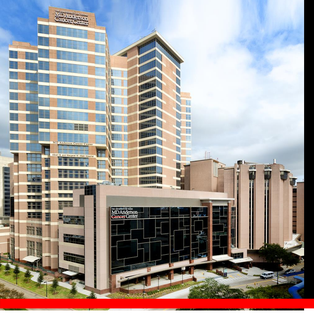

Development of a "Universal" Phantom for Standardization of Chemical Exchange Saturation Transfer (CEST) MRI

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Background

- Chemical Exchange Saturation Transfer (CEST) MRI is an emerging molecular imaging method for improving cancer diagnoses.
- A variety of image acquisition and analysis methods have been developed over the past few decades, which have been implemented on several clinical MRI instruments from different manufacturers and at different magnetic field strengths.
- A standard phantom is needed to compare these acquisition and analysis methods. This standard phantom should consist of a variety of materials and chemical agents that exhibit a CEST effect, to test the ranges of CEST image contrast that can be generated.
- CEST effect depends on temperature, necessitating accurate and precise control of the temperature of the standard phantom.

Goals

- Develop a "universal" standard phantom for CEST MRI at 3T magnetic field strength that consists of 6 materials which exhibit CEST effects over a wide range of saturation frequencies.
- Develop a standard phantom for brain imaging at high field 7T field strength.
- Maintain longitudinal stability and a steady temperature of 37.0°C during CEST MRI acquisitions.

Introduction to CEST MRI

- CEST MR image contrast is generated by selectively saturating the MR frequency of an exchangeable hydrogen atom on an exogenous contrast agent, an endogenous metabolite, or endogenous proteins, followed by chemical exchange with water, which transfers the MR signal saturation to water.
- CEST contrast is dependent on many factors, such as the concentration of exchangeable protons, proton exchange rate that is dependent on pH and temperature, and tissue relaxation rate.

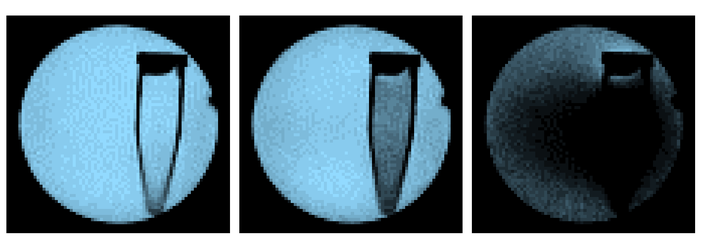

Fig. 1A. The saturation process eliminates magnetization of the hydrogen. When the hydrogen atom exchanges with a H^+ on a water molecule, the coherent magnetization of the water is reduced, causing the MR image contrast to appear darker

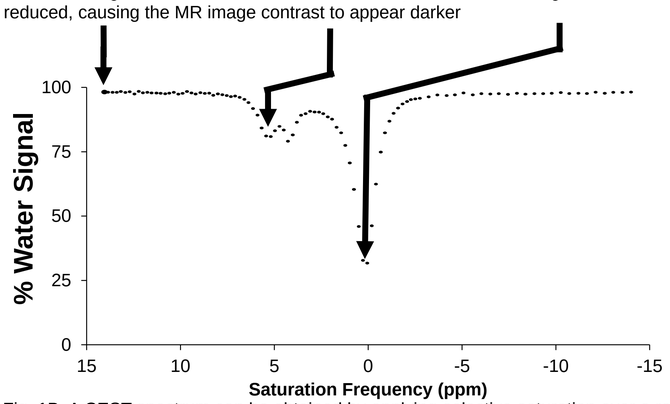

Fig. 1B. A CEST spectrum can be obtained by applying selective saturation over a range of MR frequencies and plotting the water signal amplitude as a function of saturation frequency. The maximum suppression of the water signal is used to quantitatively measure the % CEST signal, which can be used to estimate relative concentrations of proteins and metabolites in solid tumors.

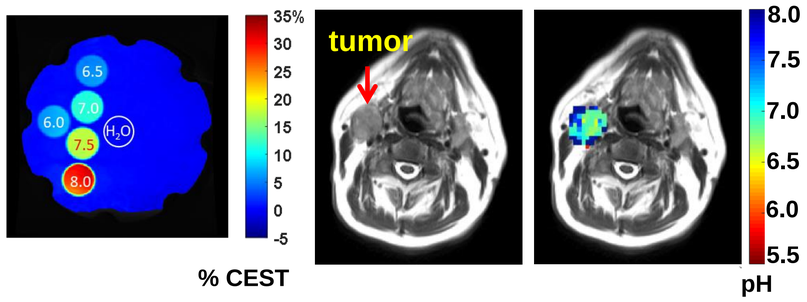

Fig. 1C. The % CEST signals of exogenous CEST agents can be used to evaluate tumor vascular perfusion and extracellular pH.

Construction of Phantom

- Base phantoms were obtained through purchase of the Diffusion Phantom from CaliberMRI and Enhanced Multi Sample 120 from Gold Standard Phantoms,
- Construction of phantoms were achieved through removing the interior materials, constructing a custom plate to enhance the number of samples that could be fitted, and filled with PureTemp37 (a liquid crystal that undergoes slow exothermic crystallization)
- Multiple samples were created of contrast, exogenous and endogenous agents, varying the pH, R1 time, and concentrations.
- Gelatin and taurine were used for the cylinder phantom while gelatin and the other agents were used in the sphere phantom.

Agent	pH range	Concentration (mM)	R1 (Gd) (s)
ParaCEST	6.2-7.4	5,10,15,20,30	1.2, 0.8, 0.4
Iopamidol	6.2-7.4	5,10,15,20,30	1.2, 0.8, 0.4
Poly-L-Lysine	6.2-7.4	100 (uM)	1.2, 0.8, 0.4
Creatine	6.2-7.4	2.5,5,10,15,20,30,50	1.2, 0.8, 0.4
Glucose	6.2-7.4	2.5,5,10,15,20,30,50	1.2, 0.8, 0.4
Gelatin$_1$	6.2-7.4	7.5% by Volume	1.2, 0.8, 0.4
Ethylene Glycol	6.2-7.4	100%	1.2, 0.8, 0.4
Taurine$_1$	6.2-7.4	10,15,20,50	1.2, 0.8, 0.4

Fig. 2. To best provide a wide variety of tests, the phantom was constructed with multiple variables including R1 (1/T1), concentration of agent, and pH range. Gelatin$_1$ and Taurine$_1$ were unique to the cylinder phantom which was also doped with a solution of gadolinium (Gd) beforehand.

Fig. 3. Cylinder phantom and sphere phantom were constructed as above. Cylinder phantom was used to test that the variables constructed would be able to be scanned properly at a 3T MRI.

Temperature Validation

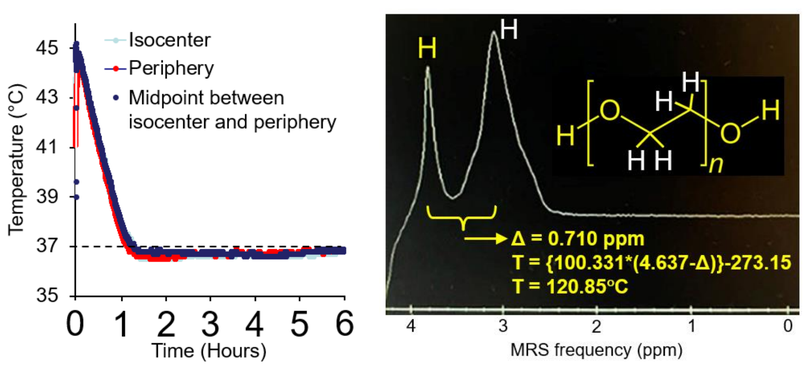

Fig. 4. The temperature of the isocenter, periphery, and midpoint of the phantom stayed relatively constant for the duration of the time measured at around thirty-seven degrees Celsius. An MR spectrum was also taken to show that MRS would be able to work for future scans.

MR Images

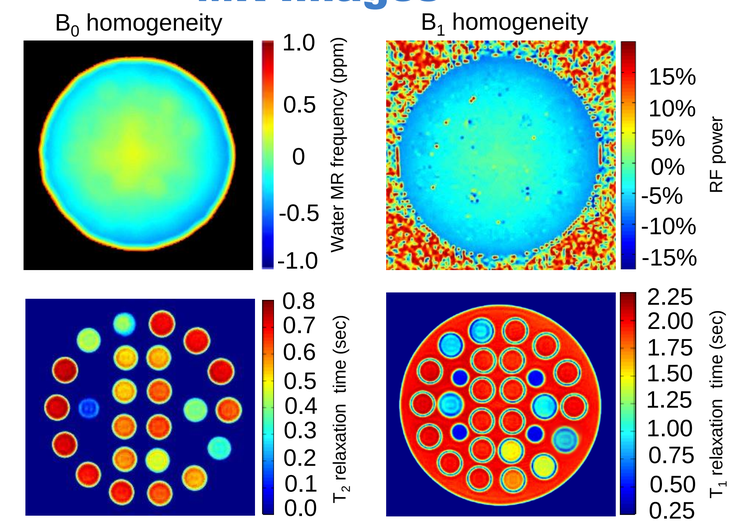

Fig. 5. B_0, B_1, T_1 and T_2 were measured and mapped.

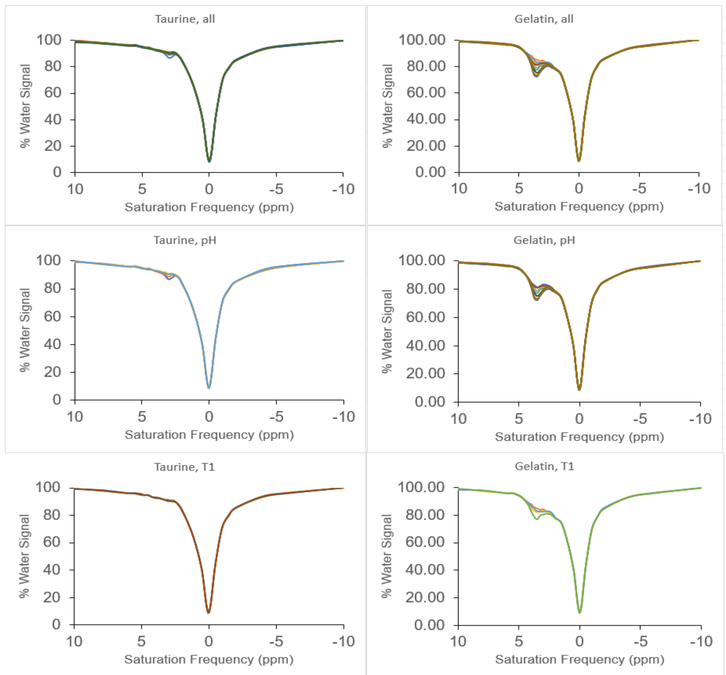

Fig. 6. CEST spectra of taurine and gelatin are shown from cylinder phantom. Taurine shows little CEST at room temperature (expected since high pH and short T1 wipes out small signal). The Gelatin samples show a relatively narrow peak, further showing a good CEST signal.

Conclusion

- B_0 and B_1 maps were homogeneous as expected. The T_1 and T_2 maps showed that doping with our contrast agent (Gd) was also successful.
- While the MR spectrum was able to be calculated, temperature shows that ethylene glycol was not pure and needs to be adjusted for the phantom
- The CEST spectra were dependent on pH for both Taurine and Gelatin. CEST spectra of Gelatin was dependent on T_1 relaxation time.
- Overall, we were able to successfully design a physical phantom to capture CEST effect and test the process of scanning the phantom.
- More work will be needed in the future to validate temporal stability and determine optimal agents for best use.

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We would like to thank QIAC for generously sponsoring and providing funding for the summer program, the Center for Advanced Biomedical Imaging at UT MD Anderson Cancer Center for access to clinical MRI instrumentation, and the Contrast Agent Molecular Engineering Lab (CAMEL) for valuable help and guidance in completing this project.