DBP: The Analysis of Brain Lesions in Neuropsychiatric Systemic Lupus Erythematosis

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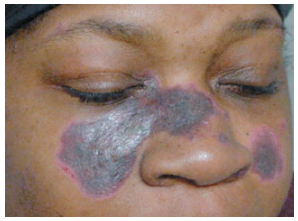
Background and Significance



- Systemic lupus erythematosus (SLE) is an autoimmune disease affecting multiple tissues, including the brain
  - the facial rash of some people with lupus looked like the bite or scratch of a wolf ("lupus" is Latin for wolf and "erythematosus" is Latin for red). patients may feel weak and fatigued, have muscle aches, loss of appetite, swollen glands, and hair loss, sometimes have abdominal pain, nausea, diarrhea, and vomiting.
- Estimates of SLE prevalence range from 14.6-372 per 10^5
  - About 1.5 million americans, 90% diagnosed are female
- Neuropsychiatric SLE (NPSLE), a term that subsumes the neurologic and psychiatric complications of SLE, occurs in up to 95% of SLE patients
- While MRI often reveals distinct white matter abnormalities in active NPSLE, the pathologic processes underlying these lesions, whether purely autoimmune or vascular (e.g., hemostasis), are unknown

Aims of the RO1 Study

- Test hypotheses concerning the possible thrombotic or embolic origin of white matter brain lesions in NPSLE
- Examine whether the incidence of lesions correlates with either levels of thrombosis markers or emboli in the blood or a potential source of emboli in the heart
- Examine whether overall lesion load or the levels of particular classes of lesion correlate with cognitive function

Background and Objective

- Critical to understanding the etiology of brain lesions in NPSLE will be the accurate measurement of their location, size, and time course.
- Lupus brain lesions are known to vary in MRI intensity and temporal evolution and include acute, chronic, and resolving cases.
- Monitoring the time course of image intensity changes in the vicinity of lesions, therefore, may serve to classify them based on their temporal characteristics.
- Major objective of this DBP will be the evaluation of existing tools and the development new tools using the NA-MIC kit for the time series analysis of brain lesions in lupus.

Goals of the NPSLE DBP

- Use and extend the NA-MIC kit to make a fully automated lesion analysis tool.
  - **Input data**
    - image data from the T1-weighted, T2-weighted, and FLAIR sequences
  - **Output data**
    - will be probability maps for each tissue class, the number of lesions, the volume of each lesion, and the total lesion volume at each time point
    - Changes in lesion size and changes in pixel intensity within the volume of each lesion will be displayed graphically
    - Time course data will also be amenable to time series analysis by statistical tools such as general linear modeling (GLM), independent component analysis (ICA), or potentially Bayesian analysis

Year 1 Work Plan

- Collect Baseline data points
- Hire experienced C++ programmer, train and mentor to become expert at using NA-MIC kit
- Evaluate the algorithm/approach performance of at least four methods for lesion segmentation of NPSLE brain images:
  - EM-Segment Method, developed by Sandy Wells
  - K-means+discriminant analysis, developed by Vincent Magnotta
  - Hybrid of EM-Segment/BRAINS, developed by Vincent Magnotta
  - Manual classification by an expert rater

We will use the STAPLE and/or a method using the Williams Index to cross-validate these methods.

Hypotheses to be studied

- Lesions within NPSLE are associated with perfusion deficits and microemboli
- Lesion location and size change over time and correlate with symptom severity

Specific Requirements

- Co-register, T1, T2, Flair
- Co-register Perfusion
  - Calculate CBF, CBV, MTT
- Segment into gray, white, csf, lesion
- Summarize location and size of lesions
- Summarize perfusion by region, within and near lesions

Data Collected to Date

- Total of 16 lupus and controls baseline cases collected so far (no followup cases collected yet)
- 7 lupus cases with lesions (indicated by neuroradiological review) have had lesions manually traced by an expert rater

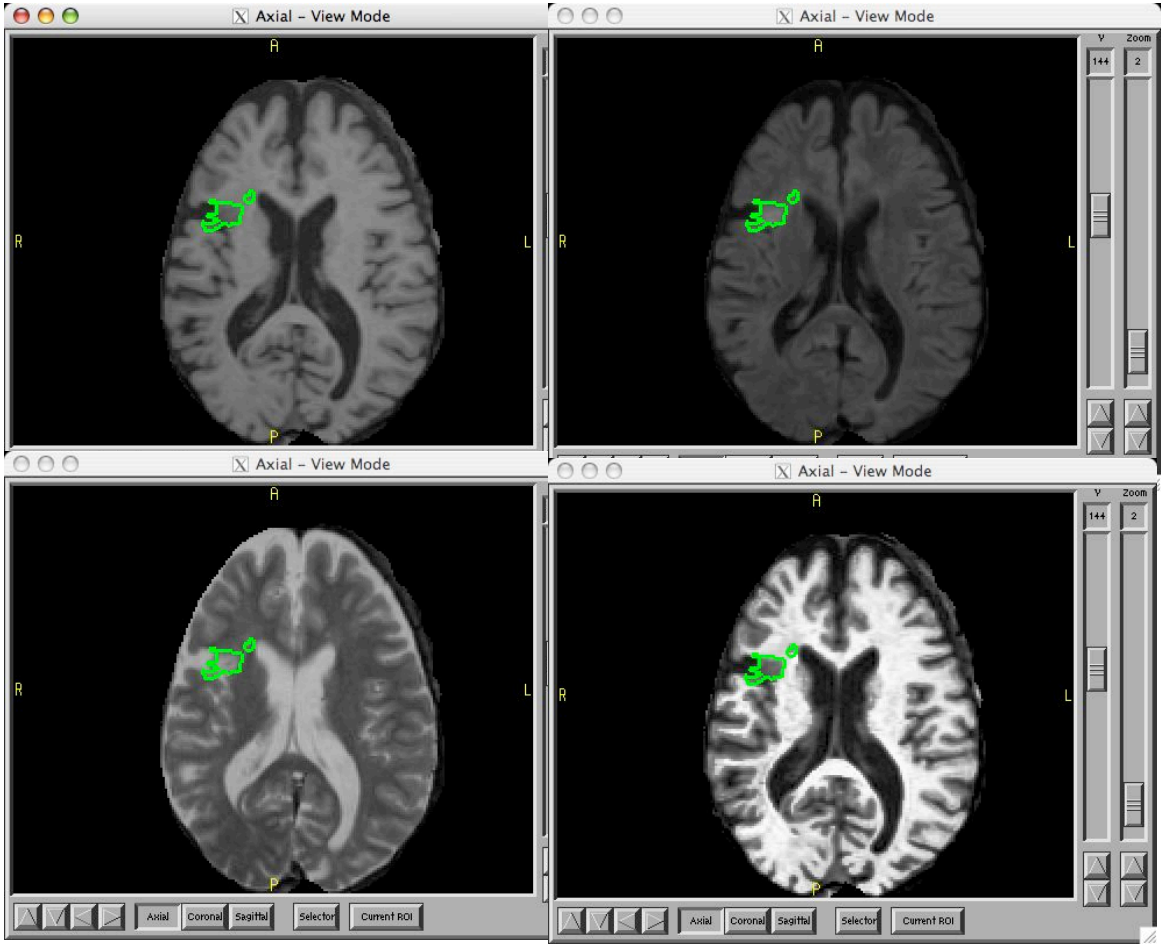
Technical Progress to date

- Baseline Data collection (16 cases with t1, t2, flair, perfusion, DTI)
- Selection of Software Engineer to start aug 1 (will attend programming week)
  - Mark Scully, has attended a MIND ITK/VTK workshop
- Initial attempts at EM Segment lesion classification in slicer 2.6x
- Initial attempts at BRAINS automated lesion classification
- Manually tracing of lesions on 7 cases

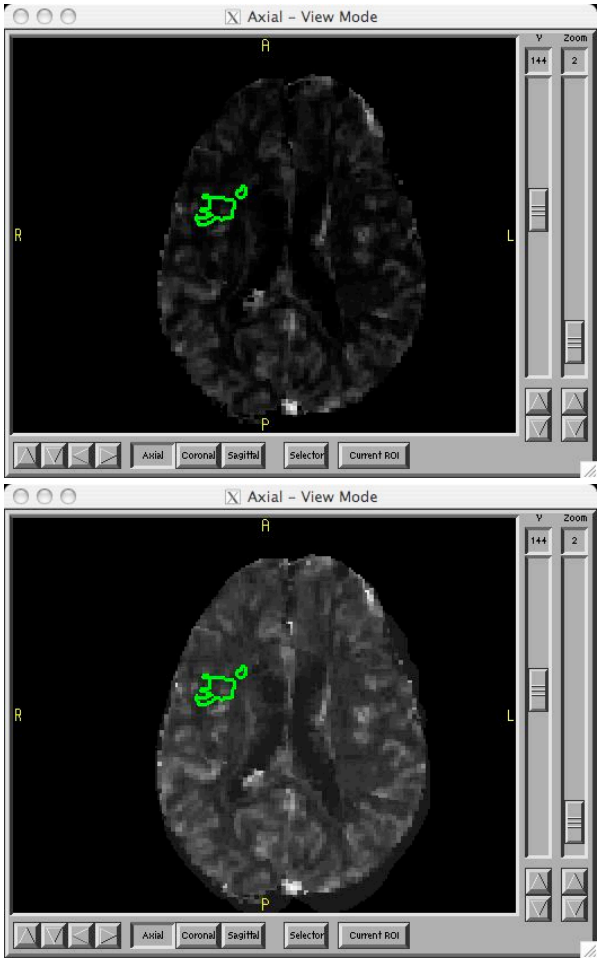
Human Resources

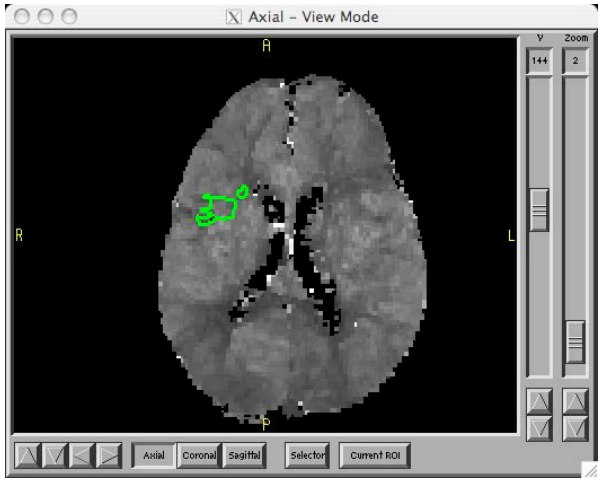
- Jeremy Bockholt (co-PI)
- Chuck Gasparovic (co-PI)
- Mark Scully (software engineer)
- Vincent Magnotta (consultant)
- Vince Calhoun (consultant)

Example Manual Lesion Classification



Example Perfusion Summary





NPSLE DBP Driving Force

- Methods developed in this DBP will have a broad impact on the study of brain diseases involving MRI-visible lesions
- Characterization of the time evolution of these lesions will undoubtedly help to elucidate not only the origins of the lesions but their relationships to disease symptoms.
- No current image analysis package currently permits this level of longitudinal automated lesion time series analysis--this will make the NA-MIC kit unique and more desirable to be used by the broader community

NPSLE DBP Summary

- Using the NA-MIC kit, we will augment, develop, and validate tools for the quantification of brain lesions thought to underlie the cognitive dysfunction of NPSLE.
- We will extend NA-MIC kit to analyze changes in these lesions with time and to relate these changes to the fluctuating symptoms of NPSLE
- We will gain greater insight of NPSLE etiology
- The automated lesion time series analyses should generalize well to other vascular disorders such as vascular dementia, myotonic dystrophy, and multiple sclerosis.