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State of the Art in Quantitative Imaging in CT, PET, and MRI

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THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

MDACC MR Research

Outline

- Technical challenges of MR quantitative imaging biomarkers (QIBs)
- Examples of clinical & clinical research MR QIBs
- Modality-specific barriers to using QIBs
- Examples of modality-specific solutions

- Educational Objectives:
  - Understand selected applications of QIBs
  - Understand factors that currently limit widespread acceptance and use of such QIBs, including sources of bias and variance
  - Understand some of the current initiatives focused on the standardization, qualification, and validation of selected QIBs

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General Challenges in MR Quantification

Arbitrary (and spatially- / temporally-dependent) signal intensity units

- Magnitude and homogeneity of B_o
- Magnetic field gradient nonlinearity and/or miscalibration
- RF coil dependency: RF coil type, B_1 sensitivity profiles, subject positioning within the coil, dielectric effects (≥3.0T)
- Slice profile variations (with RF pulse shape, flip angle, *etc*.)
- System stability issues (RF & gradient subsystems, B_o, RF coils, *etc*.)

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B_o Magnitude & Homogeneity

- In general, increasing B_0 => increasing signal
- B_0 inhomogeneity yields:
  - spatially variant signal intensities in general and spatially variant fat suppression when chemically selective saturation methods are utilized.
  - Particularly poor quality of echo-planar imaging and MR spectroscopy results

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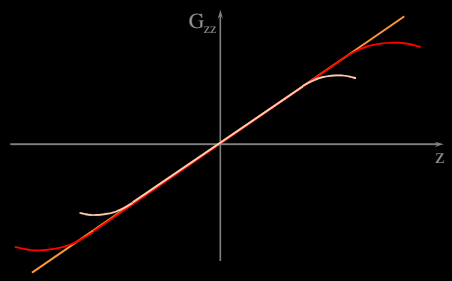
Gradient Field Nonlinearities



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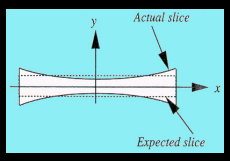
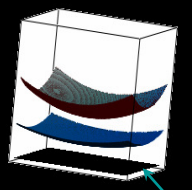
Gradient Field Nonlinearity Effects

In-Plane

Through-Plane

Through-Plane





Slice at isocenter

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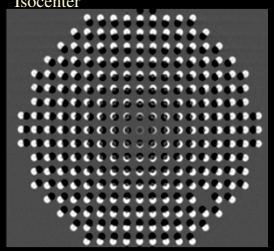
Reference: Sumanaweera TS et al., Neurosurgery 35(4):696-703, 1994

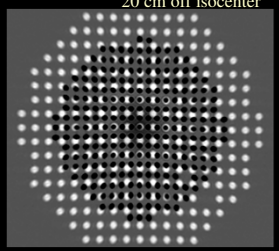
Gradient Field Nonlinearity Effects

20 cm FOV, white: w/correction, black: w/o correction

Isocenter

20 cm off isocenter





$Error_{max}$ with correction: < 1 mm @ ± 10 cm
$Error_{max}$ w/o correction: ~ 4.5mm @ ± 10 cm

$Error_{max}$ with correction: < 2 mm @ ± 10 cm
$Error_{max}$ w/o correction: ~ 5.5cm @ ± 10 cm

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Primary Limits on Spatial Accuracy

- System Limitations
  - Poor B_o homogeneity
  - Linear scale factor errors in the gradient fields
  - Field distortion due to induced eddy currents
  - Nonlinearities of the gradient fields
- Object-Induced
  - Chemical shift effects (fat / water displacement, in-plane and slice)
  - Intravoxel magnetic susceptibility differences (particularly air-tissue)
  - Effects are minimized with non-vendor specific appropriate acquisition parameters (increased BW, smaller FOV), but at the expense of SNR. [Importance of Technique!]

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General Challenges in MR Quantification

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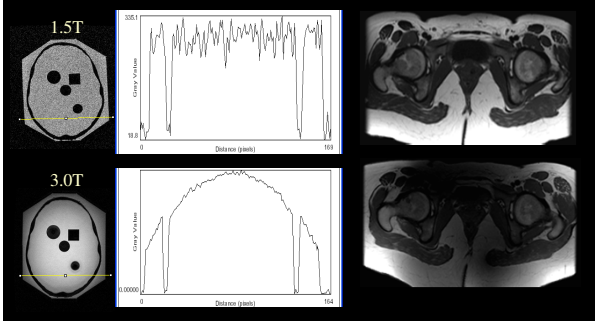
B_1 Non-Uniformity

B_1 response non-uniformity & dielectric resonance effects



General Challenges in MR Quantification

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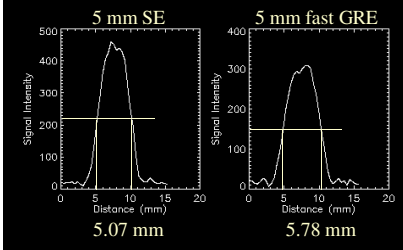
General Challenges in MR Quantification

Slice profile variations (with RF pulse shape, flip angle, *etc*.)



Typically, faster imaging sequences use increasingly truncated RF pulses resulting in thicker slice profiles for a given prescribed slice thickness. This gives rise to increased partial volume effects.

Flip angle calibrations can also be negatively affected.

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General Challenges in MR Quantification

Arbitrary (and spatially- / temporally-dependent) signal intensity units

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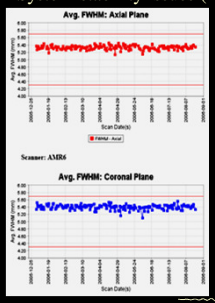
General Challenges in MR Quantification

System stability issues (RF & gradient subsystems, B_o, RF coils)



For quantitative imaging, particularly in longitudinal studies, a rigorous quality control program is critical.

Key components of frequent QC tests:

- Geometric accuracy
- Slice thickness
- Signal-to-noise ratio
- Uniformity
- High contrast spatial resolution
- Center frequency
- Transmit gain
- Contrast response

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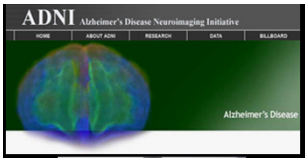
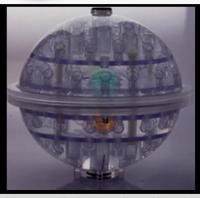
ADNI





Sphere ID	Color	Number of Spheres	Grams of Copper Sulfate Penta Hydrate per liter	Target T1 (ms)
1.0cm	none	138	0.820	
1.5cm	none	2	0.820	
3.0cm	green	1	0.220	900
3.0cm	yellow	1	0.295	750
3.0cm	red	1	0.430	600
3.0cm	orange	1	0.590	450
6.0cm	none	1	0.820	

- Multicenter, multivendor study
- Optimized pulse sequence / acquisition parameters for each platform
- MagPhan/ADNI phantom scan at each measurement point
- Access to vendor gradient correction parameters
- With full correction for gradient nonlinearities and optimized acquisition strategies, spatial accuracies of ~0.3 mm can be obtained over a ~180 mm spherical volume

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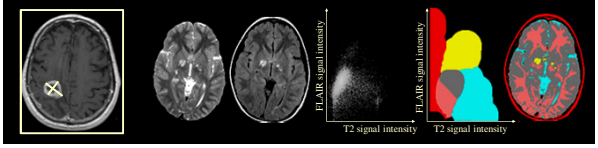
Current MR QIB Applications

Currently available MR QIBs:

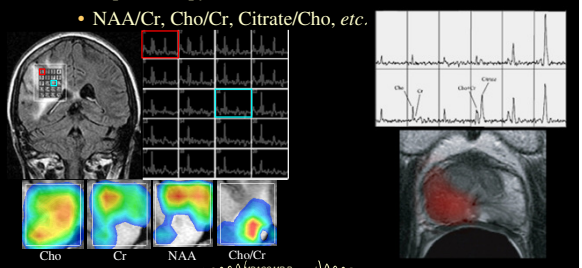
- Lesion size assessment for treatment response
  - Lesion dimension (single, dual)
    - RECIST: Response Evaluation Criteria in Solid Tumors
    - RANO: Revised Assessment in Neuro-Oncology
  - Lesion segmentation (volume calculations)
    - Single feature (single weighting) - Rare
    - Multi-feature (multiple weightings) - Very rare



Current MR QIB Applications

Currently available MR QIBs:

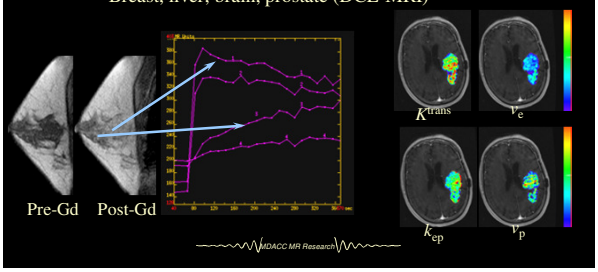
- MR Spectroscopy
  - NAA/Cr, Cho/Cr, Citrate/Cho, *etc.*



Current MR QIB Applications

Currently available MR QIBs:

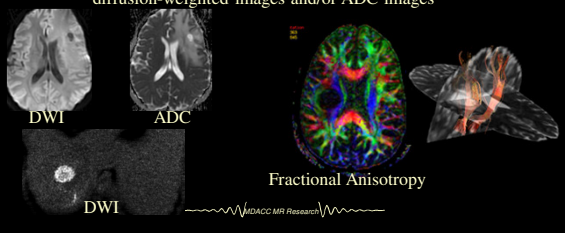
- Multiphase dynamic contrast enhanced T1-weighted MRI
  - Breast, liver, brain, prostate (DCE-MRI)



Current MR QIB Applications

Currently available MR QIBs:

- Diffusion MRI
  - Apparent diffusion coefficient (ADC)
  - Quantitative ADC seldom used clinically; qualitative review of diffusion-weighted images and/or ADC images



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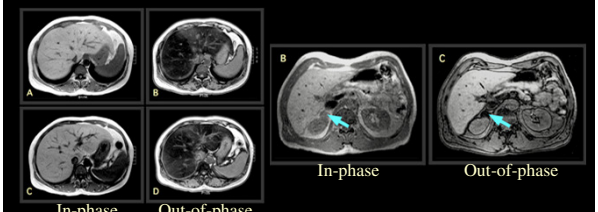
Current MR QIB Applications

Currently available MR QIBs:

- In-phase / out-of-phase imaging
  - Fatty infiltration (liver, adrenal gland)



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http://limpeter-mriblog.blogspot.com/

Current MR QIB Applications

Currently available MR QIBs:

- Flow (macroscopic)
  - Phase-sensitive MRA
    - Flow direction, speed, time-resolved (cine)

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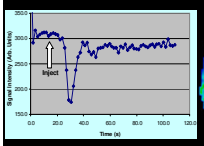
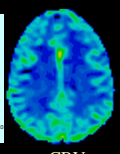
Current MR QIB Applications

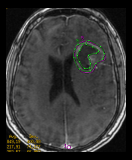
Currently available MR QIBs:

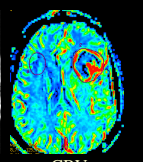
- Flow (microscopic)
  - Perfusion MRI
    - T2*-weighted Gd-enhanced DSC-MRI in brain
    - Arterial spin labeling





rCBV





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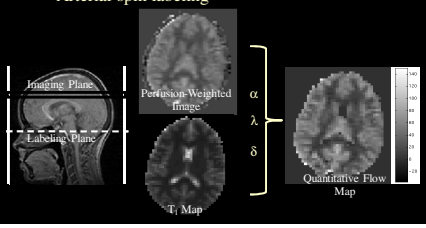
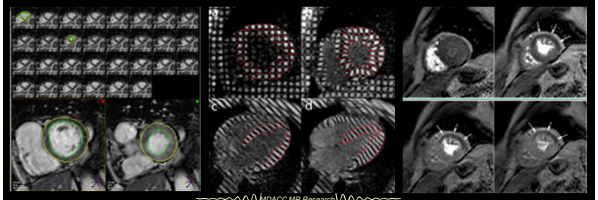


Current MR QIB Applications

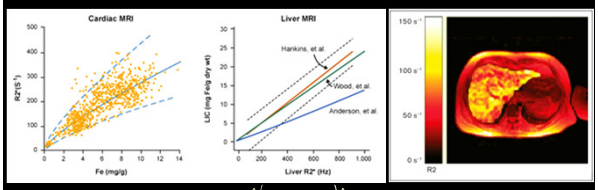
Currently available MR QIBs:

- Cardiac cine MR
  - Ejection fraction, wall thickness, *etc.*
  - Tagging – myocardial stress/strain
  - Delayed enhancement – myocardial perfusion



Current MR QIB Applications

Currently available MR QIBs:
- Iron load
  - Multi-echo T2*-weighted
    - Liver, cardiac



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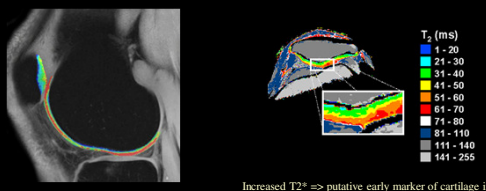
http://www.ironhealthalliance.com/diagnostics/lic-measuremen.jsp

Current MR QIB Applications

Currently available MR QIBs:
- Cartilage assessment
  - Ultrashort TE multiecho T2*-weighted



Increased T2* => putative early marker of cartilage injury

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https://irc.cchmc.org/research/msk/cartilage.php

Wow…this is great…

…so why aren't we routinely *using* all these cool MR QIBs in the clinic???

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- Technical challenges of MR quantitative imaging biomarkers (QIBs)
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Challenges for MR QIBs

- General MR QIB challenges – in addition to cost
  - Lack of detailed assessment of sources of bias and variance
  - Lack of standards (acquisition, data processing, and reporting)
    - Varying measurement results across vendors and centers
  - Lack of support from imaging equipment vendors
    - Varying measurement results across vendors
    - Varying measurement results across time for any particular vendor
  - Highly variable quality control procedures
    - Varying measurement results across centers
- Raising the bar: From morphological to functional MR QIBs
  - DCE-MRI and DSC-MRI (microvascular extraction-flow, volume, *etc.*)
  - Diffusion MRI (cellular density, cell volume fraction)
  - MR Spectroscopy (biochemical concentrations)
  - BOLD MRI (oxy- / deoxyhemoglobin ratio)

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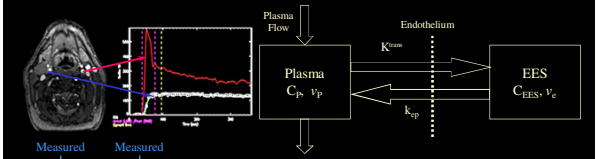
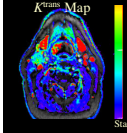
Dynamic contrast enhanced MRI



$$C_L(t) = v_P C_P(t) + v_e C_{EES}(t)$$

$$C_{EES}(t) = K^{trans} \int_0^t C_P(t')\ e^{-k_{ep}(t-t')}\ dt'$$



C_P = [Gd] in plasma (mM) = C_b / (1-Hct)
C_{EES} = [Gd] in extravascular, extracellular space (mM)
K^{trans} = endothelial transfer constant (min^{-1})
k_{ep} = reflux rate (min^{-1})
v_P = fractional plasma volume, v_e = fractional EES volume (= K^{trans} / k_{ep})

Standardized parameters as proposed by Tofts *et al., J Magn Reson Imaging*, 10:223-232, 1999.

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What are the challenges with DCE-MRI?

Signal intensity data from tumor and vascular ROIs

$$\Delta R_1 = \frac{1}{TR}\ln\frac{\left(1-\cos\alpha\, e^{-TR R_{1,0}}\right)-\frac{S}{S_0}\cos\alpha\left(1-e^{-TR R_{1,0}}\right)}{\left(1-\cos\alpha\, e^{-TR R_{1,0}}\right)-\frac{S}{S_0}\left(1-e^{-TR R_{1,0}}\right)} - R_{1,0}$$

$$[Gd] = \frac{R_1 - R_{1,0}}{r_1} = \frac{\Delta R_1}{r_1}$$

$$C_L(t) = \frac{K^{trans}\int_0^t C_P(t')e^{-k_{ep}(t-t')} + v_P C_P(t)}{1-Hct}$$

Determine v_P, K^{trans}, and k_{ep}, from non-linear fitting of $C_L(t)$ and $C_P(t)$ data

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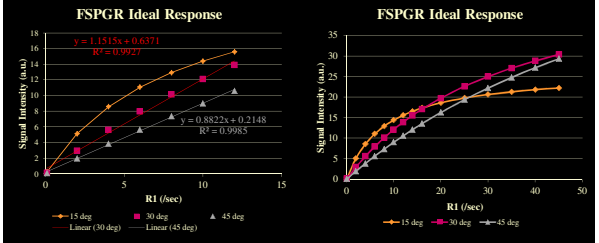
What are the challenges with DCE-MRI?

Theoretical Response (ignoring R2*)



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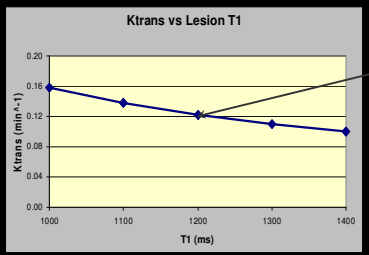
K^{trans} Simulations – T_1 Dependence



%diff T1	%diff Ktrans
-16.7	28.7
-8.3	12.6
0.0	0.0
8.3	-10.1
16.7	-18.3

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DCE-MRI data acquisition challenges

- Pulse sequence
  - Contrast response must be well characterized and maintained for duration of study (or a process for compensation for changes must be developed)
- Temporal resolution
  - Must match choice of pharmacokinetic model and parameters of interest
    - Must be rapid (≤~2-5 s) for generalized kinetic model with estimation of v_p
    - Recommended to be ≤10 s for any pharmacokinetic model
- T1 measurements
  - Required if contrast agent concentration is used in modeling
  - Must be obtained in reasonable scan time
  - Must be robust as uncertainties in T1 estimates propagate to output measures

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DCE-MRI data acquisition challenges

- Spatial resolution
  - Must be adequate for target lesion size and application
- Anatomic coverage
  - Should fully cover target lesion(s) & include appropriate vascular structure
- Motion
  - Effects should be mitigated prospectively during acquisition and/or retrospectively, *e.g.*, rigid body or deformable registration

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DCE-MRI data analysis challenges

Many choices to be made, each impacting bias and variance:

- Mitigation of motion effects (if necessary)
  - Retrospective (rigid body, deformable)
- Vascular input selection
  - Manual ROI vs. automated identification of vascular structure pixels
  - Reproducibility
- Lesion ROI(s)
  - Definition criteria
  - Reproducibility
- Fits of single averaged pixel uptake curve or pixel-by-pixel fits
- Modeling of: gadolinium concentration (requiring T1 mapping) or simple change in signal intensity data
- Reporting of results (structured reporting)

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General As Yet Unmet Needs

To move MR QIBs from exploratory / secondary endpoints to primary endpoints / surrogate markers:

- Sources of bias and variance need to be well understood and effects mitigated to the degree needed.
- There exists a need for standardized acquisition pulse sequences and analysis techniques for MR QIB studies.
- Validated phantoms (physical & digital) and test data need to be available to users in order to test new releases of pulse sequences and analysis software. (For each MR QIB of interest.)

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General As Yet Unmet Needs

To move MR QIBs from exploratory / secondary endpoints to primary endpoints / surrogate markers:

- Imaging biomarker to tissue-based and outcome measure comparisons are needed for validation.
- Reproducibility (test/retest) studies are lacking in several key areas.

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Quantitative Imaging Biomarkers – First Steps

NIST USMS Workshop 2006
Representative Agencies / Organizations

Quantitative MR Imaging Initiatives

- NCI: RIDER and Academic Center Contracts
- NCI: Imaging Response Assessment Team (IRAT)
- RSNA: Quantitative Imaging Biomarker Alliance
- ISMRM: *Ad Hoc* Committee on Standards for Quantitative MR
- AAPM: Quantitative Imaging Initiative / Working Group for Standards for Quantitative MR Measures
- NCI: Quantitative Imaging Initiative (QIN)
- Core Labs: ACRIN, CROs, *etc*.

National Cancer Institute
Cancer Imaging Program

NCI RIDER

NCI Cancer Imaging Program **RIDER**

- Reference Image Database to Evaluate Response
- Collaborative project for development and implementation of a caBIG public resource
- Series of 4 manuscripts (intro, CT, PET, MR) plus an editorial in *Translational Oncology* (Dec 2009) with data made publically available through NCIA (phantom and anonymized clinical trial imaging and meta data)

https://wiki.nci.nih.gov/display/CIP/RIDER

NCI RIDER – Available Data

National Cancer Institute
Cancer Imaging Program

UNIVERSITY OF MICHIGAN — Charles Meyer

- Images contained in "RIDER Breast MRI" Collection
- Repeat measurements: Human subjects: Breast
- DCE MRI
- ISMRM 2009 poster demonstrates how each of the "coffee break" exams were used as an estimate of each patient's null hypothesis i.e. distribution associated with no change, and thus supports the estimate of the null's 97.5 percentile for subsequent estimation of early response to neoadjuvant chemotherapy on an individual patient basis.

DUKE UNIVERSITY — Daniel Barboriak

- Images contained in "RIDER Neuro MRI" Collection
- Repeat human subject studies: Neuro
- Dynamic Contract Enhanced studies: DCE MRI:
- Diffusion weighted imaging: DWI MR
- Diffusion tensor imaging: DT MRI.

MDACC — Edward Jackson

- Images contained in "RIDER Phantom MRI" Collection
- Repeat measurement: Phantom studies
- DCE MRI
- RIDER_MR_Phantom_Data_Summary.pdf provides a summary of the images in this collection.
- RIDER_PhantomMR_Key.pdf provides a key for understanding their presentation in NBIA.

https://wiki.nci.nih.gov/display/CIP/RIDER

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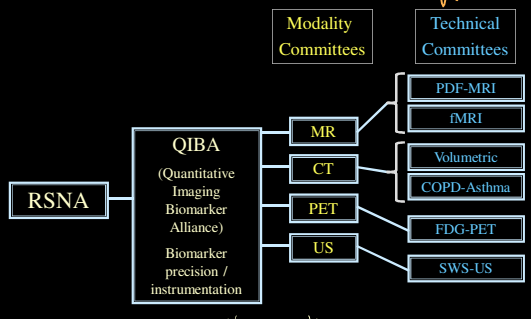
RSNA QIBA Structure



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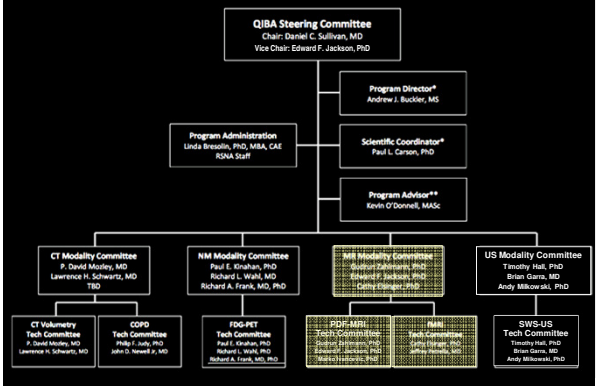
www.qibawiki.rsna.org

RSNA QIBA Structure



RSNA QIBA Approach

- Mission
  - Improve the value and practicality of quantitative imaging biomarkers by reducing variability across devices, patients, and time.
- Four components:
  - Identify sources of error and variation in quantitative results from imaging methods
  - Specify potential solutions
  - Test solutions
  - Promulgate solutions
- ~$1M / year investment by RSNA

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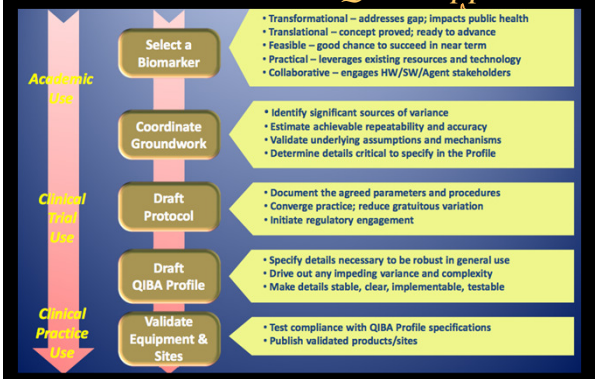
RSNA QIBA Approach



RSNA QIBA Approach

- QIBA Profiles
  - describe a specific performance claim and how it can be achieved
  - Claims: tell a user what can be accomplished by following the Profile.
  - Details: tell a vendor what must be implemented in their product; and tell a user what procedures are necessary.
- QIBA (UPICT) Protocols
  - describe how clinical trial subjects or patients should be imaged so as to achieve reproducible quantitative endpoints when those tests are performed utilizing systems that meet the specific performance claims stated in the QIBA Profiles

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RSNA QIBA Approach

- Other RSNA QIBA efforts
  - Meetings with equipment vendors
  - Education / raise awareness of quantitative imaging (radiologists, *etc*.)
  - Working with the FDA to qualify quantitative imaging biomarkers
    - First steps: Biomarker Qualification Review Team (BQRT) meetings
  - Securing (limited) funding for support of projects from the Technical Committees, *e.g*., 2-yr NIBIB contract

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RSNA QIBA Profiles

- Major components of a profile:
  - Executive Summary
  - Clinical Context and Claim(s)
  - Profile Details
    - Subject handling, imaging procedure, image post-processing, parametric image formation and analysis, archival and distribution of data, quality control, risks and risk management
  - Compliance
    - Acquisition, ancillary equipment, e.g., injectors, data analysis procedures, performance site requirements, *etc*.
  - Appendices, including model-specific instructions and parameters

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RSNA QIBA Profiles

- DCE-MRI Profile
  - Title: *Profile: DCE MRI Quantification*
  - Claim:

    Quantitative microvascular properties, specifically transfer constant (K^{trans}) and blood normalized initial area under the gadolinium concentration curve ($IAUGC_{BN}$), can be measured from DCE-MRI data obtained at 1.5T using low molecular weight extracellular gadolinium-based contrast agents within a 20% test-retest coefficient of variation for solid tumors at least 2 cm in diameter.
  - Applications:

    Profile specified for use with: **patients with malignancy**, for the following indicated biology**: primary or metastatic**, and to serve the following purpose: **therapeutic response**.

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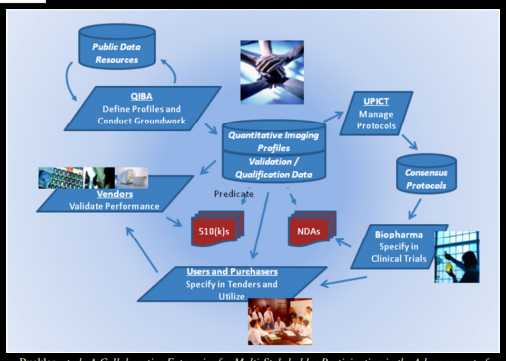

Buckler, *et al., A Collaborative Enterprise for Multi-Stakeholder Participation in the Advancement of Quantitative Imaging*, submitted, Radiology 258:906-914, 2011

RSNA QIBA Projects – Round 1

Modality	Institution	Project Title	Primary Investigator
MR			
DCE-MRI	Duke University Medical Center	Digital Reference Object for DCE-MRI analysis software verification	Daniel Barboriak, MD
	The University of Texas M.D. Anderson Cancer Center	DCE-MRI Phantom Fabrication, Data Acquisition and Analysis, and Data Distribution	Edward Jackson, PhD
	VirtualScopics, Inc.	Software Development for Analysis of QIBA DCE-MRI Phantom Data	Edward Ashton, PhD
fMRI	Duke Brain Imaging and Analysis Center	Quantitative Measures of fMRI Reproducibility for Pre-Surgical Planning - Development of Reproducibility Metrics	James Voyvodic, PhD
	Medical College of Wisconsin	Quantitative Measures of fMRI Reproducibility for Pre-Surgical Planning – Long Term and Functional Reproducibility	Edgar DeYoe, PhD
NM			
FDG-PET-CT	Johns Hopkins University School of Medicine	Analysis of SARC 11 Trial PET Data by PERCIST with Linkage to Clinical Outcomes	Richard Wahl, MD
	University of Washington	QIBA FDG-PET/CT Digital Reference Object Project	Paul Kinahan, PhD
	VU University Medical Center, The Netherlands	Meta-analysis to analyze the robustness of FDG SUV changes as a response marker, post and during systemic and multimodality therapy, for various types of solid extracerebral tumors	Otto S. Hoekstra, MD, PhD
CT			
VOL-CT	Columbia University Medical Center	Validation of Volumetric CT as a Biomarker for Predicting Patient Survival	Binsheng Zhao, DSc
	David Geffen School of Medicine at UCLA, Department of Radiology	Assessing Measurement Variability of Lung Lesions in Patient Data Sets	Michael McNitt-Gray, PhD
	Duke University Medical Center	Development of Assessment and Predictive Metrics for Quantitative Imaging in Chest CT	Samuel Richard, PhD
	University of Colorado Denver, Department of Radiology	Quantifying variability in measurement of pulmonary nodule (solid, part-solid and ground glass) volume, longest diameter and CT attenuation resulting from differences in reconstruction thickness, reconstruction plane, and reconstruction algorithm.	Kavita Garg, MD
	SUB-AWARDS:	Inter-scanner/inter-clinic comparison of reader nodule sizing in CT imaging of a phantom	Charles Fenimore, PhD (Project Mgr)

RSNA QIBA MR Projects

Round 1

Modality	Institution	Project Title	Primary Investigator
MR			
DCE-MRI	Duke University Medical Center	Digital Reference Object for DCE-MRI analysis software verification	Daniel Barboriak, MD
	The University of Texas M.D. Anderson Cancer Center	DCE-MRI Phantom Fabrication, Data Acquisition and Analysis, and Data Distribution	Edward Jackson, PhD
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	Medical College of Wisconsin	Quantitative Measures of fMRI Reproducibility for Pre-Surgical Planning – Long Term and Functional Reproducibility	Edgar DeYoe, PhD

Round 2

DCE-MRI	ACR / UPenn	Test-Retest Evaluation of Repeatability of DCE-MRI and DWI in Human Subjects	Mark Rosen, MD, PhD
fMRI	Johns Hopkins University	Validation of Breath Hold Task for Assessment of Cerebrovascular Responsiveness and Calibration of Language Activation Maps to Optimize Reproducibility	Jay Pillai, MD

RSNA QIBA Phantom & Analysis SW

- RSNA QIBA: DCE-MRI Technical Committee
  - Phantom measurements:
    - Phased array acquisition
    - Body coil acquisition
    - SNR acquisition
    - VFA T1 measurement acquisition
    - DCE acquisition

  Ratio map correction for B_1 sensitivity characteristics
  - Each of the above acquisitions repeated with phantom rotated by 90, 180, 270, and 360°
  - All acquisitions repeated one week later
  - Data from 4 vendors at 3 centers
  - Core lab data analysis (VirtualScopics)

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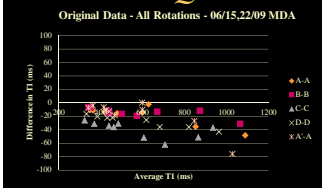
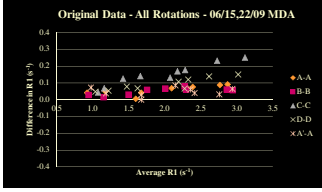
http://qibawiki.rsna.org/index.php?title=DCE-MRI

RSNA QIBA Phantom & Analysis SW

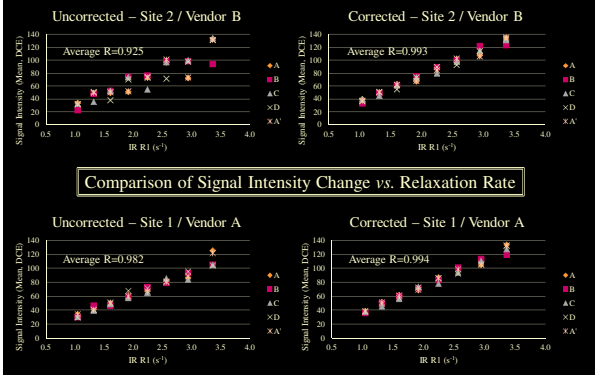


Difference in T1 from each contrast sphere, week 1 minus week 0.



Difference in R1 from each contrast sphere, week 1 minus week 0.

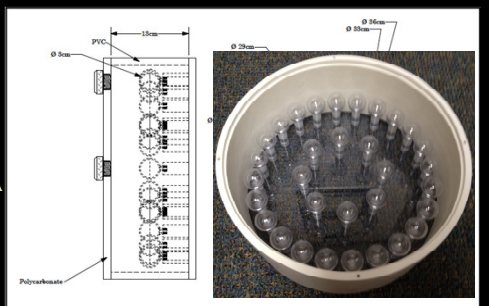
RSNA QIBA – Multiple Vendors / Three Time Points



RSNA QIBA Phantom & Analysis SW

Commercialized version of QIBA DCE-MRI phantom

Funded by RSNA / NIBIB contract; PI: E. Jackson, MDACC

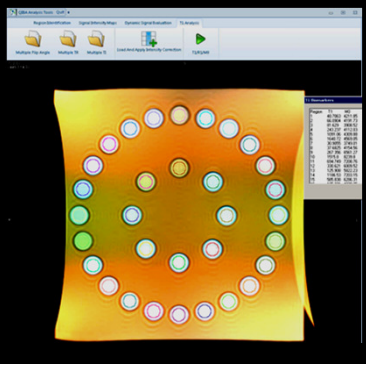


RSNA QIBA Phantom & Analysis SW

Phantom data analysis software – initial release

- Auto ROI determination
- Signal intensity correction
- R1 analysis (VFA, VTI, VTR)
- DCE analysis

Funded by RSNA / NIBIB contract; PI: Ed Ashton, VirtualScopics



RSNA QIBA Digital Reference Object

- NIBIB/RSNA Subcontract – Round 1 (PI: D. Barboriak, Duke)
  - Develop DROs for:
    - DCE-MRI signal intensity curves corresponding to varying K^{trans}, v_e, v_p, and k_{ep} values (with varying S_0 values, sampling interval, jitter, noise)
    - T1 mapping data with varying T1 and equilibrium magnetization values (with and without added noise)
  - Can be used for comparison / qualification of DCE-MRI analysis software packages.

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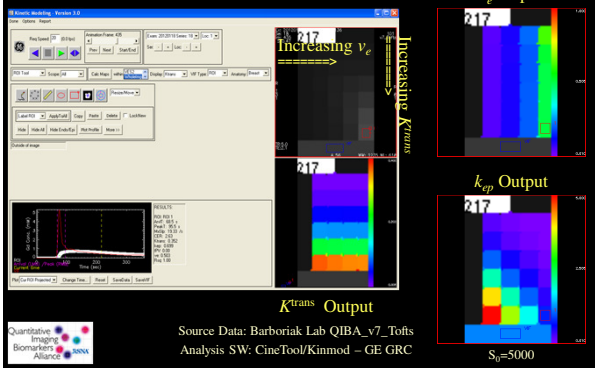
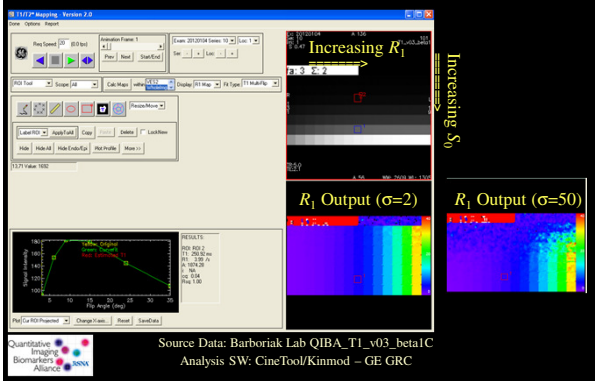
RSNA QIBA Digital Reference Object



Source Data: Barboriak Lab QIBA_v7_Tofts
Analysis SW: CineTool/Kinmod – GE GRC

RSNA QIBA Digital Reference Object



Source Data: Barboriak Lab QIBA_T1_v03_beta1C
Analysis SW: CineTool/Kinmod – GE GRC

RSNA QIBA Test/Retest Protocol

- NIBIB/RSNA Subcontract – Year 2 (M. Rosen, UPenn)
- Primary goals and objectives – *in vivo* test/retest protocol
  - 1) Determine the test-retest performance, as assessed by the coefficient of variation, of the median pixel values of K^{trans} and $IAUGC_{bn}$, using the whole prostate as the target "tumor".
  - 2) Determine the test-retest performance, as assessed by the coefficient of variation, of the median pixel value of *ADC* using the whole prostate as the target "tumor".
- ACRIN Protocol 6701

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ISMRM Ad Hoc Committee

- ISMRM: *Ad Hoc* Committee for Standards for Quantitative MR
  - Membership includes MR physicists, technologists, radiologists, NIST representatives, NIH representatives, vendors, pharma. Expertise in research trials using quantitative MR.
  - Current status:
    - White paper on quantitative MR
    - Design specifications & construction of a MR system phantom (collaboration with and funding by NIST)
    - Initial multicenter/multivendor phantom pilot studies

http://wiki.ismrm.org/twiki/bin/view/QuantitativeMR/

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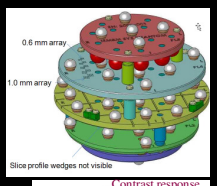
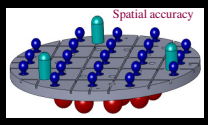
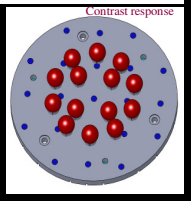
ISMRM/NIST System Phantom



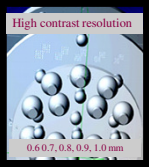
Spatial accuracy



Contrast response

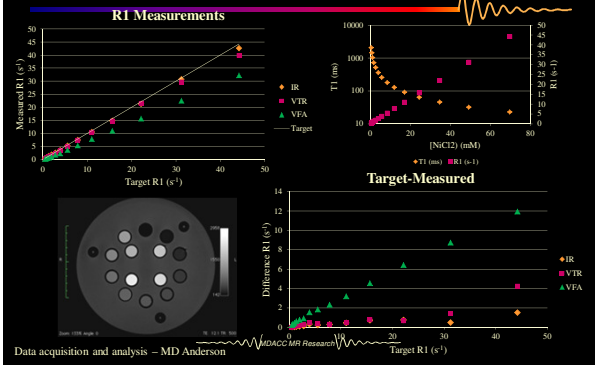


High contrast resolution



Section thickness, 10^0 ramps

R1 Measurements



Data acquisition and analysis – MD Anderson

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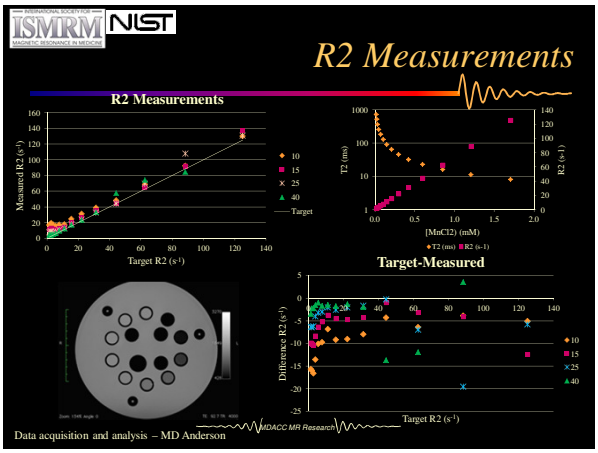
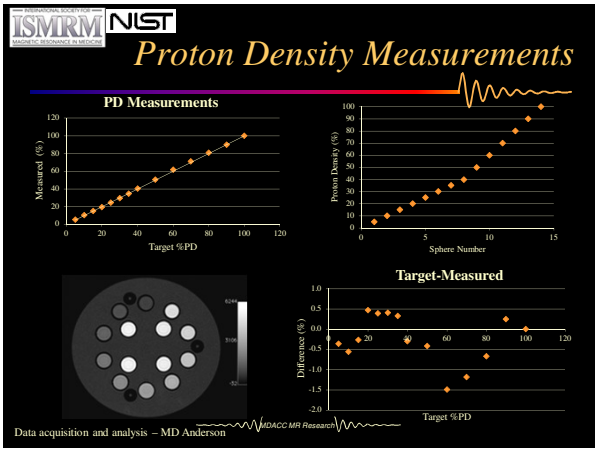
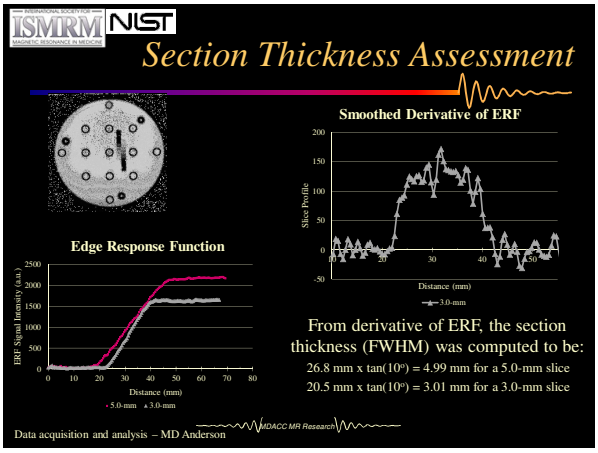
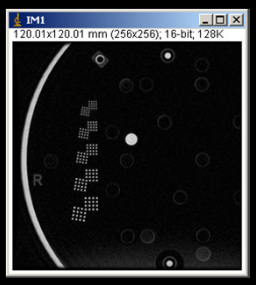

ISMRM
NIST
R2 Measurements
R2 Measurements
Measured R2 (s-1)
Target R2 (s-1)
10
15
25
40
Target
T2 (ms)
R2 (s-1)
[MnCl2] (mM)
T2 (ms) R2 (s-1)
Target-Measured
Difference R2 (s-1)
Target R2 (s-1)
10
15
25
40
MDACC MR Research
Data acquisition and analysis – MD Anderson


ISMRM
NIST
Proton Density Measurements
PD Measurements
Measured (%)
Target %PD
Proton Density (%)
Sphere Number
Target-Measured
Difference (%)
Target %PD
MDACC MR Research
Data acquisition and analysis – MD Anderson


ISMRM
NIST
Section Thickness Assessment
Smoothed Derivative of ERF
Slice Profile
Distance (mm)
3.0-mm
Edge Response Function
ERF Signal Intensity (a.u.)
Distance (mm)
5.0-mm
3.0-mm
From derivative of ERF, the section thickness (FWHM) was computed to be:
26.8 mm x tan(10°) = 4.99 mm for a 5.0-mm slice
20.5 mm x tan(10°) = 3.01 mm for a 3.0-mm slice
MDACC MR Research
Data acquisition and analysis – MD Anderson

High Contrasat Resolution



Data acquisition and analysis – MD Anderson

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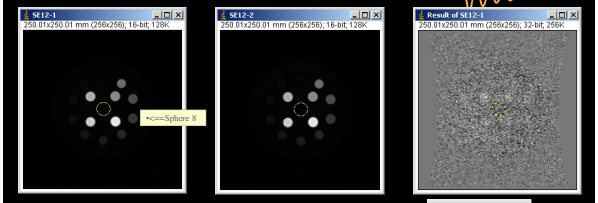
SNR



Source data: Two consecutive frames from DCE scan

SNR: 4.1 NEMA <===Flood fill
53.2 Method 1 <===Sphere 8

SNR: 4.3 NEMA <===Flood fill
62.1 Method 4 <===Sphere 8

$$SNR = \frac{\sqrt{2}\ \overline{S_{ROI}}}{\sigma_{ROI_{difference}}}$$

$$SNR = \frac{0.66\ \overline{S_{ROI}}}{\sigma_{background}}$$

Data acquisition and analysis – MD Anderson

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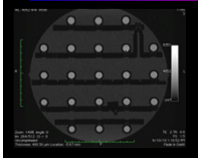
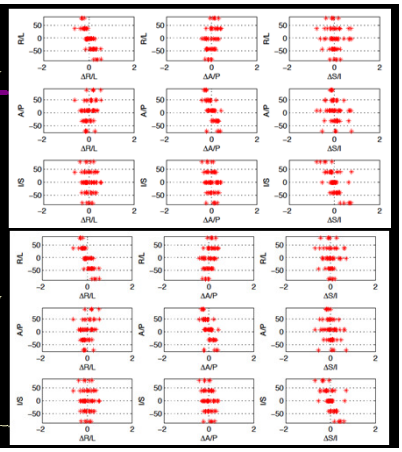
Axial w/o GW



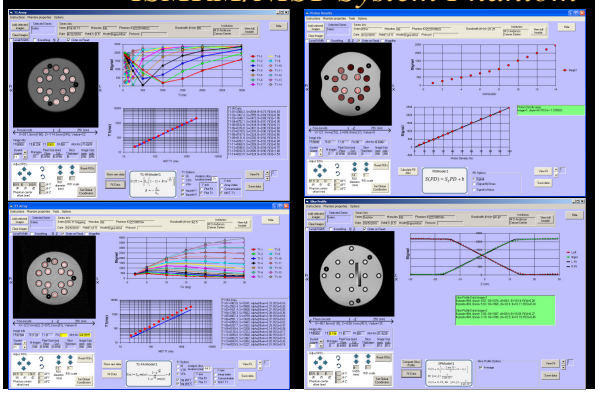
Axial w/ GW



Data Analysis:
Jeff Gunter, Mayo
(Based on ADNI project)

Data acquisition – MD Anderson

ISMRM/NIST System Phantom



ISMRM/NIST – Current Status

- Two prototypes were produced and distributed for initial testing on GE (MDACC) and Siemens (MGH) 1.5T and 3.0T scanners
- Initial prototypes being modified based on initial data review
- SBIR Phase I
  - Awarded from NIST to phantom manufacturer for development of commercial prototypes with target cost of ~$2500
- SBIR Phase II
  - Production of 50 copies for distribution to sites willing to provide (upload) data to NIST

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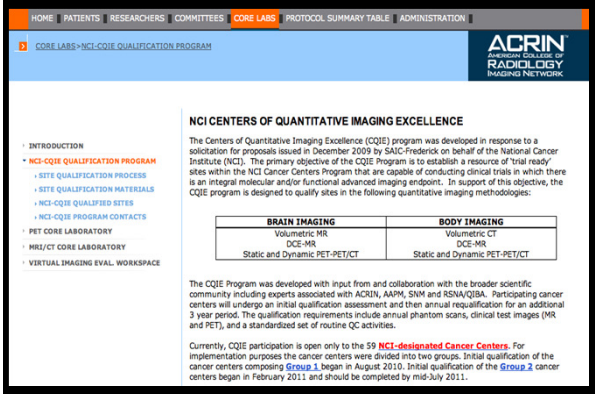
ACRIN



Quantitative Imaging Network (QIN)

- NCI-funded (CIP, U01 funding mechanism)
- QIN consists (currently) of 12 funded centers

- Five working groups:
  - Data Collection Working Group
  - Image Analysis and Performance Metrics
  - Bioinformatics/IT and Data Sharing
  - Clinical Trial Design and Development
  - Outreach: External/Industrial Relations

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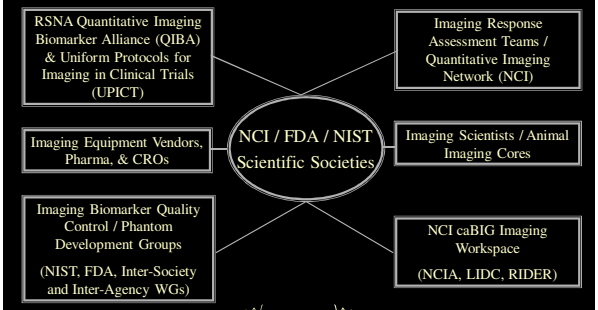
Quantitative Imaging Biomarker Efforts



MDACC MR Research

Modality-Independent Issues

The Toward Quantitative Imaging (TQI) task force of the RSNA definition:

- *"Quantitative imaging is the extraction of quantifiable features from medical images for the assessment of normal or the severity, degree of change, or status of a disease, injury, or chronic condition relative to normal. Quantitative imaging includes the development, standardization, and optimization of anatomical, functional, and molecular imaging acquisition protocols, data analyses, display methods, and reporting structures. These features permit the validation of accurately and precisely obtained image-derived metrics with anatomically and physiologically relevant parameters, including treatment response and outcome, and the use of such metrics in research and patient care."*

Buckler, *et al.*, A Collaborative Enterprise for Multi-Stakeholder Participation in the Advancement of Quantitative Imaging, *Radiology* 258:906-914, 2011

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Buckler, *et al*., A Collaborative Enterprise for Multi-Stakeholder Participation in the Advancement of Quantitative Imaging, *Radiology* 258:906-914, 2011

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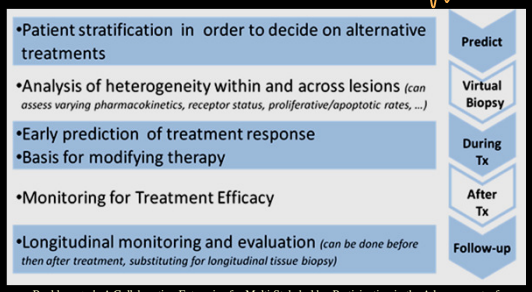
The promise of quantitative imaging



Buckler, *et al*., A Collaborative Enterprise for Multi-Stakeholder Participation in the Advancement of Quantitative Imaging. *Radiology* 258:906-914, 2011

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Modality-Independent Issues

General quantification challenges

- Lack of detailed assessment of sources of bias and variance
- Lack of standards (acquisition, analysis, and reporting)
  - Varying measurement results across vendors and centers
- Lack of support from imaging equipment vendors
  - No documented competitive advantage of QIB (regulatory or payer)
    - Varying measurement results across vendors
    - Varying measurement results across time for any particular vendor
- Highly variable quality control procedures
  - QC programs, if in place, typically not specific for *quantitative* imaging
    - Varying measurement results across centers

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Modality-Independent Challenges

- Some key challenges:
  - Cost of QIB studies (comparative effectiveness)
  - Radiologist acceptance
    - QIBs are not a part of radiologist education & training. (RSNA TQI)
    - The software and workstations needed to produce the QIBs are not integrated into the radiologists' workflow.
    - There are few guidelines for QIB reporting.
    - Clinical demand on radiologists is high --- "time is money".
  - Resource availability
    - Technologists trained in advanced, quantitative, protocols
    - Physicists and/or imaging scientists, data processing capabilities, *etc*.

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Modality-Independent Challenges

Single-vendor, single-site studies:

- Acquisition protocol optimization
  - Scan mode and acquisition parameter optimization for:
    - contrast response and CNR
    - temporal resolution (for dynamic imaging)
    - spatial resolution
    - anatomic coverage
  - Application specific phantom needed for initial validation scans and ongoing quality control
    - phantom acquisition and data analysis protocols
    - established frequency of assessment and data reporting
- Mechanism for detecting and addressing changes in measured response due to system upgrades (Quality Control)
  - Vendors focused on "competitive advantage" in radiology, not on quantitative imaging applications; no focus on maintaining signal response characteristics over time

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Modality-Independent Challenges

Single- to multi-vendor studies:

- Acquisition protocol harmonization
  - Scan mode and acquisition parameter selection for matched:
    - contrast response and CNR
    - temporal resolution (for dynamic imaging)
    - spatial resolution
    - anatomic coverage
  - Application specific phantom needed for initial validation scans and ongoing quality control
    - phantom acquisition and data analysis protocols
    - established frequency of assessment and data reporting
  - Can be achieved, but requires effort at start up and, subsequently, constant monitoring for changes in hardware/software (need for ongoing quality control)
- Vendors focused on "competitive advantage" in radiology, not on quantitative imaging applications

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Modality-Independent Challenges

Single- to multi-center studies:

- Acquisition protocols
  - Harmonization across centers and vendors
  - Distribution and activation of protocols
    - Distribute/load electronically
    - Provide expert training and initial protocol load/test
    - Develop / utilize local expertise
  - Compliance with protocol
    - Local radiologists, technologists
- Widely varying quality control
  - Ranging from specific for a given imaging biomarker, to ACR accreditation, to none
  - Even if QC program is in place, it may not test parameters relevant to the study
- "Scanner upgrade dilemma"
- Data management and reporting

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Modality-Independent Challenges

- Data analysis implementation strategies are often as variable as acquisition strategies
- Choice of model must match data acquisition strategy, *e.g.*, temporal resolution of the acquired data
- To facilitate testing/validation of various analysis packages, readily available, standardized test data and analysis results are needed:
  - Digital reference objects
  - Physical phantoms
  - Test/retest human subject data

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Modality-Independent Issues

- Limitations of the selected imaging biomarker technique
- Radiologist "buy in"
- Data acquisition:
  - Optimization, standardization, harmonization
  - Agent selection and standardization
  - Patient prep and injection technique (site, rate, delay, *etc.*) standardization
  - Acquisition protocol implementation
  - Motion mitigation, if necessary
  - Site qualification
  - Ongoing QC
- Data analysis and display:
  - Optimization, standardization, harmonization
  - Motion mitigation / registration
  - Validation against vetted databases
  - Ongoing QC
- Structured reporting
- Imaging biomarker qualification / validation => FDA => CMS

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