

# Relating multi-sequence longitudinal data from MS lesions on structural MRI to clinical covariates and outcomes

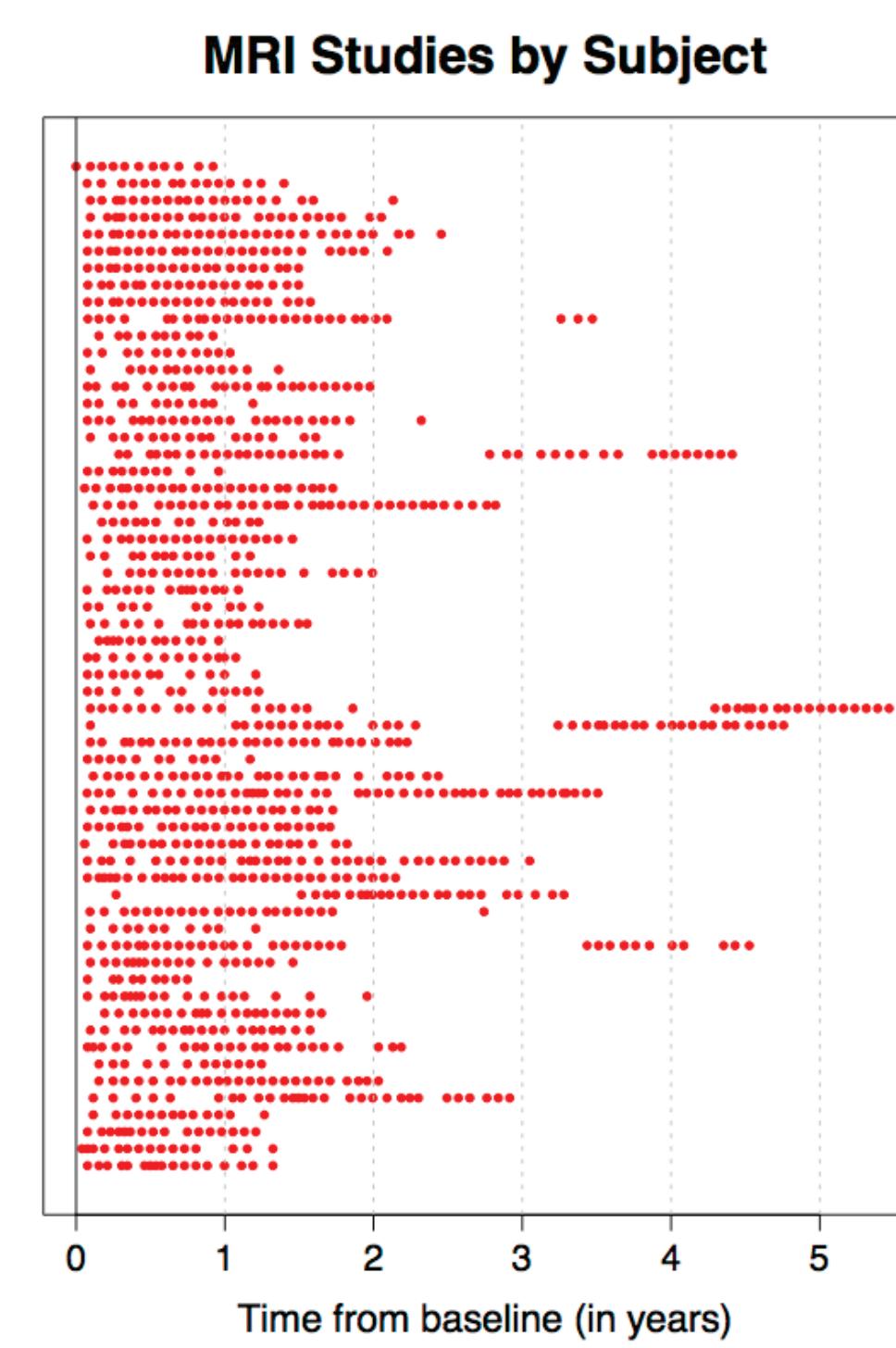


**SMART**  
Johns Hopkins University  
STATISTICAL METHODS AND APPLICATIONS FOR RESEARCH IN TECHNOLOGY

Elizabeth M. Sweeney<sup>1,2</sup>, Russell T. Shinohara<sup>2,3</sup>, Blake E. Dewey<sup>2</sup>, Mather Schindler<sup>2</sup>, Daniel S. Reich<sup>1,2</sup>, Ciprian M. Crainiceanu<sup>1</sup>, Ani Eloyan<sup>1</sup>  
<sup>1</sup>Department of Biostatistics, The Johns Hopkins University, Baltimore, MD 21205; <sup>2</sup>Translational Neuroradiology Unit, Neuroimmunology Branch, National Institute of Neurological Disease and Stroke, National Institute of Health, Bethesda, MD 20892; <sup>3</sup>Department of Biostatistics and Epidemiology, Center for Clinical Epidemiology and Biostatistics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104

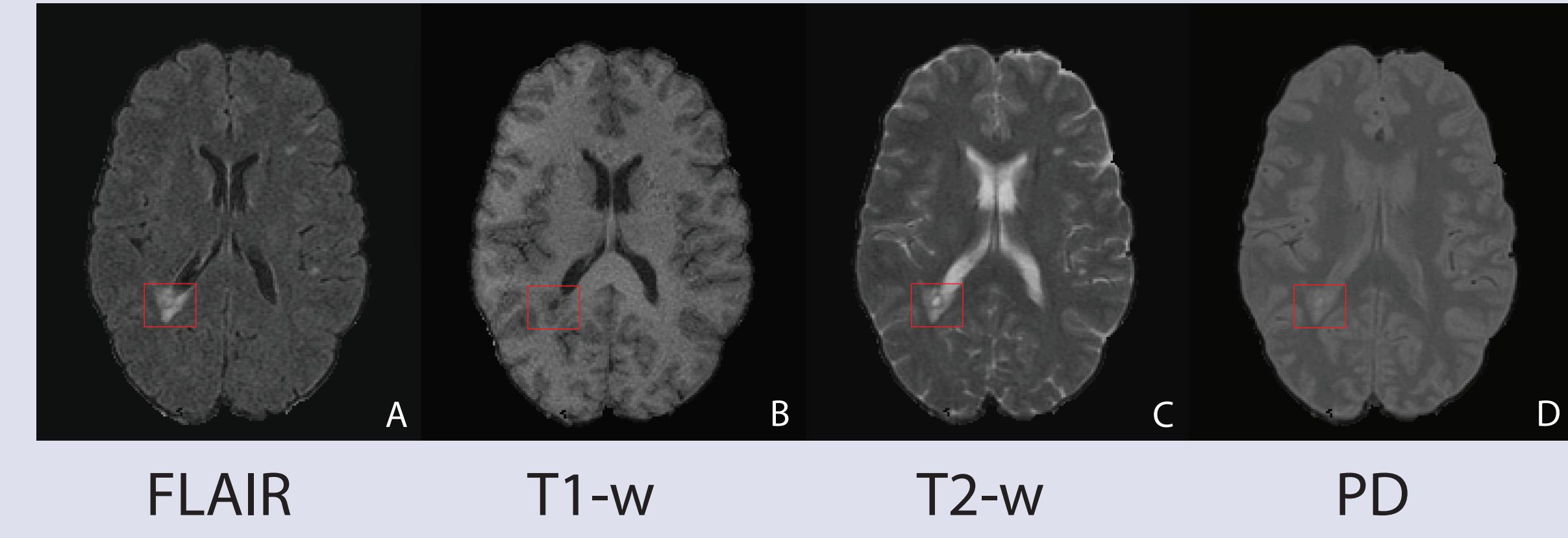
## Abstract

Structural magnetic resonance imaging (MRI) can be used to detect lesions in the brains of multiple sclerosis (MS) patients. The formation of these lesions is a complex sequence of inflammation, degeneration, and repair that MRI has been shown to be sensitive to. Previous work has characterized the lesion process using only proton density (PD) volumes [1]. We characterize the lesion formation process with multi-sequence structural MRI. Each study consists of a T1-weighted, T2-weighted, fluid attenuated inversion recovery (FLAIR) and PD volume. We extract the multi-sequence longitudinal data of the voxel intensities from the four volumes and use principal component analysis to identify voxels that contain permanent damage and repair. Future work is to investigate this repair and permanent damage in relation to clinical covariates such as disease duration, MS subtype, Expanded Stability Status Score (EDSS), and treatment.



## Lesion Repair and Damage

### 1) Image Preprocessing

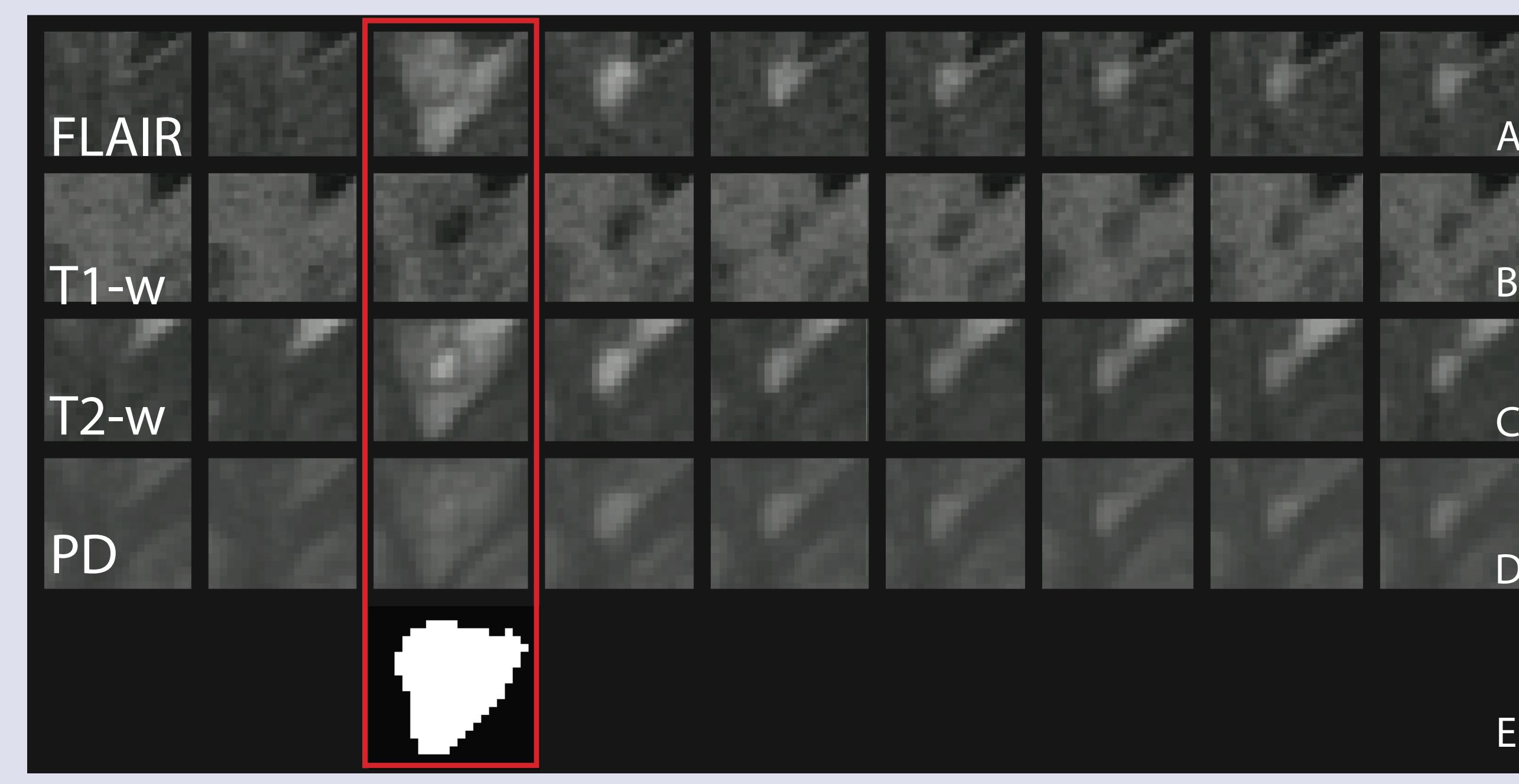


Subjects were imaged at the National Institutes of Health, on a General Electric 1.5 tesla scanner. The scanning parameters were optimized for each acquired image.

### 2) Intensity Normalization

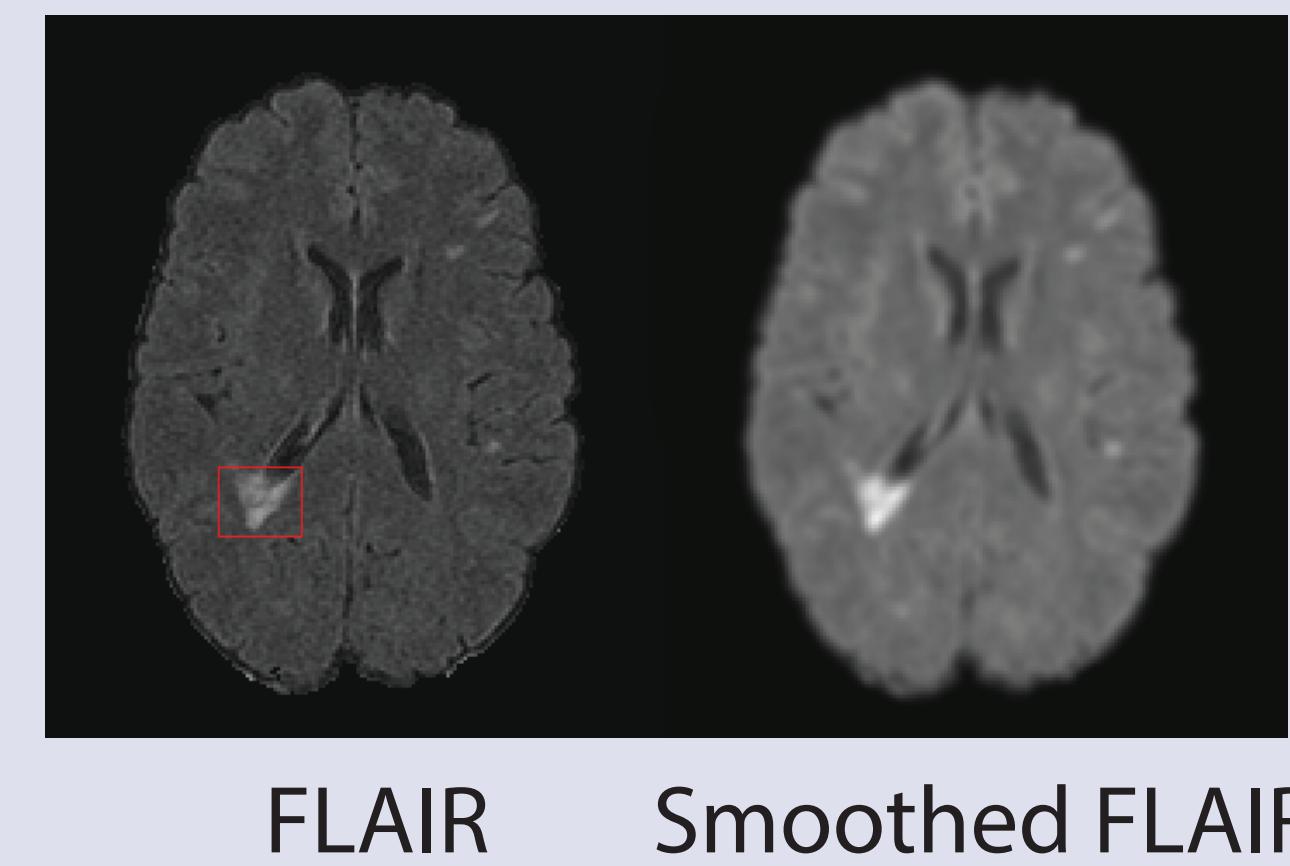
Intensities in each scan were normalized with respect to the normal appearing white matter using the methods outlined in [2].

### 3) SuBLIME



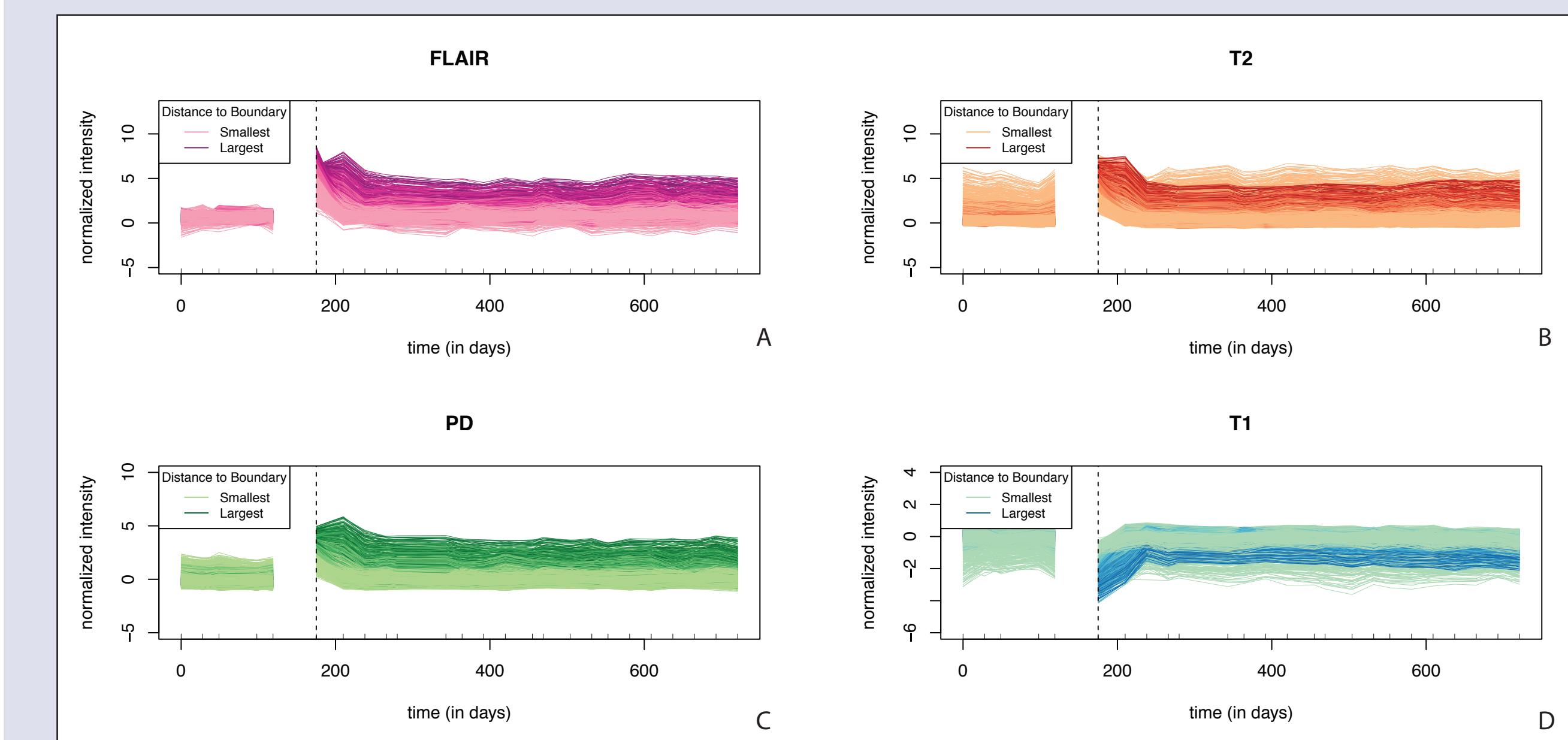
Segmentations of incident and enlarging lesion voxels were created using SuBLIME [3].

### 4) Spatial Smoothing



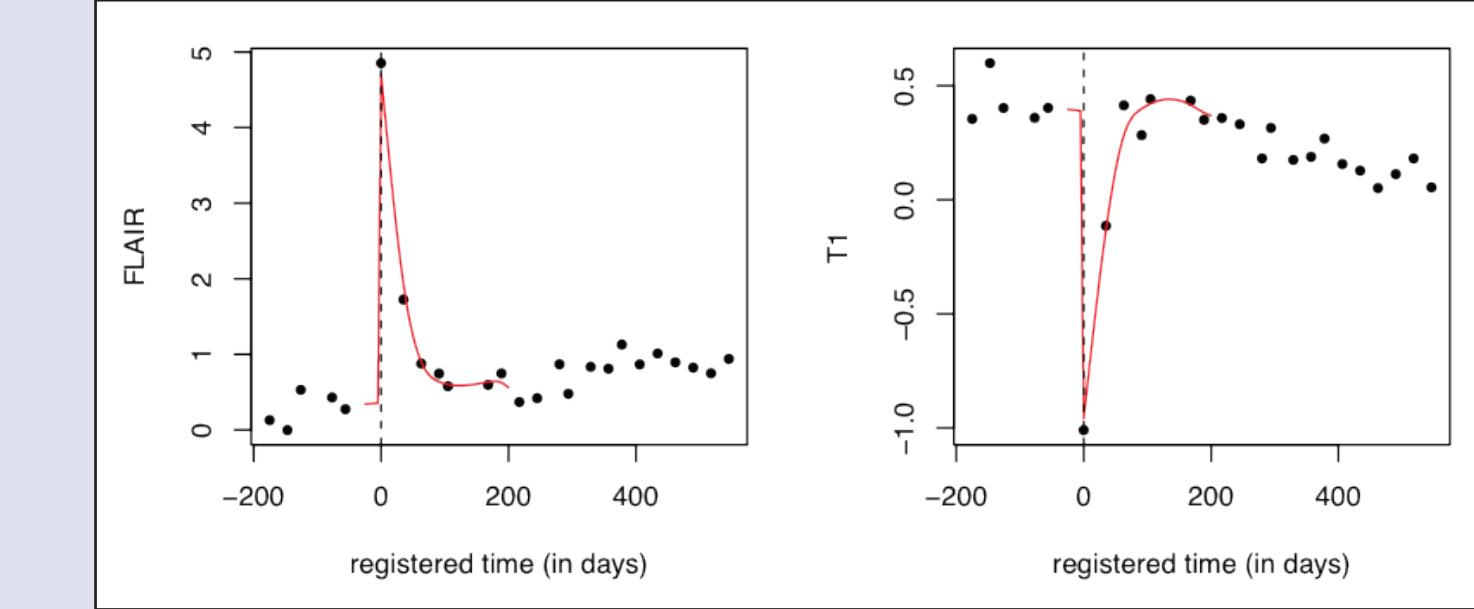
Each volume was smoothed using a Gaussian smoother with kernel window size of 5mm.

## 5) Longitudinal Lesion Intensities



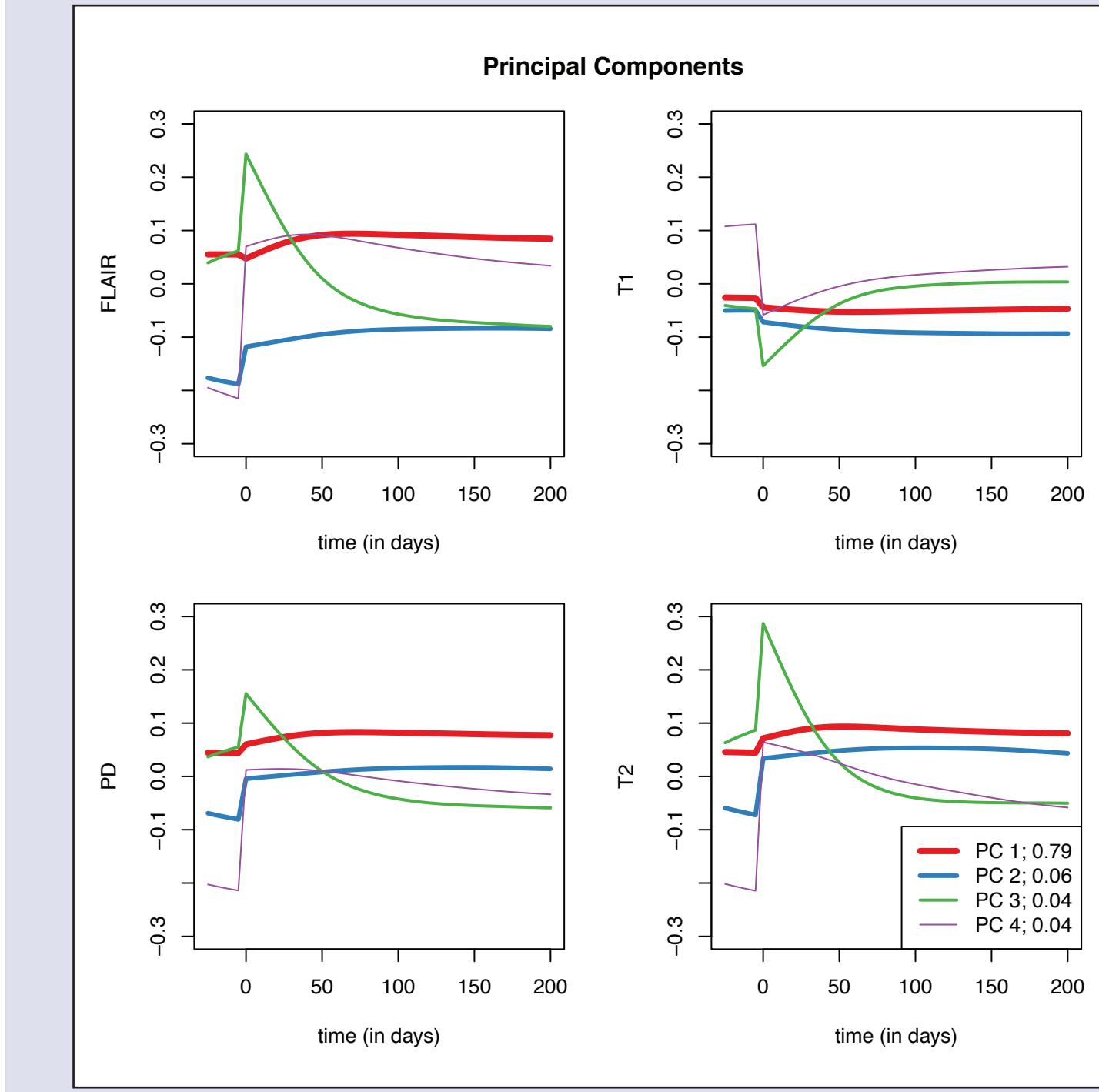
Using the SuBLIME maps, the longitudinal intensities in lesion voxels in the FLAIR, T2-w, T1-w and PD are extracted.

## 6) Temporal Registration and Smoothing



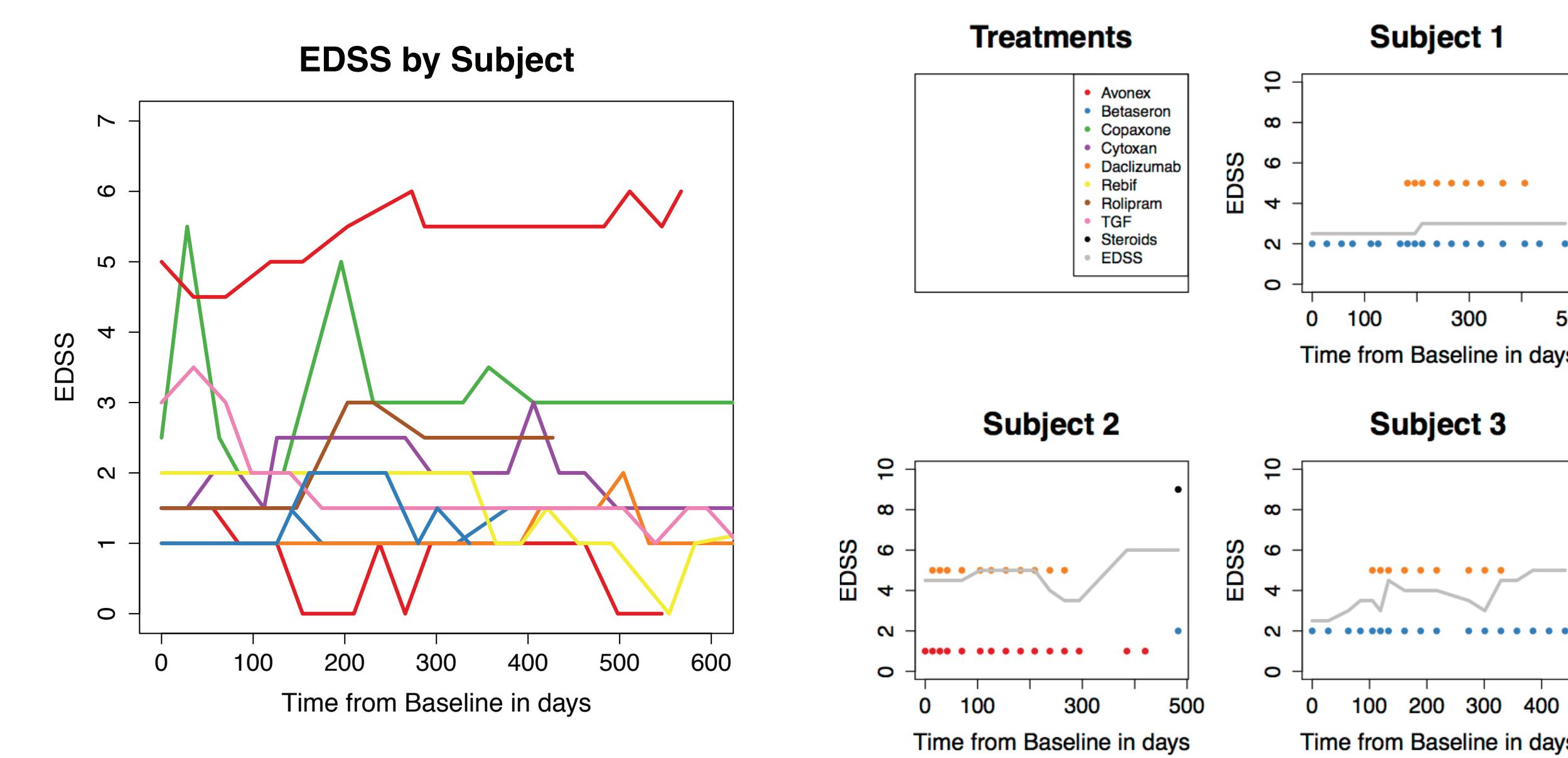
The intensities in each voxel are registered by the time the lesion is identified by SuBLIME. The intensities are interpolated to be on the same time grid.

## 7) Principal Component Analysis



The voxels from each lesion, from each subject are pooled and a principal component analysis is performed. The scores from the first principal component identifies areas of repair and permanent damage.

## Clinical Covariates



Future work is to investigate repair and permanent damage in relation to clinical covariates such as disease duration, MS subtype, Expanded Stability Status Score (EDSS), and treatment.

- [1] Meier, Dominik S., and Charles RG Guttmann. "Time-series analysis of MRI intensity patterns in multiple sclerosis." *NeuroImage* 20.2 (2003): 1193-1209.
- [2] Shinohara, R. T., Crainiceanu, C. M., Caffo, B. S., Gaitán, M. I., & Reich, D. S. (2011). Population-wide principal component-based quantification of blood-brain-barrier dynamics in multiple sclerosis. *NeuroImage*, 57(4), 1430-1446.
- [3] Sweeney, E. M., Shinohara, R. T., Shea, C. D., Reich, D. S., & Crainiceanu, C. M. (2013). Automatic lesion incidence estimation and detection in multiple sclerosis using multisequence longitudinal MRI. *American Journal of Neuroradiology*, 34(1), 68-73.