
BIOGRAPHICAL SKETCH FOR SHIV SAIDHA

NAME Shiv Saidha	POSITION TITLE Associate Professor of Neurology		
eRA COMMONS USER NAME ssaidha2			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
National University of Ireland, Galway	MBBCh	1998-2004	Medicine
Galway University Hospitals, Galway, Ireland		2004-2006	Internal Medicine
Royal College of Physicians of Ireland	MRCPI	2006	Internal Medicine
Galway University Hospitals, Galway, Ireland		2006-2009	Neurology
Johns Hopkins University, Baltimore, US		2009-2012	Neuroimmunology
Beaumont University Hospital, Dublin, Ireland		2012-2013	Neurology
National University of Ireland, Galway	MD	2013	Neuroimmunology

A. Personal Statement

My research interests have predominantly focused on the non-invasive interrogation of retinal structures using optical coherence tomography (OCT) in multiple sclerosis (MS), in order to identify and investigate novel outcome strategies for assessing and monitoring neuroprotection and neurorestoration in MS, as well as to further our understanding of the pathobiology of MS, including how retinal pathology in MS may be related to global central nervous system disturbances. I have been at the fore of discovering and demonstrating that inner and outer retinal layer pathology occur within the unmyelinated retina in MS (both quantitatively and qualitatively). I am committed to continuing to delineate and ascertain the mechanisms involved in the development of these findings, the clinical relevance of these changes (both locally in the retina, as well as more globally), their global biological relationships, and determine if this information may be used to guide the development of new, and potentially unique/novel effective MS therapies, particularly at the individual patient level. My work to date has been primarily structurally focused (both within the retina using OCT, as well as more globally within the central nervous system through the assessment of brain substructure volumes, diffusion tensor imaging & magnetization transfer ratio metrics within specific pathways in MS). I also have expertise in the functional assessment of the anterior visual pathway in MS through the application of multifocal electroretinography and pupillometry techniques amongst others. In addition, I have expertise linking changes in the retina in MS with global alterations in the biology of the underlying disease process.

B. Positions and Honors**Positions and Employment**

2004-2006	Internal Medicine, Galway University Hospitals, Galway, Ireland
2006-2009	Neurology Residency, Galway & Cork University Hospitals, Ireland
2009-2012	Fellowship, Neuroimmunology, Johns Hopkins University, Baltimore, US
2012-2013	Specialist Registrar, Neurology, Beaumont University Hospital, Dublin, Ireland
2013-2016	Assistant Professor of Neurology, Johns Hopkins University School of Medicine
2016-present	Associate Professor of Neurology, Johns Hopkins University School of Medicine

Other Experience and Professional Membership

- I. Member of the Royal College of Physicians of Ireland (MRCPI), the American Academy of Neurology, and the New York Academy of Sciences.
- II. Actively serve on the Johns Hopkins Junior Faculty Resource Advisory Council (JRAC)
- III. Actively serve on the steering committee of the International Multiple Sclerosis Visual System consortium (IMSVISUAL)

Honors

2015 Sole recipient of a large competitive research grant open to all US based MS researchers from Genentech

2013 Recipient of the Race to Erase MS (formerly Nancy Davis Foundation) junior faculty research support award for 3 years; a competitive award, open to all junior faculty specializing in MS within the US

2010 Winner of the Multiple Sclerosis International Federation (MSIF) prize for best oral presentation by a young investigator at ECTRIMS & Young MS investigator of the year award

C. Contributions to science (selected from over 70 publications)

I. A primary focus of my research to date has been the application of high resolution imaging techniques such as OCT and MRI in-vivo in MS patients for the purpose of investigating mechanisms of neurodegeneration and the identification of novel outcome strategies for accurately quantifying neurorestoration and remyelination. I have been at the fore of advancing OCT as a technology for investigating neurological disorders, and was the first investigator to implement OCT-segmentation techniques, enabling accurate quantification of discrete macular layer components, in neurological disorders, and in particular MS, for the purpose of investigating axonal and neuronal subcompartments within the retina. One of my main objectives has been to link the occurrence of pathology within the retina of MS patients (both structurally and functionally) with more global disturbances operative as part of the MS disease process. I have had a central role in the pivotal studies relating OCT derived measures to non-conventional MRI derived brain metrics in MS.

1. **S. Saidha**, S. Syc, M. Ibrahim, C. Eckstein, C. Warner, S. Farrell, J. Oakley, M. Durbin, S. Meyer, L. Balcer, E. Frohman, J. Rosenzweig, S. Newsome, J. Ratchford, Q. Nguyen, P. Calabresi. Primary retinal pathology in multiple sclerosis as detected by optical coherence tomography. (*Brain*, 2011 Feb; 134(2): 518-33) (Article featured in *F1000*, *MDLinx* and *Practical Neurology*)
2. C. Warner, S. Syc, A. Stankiewicz, G. Hiremath, S. Farrell, A. Conger, T. Frohman, E. Bisker, L. Balcer, E. Frohman, P. Calabresi, **S. Saidha**. The impact of utilizing different optical coherence tomography devices for clinical purposes and in multiple sclerosis trials. (*PLoS ONE*, 2011;6(8):e22947)
3. **S. Saidha**, S. Syc, M. Durbin, C. Eckstein, J. Oakley, S. Meyer, A. Conger, T. Frohman, S. Newsome, J. Ratchford, E. Frohman, P. Calabresi. Visual dysfunction correlates better with macular ganglion cell layer thickness than peripapillary retinal nerve fibre layer thickness as measured by optical coherence tomography. (*Multiple Sclerosis Journal*, 2011 Dec; 17(12):1449-63) (Article featured in *MDLinx*)
4. S. Syc, **S. Saidha**, S. Newsome, J. Ratchford, J. Oakley, M. Durbin, S. Meyer, E. Frohman, L. Balcer, P. Calabresi. Optical coherence tomography segmentation reveals ganglion cell layer pathology after optic neuritis. (*Brain*, 2012 Feb; 135(Pt 2):521-33)
5. M. Seigo, E. Sotirchos, S. Newsome, A. Babiarcz, C. Eckstein, E. Ford, J. Oakley, S. Syc, T. Frohman, J. Ratchford, L. Balcer, MD, E. Frohman, P. Calabresi, **S. Saidha**. *In-vivo* assessment of retinal neuronal layers in multiple sclerosis with manual and automated optical coherence tomography segmentation techniques. (*Journal of Neurology*, 2012 Mar 15 [Epub ahead of print])
6. J. Oh, K. Zackowski, M. Chen, S. Newsome, **S. Saidha**, S. Smith, M. Diener-West, J. Prince, C. Jones, P. Zijl, P. Calabresi, D. Reich. Multiparametric MRI correlates of sensorimotor function in the spinal cord in multiple sclerosis. (*Multiple Sclerosis Journal*, 2012 Aug 13 [Epub ahead of print])
7. E. Sotirchos, M. Seigo, P. Calabresi, **S. Saidha**. Comparison of point estimates and average thicknesses of retinal layers measured using manual optical coherence tomography segmentation for quantification of retinal neurodegeneration in multiple sclerosis. (*Current Eye Research*, 2012 Sep 6 [Epub ahead of print])
8. **S. Saidha**, E. Sotirchos, J. Oh, S. Syc, M. Seigo, N. Shiee, C. Eckstein, M. Durbin, J. Oakley, S. Meyer, T. Frohman, S. Newsome, J. Ratchford, L. Balcer, E. Frohman, D. Pham, C. Crainiceanu, D. Reich, P. Calabresi. Relationships between retinal axonal and neuronal measures and global central nervous system pathology in multiple sclerosis. (*JAMA Neurology*, 2012 Oct 1 [Epub ahead of print]) (Received editorial) (Article featured in *JAMA* podcast)
9. **S. Saidha**, E. Sotirchos, M. Ibrahim, J. Gelfand, Y. Sepah, J. Ratchford, J. Oh, M. Seigo, S. Newsome, L. Balcer, E. Frohman, C. Crainiceanu, A. Green, Q. Nguyen, P. Calabresi. Microcystic macular oedema, thickness of the inner nuclear layer of the retina, and disease characteristics in multiple sclerosis: a retrospective study. (*Lancet Neurology*, 2012 Oct 4 [Epub ahead of print]) (Received editorial)
10. J. Ratchford*, **S. Saidha***, E. Sotirchos, J. Oh, M. Seigo, C. Eckstein, M. Durbin, J. Oakley, S. Meyer, A. Conger, T. Frohman, S. Newsome, L. Balcer, E. Frohman, P. Calabresi (Co-First authors*). Active MS is associated with accelerated retinal ganglion cell/inner plexiform layer thinning. (*Neurology*, 2013 Jan 1 [Epub ahead of print]) (Received editorial)

11. J. Oh, **S. Saidha**, M. Chen, J. Prince, S. Smith, C. Jones, P. Zijl, D. Reich, P. Calabresi. Spinal cord quantitative MRI discriminates between disability levels in multiple sclerosis. (*Neurology*, 2013 Jan 16 [Epub ahead of print])
12. S. Syc, D. Harrison, **S. Saidha**, M. Seigo, P. Calabresi, D. Reich. Quantitative MRI demonstrates abnormality of the fornix and cingulum in multiple sclerosis. (*Multiple Sclerosis International*, 2013 Feb 16 [Epub ahead of print])
13. **S. Saidha**, P. Calabresi Optical coherence tomography should be part of the routine monitoring of patients with MS: Yes. (*Multiple Sclerosis Journal*, 2014 Sep 20 [Epub ahead of print])
14. D. Kimbrough, E. Sotirchos, J. Wilson, O. Al-Louzi, A. Conger, D. Conger, T. Frohman, **S. Saidha**, A. Green, E. Frohman, L. Balcer, P. Calabresi. Retinal damage and vision loss in African-American multiple sclerosis patients. (*Annals of Neurology*, 2014 Nov 8 [Epub ahead of print])
15. J. Oh, E. Sotirchos, **S. Saidha**, A. Whetstone, M. Chen, S. Newsome, K. Zackowski, L. Balcer, E. Frohman, J. Prince, M. Diener-West, D. Reich, P. Calabresi. Relationships between quantitative spinal cord MRI and retinal layers in multiple sclerosis. (*Neurology*, 2015 Jan 21 [Epub ahead of print])
16. A. Lang, A. Carass, E. Swingle, O. Al-Louzi, P. Bhargava, **S. Saidha**, H. Ying, P. Calabresi, J. Prince. Automatic segmentation of microcystic macular edema in OCT. (*Biomedical Optical Express*, 2015 Jan 1 [Epub ahead of print])
17. E. Swingle, A. Lang, A. Carass, O. Al-Louzi, **S. Saidha**, J. Prince, P. Calabresi. Segmentation of microcystic macular edema in Cirrus OCT scans with an exploratory longitudinal study. (*Proc SPIE Int Soc Opt Eng*, 2015;9417)
18. P. Bhargava, A. Lang, O. Al-Louzi, A. Carass, J. Prince, P. Calabresi, **S. Saidha**. Cross-platform comparison of optical coherence tomography derived retinal layer segmentation in Multiple Sclerosis utilizing a novel open-source automated segmentation algorithm. (*Multiple Sclerosis International*, 2015 May 18 [Epub ahead of print])
19. **S. Saidha**, O. Al-Louzi, J. Ratchford, P. Bhargava, J. Oh, S. Newsome, J. Prince, D. Pham, S. Roy, P. van Zijl, L. Balcer, E. Frohman, D. Reich, C. Crainiceanu, P. Calabresi. Retinal measures reflect brain atrophy: A four year longitudinal study of optical coherence tomography in multiple sclerosis. (*Annals of Neurology*, 2015 July 24 [Epub ahead of print])
20. O. Al-Louzi, P. Bhargava, S. Newsome, L. Balcer, E. Frohman, C. Crainiceanu, P. Calabresi, **S. Saidha**. Outer retinal changes following acute optic neuritis; A novel disease mechanism. (*Multiple Sclerosis Journal*, 2015 July 24 [Epub ahead of print])
21. Martinez-Lapiscina EH, Arnov S, Wilson JA, **Saidha S**, Preiningerova JL, Oberwahrenbrock T, Brandt AU, Pablo LE, Guerrieri S, Gonzalez I, Outteryck O, Mueller AK, Albrecht P, Chan W, Lukas S, Balk LJ, Fraser C, Frederiksen JL, Resto J, Frohman T, Cordano C, Zubizarreta I, Andorra M, Sanchez-Dalmau B, Saiz A, Bermel R, Klistorner A, Petzold A, Schippling S, Costello F, Aktas O, Vermersch P, Oreja-Guevara C, Comi G, Leocani L, Garcia-Martin E, Paul F, Havrdova E, Frohman E, Balcer LJ, Green AJ, Calabresi PA, Villoslada P; IMSVISUAL consortium. Retinal thickness measured with optical coherence tomography and risk of disability worsening in multiple sclerosis: a cohort study. (*Lancet Neurol*, 2016 May;15(6):574-84)
22. J. Button, O. Al-Louzi, A. Lang, P. Bhargava, S. Newsome, T. Frohman, L. Balcer L, E. Frohman E, J. Prince, P. Calabresi P, **S. Saidha**. Disease-modifying therapies modulate retinal atrophy in multiple sclerosis: A retrospective study. (*Neurology*, 2017 Jan 11 [Epub ahead of print])

II. Resulting from my recognition as an expert in structural imaging in MS I have been invited to partake in collaborations seeking my advice and input regarding the study of imaging techniques such as OCT, not only in MS, but also in several other neurological disorders. I therefore also have significant experience applying imaging techniques such as OCT across a wide variety of neurologic disorders including neurosarcoidosis, Parkinson's disease, as well as Amyotrophic Lateral Sclerosis, among many others. The formation of these collaborations underpins the far reaching effects and implications of the research I have performed beyond MS alone. Along these lines, and recognizing the work of others, I also strive to advance findings from other disciplines that could be of relevance and have utility in MS research.

1. C. Eckstein*, **S. Saidha***, S. Syc, G. Byraiah, M. Seigo, A. Stankiewicz, E. Ford, E. Sotirchos. S. Sharma, P. Calabresi, C. Pardo (Co-First authors*). Detection of clinical and subclinical retinal abnormalities in neurosarcoidosis with optical coherence tomography. (*Journal of Neurology*, 2012 Jan 4. [Epub ahead of print])

2. N. Roth, **S. Saidha**, H. Zimmerman, A. Brandt, T. Oberwahrenbrock, H. Tumani, A. Ludolph, T. Meyer, P. Calabresi, F. Paul. Optical coherence tomography does not support optic nerve involvement in amyotrophic lateral sclerosis. (*European Journal of Neurology*, 2013 April 14 [Epub ahead of print])
3. N. Roth, **S. Saidha**, H. Zimmermann, A. Brandt, J. Isensee, A. Benkhellouf-Rutkowska, M. Dornauer, A. Kühn, T. Müller, P. Calabresi, F. Paul MD. Photoreceptor layer thinning in idiopathic Parkinson's disease. (*Movement Disorders*, 2014 April 13 [Epub ahead of print])
4. A. Brandt, F. Paul, **S. Saidha**. Re: Photoreceptor layer thinning in Parkinsonian syndromes. (*Movement Disorders*, 2014 June 7 [Epub ahead of print])
5. A. Brandt, P. Calabresi, **S. Saidha**. Re: Photoreceptor layer thinning is not specific to Parkinson's disease. (*Movement Disorders*, 2014 July 1 [Epub ahead of print])

III. I am committed to unraveling the immunopathobiology of MS, identifying and developing novel MS therapies, as well as novel strategies, both for the purpose of monitoring the MS disease process, as well as for management. Stemming from this, I have been involved in multiple invited comprehensive chapters, editorials and reviews of MS.

1. **S. Saidha**, C. Eckstein, J. Ratchford. Optical Coherence Tomography as a marker of axonal damage in Multiple Sclerosis. (*Current Medical Literature – Multiple Sclerosis* 2010 Oct; 2(2): 33–43)
2. C. Eckstein, S. Syc, **S. Saidha**. Differential diagnosis of longitudinally extensive transverse myelitis in adults. (*European Neurological Journal*, 2011 Jul; 3(1): 27-39)
3. **S. Saidha**, C. Eckstein, P. Calabresi. New and emerging disease modifying therapies for multiple sclerosis. (*Annals of the New York Academy of Sciences*, 2012 Jan; 1247:117-137)
4. C. Eckstein*, **S. Saidha***, M. Levy (Co-First authors*). A differential diagnosis of central nervous system demyelination; beyond multiple sclerosis. (*Journal of Neurology*, 2011 Sep 20. [Epub ahead of print])
5. **S. Saidha**, P. Calabresi. Anti-interleukin-2 receptor alpha for multiple sclerosis? (*Lancet*, 2013 Apr 3 [Epub ahead of print])
6. **S. Saidha**. Optical coherence tomography and brain magnetic resonance imaging in multiple sclerosis. Chapter 12 Optical coherence tomography in neurologic diseases. *Cambridge University Press*. 2015
7. E. Sotirchos, **S. Saidha**. Optical coherence tomography and retinal segmentation. Chapter 15 Optical coherence tomography in neurologic diseases. *Cambridge University Press*. 2015
8. S. Saidha, P. Calabresi. Optical coherence tomography in relapsing remitting multiple sclerosis. Clinical application of OCT in multiple sclerosis. *Springer*. 2015
9. O. Al-Louzi, **S. Saidha**. Pathophysiology of optic neuritis. Multiple sclerosis: A mechanistic view. *Elsevier*. 2016
10. **Saidha S**, Calabresi P. Phenytoin in acute optic neuritis: neuroprotective or not? (*Lancet Neurology*, 2016 Jan; Epub ahead of print)
11. Sotirchos E, **Saidha S**. Other types of MS and related disorders: Neuromyelitis Optica. Chapter 9 Case studies in multiple sclerosis. *Springer*. (In press)
12. P. Bhargava, **S. Saidha**. Multiple Sclerosis: Monitoring disease activity and progression. Neurobiology of disease. *Elsevier*. (In press)

D. Research Support

Ongoing Research Support

7/1/16-6/30/17	Mechanisms of trans-synaptic degeneration in MS G-40906 Genentech Corporation \$89,600 PI: Saidha S This study will elucidate mechanisms of trans-synaptic degeneration in MS by longitudinally assessing the relationships between anterior visual pathway and posterior visual pathway changes in MS.
4/1/17 – 3/31/20	<i>In-vivo</i> investigation of trans-synaptic neurodegeneration in multiple sclerosis RG-1606-08768 National MS Society

\$ 500,000

PI: Saidha S, 27%

The main goal of this award is to investigate the longitudinal relationships between OCT and MRI in MS patients or high risk clinically isolated syndrome patients experiencing acute optic neuritis in order to determine mechanisms and clinical relevance of trans-synaptic degeneration *in-vivo* in MS by longitudinally assessing the relationships between anterior visual pathway and posterior visual pathway changes in MS, and their relationships with clinical parameters.

4/1/14–3/31/18

Open-label, single-arm extension study to the double-blind, randomized, multicenter, placebo-controlled, parallel-group study comparing the efficacy and safety of 0.5mg FTY720 administered orally once daily versus placebo in patients with primary progressive multiple sclerosis

FTY720D2306E1

Novartis Pharmaceuticals

\$ 233,285.05

PI: Saidha S, 1.02%

This is a multi-center extension study to assess the efficacy of FTY720 (fingolimod), an approved and effective therapy licensed for relapsing remitting MS, in primary progressive MS, for which there are currently no approved therapies.

4/1/13-3/31/18

Imaging neurodegeneration in MS

R01NS082347

NIH

\$ 1,251,112.00

PI: Calabresi P

Co-Investigator, 31%

This study investigates novel high resolution and in particular new MRI techniques for monitoring neurodegeneration in MS. My role in this study is as a co-investigator. I am responsible for the design of the studies, review and analysis of data and preparation of publications.

Previous

12/19/08–12/31/15

A double-blind, randomized, multicenter, placebo-controlled, parallel-group study comparing the efficacy and safety of 0.5mg FTY720 administered orally once daily versus placebo in patients with primary progressive multiple sclerosis

FTY720D2306

Novartis Pharmaceuticals

\$391,137.68

PI: Saidha S, 0%

This was a multi-center study to assess the efficacy of FTY720 (fingolimod), an approved and effective therapy licensed for relapsing remitting MS, in primary progressive MS, for which there are currently no approved therapies.

7/1/13 – 6/30/16

Optical Coherence Tomography in MS

90056516

Race to Erase MS

\$ 225,000

PI: Saidha S, 36.7%

The main goal of this junior faculty award is to investigate the longitudinal relationships between OCT and MRI in MS, and in particular to investigate whether rates of atrophy of specific retinal layers mirrors rates of atrophy of discrete brain substructures.

11/1/12-10/31/16

Mechanisms of retinal neurodegeneration and visual pathway axonal loss in MS

RG4649A5/1

National MS Society

\$ 509,875

PI: Balcer L

Co-investigator, 1.28%

This study investigates the chronology of change in OCT and the relationships of such change to high and in particular low contrast visual function change over time in MS. My role in this study is as a site investigator. I am responsible for recruiting patients and for the review and preparation of publications.

1/1/16- 10/31/16

The international multiple sclerosis visual consortium (IMSVISUAL)

PA150102734

International Progressive MS alliance division of the National MS Society

\$60,000

PI: Calabresi P

Co-investigator, 0%

This is a planning award in order to establish IMSVISUAL as an international collaboration, thereafter allowing the consortium led by its steering committee to apply for a much larger grant of 1 million euros per year for 5 years.