Libertas Academica
FREEDOM TO RESEARCH

NEW CONCEPTS IN MAGNETIC RESONANCE AS APPLIED TO CELLULAR AND *IN VIVO* APPLICATIONS

- **Melanie Martin**
  Professor of Physics, University of Winnipeg, Winnipeg, MB, Canada. Director, Magnetic Resonance Microscopy Centre, University of Manitoba, Winnipeg, MB, Canada.
- **Benedict Albensi**
  Associate Professor of Pharmacology & Therapeutics, University of Manitoba, Winnipeg, MB, Canada. Principal Investigator, Synaptic Plasticity and Cellular Memory Dysfunction Lab, Division of Neurodegenerative Disorders, St. Boniface Hospital, Winnipeg, MB, Canada.
- **Albert Cross**
  Adjunct Professor of Physics, University of Lethbridge, Lethbridge, AB, Canada.
- **Rachel Katz-Brull**
  Senior Lecturer of Imaging, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.
- **Jonathan Thiessen**
  Imaging Scientist, Lawson Health Research Institute, London, ON, Canada. Assistant Professor of Medical Biophysics, Western University, London, ON, Canada.
- **Scott King**
  Team Lead for RF Electronics and Engineering, Medical Devices Portfolio, National Research Council Canada, Winnipeg, MB, Canada.
- **Alexander Lin**
  Director, Center for Clinical Spectroscopy, Department of Radiology, Brigham and Women's Hospital, Boston, MA, USA. Assistant Professor of Radiology, Harvard Medical School, Harvard University, Boston, MA, USA.

Supplement Aims and Scope

This supplement focuses on new concepts in magnetic resonance as applied to cellular and *in vivo* applications. Advanced imaging sequences for rapid and parallel imaging/spectroscopy, high-speed multi-dimensional MR techniques and quantitative image and spectral processing techniques are included within the supplement's scope.

Magnetic Resonance Insights aims to provide researchers working in this complex, quickly developing field with online, open access to highly relevant scholarly articles by leading international researchers. In a field where the literature is ever-expanding, researchers increasingly need access to up-to-date, high quality scholarly articles on areas of specific contemporary interest. This supplement aims to address this by presenting high-quality articles that allow readers to distinguish the *signal from the noise*. The editor-in-chief hopes that through this effort, practitioners and researchers will be aided in finding answers to some of the most complex and pressing issues of our time.

Articles in this supplement focus on new concepts in magnetic resonance as applied to cellular and *in vivo* applications:

- Advanced imaging sequences for rapid and parallel imaging/spectroscopy
- High speed multi-dimensional MR techniques
- Quantitative image and spectral processing techniques.

The two main focuses of the supplement are:

- Contrast-enhanced cellular imaging with MRI
- Applications and Analysis of Functional Neuroimaging.

MRI has proven to be a powerful clinical tool, but surprisingly it is still underutilized in many clinical settings. Presumably costs and a lack of awareness for its true capabilities are responsible for this situation. Hopefully, numerous advances over the last decade that have demonstrated its utility in the diagnosis of many disorders and experimental conditions will convince hospital administrators, government leaders, and other health care professionals to embrace this powerful imaging modality more fully.

Indeed, new concepts and approaches in magnetic resonance as applied to cellular and *in vivo* applications have provided both the clinical community and the basic science community with a new impetus to use MRI beyond routine diagnosis.

Research areas involving iron contrast, fMRI of the spine, ultra high-performance computing, ^{19}F imaging in stroke, MEMRI, two proton MRS, GABA measurements, and hyperpolarized probes are just an inkling of the new developments in this exciting field.

Contrast-enhanced cellular imaging with MRI has many clinical applications as described in several articles in this supplement. Korchinski et al demonstrate how iron oxide particles can be used to track cells in MRI with both in vivo and ex vivo labeling methods. Iron oxide particles can be used to track variety of cells, including stem cells, red blood cells, macrophages, monocytes, and nonlymphocytes. These techniques have a wide variety of potential clinical applications, including imaging of ischemic stroke, multiple sclerosis, cancer, and vascular diseases.

Goldhawk et al describe the application of magnetosome genes capable of producing iron biominerals detectable by MRI. Expression of a magnetotactic bacterial protein (MagA) in several mammalian cell types can be used to endogenously increase cellular iron content with iron supplementation. This gene-based approach has the potential to both track cells and monitor their cellular function throughout the cell's life cycle. While long-term cell tracking is a distinct advantage over most iron oxide labelling methods, gene-based contrast has several hurdles to overcome, including significantly smaller effects on MR signal and challenges related to cellular iron regulation.

Fluorinated compounds can be tracked using ^{19}F MRI, with similar SNR for the same concentration of 1H and negligible endogenous concentrations of ^{19}F in the body. As outlined by Fox et al, the use of fluorinated compounds has a wide variety of potential applications, including the imaging of micro and macro-biological environments.

The dissolution-dynamic nuclear polarization (DNP) technique has revolutionized the solution state and *in vivo* nuclear magnetic resonance (NMR) spectroscopy field, by offering an increase of more than 10,000-fold in signal. However, this approach is limited by the need to obtain a substrate molecule that has a reporting nucleus with long T_1. Jupin et al show that the steady-state variable nutation angle approach is faster and may be better suited for the determination of relatively long T_1s in thermal equilibrium than other approaches to determining the long T_1 of the nuclei.

Molecular imaging probes rely on a variety of contrast mechanisms to boost MR contrast, including: chelates of paramagnetic metals such as gadolinium or manganese, which shorten the T_1 relaxation time, superparamagnetic iron oxide, which shortens the T_2 relaxation time, and hyperpolarized substances containing ^{129}Xe, ^{3}He, or ^{13}C, which can boost the MR signal up to 100,000X. Despite these signal enhancements, the injected dose usually needs to be on the order of millimolar concentrations. As demonstrated by Cross et al, the administration of contrast agents such as $MnCl_2$ may have adverse effects, necessitating caution when translating molecular MR imaging probes from bench to bedside. While the toxicity issues of $MnCL_2$ prevent it as a candidate for human studies, it has potential to be a unique and valuable research tool for functional imaging studies of freely behaving rodents. In contrast, positron emission tomography (PET) can detect nanomolar concentrations of radiolabeled tracers, making it both uniquely sensitive and safe. Alongside purely MR-based molecular imaging techniques, there are new avenues of research available with the introduction of preclinical and clinical hybrid PET/MRI systems.

Unlike most imaging modalities, MRI is capable of generating contrast based on functional and structural features without the addition of a contrast agent. This unique capability is demonstrated by the second group of papers, including detecting blood-oxygen-level dependent (BOLD) contrast in the human spinal cord, improving measurements of the inhibitory neurotransmitter GABA with MR spectroscopy, correlation of intraplaque hemorrhage and stroke measured with 1.5T and 3T MRI, and the utility of ultra-high-performance computing for the analysis of neuroimaging.

Kolesar et al review the application of fMRI for assessing nociception in the spinal cord. Although still restricted to a research setting with a large variety of methodological approaches, spinal fMRI shows promise for assessing acute and chronic pain in patients.

Due to the low concentration and overlapping resonances in neurospectroscopy, the measurement of GABA in the brain can be challenging. Wang et al compare two different MRS sequences that focus on the detection of GABA levels in data acquired from solutions with known concentrations of GABA in order to determine the accuracy of the two methods. The results demonstrate that the localized two-dimensional correlated spectroscopy (L-COSY) performs better than the more conventional MEGAPRESS sequence with the added benefit of allowing detection of many other metabolites simultaneously.

With larger data sets and more sophisticated analyses, it is becoming increasingly common for MRI researchers to exceed the limitations of standalone computer workstations. Shatil et al summarize the main advantages of computing clusters, grids, and clouds, and when it would be advisable to use them, review potential problems and barriers to access, and give practical suggestions for how interested new users can start analyzing their neuroimaging data using cloud resources.

Treiman et al explain how only MRI has the ability to identify and measure the detailed components and morphology of carotid plaques, and how it provides more detailed information than other currently available techniques. Carotid plaque composition is important in risk stratification and is better than current risk stratification based on percent stenosis, which does not provide specific information on the

actual risk of stroke for most individuals. They show that MRI can accurately detect carotid hemorrhage, and MRI identifies carotid hemorrhage correlates with acute stroke, which emphasizes the importance of MRI for clinical use.

The articles in this supplement clearly show the growing ability of MRI to be applied to cellular and in vivo applications. As the abilities of MRI grow, the applications of MRI will increase and the clinical use of MRI will also increase.

Lead Guest Editor **Dr. Melanie Martin**

Dr. Melanie Martin is a Professor of Physics at The University of Winnipeg and the Director of the Magnetic Resonance Microscopy Centre at the University of Manitoba. She completed her PhD at Yale and has previously worked at Caltech. She now works primarily in Magnetic Resonance Imaging. Dr. Martin is the author or co-author of 30 published papers and has presented at numerous conferences, and holds an editorial board appointment at Magnetic Resonance Insights.

mri.uwinnipeg.ca
m.martin@uwinnipeg.ca

Guest Editors

DR. BENEDICT ALBENSI

Dr. Benedict Albensi is an Associate Professor of Pharmacology & Therapeutics at University of Manitoba and Principal Investigator in the Synaptic Plasticity and Cellular Memory Dysfunction Lab, Division of Neurodegenerative Disorders at St-Boniface Hospital. He also holds the Manitoba Dementia Research Chair and the Everett Chair. He completed his PhD at the University of Utah and has previously worked at the Cleveland Clinic, Case Western University, and Pfizer. He now works primarily in understanding memory impairments in Alzheimer's disease. Dr. Albensi is the author or co-author of over 160 published papers, reviews, book chapters and abstracts, and has presented at over 50 conferences or seminars. He is the Associate Editor for the journal *Brain Injury* and has been a special guest editor for several journals.

http://www.sbrc.ca/dnd/faculty/dr-benedict-c-albensi/
balbensi@sbrc.ca

DR. ALBERT CROSS

Dr. Albert Cross spent 10 years as an Assistant Professor of Neuroscience and Physics at University of Lethbridge and is currently an Adjunct Professor of Physics at University of Lethbridge. He completed his PhD at University of New Brunswick and has previously worked at University of Waterloo, University of Toronto and Carleton University. He now works on MRI technical applications and is the founder of AC^2 Scientific. Dr. Cross is the author or co-author of 30 published papers and has presented at 50+ conferences.

http://directory.uleth.ca/users/albert.cross
albert.cross@uleth.ca

DR. RACHEL KATZ-BRULL

Dr. Rachel Katz-Brull is a Senior Lecturer of Imaging at Hadassah-Hebrew University Medical Center. She completed her PhD at Weizmann Institute and has previously worked at Beth Israel Deaconess Medical Center and Harvard Medical School. She now works primarily in the field of Hyperpolarized MRI. Dr. Katz-Brull is the author 25 published papers and has presented at numerous conferences.

www.katz-brull-lab.org
rkb@hadassah.org.il

DR. JONATHAN THIESSEN

Dr. Jonathan Thiessen is an Imaging Scientist at the Lawson Health Research Institute and Assistant Professor of Medical Biophysics at Western University. He completed his PhD at the University of Manitoba and has previously worked at the University of Winnipeg. He now works primarily in the field of Hybrid PET/MRI. Dr. Thiessen is the author or co-author of 15 published papers and has presented at numerous conferences.

https://www.lawsonimaging.ca/imaging/user/2106/profile
jthiessen@lawsonimaging.ca

DR. SCOTT KING

Dr. Scott King is the Team Lead for RF Electronics and Engineering in the Medical Devices portfolio of the National Research Council of Canada. He completed his PhD at the University of Manitoba and has previously worked at MRI Devices Corp as a R&D Engineer. He now works primarily in advanced MRI technologies and general medical device development. Dr. King is the author or co-author of 12 published papers, 10 patents, and has presented at numerous conferences, including five ISMRM weekend educational teaching seminars and is a referee for 15 different journals and granting agencies.

scott.king@nrc-cnrc.gc.ca

DR. ALEXANDER LIN

Dr. Alexander Lin is the Director of the Center for Clinical Spectroscopy, Department of Radiology, Brigham and Women's Hospital and an Assistant Professor of Radiology at Harvard Medical School. He completed his PhD at California Institute of Technology and has previously worked at Huntington Medical Research Institutes and National Institutes of Health in Bethesda. He is also a visiting associate at University of Illinois Chicago, Children's Hospital Boston, and Massachusetts General Hospital. He now works primarily in clinical applications of multinuclear magnetic resonance spectroscopy in the brain, breast, and liver and cardiovascular magnetic resonance imaging. Dr. Lin is the author or co-author of 42 published papers and has presented at numerous conferences, and holds an editorial board appointment at the Journal of Neuroimaging.

http://bit.ly/bwh_spectro
aplin@bwh.harvard.edu

SUPPLEMENT TITLE: New Concepts in Magnetic Resonance as Applied to Cellular and *In Vivo* Applications

CITATION: Martin et al. New Concepts in Magnetic Resonance as Applied to Cellular and *In Vivo* Applications. *Magnetic Resonance Insights* 2015:8(S1) 49–52 doi:10.4137/MRI.S37997

TYPE: Editorial

FUNDING: Authors disclose no external funding sources.

COMPETING INTERESTS: Authors disclose no potential conflicts of interest.

CORRESPONDENCE: m.martin@uwinnipeg.ca

All authors have provided signed confirmation of their compliance with ethical and legal obligations including (but not limited to) use of any copyrighted material, compliance with ICMJE authorship and competing interests disclosure guidelines.