Clinical MR Neuro Imaging at Ultra-High Field (9.4 Tesla)

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Abstract: Ultra-high field magnetic resonance (MR) imaging (greater than 3.0 Tesla) for clinical management of patients is in its infancy. The Food and Drug Administration (FDA) guideline for insignificant risk of static magnetic field exposure to humans is currently set at 8.0 Tesla. There are now dozens of 7.0 Tesla research systems and three 9.4 Tesla (limited by the current density of modern superconducting wire technology at 4.2°K over 80cm diameter clear bore) scanners available worldwide that have been designed for performing human MR studies. Just as the introduction of first FDA approved 3.0 Tesla clinical scanners came within 5 years of the initial successful experience of a 3.0 Tesla research scanner based on a clinical platform [1,2], the improved signal-to-noise (SNR) performance achieved on the now numerous ultra-high field (7.0 and 9.4 Tesla) research scanners over the last 5 years suggests that clinical applications are sure to follow.

Skeptics and naysayers of ultrahigh field human MR imaging have focused on hypothetical safety issues and perceived engineering challenges similar to those that confronted whole body imaging at 3.0 Tesla more than a decade ago. Over the last 5 years, safety of MR imaging protocols, under the guidance of the Federal Drug Administration (FDA) of the USA government and supervision of the institutional review board (IRB) of the University of Illinois, have been evaluated for normal adult humans and selected patient populations on a 9.4 Tesla scanner designed for human neuroimaging. All other FDA guidelines for imaging gradient strength and switching rate have been followed. Although above the current 8 Tesla limit of static magnetic field exposure set for humans, no detectable irreversible adverse effects have been detected. These initial studies have been published in two peer-reviewed articles [3,4]. As no significant adverse effects have been observed in vital signs or cognitive function, neuroimging studies have been broadened to all patient populations for which there are no MRI contraindications. Similarly, the numerous ultra-high field research scanners being used daily for human imaging demonstrate that the technical challenges of building and integrating an ultra-high field human scanner can not only be surmounted but such MR scanners offer new information for medical management.

The greatly enhanced MR sensitivity at 9.4 Tesla has enabled imaging protocols to acquire the MR signals from sodium (23Na) and oxygen (17O) that have been previously considered too impractical for clinical applications to be developed as imaging protocols to generate new clinically relevant information. These non-proton nuclei have much lower resonance frequencies than proton which reduce some of the technical challenges of ultra-high field imaging. RF coil design and operation (e.g. RF shimming) can build on the vast experience of 3.0 Tesla proton imaging at 128MHz. This strategy has successfully prevented the challenges of 400MHz proton imaging at 9.4 Tesla from retarding the progress at ultrahigh field imaging. Along with non-proton MR imaging applications, the quantification of the

MR signal has been emphasized to move medical imaging from its focus on the late signs of distorted anatomy to metabolic parameters that are sensitive to early stages of disease. Such quantification, while challenging, is more easily and accurately achieved at the improved SNR that comes with ultrahigh field. Spatially resolved biochemistry has the advantages of less biological variation across normal subjects and across time in longitudinal studies of normal subjects until pathology strikes. This reduced biological variation permits more sensitive detection of pathology at earlier stages of disease.

As an example of the use of such parameters, I will present a simple two-compartment model of brain tissue in which the measured sodium concentration is the volume fraction weighted sum of the intra- and extracellular compartments [5]. This model allows the TSC (see Figure 1) and tissue cell fraction (TCF, cell density) to be measured in regions of the brain where diseases kill cells. An example is the loss of cells in the hippocampal regions but not in motor cortex in the setting of Alzheimer's disease. This TCF parameter can also be used to assess tissue salvage in the treatment of stroke and tumor cell kill in the treatment of brain tumors.

The important issue for choosing the optimal field strength at which to perform these types of measurements is dependent on the nuclear properties of the signal. For clinically relevant acquisition times, the 23Na signal, with quadrupolar properties that imply biexponential transverse relaxation behavior, can only be encoded at a biologically appropriate spatial resolution at ultra-high field. Even 3.0 Tesla is insufficient to achieve a real isotropic spatial resolution of less than 8x8x8 mm^3 with sufficient SNR for quantification for signals with transverse relaxation times of only a few milliseconds.

The direct quantitative MR imaging of the 17O signal of water produced in the brain of a subject breathing enriched 17O oxygen gas will also be described in quantitative terms of cerebral metabolic rate of oxygen consumption (CMRO2). This parameter is corrected for tissue cell density using 23Na imaging and compared to age-matched 15O positron emission tomography (15O PET) data from the literature. PET promised a role for this parameter in the setting of cerebrovascular disease but failed to deliver routinely because of the lack of availability of PET scanners with an associated cyclotron required for generating the short-lived 15O radioisotope. As 17O is stable, enriched 17O oxygen gas is readily stored and shipped to sites with ultrahigh field scanners. The metabolic model for CMRO2 measurement will be described briefly [6].

If time permits, I will describe the imaging of 31P bioenergetics in the human brain that is not possible at lower clinical fields of 3.0 Tesla based on spatial resolution and SNR criteria.

These bioscales based on 23Na, 17O and 31P MR signals and accessible in clinically acceptable acquisition times only by ultra-high field scanners could be transformative for medical care across a range of neurodegenerative and cerebrovascular diseases through the increased sensitivity to earlier stages of disease and for quantitative intervention monitoring.

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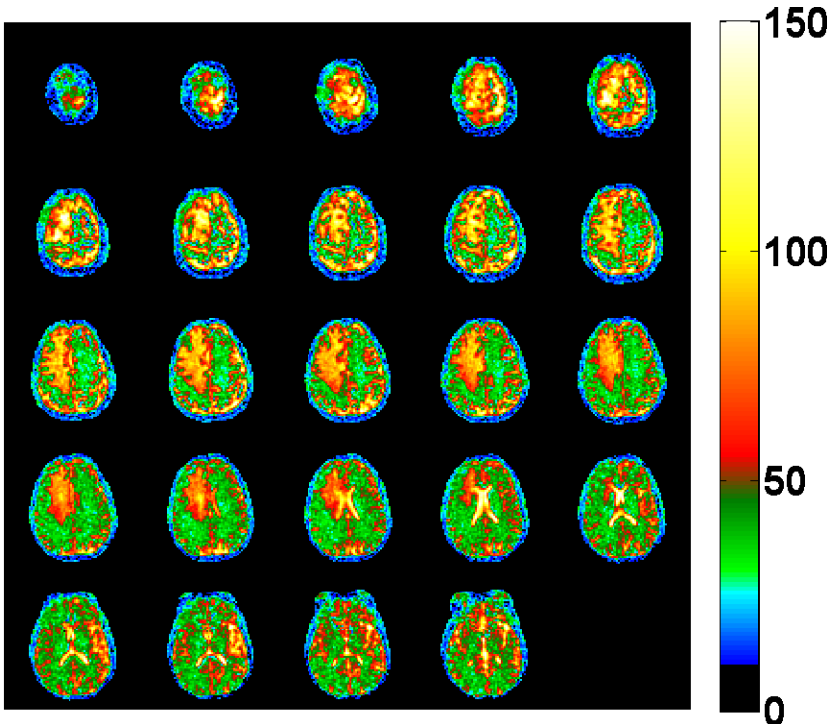

Figure 1: Selected cross sections from the quantitative TSC bioscale, showing sodium concentration from 0 to 150 mM, acquired at 9.4T in 10 minutes on a brain tumor patient.