

**From: Jonathan S. Lewin, M.D., F.A.C.R.**  
Martin Donner Professor and Director  
Russell H. Morgan Department of Radiology and Radiological Science

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Edward D. Miller, M.D.  
Dean of the Medical Faculty  
Chief Executive Officer, Johns Hopkins Medicine  
Broadway Research Building, Suite 100  
733 N. Broadway Street  
Baltimore, MD 21205-2196

Dear Dr. Miller:

It is a pleasure to recommend the promotion of Dara L. Kraitchman, V.M.D., Ph.D., F.A.C.C. for promotion to Professor in the Johns Hopkins School of Medicine.

Abstract

**Dara L. Kraitchman**, V.M.D., Ph.D., F.A.C.C. is a full-time Associate Professor in the Division of Magnetic Resonance (MR) Research, Russell H. Morgan Department of Radiology and Radiological Science since 2004 with a Joint appointment in Molecular and Comparative Pathobiology since 2009 and affiliate faculty in the Institute for NanoBioTechnology and Center for Computation Mathematics. Promotion to full professor is proposed for advancement based upon accomplishments as a biomedical scientist and veterinarian. She is a world leader in developing new methods to label stem cells for tracking in cardiovascular disease, specifically and primarily for the development of superparamagnetic iron oxide (SPIO) labeling for magnetic resonance imaging (MRI) tracking of stem cells for the treatment of ischemic cardiovascular disease. Moreover, she developed one of the first methods for positive contrast imaging of SPIOs labeling. More recently, she has discovered a novel way to label stem cells for tracking with conventional X-ray systems used for cardiac interventions. She is also accomplished in multimodality imaging and interventional techniques. Dr. Kraitchman has achieved an international reputation as the leader in this highly focused field. In addition, she has cultivated expertise and reputation in the development of minimally invasive large animal models of cardiovascular disease with a focus on relevant models for rapid clinical translation of therapies and imaging techniques.

Introduction

Dr. Kraitchman joined the full-time faculty at Hopkins in 1996 as a Research Associate in the Russell H. Morgan Department of Radiology and was promoted to an Instructor in Radiology shortly thereafter. In 1998, she was appointed as Assistant Professor and subsequently advanced to Associate Professor in 2004.

Dr. Kraitchman's education included obtaining a doctor of veterinary medicine degree at the University of Pennsylvania from 1989 through 1992 where she graduated Magna Cum Laude. She also obtained her Masters and Ph.D. in Bioengineering in 1993 and 1996 after being selected as one of two veterinarians that year in the US who participated in the Medical Science Training Program sponsored by the National Institutes of Health. She received her bachelor's degree in Electrical Engineering from Carnegie Mellon University in 1984. From 1984-1986, she was a Member of Technical Staff at Bell Laboratories prior to returning for Masters work at the University of Illinois at Urbana-Champaign in 1986.

Research Scholarship

As noted in Dara's curriculum vitae, there are currently 67 peer-reviewed publications, 2 non-peer-reviewed publications, 2 editorials, and 7 book chapters. She is also the editor of a book in press on the topic of stem cell labeling as well as the senior inventor on 3 patent applications in the area of stem cell labeling and non-invasive imaging techniques. Her research focus on novel contrast mechanisms for non-invasive imaging in cardiovascular disease is evident since >90% of her peer-reviewed publications deal with this topic. Of these peer-reviewed publications, she is first author on 12 and senior author on 15, for a first/senior author proportion of 40% (27/67). Many of these publications are in highly regarded journals with high impact factors, including *Circulation*, *The Journal of American College of Cardiology*,

Radiology, and The Journal of the Society of Nuclear Medicine. One should also note that the majority of her publications in the past 5 years, including six of the book chapters, are focused upon stem cell labeling techniques. Since joining the Hopkins faculty in 1996, she has averaged 5 peer-reviewed publications per year, with a maximum of 10 in both 2008 and 2009. The latter figure represents the more intense focus on stem cell labeling in cardiovascular disease after she acquired her NIH-funded R21/R33 with ~\$1.8M in direct costs in response to a targeted nanotechnology RFA.

Recognition of the published works as unique and valuable can be gleaned from the extensive local, national, and international invitations to discuss her work. Over the past 5 years, she has averaged 10 invited lectures per year, including invitations to major conferences nationally (American Heart Association, Radiological Society of North America, Society for Cardiovascular Medicine, Society of Nuclear Medicine, etc.) and internationally (European Heart Society, International Society of Magnetic Resonance, International Conference on Cell Therapy for Cardiovascular Disease, International Academy of Cardiology, Chinese Congress of Radiology, etc.).

Dr. Kraitchman's major contributions have been in the novel application of contrast mechanisms for identifying ischemic tissue and tracking stem cells. Her doctoral thesis combined measurement of cardiac function by MRI with perfusion using gadolinium contrast agents shortly after these agents had been approved for clinical use (1,2,3,5). The imaging processing methods developed by Dr. Young and her for tracking tagged cardiac MRI is still utilized by a GE Healthcare and academic research groups (1,2, SPAMMVU Copyright). Her continued contribution to the use of contrast-enhanced (CE) MRI is evident in her highly-cited work relating to the best methodology to analyze CE MRI for measuring myocardial infarction size (29). She was also at the forefront performing preclinical work with one of the few FDA-approved MRI contrast agents, gadofosveset trisodium (Vasovist, AngioMark, MS-325). Although this new agent was designed for use for MR angiography, she demonstrated the utility of this contrast agent for first-pass perfusion imaging of coronary artery stenosis (13) and in the process developed a new minimally invasive large animal model of coronary artery disease (10). Dr. Kraitchman achieved more widespread recognition in both Cardiology and Radiology for her development of a method to track stem cells in the heart using an FDA-approved MR contrast agent (18, 25, 27). She subsequently performed the first radiotracer direct-labeling and reporter gene labeling of stem cells in a large animal model of myocardial infarction for tracking stem cells (35, 51). Because her work is performed using clinical imaging scanners in large animal models of cardiovascular disease, she is a leader in the field aiding to the clinical translation of these stem cell labeling techniques. Currently, she is a co-editor with Dr. Joseph Wu, a cardiologist at Stanford University, of the first book devoted to cardiac stem cell labeling that is anticipated to be published this summer.

Dr. Kraitchman has also shown a keen interest in the development of interventional MRI. She was a collaborator in some of the early work demonstrating the feasibility of intravascular MR imaging using MR coils incorporated into catheters (6,7). She remains active in this arena with a recent publication using intravascular MRI in atherosclerotic disease that demonstrate the value for the higher spatial resolution intravascular MRI technique compared to conventional angiography or intravascular ultrasound (60). However, her biggest contribution to interventional MRI has been in the development of devices and a platform for delivery of MRI-labeled cellular therapies in the MRI scanner (22, 34, 40,45).

One of the major limitations of MRI-visible stem cells is that stem cells labeled with iron oxide contrast agents appear as a signal void. Dara has, in concert with Drs. Stuber and Gilson, developed an ingenious method to make these signal voids not only appear bright on MRI, but also provide an ability to quantify the signal (42, 45, US Patent Application 06/03832). This technique has been adapted for MR angiography, MR lymphography, and interventional techniques (49, 50) and has been further developed by both Philips and Siemens Medical Systems for clinical MRI systems. Thus, this patented technique appears to have tremendous potential.

Dr. Kraitchman continues to remain inventive by developing new ideas and methods for labeling stem cells for a variety of imaging modalities. She in concert with Drs. Arepally, Barnett, and Bulte recently developed the first method to track stem cells using X-ray imaging (39, 61, US Patent Application 07/009992). This technology is the focus of her current nanotechnology R21/R33 and provides a method to not only visualize stem cells using X-rays but enhances stem cell survival using microencapsulation and thereby provides a better therapeutic product. She has continued to seek out new discoveries and has recently in collaboration with Drs. Mao and Wang further developed this microencapsulation technique to enable single cell encapsulation in a high-through put manner (US Provisional Patent filed October 2010). This most recent invention may not only prove revolutionary in the stem cell therapeutic field, but also occupies a new niche in the chemoembolic therapy field by providing the first radiographically visible embolic bead therapy. Dr. Kraitchman's enthusiasm for pursuing these new avenues of research is infectious and in part the reason that she has collaborated with such a great number of individuals at Johns Hopkins and around the world.

## **Teaching Scholarship**

While Dr. Kraitchman's appointment in Radiology has primarily a research focus, she is involved in teaching at various levels. Within the Division of MR Research in the Department of Radiology, teaching occurs at several levels. Since 1999, Dr. Kraitchman has mentored Visiting Scientist and Postdoctoral Fellows from academic centers and hospitals in Europe, Asia, South American, and the US. She has been a member of the thesis committee for three Johns Hopkins biomedical engineering Ph.D. candidates and the thesis advisor for a biomedical engineering Masters candidate. This is in addition to numerous biomedical engineering and public health undergraduate students that she has mentored with independent research projects over the past 10 years. With her appointment in 2009 in the Department of Molecular and Comparative Pathobiology (MCP), she has a more formal role in mentoring the post-doctoral fellows and laboratory animal residents. She is now the direct mentor of one MCP post-doctoral fellow. She has also been the mentor for five additional post-doctoral fellows that she has fully supported financially through her grants from the National Institutes of Health including a minority supplement to one of her NIH-R01s. The quality of Dr. Kraitchman's mentorship in research can be judged by the large number of young investigator finalists and awardees from her laboratory and the current academic positions of her former mentees. In a more informal manner, she interacts with medical students, residents, fellows, and visiting scientists in Radiology, who observe or participate in her research studies. She has also participated in a more formal manner with introduction to research seminars for Radiology fellows and residents and lectures as part of the Electrical and Computer Engineering/Biomedical Engineering Department MRI Course.

Dr. Kraitchman spearheaded a research seminar in MRI for the research and clinical faculty, staff, and fellows from 2001-2006. She recruited speakers internally within the Department, School of Medicine, Johns Hopkins University, and other academic centers within the USA and abroad to present lectures on current research topics relevant to MRI research. She sought external funding from Berlex Laboratories to defray the cost of hosting external speakers. This program was extremely well attended and provided a forum for the development of new research ideas and collaborations both internally and externally. This forum led to the development of the research seminar now hosted by the In Vivo Cellular and Molecular Imaging Center (ICMIC).

Dr. Kraitchman has also developed continuing veterinary medical education courses that utilize the X-ray angiographic suite that was upgraded as a result of her Shared Instrumentation Grant. These courses have received accreditation from the Veterinary Board of the State of Maryland and have been performed independently at Johns Hopkins as well as in collaboration with national veterinary meetings, e.g., American College of Veterinary Internal Medicine.

Dr. Kraitchman holds the position of Research Faculty Administrator for the Division of MR Research supervising the two 1.5T MR scanners, two 3T MRI scanners and X-ray Angiographic suite. She facilitates faculty members who desire to perform imaging research in the MR Division. She oversees the training of new researchers and staff. This has included developing an online radiation safety course for all new users of the Angiographic system. She has also supervised the education of individuals who operate the MR-compatible cryoablation system, MR-compatible anesthesia system, MR-compatible physiological monitoring system, and Siemens X-ray angiographic system.

Dr. Kraitchman has also demonstrated her mentoring capabilities outside the institution. As Chair of the Science Committee of the Society for Cardiovascular Magnetic Resonance (SCMR), she initiated a committee consensus paper on MRI first-pass perfusion imaging. This initiative of hers has set the bar for the direction of this committee over the past several years after she stepped down as chair. In the last year, she designed and initiated a new mentorship program for the SCMR that involves pairing of mentors and mentees within the society based on similar scientific interests. The program was adopted at their most recent annual meeting and was extremely successful with over 50 mentor-mentee pairs. As such, Dr. Kraitchman has been invited to continue the supervision of the program for the next annual meeting.

#### Organizational/Administrative Activities

Dr. Kraitchman was recruited to Hopkins in 1996 by Dr. Elias Zerhouni to oversee preclinical MRI animal studies of cardiovascular disease. In 2002, she received a shared instrumentation grant that enabled the installation of a state-of-the-art X-ray angiographic system and a refurbished cardiac angiographic system from Toshiba Medical Systems in the Radiology Research Laboratory. She was responsible for all aspects of the design and build of this equipment that was dedicated to preclinical animal imaging. Subsequently, she has become an invaluable asset in the installation of the recent upgrade to the clinical field strength MRI scanners in the Division of MR Research. Next, Dr. Kraitchman became one of the lead MR researchers guiding the installation of the first combined X-ray fluoroscopy-3T MRI scanner systems in the country. Her expertise in this first of a kind installation was extremely useful. With the upgrade of the clinical inpatient and research MRI suites, I designated Dr. Kraitchman as the primary Division of MR Research faculty member overseeing the University MRI Siemens system upgrades. Dr. Kraitchman worked closely with Dr. Bluemke, the Director of Body MRI at that time, to ensure that the clinical and research needs were met in this combined MRI suite area. Due to her efforts, there is now a synergistic relationship between clinical and research development in MRI that is enhancing the

rapid translation of research in MRI. Dr. Kraitchman continues to oversee these Division of MR Research MRI and X-ray angiographic facilities. As a result of her efforts, we have one of the few MR-compatible cryoablation systems installed in the US, and interventional radiologists in the Department are making the transition from conventional X-ray angiographic techniques to MRI-based interventions. In part, due to her efforts, Johns Hopkins University is now recognized as a powerhouse in the area of interventional MRI.

Dr. Kraitchman is also a member of The Johns Hopkins Institutional Animal Care and Use Committee. Because of concerns about animal rights activists, individuals who are voting members of this committee perform much of their work largely unseen to the Johns Hopkins community. Because of Dr. Kraitchman's veterinary expertise with an emphasis on large animal models as well as medical imaging, she offers a unique perspective to this committee beyond the typical academic researcher or clinician-scientist. She has been instrumental in raising awareness in the committee about concerns about radiation dose and hearing protection in the MRI environment. Her willingness to raise and speak out on controversial issues prevents complacency within the IACUC and therefore assists the institution in being pre-emptive in the welfare and care of animals used in research. As more researchers have moved to mouse and rat models, expertise like hers in large animals is extremely valuable.

On a more personal note, Dr. Kraitchman is a member of the Johns Hopkins Green Team. This organization is a grass-root organization that has shown a commitment to sustainability and the adoption of green measures within the hospital. She personally oversaw the roll-out of recycling within the Division of MR Research. As a small group, the Green Team has been working hard to advance these efforts and provide a better environment currently with the introduction of the Farmer's market and for the future by recycling everything from bottles and cans to eyeglasses, pens, and computers.

### **Citizenship in Academic Medicine and Commitment to Hopkins**

Dara is widely recognized as an expert in her scientific area B stem cell imaging and interventional technique. Her research activities have been supported continuously since 1996 by RO1/R33 awards from the National Institutes of Health, and prior to that by smaller awards by such agencies as the American Heart Association. Her expertise has been recognized through invitations to participate in peer-review of NIH and NSF grants since 2002, and she was likewise a member from 2005 to 2008 of the Clinical and Integrative Cardiovascular Sciences (CICS) Integrate Review Group (IRG) Program B the cardiovascular clinical trial study section at the NIH. Since 2007, she has been a standing member of the American Heart Association Radiology, Imaging, and Surgery Grant Reviews Section. She has given 72 invited lectures, participated in the NIH Working Groups on the Translation of Therapies for Protecting the Heart from Ischemia and Advancing Vascular Interventional Discoveries, and numerous scientific lectures at National and International Conferences, Meetings, and Symposia. She is on the Editorial Board for 3 National Journals, including The Journal of the American College of Cardiology Cardiovascular Imaging, The Journal for the Society for Cardiovascular Magnetic Resonance, and NanoMedicine. In addition, she regularly reviews papers for 20 different journals, including Circulation, Science Clinical Translation, The Journal of the American College of Cardiology, and Radiology. She has been chair of the Science and Publication Committees of the Society for Cardiovascular Magnetic Resonance. She has published 7 book chapters focusing on MRI and stem cell labeling. She is the co-editor of a the first book devoted to stem cell labeling and non-invasive imaging that will be published in the Summer of 2011. She was also recognized for her contributions to Cardiology when she was elected as a Fellow of the American College of Cardiology. This is an honor that is bestowed on few non-physicians, and she may very well be the only veterinarian ever elected to the College.

### **Anticipated Future Progress**

Dr. Kraitchman's success with obtaining research funding along with her innovative approach to translational research has driven the opportunity to expand scientific investigation and allowed the development of new interventional imaging techniques focused on stem cell therapies at Hopkins. Dara has strongly pursued preclinical models of stem cell therapy as the cornerstone of her career and hopes to further this by expanding programs in minimally invasive therapies in companion animals at Hopkins as a bridge to Phase I clinical trials. It is hoped that stem cell microencapsulation program of which she is PI will develop into a strong program with clinical activities (such as the treatment of patients with peripheral arterial disease and ischemic heart disease). She is already active in teaching stem cell labeling techniques to physicians and scientists throughout the world to enhance expansion of these techniques to patients. She is a sought out mentor for young scientists and physicians who desire to pursue a focus in stem cell imaging and interventional MRI. As a result of her success in this area, Johns Hopkins is recognized as one of the leaders in stem cell tracking and minimally invasive imaging.

### **Summary Statement**

Dara L. Kraitchman, V.M.D., Ph.D. is one of a few world experts and leaders in the field of stem cell labeling and interventional MRI. She has made substantial and important contributions to the vitality of the research and clinical community of Hopkins, Maryland, the United States, and on a global basis. Dr. Kraitchman has achieved international recognition by virtue of her outstanding career in imaging research, her publication record, her presentations at world forums, and her impact in imaging and cardiology subspecialty societies. I recommend her promotion to professor with the highest enthusiasm.

Sincerely,

Jonathan S. Lewin, M.D., F.A.C.R.  
Martin Donner Professor and Director