# Faculty of Medicine of Harvard University Curriculum Vitae

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Place of Birth: Leiden, the Netherlands

### Education

2002	MD	Medicine	Catholic University of Leuven
2016	PhD	Medicine (S K Warfield)	Utrecht University
Postdoctor	al Training		
07/02 - 04/03	3 Resident	Adult Neurology (Program Director: Professor Jan J. Heimans, MD, PhD)	VU University Medical Center
04/03 - 06/06	8 Resident	Adult Neurology (Program Director: Sebastiaan F.T.M. de Brujin, MD, PhD)	Haga Teaching Hospital
07/06 - 06/07	' Clinical Fellow	Epilepsy and Clinical Neurophysiology (Program Director: Blaise F.D. Bourgeois, MD)	Boston Children's Hospital, Harvard Medical School
07/07 - 06/10	) Resident	Child Neurology (Program Directors: Basil T. Darras, MD, David K. Urion, MD)	Boston Children's Hospital, Harvard Medical School
07/10 - 06/11	Intern	Pediatrics (Program Directors: Theodore C. Sectish, MD, Robert J. Vinci, MD)	BCRP – Boston Combined Residency Program in Pediatrics, Harvard Medical School
07/11 - 06/12	Research Fellow	Basic Neuroscience, ABPN Neuroscience Track	Boston Children's Hospital, Harvard Medical School

(Program Director: Mustafa Sahin,

MD, PhD)

**Faculty Academic Appointments** 

07/12 - 02/14 Instructor Harvard Medical School Neurology

02/14 -Harvard Medical School Assistant Neurology

Present Professor

Appointments at Hospitals/Affiliated Institutions

Current

07/12 -Assistant Neurology Boston Children's Hospital

Present

**Other Professional Positions** 

2018 - 2019 Okulus LLC Consultant Epidiolex(R) P&T simulations

2019 - 2020 Consultant Philips Neuro Inc. High Density EEG

Greenwich Biosciences Inc. 2019 - Present Consultant Phase III trial of Epidiolex(R)

> in infants with TSC Epidiolex(R) in TSC

Scientific Advisory

Board

Speakers Bureau Epidiolex(R) in TSC

2020 - Present Consultant **CRICO** Medicolegal expertise

Adler, Cohen, Harvey,

Wakeman and Guekguezian

LLP

2020 - Present Consultant **Novartis Tuberous Sclerosis Complex** 

Neurelis Inc.

Curriculum and TSC Seizure

Clinical Data

2020 - Present Consultant

Speakers Bureau Scientific Advisory

Board

Valtoco(R)

**Major Administrative Leadership Positions** 

<u>Local</u>

2013 - Present Co-Director, Clinical Neurophysiology Boston Children's Hospital

Core, Translational Neuroscience Center

2014 - Present Director, Computational Boston Children's Hospital

Neurophysiology, Division of Epilepsy &

Clinical Neurophysiology

2015 - Present Director, BIDMC/BCH Clinical Boston Children's Hospital

Neurophysiology Fellowship Program

2019 - Present Director, BCH/BIDMC Epilepsy Boston Children's Hospital

Fellowship Program

Regional

2020 - Present President, Greater Boston Epilepsy Greater Boston

Society (GBES)

**Committee Service** 

<u>Local</u>

2013 - 2016 Career Development Curriculum Boston Children's Hospital

2013 - 2016 Committee member, lecturer

2013 - 2016 Epilepsy Surgery Scheduling Boston Children's Hospital

Improvement Committee

2013 - 2016 Epilepsy Representative

2019 - Present Graduate Medical Education Committee Boston Children's Hospital

(GMEC)

2019 - Present Member, Annual Program Review

Subcommittee

**National** 

2016 - Present American Board of Clinical Member, Examination Development

Neurophysiology (ABCN) Committee Item Writing Panel

2016 - 2019

2019 - Present Co-Chair, Pediatric EEG Board Exam

2018 - Present High Density EEG (hdEEG) Consortium Founding Member

2018 - Present

**Professional Societies** 

2003 - Present Dutch Association of Clinical Neurophysiology (NVKNF)

2003 - Present Dutch Association of Neurology (NVN)

2006 - Present American Epilepsy Society

2016 - 2019 Member, Student and Resident Education

Subcommittee, EEG Section Workgroup

2007 - Present American Association of Neurology (AAN)

2007 - Present Child Neurology Society (CNS)

2007 - Present Massachusetts Medical Society

2011 - Present American Clinical Neurophysiology Society

2012 - 2015 Member, Membership Committee 2016 - 2017 Co-Chair, Membership Committee

2012 - Present International Child Neurology Association (ICNA)

#### **Grant Review Activities**

2014 Action Medical Research, West Sussex,

United Kingdom

2014 Reviewer

2017 Nationaal Epilepsie Fonds (NEF)

2017 Reviewer

2017 - Present Scientific Review Group, NST-1 study National Institutes of Health/NINDS

section

2017 - Present Ad-hoc member and reviewer

2018 Medical Research Council (MRC)

2018 Reviewer

2018 Tuberous Sclerosis Alliance

2018 Reviewer

#### **Editorial Activities**

Ad hoc Reviewer

Acta Neurologica Belgica

American Journal of Case Reports

Annals of Neurology

BioMed Research International

BMJ Case Reports

Cognitive Neurodynamics

Developmental Neurorehabilitation

Developmental Science

Emerging Infectious Diseases

Epilepsia

Epilepsia Open

Epilepsy and Behavior

Epilepsy Research

European Journal of Paediatric Neurology

European Neurology

European Radiology

IEEE Journal of Biomedical and Health Informatics

IEEE Transactions on Neural Systems and Rehabilitation Engineering

Journal of Child Neurology

Journal of Clinical Neurophysiology

Journal of Neuroimaging

Journal of Neurology, Neurosurgery, and Psychiatry

Journal of Pediatric Neurology

Journal of Pediatrics

Molecular Neurobiology

Neuroepidemiology

Neurolmage Clinical

Neuropsychiatric Electrophysiology

Pediatric Neurology

**Pediatrics** 

PLOS ONE

Seizure - European Journal of Epilepsy

#### Other Editorial Roles

2012 Editor, Book Handbook of Pediatric Neurology

Sims KC, Senior Editor. Peters JM, Musolino P, Elibol Ward Z, Junior Editors. Lippincott

Williams & Wilkins, Nov 2013. ISBN 1451175485.

2016 - Present Editor, Journal Editor

European Journal of Paediatric Neurology

#### **Honors and Prizes**

2003	Young Scientist Scholarship	International Society for Brain Electromagnetic Topography, Santa Fe, NM
2006	TopScholar Epilepsy Fellows Scholarship	Annual Meeting of the American Epilepsy Society, San Diego, CA
2008	Von L. Meyer travel award	Boston Children's Hospital
2010	The J. Kiffin Penry Pediatric Epilepsy MiniFellowship Program	J. Kiffin Penry Pediatric Epilepsy Mini-Fellowship Network
2015	Faculty Innovated Research Award	Boston Children's Hospital Medical Staff Organization
2020	Fellow of the American Clinical Neurophysiology	American Clinical Neurophysiology Society

Society (FACNS)

# Report of Funded and Unfunded Projects

# **Grants and Sponsored Research**

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2012 - 2013 Faculty Development Fellowship, Department of Neurology, Boston Children's Hospital

Harvard Medical School Foundation funds, the Eleanor and Miles Shore 50th

Anniversary Fellowship Program for Scholars in Medicine

PI, Direct Costs: \$25,000

Study of implementation, accuracy and clinical impact of high density EEG in the

pediatric Epilepsy Monitoring Unit

2012 - 2013 Development of a web-based EEG platform for remote reading, teaching, and data

exchange

World Federation of Neurology Pilot Grant

PI, Direct Costs: \$12,000

Development and implementation of an open-source, open-access web-based EEG platform for remote EEG reading, EEG teaching, EEG archiving, and data exchange in

developing and low-resource countries.

2012 - 2015 Epilepsy Center Without Walls: Potential EEG biomarkers and antiepileptogenic

strategies for epilepsy in TSC

NIH/NINDS, P20 1P20NS080199

Investigator (PI: E Bebin)

5-center prospective study with serial imaging, EEG, clinical examination and neuropsychological assessments of your patients with TSC toexplore potential EEG biomarkers and antiepileptogenic strategies for epilepsy in TSC.

2012 - 2019 Early Biomarkers of Autism Spectrum Disorders in Infants with TSC - Autism Centers of

Excellence (ACE) 2012 Network Grant

NIH/NINDS, 1U01NS082320

Investigator (PI: Mustafa Sahin, PI: D Krueger)

5-center prospective study with serial imaging, EEG, clinical examination and neuropsychological assessments of young patients with TSCto explore potential early

biomarkers for Autism Spectrum Disorders in TSC.

2013 - 2019 MRI Biomarkers of Patients with Tuberous Sclerosis Complex and Autism

NIH, 1R01 NS079788

Investigator (PI: S Warfield)

Development and validation of a set of advanced MRI measures in a longitudinal study of young children with autism from known (TSC) and unknown causes, which uniquely identify the brain changes that underlie autism, to identify infantsat increased risk autism, to allow for monitoring of response to drug therapy, and ultimately to tailor interventions to alter the developmental trajectory.

2015 - 2016 Functional and structural connectivity and anatomopathological correlation of

epileptogenesis in Tuberous Sclerosis Complex

Harvard Catalyst Early Clinical Data Support for Grant Submissions

PI, Direct Costs: \$30,000

Ex-vivo tissue imaging study with registered and quantitative neuropathological correlation to assess abnormal connectivity and disrupted microcircuitry beyond tubers,

in the vicinity of the epileptogenic focus.

#### Current

2017 - 2022 Preventing Epilepsy Using Vigabatrin in Infants with Tuberous Sclerosis Complex (PREVeNT Trial)

NIH/NINDS, NIH 1U01NS092595-01A1

Investigator (PI: Martina Bebin)

The central hypothesis of this proposal is that through early identification of electroencephalography (EEG) biomarkers we can identify at risk infants with TSC and that early treatment versus delayed treatment with vigabatrin in this population will prevent further progression of epileptogenesis and have direct favorable impact on disease severity and epilepsy-associated comorbidities.

2017 - 2021 Dense array image-compatible EEG for enhanced neonatal care

NIH/NINDS, 5R01EB024343-03

Co-Investigator (PI: Giorgio Bonmasser)

The goal of this project is to demonstrate the feasibility and safety of developing a dense array, image-compatible, neonatal EEG net "NeoNet" (hdEEG) using novel conductive Thin Film technologies.

2018 - 2020 Interictal Frequency Oscillations as Non-Invasive Biomarkers of Epileptogenicity in Pediatric Patients

NIH/NINDS, 1R21NS101373-01A1

Co-Investigator (PI: Christos Papadelis, PI: Steven Stufflebeam)

This R21 application aims to non-invasively detect and reliably localize HFOs from pediatric patients with refractory epilepsy using high-density scalp electroencephalography (EEG) and magnetoencephalography (MEG), identify their onset generator, and correlate the resection of this generator with patients' postsurgical

outcome.

2020 - 2021 A Phase 2 Open-label 12-Week Trial of Adjunctive Ganaxolone Treatment (Part A) in Tuberous Sclerosis Complex-related Epilepsy followed by Long-term Treatment (Part B)

Marinus Pharmaceuticals

Site PI

The goal of this study is to assess preliminary safety and efficacy of ganaxolone as adjunctive therapy for the treatment of primary seizure types in patients with genetically or clinically confirmed TSC-related epilepsy through the end of the 12 week treatment period. NCT04285346.

#### **Current Unfunded Projects**

2013 - Present DTI tractography in Sclerosis Complex and non-syndromic Autism Spectrum disorder

Study of microstructural integrity of multiple anatomical and functionally relevant major white matter pathways in TSC and ASD to identify biomarkers of neurological phenotype.

2014 - Present Multiple projects involving improved electrical source imaging (ESI)

Co-investigator and PI

Multiple projects involving improved electrical source imaging (ESI), including identifying dynamic patterns in scalp EEG of epileptic patients and applying source localization techniques to these dynamics. Responsible for analysis of clinical and

hdEEG data, and provided expertise in the clinical evaluation of epilepsy to ensure that techniques developed have direct clinical relevance for epilepsy surgery.

2017 - Present Serial DTI in Tuberous Sclerosis Complex and localization of the epileptogenic zone

Study of longitudinal DTI evolution in the normal appearing white matter, the perituber region and the tubers in TSC to assess location of epileptogenic zone.

# Report of Local Teaching and Training

Formal Teaching of Residents, Clinical Fellows and Research Fellows (post-docs)

2012 - Present Inpatient service case discussions Boston Children's Hospital

Boston, Massachusetts.

**United States** 

Pediatric Neurology residents and Epilepsy fellows 4 lectures per year

2013 - Present Neuropathology lecture series Boston Children's Hospital

Boston, Massachusetts,

**United States** 

Pediatric Neurology residents 2 lectures per year

2014 - Present Epilepsy lecture series Boston Children's Hospital

Boston, Massachusetts,

**United States** 

Pediatric Neurology residents and Epilepsy fellows 2 lectures per year

Clinical Supervisory and Training Responsibilities

2012 - Present Inpatient service Pediatric Neurology, Epilepsy and

neurological ICU consultation team / Pediatric

Neurology residents and Epilepsy fellows

Boston Children's Hospital

8 weeks/year, full-time

Formally Mentored Harvard Medical, Dental, and Graduate Students

2010 Danielle Pier, HMS class of 2010 / Pediatric Neurologist, Massachusetts General

Hospital for Children

Guillain-Barre syndrome in a child with pain: lessons learned from a late diagnosis -

First authorship on case report: PMID 20456276.

2012 Jolene M Singh, Harvard University class of 2014 / Computational Radiology

Laboratory, Boston Children's Hospital

Tubers Are Neither Static Nor Discrete: Evidence From Serial Diffusion Tensor Imaging - Epilepsy Foundation Student Fellowship. Co-author on paper on longitudinal diffusion

changes in tuberous sclerosis complex: PMID 26432846.

Other Mentored Trainees and Faculty

2008 - 2012 Ivan Sanchez Fernandez, MD / Clinical and Research Fellow, Boston Children's

Hospital

Career Stage: Clinical Fellow in Neurology Mentoring Role: Supervisor

Accomplishments: Multiple first-author original publications in Epilepsia, Neurology, and others; Epilepsy Fellowship at Boston Children's Hospital; local, regional and national (invited) talks: Department of Child Neurology, Hospital Sant Joan de Déu, Universidad de Barcelona, Spain. PMIDs 21399511, 22532549, 22578248, 23163318, 23445896.

Meritxell T Fernandez, BSc / Resident in Pediatrics, Universidad de Lleida, Spaini Career Stage: Undergraduate student, Quiron Hospital Group, Barcelona, Spain Mentoring Role: Supervisor Accomplishments: BSc at Quiron Hospital Group,

Barcelona, Spain. Neurology Research elective. Second authorship on research paper on use of EEG during Wada test: PMID 22341967.

2011 - 2012 Jacqueline Tan, BSc

Career Stage: Undergraduate student, VU University Medical Center, Amsterdam, the Netherlands *Mentoring Role:* Supervisor *Accomplishments:* Brain Functional Networks in Syndromic and Non-Syndromic Autism: A Graph Theoretical Study of EEG Connectivity - BSc. Co-authorship on EEG connectivity study in autism spectrum disorder: PMID 23445896.

2012 - 2014 Anna K Prohl, BSc / Medical Student, Quinnipiac University

Career Stage: Undergraduate student, Bowdoin College, Brunswick ME Mentoring

Role: Supervisor Accomplishments: Tuberous sclerosis complex and diffusion tensor imaging - Epilepsy Foundation Student Fellowship. Co-authorship on original research papers: PMIDs 24315019, 24489482, 26432846.

2012 - 2016 Archana Patel, M.D., M.P.H. / Assistant in Neurology, Instructor in Neurology, Boston Children's Hospital and Harvard Medical School Career Stage: Resident, Fellow Mentoring Role: Supervisor Accomplishments: Supervisory role in the development of a questionnaire-based diagnostic and therapeutic approach to pediatric epilepsy, Muhimbili National Hospital, Tanzania. First authorship of paper on the use of questionnaire for pediatric epilepsy, PMID 27088519.

2013 - Present Peter E Davis, MD / Assistant in Neurology, Instructor in Neurology, Boston Children's Hospital and Harvard Medical School

Career Stage: Assistant in Neurology Mentoring Role: Co-mentor Accomplishments:

Co-author in review on TSC and Autism Spectrum Disorder, PMID 25986747. PMIDs

29101226, 31297797, 31812987, 31838998.

2014 Merel Boom, MSc

Career Stage: Graduate student, University of Amsterdam, the Netherlands *Mentoring Role:* Supervisor *Accomplishments:* Lesion-Constrained Electrical Source Imaging: A Novel Approach in Epilepsy Surgery for Tuberous Sclerosis Complex - MSc. Research elective on tuberous sclerosis complex and electrical source localization for epilepsy surgery. First author on review paper on TSC and epilepsy surgery. Co-author on original research paper on TSC epilepsy surgery and electrical source imaging, PMID 31261349.

2014 Robbert R Struyven, MD / Student, Master of Science in Data Science, Harvard University

Career Stage: Medical student, Catholic University of Leuven, Belgium Mentoring Role: Supervisor Accomplishments: Diffusion Imaging in Tuberous Sclerosis Complex - Correlation with Neuropathology. Medical student research elective, ranked 2<sup>nd</sup> in "Abstract competition" of the Student Health Science Symposium. Co-first author on original paper on this topic: PMID 31353853.

John J Bushman, BSc in Biomedical Engineering / Associate Research Engineer, A123
Systems
Career Stage: Undergraduate student, Rochester Institute of Technology, Rochester

NY Mentoring Role: Supervisor Accomplishments: White Matter Mean Diffusivity Correlates With Myelination in Tuberous Sclerosis Complex - Two-month summer Internship on the coregistration of tissue pathology and ex-vivo MRI. Co-authorship on TSC ex-vivo imaging paper, PMID 31353853.

2016 Emma A van der Poest Clement, MSc

> Career Stage: Graduate student, Erasmus University, Rotterdam, the Netherlands Mentoring Role: Supervisor Accomplishments: Erasmus University, Rotterdam, the Netherlands. Vigabatrin for Epileptic Spasms and Tonic Seizures in Tuberous Sclerosis Complex - Research elective on the use of vigabatrin in tuberous sclerosis complex. First authorship on original research paper on vigabatrin in TSC, and on case report:

PMIDs 31912454, 29687739

2017 Anne-Elise de Groen, MSc

> Career Stage: Graduate student, University of Amsterdam, the Netherlands Mentoring Role: Supervisor Accomplishments: The Evolution of Subclinical Seizures in Children With Tuberous Sclerosis Complex - MSc. Research elective on electrographical seizures in tuberous sclerosis complex. First author, PMID 31290714.

2018 Brechtie Mulder, MSc

> Career Stage: Graduate student, VU Free University, Amsterdam, the Netherlands Mentoring Role: Supervisor Accomplishments: Tuberous sclerosis complex lesion network mapping in infantile spasms - MSc. Six-month research elective for master's thesis. Co-author on original paper on TSC lesion network mapping in infantile spasms (in progress), and platform presentation at international meeting.

2019 Maaike Nijman, MSc

> Career Stage: Graduate student, University of Amsterdam, the Netherlands Mentoring Role: Supervisor Accomplishments: Structural MRI markers of epileptogenic zone in tuberous sclerosis complex - MSc. Six-month research elective for master's thesis. First author on original paper on structural MRI markers of the epileptogenic zone in TSC (in progress.)

# **Formal Teaching of Peers**

No presentations below were sponsored by 3<sup>rd</sup> parties/outside entities

2013 Non-epileptic events in pediatrics One hour lecture

> Seminar Series, Department of Boston, Massachusetts

**Psychiatry** 

Boston Children's Hospital

2013 - Present 1. Fits, faints and funny turns: 2 lectures per year

> Non-epileptic paroxysmal events in childhood. 2. Bayesian and conventional interpretation of diagnostic testing

Satellite Seminar Series (Boston

Children's North)

Boston Children's Hospital

Peabody, Massachusetts

Advanced neurophysiology techniques

Michael J. Bresnan Child Neurology

Course

2014

Boston Children's Hospital

One lecture per course Boston, Massachusetts

2016	1. Seizure or NOT? 2. Epilepsy, Boston Children's Hospital, and the WHO (International Neurology Colloquium) Michael J. Bresnan Child Neurology Course Boston Children's Hospital	Two lectures per course  Boston, Massachusetts
2018	Computational Neurophysiology Lennox-Lombroso Pediatric Epilepsy Conference Boston Children's Hospital	One lecture per course Boston, Massachusetts
2018	Seizure or NOT? Paroxysmal non-epileptic events in pediatrics Michael J. Bresnan Child Neurology Course Boston Children's Hospital	One lecture per course Boston, Massachusetts
2020	Paroxysmal non-epileptic events in pediatrics Michael J. Bresnan Child Neurology Course Boston Children's Hospital	One lecture per course Boston, Massachusetts

# **Local Invited Presentations**No presentations below were sponsored by 3<sup>rd</sup> parties/outside entities

2009	S below were sponsored by 3° parties/outside entities  Non-epileptic paroxysmal events in children / Grand Rounds  Department of Medicine, Boston Children's Hospital
2011	Computational EEG Analysis, a Clinician's and a Physicist's Perspective / Seminar Epilepsy Research Seminar Series Boston Children's Hospital
2012	A graph theoretical approach to functional connectivity in autism / Oral Presentation Fetal-Neonatal Neuroimaging & Developmental Science Center, Boston Children's Hospital
2012	Brain Functional Networks in Tuberous Sclerosis Complex and Autism: a Graph Theoretical Study of EEG Connectivity / Research Seminar Center for Pain and the Brain, Boston Children's Hospital
2013	Brain networks and EEG functional connectivity in autism and TSC / Lab meeting Cash Lab, Massachusetts General Hospital
2013	EEG Source Localization: Improving Diagnostics Through Advanced Engineering / Seminar Epilepsy Research Seminar Series Boston Children's Hospital
2014	Neuroimaging and Neurophysiology correlates of autism in Tuberous Sclerosis Complex / Oral Presentation Monthly autism meeting Boston Children's Hospital

2015	Rapid advances in neuroimaging, neurophysiology, and targeted treatment of Tuberous Sclerosis Complex / Oral Presentation Neuroradiology lecture series Boston Children's Hospital
2016	Seizure or NOT? Non-epileptic paroxysmal events in children / Conference Neurology Nursing Teaching Conference Boston Children's Hospital
2017	Localization and prediction of epilepsy in Tuberous Sclerosis Complex / Grand Rounds Longwood Epilepsy Grand Rounds Boston Children's Hospital
2018	Tuberous Sclerosis Complex: Towards systemic and surgical prevention of epilepsy / Lecture Fetal-Neonatal Neuroimaging & Developmental Science Center (FNNDSC) Boston Children's Hospital
2018	Tuberous Sclerosis Complex: Towards systemic and surgical prevention of epilepsy / Lecture Joint laboratory meeting of Kwiatkowski, Priolo, Henske and Sahin Brigham and Women's Hospital
2019	Tuberous Sclerosis Complex: Prevention of epileptic encephalopathy in multilesional epilepsy / Grand Rounds Longwood Neurology Grand Rounds Harvard Institutes of Medicine

Report of Regional, National and International Invited Teaching and Presentations
Those presentations below sponsored by 3rd parties/outside entities are so noted and the sponsor(s) is identified.

Regional 2009	Jeavons syndrome: More than meets the eye? / Oral Presentation - Presenter Greater Boston Epilepsy Society, Fall Meeting 2009 Boston, Massachusetts
2012	Brain functional networks in tuberous sclerosis complex and autism: a graph theoretical study of EEG connectivity / Oral Presentation - Presenter Autism Consortium 2012 Symposium Boston, Massachusetts
2016	Imaging and EEG to guide early treatment of TSC: can we improve neurological outcome? / Oral Presentation - Presenter TSC Medical Symposium University of Connecticut, Connecticut Children's Medical Center Hartford, Connecticut
2016	Tubers are neither static nor discrete: Lines of evidence and clinical implications / Oral Presentation - Presenter Greater Boston Epilepsy Society Boston, Massachusetts
2018	Tuberous Sclerosis Complex: Novel techniques for prediction and localization of epilepsy

Dartmouth Hitchcock Medical Center, Geisel School of Medicine Dartmouth, New Hampshire National 2000 Population study of Benign Rolandic Epilepsy: Is treatment needed? / Oral Presentation -Annual Meeting of the Child Neurology Society St. Louis, Missouri 2012 Loss of white matter microstructural integrity is associated with adverse neurological outcome in tuberous sclerosis complex / Oral Presentation - Presenter 64th Annual meeting of the American Academy of Neurology New Orleans, Louisiana 2013 Brain Functional Networks in Tuberous Sclerosis Complex and Autism: a Graph Theoretical Study of EEG Connectivity / Oral Presentation - Presenter 65th Annual Meeting of the American Academy of Neurology San Diego, California 2014 Advanced neuroimaging and neurophysiological measure of tuberous sclerosis complex: Pathology beyond tubers / Oral Presentation - Presenter Special Interest Group (SIG) meeting, 68th Annual meeting of the American Epilepsy Society Seattle, Washington 2014 Neuroimaging and neurophysiological correlates of autism in Tuberous Sclerosis Complex / Grand Rounds - Presenter **UCLA Semel Institute Grand Rounds** University of California, Los Angeles Los Angeles, California Case presentation I: Implantation Strategy. Electrocorticography and intracranial EEG 2015 course / Teaching Presentation - Presenter American Clinical Neurophysiology Society, Annual Meeting and Courses Houston, Texas 2015 Electrocorticography during pediatric epilepsy surgery. Intraoperative Monitoring course, part II / Teaching Presentation - Presenter American Clinical Neurophysiology Society, Annual Meeting and Courses Houston, Texas 2015 Rapid advances in neuroimaging, neurophysiology, and targeted treatment of Tuberous Sclerosis Complex / Lecture - Invited Speaker Weill Cornell Medical Center New York, New York 2016 Targeted treatment of Tuberous Sclerosis Complex: Insights from neurophysiology and neuroimaging / Grand Rounds - Presenter Neurology Grand Rounds University of Connecticut, Connecticut Children's Medical Center

/ Grand Rounds - Invited Speaker

Neurology Grand Rounds

Hartford, Connecticut

2016 MRI biomarkers and early medical interventions in Tuberous Sclerosis Complex / Oral Presentation - Presenter 4th Annual Flux Congress Washington University St. Louis, Missouri 2016 Pediatric State of the Art Symposium / Lecture - Chair 2016 Annual Meeting of the American Epilepsy Society Houston, Texas Tuberous Sclerosis Special Interest Group (SIG): Biomarkers and Risk Factors for 2017 Epilepsy in TSC: Diagnosis, Prediction and Prevention / Oral Presentation - Author & Presenter (Selected Oral Abstract) 2017 Annual Meeting of the American Epilepsy Society Washington, District of Columbia 2018 Technological advances in pediatric epilepsy surgery: implications for Tuberous Sclerosis Complex / Grand Rounds - Invited Speaker Department of Neurosurgery **Baylor College of Medicine** Houston, Texas High density EEG: Application in multilesional epilepsy / Oral Presentation - Author & 2018 Presenter (Selected Oral Abstract) Inaugural High Density Consortium Meeting Tampa, Florida 2018 Tuberous Sclerosis Complex: Towards preventative and targeted treatment of epilepsy / Grand Rounds - Invited Speaker **UVM Neuroscience Grand Rounds** University of Vermont Medical Center Burlington, Vermont 2018 Tuberous Sclerosis Complex: Novel localization techniques for early epilepsy surgery / Grand Rounds - Invited Speaker **Epilepsy Rounds** University of Alabama Birmingham Birmingham, Alabama 2018 Tuberous Sclerosis Complex: Towards prevention of epilepsy / Grand Rounds - Invited Speaker Pediatric Grand Rounds University of Alabama Birmingham Birmingham, Alabama 2019 Methods for HD EEG ESI and Lesion-Constrained ESI. In concurrent session "Current and Future Clinical Practice of High Density EEG and Electrical Source Imaging in Epilepsy" / Lecture - Invited Speaker American Clinical Neurophysiology Society Annual Meeting Las Vegas, Nevada 2019 Epilepsy in Tuberous Sclerosis Complex: Insights from advanced EEG and imaging techniques / Grand Rounds - Invited Speaker Epilepsy Lecture Series, Northwestern Comprehensive Epilepsy Center

Northwestern University

Chicago, Illinois

2020 Tuberous Sclerosis Complex: Prevention of epileptic encephalopathy in multilesional

epilepsy / Grand Rounds - Invited Speaker Grand Rounds, Department of Neurology

Vanderbilt University Nashville, Tennessee

2020 Epilepsy surgery in tuberous sclerosis complex: research priorities and study design /

Investigators Workshop - Chair

2020 Annual Meeting of the American Epilepsy Society

Virtual Event

2021 Prevention of epileptic encephalopathy in multilesional epilepsy / Grand Rounds - Invited

Speaker

Grand Rounds, Department of Neurology

Columbia University New York, New York

2021 Preventative medical and early surgical treatment of epilepsy in Tuberous Sclerosis

Complex / Grand Rounds – Invited Speaker Grand Rounds, Department of Pediatrics Oregon Health & Science University

Portland, Oregon

<u>International</u>

2003 Benigne Rolandische Epilepsie: Is behandeling nodig? / Oral Presentation - Presenter

Children and epilepsy: towards an individualized treatment regimen

Utrecht, Netherlands

2005 Computer-assisted EEG interpretation / Oral Presentation - Author & Presenter (Selected

Oral Abstract)

Annual Meeting of the Dutch Society of Clinical Neurophysiology

St Michelsgestel, Netherlands

2009 EEG and Imaging in the Diagnosis of Pediatric Epilepsy / Invited Presentation - Invited

Speaker

Symposium: Epilepsy and Stigma: How do we conquer it in Africa

Lusaka

2013 Brain Functional Networks in Tuberous Sclerosis Complex and Autism: a Graph

Theoretical Study of EEG Connectivity / Oral Presentation - Presenter

International Research Conference on TSC and Related Disorders: From molecules to

Medicines

Washington, District of Columbia

2015 Recent advances in neuroimaging, neurophysiology, and targeted treatment of Tuberous

Sclerosis Complex / Invited lecture - Invited Speaker

Epilepsy Research rounds

Utrecht University Utrecht, Netherlands

2016	White matter diffusivity reflects cumulative neurological comorbidity in Tuberous Sclerosis Complex / Platform Presentation - Presenter International Child Neurology Association (ICNA) meeting Amsterdam, Netherlands		
2016	Autism spectrum disorder and tuberous sclerosis complex / Lecture - Invited Speaker International Scientific Symposium on Syndromic Autism (Syndromaler Autismus Interprofessionelle Tagung) Kork (Kehl), Germany		
2018	Tuberous Sclerosis Complex: Towards Prevention of Epilepsy / Grand Rounds - Invited Speaker Pediatric Neurology Grand Rounds Amsterdam University Medical Center Amsterdam, Netherlands		
2018 - 2018	Clinical Neuroscience Minor (elective), Computer analysis of the EEG, Peers – Lecturer Amsterdam University Medical Centre Amsterdam, Netherlands		
2018 - 2018	Clinical Neuroscience Minor (elective), EEG and pediatric epilepsy, Peers – Lecturer Amsterdam University Medical Centre Amsterdam, Netherlands		
2018	Computer Analysis of the EEG / Lecture - Invited Speaker Amsterdam University Medical Centre, Clinical Neuroscience Minor (elective) Amsterdam, Netherlands		
2018	EEG and Pediatric Epilepsy / Lecture - Invited Speaker Amsterdam University Medical Centre, Clinical Neuroscience Minor (elective) Amsterdam, Netherlands		
2019	Tubers associated with Infantile Spasms impact a common brain network in tuberous sclerosis complex / Oral Presentation - Co-Author 2019 International Tuberous Sclerosis Complex Research Conference Toronto, Canada		
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# **Report of Clinical Activities and Innovations**

# **Current Licensure and Board Certification**

2002 - Present	Dutch Medical License (full)
2006 - Present	Educational Commission for Foreign Medical Graduates certification
2010 - Present	Registration as Neurologist in the Netherlands
2012 - Present	Massachusetts Medical License (full)
2013 - Present	American Board of Clinical Neurophysiology (ABCN)

2014 - Present American Board of Psychiatry and Neurology (ABPN), with Special Qualification in

Child Neurology

2016 - Present Subspecialty Certification in Epilepsy, American Board of Psychiatry and Neurology

(ABPN)

#### **Practice Activities**

2012 - Present	Ambulatory care	Comprehensive Tuberous Sclerosis Program, Boston Children's Hospital	2 sessions/month
2012 - Present	Ambulatory care	Pediatric Neurology/Epilepsy (BCH Peabody), Boston Children's Hospital	4 sessions/month
2012 - Present	Electrical Source Imaging	Division of Epilepsy and Clinical Neurophysiology, Boston Children's Hospital	2-4 sessions/month
2012 - Present	Inpatient service	Epilepsy Service, Boston Children's Hospital	6 weeks/year
2012 - Present	Outpatient EEG interpretation	Division of Epilepsy and Clinical Neurophysiology, Boston Children's Hospital	1-2 sessions/month
2016 - Present	Ambulatory care	Pediatric Neurology (BCH Lexington), Boston Children's Hospital	2 sessions/month
2016 - Present	Ambulatory care	Pediatric Neurology/Epilepsy (BCH Lexington), Boston Children's Hospital	2 sessions/month

#### **Clinical Innovations**

Continuous Spike and Wave during Sleep Syndrome (CSWS) characterization -Boston Children's Hospital (2012 - 2014) As a member of a research group studying CSWS at BCH, we revised and outlined diagnostic criteria, characterized longitudinal clinical course of the condition, outlined techniques for spike quantification on the EEG, and provided additional etiological insights based on MR imaging.

# Report of Technological and Other Scientific Innovations

Advanced neuroimaging and neurophysiology in Tuberous Sclerosis Complex (2011 -Present) I am the dedicated epileptologist in the multidisciplinary TSC program at Boston Children's Hospital, and TSC forms a major research focus. With my collaborators we were the first to describe decreased microstructural integrity in autism, suggesting the use of DTI as a biomarker for neurological outcome in TSC. Next, using EEG functional connectivity measures, we found alterations of brain network properties common to both idiopathic and TSC-related autism, suggesting a common biological mechanism. Based on my previous work and

expertise, I am responsible for EEG interpretation in two large NIH-funded prospective multicenter trials studying early EEG and advanced neuroimaging predictors of epilepsy and autism in TSC. In addition, I am developing a longitudinal imaging technique called Epilepsy Longitudinal Diffusion Imaging (ELoDI) which allows the visualization of diffusion changes over time associated with epileptogenicity.

Web-based EEG platform (2012 - 2013)

I designed a novel software system which is an open-source, open access, web-based EEG platform. Locally recorded EEGs can be stored on a server, and remotely and securely accessed via any internet browser without installation of software. It allows for near real-time or offline remote EEG reading, data-exchange, and teaching. Vector-based graphics adjust to screen resolution and connection speed is typically not a limiting factor as the signal gets downsampled, and an image gets generated locally on demand only. While digitized EEGs may be available now in limited resource regions, pediatric EEGs are often not interpreted properly or timely, creating a clinical deficiency in diagnosis and treatment of epilepsy. The system also allows for researchers to become less dependent on data transfer of large files, and data can be read "streaming" and nearly in real-time. The software is currently piloted in Zambia (clinical service, and teaching) and Tanzania (research).

Density Weighted Statistics (DWS) in Diffusion Tensor Imaging (DTI) tractography (2012 -2015) Together with my mentor, Dr. Simon K. Warfield, Ph.D., we describe a novel solution for the problem of partial volume averaging in region-of-interest (ROI) analysis with DTI tractography. When voxels associated with a fiber tract are identified, the proportion of the voxel associated with the fiber tract is important. A common strategy to select a tract-based ROI has been to threshold the streamline density to identify voxels associated with a particular white matter tract. Average DTI parameters of the region are then assessed by computing the mean value by summing the parameter over all the voxels above the threshold and dividing by the number of voxels in the region. However, partial volume effects confound the analysis. We describe the use of streamline density directly to enable an appropriate weighted average of diffusion tensor parameters. In our analysis, the diffusion tensor parameters of a region are calculated on the basis of equal weighting of each of the trajectories, rather than equal weighting of each voxel.

EEG dynamics and electrical source imaging (ESI) (2013 - Present)

As a member of the Computational Radiology Laboratory, I collaborate with Drs. Hyde, Warfield, and Erem on a number of studies identifying dynamic patterns in scalp EEG of epileptic patients. We apply novel source localization techniques to these dynamics using the DESI algorithm we developed. In these studies, I am responsible for analysis of clinical and hdEEG data, and provide expertise in the clinical evaluation of epilepsy to ensure that the techniques developed have direct clinical relevance for improving epilepsy surgery.

# Report of Education of Patients and Service to the Community

#### **Activities**

No activities below were sponsored by 3<sup>rd</sup> parties/outside entities 2011 BNN Radio (The Netherlands) / Health Care Correspondent

Radio interview regarding current affairs of health care in Massachusetts and USA

2013 Interview Dradio (Deutschlandradio), with Leonie Seng / Science Report on EEG Network Analysis 2015 TSC Family Day, Waltham, MA / Speaker Oral presentation, "Epilepsy and Tuberous Sclerosis Complex: How to optimize 12 developmental outcome" Journal of Child Neurology Podcast / Guest Speaker 2019 Electrographic Seizures in Tuberous Sclerosis Complex

Interview for the JCN Podcast

# Educational Material for Patients and the Lay Community No materials below were sponsored by 3<sup>rd</sup> parties/outside entities

No materials below were sponsored by 3 <sup>rd</sup> parties/outside entities			
Books, monogr 2011	raphs, articles and presentations i Amerikaanse teamgeest inspireert Nederlandse kinderneuroloog	Full-length biographical interview for De Neuroloog, the Dutch Neurological Association's professional magazine	Maathuis M. Amerikaanse teamgeest inspireert Nederlandse kinderneuroloog. De Neuroloog 2009;16(1):11- 12
2011	Hot topics in Pediatric Neuroradiology	Invited editorial on DTI and autism in TSC study	Poussaint, T.Y. Diffusion Imaging Provides Insight into White Matter Microstructural Integrity in Tuberous Sclerosis Complex. AJNR 2011; 32(6):993-997
2012	Autism may involve disordered white matter in the brain	Interview for Boston Children's Hospital science and clinical innovation blog, Vector	Fliesler N. A view of autism: altered brain pathways, disordered white matter. http://vectorblog.org/2011/12/aview-of-au tism-altered-brainpat hways-disordered-w hitematter. Published Dec 8, 2011. Accessed Jun 10, 2013.
2013	'Network' analysis of brain may explain features of autism	Interview for Boston Children's Hospital science and clinical	Fliesler N. Could "network" analysis of the brain explain autism's features

		innovation blog, Vector	http://vectorblog.org/ 2013/03/co uld-network-analysis -of-thebrain-explain- autisms-features Published Mar 1, 2013. Accessed Jun 10, 2013.
2013	Autistische hersenen zijn fijner geweven	Coverage of autism network analysis in the Dutch newspaper	Volkskrant reporter. Autistische hersenen zijn fijner geweven. http://www.volkskran t.nl/vk/nl/2844/ Archief/archief/articl e/detail/340 1159/2013/02/28/ Autistischehersenen -zijn-fijnergeweven.d html Published Feb 28, 2013. Accessed Jun 20, 2013
2013	Brain connectivity differs in children with autism	Interview and research summary for Neuropsychiatry "News" section.	Freeston, S. News: Brain connectivity differs in children with autism, EEG study suggests. Neuropsychiatry 2013;3(2):131-132
2013	Falsch verbunden: Hirnregionen autistischer Kinder sind auf ungewöhnliche Weise miteinander vernetzt.	Interview with "Gehirn und Geist" the German edition of Scientific American's "Brain and Mind"	Klotzbücher, L. Falsch verbunden Hirnregionen autistischer Kinder sind auf ungewöhnliche Weise miteinander vernetzt. http://www.gehirn-un dgeist.de/alias/autis mus/falschverbunde n/1185521. Published Feb 28, 2013. Accessed Jun 20, 2013
2013	Redondance et déconnexion	Invited	Taquet M. & Peters

		commentary to the autism network analysis study in Nouvelles magazine	J.M. Le réseau cérébral fonctionnel des enfants atteints d'autisme: Redondance et déconnexion. Article in French. Nouvelles, Med Sci (Paris) 2013; 29(6-7):567-9.
2016	A new model for detecting seizures in the neuro ICU	Press coverage in Neurology Today, the AAN's news outlet	Tailan, J. A new model for detecting seizures in the neuro ICU. Neurology Today 2016;16(1):1, 12-13
2016	Seizure or not? Nonepileptic paroxysmal events in pediatrics	Featured in Boston Children's Hospital Clinical Health Blog	https://notes.childre nshospital.org/seizur e-or-not-non-epilepti cparoxysmal-events -inpediatrics/ Published Nov 2, 2016. Accessed Nov 8, 2016.

# Recognition

2010 - 2016 Patient's Choice Award,

Compassionate Doctor Award

Rated and awarded by patients on

Vitals.com

# **Report of Scholarship**

ORCID: 0000-0002-6725-2814

# Peer-Reviewed Scholarship in print or other media

#### **Research Investigations**

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# **Narrative Report**

My Area of Excellence is Clinical Expertise and Innovation. As an adult neurologist, a child neurologist, and clinical neurophysiologist, with specific expertise in EEG signal processing, advanced neuroimaging techniques and their clinical application to patients with intractable epilepsy, tuberous sclerosis (TSC), and autism, I spend approximately 50% of my time in clinical research and innovation—mostly in the computational radiology laboratory (CRL) and covered in full by NIH funds. I spend 45% in clinical care, in the Multidisciplinary Tuberous Sclerosis Program, in the Comprehensive Epilepsy Clinic, and in a satellite clinic (general Pediatric Neurology), and approximately 5% in teaching activities.

Throughout my career, I have operated on the boundary between clinical care and cutting edge technology, applying innovations in EEG signal processing and advanced neuroimaging.

First, for children undergoing epilepsy surgery, my collaborators and I provide tailored imaging and EEG solutions for specific clinical problems, to optimize the chances of successful surgery and minimize surgical injury to functional areas. These innovations include the clinical application of patient-specific DTI tractography, 3D-renderings of the subdural electrode grids on the MRI brain surface, quantitative validation of the use of EEG during the Wada test, examination of the clinical impact of temporal lobe spike propagation in the MEG, and novel electrical source imaging modeling approaches.

Second, I am the main epileptologist in the multidisciplinary TSC program at Boston Children's Hospital, and TSC forms a major research focus. With my collaborators, I was the first to describe an altered microstructural integrity in autism, suggesting the use of DTI as a biomarker for neurological outcome in TSC. Next, using EEG functional connectivity measures, we found alterations of brain network properties common to both idiopathic and TSC-related autism, suggesting a common biological mechanism. Recently, I published data on longitudinal changes in DTI in TSC, providing imaging evidence that tubers and their direct environment are neither static nor discrete. Based on my previous work and expertise, I am responsible for EEG interpretation in two large NIH-funded prospective multicenter trials studying early EEG and advanced neuroimaging predictors of epilepsy and autism in TSC, and receive funding through a third NIH-grant in the expansion of this work to non-syndromic autism.

Finally, again focused on the integration of technological innovation and clinical care, as the past recipient of a World Federation of Neurology Pilot Grant, I have developed a web-based EEG platform for remote EEG reading, teaching, and data exchange. The platform was piloted in two sub-Saharan African nations.

Among my **Teaching** activities, I have mentored 15 undergraduate and graduate students, residents, fellows, and visiting physicians from institutions around the world. I supervise medical students, residents and fellows in the pediatrics, child neurology and clinical neurophysiology programs, and I have been invited to talk in CME-accredited teaching sessions in the medicine, psychiatry and nursing departments. Over the past years, I have received numerous invitations to present my work on DTI, abnormal EEG connectivity and brain functional networks, autism, and tuberous sclerosis complex, including invitations to national and international conferences. This work has also been featured in numerous professional and public news outlets.

In summary, within my **Area of Excellence in Clinical Expertise and Innovation**, I have an outstanding record of successful implementation and clinical application of technological advancements in the patient setting, highlighting my unique skillset of both clinical expertise and understanding of physics and engineering. My current expertise and experience allow me to continue to interact and collaborate with both computational scientists and child neurologists, and place me in an excellent position to continue

making important contributions to the field directly and to exert future influence through the researchers I train.