Multisite Investigation of the Effect of Site and Protocol Variation on Fractional Anisotropy

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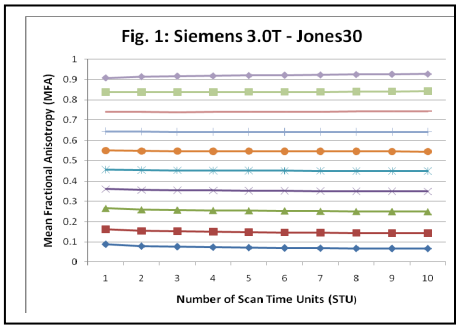
Introduction: Multi-site studies have become ubiquitous when large numbers of subjects are needed. Therefore, the characterization of site effects has become increasingly important. Studies have been undertaken to look at diffusion tensor imaging (DTI) metric reproducibility, e.g. [1], but little work has been done that includes site effects. The goals of this study were to 1) characterize the site effects on fractional anisotropy (FA), 2) determine the effect of number of gradient directions at each site, and 3) establish methods by which those wishing to include DTI in their multi-site study protocol can characterize their sites prior to the start of data acquisition and after hardware and/or software upgrades. The metric used was the reproducibility of FA as the amount of data used in the calculation was varied [2].

Materials and Methods: Five locally-recruited subjects were scanned at each of five sites. Three scanner vendors were represented: Siemens (2 sites), GE (1 site), and Philips (2 sites). Five of the sites had field strengths of 3.0T; the 6th site (Philips2) was 1.5T. Ten DTI scans were performed on each subject, using the Jones 30 set of diffusion-weighted directions (DWD) and 5 b=0 scans. Each Jones30/5 b=0 set was defined to be one "scan-time unit" (STU). Other protocol parameters include: b-value of 1000 s/mm^2, 2.5 mm^3 isotropic voxels, acquired matrix size: 96 x 96, full k-space coverage, FOV: 240 x 240 mm, number of slices: 25, parallel imaging: SENSE (p = 2) for Philips and GRAPPA for Siemens, 1 average, TR/TE (ms) were: Siemens = 4000/98.0 (site1), 3800/98.0 (site2); GE = 5200/99.5; Philips = 4000/101.19 (site2), 4000/100.00 (site1). In these scans TR and TE were harmonized as much as possible given the constraints set by different manufacturers. The final TE was dictated by the longest minimum TE achievable over all the sites. A separate set of 5 subjects was acquired was acquired on the GE scanner using their minimum TE (69.8 ms) with the chosen diffusion parameters, to determine the effect on FA of minimizing TE, a commonly used scenario. The achievable TR/TE is dictated by the achievable duty cycle of the scanner, the maximum gradient strength, and the scheme by which k-space is traversed. Data sets with different numbers of STU were constructed by concatenating a sequentially increasing number of data sets together before calculation of the tensors and associated metrics, i.e., data set 1 (STU=1), data set 1 and 2 (STU=2), data sets, etc. Each frame within the concatenated data set was registered to the first b=0 frame using a 12 degree-of-freedom registration code. Tensors and tensor metrics were calculated using in-house code written in C. Noise and skull voxels were removed using a combination of Brain Extraction Tool (FSL, University of Oxford) and in-house code written in IDL (ITT-VIS).



Analysis: Whole-brain FA histograms were calculated and divided into 0.1-wide bin ranges from 0.0 to 1.0; the mean FA value was calculated for each bin range. The STU=10 data set, calculated using all 10 co-registered runs, was used as a "gold standard" and to identify the bin-range membership of each brain voxel. The corresponding bin means were then calculated at each STU value using those voxels identified as belonging in a given bin for the STU=10 data. This gave estimates for the effect of decreasing the amount of data used in the tensor calculation for each site. The data was sub-sampled to smaller numbers of directions (15, 10, 6 directions) and the same analysis was repeated to discover the effect of reducing the number of gradient directions on FA reproducibility as STU was changed. Mean FA vs. STU for 6 brain structures (internal capsule {IC}, frontal white matter {FW}, centrum semiovale {CS}, globus pallidus {GP}, putamen {PUT}, and the splenium of the corpus callosum {SCC}) were generated from the Jones30 data. In addition, p-values were calculated to observe differences in bin means 1)at each STU level between vendors, 2)for different TE values within a vendor (GE), and 3) between field strengths.

	Jones30	PE15	PE10	PE6	mean	stdev
Siemens1 vs Siemens2 (both 3.0T)	1	0	3	4	2	2
GE1 vs GE1 (min TE vs long TE)	42	46	41	36	42	4
Siemens1 vs Philips1 (both 3.0T)	25	23	24	19	23	3
Siemens1 vs GE (both 3.0T)	6	4	1	2	3	2
Philips1 vs GE (both 3.0T)	11	16	13	10	12	3
Philips2 vs Philips1 (1.5T vs 3.0T)	19	30	34	54	34	15
Philips2 vs GE (1.5T vs 3.0T)	23	27	44	57	38	16
Philips2 vs Siemens1 (1.5T vs 3.0T)	24	27	35	44	32	9

Results and Discussion: As an example of the analysis, Fig. 1 shows for a Siemens scanner that ~2 STU of data is needed to eliminate the upward bias in the FA = 0.0- 0.1 bin at 3.0T for the Jones30 set of DWD's. At a sub-sampling to 6 DWD's, 5-6 STU's of data are needed (data not shown). This increase holds across vendor at 3.0T. With a field strength of 1.5T, 9 STU are needed to accurately measure FA values in the 0.0-0.1 bin. The table shows the number of significant differences in the 100 possible mean bin FA values (10 FA bins, 10 STU). There is very little difference between site, but within vendor (Siemens1 vs Siemens2). The largest differences are for the same site, but with TE minimized vs using the 'consortium' minimum TE value. In addition, the number of significant differences increases in the 1.5T vs 3.0T case as the number of gradient directions is reduced.

References: [1] Pfefferbaum, et al., JMRI, 18:427 (2003); [2] Farrell, et al., JMRI, 26:756 (2007).