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Previous MRI studies in MS have retrospectively analyzed normal-appearing brain tissue in locations where typical MS lesions ultimately appeared, finding pre-lesional changes in several MRI metrics. However, studies have not been entirely consistent and the development of a prototypical MS lesion cannot as yet be prospectively predicted. The primary objective of this project is to validate the "preactive" lesion hypothesis in MS by identifying the spatiotemporal imaging signature of white matter destined to undergo acute, focal inflammation and demyelination—specifically, one that will allow reliable, prospective detection of nascent lesions before they appear on conventional (non-quantitative) imaging. The specific aim is to acquire a longitudinal set of quantitative MRI metrics in MS patients and perform a multivariate spatiotemporal analysis of pre-lesional, normal-appearing white matter, seeking spatially clustered interval changes that presage the appearance of a typical MS plaque.

Over the past year, the quantitative MRI protocol has been developed and optimized; enrollment and scanning of subjects is awaiting IRB approval of the study protocol, which is imminent.

15. SUBJECT TERMS
Multiple sclerosis, magnetic resonance imaging, longitudinal studies, preactive lesions
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INTRODUCTION: Previous MRI studies in MS have retrospectively analyzed normal-appearing brain tissue in locations where typical MS lesions ultimately appeared, finding pre-lesional changes in several MRI metrics. However, studies have not been entirely consistent and the development of a prototypical MS lesion cannot as yet be prospectively predicted. The primary objective of this project is to validate the “preactive” lesion hypothesis in MS by identifying the spatiotemporal imaging signature of white matter destined to undergo acute, focal inflammation and demyelination—specifically, one that will allow reliable, prospective detection of nascent lesions before they appear on conventional (non-quantitative) imaging. The specific aim is to acquire a longitudinal set of quantitative MRI metrics in MS patients and perform a multivariate spatiotemporal analysis of pre-lesional, normal-appearing white matter, seeking spatially clustered interval changes that presage the appearance of a typical MS plaque.

BODY: We have completed the development and optimization of the quantitative MRI pulse sequences to be used for the project, summarized as follows: (1) myelin water mapping based on the mcDESPOT pulse sequence as originally reported by Deoni et al [1] and adapted by our group [2,3]; (2) magnetization transfer (MT) imaging as adapted and optimized by our group [4-9]; and hybrid diffusion imaging (HYDI), developed and optimized by our group [10-12]. Additionally, we developed the post-processing pipeline to be used for these multiparametric images, with key stages including brain extraction, co-registration of images from different modalities and time-points, and segmentation of normal-appearing white matter. We are currently enrolling and scanning subjects. Three subjects have been enrolled to date; one had to be dropped from the study because of an acute exacerbation in his disease that required him to begin disease-modifying therapy, which is one of the exclusion criteria.

KEY RESEARCH ACCOMPLISHMENTS: Novel approaches to improve the accuracy and reliability of quantitative MRI (qMRI) targeting cerebral white matter have been developed as detailed in previous progress reports. We are now scanning subjects and further accomplishments await completion of scanning in all subjects and data analysis.

REPORTABLE OUTCOMES: Several of our technical developments that preceded the initiation of scanning have been reported [2-9, 12]. Further reports now await completion of scanning in all subjects and data analysis.

APPENDICES: None.

SUPPORTING DATA:

The following abstracts resulting from this work were presented or accepted for presentation at national/international meetings since the previous reporting period:


REFERENCES:


