I will be discussing “off-label” use of Gadolinium based Contrast agents
The major focus will be on non-neuro applications

Issues-quantitation, relationship to physiology, metabolism

Examples-DCEMRI, ASL, DWI, MRS

Issues

• Quantitation-accuracy, precision, detection limits
• Standardization-acquisition, processing/analysis
• Validation

ADNI, NIHPD, OAI, RSNA-QIBA, ACRIN
Inter-vendor and intra-vendor variability
Software and hardware upgrades

ACR MRI Phantom

Automated Analysis of Multi Site MRI Phantom Data for the NIHPD Project

Luke Fu, Vladimir Fonov, Bruce Pike, Alan C. Evans, and D. Louis Collins

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{vfonov, bruce, alan}@bic.mni.mcgill.ca
www.bic.mni.mcgill.ca/nihpd/

https://nihpd.crbs.ucsd.edu/nihpd/info/data_access.html

Fig. 1. Plot of SNR, PIU, phantom diameter and height vs. site for the TI modality. The horizontal line represents the grand mean of all sites, while the diamond represents 95% normal confidence interval centered at the sample mean.
Fig. 2. Longitudinal T1 plots of PIU, SNR, diameter and height for all sites. The legend is as follows: Red = Site 1, Green = Site 2, Blue = Site 3, Orange = Site 4, Lime = Site 5, Purple = Site 6, Aqua = Site 7.
Table 2
ACR phantom results from 4 scanners. Siemens shows approximately 30 ms prolonged peak T2 compared to GE and Philips. GE showed 10 ms variance between scanners.

<table>
<thead>
<tr>
<th>ACR phantom peak T2 and histogram width</th>
<th>GE HDx</th>
<th>GE Signa Excite</th>
<th>Philips Intera</th>
<th>Siemens Avanto</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak T2 (ms)</td>
<td>145</td>
<td>135</td>
<td>140</td>
<td>170</td>
</tr>
<tr>
<td>T2 histogram width</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>55</td>
</tr>
</tbody>
</table>

Table 1
Subject gender breakdown by vendor and diagnostic group (female/male).

<table>
<thead>
<tr>
<th>Subject enrollment table</th>
<th>Philips</th>
<th>GE</th>
<th>Siemens</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>6/3</td>
<td>5/13</td>
<td>4/4</td>
<td>15/20</td>
</tr>
<tr>
<td>MCI</td>
<td>2/5</td>
<td>7/6</td>
<td>7/4</td>
<td>16/15</td>
</tr>
<tr>
<td>AD</td>
<td>4/7</td>
<td>6/4</td>
<td>6/4</td>
<td>16/15</td>
</tr>
<tr>
<td>Total</td>
<td>12/15</td>
<td>18/23</td>
<td>17/12</td>
<td>47/50</td>
</tr>
</tbody>
</table>
Contrast Enhanced MRI Has Diagnostic Value in Oncology Breast, Lung, Prostate, etc.
Behavior of Contrast Agent in the Body

Depends on:

- Cellular density or "Extracellular Volume Fraction"
- Blood vessel permeability "Microvascular Permeability"
Dynamic Contrast Enhanced MRI (DCEMRI)

Components

- “High-field” MRI machine (1.0 tesla or greater)
- Phased array coil
- Gadolinium contrast agent (GdDTPA)
- Images taken at several time points (spatial vs temporal resolution)
- Software algorithm processes data for either parametric maps or semi-quantitative plots
Juergen F. Schaefer, Joachim Vollmar, Fritz Schick, Reinhard Vonthein, Marcus D. Seemann, Herrmann Aebert, Rainer Dierkesmann, Godehard Friedel, and Claus D. Claussen

Solitary Pulmonary Nodules: Dynamic Contrast-enhanced MR Imaging—Perfusion Differences in Malignant and Benign Lesions

Radiology August 2004 232:544-553;
Tofts Model Equation

\[ SI = \left[ a_1(e^{-k_{\text{trans}}t/ve}) - e^{-m_1t}/(m_1-k_{\text{trans}}/ve) \right] + \left[ a_2(e^{-k_{\text{trans}}t/ve}) - e^{-m_2t}/(m_2-k_{\text{trans}}/ve) \right] + a_1 e^{-m_1t} + a_2 e^{-m_2t} \times d * k_{\text{trans}} \]

Two Compartment Model
Negligible vascular space
Idealized arterial input function
(SI linear with Gd Agent Concentration)

Challenges/Issues

How accurate is the model?
How precise are the values of Ktrans and Ve?
What is the influence of SNR and temporal resolution?
• Modified ADNI/IRAT phantom for DCE-MRI
• Defined generic DCE-MRI acquisition protocols
• Conduct multi-center phantom reproducibility study
• Define procedure for routine phantom use
• Develop simulated data set for algorithm testing

http://www.rsna.org/research/qiba.cfm
**RSNA QIBA DCE-MRI Phantom v1 Studies**

- Phantom measurements (overview):
  - Phased array acquisition
  - Body coil acquisition
  - SNR acquisition
  - Variable flip angle T1 measurement acquisition
  - DCE acquisition

- Each of the above acquisitions repeated with phantom rotated by 90, 180, 270, and 360°

- All acquisitions repeated one week later

**Sites / vendors**
- MDACC
- UPenn
- Univ Chicago
- Duke Univ
- Univ CA Davis
- GE (new)
- Siemens (2)
- Philips
- Philips
- GE (old)

<table>
<thead>
<tr>
<th>Site</th>
<th>Vendor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A</td>
</tr>
<tr>
<td>2</td>
<td>B</td>
</tr>
<tr>
<td>3</td>
<td>C</td>
</tr>
<tr>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>5</td>
<td>A</td>
</tr>
</tbody>
</table>

**RSNA QIBA – Multiple Vendors / Three Time Points**

- Difference in T1 from each contrast sphere, week 1 minus week 0.
- Difference in R1 from each contrast sphere, week 1 minus week 0.
Requirements for validating imaging biomarkers

• Standardized acquisition, processing, and analysis
• Implementation in prospective multicenter clinical trials
• Comparison with gold standards such as pathology or other imaging techniques
• Validation with clinical outcome (e.g. survival, quality of life)

Anatomic T2W and T1W early subtraction images and parametric maps for rBV and Ktrans at baseline and following 2 cycles of neoadjuvant chemotherapy in a clinically and pathologically (A) responding patient and (B) nonresponding patient.

©2008 by American Association for Cancer Research
Change in MRI-derived tumor size and DCE-MRI kinetic parameters according to (A) clinical tumor response and (B) pathologic tumor response.
Early changes at 1 mo in blood flow and tumor size compared with delay of progression of the disease after initiation of the treatment.


©2008 by American Association for Cancer Research
Predicting and Monitoring Cancer Treatment Response with Diffusion-Weighted MRI

Harriet C. Thoeny, MD and Brian D. Ross, PhD

Figure 1. Schematic representation of the relationship between change in cellular density following an effective therapy and the corresponding distribution of water diffusion values within the tumor. Note that the mean diffusion value of a tumor increases early following the loss of cellular density. (Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.)
Malignant renal neoplasms: correlation between ADC values and cellularity in diffusion weighted magnetic resonance imaging at 3 T

Neoplasie renali maligne: correlazione tra valori di ADC e cellularità nelle sequenze pesate in diffusione con risonanza magnetica a 3 T

G. Manenti\(^1\) · M. Di Roma\(^1\) · S. Mancino\(^1\) · D.A. Bartolucci\(^1\) · G. Palmieri\(^2\) · R. Mastrangelo\(^1\)
R. Miano\(^3\) · E. Squillaci\(^4\) · G. Simonetti\(^1\)

\[ r = -0.73 \quad p < 0.01 \]

Fig. 7. Correlation between apparent diffusion coefficient and cellularity.
NdH/dT: A new quantitative measure for Diffusion Weighted Imaging based evaluation of abdominal tumor response to therapy

Moti Freiman¹, Stephan Voss², Simon K. Warfield¹.

¹Computational Radiology Laboratory, Children’s Hospital, Harvard Medical School, Boston MA USA
²Dept. Of Radiology, Children’s Hospital, Harvard Medical School, Boston MA USA

Submitted to: ISMRM’2011
Our approach

- NdH/dT: Normalized cumulative histogram difference over time
  - Difference between the Cumulative histograms of the tumor ADC values
  - Area Under the Curve (AUC) represent the overall change in tumor diffusivity
  - Normalization by the AUC of healthy tissue sample produce absolute global measure

✓ Single number
✓ Intuitive to interpret
✓ No non-rigid registration is required
✓ Capture tumor heterogeneity

NdH/dT: Representative examples

Figure 1. Images and histograms of two patients. (a,e) DWI images (b-value=400) before (left) and after (right) therapy. (b,f) ADC maps before (left) and after (right) therapy. The tumors are encluted in red. (c,g) Cumulative histograms of the ADC values, before (red) and after (green) therapy. (d,h) The differences between time-points histograms.
REVIEW

Clinical Utility of Proton Magnetic Resonance Spectroscopy in Characterizing Breast Lesions

Rachel Katz-Brull, Philip T. Lavin, Robert E. Lenkinski
### Table 2: Breast proton magnetic resonance spectroscopy (1H MRS) studies and results

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of malignant tumors</th>
<th>No. of benign tumors</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>No. of true positives</th>
<th>No. of true negatives</th>
<th>No. of false negatives</th>
<th>No. of false positives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cecil et al. (16)</td>
<td>19</td>
<td>14</td>
<td>100</td>
<td>93</td>
<td>19</td>
<td>13</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Young et al. (19)</td>
<td>23</td>
<td>6</td>
<td>96</td>
<td>83</td>
<td>22</td>
<td>5</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Reuber et al. (18)</td>
<td>10</td>
<td>6</td>
<td>70</td>
<td>100</td>
<td>7</td>
<td>6</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>26</td>
<td>92</td>
<td>92</td>
<td>48</td>
<td>24</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

*Cases in which hardware failed, the patient moved during examination, MRS was done after fine-needle aspiration procedure, and cases of tubular adenoma (in studies where these cases were reported in detail) were excluded. Data were reproduced from studies cited or calculated from data presented therein.

---

**Figure**: Percentage of choline (Cho) and lactate (Lac) concentrations expressed as a percentage of the total peak area. Panels A-D show examples of magnetic resonance spectroscopy (MRS) findings: (A) Cho = 4.6 mmol/kg, LD = 4.0 cm; (B) Cho = 3.7 mmol/kg, LD = 4.0 cm; (C) Cho = 0.9 mmol/kg, LD = 1.7 cm; (D) Cho = 4.1 mmol/kg, LD = 1.7 cm.

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Treatment Monitoring of Breast Cancer with MRI and MRSI

http://www.acrin.org/

ACRIN protocol 6657 (open)
ACRIN Principal Investigator
Nola M. Hylton, PhD
University of California, San Francisco
San Francisco, CA
Can immediate (1-3 days) change in [tCho] predict response?

- PI: Nola Hylton & Laura Esserman, UCSF
- Single voxel MRS, T2-corrected water as internal reference
- 1.5T and 3T, GE/Siemens/Philips
- Central MRS analysis (UMN – Bolan)
- Fall 2010: 114/144 subjects completed

QC Protocol
- Standard phantoms
- Qualifying and weekly QC scanning
- Choline + and control phantoms

Bolan et al., ISMRM 2008
Example Case
1.5 T MRI
7 mL voxel
Water T$_2$ = 103 ms
[tCho] = 6.2 mmol/kg

MRI Biomarkers
DCEMRI-Vascular permeability
ASL-tissue perfusion
DWI-cellularity
MRS-metabolism (choline)
MRI/MRS is Complicated
Navigating through the maze to reach quantitation requires a systematic approach