## **Biographical Sketch**

## NAME: Donahue, Manus Joseph

## eRA COMMONS USER NAME: donahumj

## POSITION TITLE: Professor of Radiology, Neurology, and Psychiatry

### EDUCATION/TRAINING:

Institution and location	Degree	Completion date	Field of study
Duke University Durbam NC USA	BS	05/2003	Physics
Duke Oniversity, Dumani, NC, USA	00	0372003	r Hysics
Duke University, Durham, NC, USA	BA	05 / 2003	Philosophy
Johns Hopkins, Baltimore, MD, USA	PhD	11 / 2007	Biophysics
University of Oxford, Oxford, Oxfordshire, UK	Postdoctoral	11 / 2009	Clinical Neurology

## A. Personal Statement

I am a Professor of Radiology and Radiological Sciences and my work focuses on developing and implementing novel magnetic resonance imaging (MRI) approaches to better understand tissue function in diseases of the circulation. To this end, I have worked on developing new methods for quantifying physiological parameters such as blood flow, blood volume, tissue sodium, lymphatic flow, oxygen extraction fraction, the metabolic rate of oxygen consumption, and structural and functional connectivity both in the central nervous system and periphery. A major emphasis of my work is to identify functional biomarkers that precede overt symptoms and clinical disease manifestations and to use these biomarkers to triage patients for disease-modifying therapies. Applications of this work by my lab and my immediate collaborators focus on vascular disease and stroke, lymphatic disorders, neonatal hypoxia, cerebral plasticity, anemia, fat disorders, and neurodegeneration (Parkinson's disease and Huntington's disease). Over the past six years, I have also been the Principal Investigator of four NIH-funded studies in which these approaches have been applied in patients with atherosclerotic vascular disease, moyamoya disease and syndrome, and lymphatic disorders. I serve as Vice Chair of the Vanderbilt Institutional Review Board Human Subjects Protections Committee; teach courses on imaging science; and I oversee multiple PhD students, medical students and residents, and post-doctoral fellows.

- Rane S, Donahue PM, Towse T, Ridner S, Chappell M, Jordi J, Gore J, <u>Donahue MJ</u>. Clinical feasibility of noninvasive visualization of lymphatic flow with principles of spin labeling MR imaging: implications for lymphedema assessment. *Radiology*. 2013; 269(3):893-902. PMCID: <u>PMC4485559</u>
- 2. <u>Donahue MJ</u>, Near J, Blicher JU, Jezzard P. Baseline GABA concentration and fMRI response. *Neuroimage*. 2010; 53(2):392-8. PMID: <u>20633664</u>
- Donahue MJ, Dethrage LM, Faraco CC, Jordan LC, Clemmons P, Singer R, Mocco J, Shyr Y, Desai A, O'Duffy A, Riebau D, Hermann L, Connors J, Kirshner H, Strother MK. Routine clinical evaluation of cerebrovascular reserve capacity using carbogen in patients with intracranial stenosis. *Stroke*. 2014; 45(8):2335-41. PMCID: <u>PMC4118584</u>
- Jordan LC, Gindville MC, Scott AO, Juttukonda MR, Strother MK, Kassim AA, Chen SC, Lu H, Pruthi S, Shyr Y, <u>Donahue MJ</u>. Non-invasive imaging of oxygen extraction fraction in adults with sickle cell anaemia. *Brain*. 2016; 139(Pt 3):738-50. PMCID: <u>PMC5014126</u>

# B. Positions and Honors

Positions and Employment

2005-2007	MR Technologist, Kennedy Krieger Institute, Baltimore, MD, USA
2008-2009	Dunhill Fellow in Neuroimaging, Oxford University, Oxford, UK
2009-2010	Assistant Professor, Radiology, Johns Hopkins University, Baltimore, MD, USA
2010-2015	Assistant Professor, Radiology, Vanderbilt University Nashville, TN, USA
2015-2019	Associate Professor, Radiology, Vanderbilt University Medical Center, Nashville, TN, USA
2019-	Professor, Radiology, Vanderbilt University Medical Center, Nashville, TN, USA
2019-	Editorial board member, Journal of Cerebral Blood Flow and Metabolism
2020-	Vice Chair, Human Subjects Protections Committee, Vanderbilt University Medical Center

Honors

**1995** Eagle Scout

# C. Contribution to Science

The following contributions are summarized from more than 115 peer-reviewed manuscripts

**1.** Development of magnetic resonance imaging and spectroscopy approaches for quantifying human tissue function. As an imaging scientist, I have developed imaging tools designed to extract quantitative measures of tissue physiology (e.g., blood flow, blood volume, oxygen extraction and consumption, lymphatic flow, neurotransmitter concentration, and vessel wall properties). I have experience developing these tools at the standard clinical field strength of 3 Tesla as well as at typically the highest human field strength of 7 Tesla.

- 1. <u>Donahue MJ</u>, Lu H, Jones CK, Edden RA, Pekar JJ, van Zijl PC. Theoretical and experimental investigation of the VASO contrast mechanism. *Magn Reson Med*. 2006; 56(6):1261-73. PMID: 17075857
- Donahue MJ, Hoogduin H, van Zijl PC, Jezzard P, Luijten PR, Hendrikse J. Blood oxygenation leveldependent (BOLD) total and extravascular signal changes and ΔR2\* in human visual cortex at 1.5, 3.0 and 7.0 T. NMR Biomed. 2011; 24(1):25-34. PMID: 21259367
- Donahue MJ, Blicher JU, Østergaard L, Feinberg DA, MacIntosh BJ, Miller KL, Günther M, Jezzard P. Cerebral blood flow, blood volume, and oxygen metabolism dynamics in human visual and motor cortex as measured by whole-brain multi-modal magnetic resonance imaging. *J Cereb Blood Flow Metab.* 2009; 29(11):1856-66. PMID: <u>19654592</u>
- 4. **Donahue MJ**, Near J, Blicher JU, Jezzard P. Baseline GABA concentration and fMRI response. *Neuroimage*. 2010; 53(2):392-8. PMID: <u>20633664</u>

**2.** Development of imaging tools for visualizing the lymphatic circulation. The lymphatic system is fundamental to a spectrum of devastating diseases, including cancer, cancer-treatment morbidity, obesity, and immune disorders. In this line of work, I have developed new imaging tools to quantify lymphatic dysfunction and our group is applying these tools in trials of secondary lymphedema, immunodeficiency (i.e., HIV) and lipedema.

- Rane S, Donahue PM, Towse T, Ridner S, Chappell M, Jordi J, Gore J, <u>Donahue MJ</u>. Clinical feasibility of noninvasive visualization of lymphatic flow with principles of spin labeling MR imaging: implications for lymphedema assessment. *Radiology*. 2013; 269(3):893-902. PMCID: <u>PMC4485559</u>
- Donahue MJ, Donahue PCM, Rane S, Strother MK, Scott A, Smith SA. Assessment of lymphatic impairment and interstitial protein accumulation in patients with breast cancer treatment-related lymphedema using CEST MRI. *Magn Reson Med*. 2016; 75(1):345-55. PMCID: PMC4561605
- Crescenzi R, Donahue PM, Hartley KG, Desai AA, Scott AO, Braxton V, Mahany H, Lants SK, <u>Donahue</u> <u>MJ.</u> Lymphedema evaluation using noninvasive 3T MR lymphangiography. *J Magn Reson Imaging*. 2017. PMCID: <u>PMC5573666</u>
- 8. Donahue PM, Crescenzi R, Scott AO, Braxton V, Desai A, Smith SA, Jordi J, Meszoely IM, Grau AM, Kauffmann RM, Sweeting RS, Spotanski K, Ridner SH, **Donahue MJ**. Bilateral Changes in Deep Tissue

Environment After Manual Lymphatic Drainage in Patients with Breast Cancer Treatment-Related Lymphedema. *Lymphat Res Biol.* 2017; 15(1):45-56. PMCID: PMC5369395

**3.** Clinical implementation of magnetic resonance imaging protocols in patients with ischemic cerebrovascular disease. I have worked on incorporating vascular imaging protocols into the radiological infrastructure at Vanderbilt. In addition to this clinical work, this line of research has been the topic of three clinical trials that focus on using imaging biomarkers of tissue physiology to evaluate infarction risk in patients with atherosclerotic and non-atherosclerotic (i.e., moyamoya) vasculopathy.

- Donahue MJ, Dethrage LM, Faraco CC, Jordan LC, Clemmons P, Singer R, Mocco J, Shyr Y, Desai A, O'Duffy A, Riebau D, Hermann L, Connors J, Kirshner H, Strother MK. Routine clinical evaluation of cerebrovascular reserve capacity using carbogen in patients with intracranial stenosis. *Stroke*. 2014; 45(8):2335-41. PMCID: PMC4118584
- Cogswell PM, Davis TL, Strother MK, Faraco CC, Scott AO, Jordan LC, Fusco MR, Frederick BD, Hendrikse J, <u>Donahue MJ</u>. Impact of vessel wall lesions and vascular stenoses on cerebrovascular reactivity in patients with intracranial stenotic disease. *J Magn Reson Imaging*. 2017; 46(4):1167-1176. PMCID: <u>PMC5500451</u>
- Arteaga DF, Strother MK, Davis LT, Fusco MR, Faraco CC, Roach BA, Scott AO, <u>Donahue MJ</u>. Planningfree cerebral blood flow territory mapping in patients with intracranial arterial stenosis. *J Cereb Blood Flow Metab.* 2017; 37(6):1944-1958. PMCID: <u>PMC5464691</u>
- Donahue MJ, Strother MK, Hendrikse J. Novel MRI approaches for assessing cerebral hemodynamics in ischemic cerebrovascular disease. *Stroke*. 2012; 43(3):903-15. PMCID: <u>PMC6939674</u>

**4.** Hemodynamic and metabolic indicators of treatment response and stroke risk in patients with sickle cell disease (SCD). I have applied new imaging approaches that report on quantitative measures of cerebral blood flow, oxygen extraction, and arterio-venous capillary shunting to understand how these parameters can be used to triage adult and pediatric patients with SCD for personalized therapies (i.e., hydroxyurea, transfusion, or stem cell transplant). I also serve on the Food and Drug Administration (FDA) and American Society of Hematology (ASH) advisory boards to recommend neurologically-focused endpoints in clinical trials of SCD.

- Jordan LC, Gindville MC, Scott AO, Juttukonda MR, Strother MK, Kassim AA, Chen SC, Lu H, Pruthi S, Shyr Y, <u>Donahue MJ</u>. Non-invasive imaging of oxygen extraction fraction in adults with sickle cell anaemia. *Brain*. 2016; 139(Pt 3):738-50. PMCID: <u>PMC5014126</u>
- Juttukonda MR, Jordan LC, Gindville MC, Davis LT, Watchmaker JM, Pruthi S, <u>Donahue MJ</u>. Cerebral hemodynamics and pseudo-continuous arterial spin labeling considerations in adults with sickle cell anemia. *NMR Biomed*. 2017; 30(2). PMCID: <u>PMC5351809</u>
- Jordan LC, Juttukonda MR, Kassim AA, DeBaun MR, Davis LT, Pruthi S, Patel NJ, Lee CA, Waddle SL, <u>Donahue MJ</u>. Haploidentical bone marrow transplantation improves cerebral hemodynamics in adults with sickle cell disease. *Am J Hematol.* 2019; 94(6):E155-E158. PMCID: <u>PMC6939674</u>
- Jordan LC, Kassim AA, <u>Donahue MJ</u>, Juttukonda MR, Pruthi S, Davis LT, Rodeghier M, Lee CA, Patel NJ, DeBaun MR. Silent infarct is a risk factor for infarct recurrence in adults with sickle cell anemia. *Neurology*. 2018; 91(8):e781-e784. PMCID: <u>PMC6107269</u>

**5. Imaging biomarkers of neurodegeneration and pharmacological response.** I oversee the imaging components of several trials where neuroimaging is applied to understand cognitive response to exploratory therapies in patients with central and peripheral  $\alpha$ -synucleinopathies (Parkinson's disease and pure autonomic failure) or dementia (mild cognitive impairment, vascular dementia, ICU delirium, and Alzheimer's disease).

- Claassen DO, Stark AJ, Spears CA, Petersen KJ, van Wouwe NC, Kessler RM, Zald DH, <u>Donahue MJ</u>. Mesocorticolimbic hemodynamic response in Parkinson's disease patients with compulsive behaviors. *Mov Disord*. 2017; 32(11):1574-1583. PMCID: <u>PMC5681361</u>
- Rane S, Ally BA, Hussey E, Wilson T, Thornton-Wells T, Gore JC, <u>Donahue MJ</u>. Inverse correspondence between hippocampal perfusion and verbal memory performance in older adults. *Hippocampus*. 2013; 23(3):213-20. doi: 10.1002/hipo.22080. Epub 2012 Oct 26. PMCID: <u>PMC3878078</u>

- Talati P, Rane S, Kose S, Blackford JU, Gore J, <u>Donahue MJ</u>, Heckers S. Increased hippocampal CA1 cerebral blood volume in schizophrenia. *Neuroimage Clin*. 2014; 5:359-64. doi: 10.1016/j.nicl.2014.07.004. eCollection 2014. PMCID: <u>PMC4141978</u>
- Juttukonda MR, Franco G, Englot DJ, Lin YC, Petersen KJ, Trujillo P, Hedera P, Landman BA, Kang H, <u>Donahue MJ</u>, Konrad PE, Dawant BM, Claassen DO. White matter differences between essential tremor and Parkinson disease. *Neurology*. 2019; 92(1):e30-e39. PMCID: PMC6336163

#### Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/pubmed/?term=manus+donahue+OR+donahue+MJ+and+vanderbilt

### D. Research Support

## **Ongoing support**

1R01 NS097763-01 NIH/NINDS Imaging collaterals and tissue metabolisn <i>Role: PI</i>	Donahue (PI) n in patients with Moyamoya syndrome	07/01/2016 – 06/30/2021
1R01 NR015079-06S1 NIH/NIA (R01 supplement) Quantification of glymphatic dysfunction i <i>Role: Pl</i>	Donahue (PI) n patients with Alzheimer's disease and	08/01/2019 – 07/31/2020 d related dementias
1R01 NR015079 NIH/NINR Imaging biomarkers of lymphatic dysfunc <i>Role: Pl</i>	Donahue (PI) tion	07/1/2018 – 06/30/2022
LFA12 Lipedema Foundation Utilizing Molecular Tissue Profiles and Patients with Lipedema <i>Role: Pl</i>	Donahue (PI) Lymphatic Clearance to Improve Clin	09/01/2017 – 08/31/2019 (no cost extension) ical Discriminatory Capacity in
5R01NS09751202 NIH/NINDS Mechanisms of cerebrovascular reactivity <i>Role: Vanderbilt site PI (subcontract with</i>	Frederick /Donahue (Multi PI) / in health and disease <i>Harvard Medical Center)</i>	09/01/2016 – 05/31/2022
Strategically focused research network American Heart Association Microvascular disease determines limb or <i>Role: Co-Investigator</i>	Beckman J (PI) utcomes in peripheral artery disease	04/01/2018 – 03/31/2021
1K24 HL147017 NIH/NINDS Mentoring in patient-oriented research for <i>Role: Co-investigator</i>	Jordan (PI) cused on neurological complications of	09/01/2019 – 08/31/2022 sickle cell disease
1R01-NS096127-01 NIH/NINDS MRI-based quantitative brain oxygen met <i>Role: Co-Investigator</i>	Jordan (PI) abolism identifying high risk of infarct r	03/01/2016 – 02/28/2021 ecurrence in sickle cell anemia

1R01NS100980-01A1

NIH/NIA Cardiovascular predictors of cerebrovascular <i>Role: Co-investigator</i>	r health in older adults	
5R01NS097783 NIH/NINDS Biological determinants of impulsivity in Park <i>Role: Co-investigator</i>	Claassen (PI) inson's disease	08/01/2016 – 05/31/2021
Completed support (recent selected)		
2R01MH070560-07A1 NIH/NIMH Imaging Hippocampal Function in Psychosis <i>Role: Co-investigator</i>	Heckers (PI)	09/27/2013 – 07/31/2018
1R01 NR015079	Donahue (PI)	07/01/2014 - 06/30/2018
Imaging Lymphatic function in Patients with I Role: PI	Breast Cancer Related Lymphedema	
14CSA20380466	Donahue/Jordan (Multi PI)	07/01/2014 - 06/30/2017
MRI-based quantitative brain oxygen metabo Role: Co-PI	blism mapping in sickle cell anemia	
5R01 NS078828	Donahue (PI)	06/01/2012–04/30/2017
Characterizing Hemodynamic Compensation Role: Pl	and Stroke Risk in Stenosis Patients	
14GRNT20150004	Donahue (PI)	07/01/2014 - 06/30/2016
Characterization of Regional Chemical and Role: Pl	/ascular Uncoupling in Following Ischem	ic Stroke
5R01EB016695-02	Grissom (PI)	04/10/2014 - 03/31/2018
Three-dimensional Patient-tailored RF pulse Role: Co-investigator	s for spin echo neuroimaging at 7T	
1R21 MH099218-01A1	Taylor (PI)	07/15/2013 - 06/30/2015
Frontal Hypo Perfusion Effects on Antidepres Role: Co-investigator	ssant Outcomes in Geriatric Depression	
322653 Michael L Fex Foundation	Rane (PI)	07/01/2014 - 06/30/2016
Cortical and Functional Distinctions in Alzhei Role: Administrative Co-PI	mer's and Parkinson's Disease	
SPRINT-MIND	Donahue (PI)	10/01/2011 - 09/30/2015
Assessing performance of blood pressure m Role: PI (Vanderbilt Site)	edication using 3T MRI	