OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Nicholas J. Tustison, D.Sc.

eRA COMMONS USER NAME (credential, e.g., agency login): tustison

POSITION TITLE: Associate Professor of Radiology and Medical Imaging

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

| INSTITUTION AND LOCATION | DEGREE  (if applicable) | Completion Date  MM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| Brigham Young University | BS | 04/1998 | Applied Physics: Computer Science Emphasis |
| University of Virginia | MS | 05/2000 | Biomedical Engineering |
| Washington University in St. Louis | DSc | 08/2004 | Biomedical Engineering |
| University of Pennsylvania | Postdoctoral | 09/2006 | Medical Image Analysis |

**A. Personal Statement**

I am well-suited to significantly contributing to the quantitative analyses proposed in this “Pilot Study to Determine Health Effects of e-cigarette in Healthy Young Adults.” I have authored several articles detailing novel image analysis techniques, including registration and segmentation, for pulmonary studies utilizing hyperpolarized gases. As a core developer of the open source Insight Toolkit (National Library of Medicine) and the popular Advanced Normalization Tools (ANTs), I have extensive experience with robust software and algorithm development and employing these tools in robust pipelines for large-scale studies.

1. Filiano AJ, Xu Y, Tustison NJ, Marsh RL, Baker W, Smirnov I, Overall CC, Gadani SP, Turner SD, Weng Z, Peerzade SN, Chen H, Lee KS, Scott MM, Beenhakker MP, Litvak V, Kipnis J. Unexpected role of interferon-γ in regulating neuronal connectivity and social behaviour, Nature, 2016 Jul, 535(7612):425-9. PMCID: PMC4961620.
2. Tustison NJ, Cook PA, Klein A, Song G, Das SR, Duda JT, Kandel BM, van Strien N, Stone JR, Gee JC, Avants BB: Large-Scale Evaluation of ANTs and FreeSurfer Cortical Thickness Measurements, NeuroImage, 2014 October, 99:166-79. PMID: 24879923.
3. Avants BB, Tustison NJ, Song G, Cook PA, Klein A, Gee JC: A reproducible evaluation of ANTs similarity metric performance in brain image registration, Neuroimage 2011 February, 54(3):2033-2044. PMCID: PMC3065962.
4. Tustison NJ, Avants BA, Cook PA, Zheng Y, Egan A, Yuskevich PA, Gee JC: N4ITK: improved N3 bias correction, IEEE Trans Med Imag, 2010 June; 29(6):1310-1320. PMCID: PMC3071855.

**B. Positions and Honors**

**Positions and Employment**

2004-05 Research Fellow, Penn Image Computing and Science Laboratory, University of Pennsylvania, Philadelphia, PA

2005-2010 Senior Research Investigator, Penn Image Computing and Science Laboratory, University of Pennsylvania, Philadelphia, PA

2010- Assistant Professor, Department of Radiology, University of Virginia, Charlottesville, VA

**C. Contribution to Science**

* + - 1. **Working with colleagues from the University of Pennsylvania, I have made important contributions (both practical and theoretical) to image registration—a fundamental processing step in many medical image analysis tasks. These include contributions to biological modeling using parsimonious transformations described by diffeomorphisms which are smooth transforms with differentiable inverses. The utility of such transforms spans the gamut of possible applications from cardiac and lung mechanics to brain mapping. Other utilities have included point set similarity metrics for other application domains. In support of open science and reproducibility, I have made these contributions available through the Insight Toolkit (ITK) of the National Institutes of Health for other researchers to use. Additionally, my colleagues and I have won several competitions related to our image registration contributions. Specifically, the EMPIRE10 (registration of CT lung images) and STACOM2014 (cardiac motion estimation) challenges were both won using our image registration contributions.**

1. Avants BB, Tustison NJ, Stauffer M, Song G, Wu B, Gee JC: The Insight ToolKit image registration framework, 2014 April, 8:44. PMCID4009425
2. Tustison NJ, Avants BB: Explicit B-spline regularization in diffeomorphic image registration, Front Neuroinform, 2013 December, 7:39. PMCID: PMC3870320
3. Tustison NJ, Awate SP, Song G, Cook TS, Gee JC: Point set registration using Havrda-Charvat-Tsallis entropy measures, IEEE Trans Med Imag, 2011 February, 30(2):451—460. PMID: 20937578
4. Tustison NJ, Avants BA, Gee JC: Directly manipulated free-form deformation image registration, IEEE Trans Image Process, 2009 March; 18(3):624-635. PMID: 19171516
   * + 1. **In general, my contributions have been methodological. Most importantly, these contributions have been made available as open source software through the Advanced Normalization Tools (ANTs) and the underlying Insight Toolkit (ITK) of the National Library of Medicine of the NIH. ANTs was first created to rapidly disseminate our latest research to the community of scientists who depend on imaging analytics and to allow them to study different organ systems, species or modalities with the same sound foundation. While originally focused on diffeomorphic image registration, ANTs now incorporates novel and cutting-edge methods for image cleaning, segmentation, feature extraction and, more recently, complete statistical pipelines via ANTsR. In 2014, there were nearly 2,000 citations to ANTs and the software is cloned, downloaded or otherwise accessed over 100-200 times per week, on average at github. The sourceforge site hosts a similar number of visits and downloads. ANTsR is accessed on average 50 times per week---a substantial number for new software. There are also over 500 discussion topics on the ANTs sourceforge community site, nearly 100 topics on the github site and over 50 help-focused emails to the personal addresses of developers. Generally, response time to requests for help is within a few hours with rare occasions taking up to a day or two and is primarily split between myself and my colleague, Brian Avants. Recent development includes the open-source ANTsRNet (https://github.com/ntustison/ANTsRNet)---an R-based implementation of common deep learning architectures.**
5. Tustison NJ, Cook PA, Klein A, Song G, Das SR, Duda JT, Kandel BM, van Strien N, Stone JR, Gee JC, Avants BB: Large-Scale Evaluation of ANTs and FreeSurfer Cortical Thickness Measurements, NeuroImage, 2014 October, 99:166-79. PMID: 24879923.
6. Avants BB, Tustison NJ, Song G, Cook PA, Klein A, Gee JC: A reproducible evaluation of ANTs similarity metric performance in brain image registration, Neuroimage 2011 February, 54(3):2033-2044. PMCID: PMC3065962.
7. Avants BB\*, Tustison NJ\*, Wu J, Cook PA, Gee JC: An open source framework for *n*-tissue segmentation with evaluation on public data, Neuorinformatics, 2011 Dec, 9(4):381-400, PMCID: PMC3297199. \*Joint first authorship
8. Tustison NJ, Avants BA, Cook PA, Zheng Y, Egan A, Yuskevich PA, Gee JC: N4ITK: improved N3 bias correction, IEEE Trans Med Imag, 2010 June; 29(6):1310-1320. PMCID: PMC3071855.
   * + 1. **My colleagues and I have also raised very important critiques with respect to foundational tools used in neuroimaging research and general scientific practices. In one publication, we demonstrated how a common image mapping technique for determining statistical differences in populations results in significant false positives. This issue dovetails with related selection bias issues in the fMRI literature and in neuroscience research practices. We have also provided researchers and reviewers with guidelines for assessing the relative performance of scientific software and the pitfalls associated with instrumentation bias where software is viewed as a scientific instrument requiring proper usage.**

1. Tustison NJ, Avants BB, Cook PA, Kim J, Whyte J, Gee JC, Stone JR: Logical circularity in voxel-based analysis: normalization strategy may induce statistical bias, Hum Brain Mapp, 2014 March, 35:745--759 PMID: 23151955.
2. Tustison NJ, Johnson HJ, Rohlfing T, Klein A, Ghosh SS, Ibanez L, Avants BB: Instrumentation bias in the use and evaluation of scientific software: recommendations for reproducible practices in the computational sciences, Front Neurosci, 2013 September, 7:162, PMCID: PMC3766821.

**Complete List of Published Work in MyBibliography:** [**https://www.ncbi.nlm.nih.gov/myncbi/1TywuikZnK45a/bibliography/public/**](https://www.ncbi.nlm.nih.gov/myncbi/1TywuikZnK45a/bibliography/public/)

**D. Research Support**

**Ongoing Research Support**

**(Gee, JC) 06/01/2017 – 05/31/2022**

NIH-NLM

University of Pennsylvania

ITK-Lung: A software framework for lung image processing and analysis

This project brings together leading expertise in lung imaging research at Penn and UVa to develop, evaluate and deploy under community support an open-source software toolkit targeted for pulmonary imaging research.

Role: PI of UVa subcontract

**Completed Research Support**

**NNX13AJ92G (DR Roberts) 5/16/2013 - 5/15/2018**

NASA/Medical University of South Carolina

Human Cerebral Vascular Autoregulation and Venous Outflow In Response to Microgravity-Induced Cephalad Fluid Redistribution

The goal of this study is to understand how cerebral vascular autoregulation is influenced by astronauts traveling in the space shuttle, and by the training they undergo to get adjusted to microgravity.

Role: Co-investigator

**#S-1163-01 (JR Stone) 1/1/2013 – 5/31/2015**

The Geneva Foundation

Brain Injury Biomarkers and Behavioral Characterization of mTBI in Soldiers Following Repeated, Low-Level Blast Exposure

The goal of the present project is to longitudinally evaluate repetitive low-level blast exposure in a population of New Zealand Breachers over a four-year period. The length of this project will allow for multiple evaluations in a longitudinal fashion of the same subject thus affording the opportunity to characterize the natural history of any neurological alterations observed in military breachers exposed to low-level blast.

Role: Co-investigator

**2R44 HL087550-04A1 (I Ruset) 9/1/2011 –** 1**/31/2015**

Xemed, LLC/NIH-NHLBI

Regulatory Advancement of HXe as an MRI Contrast Agent

The primary goal is to validate the effectiveness of HXe ventilation MRI for delineating regions of normal and abnormal lung ventilation.

Role: Co-investigator on UVA subcontract (UVA PI: T. Altes)

**(Gee, JC)**  **7/1/2011 –** **6/30/2012**

NIH-NLM

University of Pennsylvania

Fundamental Refactoring of Deformable Image Registration in ITK with Distributed Computing and GPU Acceleration

UVA will be a subcontractor to the University of Pennsylvania (P.I. James C. Gee) on simplifying and enhancing the registration framework of the Insight Toolkit (ITK) of the National Institutes of Health to attract the broad neuroimaging community. The former seeks to ease ITK use for non-C++ programmers whereas the latter aims to add high performance registration strategies to ITK. The University of Virginia will carry the following responsibilities for this project: to collaborate with University of Pennsylvania personnel to simplify the ITK registration framework and to develop the proper testing environment to ensure integrity of the new ITK software developments. Dr. Tustison will oversee the efforts of the University of Virginia collaborators. He will play a leading role in software developments specifically as it relates to novel registration developments involving Bsplines.

Role: PI of UVA subcontract

**PJMR005\_1050033 (TA Altes) 10/15/2010 – 5/31/2014**

Novartis Pharmaceuticals Corp.

Hyperpolarized noble-gas enhanced imaging of b2-agonist pharmacodynamics and pharmacokinetics in mild to moderate asthma

The goal is to assess the utility of hyperpolarized helium-3 MRI to detect changes in lung ventilation in asthmatics treated with beta agonists.

Role: Co-investigator

**R44 HL1123971 (I Ruset) 12/1/2011 - 5/31/2015**

Xemed, LLC/NIH-NHLBI

Single-session bronchial thermoplasty for severe asthmatics guided by Hxe MRI

UVA will be a subcontractor to Xemed on the three center trial (Xemed, UVA, and University of Washington) to assess the potential utility of using hyperpolarized xenon MRI to guide a newly FDA approved endobronchial treatment for asthma, bronchial thermoplasty. Image guidance has the potential to reduce the number of treatment sessions for bronchial thermoplasty from 3 to 1 which would result in significant reductions in both cost and risk associated with this procedure. The University of Virginia will carry two responsibilities for this project: to refine innovative software methods for indentifying problematic airways and quantifying their disease (throughout Phase I and Phase II), and to serve as the blinded reading site masked to which patients are in which treatment group (primarily at the end of Phase II).

Role: PI on UVA subcontract