Brain Phantoms for Ultra High Field MRI

By

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I. Abstract

The challenge of neuroimaging at 7T is that the wavelength associated with the radiofrequencies (RF) used (determined by the Larmor relationship) is a function of the permittivity and conductivity of the head and is comparable to the dimensions of the human head. The result is that brain images at 7T have shading and bright spots that compromise image homogeneity.

To optimize RF coils at 7T and study the effect of mitigating approaches such as shimming of the radio frequencies produced by multiple transmitters, I am putting together a head mimicking phantom with the appropriate structure, electrical, and wave properties and magnetic resonance relaxation times. I created multiple plates from an MRI of a human head and used this to generate NC mill forms that can be used to build a realistic model of a human brain, slice by slice. The forms will be filled with certain concentrations of agarose and gadolinium choride to get the right relaxation times as well as electrical properties and assembled into a 3D model of the human brain. Such a phantom would be unique. It would allow the ability to instrument the phantom and measure RF power deposition and optimize RF shimming techniques using multiple transmitters. Both of which are major challenges currently.

II. Introduction

Imaging at 7T magnetic fields has various advantages as well as downfalls. The development of a tissue-mimicking phantom with dielectric properties and other tissue specific characteristics is the first step to understanding the problems with imaging at such a high magnetic field. The main objective of my work was to develop an agarose gel and saline solution phantom to mimic properties of the human brain for imaging at 7T. This phantom will contain
solutions that have the same white matter and grey matter T1 and T2 relaxation times as well as similar dielectric properties and anatomical structure of a human brain to simulate its radio frequency (RF) loading and magnetic behaviour.

III. Theory

III.1 An Introduction to MRI

Magnetic Resonance Imaging (MRI) is an imaging modality that incorporates the use of nuclear magnetic resonance of protons to produce proton density images (7). An MRI is capable of producing very clear and detailed images of the body’s soft tissues without exposure to radiation. The biggest and most important component in an MRI system is the magnet (8). The strength of the magnet is rated using a unit of measure known as a tesla (T). The magnets clinically used today in MRI are in the 0.5T to 2T range. Magnetic fields greater than 2T have not been approved for use in medical imaging, though ultra high field magnets are used in research.

As stated above, the M in MRI stands for magnetic. Magnetism is a property of matter that is a result of atoms having orbiting electrons. The orbiting electrons cause the atoms to have a magnetic moment associated with an intrinsic angular momentum called ‘spin’. The microscopic magnetization of protons in a magnetic field causes them to spin at a rate of precession referred to as the Larmor frequency. Protons in the body will align with the main magnetic field, Bo, resulting in a net magnetization pointing in the direction of the main magnetic field. Exposure of individual nuclei to RF radiation (B1 field) at the Larmor frequency causes nuclei to transition from the lower energy state to the higher energy state (7).

Exposure of an object or person to RF radiation at the Larmor frequency, causes the net magnetization to spiral away from the Bo field. In the rotating frame of reference, the net magnetization vector rotate from a longitudinal position a distance proportional to the time length of the RF pulse. After a certain length of time, the net magnetization vector rotates 90 degrees and lies in the transverse or x-y plane. It is in this position that the net magnetization can
be detected on MRI. The angle that the net magnetization vector rotates is commonly called the ‘flip’ angle (7).

The return of excited nuclei from the high energy state to the ground state is associated with loss of energy to the surrounding nuclei. T1 (spin-lattice) relaxation is characterized by the longitudinal return of the net magnetization to its ground state of maximum length in the direction of the main magnetic field. The T1 relaxation time is the time for the magnetization to return to 63% of its original length. T1 relaxation is dependent on the main magnetic field strength that specifies the Larmor frequency (8). Higher magnetic fields are associated with longer T1 times.

T2 (spin-spin) relaxation occurs when spins in the high and low energy state exchange energy but do not lose energy to the surrounding lattice. This results in loss of the transverse magnetization. In biological materials, the T2 time is considerably shorter than the T1 time. T2 relaxation occurs exponentially like T1 relaxation with 63% of the transverse magnetization gone after one T2 period (8).

Each tissue has its own characteristic T1 and T2 relaxation times which varies with the magnetic field applied to the tissue. At 7T, human grey matter from the brain has a T1 of 2000ms and a T2 of 55ms, whereas the white matter has a T1 of 1300ms and a T2 of 45ms (3, 4).

III.II Imaging at Ultra High Magnetic Fields

Imaging at high magnetic field strengths has many advantages. For one, an increase in the field is accompanied by a larger difference between the amount of parallel and antiparallel spins, according to the Boltzmann distribution (7). This results in an increase in the signal, which is proportional to the square of the main magnetic field. Thus, the signal-to-noise (SNR) ratio follows a linear relation with the value of the field. An increase in SNR results in a higher image quality, higher speed of image acquisition, and higher spatial resolution. Also, longer T1 and T2 relaxation times at higher fields result in higher blood/tissue contrast (8).
Although imaging at ultra high magnetic fields (higher than 3T) has many advantages, such as increased signal-to-noise (SNR) and spatial resolution, there are certain concerns regarding the effects of magnetic fields of such high strength on human tissue. For one, at ultra high field, there is a rapid increase in the quantity of RF energy deposited; which is proportional to the square of the value of the main magnetic field (8). During an MR procedure, the patient absorbs a portion of the transmitted RF energy, which may result in tissue heating and other adverse effects, such as alterations in visual, auditory and neural functions. The Specific Absorption Rate (SAR), measured in Watts/kg, is the RF power absorbed per unit mass of tissue. Strict limits to the SAR levels are imposed by patient safety international regulations and SAR measurements must be monitored during a scan to ascertain that levels do not approach the limit.

As previously stated, high magnetic fields also induce changes in dielectric properties. The various conductivity effects of the different tissues of the body cause heterogeneity in RF excitations. These are seen as an image with a non uniform signal and varying degrees of signal loss. This consequence can be seen in figure 1, in which there is shading and bright spots that compromise image homogeneity. Reducing these artifacts involves optimizing the coils and RF emission, as well as developing parallel emission techniques adapting RF emission to heterogeneous environments.

Figure 1. Magnetic resonance image of an axial slice through the human brain at 7T with image heterogeneity.
The Importance of Phantoms in Medical Imaging

In regards to medical imaging, a phantom is an artificial object of known size and composition that is imaged to test, adjust or monitor an MRI system’s homogeneity, imaging performance, and orientation aspects (8). It is advantageous to have a phantom that exhibits the same or similar properties to human tissue. These properties include T1 and T2 relaxation times, conductivity and permittivity, as well as size and structure. A phantom with these characteristics is very useful because it is not always practical or ethical to try various novel tests with high field MRI on a human. A phantom that is comparable to the human brain would mean that tests done with it can be better applied to biological conditions.

IV. Method

IV.1 Part 1 – Phantom Composition

It was determined that gadolinium chloride is a good T1 modifier, whereas agarose is a good T2 modifier (6). The relaxivity of varying concentrations of gadolinium chloride (GdCl3) and agarose were measured in order to find tissue equivalents. A range of concentrations were prepared in 8-ml sample tubes and T1 and T2 values were determined via fitting of segmented inversion recovery and multi echo spin imaging experiments.

Concentrations of GdCl3 and agarose were chosen to provide T1 and T2 values that match average human grey matter and white matter values, as reported in the literature (3, 4). A 15.2 cm PVC pipe was used as a former and filled with grey-matter-mimicking and white-matter-mimicking gels in concentric annuli, with a CSF-mimicking 50-mM NaCl solution (2) in a central spherical compartment and in a thin annulus around the periphery. A schematic of the phantom that was constructed is illustrated in figure 2. Phantom size was chosen to match the average human brain by mass (~3 kg) (5).
The detailed procedure that was taken for building of the concentric phantom illustrated in figure 2 is as follows:

- GdCl3 was diluted to desired volume and concentration.
- NaCl was weighed out and added to the solution
- Solution is heated on a hot plate to 60 degrees Celsius, at this time; the appropriate amount of agarose was added to solution and stirred with a magnetic stirrer
- Once heated to approximately 90 degrees Celsius, the solution was considered completely dissolved and became transparent
- At this point, the solution was cooled for 10 minutes and brought to the fume hood where the desired amount of NaN3 (antiseptic) was added
- Finally, the solution was poured into the PVC mold and was left to solidify into a gel.
- Once both solutions (grey matter and white matter) were solidified, saline was added around the periphery and then the container was sealed with PVC glue

**IV.II Part 2 – Phantom Size and Structure**

The phantom that was previously described is symmetrical in shape. Yet, the human brain is not symmetrical, therefore the next step in my project was to design a phantom with similar anatomical structure as the human brain. Axial images of brain slices were obtained from *Brain Web – Simulated Brain Database* (1). These images represent the standard size and structure of the human brain. There was 36 axial slices of the brain each with a slice thickness of 5mm. The modality used to acquire the images was T1-weighted and there was zero noise and intensity non-uniformity (RF) in the images.
Of the 36 brain slices, 14 were selected, as shown in figure 3. Each image was modified using ImageJ. These modifications included image sharpening and contrast enhancement by adjusting window and level in order to maximize the contrast between grey matter, white matter, and CSF. The 14 images were then printed.

Each image was manually outlined to distinguish unambiguously between the three different compartments; white matter, grey matter, and cerebrospinal fluid. The tracings were scanned and made binary using ImageJ. Each outlined image was then formatted from JPG to PDF using the Cute PDF Writer and then subsequently saved as a DXF file using Aide PDF to DXF converter. Solid Works was then used to convert the DXF file into a SAT file.

Once all images were converted into SAT files they were opened into MasterCam Mill 9. In this program, changes were made to ensure all lines were continuous and to make deletions of unnecessary detail where needed. Once each brain slice was compartmentalized into MasterCam, they can be milled out of plastic and eventually filled with the appropriate brain-mimicking substances. Figure 4 shows an outline of the steps taken in converting a single image into a SAT file. These steps were repeated for all 14 brain slices.

Figure 4. Procedure of image formatting. i) Image slice obtained from Brain Web, ii) Image outlined and made binary with ImageJ, iii) Image formatted to SAT with Solid Works, iv) Image is modified and ready to be milled in MasterCam.
V. Results

T1 and T2 contrasts matching grey and white matter were successfully created, as demonstrated in figure 5. Figure 5 are T1-weighted images of the same slice of the phantom with different inversion times. They successfully demonstrate the differences in T1 values between the tissues, and ultimately the presence of contrast between grey matter, white matter, and CSF.

![Figure 5: T1W MPRAGE images of the same slice of the phantom with different inversion times. Left: T1= 500ms, Mid: 1400 ms to null GM, Right: 900 ms to null WM.](image)

The resulting concentrations of GdCl3 and agarose to mimic grey matter and white matter are indicated in table 1. With these concentrations, the phantom will exhibit the target T1 and T2 values, as stated in the table, when scanned in a 7T MRI. For graphical figures showing the T1 and T2 values for agarose concentrations ranging from 0 to 2.2% and GdCl3 concentrations from 0uM to 150uM, refer to the Appendix (IX).

Table 1: Agarose % and [Gd] chosen to match grey and white matter contrast.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Target T1 (ms)</th>
<th>Target T2 (ms)</th>
<th>% agarose</th>
<th>[GdCl3] (uM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grey matter</td>
<td>2000</td>
<td>55</td>
<td>2.1%</td>
<td>8</td>
</tr>
<tr>
<td>White matter</td>
<td>1300</td>
<td>45</td>
<td>2.2%</td>
<td>22</td>
</tr>
</tbody>
</table>

Coil loading was measured by tuning, matching, and decoupling a 6-channel transceiver array for a human head and comparing the S11 and S12 parameters when loaded with the phantom. The inclusion of the conductive CSF-mimicking 50-mM NaCl solution in the center and periphery of the phantom was found necessary to achieve coil-loading effects that matched
the human head (as determined by S11 measurements). Coil coupling (S12) was worse than in the head by roughly 3dB per channel pair, due to the phantom coupling more to the coils. This increase in coupling, as compared to the head, is also visible in the amount of RF power required for excitation, which is nearly 5dB less in the phantom. B1+ spatial behavior is similar to that in the head, as demonstrated by the intensity patterns in figure x.

B1+ effects, also known as the radiofrequency magnetic field effects, were empirically determined via imaging experiments with multi-channel transmit arrays, noting the location of signal nulls in the phantom and in a human volunteer for two driving configurations: single channel transmission, and 6-channel transmission phases set randomly to induce B1+ spatial cancellations. Results are shown in figure 6. In this figure it is clear that the phantom behaves in a similar fashion to the human brain because it has shading and bright spots in approximately the same locations.

![Figure 6: Comparison of RF interference patterns. Top row: Single element transmitting (located at back of head). Bottom row: All elements transmitting with random phases to produce interferences.](image)

Once the right concentration of GdCl3 and Agarose to mimic human grey and white matter were determined the shape and anatomical structure of the phantom was developed. The final model of the segmented phantom having compartments for grey matter, white matter, and
CSF is shown in figure 7 for one brain slice. In the figure, the pockets represent different compartments of the brain slice that will be milled out of plastic.

![Image](image.png)

**Figure 7.** i) Pockets in blue represent regions that will be milled, ii) Model represents how the tool will mill out each compartment.

Once each brain slice, 1cm in thickness, are milled out of plastic, they will each be individually filled with the appropriate brain mimicking solution for grey matter and white matter and left to solidify into a gel. Once solidified, each cross section will be stacked one on top of the other and assembled into a 3-dimensional representation of the brain. The phantom will be the same size as the average brain with a width of 140mm, length of 167mm, and height of 93mm.

**VI. Discussion**

An agarose gel and saline solution phantom was developed to mimic properties of the human brain for imaging at 7T. A phantom was created with the same anatomical structure and size as a brain with grey matter/white matter contrast created via altering the agarose gel concentration to produce T2 differences, while T1 was modulated via doping with Gadolinium salts. Saline compartments mimicking the ventricles and peripheral cerebrospinal fluid (CSF) allow for proper loading and decoupling behaviour of RF coils tuned for the head. Additionally,
the compartmentalized nature of the gel provides B1+ behaviour similar to that in the head. With these features, this phantom design is useful for evaluating sequence contrast, coil design, and B1 shimming at 7T.

VII. Conclusion

High field MRI is a very prominent field of medical imaging research and phantoms are used very frequently. Yet, a phantom with the above mentioned characteristics would be unique. It would be very useful in high field MRI because the closer its’ properties resemble that of the human brain, the better MRI tests done with the phantom can be related to biological conditions. This head-mimicking phantom has two major benefits; it would (1) allow the ability to instrument the phantom and measure RF power deposition (SAR) and (2) optimize RF shimming techniques using multiple transmitters. Both of which are major challenges currently.
VIII. References


IX. Appendix

**Figure 8.** T1 vs. concentration of GdCl3 for various % agarose.

**Figure 9.** T2 vs. % agarose for various GdCl3 concentrations.