Rulers for Radiologists: Developing Standards for Quantitative Magnetic Resonance Imaging

Michael Boss
National Institute of Standards and Technology, Physical Measurement Laboratory, Magnetic Imaging Group

NIST
National Institute of Standards and Technology
U.S. Department of Commerce

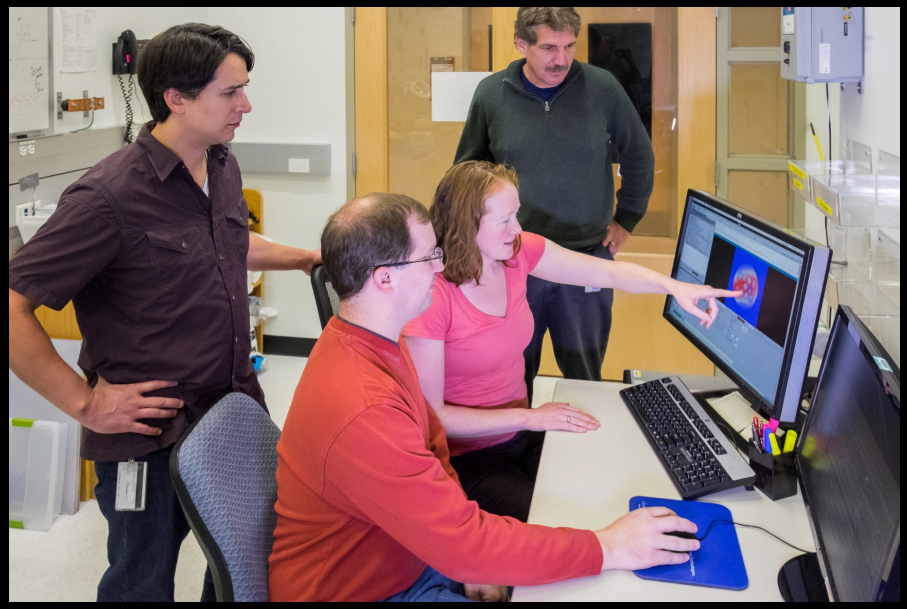
Overview

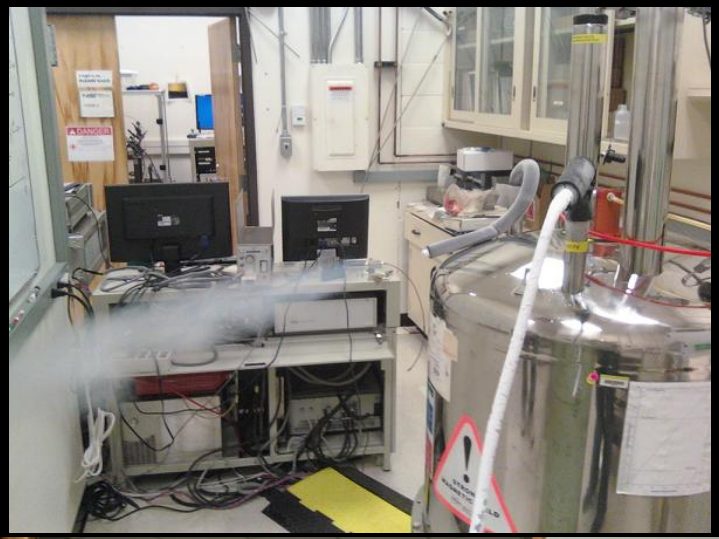
- Introduction
- MRI 101
- Approaches
  - ISMRM System Phantom
  - NCI/RSNA QIBA Diffusion Phantom
  - UCSF Breast Phantom
- Future Directions
- Conclusions

Why be quantitative?

- Provides metrics to establish measurement reproducibility
  - Geometry
  - Modality-specific biomarkers
  - Diffusion
  - Temperature
- Better disease detection and treatment monitoring
- Ensure safety

The NIST MRI Team





- Steve Russek (project leader), Michael Boss, Katy Keenan, Karl Stupic, Brian Yunker
- John Moreland (group leader), Gary Zabow, Josh Biller
- Two magnets used in unique ways

What are our goals?

- Facilitate development of novel, quantitative MR techniques
- Establish traceable, ground truth reference values for MR community
- Develop quantitative, biomimetic phantoms

Our partners

ISMRM ONE COMMUNITY FOR CLINICIANS AND SCIENTISTS

Quantitative Imaging Biomarkers Alliance RSNA

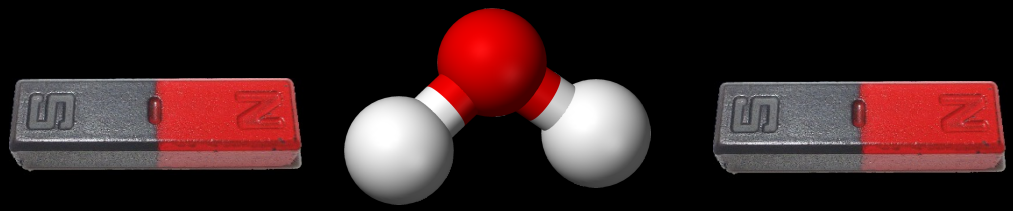
NATIONAL CANCER INSTITUTE

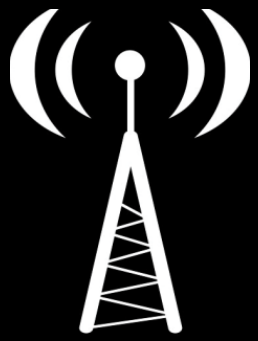
NIH National Institute of Biomedical Imaging and Bioengineering

CENC Chronic Effects of Neurotrauma Consortium

MR Basics

- Magnetic Resonance Imaging (MRI) is an imaging technique that detects hydrogen atoms in your body
- Based on Nuclear Magnetic Resonance (NMR)
- Uses strong magnets and radio waves to detect a signal
- Magnetic field gradients allow localization of signal





MR Basics: Signal Generation

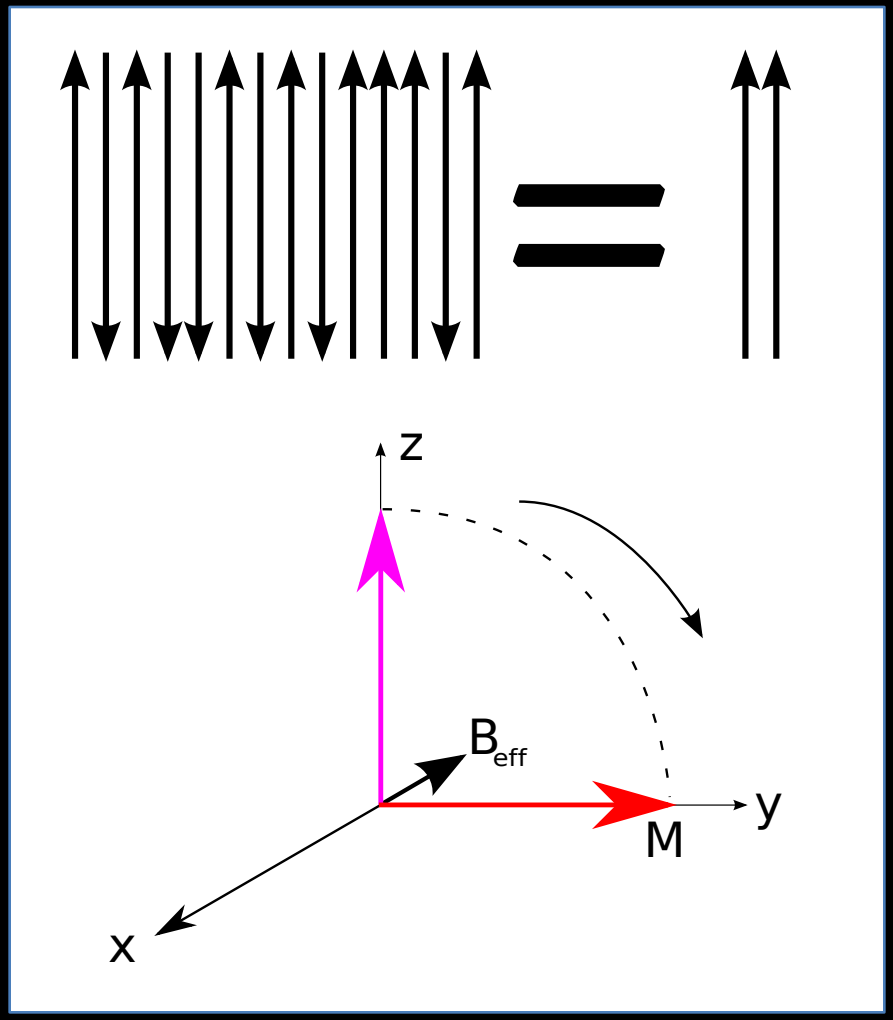
- The hydrogen nucleus is like a tiny bar magnet
  - Thermal equilibrium: align parallel or anti-parallel in a magnetic field
  - Slight preference for parallel creates a net magnetization, *M*
- Apply a pulsed RF field at the Larmor frequency
  - In rotating frame, net magnetization rotates
  - Can be placed into a plane transverse to the external field

$$\omega = \gamma B_0$$

ω : Larmor frequency

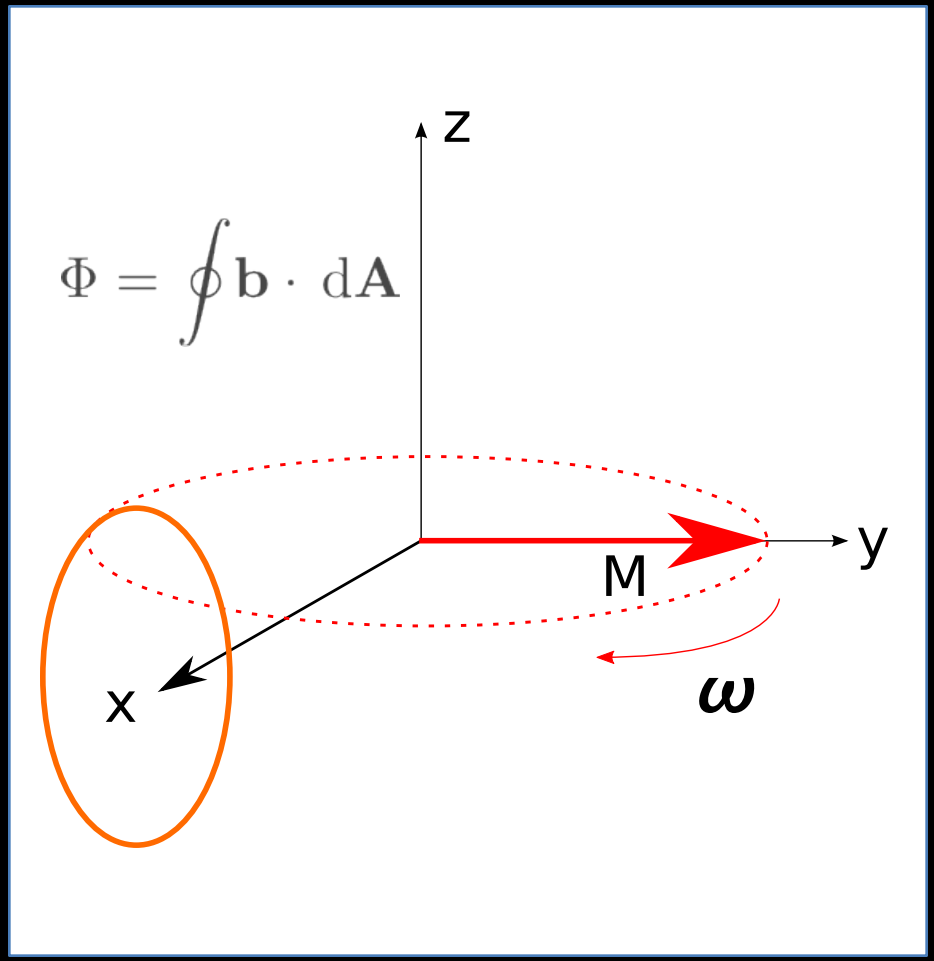
γ : Gyromagnetic ratio

B_0 : External magnetic field strength



MR Basics: Inductive Detection

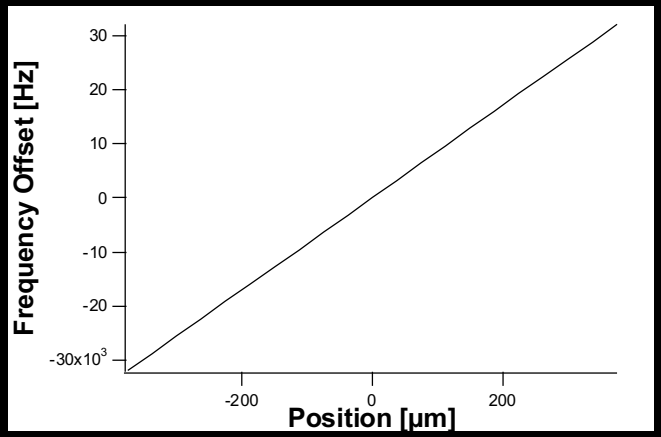
- Magnetization rotates at the Larmor frequency in the transverse plane
- A *changing* magnetic flux will *induce* a voltage in a closed loop conductor
- The voltage is proportional to the number of spins

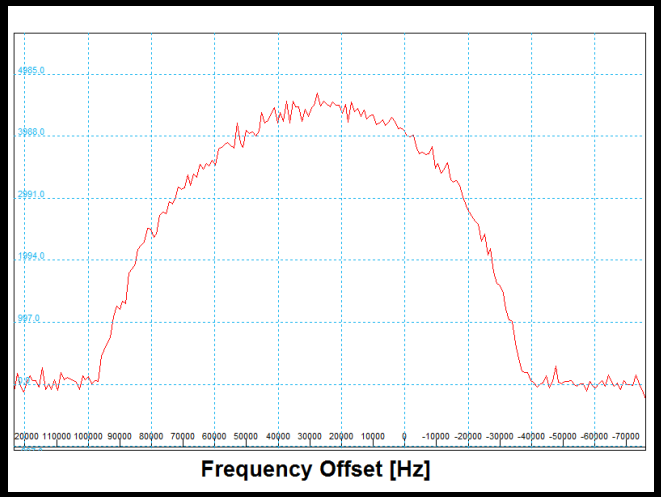


So which spins come from where?

MR Basics: Signal Localization

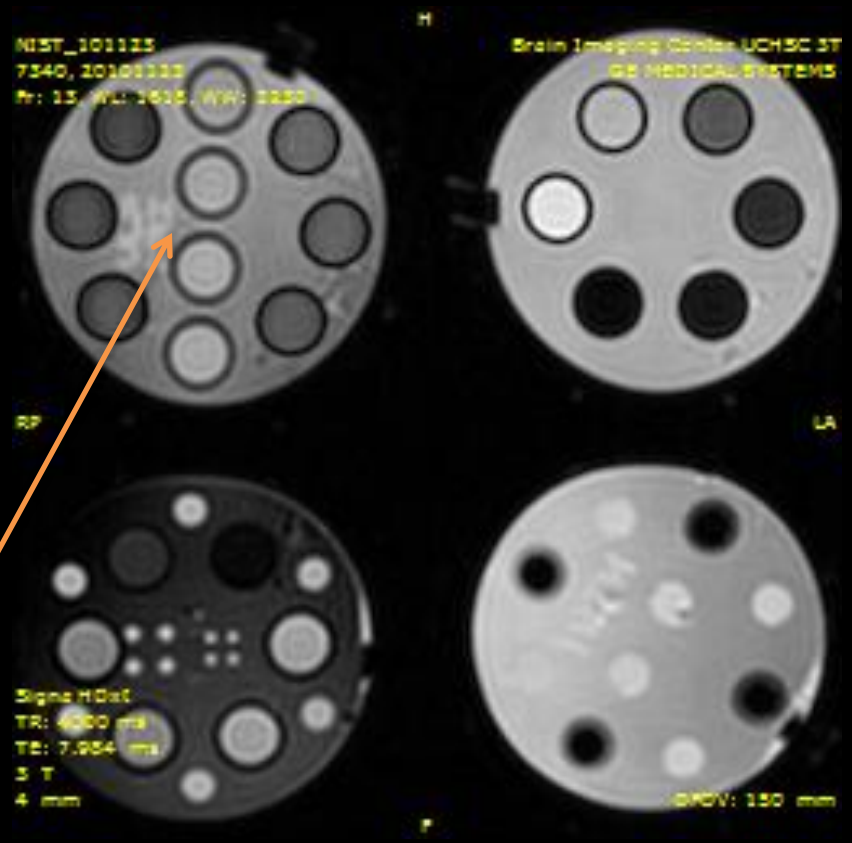
- Larmor frequency scales with external magnetic field
- By applying magnetic field gradients, the field will vary linearly as a function of position along a given direction (x, y or z)
  - Larmor frequency is position-dependent
  - Signal intensity as a function of frequency tells where hydrogen nuclei (protons) are



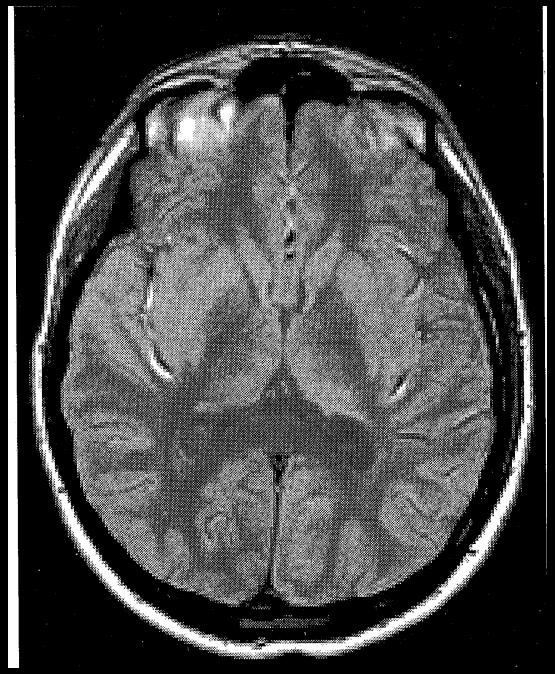


MRI Basics: Contrast

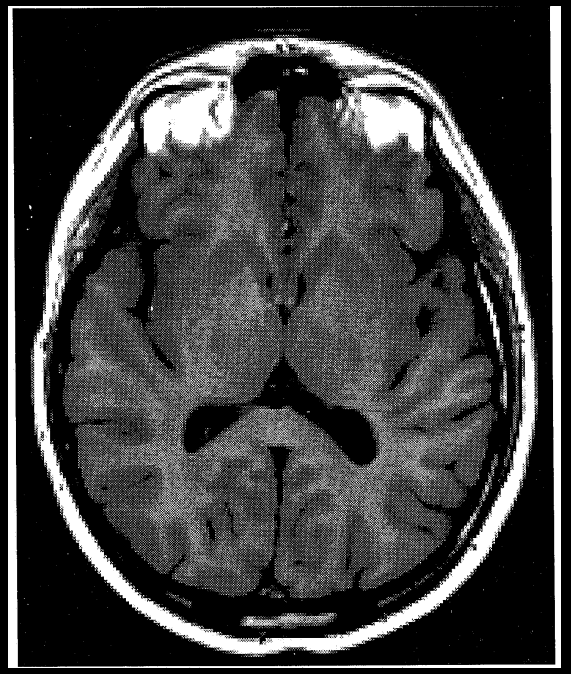
- One obvious mechanism: proton density
- MR signal does not last forever
  - Signal intensity decays according to two time constants, T_1 and T_2
  - Differences in relaxation times can be taken advantage of to generate contrast in images



MRI Basics: T_1 (longitudinal) Relaxation



Normal Image

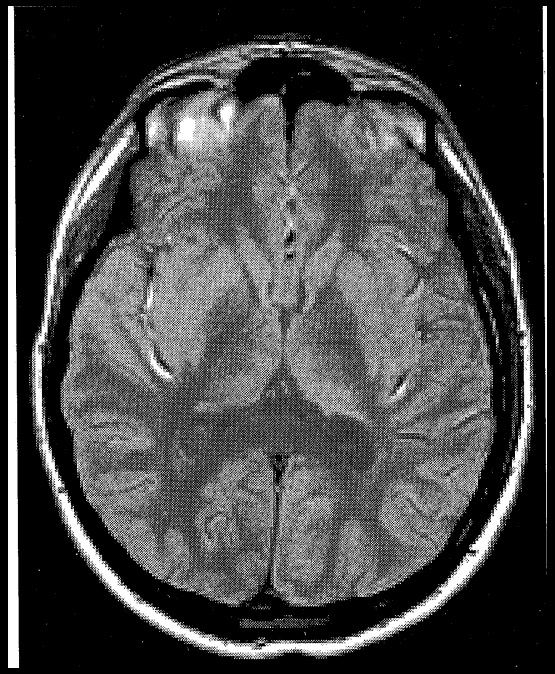


T_1-weighted Image

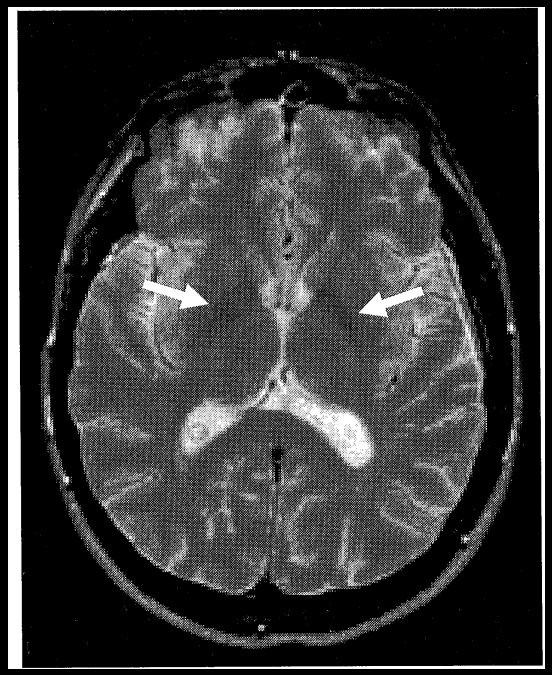
Images from E. Haacke et al., Magnetic Resonance Imaging: Physical Principles and Design Sequences

- Spins return back to equilibrium in a characteristic time T_1
- Short T_1 appear bright, long T_1 dark
- T_1 affects how fast data can be acquired: repetition time (TR)

MRI Basics: T_2 (transverse) Relaxation



Normal Image



T_2-weighted Image

Images from E. Haacke et al., Magnetic Resonance Imaging: Physical Principles and Design Sequences

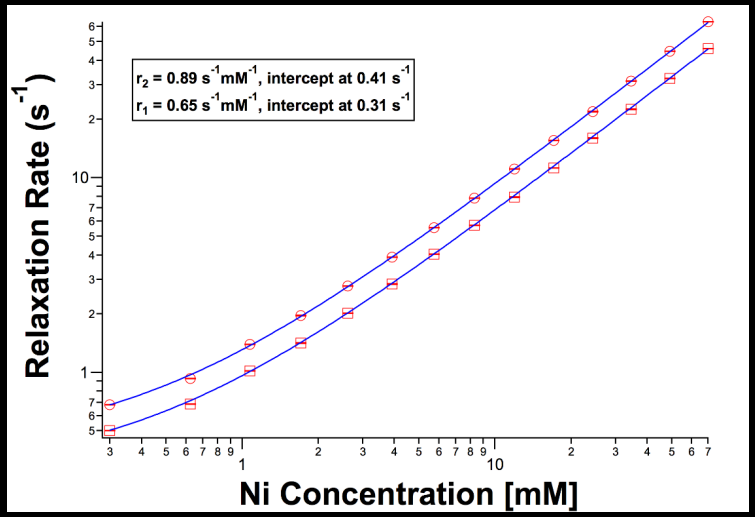
- Spins dephase due to different Larmor frequencies
- Short T_2 appear dark, long T_2 bright

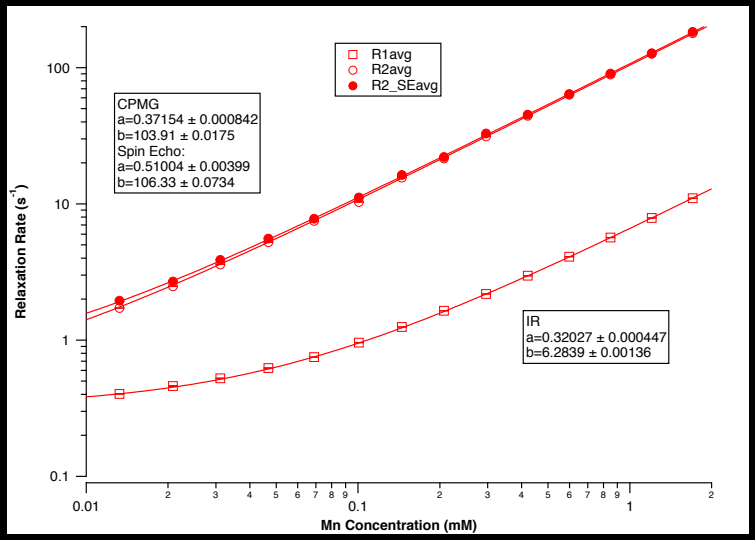
NIST/ISMRM System Phantom

- Worked with ISMRM Ad Hoc Committee for Standards in Quantitative Magnetic Resonance
- Developed phantom for basic MR parameter quantification
  - Based on ADNI shell
  - Materials chosen to match physiological values
- Ground truth to be established by NIST
  - NIST MRI
  - NIST NMR

System Phantom: Ground Truth Measurements

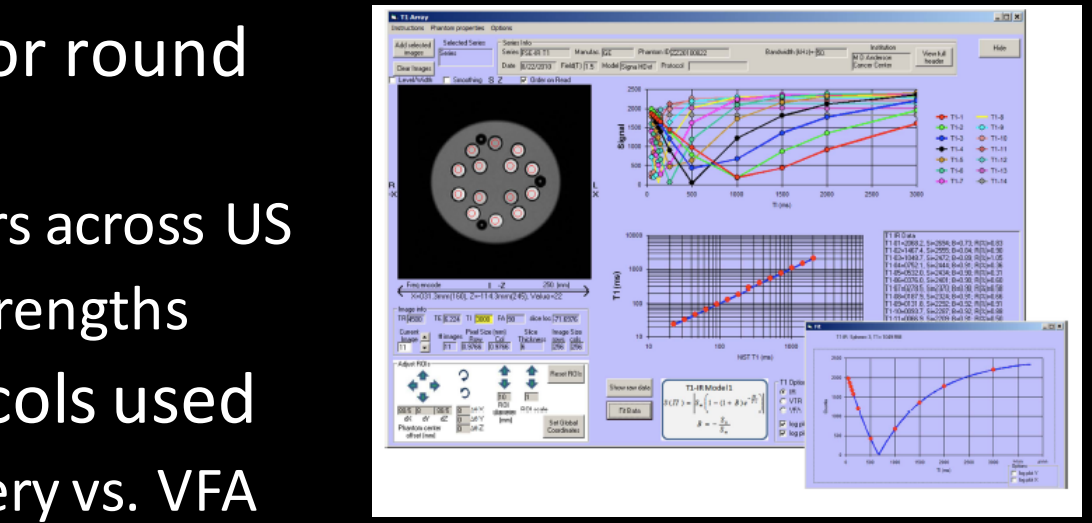
- Measure ground truth at appropriate field strengths and temperatures
  - 1.5 and 3 tesla
  - 10-37 °C
- Use gold standard techniques
  - Inversion Recovery
  - Carr-Purcell-Meiboom-Gill
- Measurements must be physically consistent

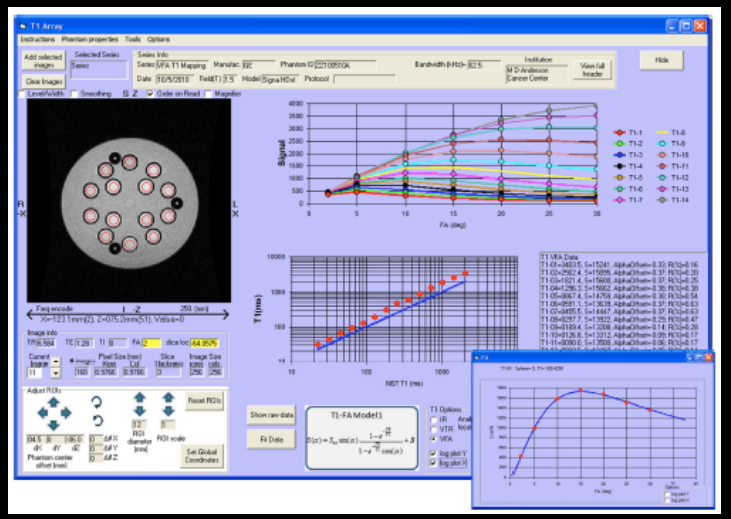




System Phantom: Field Testing

- Phantom sent out for round robin testing
  - 18 different scanners across US
  - 3 vendors, 2 field strengths
- Standardized protocols used
  - T_1: Inversion Recovery vs. VFA
  - T_2: Spin Echoes
- Data analyzed at NIST using custom software, PhantomViewer





System Phantom: Data Analysis

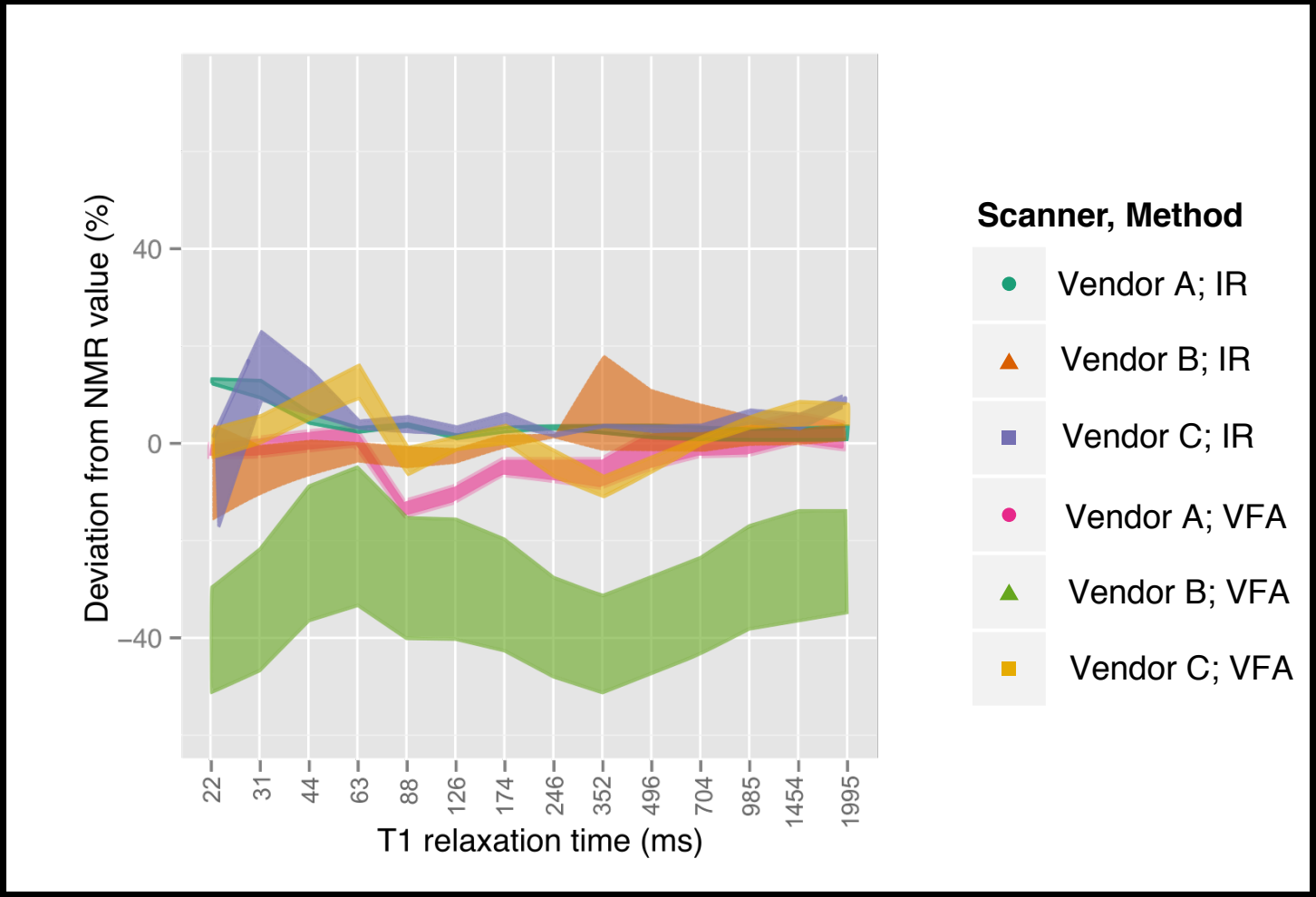
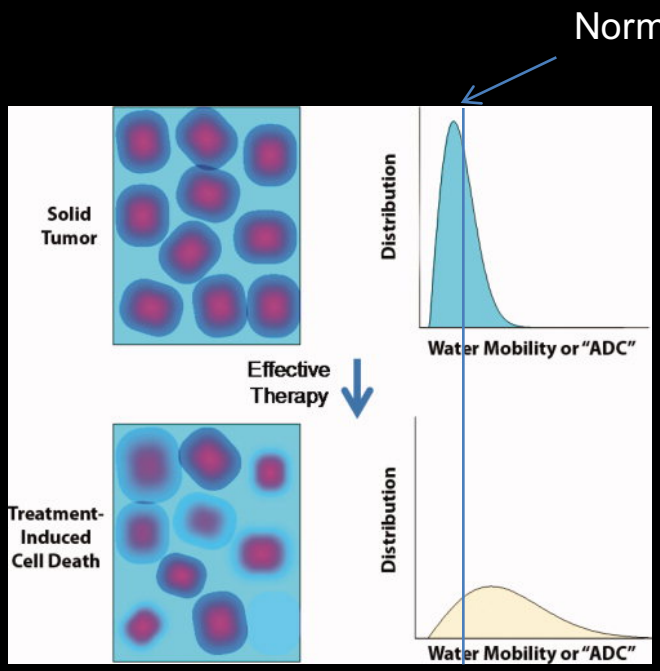


Image courtesy of Katy Keenan

Approaches: NIST/NCI/RSNA QIBA Diffusion Phantom

- Diffusion-weighted MRI (DWI) can reveal microscopic structural information
- Tumors/lesions often exhibit different **apparent diffusion coefficient** (ADC) than healthy tissue
  - Enables diagnosis and treatment monitoring
- **Goal**: Generate QIBA Profile for DWI using ADC as quantitative imaging biomarker
  - Literature search for claim justification
  - Phantom for QC



Often, tumors are highly cellular with restricted diffusion

Treated tumors often show apoptosis or necrosis with increase in diffusion

Thoeny HC and Ross BD, J. Magn. Reson. Imag., 32:2-16 (2010)

Diffusion Phantom: Background and Inspiration

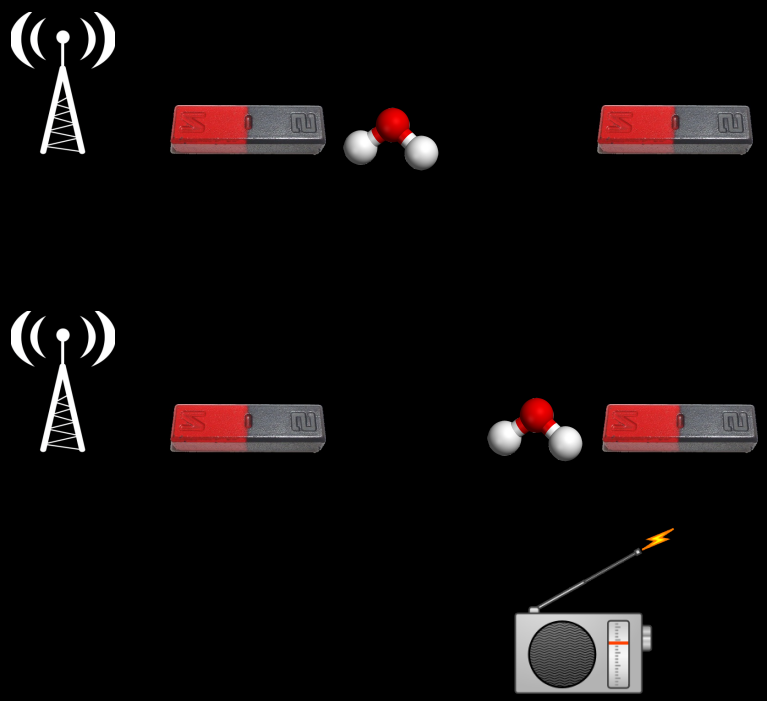
Table 1. Apparent diffusion coefficient values measured in normal liver at 1.5 T

Reference	Mean ADC (10^{-3} mm^{2}s^{-1})	Standard deviation	Range	Number of subjects	*b*-values (s mm^{-2})	Comments
Taouli et al [10]	1.60	0.13	1.44–1.88	10 v	0, 500	Conventional
	1.52	0.15	1.28–180			With parallel imaging
	1.51	0.21	1.27–1.99			Diffusion tensor/ parallel imaging
Mürtz et al [11]	0.92–0.96[a]	0.09–0.14	0.62–1.20	12v	50, 300, 700, 1000, 1300	Pulse Triggered
	1.03–1.14	0.22–0.40	0.67–2.57			Non-triggered
Kim et al [12]	1.05/1.02[b]	0.30/0.25		6 v/126 p	3, 57, 192, 408, 517, 850	
	1.55/1.16	0.37/0.42			3, 57, 192, 408, 192, 408	
	4.8/3.55	2.37/1.75			3, 57	
Ichikawa et al [13]	2.28	1.23		46 p	1.6, 55	
Taouli et al [14]	1.83	0.36	1.4–2.55	66 p	0, 500	
	1.51	0.49	1.12–2.71		0, 134, 267, 400	
Kwee et al [15]	1.60/1.62/1.57[c]	0.14/0.18/0.15		11 v	0, 500	Breath-hold
	2.13/2.27/2.07	0.33/0.47/0.43				Respiratory triggered
	1.65/1.62/1.65	0.09/0.16/0.17				Free breathing (7 mm slice)
	1.64/1.66/1.57	0.13/0.11/0.19				Free breathing (5 mm slice)
Yamada et al [16]	0.87	0.26		78 p	30, 300, 900,1100	ADC
	0.76	0.27				Diffusion coefficient (DC)
Müller et al [17]	1.39	0.16		10 v+9 p	8 *b*-values; b_{max} 328–454	
Namimato et al [18]	0.69	0.31		51 p	30, 1200	
This study	1.04	0.05	0.95–1.11	10 v	100, 200, 500, 750, 1000	Free breathing

ME Miquel, *et al*., Brit. J. Rad., **85**:1507-1512 (2012)

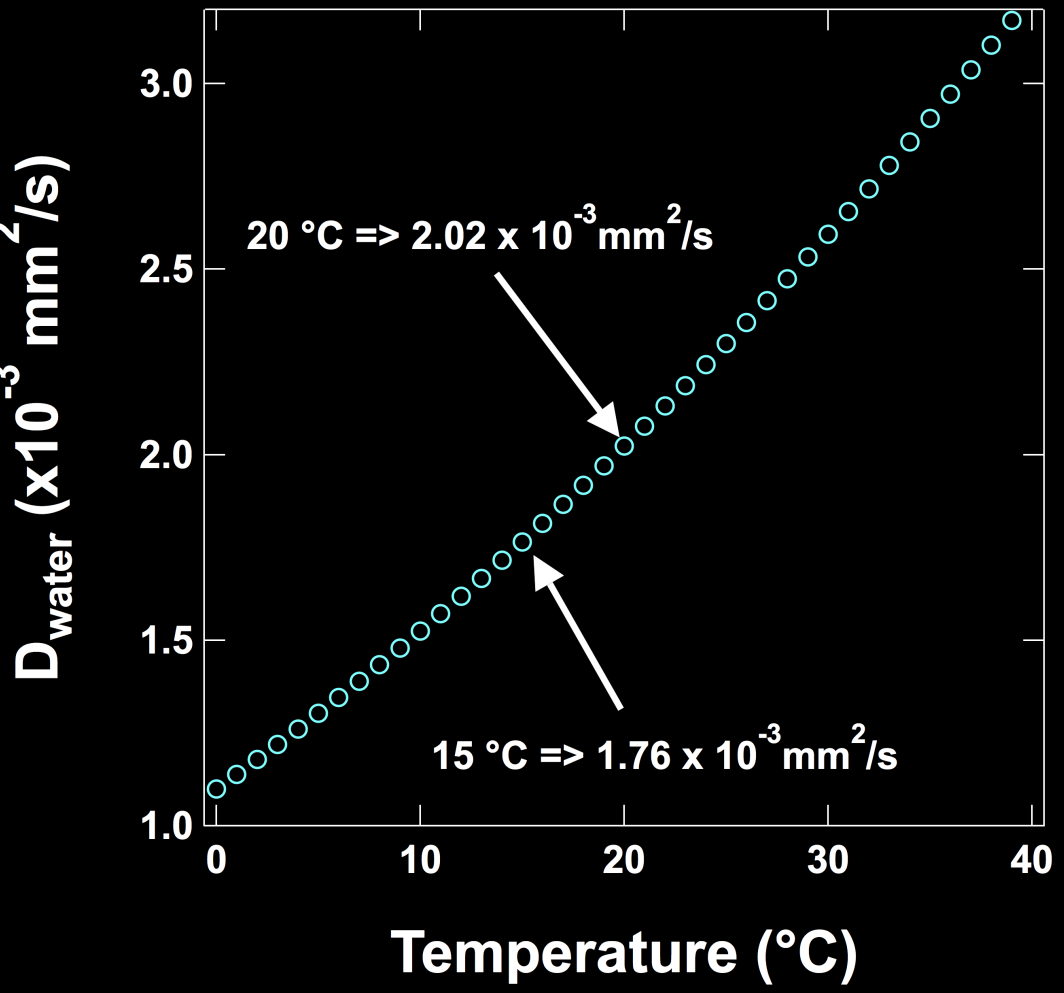
Measuring diffusion with RF

- Basic concept
  - Each water molecule in the body can serve as an RF transmitter/receiver
  - Tag hydrogen (proton) spins with phase as a function of position
  - Let spins move around
  - Reverse phase change
  - Signal attenuation due to imperfect refocusing provides information about motion



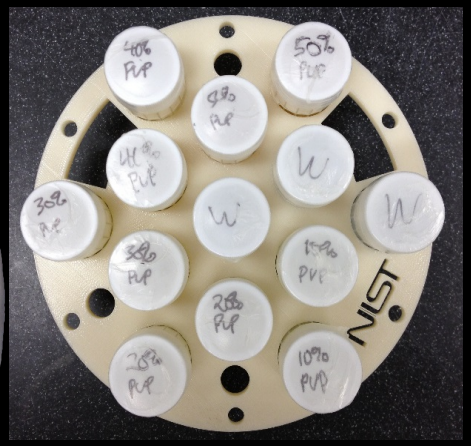
Diffusion is temperature dependent

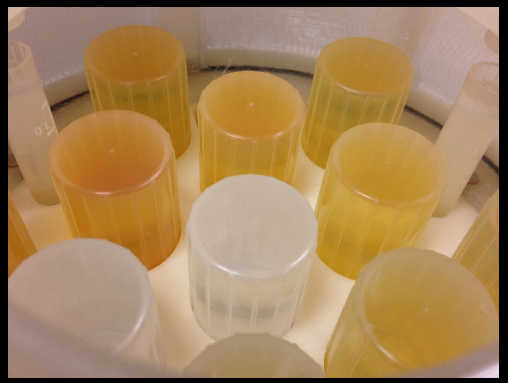
- Apparent Diffusion Coefficient (ADC) of water increases by 2-3%/°C
- Good phantom needs temperature monitoring or control



Holz et al., PCCP **2**:4740 (2000)

NIST/NCI/QIBA Isotropic Diffusion Phantom



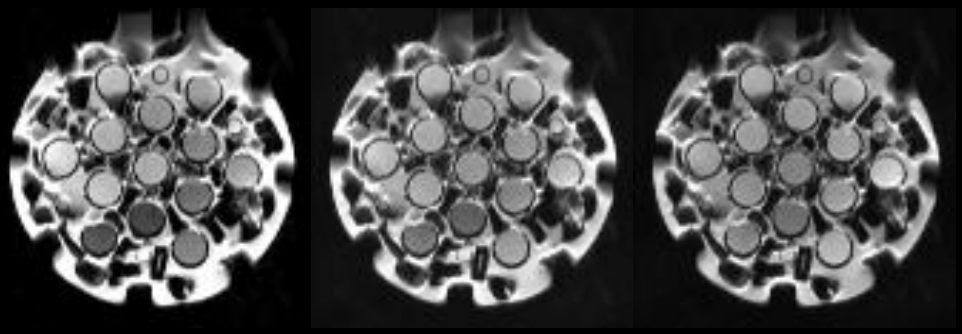


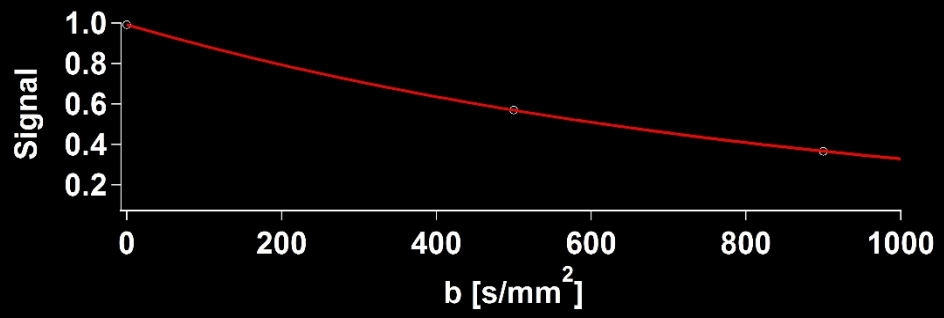
- Goals
  - Establish linearity of ADC over relevant physiological range
  - Characterize off-isocenter effects (e.g. gradient linearity)
- Approach
  - Use non-toxic polymer to tune ADC of water molecules
  - Spread diffusion media over wide area
  - Minimize thermal effects by use of an ice-water bath

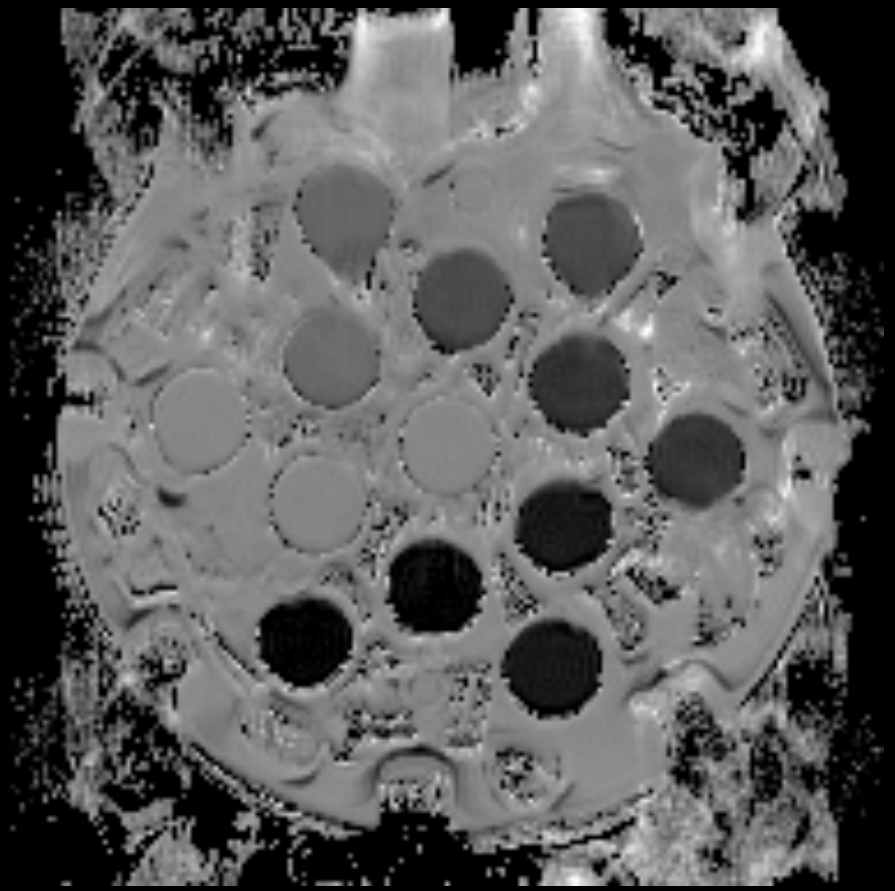
Commercially available at High Precision Devices, Inc.
http://www.hpd-online.com/diffusion-phantom.php

Prototype Diffusion Phantom Round Robin

- Prototype phantoms sent to collaborators in US and EU
- Measured on all major vendors, using a standardized protocol (b=0, 500, 900 s/mm^2)

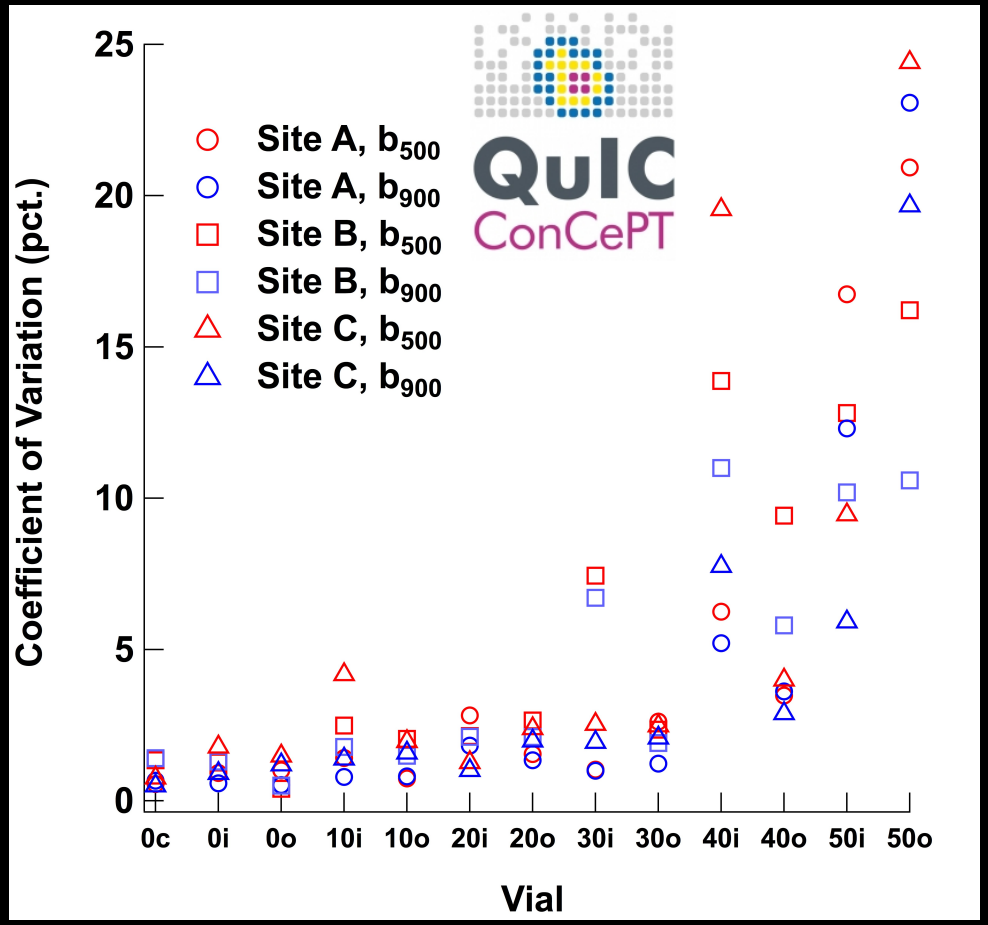






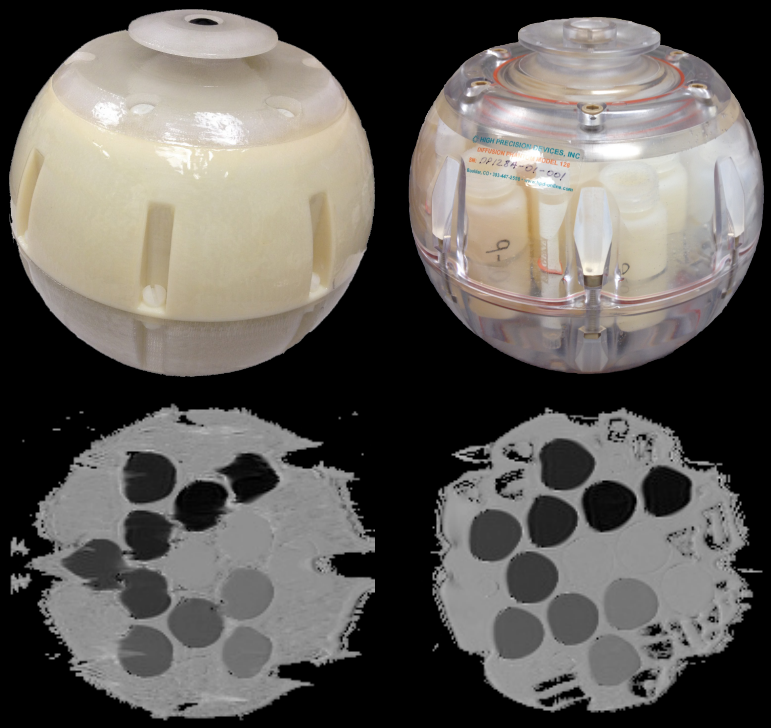
Prototype Diffusion Phantom Round Robin

- Assessed ADC in each vial using different b-values (2-point fit)
- As ADC decreased, coefficient of variation increased
- b_{900} resulted in lower CoVs than b_{500}



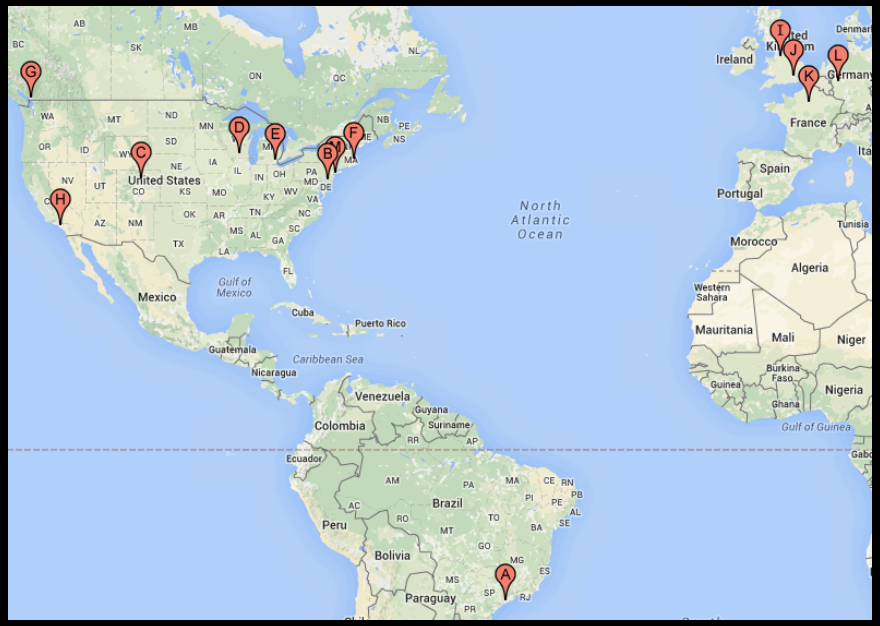
Diffusion Phantom: Prototype to Product

- Moved from 3D-printing to injection molded manufacturing
  - More robust material
  - Transparent shell allows ice to be more easily seen
- Minor design changes
  - Larger vials
  - Susceptibility-matching plugs to mitigate image artifacts



Diffusion Phantom: New Round Robin

- Phantom copies sent to a larger number of sites:

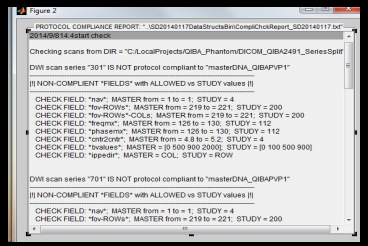


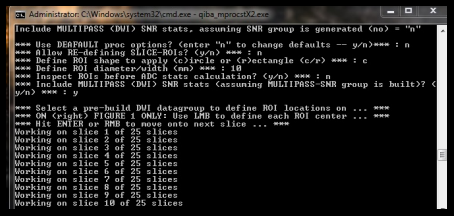
- Modified imaging protocol:
  - 4 b-values: 0, 500, 900, 2000
  - Interested in seeing effect of b_{2000} on CoV of high-PVP solutions (low ADC)
- Day 1: test-retest of all 4 b-values across all 3 orientations (done sequentially, 4 passes)
- Day 2: repeat of Day 1
- Data stored on Quantitative Imaging Data Warehouse: http://qidw.rsna.org/community/10
- Automated software analysis with **QIBAPhan**

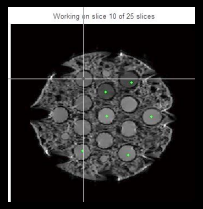
Diffusion Phantom: Achieving Consistent Analysis: **QIBAPhan**

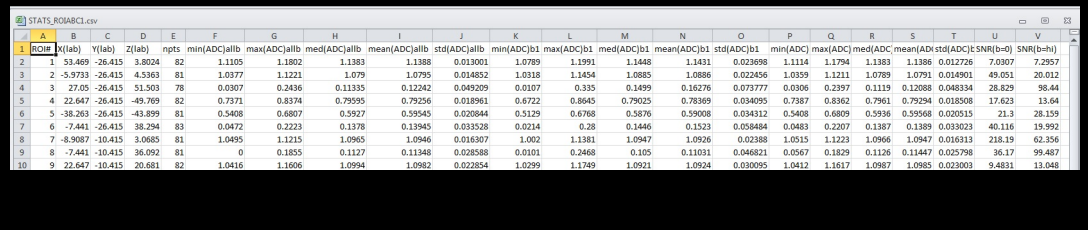
Project Goal: Automated derivation and analysis of key system DWI performance metrics for cross-vendor/site certification and quality control utilizing phantom data

Authors: Tom Chenevert and Dariya Malyarenko





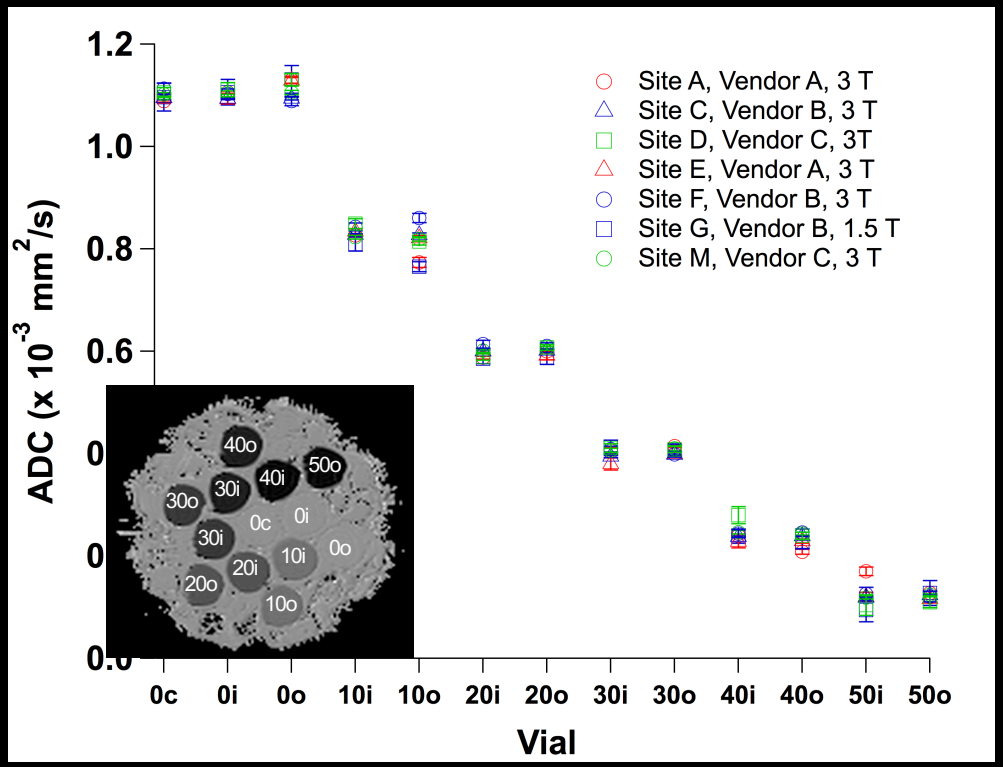




ROI#	X(lab)	Y(lab)	Z(lab)	npts	min(ADC)allb	max(ADC)allb	med(ADC)allb	mean(ADC)allb	std(ADC)allb	min(ADC)b1	max(ADC)b1	med(ADC)b1	mean(ADC)b1	std(ADC)b1	min(ADC)	max(ADC)	med(ADC	mean(ADC	std(ADC)b	SNR(b=0)	SNR(b=hi)
1	53.469	-26.415	3.8024	82	1.1105	1.1802	1.1383	1.1388	0.013001	1.0789	1.1991	1.1448	1.1431	0.023698	1.1114	1.1794	1.1383	1.1386	0.012726	7.0307	7.2957
2	-5.9733	-26.415	4.5363	81	1.0377	1.1221	1.079	1.0795	0.014852	1.0318	1.1454	1.0885	1.0886	0.022456	1.0359	1.1211	1.0789	1.0791	0.014901	49.051	20.012
3	27.05	-26.415	51.503	78	0.0307	0.2436	0.11335	0.12242	0.049209	0.0107	0.335	0.1499	0.16276	0.073777	0.0306	0.2397	0.1119	0.12088	0.048334	28.829	98.44
4	22.647	-26.415	-49.769	82	0.7371	0.8374	0.79595	0.79256	0.018961	0.6722	0.8645	0.79025	0.78369	0.034095	0.7387	0.8362	0.7961	0.79254	0.018508	17.623	13.64
5	-38.263	-26.415	-43.899	81	0.5408	0.6807	0.5927	0.59545	0.020644	0.5129	0.6768	0.5876	0.59008	0.034312	0.5408	0.6809	0.5936	0.59568	0.020515	21.3	28.159
6	-7.441	-26.415	38.294	83	0.0472	0.2223	0.1378	0.13945	0.033528	0.0214	0.28	0.1446	0.1523	0.059484	0.0483	0.2207	0.1387	0.1389	0.033023	40.116	19.992
7	-8.9087	-10.415	3.0685	81	1.0495	1.1215	1.0965	1.0946	0.016307	1.002	1.1381	1.0947	1.0926	0.02388	1.0515	1.1223	1.0966	1.0947	0.016313	218.19	62.356
8	-7.441	-10.415	36.092	81	0	0.1855	0.1127	0.11348	0.028588	0.0101	0.2468	0.105	0.11031	0.046821	0.0567	0.1829	0.1126	0.11447	0.025798	36.17	99.487
9	22.647	-10.415	20.681	82	1.0416	1.1606	1.0994	1.0982	0.022854	1.0299	1.1749	1.0921	1.0924	0.030095	1.0412	1.1617	1.0987	1.0985	0.023003	9.4831	13.048

- Reads in DW-MRI multi-vendor multi b-value classic DICOM images of the phantom
- Outputs scan series catalogue with acquisition protocol compliance check
- Displays DWI and derived ADC maps for user-supervised ROI loci definition
- Tabulates ROI summary statistics for ADC, DWI and SNR for individual b-values and repeat scans

Diffusion Phantom: Results



- Standardized image analysis performed
- Excellent repeatability
  - CoV<1.7 % for ADC>0.4 x 10^{-3} mm^2/s
  - 3-3.4 % for PVP-40 (~0.24 x 10^{-3} mm^2/s)
  - 7.5-11.0 % for PVP-50
- Interscanner reproducibility
  - CoV<4.1 % for ADC>0.4 x 10^{-3} mm^2/s
    - <1% for innermost water vials
  - 5.6-6.8 % for PVP-40 (~0.24 x 10^{-3} mm^2/s)
  - 5.4-19.7 % for PVP-50
- Phantom in clinical trial (TRACK-TBI)

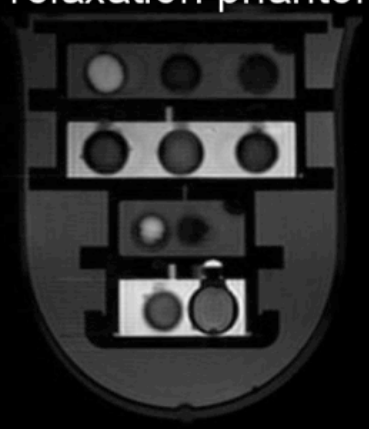
Approaches: NIST/UCSF breast phantom

Quantitative MRI measures:

- Compare T_1 measurement techniques
- Compare diffusion imaging methods
- Measure tumor volumes
- Assess fat suppression

Diffusion phantom

T1 relaxation phantom

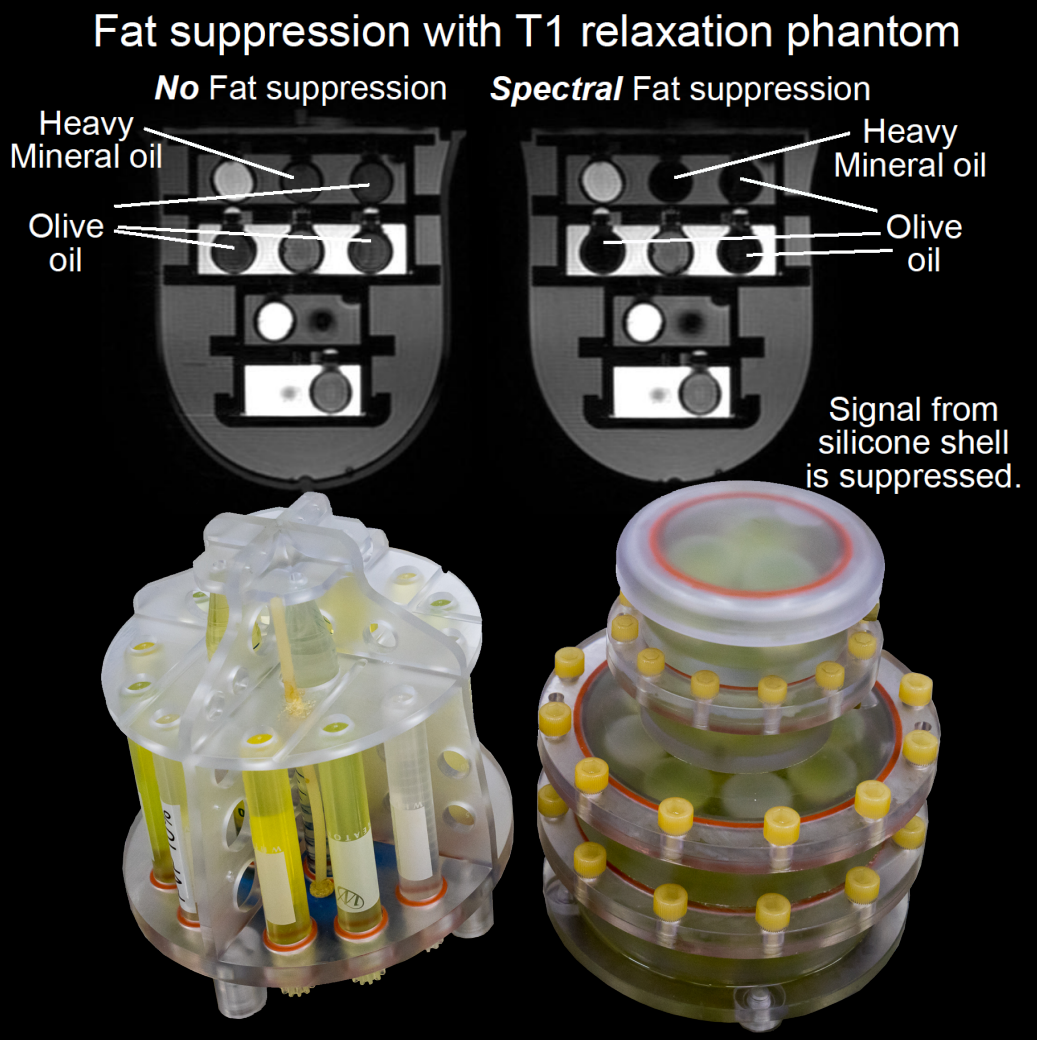


Collaboration with Dr. Nola Hylton at University of California San Francisco (UCSF) for the ACRIN 6698/I-SPY 2 trial

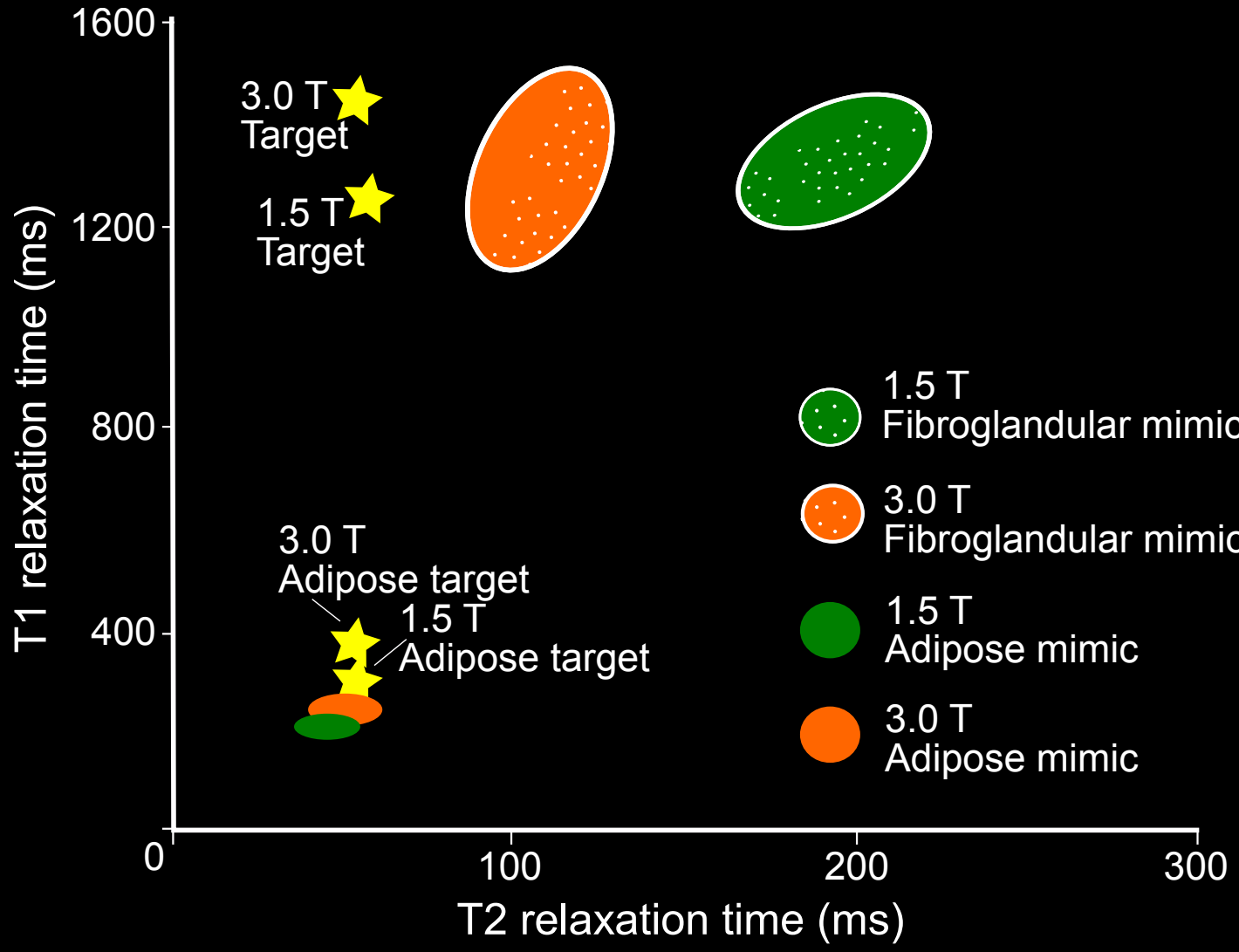
Slide courtesy of Katy Keenan

Breast Phantom

- Geometric array
- Diffusion components
- Fibroglandular and fat Mimics
- T_1 components
- Universal fit in wide range of breast coils
- Development through 2 rounds of SBIR



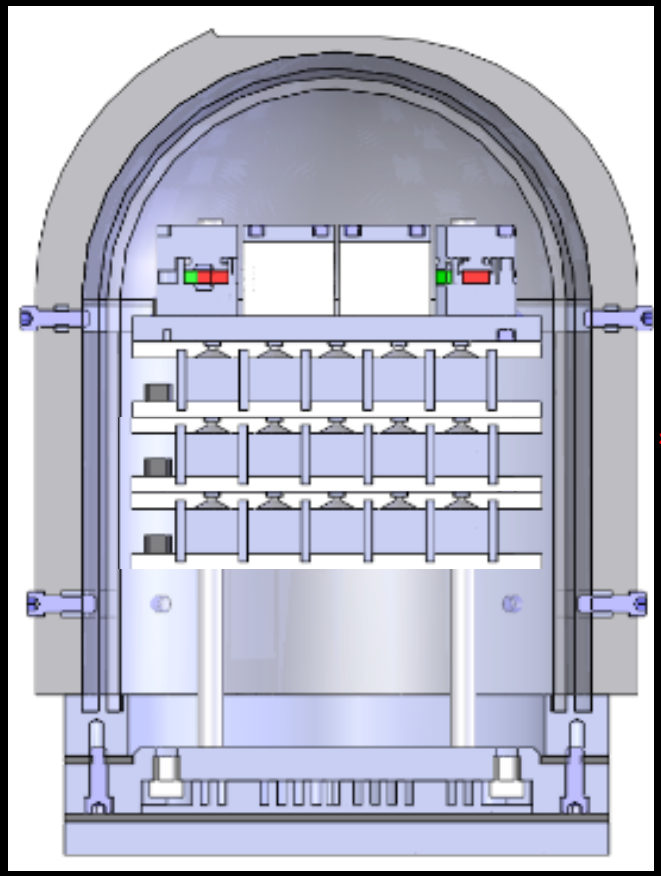
T1 relaxation results

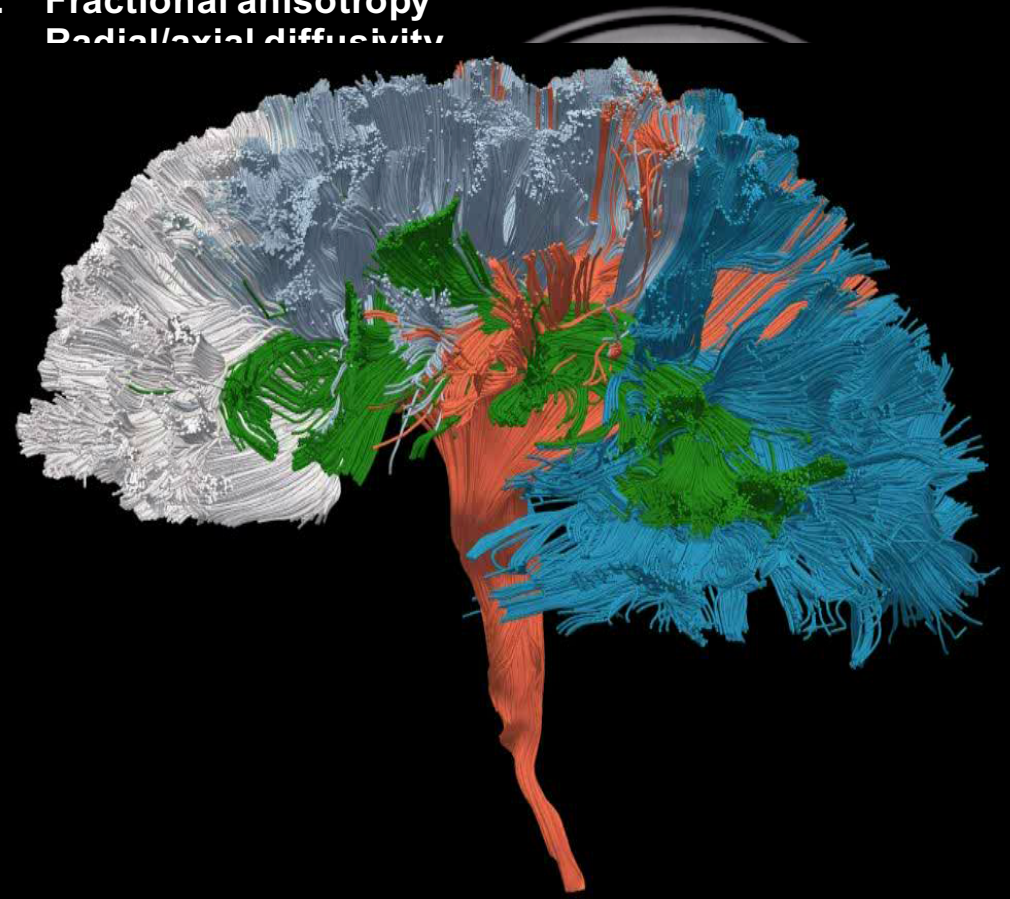


Target *in vivo* values from Rakow-Penner et al., JMRI 23(1):87-91, 2006

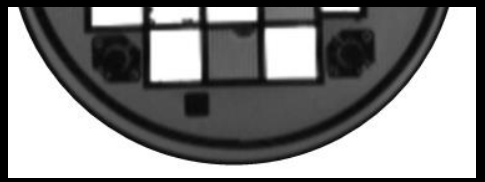
Future Directions: CENC "universal" phantom

1. Fractional anisotropy
2. Radial/axial diffusivity
3.
4.
5.





1.
2. Proton density
3. Apparent Diffusion Coefficient (ADC)

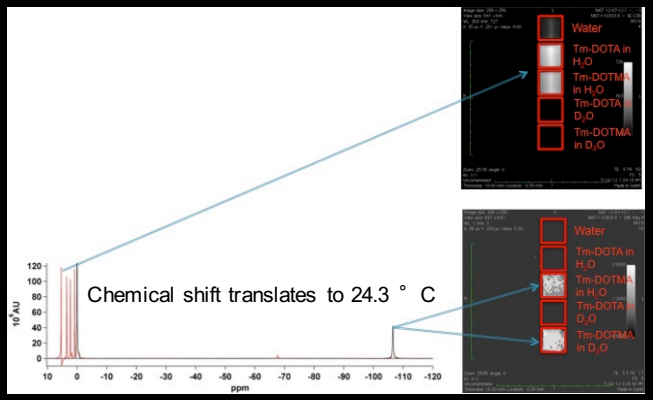


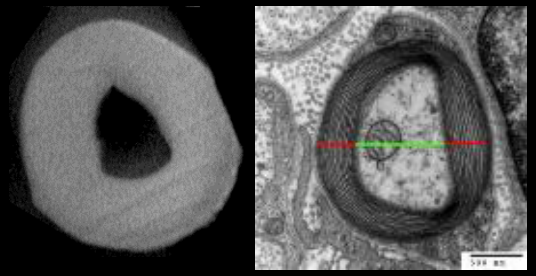
Veterans Health Administration R&D www.research.va.gov

CENC Chronic Effects of Neurotrauma Consortium

Future Directions: CENC "universal" phantom

Additional quantitative biomarkers



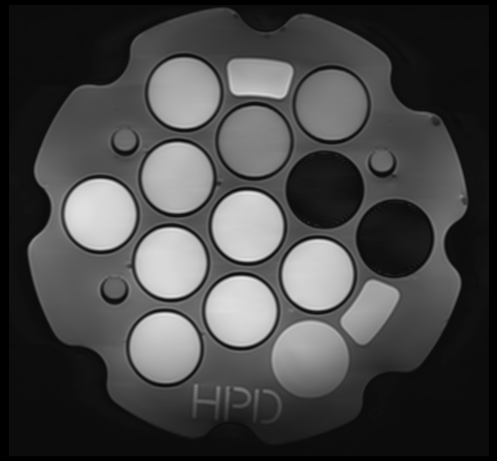


Need better biomimetic materials and structures

Develop novel techniques to interrogate additional physical parameters

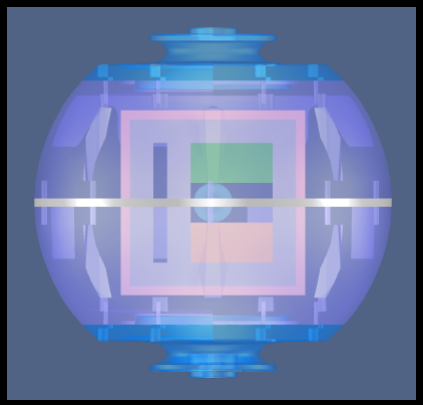
Future Directions: Additional Phantom Efforts

T2* / Dynamic Susceptibility Contrast
Phantom with RSNA-QIBA



Quantitative Imaging Biomarkers Alliance
RSNA

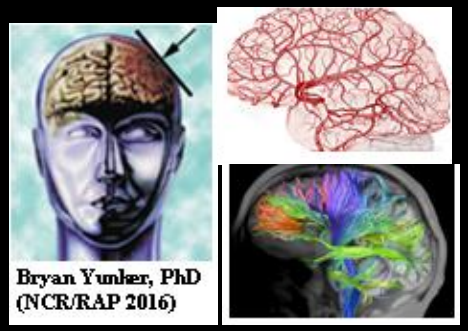
PET-MR phantom with NIST Gaithersburg and UCSF
Challenge: determining attenuation from MR for calculation of PET maps



Skin
Bone
Soft tissue 1
Soft tissue 2
Calibrated PET source

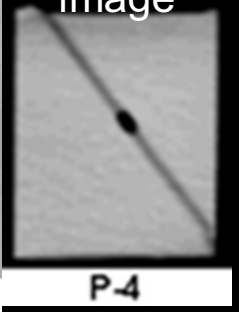
UCSF
University of California San Francisco

CT-Ultrasound-MR-PET Multimodality Phantoms
Challenge: discover materials that mimic tissue and impact damage across modalities



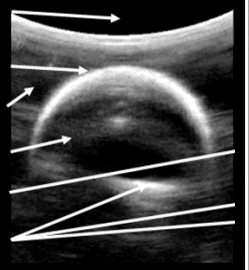
Sample

CT image

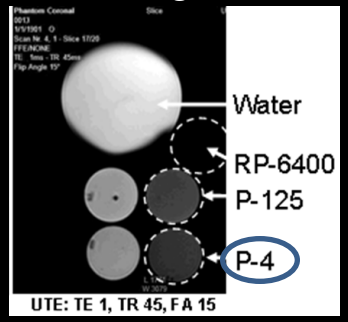


Industrial casting compound with water cavity

Ultrasound image



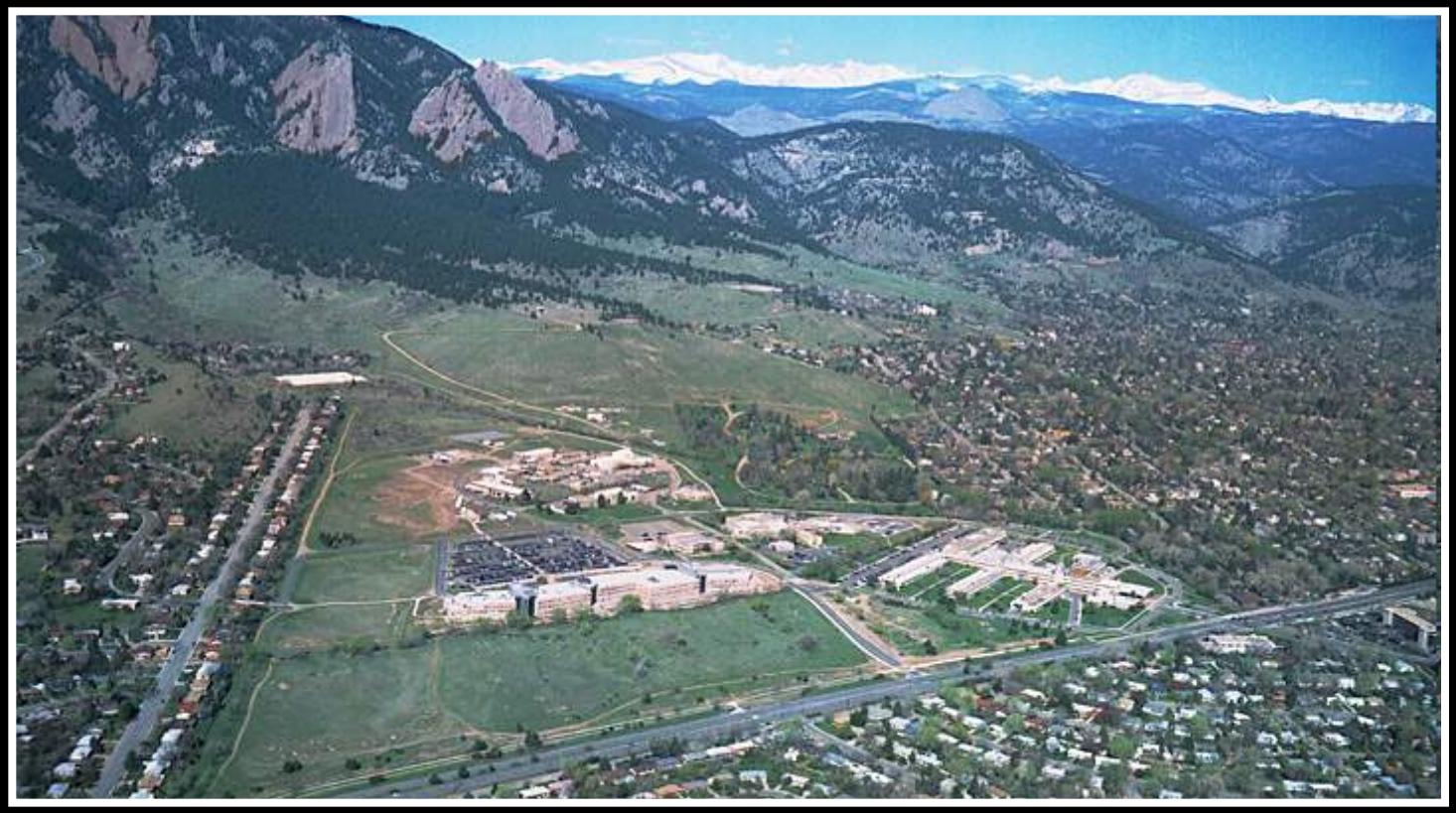
MR image



Conclusions

- **Goals: To provide long-term monitoring of traceable materials/objects that:**
  - Have ground truth
  - Sanity check for existing MR techniques
  - Expedite development of new imaging techniques
  - Improve patient care through non-invasive, reproducible measurement of physical parameters
- **Explored several approaches**
  - Professional societies
  - Round robins
  - Academic collaborators
  - SBIR, industrial partners
- **Disseminating NIST work worldwide**

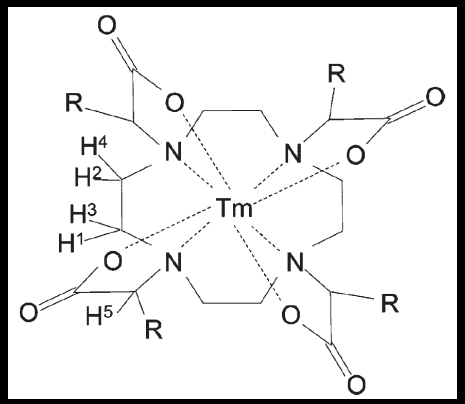
Thanks for your time!

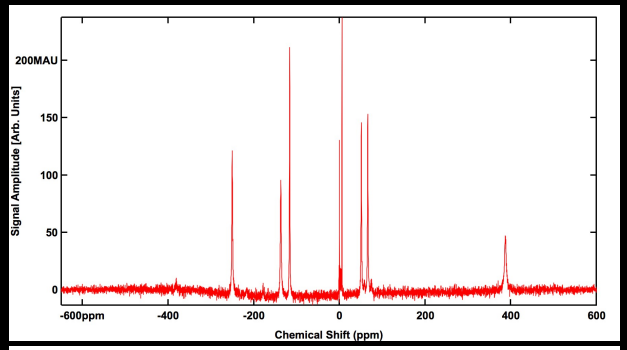


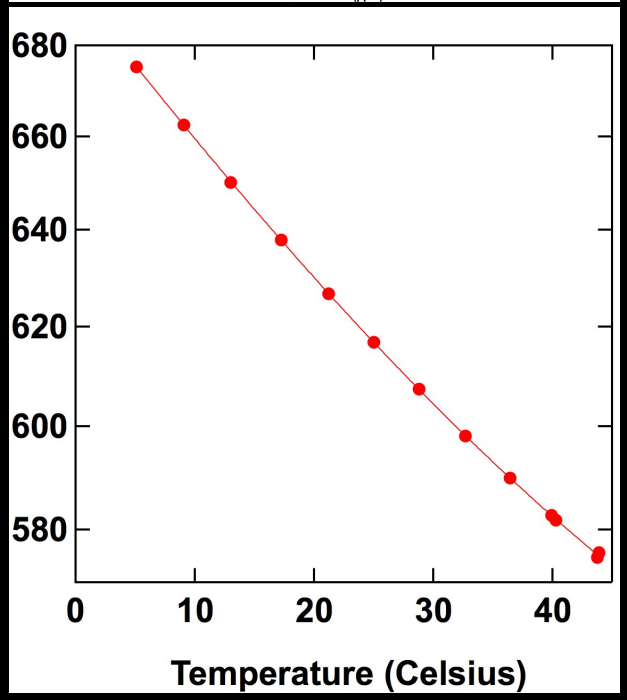
MR Thermometry

- ADC values can be very temperature dependent
- Need a way to measure temperature *in situ*
- Solution: thulium chelates, such as Tm-DOTA

Tm-DOTA







Ultra-Low Field (ULF) MRI Phantom

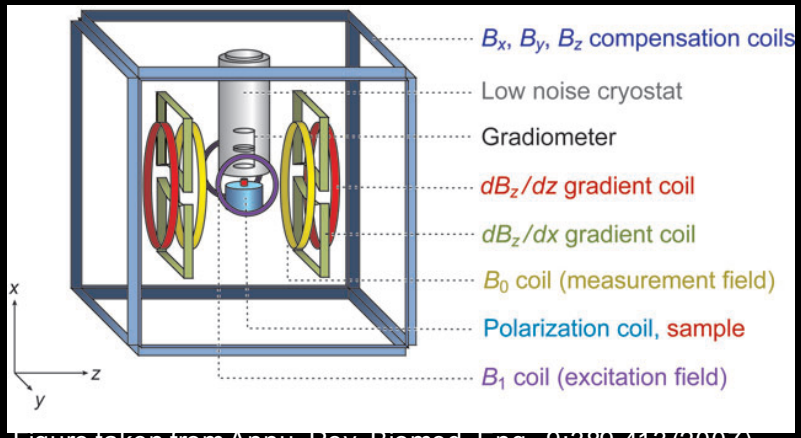
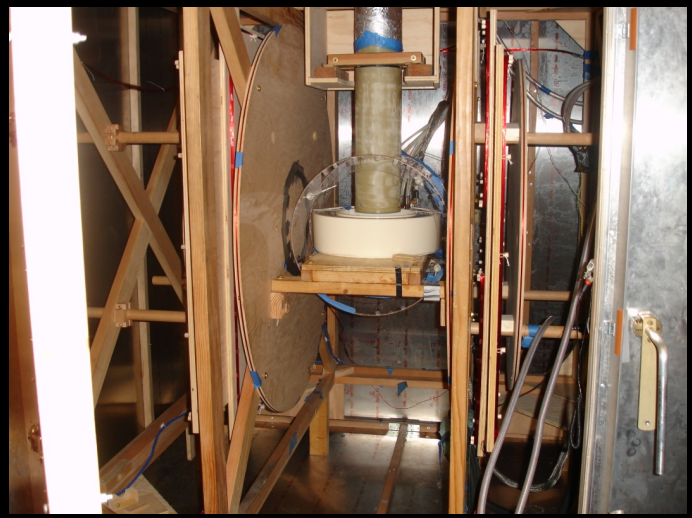
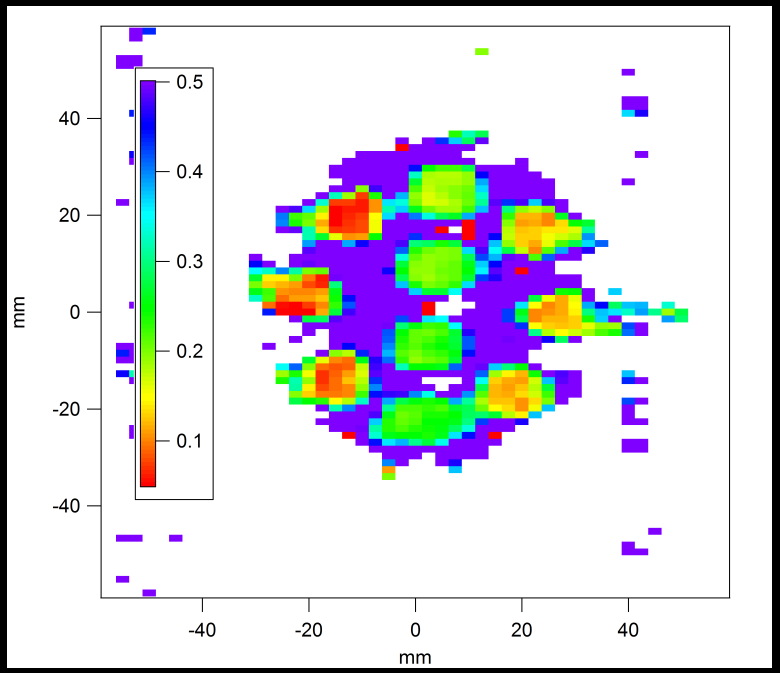


Figure taken from Annu. Rev. Biomed. Eng., 9:389-413 (2007)



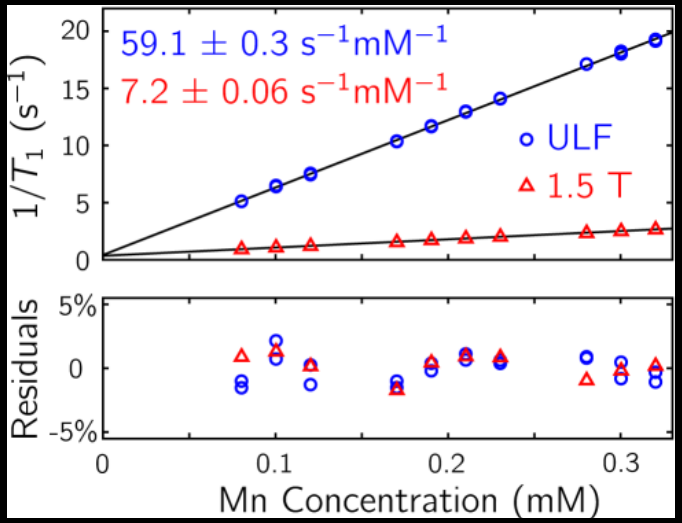
Ultra-Low Field (ULF) MRI Phantom

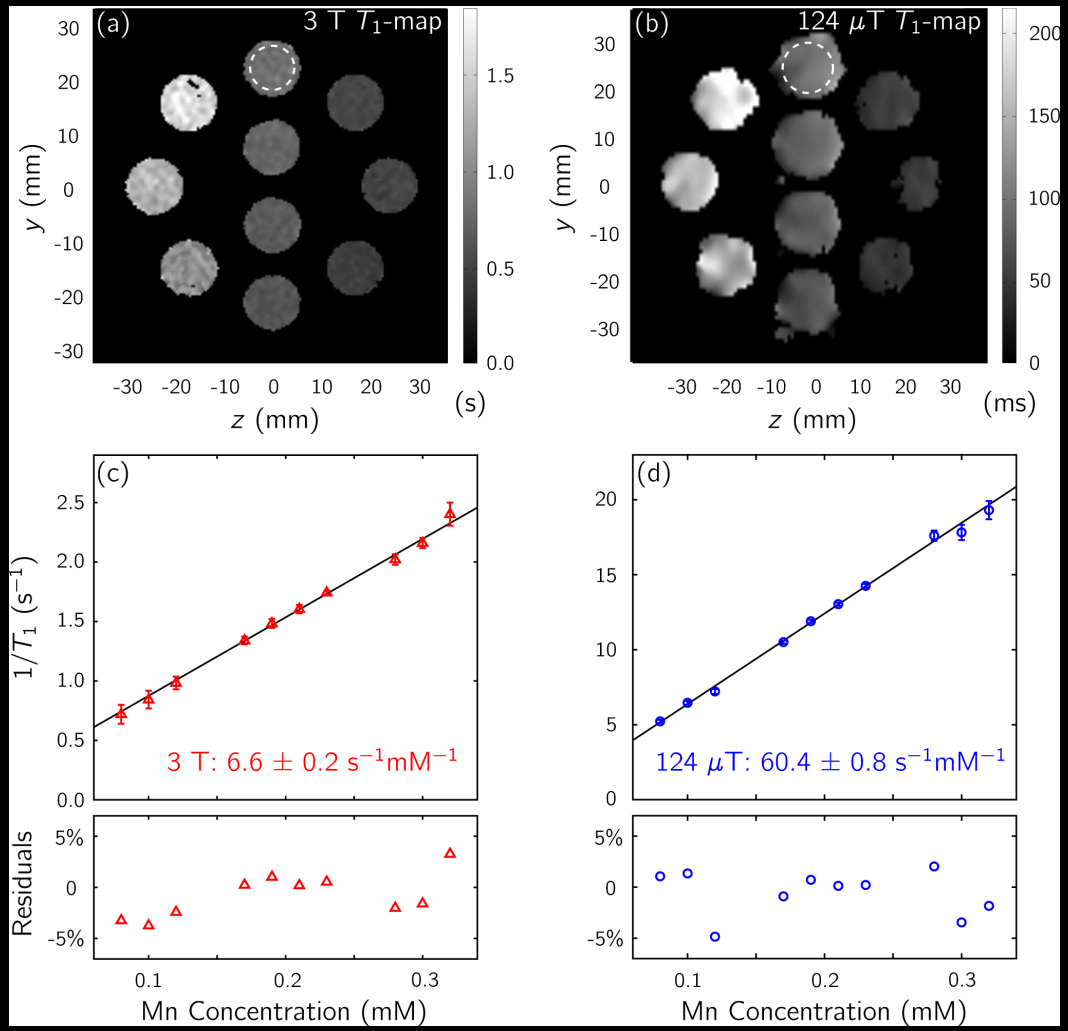
- At low field strengths, higher relaxivity -> greater contrast
- NIST ULF-MRI system
- Our phantom for ULF-MRI has been tested in collaboration with the John Clarke group at UC Berkeley
  - Low SNR at 132 µT makes scan times very long compared to clinical MRI
  - System stability is an issue raised by preliminary phantom data
  - Phantom will be crucial in assessing system performance both at Berkeley and here in Boulder



ULF-MRI at UC Berkeley: T_1

ULF-NMR and MRI T_1 data in good agreement





ULF-MRI at UC Berkeley: resolution