BIOGRAPHICAL SKETCH

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NAME: Spielman, Daniel M

eRA COMMONS USER NAME (agency login): SPIELMAN.DANIEL

POSITION TITLE: Professor - Department of Radiology

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Mass. Inst. of Technology, Cambridge, MA	BS	06/1983	Electrical Engineering
Stanford University, Stanford, CA	MS	06/1984	Electrical Engineering
Stanford University, Stanford, CA	MS	06/1987	Statistics
Stanford University, Stanford, CA	PHD	01/1991	Electrical Engineering

A. Personal Statement

Originally trained as an Electrical Engineer, I now have over 25 years of experience as a medical imaging researcher. My primary interests are in the field of in vivo magnetic resonance imaging (MRI) and spectroscopy (MRS) and the development of new methods of imaging metabolism within the body. Current projects include ^{13}C MRS of hyperpolarized substrates for the assessment of glycolysis, oxidative phosphorylation, and other key metabolic pathways, optimized mapping of ^{1}H metabolite distributions throughout the body, and quantifying neurotransmitter levels and cycling rates in the brain. In my laboratory, we focus on advancing a novel array of both acquisition and analysis techniques for use in preclinical and clinical studies. These developments, which include improved spectroscopic imaging and shimming methods, multinuclear NMR studies, application of estimation theory for metabolic modeling and optimal data quantification, address the inherent difficulties of low concentrations of the targeted components, overlapping resonances, and magnetic field inhomogeneities caused by imperfect magnets and magnetic susceptibility variations with the body. Primary applications of this work include cancer diagnosis, treatment monitoring, and prediction of response to therapy, assessment of cardiac function, improved understanding and treatment of metabolic diseases (e.g. diabetes, liver failure) and neurologic disorders including Alzheimer's disease, schizophrenia, and epilepsy.

B. Positions and Honors

Positions and Employment

1985 - 1986 Engineer, Hughes Aircraft Company, El Segundo, CA
1986 - 1990 Research Assistant - Department of EE, Stanford University
1990 - 1993 Research Affiliate – Department of Radiology, Stanford University
1993 - 2000 Assistant Professor - Radiology, Stanford University
2000 - 2010 Associate Professor - Department of Radiology and EE (courtesy), Stanford University
2010 - Professor - Department of Radiology and EE (courtesy), Stanford University

Other Experience and Professional Memberships

Member of the International Society of Magnetic Resonance in Medicine (ISMRM), Radiological Society of North America (RSNA), and IEEE.

Honors

1983 U.S. Army Research Office 3-yr Fellowship, DOD
1983 Tau Beta Pi and Eta Kappa Nu, Engineering Honor Societies
2005 Outstanding Teacher Award, ISMRM
2012 Balchandani P (trainee) awarded ISMRM Junior Fellow, ISMRM
2012 Research Council Distinguished Investigator Award, Academy of Radiology
2012-5 Distinguished Reviewer, Magnetic Resonance in Medicine
2012 Magna Cum Laude Award, "STABLE-2: A shorter, more B0-insensitive option for adiabatic

slice-selective excitation", ISMRM

2014 Summa Cum Laude Award, "Skeletal Muscle Metabolism Measured by Hyperpolarized 13C MR Spectroscopy", ISMRM

2014 Summa Cum Laude Award, "Metabolic Changes in a Rat Glioma Model After Anti-Angiogenic Treatment Measured by MR Spectroscopic Imaging of Hyperpolarized [1-13C]Pyruvate", ISMRM

2014 Summa Cum Laude Award, "Assessment of Diabetic Skeletal Muscle Metabolism Using Hyperpolarized 13C MR Spectroscopy", ISMRM

2014 Park, JM (trainee) awarded ISMRM Junior Fellow, ISMRM

2015 Summa Cum Laude Award, "13C MRS of the Brain Without Decoupling", ISMRM

C. Contribution to Science

1. One of my most significant contributions has been the development of improved methods for addressing the magnetic field inhomogeneities limiting many MRI applications. As part of this work, I developed the fast field mapping and regularized least-squares reconstruction method that is now included on all GE Healthcare MR scanners.

a. Webb P, **Spielman D**, Macovski A, "Inhomogeneity Correction Using High Resolution Water Referencing", Magn Reson Med, 1991; 23: 1-11.
b. Morrell G, **Spielman D**, "Dynamic Shimming for Multislice MRI", Magn Reson Med, 1997; 38: 477-483.
c. **Spielman D**, Adalsteinsson E, Lim, K, "Quantitative Assessment of Improved Homogeneity Achievable Using Linear Versus Higher Order Shims for Spectroscopic Imaging of the Brain", Magn Reson Med, 1998; 40(3): 376-382.
d. Kim DH, Adalsteinsson E, Glover GH, **Spielman DM, "**Regularized higher-order in vivo shimming", Magn Reson Med. 2002 Oct;48(4):715-22

2. I introduced the idea of using variable-density spirals for use with dynamic MR imaging. This technique provides a highly efficient and flexible approach for achieving optimal spatial versus temporal tradeoffs and is now broadly used in both MRI and spectroscopic imaging (MRSI) applications.

a. **Spielman D**, Pauly J, "Spiral Imaging on a Small-bore System at 4.7T", Magn Reson Med, 1995; 34: 580-585.
b. **Spielman DM**, Pauly JM, Meyer CH, "Variable-Density Spirals for MR Fluoroscopy", Magn Reson Med, 1995; 34: 388-394.
c. Kim DH, Adalsteinsson E, , **Spielman DM**. , Simple Analytic Variable Density Spiral Design., Magn Reson Med. 50:214-9, 2003
d. Adalsteinsson E, Star-Lack J, Meyer C, and **Spielman D**, "Reduced Spatial Side Lobes in Chemical Shift Imaging", Magn Reson Med, 1999; 42(2): 314-323.

3. Proton spectroscopic imaging provides unique insights into in-vivo metabolism, but is hindered by low SNR requiring long scan times to overcome. It is thus inefficient to sequential interrogate individual tissue voxels. My trainees and I developed spiral ^{1}H MRSI as a robust and highly efficient method of collecting both multislice and volumetric spectroscopic information.

a. **Spielman D**, Pauly J, Macovski A, Glover G, Enzmann D, "Lipid-suppressed Single and Multiple Slice Proton Spectroscopic Imaging of the Human Brain", JMRI, 1992; 2: 253-262.
b. Adalsteinsson E, Irarrazabal P, Topp S, Meyer C, Macovski A, **Spielman D**, "Volumetric Spectroscopic Imaging with Spiral-Based k-Space Trajectories", Magn Reson Med, 1998; 39: 889-898.
c. Kim DH, Adalsteinsson E, **Spielman DM**, Spiral Readout Gradients for the Reduction of Motion Artifact in Chemical Shift Imaging., Magn Reson Med, 51(3):458-63, 2004
d. Kim DH, **Spielman DM**. Reducing gradient imperfections for spiral magnetic resonance spectroscopic imaging. Magn Reson Med. 2006 Jul;56(1):198-203.

4. The most significant application of MR spectroscopy as been in the study of brain function and metabolism. Colleagues and I developed a number of advancements in the use of specialized Rf pulses and pulse sequence refinements for use with ^{1}H MRS, including the use of spectral-spatial Rf pulses, novel adiabatic pulse design methods, and techniques for distinguishing the overlapping resonances from brain glutamate and glutamine.

a. **Spielman D**, Meyer C, Macovski A, Enzmann D, "Proton Spectroscopic Imaging Using a Spectral-Spatial Excitation Pulse", Magn Reson Med, 1991; 18: 269-279.
b. Mayer D, **Spielman DM** "Detection of glutamate in the human brain at 3 T using optimized constant time point resolved spectroscopy." Magn Reson Med. 2005; 54: 2: 439-42.
c. Balchandani P, Pauly J, **Spielman D**. Slice-selective tunable-flip adiabatic low peak-power excitation (STABLE) pulse. Magn Reson Med. 2008 May;59(5):1072-8, PMCID: PMC2692522.
d. Gu M, Zahr NM, **Spielman DM**, Sullivan EV, Pfefferbaum A, Mayer D. Quantification of glutamate and glutamine using constant-time point-resolved spectroscopy at 3 T. NMR Biomed. 2013 Feb;26(2):164-72. PubMed PMID: 22761057.

5. The recent development of ^{13}C MRSI of hyperpolarized ^{13}C-labeled substrates provides a powerful new approach for interrogating metabolic pathways and associated enzyme activities in vivo at unprecedented spatial and temporal resolution. The new area of research is ideally suited for fast spectroscopic imaging methods due to the rapidly decaying hyperpolarized magnetization. My team has made several significant contributions to this field including novel fast spectroscopic imaging methods, metabolic modeling tools, and assessment of applications for brain, cardiac, and liver imaging.

a. Mayer D, Yen YF, Tropp J, Pfefferbaum A, Hurd RE, and **Spielman DM**, Application of sub-second spiral chemical shift imaging to real-time multi-slice metabolic imaging of the rat in vivo after injection of hyperpolarized (13)C1-pyruvate, Magn Reson Med, 2009, 62(3):556-564, PMCID: PMC2782691.
b. Mayer D, Yen YF, Josan S, Park JM, Pfefferbaum A, Hurd RE, **Spielman DM**. Application of hyperpolarized [1-^{13}C]lactate for the in vivo investigation of cardiac metabolism. NMR Biomed. 2012 Oct;25(10):1119-24. PMID: 22278751; PubMed Central PMCID: PMC3357452.
c. Josan S, Xu T, Yen YF, Hurd R, Ferreira J, Chen CH, Mochly-Rosen D, Pfefferbaum A, Mayer D, **Spielman D**. In vivo measurement of aldehyde dehydrogenase-2 activity in rat liver ethanol model using dynamic MRSI of hyperpolarized [1-(13) C]pyruvate. NMR Biomed. 2013 Jun;26(6):607-12. PubMed PMID: 23225495; PubMed Central PMCID: PMC3634870.
d. Park JM, Josan S, Jang T, Merchant M, Watkins R, Hurd RE, Recht LD, Mayer D, **Spielman DM**. Volumetric spiral chemical shift imaging of hyperpolarized [2-(13)c]pyruvate in a rat c6 glioma model. Magn Reson Med. 2015 May 6, PubMed PMID: 25946547

Complete List of Published Work in My Bibliography (124 total):
http://www.ncbi.nlm.nih.gov/myncbi/daniel.spielman.1/bibliography/41155633/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

NIH R01 CA176836 (PI: Lawrence Recht) 05/09/14-04/30/19
"Metabolic therapy of GBM guided by MRS of hyperpolarized 13C-Pyruvate"
The goal of this project is to link bevacizumab's treatment effect with an optimal "lactate/bicarbonate ratio" that can be used clinically as a measure of effectiveness and therapeutic goal.
Role: Co-PI

NIH R21 EB019665 (PI: Daniel Spielman) 09/01/14-8/31/16
"Novel MRS methods for measuring brain energetics and neurotransmitter cycling"
The overall goal of this two-year technical development project is to develop optimized magnetic resonance methods for the noninvasive measurement of neuroenergetics and neurotransmitter cycling throughout the human brain.

NIH P41 EB015891 (PI: Gary Glover) 01/01/95-03/31/15
"Center for Advanced Magnetic Resonance Technology at Stanford"
The major goals of this project are to develop innovative MR techniques for fundamental anatomic, physiologic and pathophysiologic studies involving animals and humans and to serve the academic and scientific community through collaborations, education, and access to Center facilities and resources.
Role: Co-Pi

NIH R01 HD084214 (PI: Fred Chin) 9/22/2014-5/31/2019
"Cross-species mutli-modal neuroimaging to investigate GABA physiology in fragile X syndrome"

The goal of this project is to significantly contribute new discoveries by studying both animals and humans with FXS, and undertaking research from a developmental perspective and at multiple levels of scientific analysis.
Role: Co-Investigator

Stanford BioX Seed Grant (PI: Daniel Spielman) 10/01/14-9/30/16
"In vivo Metabolic Imaging of Senescent Cells Using Hyperpolarized 13C MRS"
The goal of this project is to develop multi-modal imaging methods for detecting and quantifying senescent cells.

GE-Stanford Blue Sky Research Funding (PIs: D. Spielman and J. Willmann) 5/1/2014-6/30/2015
"Fused Hyperpolarized MRS/PET/Molecular Ultrasound Imaging for Improved Diagnosis of Prostate Cancer"
The goal of this multidisciplinary proposal is to increase the diagnostic accuracy of guided prostate cancer biopsy by developing and testing a novel, clinically translatable real-time acquisition and analysis platform for acquiring fused hyperpolarized 13C MRS, PET, and molecular ultrasound imaging data sets.

Completed Research Support

NIH S10 OD012283 (PI: Daniel Spielman) 05/01/13-04/30/15
"Hyperpolarizer for ^{13}C MR Metabolic Imaging of human subjects and animal models"
This high-end shared instrumentation grant was for the purchase of a GE SpinLab dynamic nuclear polarizer and quality control system.

NIH R01 AA018681 (PI: Daniel Spielman) 1/1/2010-12/31/2014
"Metabolic Imaging of the Cardioprotective Effects of Alcohol and ALDH2 Activators"
The goal of this project was to develop hyperpolarized ^{13}C MRS methods for imaging ALDH2 activity for the assessment of cardiac metabolism.

DOD Prostate Cancer Development Award W81XWH-11-1-0602 (PI: Daniel Spielman) 7/15/2011-7/14/2014
"In-Vivo Imaging of Branched Chain Amino Acid Metabolism in Prostate Cancer"
The overall goal of this proposal was to evaluate ^{13}C-MRS of hyperpolarized alpha-ketoisocaprioic acid (KIC) as a powerful new approach to image underlying metabolic processes differentiating normal and malignant tissues and thus to develop a novel diagnostic tool for optimizing treatment choice and therapy monitoring.

NIH R01 MH080913 (PI: Daniel Spielman) 7/1/2008-4/30/2013
"1H MRSI of the Human Brain at 7T"
The goal of this project was to develop optimized novel methods for spectroscopic imaging of the human brain at ultra-high fields.

NIH R01 CA048269, (PI: Daniel Spielman) 7/23/1990-7/31/2006
"Magnetic Resonance Spectroscopic Neoplasm Imaging"
The goal of this project was to develop volumetric 1H spectroscopic imaging methods for the diagnosis and monitoring of cancer.

NIH R01 AG018942, (PI: Daniel Spielman) 3/1/2001-2/28/2005
"Magnetic Resonance Spectroscopic Imaging in Alzheimer's Disease"
The goal of this project was to assess the utility of 1H MR spectroscopic imaging of the brain as a tool for the assessment of Alzheimer's Disease.