## BIOGRAPHICAL SKETCH

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NAME: Andreas H. Hielscher

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POSITION TITLE: Professor of Biomedical Engineering, Electrical Engineering, and Radiology

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 | Completion Date | FIELD OF STUDY |
|---|---|---|---|
| University of Hannover, Germany | B.S. | 06/1987 | Physics |
| University of Hannover, Germany | M.S. | 06/1991 | Applied Physics |
| Rice University, Houston, TX | Ph.D. | 05/1995 | Electrical & Comp. Eng. |
| Los Alamos National Lab., Los Alamos, NM | Postdoc | 03/1997 | Biomedical Engineering |

### A. Personal Statement

I have been trained and perform research in the general area of biomedical imaging. Over the last decade my work has focused on the development of state-of-the-art imaging software and hardware for optical tomography. I have applied this technology to diagnose and treat peripheral artery disease, arthritis, prostate cancer and skin cancer. Among my main contributions to this field are the introduction of transport-theory-based reconstruction algorithms both for absorption and fluorescence imaging, the development of the first fully digital-signal-processor (DSP) based optical tomographic imaging system, and the first three-dimensional optical tomographic reconstruction of a complete rat brain and the human frontal lobe. In addition, my team was the first to introduce a dynamic optical tomographic breast imaging system capable of imaging both breasts at the same time. Employing this system, we have performed one of the largest neo-adjuvent chemotherapy monitoring study to date. All breast cancer related studies have been performed in close collaboration with Prof. Hershman, the leader of the Breast Cancer Program at Columbia's Cancer Center. I have published more than 200 articles in peer-reviewed scientific journals and conference proceedings, which have been cited over 8000 times. In addition to these research efforts, I have also been deeply involved in educational aspects of novel imaging methods as Co-PI of NIAMS T32 grant on "Multidisciplinary Engineering Training in Musculoskeletal Research" and an NSF funded Integrative-Graduate-Education-and-Research-Traineeship (IGERT) Program in which we have taught students on techniques for optical actuation, sensing, and imaging of biological systems. Furthermore, I have increasingly focused on translational aspects of biomedical engineering. For our Department of Biomedical Engineering, I secured funding for the department from the Wallace H. Coulter Foundation under their Translational Partners in Biomedical Engineering - Phase II program. The goal of this program is to position promising biomedical technologies for licensing to commercial partners who bring new technologies to the clinical. I hold numerous patents on various aspects of this technology and together with Columbia's Technology Transfer Office we are actively commercializing our imaging systems.

### B. Positions and Honors

**Professional Experience**

1992-95 **Graduate Research Assistant**, Rice University, Dept. Elec. & Comp., Houston, TX
1995-98 **Postdoctoral Fellow**, Los Alamos Nat. Lab., Bioscience & Biotechnology Group, Los Alamos, NM
1998-01 **Assistant Professor of Pathology**, Dept. Pathology, SUNY Health Science Center, Brooklyn, NY
1999-02 **Adjunct Professor of Electrical Engineering**, Dept. of Electrical Engineering, Polytechnic University, Brooklyn, NY

2001-05 **Adjunct Professor of Pathology**, Dept. of Pathology., SUNY Health Science Center, Brooklyn, NY
2001-06 **Associate Professor of Biomedical Engineering and Radiology (non-tenured)**, Depts. of Biomedical Engineering & Radiology, Columbia University, New York, NY
2006-10 **Associate Professor Biomedical Engineering and Radiology (tenured)**, Depts. of Biomedical Engineering & Radiology, Columbia University, New York, NY
2010- **Professor of Biomedical Engineering, Electrical Engineering and Radiology**, Depts. of Biomedical Engineering, Electrical Engineering and Radiology, Columbia University, New York, NY
2011-12 **Chair**, Dept. of Biomedical Engineering, Columbia University, New York, NY

**Other Experience and Professional Memberships**

2010 Member of Scientific Review Special Emphasis Panel on "BMIT/CMIP/MEDI Imaging Applications", Center for Scientific Review at NIH, June 24.
2011 Member of Conference Program Committee, "Biomedical Applications in Molecular, Structural, and Functional Imaging," SPIE Medical Imaging Conference, San Diego, CA , Feb. 2009, 2010 and 2011.
2011 Member of the "In vivo Cellular and Molecular Imaging Centers (ICMIC - P50)" Review Group, National Cancer Institute (NCI) at NIH, March 15-16.
2011 Member of Technical Program Committee, 5th International Conference on Bioinformatics and Biomedical Engineering (iCBBE 2011), Wuhan, China, May 10-12.
2011 Chair of Conference on *Diffuse Optical Imaging* at the European Conference on Biomedical Optics, Munich, Germany, June 2009, May 2011.
2011 Theme Chair, Biomedical Image and Image Processing, *33rd Annual International Conference of the IEEE Engineering in Medicine and Biology Societ*y (EMBS'2011), Boston, MA, Aug. 30 – Sept. 1.
2012 Member of review panel for "Point-of-Care Technologies Research Network (U54)", Center for Scientific Review at the National Institutes of Health (NIH), Bethesda, MD, March 28-29.
2012 Member of Advisory Board to the German Federal Ministry of Education and Research (BMBF) on "Science-Driven Evaluation of Large Research Infrastructure Projects for a National Roadmap," Berlin, Germany, April 16-17.
2013 Program Chair, European Conference on Biomedical Optics (ECBO), Munich, Germany
2015 General Chair, European Conference on Biomedical Optics (ECBO), Munich, Germany
2017 Member of review panel and site-visit team for the Collaborative Research Center (CRC) 824 "Imaging for Selection, Monitoring and Individualization of Cancer Therapies" at Technical University Munich, Germany, organized by the German Research Foundation (Deutsche Forschungsgemeinschaft - DFG), December 8-9, 2017.
2016 to 2018 Member of the "Committee for Science-Driven Evaluation of Large-Scale Research Infrastructure Projects," (Project Costs > €50,000,000), German Council of Science and Humanities (Deutscher Wissenschaftsrat), since November 2016.
2018 Ad-hoc Member of NIH study section on Clinical Molecular Imaging and Probe Development (CMIP), Washington, DC, February 7-8, 2018

**Honors and Awards**

1992 Robert A. Welch Foundation Predoctoral Fellowship
1995 Los Alamos National Laboratory Director's Postdoctoral Fellowship
1999 Whitaker Foundation Young Investigator Award
1999 Young Investigator Award - The New York City Council Speaker's Fund for Biomedical Research at the New York Academy of Medicine
2000 Young Investigator Award - National Institute of Arthritis and Musculoskeletal and Skin Diseases
2003 Fellow of the Institute for Biomedical Engineering and Laser Medicine, Free University, Berlin, Germany
2012 Elected Fellow of the American Institute for Medical and Biological Engineering (AIMBE)

## C. Contribution to Science

**C.1. *Theoretical Basis for Optical Tomographic Imaging (OTI) with the Equation of Radiative Transfer:*** Of considerable impact is my work on optical tomographic imaging using the equation of radiative transfer (ERT), also called transport equation. Unlike the widely used diffusion approximation (DA) to the ERT, employing the ERT allows for accurately modeling the image problem for tissue that contain low-scattering fluids, highly absorbing media, and small tissue geometries. Examples for case where ERT-based methods are more appropriate than DA-based approaches are brain imaging, imaging of finger joints, and small animal imaging. I trained in the world's foremost institution on numerically modeling with the ERT, Los Alamos National Laboratory, where the first atomic bomb was developed relying on exactly this equation. I was the first to realize the potential of using the ERT in the emerging field of optical tomographic imaging of biological tissue. An early papers on topic is still the defining work on the question of when the DA can be used to model light propagation in tissue, and when it has to be replaced by the more generally applicable ERT (a). Subsequently I published a series of papers in which he laid out the theoretical framework for finding cross-sectional images of the internal structure of biological tissues from optical measurements performed on the surface of these tissues (b – e). Overall my group has published over 20 manuscript in this area, which together been cited over to 2000 times.

a. AH Hielscher, RE Alcouffe, RL Barbour :Comparison of finite-difference transport and diffusion calculations for photon migration in homogeneous and heterogeneous tissues," *Physics in Medicine and Biology* 43, pp. 1285-1302 (1998). [341 citations]
b. AD Klose, U Netz, J Beuthan, AH Hielscher "Optical tomography using the time-independent equation of radiative transfer. Part 1: Forward model & Part 2: Inverse model, " *J Quantitative Spectroscopy and Radiative Transfer*, Vol 72/5, pp 691-732 (2002). [228+171=399 citations]
c. K Ren, G Bal, AH Hielscher, "Frequency domain optical tomography based on the equation of radiative transfer," *SIAM Journal on Scientific Computing* 28 (4), 1463-1489 (2006). [135]
d. HK Kim, M Flexman, DJ Yamashiro, JJ Kandel, AH Hielscher, "PDE-constrained multispectral imaging of tissue chromophores with the equation of radiative transfer," *Biomedical Optics Express* 1 (3), 812-824 (2010). [53 citations]

***C.2. Instrument Development for Optical Tomographic Imaging (OTI):*** For the last decade my group has also focused on the development of novel imaging system that are capable of acquiring the necessary data for the image reconstruction codes. In 2002, we introduced the first "*dynamic"* optical tomographic imaging system, which allowed for full tomographic data capture in less than a second (a). The fastest OTI system at that time, it was the first that was capable of tomographic imaging of subsecond hemodynamic vascular effects. Subsequently, we further advance this technology by developing the first all digital imaging system (b). This substantially improved signal to noise as well as data acquisition speed. After implementing an general imaging system of this type, we adapted and advanced that technology for the specific application of breast cancer imaging (c). Furthermore, we developed the first non-contact camera-based frequency-domain tompgraphic system that can operate up to 1GHz. The system is used for arthritis (RA) (d). Finally, most recently we introduced a novel portable wireless handheld imaging system, that together with a novel spectral constrained evolution strategies can obtain information about tissue optical parameters at a very low cost in low resource settings (e).

a. CH Schmitz, M Löcker, JM Lasker, AH Hielscher, RL Barbour, Instrumentation for fast functional optical tomography," *Review of Scientific Instruments* 73 (2), 429-439 (2002). [197 citations]
b. JM Masciotti, JM Lasker, AH Hielscher, "Digital lock-in detection for discriminating multiple modulation frequencies with high accuracy and computational efficiency," *IEEE Transactions on Instrumentation and Measurement* 57 (1), 182-189 (2008). [88]
c. ML Flexman, MA Khalil, R Al Abdi, HK Kim, CJ Fong, E Desperito, D. Hershman, A.H. Hielscher, "Digital optical tomography system for dynamic breast imaging," *J Biomedical Optics* 16 (7), 076014-076014-16 (2011). [77]
d. UJ Netz, J Beuthan, AH Hielscher, "Multipixel system for gigahertz frequency-domain optical imaging of finger joints," Review of Scientific Instruments 79 (3), 034301 (2008). [38]
e. ML Flexman, HK Kim, R Stoll, MA Khalil, CJ Fong, AH Hielscher, "A wireless handheld probe with spectrally constrained evolution strategies for diffuse optical imaging of tissue," *Review of Scientific Instruments* 83 (3), 033108 (2012). [26]

***C.3. Diagnosis and Treatment Monitoring of Rheumatoid Arthritis with OTI:*** With the hardware and software to perform optical tomographic imaging in place, my group has increasingly applied this technology to clinical problems. With over a decade of support from the National Institute of Arthritis and Musculo-skeletal and Skin Diseases, we have developed and perfected optical imaging methods for the detection and treatment monitoring of rheumatoid arthritis. Employing frequency-domain technology, our 2012 study is still the largest clinical study on RA using OTI. With data from over 200 finger joints we were able to show that joints affected by RA can be clearly distinguished from joints not affected by RA at a light intensity modulation of 600 MHz. In more recent years, my team has been focusing on machine learning algorithm that can be used to perform smart analysis of complex data sets. Introducing this novel approach to the imaging of joints, we recently report on unprecedented sensitivities and specificities that surpass 90%.

a. AK Scheel, M Backhaus, AD Klose, B Moa-Anderson, UJ Netz, ..., AH Hielscher, " First clinical evaluation of sagittal laser optical tomography for detection of synovitis in arthritic finger joints," *Annals of the Rheumatic Diseases* 64, pp. 239-245 (2005). [108 citations]
b. AH Hielscher, AD Klose, AK Scheel, B Moa-Anderson, M Backhaus, ... "Sagittal Laser Optical Tomography for Imaging of Rheumatoid Finger Joints," *Physics in Medicine and Biology* 49(7), pp. 1147 - 1163 (2004). [155 citations]
c. AH Hielscher, HK Kim, U Netz, L Montejo, S Blaschke, PA Zwaka, ..., "Frequency-Domain Optical Tomographic Imaging of Arthritic Finger Joints," *IEEE Transaction on Medical Imaging* 30 (10), 1725 – 1736 (2011). [28 citations]
d. LD Montejo, J Jia, HK Kim, UJ Netz, S Blaschke, GA Müller, ..., AH Hielscher, "Computer-aided diagnosis of rheumatoid arthritis with optical tomography, Part 1: feature extraction & Part 2: image classification, *J Biomedical Optics* 18 (7), 076001-076001 & 076002-076002 (2013). [16+12=28]

**C.4. Dynamic OTI in management and treatment and management of Breast Cancer (BC) and Peripheral Artery Disease (PAD):** In addition to exploring the clinical utility of frequency-domain OTI, my group has explored the potential impact of dynamic OTI in treatment monitoring of breast cancer patients and patients suffering from peripheral artery disease (PAD). We developed the first full tomographic breast imaging system that can gather dynamic data from both breast at the same time (see 2c). With this we were able to show in a 29 patient study that hemodynamic features can be used to identify breast cancer (b). We have recently completed a 40-patient study with patients that undergo neoadjuvent chemotherapy (NACT) and are in the process of publishing this data (a). Furthermore, we have made big strides towards a clinically useful imaging system for patients with peripheral artery disease. In the largest clinical study involving OTI for the detection of PAD, we recently showed that dynamic imaging features can identify PA in diabetic patients, for whom traditional diagnostic methods are unreliable.

a. J.E. Gunther, E. Lim, H.K. Kim, M. Flexman, J.A. Campbell, H. Hibshoosh, K. Crew, K. Kalinsky, D.L. Hershman, A.H. Hielscher, "Dynamic diffuse optical tomography for monitoring neoadjuvant chemotherapy in breast cancer patients," Radioloy 2018 Feb 12:161041. doi: 10.1148/radiol.2018161041. [Epub ahead of print]
b. E.A. Lim, J.E. Gunther, H.K. Kim, M.Flexman, H. Hibshoosh, K. Crew, B. Taback, J. Campbell, K. Kalinsky, A.H. Hielscher, D.L. Hershman, "Diffuse optical tomography changes correlate with Residual Cancer Burden after neoadjuvant chemotherapy in breast cancer patients" Breast Cancer Research and Treatment 162(3), pp. 533-540 (April 2017) doi:10.1007/s10549-017-4150-7
c. MA Khalil, HK Kim, JW Hoi, I Kim, R Dayal, G Shrikhande, AH Hielscher, "Detection of Peripheral Arterial Disease Within the Foot Using Vascular Optical Tomographic Imaging: A Clinical Pilot Study," *European Journal of Vascular and Endovascular Surgery* 49 (1), 83-89 (2015). [15]
d. ML Flexman, HK Kim, JE Gunther, EA Lim, MC Alvarez, E Desperito, ..., D Hershman, AH Hielscher, "Optical biomarkers for breast cancer derived from dynamic diffuse optical tomography, *Journal of Biomedical Optics* 18 (9), 096012-096012 (2013). [37]
e. MA Khalil, HK Kim, IK Kim, M Flexman, R Dayal, G Shrikhande, ..., AH Hielscher, "Dynamic diffuse optical tomography imaging of peripheral arterial disease," *Biomedical Optics Express* 3 (9), 2288-2298 (2012). [23]

**C.5. Optical Tomographic Imaging for Preclinical Small Animal Studies:** In addition to the clinical studies, my group has performed preclicinal studies involving small animal models for human diseases. In particular, we have employed our dynamic imaging systems to study hemodynamic effects in the brain of rodents (a,b). In studying these effects, our group was the first to perform full three-dimensional optical

tomography a rodent brain (b). Furthermore, we found imaging biomarkers that can predict outcome of cancer treatments with anti-angiogenic drugs within 3 days of treatment initiation (c). Most recently we have introduce the first non-contact animal imaging system that can gather angular resolved data for fluorescence, bioluminescence, and absorption imaging (d). Angular resolved data is crucial to make use of the most accurate image reconstruction algorithms, which are based on the equation of radiative transfer (ERT). Unlike the diffusion approximation, the ERT is angular dependent.

a. AH Hielscher,"Optical tomographic imaging of small animals," Current Opinion in Biotechnology 16 (1), 79-88 (2005). [233]
b. AY Bluestone, M Stewart, J Lasker, GS Abdoulaev, AH Hielscher, "Three-dimensional optical tomographic brain imaging in small animals, Part 1: hypercapnia & Part 2: unilateral carotid occlusion," Journal of Biomedical Optics 9 (5), pp/ 1046-1062 & pp.1063-1073 (2004). [135]
c. ML Flexman, F Vlachos, HK Kim, SR Sirsi, J Huang, SL Hernandez, ..., J. Kandel, AH Hielcsher, "Monitoring early tumor response to drug therapy with diffuse optical tomography," Journal of Biomedical Optics 17 (1), 0160141-0160148 (2012) [18]
d. JH Lee, HK Kim, C Chandhanayingyong, FYI Lee, AH Hielscher, Non-contact small animal fluorescence imaging system for simultaneous multi-directional angular-dependent data acquisition," Biomedical Optics Express 5 (7), 2301-2316 (2014) [10]

**Complete List of Published Work in MyBibliography:**
< http://www.ncbi.nlm.nih.gov/pubmed/?term=Hielscher+AH>
(see also < https://scholar.google.com/citations?user=teOwN30AAAAJ&hl=en> for a more complete list, including conference proceedings and patents)

**D. Research Support**

**Active**

NHLBI - 1R01-HL115336-01A1 Hielscher (PI) 08/01/2013 - 07/30/2018
*Title: Optical Tomographic Imaging of Peripheral Arterial Disease*
The goal of this study is to build and test a dynamic optical tomography system in a study involving 100 patients with peripheral arteral disease. There is no overlap with the proposed project.

**Recently Completed**

BioAccelerate NYC Partnership Fund Hielscher (PI) 09/01/2014 -3/31/2017
*Title: Intraoperative optical imaging system for the assessment of lower limb reperfusion*
The goal of this study is to develop a low-cost optical imaging system that can be used during vascular sugery to assess reperfusion. There is no overlap with the proposed project.

Columbia-Coulter Translations Research Partnership Spotnitz/Hielscher (Co-PIs) 09/01/2015 -12/31/2016
*Title: Ultraviolet Laser Sleeve*
The goal of this pilot study is to develop a narrow-UV-light delivery system that can be used to eliminate or considerably reduce bacterial infections along percutaneous drivelines. There is no overlap with the proposed project.

NIAMS - 3R01AR050026-09S1 Bathon, Hielscher (Co-PIs) 07/01/2013 - 06/30/2015
*Title: Inflammation and cardiovascular disease in RA*
The goal of this supplement was to assess if optical tomographic imaging can predict treatment outcome in patients receiving TNF-a therapy. There is no overlap with the proposed project.

Department of Defense (DOD-OR090175) F.Y. Lee (PI) 07/01/2010 - 06/30/2015
*Title: Ready-to-use tissue constructs for military bone and cartilage trauma*
The goal of this grant was to develop tissue constructs that can be used in the field for acute replacement of bone and cartilage. The constructs were tested and imaged in animal models. There is no overlap with the proposed project. (Role: Collaborator)

NCI - 5R33CA118666 Hielscher (PI) 08/01/2008 - 07/31/2013
*Title: Small animal tomography system for green fluorescent protein imaging*
The goal of this project was to design and build a small animal imaging system for tomographic imaging of fluorescence markers. There is no overlap with the proposed DOD project.

Technology Transfer Incentive Program - C020041 Hielscher (PI) 3/15/2006 to 12/31/2012

(New York State Office of Science, Technology and Academic Research)
*Title: Breast Cancer Imaging using Optical Tomography*
The goal of this grant was to develop an optical tomographic breast imaging system that can provide data on hemodynamics in both breast at the same time. The system was tested in a clinical study with 30 patients and is still used for other ongoing studies. The two new systems to be build under the DOD grant will be based on this original design, but contain various improvements. There is no overlap with the proposed project.