,06 | 0,04 | 0,05 | 0,05 | 0,02 |
| *CCS* | 0,47 | 0,42 | -0,20 | 0,55 | 0,54 | -0,04 | 0,07 | 0,07 | 0,01 | 0,09 | 0,09 | 0,03 | 0,05 | 0,04 | 0,01 |
| *TC* | 0,64 | 0,69 | 0,91 | 0,50 | 0,47 | 0,92 | 0,04 | 0,05 | 0,04 | 0,05 | 0,04 | 0,04 | 0,02 | 0,03 | 0,03 |
| *Fornix* | 0,12 | 0,35 | 0,42 | 0,31 | 0,29 | 0,49 | 0,06 | 0,04 | 0,03 | 0,03 | 0,05 | 0,05 | 0,11 | 0,10 | 0,10 |
| *FOF* | 0,74 | 0,78 | 0,91 | 0,85 | 0,76 | 0,96 | 0,06 | 0,07 | 0,03 | 0,05 | 0,06 | 0,04 | 0,07 | 0,07 | 0,05 |
| *AF* | 0,96 | 0,96 | 0,93 | 0,98 | 0,99 | 0,96 | 0,08 | 0,10 | 0,05 | 0,09 | 0,09 | 0,04 | 0,08 | 0,09 | 0,03 |
| **Regions** | ***GFA*** | ***FA*** | ***ADC*** | ***GFA*** | ***FA*** | ***ADC*** | ***GFA*** | ***FA*** | ***ADC*** | ***GFA*** | ***FA*** | ***ADC*** | ***GFA*** | ***FA*** | ***ADC*** |
| *CCS* | 0,86 | 0,66 | 0,14 | 0,96 | 0,77 | 0,83 | 0,06 | 0,05 | 0,04 | 0,05 | 0,03 | 0,04 | 0,07 | 0,03 | 0,05 |
| *CTS* | 0,94 | 0,94 | 0,55 | 0,98 | 0,95 | 0,52 | 0,06 | 0,07 | 0,03 | 0,06 | 0,06 | 0,05 | 0,07 | 0,08 | 0,02 |
| *UF* | 0,75 | 0,44 | 0,64 | 0,88 | 0,31 | 0,75 | 0,07 | 0,10 | 0,07 | 0,08 | 0,08 | 0,06 | 0,10 | 0,03 | 0,05 |

***References:** [1] V.J Wedeen et al / NeuroImag 41 (2008), [2] C. Vollmar et al / NeuroImage 51 (2010), [3] (http://surfer.nmr.mgh.harvard.edu/), [4] (http://www.fmrib.ox.ac.uk/fsl/), [5] Diffusion Toolkit, [6 ]D.S Tuch Magnetic Resonance in Medicine 52 (2004), [7] Shrout & Fleiss, Psychological Bulletin Vol. 86, No 2 1979. [8] S.Marenco et al / Psychiatry Research: Neuroimaging 147 (2006)*

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