

Reproducibility of brain atrophy measures assessed with ADNI back-to-back MRI scans

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Purpose

To compare the reproducibility of the FSL/Siena [1] whole brain atrophy measure for 44 different combinations of options and two MRI field strengths (1.5T and 3T). This study provides a check of recent results on the optimum parameters for FSL/Siena [3] using a different data set and methodology.

Methods

FSL/Siena [1] (<http://www.fmrib.ox.ac.uk/fsl>) is a commonly used and fully automatic software for measuring percentage brain volume change (PBVC) between two MRI scans of the same subject separated by time. For at least 118 subjects in the ADNI1 study, the back-to-back (BTB) MPRAGEs were acquired at two different field strengths (1.5T and 3T) for each patient visit. Because each patient visited multiple times, 200 time point pairs of BTB MPRAGEs with 12 to 18 months between patient visits were available at both field strengths.

1600 MPRAGE image volumes were processed in this study. Two MPRAGEs were acquired at each of the two field strengths for each patient visit. FSL/Siena required MPRAGEs from two separate patient visits and there were 200 such patient visit pairs.

FSL/Siena v4.1.4 was run on the 1600 MPRAGEs for each of 44 combinations of options. Four FSL/Siena parameters (-S, -R, -B, and default [--]) were combined with 11 different values of the f value (0.0, 0.1, 0.2, ..., 1.0). "g" was left as its default. The total computation time required for the study was 9 core-years.

The BTB reproducibility for each set of options for FSL/Siena was calculated by finding the 50th percentile of the absolute value of the BTB difference in the PBVC for the 200 patient visit pairs [1,2]. Bootstrapping with 10,000 repetitions was used to estimate the 95 percentile error bounds on the reproducibility.

Best FSL/Siena Options			Worst FSL/Siena Options		
Options	Reproducibility		Options	Reproducibility	
-B 0.2 1.5T	0.26	0.26 0.29	-S 0.9 1.5T	0.91	0.77 0.82
-B 0.1 1.5T	0.21	0.27 0.30	-S 0.8 3.0T	0.88	0.78 0.83
-R 0.6 1.5T	0.26	0.27 0.31	-- 0.9 3.0T	0.78	0.78 0.87
-B 0.3 1.5T	0.27	0.27 0.31	-- 0.8 3.0T	0.78	0.80 0.80
-B 0.2 3.0T	0.28	0.28 0.31	-S 0.9 3.0T	0.80	0.83 0.88
-R 0.4 1.5T	0.25	0.28 0.31	-- 0.8 1.5T	1.00	0.85 1.00
-R 0.5 1.5T	0.23	0.28 0.28	-R 0.9 1.5T	0.88	0.86 1.00
-R 0.4 3.0T	0.28	0.28 0.32	-B 0.7 1.5T	0.74	0.91 0.91
-- 0.4 3.0T	0.29	0.28 0.33	-S 1.0 3.0T	0.98	0.99 0.99
-- 0.6 1.5T	0.24	0.28 0.35	-- 1.0 3.0T	1.00	1.03 0.99
-B 0.1 3.0T	0.27	0.29 0.33	-B 0.7 3.0T	0.77	1.03 1.00
-R 0.6 3.0T	0.27	0.30 0.25	-B 0.0 3.0T	1.13	1.13 1.18
-S 0.4 3.0T	0.29	0.30 0.30	-B 0.8 1.5T	0.98	1.18 1.00
-- 0.0 1.5T	0.33	0.34 0.34	-R 1.0 3.0T	0.98	1.19 1.00
-R 0.5 3.0T	0.28	0.30 0.36	-B 0.0 1.5T	1.07	1.24 1.00
-S 0.5 3.0T	0.28	0.31 0.33	-B 0.8 3.0T	1.03	1.32 1.00
-B 0.5 1.5T	0.30	0.31 0.40	-B 0.9 1.5T	1.00	1.92 1.00
-S 0.4 1.5T	0.27	0.32 0.32	-R 1.0 1.5T	1.00	1.95 1.00
-R 0.7 1.5T	0.27	0.32 0.32	-B 0.9 3.0T	1.00	1.96 1.71
-R 0.7 3.0T	0.28	0.32 0.34	-B 1.0 3.0T	1.00	2.47 1.00
-- 0.5 3.0T	0.28	0.32 0.35	-B 1.0 1.5T	0.98	4.56 0.99

Table 1. Reproducibility, with 95% error bounds, of the back-to-back (BTB) ADNI1 MPRAGEs for a range of FSL/Siena options and two field strengths. Each reproducibility is the median of the absolute value of its respective BTB distribution.

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ADNI1 Back-to-Back MPRAGEs

While rarely mentioned in the literature, as part of the first Alzheimer's Disease Neuroimaging Initiative (ADNI1) study, the 3D T1-weighted MRI scans (the so-called MPRAGE sequences) were acquired in duplicate during each patient visit - with the acquisition of the second MPRAGE starting within seconds of completion of the first. As ADNI has over 800 subjects - with an average of 6 visits each - spread over several years, roughly 9,000 back-to-back (BTB) MPRAGE were available to probe the performance of brain atrophy measures [2].

Results

The FSL/Siena option combination that yielded the best 50% reproducibility was "-B f=0.2" on 1.5T and yielded 0.26% PBVC. However 10 other option combinations fell with the 95% error bound of the best. The 0.26% is comparable to smallest averaged treatment effect per subject.

Of the best 11 option combinations 7 were 1.5T while the remaining 4 were 3T with "-B f=0.2" also being the best 3T option. Thus the PVBC reproducibility at 3T is no better, and perhaps slightly worse than 1.5T.

While, for the most reproducible results, bootstrapping yielded reasonable estimates of the 95% error bounds, it occasionally yielded unreasonable results, especially for the options with the poorest reproducibility. Poor bootstrapping is an indication of a BTB distribution departing even farther from Gaussian than shown in Figure 1.

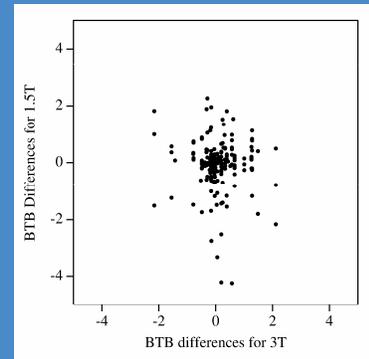


Figure 1. BTB reproducibility for 3T versus 1.5T by subject for the best 1.5T and 3T options. The large number of outliers indicates the BTB distributions depart from Gaussian. The 2D distribution indicates poor reproducibility is not a characteristic of a subject [2].

Conclusions

- The most reproducible combination of options for FSL/Siena at both 1.5 and 3T was "-B f=0.2", inline with recent reports [3].
- The reproducibility of the 3T MPRAGEs was no better than 1.5T and perhaps slightly worse.
- The large shoulders on the BTB distribution at both field strengths poses a significant problem for robust statistical analysis of FSL/Siena results.

References: [1] Smith SM et al. *NeuroImage* 2007;36:1200. [2] Cover KS, et al. *Psychiatry Research: Neuroimaging*. 2011;193:182. [3] Popescu V et al. *NeuroImage* 2012 Epub.