# Improved longitudinal gray matter atrophy assessment via a combination of SIENA and a 4-dimensional hidden Markov random field model

Michael G Dwyer[1], Niels P Bergsland[1], and Robert Zivadinov[1]

[1]*Buffalo Neuroimaging Analysis Center, University at Buffalo, Buffalo, NY, United States*

## TARGET AUDIENCE

This research is aimed at researchers and/or clinicians seeking to better understand tissue-specific brain atrophy via serial MRI analysis. This includes those involved in basic science and aging research, pathologic research, and clinical trials.

## PURPOSE

Although excellent longitudinal whole-brain atrophy measurements techniques such as SIENA have been developed, tissue-specific gray/white matter atrophy has proven more difficult. Techniques such as SIENAX and others can be used longitudinally, but are not as direct as SIENA and are generally far less precise. We sought to combine elements of SIENA with improvements to FSL's FAST to create a significantly more precise serial tissue-specific atrophy tool called SIENAX-MTP (multiple time point).

## METHODS

First, we extended FSL's FAST tool from a 3-dimensional hidden Markov random field (HMRF) model to a 4-dimensional model. This allows FAST to consider multiple images at once as temporal neighbors, and to avoid arbitrarily classifying voxels of ambiguous intensity differently at different time points. Second, to address scanner- and position-related scaling issues we used SIENA's skull-constrained approach to determine a joint scaling factor between the two images and to put them together into an unbiased halfway space. Finally, to prevent discrepancies in brain extraction from contributing to atrophy measurement, we did all analysis using a unified brain mask in the halfway space.

To evaluate the performance of SIENAX-MTP, we used both simulation and testing on a clinical dataset of patients with MS and matched healthy controls. For simulation, we used scan-rescan images of healthy volunteers, and artificially scaled them to create known changes. For the clinical dataset, we evaluated a matched set of 128 patients, 64 of whom clinically progressed and 64 who did not progress over a 5 year period. For both datasets, we performed conventional SIENAX and SIENAX-MTP in parallel.

## RESULTS

Direct scan-rescan showed much better reproducibility with our approach (Fig. 1). Simulation also showed that SIENAX-MTP agreed much better with the actual scaling values applied (R=0.83 compared to R=0.23 for SIENAX, Fig. 2). In addition, variance within the cases for each scaling value was reduced in SIENAX-MTP results as compared to standard SIENAX. For the clinical evaluation, SIENAX MTP showed reduced variance and a larger effect size than SIENAX for all measures evaluated. For GM, it showed a significant difference of p=0.002, whereas SIENAX along showed only a trend of p=0.056. SIENAX-MTP measures also correlated better with SIENA than did standard SIENAX measures.

## CONCLUSIONS

SIENAX-MTP provides significantly more precise serial GM/WM atrophy assessment than the comparison of two independent SIENAX analyses. It also shows more clinically significant differences, and may therefore provide more statistical power in applicable research and related clinical trials.



**Figure 1.** Scan-rescan results. Difference should be null.



**Figure 2.** Simulation results show much more variance for SIENAX than for SIENAX-MTP.

## REFERENCES

1. S.M. Smith, N. De Stefano, M. Jenkinson, and P.M. Matthews. Normalised accurate measurement of longitudinal brain change. Journal of Computer Assisted Tomography, 25(3):466-475, May/June 2001.

2. S.M. Smith, Y. Zhang, M. Jenkinson, J. Chen, P.M. Matthews, A. Federico, and N. De Stefano. Accurate, robust and automated longitudinal and crosssectional brain change analysis. NeuroImage, 17(1):479-489, 2002.

3. Winkler, G. Image Analysis, Random Fields and Markov Chain Monte Carlo Methods: A Mathematical Introduction (2nd ed.). Springer, 2006.

4. Zhang, Y. and Brady, M. and Smith, S. Segmentation of brain MR images through a hidden Markov random field model and the expectation-maximization algorithm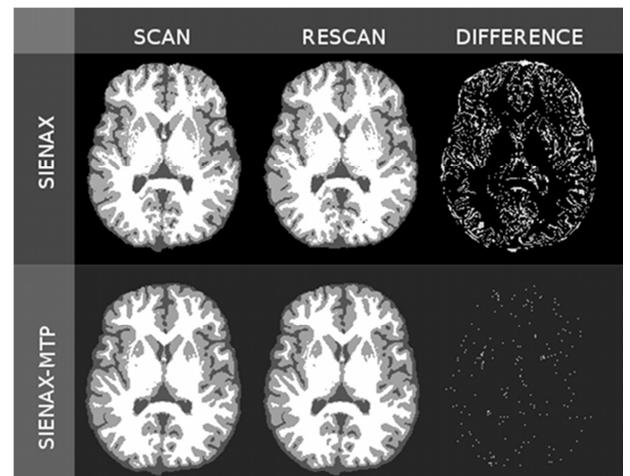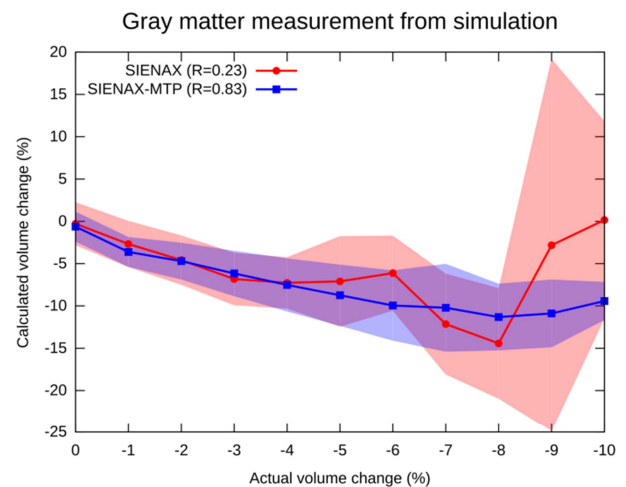. IEEE Trans Med Imag, 20(1):45-57, 2001.