BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.

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NAME Gauthier, Susan Angela	POSITION TITLE Associate Professor of Clinical Neurology, Department of Neurology, Weill Cornell Medical College
eRA COMMONS USER NAME SAG2015	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University at Buffalo, Buffalo N.Y.	BS	1992	Biological Sciences
Philadelphia College of Osteopathic Medicine, Philadelphia, PA	DO	1997	
Harvard School of Public Health, Boston, MA	MPH	2005	

A. Personal Statement

My passion lies in uncovering the underlying principles that govern disease progression in multiple sclerosis (MS). Despite potent anti-inflammatory treatment and other strides in MS, predicting a patient's disease progression still eludes us. Furthermore, there has been very little impact on altering the clinical course of MS once patients enter the progressive phase. Through my research and collaboration I am firmly convinced that a deep understanding of the unique pathophysiology of progressive MS is vital to the development of effective therapies in thwarting progression. To that end, my career is focused on the research and development of relevant pathophysiologic mechanisms of MS through the use of novel quantitative neuroimaging techniques.

My research career began at The Partners Multiple Sclerosis Center at Brigham and Women's Hospital, where I received clinical training in MS and focused my fellowship on gaining skills in clinical research and clinical trial design. I bolstered these skills through the Clinical Effectiveness Program and a Master of Public Health at the Harvard School of Public Health. At the Partner's MS Center, I led the CLIMB study, currently the largest longitudinal observational cohort study in MS. My experience as Medical Director for the CLIMB study allowed me to be selected to be the Director of Clinical Research at Weill Cornell Medical College. This role enabled me to able conceive and launch the MS clinical research program at Weill Cornell. In my role as director, I have built and led teams that have developed robust clinical research infrastructure that is underpinned by sophisticated clinical and MRI databases. This platform manages longitudinal data on over 1,000 patients on an ongoing basis. The platform's multi-modality incorporates both animal and human imaging, utilizing both MRI and Positron Emission Tomography (PET).

In addition, I have developed strong collaborative relationship with Weill Cornell's departments of radiology. This collaboration began with a focus on early-stage imaging techniques, which then led to an exploration of the biological mechanisms at play in MS. Over time, this work will further refine the accuracy of our predictive models. With the infrastructure, platform and relationships in place, my team and I are focused specifically on applying markers to the quantification of myelin and inflammation. By researching and validating novel imaging MS biomarkers, and utilizing these imaging modalities to make discoveries regarding the ongoing pathological processes, we can further enhance our understanding of potential therapeutic targets.

Furthermore, as novel therapeutics focused on repair and neuroprotection are developed in MS, the need for accurate markers are even more essential. Our aim is that the result of our work can be utilized for exploratory clinical trials of regeneration, specifically re-myelination.

With the clinical research infrastructure foundation in place, my team and I have been highly productive with a number of recent publications highlighting the clinical feasibility of novel imaging techniques and their use in answering essential questions regarding the mechanisms that underlie MS. In conclusion, I feel that my passion and unique expertise provide the leadership necessary to successfully deliver my aims.

1. Kuceyeski, A, Vargas, W, Dayan, M, Monohan, E, Blackwell, C, Raj A, Fujimoto, K, **Gauthier, SA** Modeling the relationship between gray matter atrophy, abnormalities in connecting white matter and cognitive performance in early Multiple Sclerosis. AJNR Am J Neuroradiol. 2015 Apr;36(4):702-9.
2. Vargas W, Monohan E, Pandya S, Raj A, Vartanian T, Nguyen T.D, Hurtado Rúa S, **Gauthier SA** Measuring longitudinal myelin water fraction in new multiple sclerosis lesions. 2015 Neuroimage Clinical. *in press*.
3. Nguyen TD, Deh K[1], Monohan E, Pandya S, Spincemaille P, Raj A, Wang Y, **Gauthier SA .** Feasibility and reproducibility of whole brain myelin water mapping in 4 minutes using fast acquisition with spiral trajectory and adiabatic T2prep (FAST-T2) at 3T. Magn Reson Med. 2015 Aug 29.
4. Dayan M, Monohan E, Pandya S, Kuceyeski A, Nguyen TD, Raj A, **Gauthier SA** Profilometry: A new statistical framework for the characterization of white matter pathways, with application to multiple sclerosis. Hum Brain Mapp. 2015 Dec 15

B. Positions and Honors.

Professional Experience:

1997-1998	Rotating Intern, Traditional Osteopathic Rotating Internship Program, Maimonides Medical Center, Brooklyn New York
1998-1999	Intern, Internal Medicine, St. Elizabeth's Hospital, Boston Massachusetts
1999-2002	Resident, Neurology, Boston University Medical Center
2001-2002	Chief Resident, Neurology, Boston University Medical Center, Boston Massachusetts
2002- 2005	Clinical Research Fellow, Partners Multiple Sclerosis Center, Brigham and Women's Hospital, Boston Massachusetts
2002-2006	Instructor in Neurology, Harvard Medical School, Boston, Massachusetts
2002- 2006	Associate Neurologist, Department of Neurology, Brigham and Women's Hospital, Boston, Massachusetts
2007- 2014	Assistant Professor in Neurology, Weill Cornell Medical College, New York, New York
2007-	Attending Neurologist, New York Presbyterian Hospital, New York, New York
2010-	Director of Clinical Research, Judith Jaffe Multiple Sclerosis Center, Weill Cornell Medical College
2014-	Associate Professor in Clinical Neurology, Weill Cornell Medical College, New York, New York

Committee assignments:

2013-	MRI phase and Quantitative Susceptibility Mapping (QSM): steering committee member
2013-2015	Weill Cornell Medical College IRB review committee member
2013-	Weill Cornell Medical College Dept of Neurology Promotions committee
2013	National Multiple Sclerosis Society's Fellowship Advisory Committee (ad hoc)

Honors and Awards:

1992	B.S. Cum Laude, University at Buffalo, Buffalo New York
2002- 2005	Sylvia Lawry Clinical Trial Fellowship, National Multiple Sclerosis Society
2003- 2005	NIH loan repayment award

2007- 2013 Feil Family Clinical Scholar Award in Multiple Sclerosis

Licensure and Board Certification:

2003 American Board of Psychiatry and Neurology (re-certification 2013)

C. Contribution to Science

Prediction of MS disease progression: My career was at first focused on utilization of patient data and conventional MRI metrics to predict disease course. My goal was to utilize novel statistical approaches to analyze complex longitudinal data within large datasets of MS patients in order to provide a trajectory for patients. I focused on identifying the early markers associated with aggressive disease course. My contribution to the field included the introduction of a Markov model, which predicted short-term clinical disability progression by incorporating a patient's current and past disability into the model. The advantage of this model was the utilization of longitudinal clinical data that otherwise would have been ignored in the standard methods. In the end my team and I were the first to identify a conventional MRI metric, brain atrophy, as a potential biomarker to identify patients with benign MS. It was through this work that I furthered my interest in MRI metrics.

1. **Gauthier SA**, Berger AM, Liptak Z, Duan Y, Egorova S, Buckle GJ, Glanz BI, Khoury SJ, Bakshi R, Weiner HL, Guttmann CRG. Benign MS is characterized by a lower rate of brain atrophy as compared to early MS. Arch. Neurol. 2009 Feb;66(2):234-7
2. **Gauthier SA**, Mandel M, Guttmann CRG, Glanz BI, Khoury SJ, Betensky RA, Weiner, HL Predicting Short-term Disability in Multiple Sclerosis. Neurology. 2007 Jun 12;68 (24):2059-65
3. Mandel M, **Gauthier SA**, Guttman CRG, Weiner HL, Betensky R. Estimating Time to Event from Longitudinal Categorical Data: An Analysis of Multiple Sclerosis Progression. Journal of the American Statistical Association. Dec 2007;102 (480):1254-1266

Developing quantitative imaging biomarkers for multiple sclerosis: Although conventional imaging has been instrumental in early diagnosis of MS, the lack of pathological specificity prevents its use in exploring specific pathological processes that provide novel therapeutic targets. In addition, as potential re-myelination agents are being identified, a myelin biomarker is essential in understanding normal myelin dynamics within the disease, as well as function as an outcome for a clinical trial. As part of my program I have collaborated with a multidisciplinary group, which developed and optimized a signal-to-noise ratio efficient 3D spiral gradient-echo sequence, also referred to as Fast Acquisition with Spiral Trajectory and T2prep (FAST-T2). FAST-T2 enables rapid whole brain myelin water fraction, which is an indirect measure of myelin in the brain, within clinically feasible scan time at 3T. Furthermore, our group integrated a novel approach to deriving myelin maps from FAST-T2 data, which greatly improves robustness to noise, reduces spatial variations, and enhances the definition of white matter fiber bundles in the brain. Our goal is to develop this protocol into a multi-platform algorithm to be utilized for clinical trials. Recently, I have developed a strong collaboration with Dr. Yi Wang and together we have begun to explore the clinical translation of Quantitative Susceptibility Mapping (QSM) in MS. We have discovered a unique QSM signature in MS lesions, which is consistent with recent studies of iron dynamics in MS lesions. The QSM lesion and FAST-T2 work will allow us to quantitate MS lesion iron activity as well as allow the study of the significance on tissue injury as proposed in the current proposal.

1. Raj A, Pandya S, Nguyen TD, **Gauthier SA**. Multi-compartment T2 Relaxometry Using A Spatially Constrained Multi-Gaussian Model. Plos One 2014 Jun 4;9(6)
2. Nguyen TD, Wisnieff C, Cooper MA, Kumar D, Raj A, Spincemaille P, Wang Y, Vartanian, TK, **Gauthier, SA.** T2prep Three-Dimensional Spiral Imaging with Efficient Whole Brain Coverage for Myelin Water Quantification at 1.5. Magn Reson in Med. 2012 Mar:67(3);614-21
3. Kumar D ,Nguyen TD, **Gauthier, SA**, Raj A. A Bayesian Algorithm Using Spatial Priors for Multi-Exponential T2 Relaxometry from Multi-Echo Spin Echo MRI. Magn Reson in Med Magn Reson in Med. 68:1536-1543 (2012)
4. Chen W, **Gauthier SA**, Gupta A, Comunale J, Liu T, Wang S, Pei M, Pitt D, Wang Y. Quantitative susceptibility mapping of multiple sclerosis lesions at various ages. Radiology. 2014 Apr; 271(1):183-92

My complete list of published work in is listed in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/1NMuzPxUmFi/bibliography/47938733/public/?sort=date&direction=ascending

D. Research support

Current Research Support

Corporate Sponsored (Gauthier) 05/01/16 – 04/30/2018
Mallinckrodt.
T*itle: ACTH effects on myelination in multiple sclerosis.* This pilot study designed to perform a chronological measurement of myelin water fraction (MWF) in new contrast-enhancing lesions in subjects treated with ACTH during an acute exacerbation of multiple sclerosis (MS).
Role: PI

Corporate Sponsored (Gauthier)
Novartis Pharmaceutical Corporation 09/1/12-8/30/2016
Title: In vivo MRI quantification of Fingolimod induced remyelination.
The primary aim of this investigator-initiated project is measure the effect of treatment with Fingolimod on myelin content as measured by MRI (T2 relaxometry) in an animal model of MS.
Role: PI

Corporate Sponsored (Gauthier)
Genzyme 7/1/14-6/30/2018
Title: Measuring active microglia in progressive multiple sclerosis.
The primary aim of this investigator-initiated project is to determine if the innate immune response is activated in the progressive stage of MS and where these cells located. We will attempt to relate to markers of neuronal loss and disability.
Role: PI

R01NS090464 (Wang)
NIH/NINDS 4/1/2015-3/31/2020
Multiple sclerosis lesion magnetic susceptibility activity
The primary aim is to investigate the MS lesion susceptibility time course and the underlying biology and physics.
Role: Co-Investigator

Corporate Sponsored (Gauthier)
Novartis Pharmaceutical Corporation 7/1/14-6/30/2017
Title: Ascertaining the influence of Gilenya® (FTY720) on the innate immune burden
The primary aim of this investigator-initiated project is measure the effect of treatment with Natalizumab on activated monocytes as measured by PET.
Role: PI

Corporate Sponsored (Gauthier)
Biogen Idec 1/1/2015-12/31/2016
Title: Multiplatform FAST-T2 MWF Imaging (Stage 1)
The primary aim of this project is to transition our FAST-T2 myelin water map MRI sequence to different MRI platforms (specifically from GE to Siemens) with the eventual goal of having a multi-platform MRI sequence to be utilized for multi-center clinical trials related to myelin repair in MS.
Role: PI

Completed research:

National Multiple Sclerosis Society (Gauthier) 10/01/11 - 09/30/2015
Title: Developing a quantitative imaging biomarker for remyelination in multiple sclerosis.
The primary aim of this project is further develop and validate T2 relaxometry as a biomarker for myelin, which can then be utilized for clinical trials targeting remyelination in MS.
Role: PI