This is the second edition of the MRRC newsletter. In this newsletter we are including recent updates on new developments at the MRRC in arterial spin labeling, RF coil development at 7T, and whole plane spectroscopic imaging of brain at 3 and 7T. Also, we have included a technical note regarding recent developments in GABA editing measurements. Before describing these developments, I would like to thank of all you who participated in the retreat. In addition to presentations from the various MR centers at Pittsburgh and CMU, there were 48 poster presentations. However, I believe the highlights of the retreat were the discussions during lunch and the interactions amongst the presenters at their posters. It is clear that although there are multiple imaging centers at Pittsburgh and CMU, there are many common interests that we all share. Hopefully, the retreat will serve as a catalyst for greater interactions amongst all of the participants and the MR centers.

As many of you are aware, the 7T human system quenched during the last week of November. The exact cause is unknown. Luckily, the quench appears to have occurred in an orderly fashion with appropriate shunting of the energy and discharge of the helium gas. I am told this is similar to what happened about three years ago. Thus, at this time, we are optimistic that there was no internal damage and that the 7T can be brought back to field. Due to the challenges associated with Agilent's withdrawal from high field imaging (Agilent is the manufacturer of the 7T human magnets) and world-wide shortages in liquid helium, the ramp date was delayed until mid-January. We hope to have the 7T operational by the beginning of February.

This marks the end of my first year as Director of the MRRC. I want to thank our users for their patience, cooperation and support of the MRRC. Although transitions are always challenging, I believe we have made large strides in positioning the MRRC and its users for a healthy and productive future. As we are all aware, funding levels at the NIH remain at relatively low levels, and are likely do so for the next several years. Thus, it is important that we as a community leverage our joint strengths to maximize our competitiveness. Therefore I look forward in the coming year to establishing closer relationships between the MRRC and all of you to enhance our joint success in this challenging funding environment.

A Matlab-Based Toolbox for pCASL Image Analysis : Andrea G. Gillman, H. Michael Gach
Target Area of Application: Measurements of tissue perfusion
Advantages: Improved quantification of ASL data
Contact: Michael Gach (gach@pitt.edu).

Arterial spin labeling (ASL) is a non-invasive MRI technique that measures tissue perfusion, e.g. cerebral blood flow (CBF), using blood water as an endogenous tracer. ASL is a difference imaging technique in which a labeled image is subtracted from an unlabeled control image. The tissue perfusion is directly proportional to the difference image as related through the Kety/Buxton kinetic model for a freely diffusible tracer [1]. Pseudo-continuous ASL (pCASL) employs a train of RF pulses to selectively invert (or label) blood water spins as they flow through the arteries. In contrast, pulsed ASL (PASL) uses adiabatic inversion pulses to invert either the imaging volume (control) or a larger volume encompassing the imaging volume (label). Advantages of ASL over intravenous (exogenous) tracer-based perfusion methods include the avoidance of injection of gadolinium, and the ability to perform multiple measurements during a single exam. Both PASL and pCASL are commonly used at 3 T in clinical and preclinical research centers. The MR Research Center (MRRC) has extensive physics expertise in both PASL and pCASL. Researchers interested in using ASL are encouraged to work with the MRRC physicists to ensure optimization of their protocols and data analysis techniques.

Many researchers who acquire ASL data create CBF maps using the University of Pennsylvania's ASL toolbox (https://www.cfn.upenn.edu/~zewang/ASLtbx.php) that is written in Matlab and works in conjunction with Statistical Parametric Mapping (SPM). However, the ASL toolbox must be used with caution, as it assumes that images are acquired from inferior to superior, and voxels are imaged with a transit delay that is longer than the tracer arrival time. In addition, there are differences between software releases that can affect the perfusion quantification results. For example, the latest versions of the toolbox apply lower and upper cutoffs to eliminate outliers.

We have modified and updated the ASL toolbox to improve CBF quantification for pCASL acquisitions based on the kinetic model (Fig. 1). Algorithms were added to infer arrival time kinetics, and histogram feedback has been added to allow optimization of parameter thresholds and cutoffs. There are different versions of this modified toolbox available to analyze images acquired in descending, ascending, or interleaved orders. Overall, the modified toolbox is a more reliable and accurate program with enhanced operator control and flexibility.

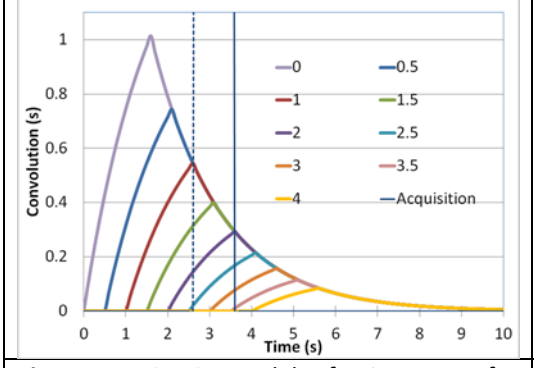

Figure 1: Kinetic model of ASL tracer for arrival times from 0 to 4 seconds. The model assumes: Label time: 1.6 s, Transit Delay: 1.1 s, Slices: 20, T_{1blood}: 1.61 s, TE: 14 ms, TR/slice: 43 ms. The ASL signals are converted to perfusion values after division by the applicable value of the convolution of the arterial input function with the tracer relaxation function.

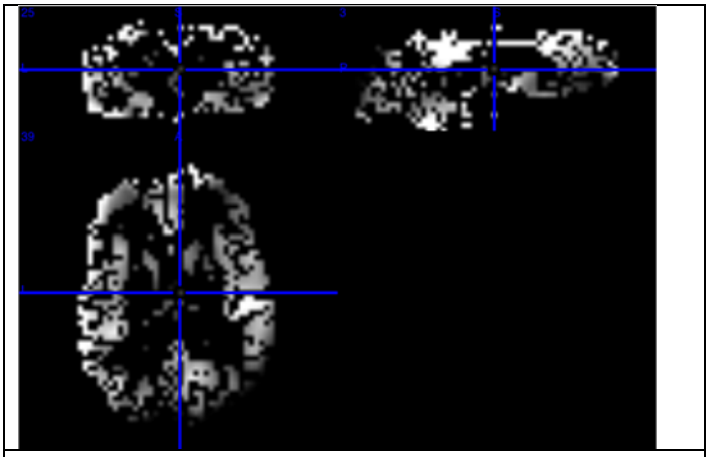

Figure 2: Mean Grey Matter CBF Maps.

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Whole Plane ^{1}H MR Spectroscopic Imaging and Analysis: HP Hetherington, JW Pan, Y Lee and T Zhao

Target Area of Application: Mapping of regional neuronal injury and impairment

Advantages: Whole slice sampling and automated detection of neuronal injury/impairment including peripheral cortex and deep white matter.

Contact: Hoby Hetherington (hetheringtonh@upmc.edu)

Typically, ^{1}H MR spectroscopic data is acquired as a single or multiple single voxel measurements to evaluate the presence of neuronal injury or changes in key neurotransmitters (e.g. glutamate and GABA). The decision to acquire data as a single measurement representing a single region (4-8cc of brain tissue) is often driven by concerns over spectral quality and limitations in shimming the main magnetic field (B_0). However, with advances in B_0 shimming technology, including software and hardware (see News Letter #1), this limitation can be overcome, allowing for the simultaneous evaluation of substantially larger brain regions. Since MRSI methods acquire data from all locations in the selected field of view (FOV) simultaneously, the signal-to-noise ratio per unit time is maximized in comparison with multiple single voxel measurements. A common method to provide this data is to add spatial encoding into a single voxel acquisition sequence (e.g. STEAM, PRESS), and to increase the size of the selected volume, typically from 1-3cm per side for a single voxel measurement to a box measuring 8-12cm per side with 1-2cm thickness and containing ~100 individual voxels (i.e. spectra). Several major limitations govern the size of the volume: 1) the need to exclude extracerebral lipid signals from the scalp and bone marrow; and 2) mis-registration artifacts arising from limited peak transmitter strength. Failure to take these limitations into consideration results in lipid contamination in the brain spectra and heavily distorted metabolite ratios from voxels at the edge of the selected volume. To enable measurements of the cortical periphery and eliminate mis-registration artifacts, we have implemented whole plane imaging sequences on the 3T and 7T systems, which suppress extracranial lipids without the use of in-plane selection pulses (1, 2). This allows us to sample the entire slice, including the peripheral cortex (Fig 1). Since the measured voxels will include varying amounts of gray and white matter, metabolite ratios and content will vary due to natural heterogeneity. To account for the tissue heterogeneity, linear regression models (3, 4) are used with tissue segmentation to provide automated statistical driven detection of regions of neuronal injury and impairment (Fig. 2). Abnormal brain regions can then be automatically detected, color coded according to their significance and overlaid on the anatomical images for reference.

Fig. 1. 7T data, green rectangle on density image displays region of display from SI data set. Representative spectrum shown below.

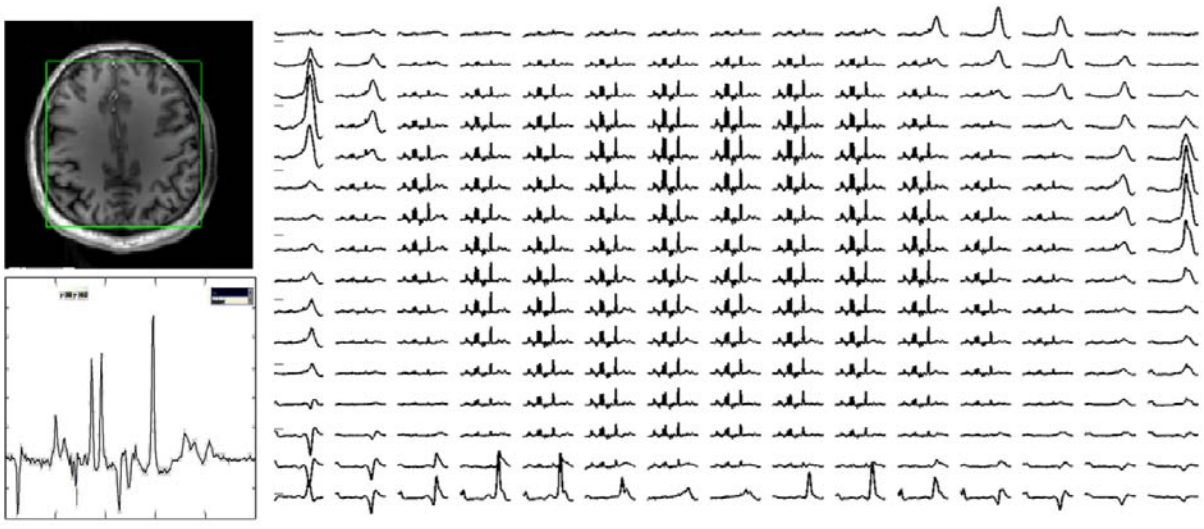
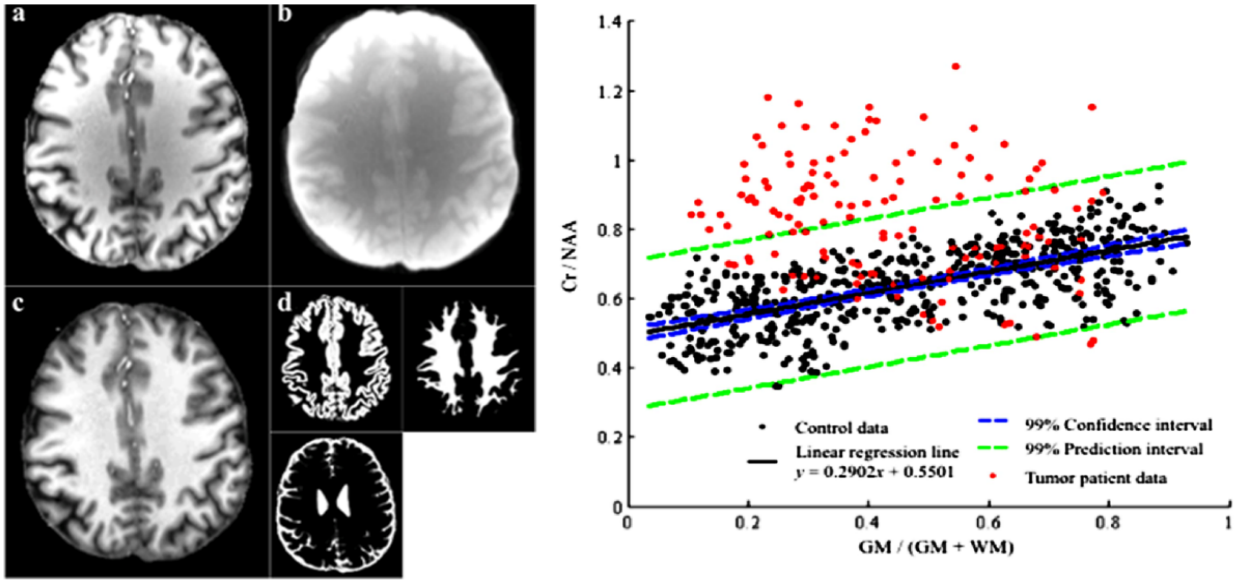


Fig. 2. Segmentation and regression analysis. Red dots - tumor patient with diffuse neuronal loss.



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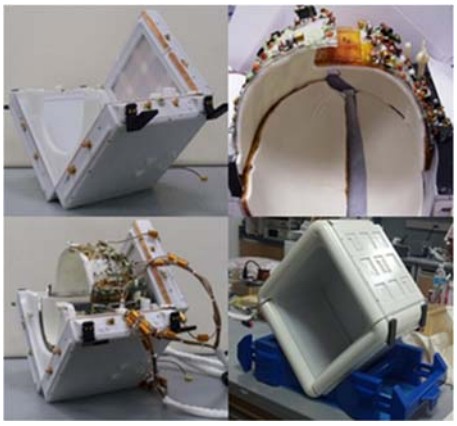
20-Ch Transmit Array with 32-Ch Receive Insert for 7T Neuro Studies
Target Area of Application: SWI, T2*, MPRAGE, Resting State fMRI
Advantages: High SNR and state of the art 7T transmit field homogeneity
Contact: Tamer S. Ibrahim (tibrahim@pitt.edu)

Addressing RF inhomogeneity and heating issues that arise at high operational frequencies is pivotal in the development of RF coils for high (≥ 3T) and ultrahigh fields (≥ 7T). At high field strengths, the human head/body size becomes comparable to the RF wavelength, and thus the interaction between the RF coil and tissue becomes increasingly sensitive to variations in the size/shape of the human head. We have developed a **20-Ch transmit array with 32-Ch Receive Insert for 7T Neuro Studies.** The coil system (Figure 1) is subject-insensitive and does not require tuning or matching for different patients. The coil system was tested with different contrast parameters: BOLD, T2*, or structural T1 weighted imaging. RF shimming, SWI and EPI images are shown in Figure 2: RF amplitude and phases were used to obtain **a whole brain + cerebellum transmit field homogeneity (max/min <2.6) with a mean SAR = 2.25 W for a continuous mean transmit field value of 2uT in the brain + cerebellum and peak/mean SAR ratio < 3.5.** Due to the array's robust insensitivity to different subjects, the images were obtained without RF field mapping utilizing an excitation mechanism obtained with numerical simulations. **This RF Tx/Rx device can be implemented without utilizing the Transmit Array System on the 7T human scanner.** ***The 3D transmit field homogeneity represents current state of the art for 7T human head imaging.***

Figure 2: 20-Ch Transmit Array with 32-Ch Receive Insert for 7T



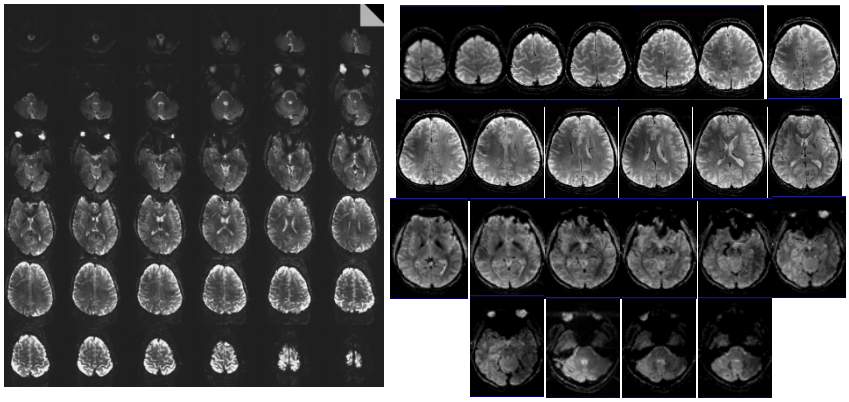


Figure 1: EPI and single-average T2* Images obtained at 7T using the 20-Ch Tx & 32-Ch Rx coils.

Measurements of Brain GABA: What you need to know …

Over the past several years, measurements of brain GABA have become more commonplace. The measurements have typically used MEGA-PRESS as a spectral editing sequence (1). In this sequence, J-evolution of the GABA resonance is modulated on alternate acquisitions such that subtraction of the scans eliminates spectral overlap of GABA with other resonances (see ref. 2 for a general description of the principles of spectral editing sequences). Despite its popularity and wide acceptance by the psychiatric and neurological communities, a number of technical issues have surfaced over the past several years. These issues include: 1) contamination from macromolecular resonances; and, 2) artifacts arising from the frequency selectivity of the sequences and magnetic field (B_0) instability.

Macromolecule Contamination: The presence of macromolecule (MM) resonances that mimic the GABA resonance were first reported in the early 1990s by Behar and Ogino (3). One of these resonances has a chemical structure that is very similar to GABA; it has J-coupled resonances at 1.7 and 3.0 ppm and GABA has J-coupled resonances at 1.9 and 3.0ppm. Further, the relative concentration of the MM resonances are similar or higher than that of GABA. In virtually all spectral editing sequences, the 3.0ppm GABA is the target resonance for observation, while its 1.9ppm J-coupled partner is the target for selective perturbation (inversion) to produce detectable signal in the difference spectrum. However, the close proximity of the 1.7 ppm MM and 1.9pm GABA resonances and their extended multiplet structures make it extremely difficult, if not impossible, to selectively excite/invert only one of these resonances (4). Thus, a variety of methods for correcting for this effect were developed in the late 1990s, including numerical corrections for the lack of selectivity (5), use of metabolite suppressed reference scans and self-correcting methods (6) The latter method, described by Henry and colleagues (6), in which the MM contamination is made constant across the two spectra so that it "subtracted out", became the clear method of choice. However, the initial reports of the MEGA-PRESS editing sequence suggested that some other means suppressed the MM resonances, thereby rendering the "correction" methods unnecessary. The simpler implementation and high apparent SNR drove the widespread adoption of MEGA-PRESS for GABA measurements. Recent work (4), though, has demonstrated that the initial claims of MM-free editing were incorrect and the excellent SNR for MEGA-PRESS measurements of GABA is likely attributable to 50% of the "GABA" resonance being MM (i.e. doubling the intensity). Since the MM resonance is not related to inhibitory neurotransmission, this represents a confounding factor in the interpretation of the data. Thus, when interpreting GABA data acquired with MEGA-PRESS, it is important to consider potential changes in MM content and its effect on the interpretation of the data. Over the coming months we will be implementing alternative sequences at 3T and 7T that provide MM free data, thereby eliminating this confounding factor (7). As these methods become available, we will make them available to all.

Frequency Selectivity and Artifacts from B0 Instability: As described, the MEGA PRESS editing sequence relies on selective perturbation of the GABA 1.9 ppm resonance to achieve "editing" of the 3.0ppm GABA resonance. Thus, errors in the applied frequency of the selective inversion pulse change the efficiency of editing and also (as described above) the distribution of GABA and MM contributions to the measured resonance. Although frequency determination is not challenging when the B_0 field is stable, time dependent variations in the B_0 field can cause significant artifacts in this measurement if not detected and corrected for. Notably, Barker and colleagues at Johns Hopkins University have recently documented the effect for GABA editing sequences following extended fMRI acquisitions, where GABA measurements artifactually decreased (10-15%) over time due to frequency shifts induced by fMRI measurements. Notably changes in the B_0 field (and therefore frequency of GABA and all other resonances) due to EPI-based acquisitions are well documented, and are caused by energy absorption and heating of passive shim elements in the magnet. This suggests that studies using both GABA and fMRI or DTI measurements should consider the temporal order of the studies. Specifically, performing the GABA measurement prior to any fMRI or DTI measurement should provide a more stable B_0 field for the GABA measurement.

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