

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

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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_1 s 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 , ^3He , 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

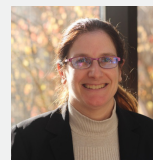


actual risk of stroke for most individuals. They show that MRI can accurately detect carotid hemorrhage, and MRI identifies carotid hemorrhage correlates with acute stroke, which emphasizes the importance of MRI for clinical use.

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.

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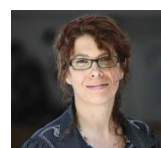
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