BIOGRAPHICAL SKETCH

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NAME: Haacke, Ewart Mark

eRA COMMONS USER NAME (credential, e.g., agency login): ak5444

POSITION TITLE: Director and Professor

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
University of Toronto, Canada	BS	06/1973	Mathematics & Physics
University of Toronto, Canada	MS	02/1975	Theoretical Physics
University of Toronto, Canada	PhD	06/1978	High Energy Physics

A. Personal Statement

My background has been in the study of the brain's vasculature and its role in disease and in the development of methods able to tackle key physiological problems from the MRI perspective. The goal of this proposal is to upgrade our small animal 7T system with new software and coils. The primary goal of my ongoing project is to unify several novel imaging concepts into one ultra-high resolution MICRO MRI to improve both qualitative and quantitative evaluation of brain arterial and venous systems at the micro level. Two major limitations to achieving practical high-resolution microvascular imaging are blood vessel contrast and SNR. The upgrade to a new 7T console will help us to overcome these two obstacles. My own research interests have been in studying abnormal vasculature in mild traumatic brain injury, multiple sclerosis, stroke and vascular dementia. We at my lab are pioneers in this area of imaging and have published extensively in this field. Further, I was a pioneer in inventing both MR angiography, susceptibility weighted imaging and super-resolution imaging techniques. Finally, I am also the director of the MR Research Facility at Wayne State University and as part of that role I am supportive of the implementation of many research related projects at both 7T and 3T throughout the University.

B. Positions and Honors

Positions and Employment

1985-1989 **Assistant Professor of Radiology and Physics**, Head, MR Physics and Basic Science. Case Western Reserve University, Cleveland, OH, USA
1989-1993 **Associate Professor**, Department of Radiology with appointments in Physics and Biomedical Engineering, Case Western Reserve University, Cleveland, OH, USA
1993-1999 **Professor of Radiology**, Director MR Imaging Research, Mallinckrodt Institute of Radiology, Washington University, St. Louis, MO, USA
1993-Present **Adjunct Professor**, Dept of Physics, Case Western Reserve University, Cleveland, OH, USA
1994-Present **President**, Magnetic Resonance Innovations, Inc., Detroit, MI, USA
1999 **Visiting Professor**, The Roentgen Professor of Physics, Wuerzburg, GERMANY
1999-Present **Director**, The MRI Institute for Biomedical Research, Detroit, MI, USA
2002-Present **Professor**, Department of Radiology, Wayne State University, Detroit, MI, USA
2002-Present **Director**, Wayne State University, Magnetic Resonance Imaging Facility, Detroit, MI, USA
2002-Present **Professor**, Department of Biomedical Engineering, Wayne State University, Detroit, MI, USA
2002-Present **Adjunct Professor**, Loma Linda University, Loma Linda, CA, USA
2005-Present **Adjunct Professor**, Department of Electrical and Computer Engineering at McMaster University and the Brain-Body Institute at St Joseph's Healthcare in Hamilton, Ontario, Canada.
2010-Present **Director**, Program in Traumatic Brain Injury Research
2012-Present **Visiting Professor**, Northeastern University, Shenyang, CHINA

2013-Present **Adjunct Professor**, Department of Medical Imaging, University of Saskatchewan, Saskatoon, Saskatchewan, CANADA
2014-Present **Visiting Professor** "Zijiang Visiting Scholar (Professor)" East China Normal University, Shanghai, CHINA
2014-Present **Visiting Professor**, The Copernicus Professor of Physics, University of Ferrara, Ferrara, ITALY
2015-Present **Director**, Joint MRI program with East China Normal University

Honors

1989 Sylvia Sorken Greenfield Award for the best paper in Medical Physics
1992 Fellow of the Society Award for the Society of Magnetic Resonance Imaging
1994 Silver Medal Award, Society of Magnetic Resonance
1997 Poster Award at the 14th Annual Meeting, European Society for Magnetic Resonance in Medicine and Biology. J.R. Reichenbach, E.M. Haacke, B.C.P. Lee, Ch. Przetak, W.A. Kaiser
1998 Marie-Sklodowska-Curie Prize for Visualization of Cerebral Venous Structures Using High Resolution MRI by J.R. Reichenbach, L.R. Schad, M. Essig, E.M. Haacke, W.A. Kaiser
1999 Awarded the Visiting Professorship as the Roentgen Professor of Physics in Wuerzburg
2004 Gold Medal Award, International Society of Magnetic Resonance in Medicine
2006 RSNA Educational Exhibit Award LL-NR4709 entitled "Susceptibility Weighted Imaging (SWI) of the Brain: Pictorial Review of the Technique, Anatomy, and Pathology" T. Hirai, MD, Kumamoto, M. Akter, M. Kitajima, MD, T. Okuda, MD, E.M. Haacke, PhD, Y. Yamashita, MD
2008 Best Abstract Award "Improving the detection of diffuse axonal injury by complementary use of advanced MRI" at the 6th North American Brain Injury (NABIS) Annual Conference. Z. Kou, R. Benson, R. Gattu, M. Haacke. The abstract presented our breakthrough on a complementary use of SWI and DTI techniques for injury detection.
2009 Regional Scholarship for Asia "Imaging the Vessel Wall in Major Peripheral Arteries using Susceptibility Weighted Imaging: Visualizing Calcifications" at the 12th Annual Society of Cardiovascular Magnetic Resonance (SCMR). Qi Yang, Kuncheng Li, Jiangtao Liu, S. Barnes, Z. Wu, J. Neelavalli, J. Hu, E.M. Haacke.
2014 Award for recognition of Susceptibility Weighted Imaging MRM 2004 as one of the Top 30 papers published in Magnetic Resonance in Medicine in the last 30 years.
2015 Summa cum laude merit Award for abstract #0945: "Gestational Age Dependent Increase in Placental Perfusion Quantified Using MRI." Pesented at the ISMRM 23rd Annual Meeting, Toronto, Ontario, Canada, May 2015. Yadav BK , Neelavalli J, Krishnamurthy U, Shen Y, Szalai G, Wang B, Chaiworapongsa T, Hernandez-Andrade E, Than NG, Haacke EM, Hassan SS, Romero R.
2015 T. David Sisk Award for Best Original Research Paper: "Is There Chronic Brain Damage in Retired NFL Players? Neuroradiology, Neuropsychology, and Neurology Examinations of 45 Retired Players." Casson IR, Viano DC, Haacke EM, Kou Z, LeStrange DG. Sports Health. 2014 Sep;6(5):384-95.
2016 Gold Medal Award for Academic Excellence, at the 6th Annual International Society for Neurovascular Disease (ISNVD) Scientific Meeting

C. Contributions to Science

1. Traumatic Brain Injury Contributions

The use of SWI for studying trauma has become a mainstay in the field. This work and extensions of it have shown that SWI is 3 to 6 times more sensitive to microbleeds than other methods. For this reason, SWI has become a standard for the study of TBI patients and more recently in terms of investigating the use of SWI in the study of venous damage in mild TBI patients where 10 to 20% are found to have some type of damage post trauma while conventional imaging showed no changes (a). Our work in stroke has also shown that not only did SWI correlate with DWI data it also correlated with perfusion data. This paper showed that SWI can detect more microbleeds than conventional imaging. As such it opened the door to the question: "Is a microbleed detected with SWI a counter indication for TPA treatment?" A recent paper from Shanghai has suggested that is the case. We also used DTI in studying TBI rather early in the field. We demonstrated that there is the potential to predict injury severity in TBI patients. Today this work has been extended to study, along with SWI and DTI (b), the ability to detect brain damage in chronic mild TBI patients. After many years of discussions and meetings with worldwide imaging experts, a consensus was reached as to how to best collect data for the study of TBI. This

multi-tiered imaging protocol has become a working model for TBI researchers around the world. It was formally adopted by the military in the summer of 2014 to be used at all there sites for TBI patients (c). The ability to detect dementia early is an important step in treating it. Cerebral amyloid angiopathy or vascular dementia is now believed to make up about one-third of dementia cases with Alzheimer's disease being considered the major cause otherwise. Using SWI, this paper shows that patients with four or more microbleeds all go on to develop dementia. Therefore, SWI could become a biomarker for the early detection of vascular dementia. Since it is now believed that patients with TBI may suffer more dementia, these works link nicely together in understanding which TBI patients may be at risk for dementia (2).

a. Tong S. et al. Hemorrhagic Shearing Lesions in Children and Adolescents with Post-traumatic Diffuse Axonal Injury – Improved Detection and Initial Results. Radiology 2003; 227:332-339. PMID 12732694.
b. Benson R.R. et al. Global White Matter Analysis of Diffusion Tensor Images is Predictive of Injury Severity in TBI. Journal of Neurotrauma 2007; 24:446-459. PMID 17402851.
c. Haacke E.M. et al. Common Data elements in radiologic imaging of traumatic brain injury. JMRI 2010; 32:516-543. PMID 20815050.

2. Flow and Angiographic Contributions

An early problem in magnetic resonance imaging (MRI) was the presence of motion. Understanding the role of motion and how to deal with it was an important step in designing better sequences. This focus eventually led to the concept of motion compensation (a). The critical "aha" came with the marriage of fast imaging and motion compensation which now made signal from the vasculature appear not as ghosting but rather a beautiful representation of the vessels. With this paper 2D time-of-flight and then 3D MRA were born. Many more papers came from Prof. Haacke in the area of clinical developments of MRA. Despite the now accepted utility of MRA, Prof. Haacke felt that image quality still suffered from signal-to-noise and slow flow effects. He then demonstrated that high resolution scanning with a contrast agent was the most effective way to image the vessels. Using a special post-processing or vessel tracking, he showed that it didn't matter if the veins got bright too as they could be extracted from the images (b). More recently, Prof. Haacke has continued to study the role of abnormal vasculature in neuro-degenerative diseases. He has shown that a fraction of idiopathic Parkinson's patients have vascular problems, particularly extracranial venous problems. Specifically, he showed that many PD patients have abnormal flow and vasculature on the left side. Some are born without any left sided jugular system and others have no flow on the left side. This finding may lead to new vascular treatments for PD patients and a better understanding of the cause of the disease for this subgroup of patients (c). Finally, it has been postulated that multiple sclerosis patients have extra-cranial venous vascular problems, particularly poor flow in the jugular veins. This finding has been questioned over the years. In this paper, we show clearly that the MS population has more stenoses and abnormal venous flow than normal healthy controls. This finding may lead to new vascular treatments for MS patients and a better understanding of the cause of the disease for this subgroup of patients (d).

a. Haacke E.M. et al. Improving Image Quality in the Presence of Motion by Using Rephasing Gradients. AJR 1987; 48:1251-1258. PMID 3495155.
b. Lin W. et al. Gadolinium-enhanced high-resolution MR angiography with adaptive vessel tracking. Preliminary results in the intracranial circulation. JMRI 1992; 2:277-284. PMID 1627862.
c. Liu M. et al. Patterns of Chronic Venous Insufficiency in the Dural Sinuses and Extracranial Draining Veins and Their Relationship with White Matter Hyperintensities for Patients with Parkinson's disease. Jrnl of Vasc Surg 2014 Mar 19; [Epub ahead of print] PMID 24655749.
d. Sethi S.K. et al. Jugular Venous Flow Abnormalities in Multiple Sclerosis Patients Compared to Normal Controls. J Neuroimaging. 2014 Oct 15. doi: 10.1111/jon.12183. [Epub ahead of print] PMID 25316522.

3. Magnetic Field Inhomogeneity Effects and Iron Quantification

Fast imaging opened the door to many practical clinical questions but at high fields there remained some unpleasant artifacts. Gradient echo images had significant signal losses if echo times exceeded 20ms. Prof. Haacke showed how to correct the problem. Today with high resolution imaging in 3D, we now take full advantage of the theory expounded in this early paper. Many papers followed in the 1990s on how to correct field effects especially in fMRI all based on the concepts in this paper (a). His work also led to an in depth theory of T2* dephasing for a number of key structures in the brain such as cerebral microbleeds and venous blood especially for the study of signal changes in fMRI (b). In an attempt to speed up data acquisition in the most efficient manner possible, Prof. Haacke introduced the use of a dual acquisition True FISP (an expression coined by him because of the rampant confusion with fast imaging acronyms in those days) sequence that was

invulnerable to local field variations to enhance signal from long T2 tissues. This was initially done by CSF but later in his book on MRA in 1993 was also applied well ahead of its time to imaging blood vessels, particularly arteries because of their long T2. Today this is an important application in imaging coronary vessels. EPI and long echo images continue to be plagued by signal losses and understanding the extravascular component of fMRI signal loss and is still an unresolved problem. Prof. Haacke showed that one could quantitate the signal loss in terms of the local field behavior and geometry (b). In 2005, he brought together work done in iron measurements with MRI over the last 20 years prior to its publication. It also set the trend for where we might go in the future. It was for years one of the most quoted papers in the Journal Magnetic Resonance Imaging (c). This work on iron led to a new imaging finding for detecting lesions in MS; lesions can be measured from their iron content. In fact, some lesions that can be seen with SWI cannot be seen with conventional imaging. Therefore, the lesion load is often under-estimated with conventional imaging. Today this has become an important area of study to evaluate what type of iron is present, whether it is in the form of iron in macrophages or micro-bleeding and to predict the advent of new lesions (d).

a. Haacke E.M. et al. Reducing T2* Dephasing in Gradient Field Echo Imaging. Radiology 1989; 70:457-462. PMID 2911669.
b. Yablonskiy D.A. et al. Theory of NMR Signal Behavior in Magnetically Inhomogeneous Tissues: The Static Dephasing Regime. MRM 1994; 32:749-763. PMID 7869897.
c. Haacke E.M. et al. Imaging Iron Stores in the Brain Using Magnetic Resonance Imaging. MRI 2005; 23:1–25. PMID 15733784. The #1 downloaded article from Science Direct, downloaded 1,276 times in 2012.
d. Haacke E.M. et al. Characterizing Iron Deposition in Multiple Sclerosis Lesions Using Susceptibility Weighted Imaging. JMRI 2009; 29:537-544. PMID 19243035.

4. Functional brain imaging and susceptibility weighted imaging

The study of MRA went hand in hand with the recognition that MR could do functional brain imaging. In fact, the early descriptions of how the process worked were incorrectly ascribed to diffusion and Prof. Haacke spent the early years in fMRI demonstrating how it was in fact the intravascular signal that led to much of the signal change at 1.5T. His work led to the first demonstration of 1mm^3 imaging of fMRI in the brain, an approach which is only now finding its return with segmented EPI techniques (a). One might argue that his early work on phase held the seeds to the future methodology with Prof. Haacke refers to today as susceptibility weighted imaging or SWI. Combining his experience in reducing field effects, he showed it was possible to understand fMRI effects. Phase results give the first hint at long echo times of 120ms that the presence of venules are manifest (b). The culmination of this fMRI and magnetic field research led to the birth of a totally new means to image veins. Today this method now referred to as SWI has shown its ability to separate arterial from venous signal, to visualize tumors clearly without a contrast agent, to examine, the vascularity of tumors, to study trauma in adults and children, to study MS vascularity and to study iron build up in normal and Alzheimer's brains. This method also is an indicator in the brain of changes in oxygen saturation and has been shown to correlate with diffusion weighted imaging results in stroke and with detecting bleeds with CT. It has become an accepted technology in neuro-radiology. It received an award from the ISMRM as one of the top 30 papers in the last 30 years in the Journal Magnetic Resonance in Medicine (c). Finally, what lies ahead? The study of fMRI relies today on EPI and a statistical armamentarium of correction algorithms for motion and field distortion. Today, Prof. Haacke is taking a pioneering approach to measure oxygen saturation using quantitative susceptibility mapping. It has potential applications in all neuro-degenerative diseases but it is particularly important in stroke imaging (d).

a. Lai S. et al. Identification of Vascular Structures as a Major Source of Signal Contrast in High Resolution 2D and 3D Functional Activation Imaging of the Motor Cortex at 1.5T. MRM 1993; 30:387-392. PMID 8412613.
b. Haacke E.M. et al. In Vivo Validation of the BOLD Mechanism: A Review of Signal Changes in Gradient Echo fMRI in the Presence of Flow. Intl J of Imaging Sys and Technology 1995; 6:153-163. PMID None.
c. Haacke E.M. et al. Susceptibility Weighted Imaging (SWI). MRM 2004; 52:612-618. PMID 15334582.
d. Haacke E.M. et al. Susceptibility mapping as a means to visualize veins and quantify oxygen saturation. J. Mag. Reson. Imaging 2010; 32:663-676. PMID 20815065.

A complete list of published work can be found in My Bibliography:
http://www.ncbi.nlm.nih.gov/pubmed/?term=haacke+em

D. Research Support:

Ongoing Research Support

1R01EB13663-01A1 **Allen (PI)** **05/01/2014 – 04/30/2018**
National Institutes of Health
Study of Advanced Eu(II)-Based Contrast Agents for Ultra-High Field Magnetic Resonance Imaging
The major goals of this proposal are (1) to chemically enhance the stabilities and imaging-relevant parameters of Eu(II)-containing complexes; (2) to characterize the toxicity of Eu(II)-containing complexes; and (3) to characterize the in vivo imaging properties of Eu(II)-containing complexes.
Role: Co-Investigator

R01 NS041922-10 **Juhasz (PI)** **07/01/2008 – 04/30/2019**
National Institutes of Health/NINDS
Longitudinal neuroimaging in Sturge-Weber syndrome
The major goal of this project is to identify imaging markers of epileptogenesis and neurocognitive decline, and to study pathomechanisms of disease progression in children with Sturge-Weber syndrome
Role: Co-Investigator

Contract C912015, Protocol H16-037 **Haacke (PI)** **06/01/2010 – 05/31/2021**
AbbVie Inc.
Multiparametric Quantitative White Matter Imaging in Healthy and Multiple Sclerosis Subjects
The major goals of this project are to investigate key Magnetic Resonance Imaging-derived measures of white matter pathophysiology in the brain and Optical Coherence Tomography-derived measures of retinal pathophysiology for 1) test-retest variability in healthy subjects (Group 1 only) and 2) the magnitude of longitudinal change associated with disease progression in multiple sclerosis patients.
Role: Principal Investigator

R01 AG011230-16 **Raz (PI)** **06/01/2010 – 05/31/2021**
National Institutes of Health/NIA
Neural Correlates and Modifiers of Cognitive Aging
The major goals of this project are continuation and expansion of the research activities of the past 16 years to describe course of differential brain aging, mechanisms of differential brain shrinkage, age-related brain changes and approach to study of the biological and cognitive change.
Role: Co-Investigator

1P30AG053760-01 **Paulson (PI)** **08/15/2016 – 06/30/2021**
National Institutes of Health/NIA
Michigan Alzheimer's Disease Core Center
The major goals of the “Michigan Alzheimer’s Disease Core Center (Michigan ADCC),” aims to build a regional center that formally links efforts at the three major research universities in Michigan (the University of Michigan (UM), Wayne State University (WSU) and Michigan State University (MSU)). Wayne State University Institute of Gerontology (IOG) activities involved in this application include Michigan ADCC Clinical Core: *E. Mark Haacke, PhD* will serve as Clinical Core Investigator. Dr. Haacke will work on analyzing microbleeds that already show the ability to detect pathological features of vascular dementia in the form of cerebral amyloid angiopathy well before patients become demented. He will be involved in helping to establish the imaging protocols, image evaluation, and biomarker determination in research subjects evaluated by the Michigan ADCC.
Role: Clinical Core Investigator