

Jorge Jovicich^{1,2}, Silvester Czanner^{1,2}, Brian Quinn^{1,2}, Jenni Pacheco^{1,2},

Andre van der Kouwe^{1,2}, Peter J Snyder⁴, Mostafa Analoui⁴, Marilyn Albert⁵, Rahul Desikan^{1,6},

Ron Killiany^{1,6}, Bruce Fischl^{1,2}, Brad Dickerson^{1,3}

¹MGH/MIT/HMS Athinoula Martinos Center for Biomedical Imaging, Charlestown, MA

Departments of ²Radiology and ³Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

⁴Pfizer Global Research & Development, Groton, CT

⁵Division of Cognitive Neuroscience, Department of Neurology, Johns Hopkins School of Medicine, Baltimore, MD

⁶Department of Anatomy and Neurobiology, Boston University, Boston, MA, USA



INTRODUCTION

- Background:** Longitudinal MRI studies offer the potential to quantify changes in brain structure over time in neurodegenerative diseases, such as Alzheimer's disease, and may ultimately provide useful biomarkers of disease progression [1]
- Limitation:** An important challenge for such studies is to minimize instrumentation-related variability in the images, thereby reducing noise and increasing power to detect potential biologic effects of interest [2].
- Goal:** Obtain estimates of variance present in imaging data when healthy older subjects are scanned at two week intervals on the same scanner and on different scanners at different platforms and field strengths.
- Note:** This initial analysis focused on the reproducibility of image intensity, which may affect tissue segmentation regardless of which particular morphometric analysis approach is used. Accompanying abstracts:
 - #847: CNR Comparison of Three Pulse Sequences for Structural MR Brain Imaging, X. Han et al.
 - #844: Test-retest reliability assessment for longitudinal MRI studies: A comparison of the effects of different T₁-weighted protocols, scanner platforms, and field strengths on semi-automated hippocampal, B. Quinn et al.

METHODS

Standardization of structural MRI protocol

- We evaluated the reproducibility of two 3D structural MRI acquisition protocols that give good gray/white matter contrast and that can be used for automated brain morphometry: MP-RAGE and multiple-flip angle acquisitions of multi-echo FLASH scans.
- The sequences were implemented on three MRI platforms with as close as possible parameters. At the time of the experiment the multi-echo FLASH was not implemented on GE platforms.

MRI Systems	Siemens Sonata (1.5T)	GE LX (1.5T)	Siemens Trio (3T)
3D T1 Acquisitions	MP-RAGE Multi-echo FLASH	MP-RAGE	MP-RAGE Multi-echo FLASH
# test-retest Scans	2	1	1

- MP-RAGE:** Two 3D sagittal, TR/TE/TI = 2.73s/3.44ms/1s, 256x192, 1.33mm thick slices, 128 sagittal slabs, flip angle= 7°
- Multiple flip angle FLASH:** Two 3D sagittal multi-echo multi flip angle (30° and 5°) FLASH volumes (651 Hz/pixel, TR=20ms, TE=(1.8+1.82*n)ms, n=0-7; both for 1.5T and 3T)
- Subjects:** 15 volunteers (ages 66-81, 8 male, 7 female) were scanned on each of the platforms (table above) within two weeks.

Image pre-processing

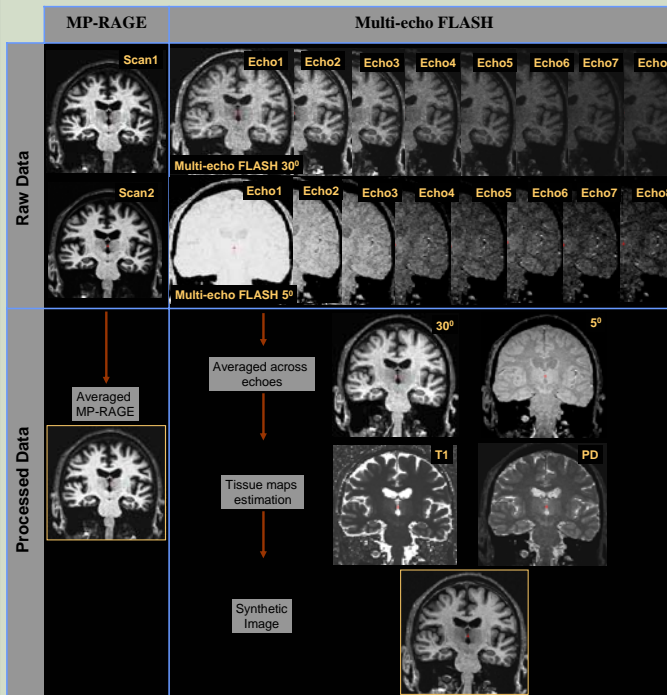
- MP-RAGE:** Two scans per session were co-registered and averaged
- FLASH:** For each flip-angle, the multi-echo images were averaged. T1 and proton density (PD) maps were derived from the two co-registered flip angle-averaged scans using the Bloch equations. A synthetic image optimally weighted to maximize gray/white matter contrast-to-noise ratio is derived from the tissue maps [3]
- The Montreal Neurological Institute tools were used for image co-registration.
- Distortion corrected (unwarped) volumes were obtained using gradient's specific non-linearity properties [2]
- Pre-processed images were skull stripped

Test-retest reproducibility evaluation

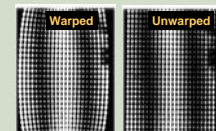
- Here we only consider the image intensity reproducibility within the Siemens Sonata and across the Siemens Sonata-Trio scanners.
- Paired test-retest scans are co-registered and normalized to have the same overall mean intensity
- For each subject we calculated image intensity variability:
 - Paired test-retest cases per acquisition: [Sonata1-Sonata2], [Sonata1-Trio1]
 - Voxel-based relative error maps
 - Global brain mean value from each variability map
 - Repeat all the above with and without distortion correction

RESULTS

1) Sample Structural Data (Siemens Sonata)

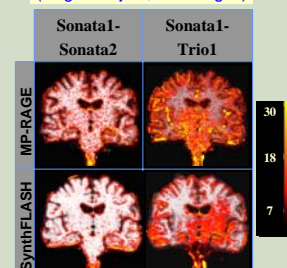


2) Distortion Correction (Siemens Sonata)



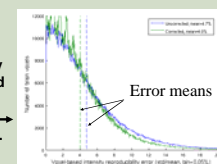
Imaging gradients have nonlinearity effects that generate distortions (left). Unwarping (right) improves geometric and image intensity accuracy [2].

3) Sample Intensity Variability Maps (single subject, % changes)



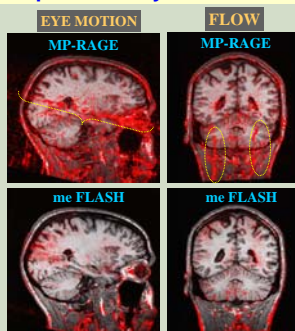
Color maps indicating voxel-based test-retest image intensity variability of unwarped images (% changes).

4) Sample Histogram (single-subject, Sonata1-Trio1)



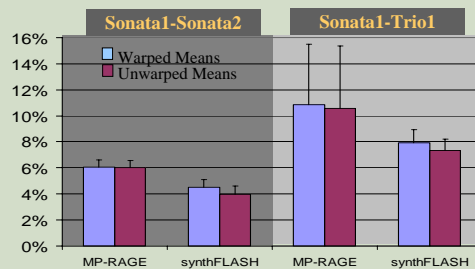
Brain histogram distribution of image intensity reproducibility errors, for corrected (green) and uncorrected (blue) data. Unwarping shifts the errors to lower mean, reducing image intensity variability marginally.

5) Sensitivity to image intensity reproducibility from motion



The higher bandwidth acquisition from multi-echo FLASH reduces sensitivity to intensity fluctuations related to eye motion and flow. Same subject scanned 4 times during one session. Image intensity fluctuations larger than 8% are in red.

6) Image Intensity Variability Measures (averages across subjects, means and std)



CONCLUSIONS

- Image intensity reproducibility:**
 - System effects:** stronger intensity variability across field strengths, probably due to larger inhomogeneities (dielectric effects) at 3T than at 1.5T.
 - Unwarping effects:** Marginal improvements, not the dominating variance source
 - Sequence effects:** Synthetic FLASH data has better image intensity reproducibility than MP-RAGE, probably due to its lower sensitivity to fluctuations from motion as well as its dependency on tissue maps, which should be less dependent on hardware after calibration).
- Next steps:**
 - Correlate image intensity reproducibility with morphometry reproducibility results

REFERENCES

- Ashburner J et al. Lancet Neurol 2003;79-88
- Jovicich J et al. ISMRM 2004
- Fischl B et al. NeuroImage 2004; 23 Suppl 1:S69-84

ACKNOWLEDGEMENTS

- This study was supported by:
- Pfizer, Inc., the NIA (K23-AG22509 & P01-AG04953)
 - NCCR BIRN Morphometry Project (U24-RR021382).

CONTACT

Contact: jovicich@nmr.mgh.harvard.edu

