

Assessing intra- and interscanner variability of automated brain volumetry using SPM12, SIENA, SIENAX

Background: Brain volume loss (BVL) has been proposed as a surrogate marker of neurodegeneration in Multiple Sclerosis (MS). Recent advances in image post-processing have fostered measures of BVL/brain atrophy in clinical trials. However, a number of confounding factors impede interpretation of brain atrophy measures on a single subject level. Among these are methodological limitations (test/re-test variability) next to biological factors like the washout of inflammatory edema leading to "pseudoatrophy" and hydration status. These issues need to be taken into account to avoid misinterpretation of findings.

Objectives: To compare intra- and interscanner variability of SPM12, SIENA, and SIENAX. For these techniques the impact of measurement variability on longitudinal volumetric studies was assessed. Minimum percentage volume differences necessary to detect a significant volume change between two intra-individual measurements were determined.

MRI data: Three-dimensional (3D) T1-weighted magnetization prepared rapid gradient echo (MPRAGE) scans of 51 healthy subjects from the Alzheimer's Disease Neuroimaging Initiative (adni.loni.usc.edu) repository were included into this study. Each subject was scanned twice on two different scanners (1.5 T and 3 T) (4 scans per patient/total=204 scans) within a few weeks. The data was acquired at 50 different imaging centers. The two scans for each patient and platform were acquired back-to-back during a single imaging session.

Methods: For each patient intrascanner (1.5 T vs. 1.5 T and 3 T vs. 3 T scan) and interscanner variability (first 1.5 T vs. first 3 T scan) was determined.

For all scans the normalized total brain volume was computed with SPM12 (1) (using default parameters, except that the image data were sampled every 2 mm instead of the default 3 mm) and FSL-SIENAX (2) (configuration BET: f=0.2 and reorientation=fslswapdim). For SPM12, normalization of brain volumes (white- and gray matter) was performed applying a method described in (3). Percentage brain volume change (PBVC) was determined based on normalized brain volumes:

$$PBVC = 100 * \frac{v2 - v1}{v1}$$

For SIENA (2) the PBVC was directly computed between the paired scans (configuration BET: -B f=0.5).

Since the scans are acquired back-to-back no brain volume change is expected (PBVC should be 0) expected. Therefore the measured PBVC between the two scans can be used as measure for the intra- and interscanner variability (measure for test-retest error). For each method the 25th percentile, the median, and the 95th percentile of the absolute PBVC values were computed (102 PBVC measures for intrascanner setting, 51 PBVC measures for the interscanner setting).

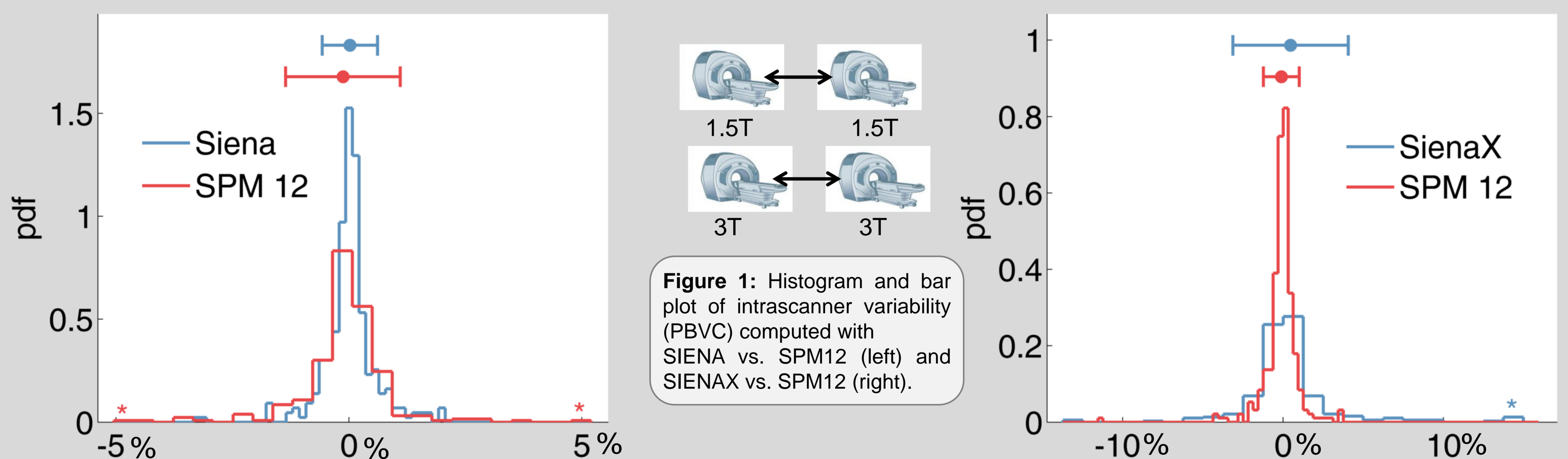


Figure 1: Histogram and bar plot of intrascanner variability (PBVC) computed with SIENA vs. SPM12 (left) and SIENAX vs. SPM12 (right).

| Method | Intrascanner variability (1.5 T vs. 1.5 T, 3 T vs. 3 T scan) [25 th percentile, median , 95 th percentile] of abs(PBVC) | Interscanner variability (1.5 T vs. 3 T scan) [25 th percentile, median , 95 th percentile] of abs(PBVC) |
|--------|---|--|
| SPM12 | [0.05, 0.24 , 1.28] | [0.21, 1.74 , 5.44] |
| SIENAX | [0.16, 1.93 , 14.38] | [0.61, 4.96 , 19.67] |
| SIENA | [0.01, 0.15 , 0.90] | [0.20, 1.57 , 4.97] |

Conclusions:

- For quantification of whole brain volume loss in longitudinal studies SIENA appears to outperform SPM12 in the intrascanner setting.
- SPM12 has a significant lower variability than SIENAX and hence is better suited for cross-sectional measurements.
- All methods feature a significantly higher variability when baseline and follow-up scans were acquired on different devices with different field strengths.
- The minimum absolute percentage volume difference between two MRI scans of the same subject (scanned on the same scanner) necessary to detect a significant volume change (p=0.05) beyond the level of intrinsic noise of the methodology is 1.28% for SPM12, 14.38% for SIENAX, and 0.9% for SIENA.

*Data used in preparation of this study were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. A complete listing of ADNI investigators can be found at: http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf

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