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14. ABSTRACT
We have been developing robust low-magnetic-field implementations of MRI (LFI) focused on brain imaging. In particular we have expanded our development of the LFI test bed to include two complimentary approaches: electromagnet and permanent magnet based test bed scanner systems. We are also developing injury-sensitive MRI based on converting the electron spin of free radicals associated with injury into nuclear polarization using the Overhauser effect and subsequently imaging that modified nuclear polarization using low-field MRI (OMRI). Much of the hardware development of the human head LFI test bed systems and the OMRI system is now complete. Application of the suite of techniques and technologies from our work could advise future development of a deployable device with a high diagnostic impact and could be transformative, enabling improved diagnosis and monitoring of battlefield injuries prevalent in TBI.

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INTRODUCTION:

This applied research program builds on recent advances by our collaboration in the development of novel methods of low-magnetic-field MRI and advanced MRI hardware. Without major innovation, high-field MRI instruments offer limited utility for imaging TBI in widely deployable contexts. We focus our research effort on the high-risk and critical challenges that must be solved to enable deployment of a transportable human-head MRI system applicable to TBI imaging in battlefield medical facilities. Our goal is to establish proof-of-principle of a suite of techniques and technologies to advise future development of a field-deployable device with high diagnostic impact. This research effort has two specific aims:

Specific Aim 1: Develop a low-field human-head MRI system (LFI) suitable for high-resolution multi-nuclear imaging, and improve the ability to attain brain images based on the intrinsic *in vivo* ^{1}H NMR signal in this scanner.

This includes the development of robust low-field scanner hardware methodologies (both electromagnet and permanent magnet based), the development of novel high-speed parallel imaging detection systems, and work on advanced adaptive reconstruction methods including navigators and sparse sampling.

Specific Aim 2: Develop injury-sensitive MRI based on converting the electron spin of free radicals associated with injury (specifically TBI) into nuclear polarization using the Overhauser effect and subsequently imaging that modified nuclear polarization using low-field MRI (**OMRI**). Successful demonstration of OMRI of free-radicals associated with injury will be directly applicable to the MRI systems of **Aim 1**, enhancing image-based injury specificity and/or shortening scan acquisition time.

The development of this new MRI contrast mechanism may provide an unambiguous non-invasive *in vivo* maker for cerebral injury, and has potential for assisting the imaging of TBI at both low and high magnetic fields.

BODY:

Progress in Year 1 focused on hardware development for both the human head **LFI** (**Aim 1**) and for the **OMRI** system (**Aim 2**).

Low Field Imager (LFI)

TASK 1A: Low-field MRI Hardware Development

We have expanded our development of the LFI test bed to include two complimentary approaches to the low-field head scanner of **Aim 1** and in **Task 1A**, and have been pursuing both electromagnet and permanent magnet based test bed scanner systems. There are two parts to this approach: the conversion of the biplanar electromagnet "hyperpolarized-gas lung imager" to a highly optimized low-field head scanner with high-performance linear gradients, and the development of second LFI test bed is based on a lightweight (45 kg) and portable permanent magnet array in a configuration known as a Halbach array.

The reconfigured biplanar electromagnet LFI provides an ideal test bed for all of the novel acquisition, detection methodologies, and reconstruction algorithms, and additionally will provide necessary experience and data to advise optimal construction and magnetic field for any future electromagnet-based deployable systems.

The second LFI test bed is based on a lightweight (45 kg) and portable permanent magnet array in a configuration known as a Halbach array. This Halbach array LFI is a highly specialized and potentially disruptive technology scanner that could greatly ease both the cost and burden of a field-forward instrument. This Halbach LFI contrasts markedly with the biplanar electromagnet LFI in that it has a highly inhomogeneous magnetic field, but we intend to use this inhomogeneity to our advantage and use it to acquire head images without the use of an additional gradient set.

Together, these LFI imager test beds are part of a suite of low-field MR imaging techniques and technologies potentially practical for operation in field hospitals or forward triage.

Biplanar electromagnet LFI optimization:

In Year 1, we have been focused on several aspects of the conversion of the low-field lung imager to a head imager. Previously, the biplanar LFI magnet superstructure was a ½" thick aluminum flange. Eddy currents induced by rapidly slewing gradients would strongly limit the rate at which imaging could be performed. We carefully re-engineering and replaced the central aluminum magnet flange with non-conducting polycarbonate and this eliminated eddy-current effects to a level where they no longer dominate the speed at which images can be acquired (**Figure 1**). Indeed, this modification now enables rapid imaging sequences that previously would have been impossible, and we are currently testing the upper limit of magnetic gradient slew-rates. We are planning on implementing and testing very rapid and efficient imaging sequences such as balanced steady-state free precession (bSSFP) in Y2 which could play a major role in successful high-speed imaging at low magnetic field.

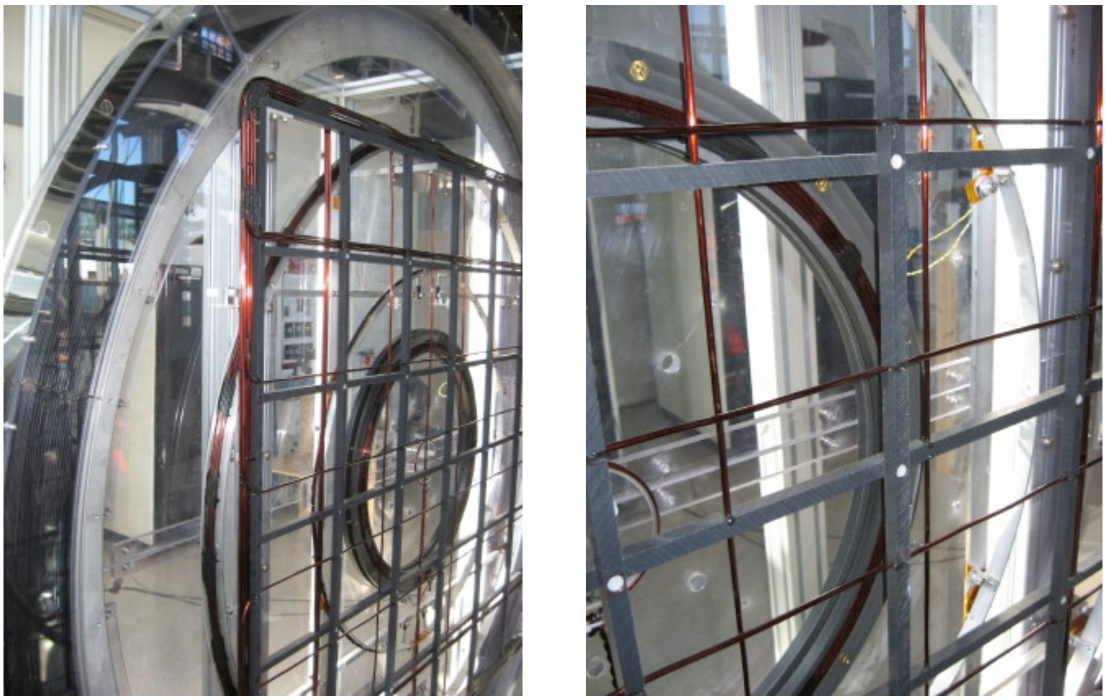


Figure 1: Photographs of one plane of the optimized biplanar LFI. The transparent flange of the modified imager main superstructure is visible, as is the transparent cooling air duct surrounding the outer electromagnet coil. The biplanar gradient coils are mounted in place on the main flange as well. **LEFT**: the inner and outer B_0 coils are visible. **RIGHT**: close-up view of the Nylatron framework holding the transverse gradient wire, and the circular aluminum frames that support the z axis gradient windings. The copper wire is coated in a heavy-build polyamide insulating layer.

We performed finite-element analysis of forced-air cooling strategies of the biplanar electromagnet to address the relative merit of conductive cooling through a chilled heat exchanger vs. forced-air cooling through a channel surrounding the electromagnet. We concluded that forced-air cooling would be feasible at least up to fields of 10 mT in the biplanar LFI. We then converted the electromagnet to forced-air cooling with a polycarbonate air duct surrounding the outer electromagnet coil (also see **Figure 1**). An airflow-based interlock outside of the RF shielded enclosure has been implemented as well which will shut down the main magnet power supply in the event of a fault in the cooling system. The LFI electromagnet is now fully converted to forced-air cooling.

We have numerically modeled and iteratively optimized the main electromagnet geometry of the open-access biplanar "lung imager" to determine the ideal arrangement of conductors for reconfiguration as a head imager. The sensitivity of the bi-planar magnet geometries to positional misalignment of any of the coils was simulated and we found that with careful alignment we should be able to obtain better than 25 ppm homogeneity over a 25 cm diameter spherical volume which is sufficient for high-resolution ^1H imaging at low magnetic field.

In its previous configuration as a lung imager, the ^1H NMR line width measured in a 20 cm diameter spherical volume was nominally 25 Hz. Once this alignment described above was performed, we found that NMR measurements from a 20 cm spherical (head sized) phantom inside of a 25 cm coil tuned at 276 kHz (6.5 mT) could regularly attain NMR specta with FWHM line widths of around 5 Hz (**Figure 2**), verifying the results of the simulations. This field homogeneity is more than sufficient for high-resolution ^1H imaging at low magnetic field, and no further optimization of the electromagnet geometry needs to be performed.

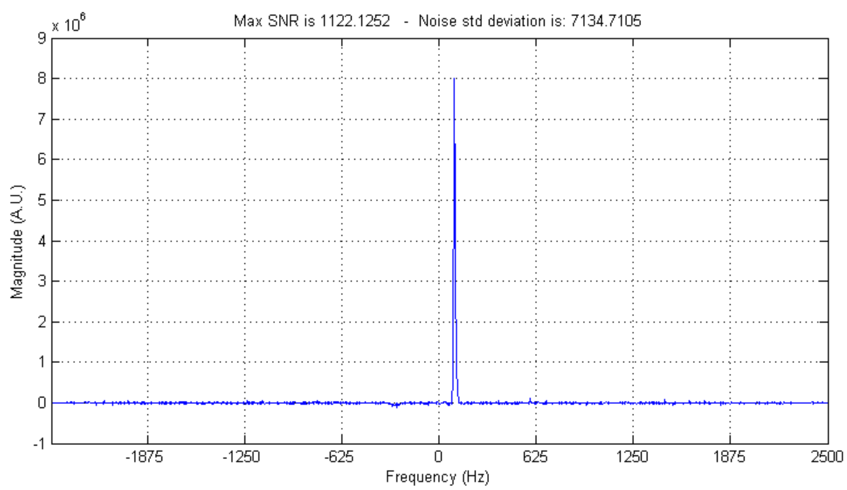


Figure 2: Single-shot ^1H spectra acquired in the reconfigured LFI at 276 kHz (6.5 mT) from a 20 cm spherical water phantom. Linewidth is ~5 Hz, and SNR is ~1100. This spectrum was obtained in a 25 cm cylindrical solenoid coil tuned to 276 kHz and matched to 50 Ohms. NMR pulse width = 350 μs, α~90°, BW=5 kHz.

A high performance gradient set is essential for the biplanar LFI. We have evaluated the need for actively shielded imaging gradients in the biplanar LFI for imaging and conclude that coupling between the slewing planar gradients and the B0 coil should have a negligible impact on high-speed head imaging. We have installed an in-house designed non-shielded biplanar gradient set in the reconfigured biplanar LFI that is contained within the individual planes of electromagnet for open access and ease of setup/transportability in a future engineered portable system. The gradient coils are mounted on the same support structure as the main magnet, allowing for an additional level of robustness for the entire system. Alignment of the magnetic gradient set is crucial to imaging performance.

We mapped the linearity of the planar gradient set, and preliminary tests have measured gradient strength and linearity for each of the three gradient coil axes. We obtained excellent gradient linearity on all three axes with typical deviations < 1% and gradient strengths up to 0.1 G/cm (1 mT/m) from this biplanar gradient set. From a thermal perspective, we have achieved our goal of employing passive convective cooling of the gradient set.

The performance of the biplanar LFI is sufficient that we can now acquire MR-based magnetic field maps. In Q3Y1 we used phase-sensitive MRI techniques to obtain image-based magnetic field maps (**Figure 3**) in the modified low-field scanner. These measurements allow us to determine the maximum attainable FOV over which MRI will be practical. These phase-sensitive images were used to fine-tune the electromagnet alignment geometry of the LFI for its use as a head imager. These maps will also be used to observe any time-dependent artifacts that thermal cycling of the system might induce. The ability to acquire image-based magnetic field maps in the biplanar LFI could be used as part of a self-aligning electromagnet-based system in future field systems where the number of degrees of freedom is limited due to the planar construction.

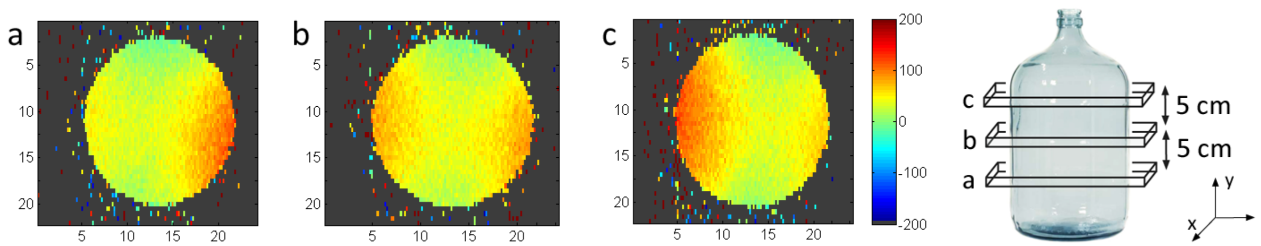


Figure 3: Magnetic field homogeneity maps (in ppm) acquired in the electromagnet LFI from a 4L water-filled bottle at 276 kHz (6.5 mT). Three representative slices (of 21 planes) are shown. **LEFT TO RIGHT:** Y = –5 cm, Y = 0 cm, and Y = –5 cm. These B0 maps are computed from the difference of two 3D gradient echo phase images acquired with different echo times (TE1, TE2). Imaging parameters were as follows: Matrix=128 × 45 × 21, FOV=256 × 225 × 210 mm^3, voxel size=2× 5×10 mm^3, TE1/TR1=27/170 ms, TE2/TR2 =47/190 ms, α=90°. Total scan time was 43 min for image TE1 and 48 min for image TE2.

Low-frequency environmental noise mitigation

Although much effort is made to increase our NMR signal sensitivity through noise-matched preamps, novel detection electronics and signal processing, equal emphasis must be placed on the minimization of both capacitively- and magnetically-coupled noise currents. Improvements in the environmental noise floor can go a long way to improve scanner sensitivity especially for a field-operated instrument that may be located in an unusual environment. Throughout Y1 we worked to optimize the noise floor of the biplanar LFI system. This is of critical importance as operation at such low magnetic field means that the intrinsic ^{1}H signal is already quite small and "bright-line" noise in particular must be suppressed.

Most electronic devices are designed not to interfere with radio signals and other wireless systems which typically operate from 50 MHz up to 10 GHz, however little attention is given to curtail device emissions in the sub-1 MHz regime. We used a spectral analyzer and a broadband pickup coil to detect sources of environmental noise in the scanner laboratory, and indeed there found many environmental noise signals within the 200–300 kHz frequency range in which we operate the biplanar LFI.

In our system, the noise floor is dominated by two key issues: bright-line common-mode noise capacitively coupling to the gradient cabling outside of the RF enclosure, and gradient feed-through filtering at the RF enclosure. We have evaluated the characteristics needed for feed-through filtering of the high-current magnetic gradient control lines into the RF shielded enclosure of the LFI. Filtering of these lines is tricky in that we need to avoid resonance effects between the gradient self-inductance and the filter capacitance as well as provide sufficient noise attenuation above the low-frequency limit of our imager (>200 kHz).

The characteristics needed for high-performance feed-through filtering of the high-current magnetic gradient control lines were evaluated in Q3, and in Q4 we continued in our design of a suitable filter to both avoid resonance effects between the gradient self-inductance and the filter capacitance, and to provide sufficient noise attenuation above the low-frequency limit of our imager (>200 kHz). In particular, we investigated various multi-order T and Pi-filter geometries. This is a non-trivial issue as the ideal "T" filters are large and heavy but more effective than "Pi" filters. We consider this filter work as ongoing. We have been able to obtain filtering performance that is "good-enough" for the biplanar LFI testbed using a pure capacitive gradient filter (and the ferrite chokes described below) but to attain the ultimate system performance will require a redesigned inductor-based filter. Several manufacturers have been contacted about this kind of filter design, but no suitable off-the-shelf solution appears to exist. As a result we will likely put on the "back burner" any additional work on the filter design as it is purely an engineering goal for future systems.

We were able to greatly suppress common-mode noise with the use of ferrite chokes of a material carefully chosen for maximum suppression at our Larmor frequency. In the case of the 6.5 mT (276 kHz) LFI, we were able to find maximum noise suppression using the "W" material from Magnetics (part number ZW44932TC, Lot C82629) which has a very large magnetic permeability (μ=10,000) and consequently a high loss tangent value of 32.5 ($\times 10^6$) at 100 kHz. We now use chokes of this material in common-mode configuration on all the lines entering the LFI RF shielded enclosure.

Finally, in late Q4Y1, we sent a set of three Techron 8607 gradient amplifiers to AE Techron, Inc. for rebuilding and effort to reduce their out-of-bandwidth noise and improve the “bright line” noise performance. These amplifiers have just been returned to us (January 2012) and have been factory reconfigured as Techron 7782 amplifiers. We anticipate testing them in the biplanar LFI in Q1Y2.

Halbach array (permanent magnet) LFI

The second LFI test bed scanner we have been developing is based around a Halbach array of permanent magnets ideal for portable MRI in that it creates a relatively uniform field transverse to the head without the use of a cryostat or power supplies. A truly portable MR system has the potential to quickly detect brain injury at the site of injury. For example hemorrhage detection is critical for both stroke patients and traumatic brain injury victims. In stroke, rapid distinction between a hemorrhagic and non-hemorrhagic event could allow administration of a clot-busting drug such as tPA (tissue plasminogen activator) in an ambulance prior to transportation to the hospital, perhaps advancing this time-sensitive treatment by up to an hour. Subdural hemorrhage (or hematoma) is a form of traumatic brain injury, in which blood gathers between the dura and arachnoid mater (in meningeal layer) and is likely to be visualized on course resolution (e.g. 5mm) T1 images.

To test the feasibility of these magnets for imaging, we have designed, modeled and constructed a small, 20 rung Halbach array with radially magnetized NdFeB N42 magnets, large enough to fit the human head. The modeled field shows a roughly quadratic field profile with a central Larmor frequency sufficient for imaging (~3.3MHz). While the homogeneity is well below that of superconducting magnets, it fits well with our light-weight and portable concept if the inhomogeneities are used in image encoding, either through spatially selective excitation coupled with localization from 32 channel parallel reception of the brain signal, or through “O-space” style encoding [**Ref 1**] induced by rotating the quadratic profile of the magnet around the head. Either case fulfills the portability criteria by eliminating the gradient coil and power supply. Note that the lead author of [**Ref 1**], Dr. Jason Stockman, has started (January 2012) a postdoctoral position in our laboratory focusing on spatial encoding in the Halbach imager.

We performed a modeling and feasibility study of a light-weight, low-field permanent magnet array for head imaging. The k=2 mode Halbach array is an 18 cm radius, 34 cm long array of N52 neodymium magnets. The configuration is shown in **Figure 4**. A calculated magnetic field plot for this magnetic geometry with 5 kHz ^{1}H Larmor frequency contours is shown in **Figure 5**. The mean frequency is 3.3 MHz, and the red inscribed circle shows 20 cm sphere at the magnet isocenter.

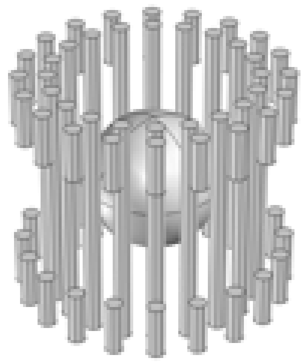


Figure 4: Halbach geometry

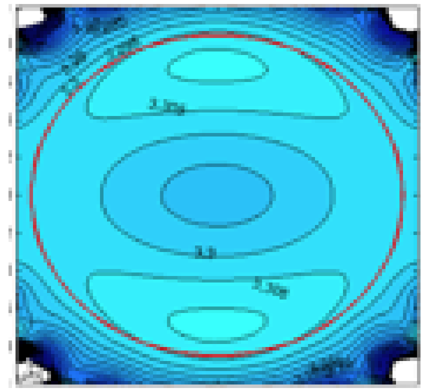


Figure 5: Calculated B field

We finalized the magnetic and mechanical design and have constructed the lightweight, low-field permanent magnet array for head imaging. Details of Halbach array LFI mechanical assembly design:

- Finite element modeling was used to simulate forces of magnets in order to design mechanical assembly.
- Smaller magnets were bonded together in a fiberglass tube to achieve the 14” length needed for the instrument. The magnetic repulsion of the individual smaller magnets makes assembly difficult, so a jig was constructed to secure the magnets in the tube.
- High tensile strength plastic rings were designed to hold the 14” magnets assemblies in place. These pieces have been cut with a water jet cutter with square magnet locating holes at precisely the correct place and angle. This preciseness is imperative to the field homogeneity. The tensile strength of these rings must be quite high as there are large forces (~ 35 lbf) pulling some magnets into the center and pushing some magnets outward.

The complete mechanical design of the system assembly is shown in **Figure 6**. We also have investigated the sensitivity of the system by generating coil sensitivity map of 32-channel parallel imaging array (**Figure 6**) and g-factor maps.

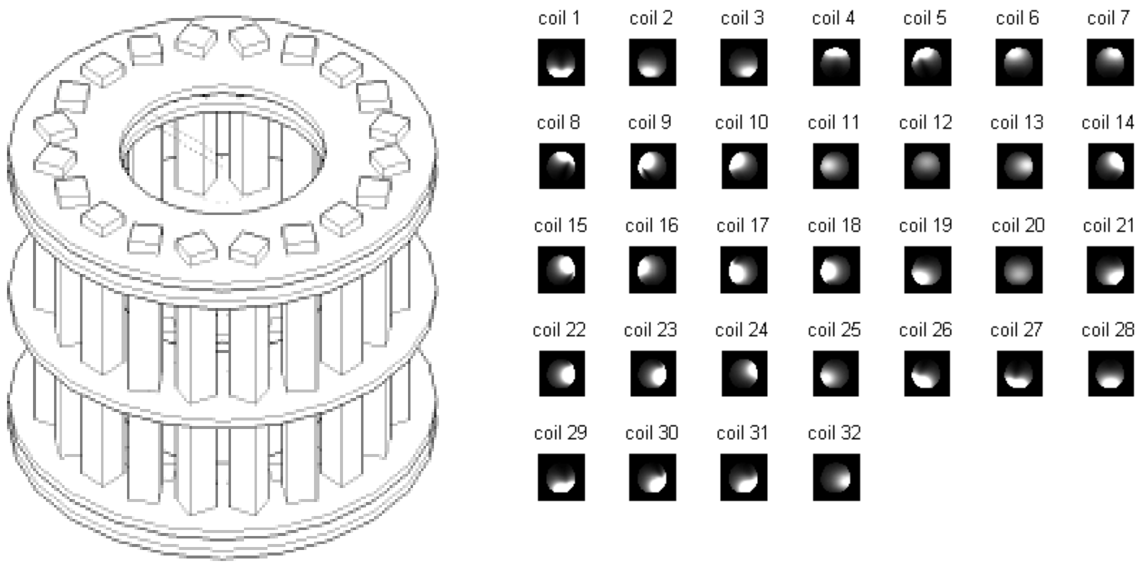


Figure 6: (**LEFT**) Mechanical design of Halbach LFI. (**RIGHT**) 32-channel parallel imaging array coil sensitivity map.

Once assembled, we were able to acquire preliminary NMR-based measurements using the Redstone console at 3.3 MHz. These measurements were used to roughly map the magnetic field and measure the spatial dependence of the NMR linewidth [see **Appendix 1**]. We are currently making detailed spatial field maps of the Halbach LFI using a 3-axis computer controlled magnetometer. We will use these detailed maps to compute the location of any additional shim magnets if needed. The broadband pre-amp described below will be tested on the Halbach LFI system, and we will then begin the design and construction of the 32-channel array coil.

Parallel-array detectors:

We have been developing low frequency surface coils for use in the parallel-array detector for both head LFI configurations. This includes the evaluation and selection of appropriate preamplifiers optimized for this application. We were in conversation with engineers at Analog Devices and initially were very excited the use of current-feedback op-amps for this novel application. However, we have since established a fruitful collaboration with Drs. Utsuzawa, Mandal and Song at Schlumberger-Doll Research Center in Cambridge MA with the focused goal of broadband inductive NMR detectors.

We have applied their methodology of a non-resonant approach to building a robust, wideband probe using a low inductance untuned coil and a transformer to our specific head-imaging application, and have built and bench tested a surface coil and broadband preamp interface for the LFI parallel imaging detector system (**Figure 7**). Using this preamp we achieved a measured gain and frequency response with a pick up coil (L = 2.6uH) of about 47 dB +/- 3 dB over the broadband range 100 kHz to 5 MHz. The use of this preamp for NMR/MRI represents a breakthrough in receiver technology with applications beyond the present work, including in high-field MRI where it could potentially eliminate the need to retune coils to accommodate the shift in coil resonance frequency owing to coil loading, or for the detection of other nuclei.

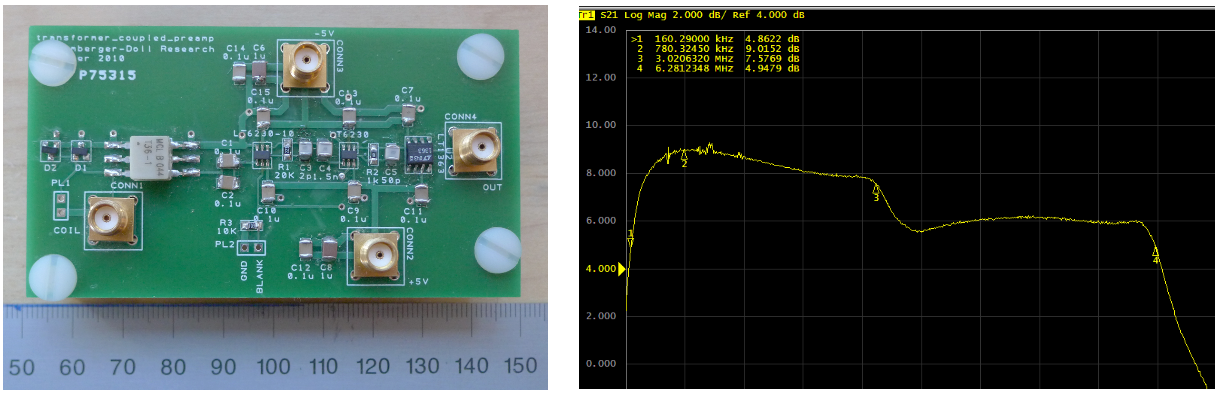
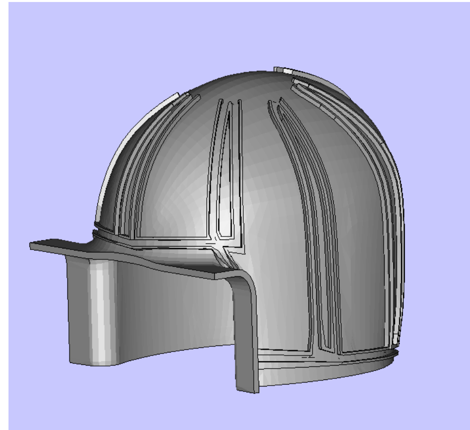


Figure 7: LEFT: Photograph of the in-house-built transformer-coupled broadband preamp circuit board developed in collaboration with the Schlumberger-Doll Research Center. Ruler units are millimeters. **RIGHT**: VNA measurement of S21, the gain characteristics of the broadband preamp, while coupled to a 3 loop pickup coil of approximate size and inductance as the individual receiver coils that will be used in the parallel-detector head-array. Frequency span plotted is 100 kHz–7 MHz. This preamp has a very flat (+/- 3 dB) response over the frequency range 200 kHz–6 MHz well suited for the NMR signal chain in the inhomogeneous field of Halbach magnet detector array.

We have begun to build the 8-channel head coil “helmet” parallel detector array for the biplanar LFI (**Figure 8**). These “helmet” detectors will be used in both the biplanar and the Halbach imagers as a way to accelerate imaging time by reducing the number of phase-encode steps through parallel detection.

Figure 8: 3D model of 8-channel head coil "helmet" parallel detector array for the biplanar LFI. Each coil in the array will be connected to an individual pre-amp, allowing parallel encoding of the image data. A similar, 32-channel coil helmet will be built for the Halbach imager. This coil form will been printed on a a 3D printer and will be tested in Y2



TASK 1B: System control and image acquisition

Acquire commercial console:

During Q1Y1, we had extensive interaction with Tecmag Inc. to put together the final design specification of the multi-channel enhanced MRI console upgrade for the LFI known as RED-STONE. This highly customized Tecmag Redstone commercial MR research console is used for RF and gradient pulse control and signal reception for the scanners in this work. It contains the same capabilities of RF and gradient pulse control and signal reception as a clinical MRI scanner, while maintaining much greater flexibility and operator control for MR sequence development. This Redstone console is the heart of the upgrade that will enable high-speed parallel imaging (including eight low-frequency receive channels) at the unusual frequency regime of low-field MRI. In Q2 we placed the order for this console, but further modified the original specification at that time to add additional features to the Redstone console. These additional features included two additional channels: a high-frequency transmit channel and a high-frequency receive channel. The addition of these channels to the Redstone offers the rather unique capability of performing simultaneous NMR/ESR in the LFI. This will provide a better workflow between the effort of Specific Aim 1 and the effort of Specific Aim 2, particularly in late Y2 and in Y3. As a result, we have successfully co-located all research efforts (both Specific Aims) to the PI's laboratory, beginning late Y1.

We received the multi-channel enhanced Redstone console Q3 and spent much of Q3 interfacing, testing, and debugging the instrument. It was discovered during this testing in our laboratory due to a manufacturing error the receiver boards had been set up to operate at the wrong intermediate frequency. One of the REDSTONE enclosures (containing 8 receiver boards) had to be sent back to Tecmag and repaired. The 9th receiver was replaced in the field. The system is now fully operational in our laboratory.

The as-built specifications of the Redstone console include nine receive channels (50 kHz-125 MHz, and two transmitter channels: one 100 kHz to 125 MHz transmitter (NMR) and one 500 kHz-500 MHz transmitter (ESR), both with 10 ns 0.0055° phase shifts, 0.0055° RF spoiled pulses, 40 ns 96-dB amplitude control, 64 million point waveform memory, 20 ns phase-continuous frequency switching, 0.19 Hz frequency resolution and nominal 1 V output.

The nine digital receivers of the system each have 14-bit 50 MHz ADC (oversampling provides an effective dynamic range of up to 24-bits) digitizing directly at the intermediate frequency, >85 dB of gain, digital filtering, receiver bandwidth of 12.5 MHz, fast acquisition recycle time of 40 μs plus one dwell period, and fast < 1 μs receiver recovery time. The minimum dwell time is 1 μs per complex point times the number of active receivers divided by the number of active signal averagers for multi-receiver, simultaneous, interleaved, acquisitions.

The DSP Pulse Programmer provides 10 ns timing and minimum pulse width, 3,072 sequence events, external trigger, 4-bit conditional branching and 8 user assignable control lines.

The Gradient control system provides each DSP waveform generator with 64 million points of waveform memory, digital on-the-fly pre-emphasis and an opto-coupled high speed 20-bit DAC. This includes a gradient rotation board for oblique imaging and shimming of Z, X and Y through the gradient coils.

The DACs of the Gradient Control System feeds directly into three Techron 8607 gradient amplifiers, which supply the MRI gradient pulses via the gradient coils described above. The Redstone console is controlled by a Dell Optiplex 780 PC running Windows 7 and TNMR software supplied by Tecmag.

Begin development of image navigation and reconstruction methods:

We have been developing a software workflow to move raw spectroscopy and image data from the Tecmag TNMR software to the MATLAB environment for processing and display. Sparse sampling and other advanced parallel and navigator reconstruction algorithms would be difficult to implement without this TNMR/MATLAB pipeline in place. As of the end of Y1, this pipeline has been coded and is fully operational (**Figure 9**).

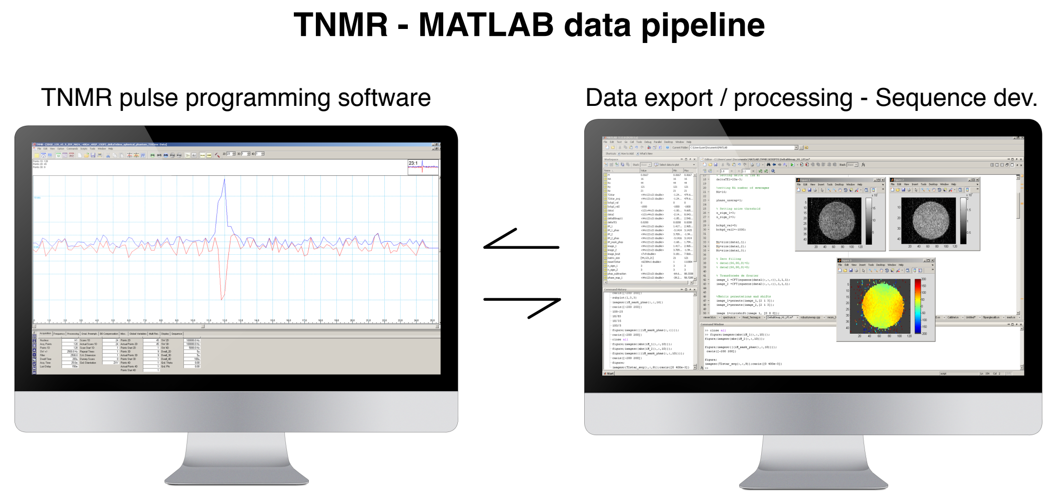


Figure 9: Screen shots of the in-house developed data processing pipeline between TNMR and MATLAB. TNMR is the pulse programming language/software used to upload sequences to and move data off of the REDSTONE console. This pipeline (written in Matlab) allows us to seamlesly move data between the acquisition computer and the processing scripts. Shown (**LEFT**) is a single gradient-echo from the full $128 \times 45 \times 21$ B0 field map data set of **Figure 3** (plotted here in the time-domain). This data is then processed and in this case, B0 field maps (**RIGHT**) are computed. This pipeline is bidirectional and allows MATLAB to directly control the TNMR pulse language and thus control the REDSTONE directly. This is an essential step for the sparse sampling approach we will use in Y2 to obtain rapid multi-channel parallel imaging.

OMRI Injury Imaging

TASK 2A: OMRI Hardware Development

The design and development of hardware systems required for Overhauser Magnetic Resonance Imaging (OMRI) is of key importance for Specific Aim 2.

Improved Overhauser MRI (OMRI) system

In the last few months we have made the decision to co-locate the low-field OMRI system with the biplanar LFI in the PI's laboratory as a way to speed development and integration between the two specific aims of this project. The modified biplanar LFI now contains the ability to produce ESR pulses in addition to NMR pulses. We added a 2nd transmit and receive channel to the Redstone system and have full control of the system through the TNMR/MATLAB pipeline described above. The OMRI system is fully operation, and results demonstrating the interaction between the biplanar LFI and the OMRI in a model system free radical system are presented in the following section.

Development of OMRI RF transmitter coils

Electromagnetic simulations were performed to evaluate designs for the coils so as to maximize the magnetic fields generated and minimize the electric fields generated so that they are suitable for applying high power excitations to phantom and biological test systems with minimal heating. We have built three cylindrical OMRI coils to test in phantom systems:

1. 12-rung bandpass birdcage coil, 21 cm diameter and 27 cm long.

2. Single loop saddle (Alderman-Grant), 7 cm diameter and 10 cm long.

3. Three-turn solenoid designed to fit a 7.5 mm NMR sample tube.

All of these coils can be tuned to the ESR resonance at the 6.5 mT field of the biplanar LFI (~200 MHz), and are well matched to 50 Ohms to provide efficient transfer to the sample. For each of these coils we have also designed and constructed a corresponding NMR coil that nests outside of the OMRI coil.

Using this system, we have measured `^{1}H NMR spectra in a model stable free radical system of 3 mM TEMPO ((2,2,6,6-Tetramethylpiperidin-1-yl)oxyl) in water with- and without the Overhauser-enhancement ESR drive field. The SNR enhancement in the free-radical solution in the presence of Overhauser hyperpolarization is ~78 (**Figure 10**). This experiment in a model system validates the operation of the OMRI system, the OMRI RF transmitter coils, and the matching NMR coils.

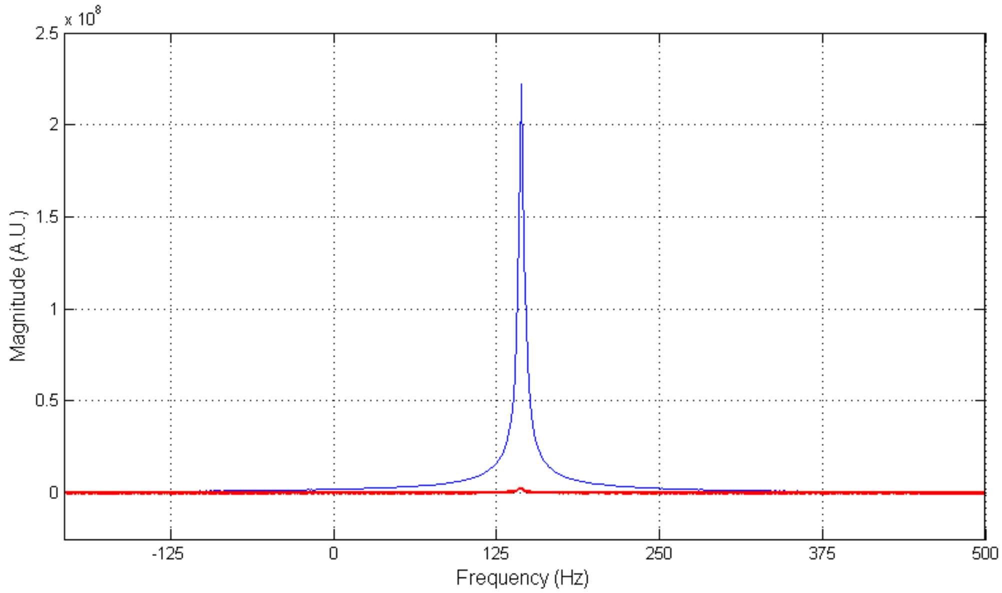


Figure 10: First demonstration of Overhauser-enhanced NMR in the biplanar LFI/OMRI system acquired at 276 kHz (6.5 mT). Shown above are single-shot NMR spectra of a 3 mM solution of TEMPO in water acquired with- (in blue) and without (in red) an ESR saturation hyperpolarization pulse. No scaling has been done. The timing of both sequences is identical. The TEMPO sample (in a 7.5 mm NMR tube) was placed inside the nested ESR/NMR OMRI coil system. The SNR enhancement in the free-radical solution in the presence of Overhauser hyperpolarization is ~78. The Overhauser drive field is a 2.5 s pulse at 235 MHz. The NMR pulse width is 140 μs (nominal 90°).

Development of CW-RF excitation profiles to maximize Overhauser enhancement.

Activities in Q3 and Q4 focused on the investigation of microwave techniques to increase the amount of nuclear polarization achievable with dynamic nuclear polarization (DNP). This is important for situations where the radical concentration is low or an inhomogeneous magnetic field broadens the electron spin resonance (ESR) line, both of which are challenges with low field Overhauser-enhanced magnetic resonance imaging. By applying pulsed frequency modulation to the microwave source at a rate much faster than the electron spin lattice relaxation time, up to an order of magnitude increase in the polarization is observed (**Figure 11**). These studies have been carried out using our high-field dynamic nuclear polarization setup in ^{29}Si, however we anticipate that the technique will be transferable to the low field OMRI system for use in free-radical Overhauser pulses. We will investigate these frequency modulated saturation pulses in the OMRI system in Y2.

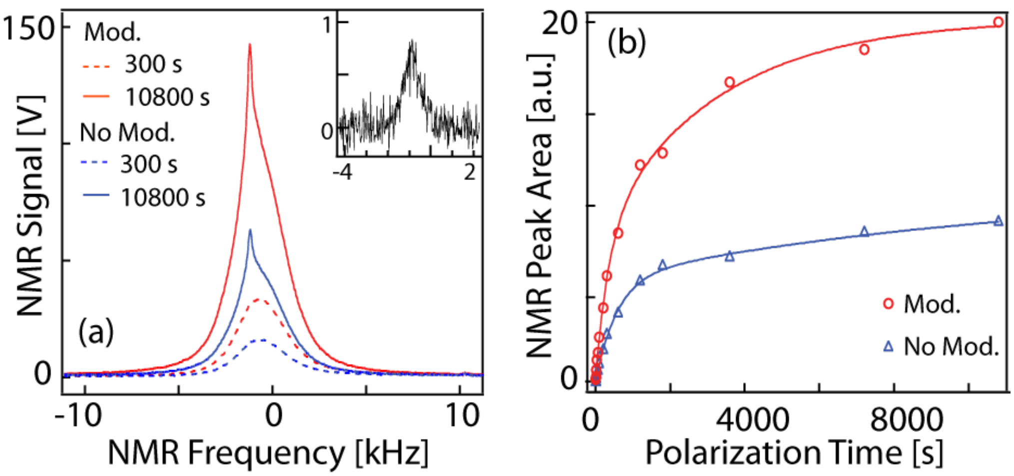


Figure 11: (**LEFT**) Single-shot ^{29}Si NMR spectra after 300 s (dashed lines) and 10800 s (solid lines) of DNP polarization for a sample of silicon particles with and without microwave frequency modulation. **Inset:** ^{29}Si spectrum acquired with no DNP and NA=200,000. (**RIGHT**) ^{29}Si NMR peak area plotted as a function of DNP polarization time with- and without frequency modulation of the microwave source. In both cases the microwave source was centered at 80.966 GHz. All spectra were acquired at 3 T.

TASK 2B: In vitro NO Overhauser enhanced proton spectroscopy

We have been developing spectroscopy protocols to enhance the detectible NMR signal from aqueous solutions of nitroxide radicals in a manner similar to that used in the TEMPO radical model system described above. Detection using Overhauser-enhancement of nitroxide may provide an unambiguous non-invasive *in vivo* marker for cerebral injury. As of December 2011, Dr. Brandon Armstrong has taken a postdoctoral position in our laboratory focused on nitroxide detection in the OMRI system. He is an expert in Overhauser spectroscopy of nitroxide and is the lead author of [**Ref 2**], “A new model for Overhauser enhanced nuclear magnetic resonance using nitroxide radicals”. We expect to move from experiments in the TEMPO model system to testing the spectroscopy protocols in nitroxide solutions beginning Y2 once the detection limits of the OMRI system have been characterized in the model system and the frequency-modulated excitation profiles described above have been implemented.

KEY RESEARCH ACCOMPLISHMENTS:

- Reconfigured and modified the biplanar electromagnet LFI as an optimized high-performance head imager test bed capable of high-speed acquisitions at low magnetic field and demonstrated its preliminary performance.
- Achieved ^{1}H line widths of 5 Hz in biplanar LFI of 20 cm spherical phantom at 276 kHz
- Acquired image-based phase-sensitive static magnetic field maps on biplanar LFI
- Designed and built a very portable 45 kg Halbach array magnet for portable brain MRI that requires no power to maintain the field. The accessibility of this magnet has the potential to offer basic head trauma and hemorrhaging detection to a broad range of applications.
- Performed NMR at 3 MHz in Halbach LFI for field mapping.
- Designed, built, and tested broadband coil parallel-array preamp system.
- Designed form for 8 coil head parallel array
- Tested and integrated Tecmag Redstone nine channel Rx/two channel Tx console.
- Set up bidirectional control and processing pipeline between TNMR and MATLAB.
- Co-located OMRI system with biplanar LFI
- Built and tested OMRI RF transmit coils
- Demonstrated Overhauser-enhanced spectroscopy in solutions of TEMPO radical.
- Investigated pulsed frequency modulation RF Overhauser excitation at high field.

REPORTABLE OUTCOMES*:*

1. Zimmerman CL, Wald LL, Rosen, M, Blau, J., "Design and construction of a Halbach array magnet for portable brain MRI", to be presented at the *2012 International Society for Magnetic Resonance in Medicine,* May 2012, Melbourne Australia.

2. Cassidy MC, Lee M, and Marcus C M, Modulation Enhanced Dynamic Nuclear Polarization in Silicon, *manuscript in preparation.*

CONCLUSION*:*

The reason MRI is not widely-deployable is that high-strength magnetic fields (of order 1 T) are necessary with conventional MRI to obtain useful brain images; however such high magnetic fields involve large, heavy, fragile, expensive equipment (such as superconducting magnets) that is incompatible with operation in field hospitals. Our hypothesis is that low-magnetic-field implementations of MRI can be developed to allow robust, transportable imaging modalities well suited to diagnose the types of battlefield injuries prevalent in TBI and practical for operation in field hospitals. Application of the suite of techniques and technologies from our work could advise future development of a deployable device with a high diagnostic impact and could be transformative, enabling improved diagnosis and monitoring of f battlefield injuries prevalent in TBI.

We expanded our development of the LFI test bed to include two complimentary approaches to the low-field head scanners, and have been pursuing both electromagnet and permanent magnet based systems. Much of the hardware development of the human head LFI test bed systems (**Aim 1)** and the **OMRI** system (**Aim 2**) is now complete.

REFERENCES:

1. Stockmann, J. P., Ciris, P. A., Galiana, G., Tam, L. & Constable, R. T. O-space imaging: Highly efficient parallel imaging using second-order nonlinear fields as encoding gradients with no phase encoding. *Magnetic Resonance in Medicine* **64**, 447–456 (2010).

2. Armstrong, B. D. & Han, S. A new model for Overhauser enhanced nuclear magnetic resonance using nitroxide radicals. *The Journal of Chemical Physics* **127**, 104508 (2007).

APPENDICIES:

We attach as an appendix the abstract submitted to the 2012 meeting of the International Society for Magnetic Resonance in Medicine detailing the Halbach LFI magnet built in our laboratory. Please note that the first author on reference 2 of the attached abstract, Jason Stockman, has begun work in our laboratory as of Jan 2012 as a postdoctoral fellow and will focus on parallel reconstruction methods to accelerate imaging in both of the LFI head scanners as well as implement his O-space methodology to the Halbach head imager.

We also attach for reference the Year 1 SOW.

Design and construction of a Halbach array magnet for portable brain MRI   Abstract ID: 3897

Clarissa L. Zimmerman, Lawrence L. Wald, Matt Rosen, James Blau

Introduction: A portable MR system has the potential to quickly detect brain injury at the site of injury. For example hemorrhage detection is critical for both stroke patients and traumatic brain injury victims. In stroke, rapid distinction between a hemorrhagic and non-hemorrhagic event could allow administration of a clot-busting drug such as tPA (tissue plasminogen activator) in an ambulance prior to transportation to the hospital, perhaps advancing this time-sensitive treatment by up to an hour. Subdural hemorrhage (or hematoma) is a form of traumatic brain injury, in which blood gathers between the dura and arachnoid mater (in meningeal layer) and is likely to be visualized on course resolution (e.g. 5mm) T_1 images. Other applications include the potential to construct higher order modes of the Halbach array which can produce strong gradients, For example providing high resolution profile imaging (1) of the brain meninges. A Halbach array of permanent magnets is ideal for portable MRI in that it creates a relatively uniform field transverse to the head without the use of a cryostat or power supplies. To test the feasibility of these magnets for imaging, we have designed, modeled and constructed a small, 20 rung Halbach array with radially magnetized NdFeB N42 magnets, large enough to fit the human head. The modeled field shows a roughly quadratic field profile with a central Larmor frequency sufficient for imaging (~3.3MHz). While the homogeneity is well below that of superconducting magnets, it fits well with our light-weight and portable concept if the inhomogeneities are used in image encoding, either through spatially selective excitation coupled with localization from 32ch parallel reception of the brain signal, or through O-space (2) style encoding induced by rotating the quadratic profile of the magnet around the head. Either case fulfills the portability criteria by eliminating the gradient coil and power supply.

Materials and Methods: The major criteria for design of the permanent magnet Halbach array are 1. maximize average field 2. allow small controlled field variation for spatial encoding. COMSOL field simulations were used to manually optimize the field based on the size and quantity of the NdFeB magnets and the radius of the cylinder. The result was a 20 magnet cylindrical array of 14"x1"x1 NdFeB magnets (Fig 1). Two smaller rings of smaller (1" cube) magnets at the top and bottom of the cylinder were added to provide end correction fields to offset the fall-off of the finite array in the z direction. A water-jet cutter was used to create the plastic rings that hold the magnets (fig 2A). In order to create the 14" magnets for the Halbach cylinder, it was necessary to glue to smaller magnets together. The smaller magnets were individually inserted into 1"x1" fiberglass tubes and floated on top of each other as they were repelled in this arrangement. A magnet loader and pushing apparatus was necessary to hold the magnets together during gluing.

Results: Figure 1(c-d) shows the COMSOL simulated field variation in 1 KHz contours. Figure 2B shows the field as a function of x, y and z location across the cardinal directions thru isocenter. The field was measured using a Tecmag console and NMR probe tuned to 3.2 MHz. Points were recorded by manually moving the NMR probe and recording FIDs. Frequency drift (Fig. 2C) was also measured by fixing the probe near the center for and tracking the NMR frequency for 20 minutes. This drift is likely due to temperature, which may be mitigated by thermal insulation. These results are shown in Figure 2. Table 1 outlines the resulting parameters of the constructed magnet.

Conclusion: The constructed magnet array achieves reasonable homogeneity for our application. It is very portable weighing only 45kg and requires no power to maintain the field. In addition to the cost of building this magnet was less than $6000. The accessibility of this magnet has the potential to offer basic head trauma and hemorrhaging detection to a broad range of applications.

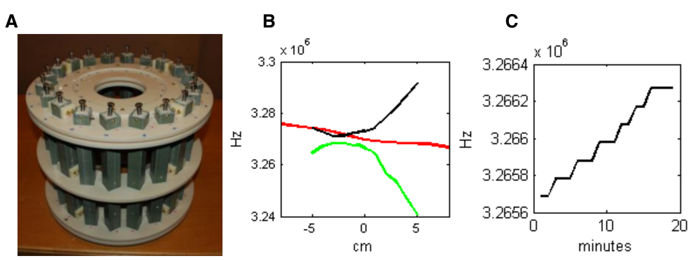


Figure 2: (A) Photo of constructed magnet (B) Measured FID frequency along the z-axis in red (axial), along the x-axis in black, along y-axis in green. (C) Measured FID frequency at one point in magnet for 20 minutes

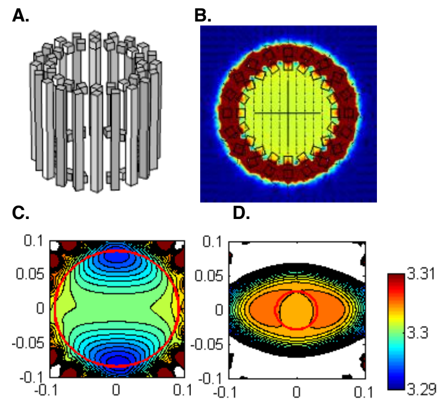


Figure 1: COMSOL simulations (A) magnet geometry, (B) field plot in center slice showing orientation of magnets and the field, (C-D) 1 Khz contour s of center slice and 5 cm above center. Red circle represents brain size.

Weight	45 kg
Center Larmor frequency	3.27MHz (77mT)
Homogeneity (over 10 cm^3)	15,000ppm
Drift of B0 over 20 minutes	586 Hz
Array radius	18cm
Array height	14"

Table 1: Properties of constructed magnet

References: (1) B. Blümich, S. Anferova, F. Casanova, K. Kremer, J. Perlo and S. Sharma, Unilateral NMR: principles and applications to quality control of elastomer products, *KGK Kautsch Gummi Kunstst* **57** (2004), pp. 346–349. (2) Stockmann, J. P., Ciris, P. A., Galiana, G., Tam, L. and Constable, R. T. (2010), *O*-space imaging: Highly efficient parallel imaging using second-order nonlinear fields as encoding gradients with no phase encoding. Magnetic Resonance in Medicine, 64: 447–456.

APPENDIX 1: Halbach-array imager submitted to 2012 ISMRM conference

Statement of Work

Year	Task	Objectives
Y1	***1. Low Field Imager***	
Q1-4	**1A** Low-field MRI Hardware Development	DEVELOPMENT of biplanar magnet and gradient coils. DEVELOPMENT of multi-coil-array parallel imaging system. DEVELOPMENT of thermal and power management systems.
Q3-4	**1B** System Control and Image Acquisition	ACQUIRE commercial MRI console. Begin DEVELOPMENT of image navigation and reconstruction methods.
Y1	***2. OMRI injury imaging***	
Q1-4	**2A** OMRI Hardware Development	DEVELOPMENT of improved low-field (5-100mT) Overhauser Magnetic Resonance Imaging (OMRI) system for small animal subjects, DEVELOPMENT of radio-frequency (RF) transmitter coils to deliver high-power (>10W) broad-band saturation pulses at frequencies corresponding to the Larmor precession frequencies of electrons over field range of 5-20mT. DEVELOPMENT of broadband, CW-RF excitation profiles to maximize Overhauser enhancement of the proton signal associated with broad EPR lines ($\Delta\omega_e$>10G).
Q3-4	**2B** *In Vitro* NO Overhauser effect-Enhanced Proton Spectroscopy (OEPS)	DEVELOPMENT of protocols for *In Vitro* OEPS in aqueous solution at a variety of NO concentrations (0.2-10 µM) at 6-15mT (“extreme narrowing limit”) for NO-Hb, at a variety of Hb concentrations.

YEAR 1 DELIVERABLES: Detailed technical reports on progress in the development of the low-field human head imager and the OMRI system optimized for imaging Overhauser-enhanced free radicals.

APPENDIX 2: Year 1 Statement of Work.