Abdomen/Pelvic Perfusion and Diffusion Imaging: Ready for Prime Time?

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University of Pennsylvania
Disclosure:
paid consultant for ACR Image Metrix, Inc.
Why Functional Imaging?

• Improved diagnostic performance?
  – Prostate: MRI + MRS + DCE + DWI

• Personalized Oncology
  – Assess tumor biology for prognostic characteristics

• Molecular Oncology
  – Prevalence of targeted therapies in current trials

• Newer imaging paradigms
  – Prognostic factors
  – Predictive factors
  – Early response assessment
GIST – Gleevec Therapy

baseline

Follow-up

We Should Desist Using RECIST, at Least in GIST

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Functional Tumor Imaging

- PET
  - FDG, FLT, F-MISO/Cu-ATSM, …
- Perfusional Imaging
  - DCE-MRI, DCE-CT, CE-US, H$_2$O-PET
- Diffusion Weighted Imaging
- MR Spectroscopy
- MR Elastography
- Optical (Near-IR) Imaging
RCC Sorafenib effect

Baseline

Day 21
Tumor Ktr effect of BAY 43-9006

<table>
<thead>
<tr>
<th>Patient</th>
<th>Pre-BAY</th>
<th>Post-BAY</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>+</td>
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<tr>
<td>2</td>
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<td>3</td>
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<td>15</td>
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<tr>
<td>16</td>
<td>-</td>
<td>+</td>
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<tr>
<td>17</td>
<td>-</td>
<td>+</td>
</tr>
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</table>

SD at 1 yr: + + + + - - - - + + - + + - + - -
Clear cell: + + + + + + - - + - + + + + - -

ACRIN Abdominal Committee
ACRIN fall meeting Abd/Gyn Scientific Ses
Sorafenib in RCC

LogRatio ≥ 0
No of Patients
Progressed
Censored
Log Ratio P-Value: 0.6587
7
6
1

LogRatio < 0
34
26
8

Progression-Free Survival Estimate

Ktrans < 0.184
No of Patients
Progressed
Censored
Ktrans > 0.184
22
21
1
13
8

Log Rank P-Value: 0.0306

Ktrans
Progression-Free Survival Time (Weeks)

Kaplan–Meier Estimate

Courtesy W Stadler, Univ. Chicago

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DCE-MRI Protocols

- Multiple variations of image acquisition
  - Single slice 2D
  - Multi-slice 2D (sequential, interleaved)
  - Single thin-slab 3D
- Injection Protocols
  - Standard: 0.1 mmol/kg @ 2cc/sec
  - Slow: 0.1 mmol/kg @ 0.3cc/sec
  - Dual:
    - 0.01 mmol/kg @ 2cc/sec (AIF)
    - 0.1 mmol/kg @ 2cc/sec (tumor)
- Temporal Resolutions: 1-15 seconds/phase
Kt = 0.31476 ± 0.22599
Ve = 0.22779 ± 0.10057
Kt = 0.3015 units [1/min]
ve = 0.2070 units %

Kt = 0.18454 ± 0.15173
Ve = 0.16865 ± 0.077324
Kt = 0.1235 units [1/min]
ve = 0.1246 units %
Patient positioning effects

ACRIN fall meeting

Abd/Gyn Scientific Session
Trade-offs in DCE-MRI

• Image Acquisition
  – Temporal resolution/image quality
  – Volumetric coverage/vascular input function
  – Motion effects (lung/liver)

• Image Analysis
  – Heuristic vs. Pharmacodynamic
  – AIF measurement
  – T1 measurement and correction
  – Pixel-based vs. other
Phase II trial of doublet targeted therapy in locally advanced/metastatic RCC
- Four arms (Avastin, sorafenib, temsirolimus)

DCE-MRI sub-study optional
- DCE prior to Tx and after cycle 2

Targets:
- ECOG: 360 patients (90/arm)
- ACRIN: 100 patients (25/arm)
ACRIN 6676 Qualification

- Identify radiologist/oncologist
- Submit magnets specs
- Implement protocol
- Phantom Imaging
- Conference call w/ACRIN
- Enroll!!
### Site Initiation

**Proposed Action**

<table>
<thead>
<tr>
<th>Action</th>
<th>Can't perform (not allowed by scanner software)</th>
<th>Can perform (Indicate new image time below)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Turn on parallel imaging (acceleration factor of 2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Change NEX to equal 0.75 (or 6/6 partial fourier)</td>
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</tr>
<tr>
<td>3. Change to minimum # of slices (no fewer than 6)</td>
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<tr>
<td>4. Increase BW to 83.3 kHz (GE) or 375 Hz/pix (Philips/Siemens)</td>
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<td></td>
</tr>
<tr>
<td>(reset TR and TE to new minimum values)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Change to 90% partial FOV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Remove slice oversampling (if possible)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Increase BW to 128 kHz (GE) or 500 Hz/pix (Philips/Siemens)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Increase FOV to 44cm and change partial FOV to 75%</td>
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<td></td>
</tr>
<tr>
<td>9. Remove anterior and posterior sat bands</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### R1 Range vs SI

- **30**: *
- **15**: *
- **5**: *

![Image of anterior coil](image_url)

![Graph showing R1 range vs SI](graph_url)
6677: Glioma Treatment Trial

- Ongoing study with RTOG
- Bevacizumab/Temazolamide treatment
- 101 patients accrued to date
- “Standard” or “Advanced” imaging options
- Advanced imaging
  - 13 patients 13%
    - 61 DCE-MRI exams
    - 43 per protocol 70%
ACRIN 6676 to date

- Initial protocol planning: April, 2005
- ECOG trial opened: Sept, 2007
- ACRIN sites: 5 qualified, 2 pending
- ECOG enrollment: 72 (as of 10/2/08)
- ACRIN enrollment: 0
Obstacles

• Co-operative trials
  – Long time frame for oncology activation
    • Changing dynamics of cancer therapy for metastatic disease
  – Enthusiasm “mismatch”
    • Interested radiologist, oncologists not participating in trial
    • Oncology interested, radiology site not

• Metastatic setting
  – DCE-MRI “evaluable” lesion
  – Needs active radiology image planning
  – Single lesion only imaging
  – Variable imaging geometries
DCE-MRI: Tumor Heterogeneity

Pre-CA4P

Post-CA4P

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Melanoma: Avastin+Gleevec

$K_{\text{trans}} \downarrow 85\%$

$K_{\text{trans}} \downarrow 35\%$

Pre-Gd

Post-Gd

Pre-Tx

Post-Tx
Effects of Motions

Bone Metastases

Lung Metastases

--- non-motion-corrected

Courtesy Masoom Haider, Univ. Toronto
Solution #1: Primary Site Trial

- Limits study to single anatomic site
  - Fixed imaging geometry
- Option to choose non-mobile regions
  - Pelvis: cervical CA, prostate CA, rectal CA
- Limits study type
  - Pre-operative assessments
    - histology correlates
  - Neoadjuvant trial (breast)
  - Unresectable disease
    - more limited population
Solution #2: Volumetric DCE-MRI

- **Novel k-space trajectories/parallel imaging**
  - More rapid imaging
  - Larger volumes without time penalty
  - Implemented for MRA (TWIST® – Siemens)

- **Golden-angle radial imaging (UPenn)**
  - 32 x 6 mm slices
  - 192 radial passes
  - Subaperture sampling @ ~1 frame/3 sec
  - KWIC processing for image reconstructions
Radial Self-Gating

- Signal at k-space center should be constant
- Any variation likely due to motion
- Slow component: Contrast agent arrival
- Rapid, periodic component: Respiratory motion

Self-gating signal

- Signal magnitude (a.u.)
- Time (sec)
Conventional vs. Gated Radial DCE-MRI
Conventional vs. Gated Radial DCE-MRI
Disclosure #2:

speaker does not profess expertise in DWI
Diffusion Imaging

- Diffusion weighted imaging useful for depicting malignant lesions
- Early treatment-induced changes in microenvironment alters tumor ADC
  - low b values: perfusion effects
  - High b values: diffusion effects
Whole Body MRI w/DWI

Non-Small Cell Lung Cancer:
Whole-Body MR Examination for M-Stage Assessment—Utility for Whole-Body Diffusion-weighted Imaging Compared with Integrated FDG PET/CT

Added value of DWI in whole body MRI for assessment of metastatic disease in NSCLC. Performance comparable to that of PET-CT.
Partially necrotic HCC post TACE

Necrotic: ADC 2.21
Viable: ADC 1.61

ADC map          Gross explant          x 20 mag.

Courtesy of Bachir Taouli, MD (NYU)
Table 2
Changes in Tumor Size, Enhancement, and ADC Value after Treatment in 13 Targeted Tumors

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before Treatment</th>
<th>After Treatment</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size of mass (cm)</td>
<td>9.4 ± 4.2</td>
<td>9.2 ± 4.7</td>
<td>.492</td>
</tr>
<tr>
<td>Percentage enhancement of mass</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial phase</td>
<td>70 ± 23</td>
<td>48 ± 30</td>
<td>.013</td>
</tr>
<tr>
<td>Venous phase</td>
<td>91 ± 12</td>
<td>66 ± 28</td>
<td>.012</td>
</tr>
<tr>
<td>ADC value ($\times 10^{-3}$ mm²/sec)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mass</td>
<td>1.65 ± 0.32</td>
<td>1.95 ± 0.25</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Liver</td>
<td>1.77 ± 0.12</td>
<td>1.82 ± 0.28</td>
<td>.339</td>
</tr>
<tr>
<td>Spleen</td>
<td>1.08 ± 0.23</td>
<td>1.17 ± 0.18</td>
<td>.434</td>
</tr>
</tbody>
</table>

Note.—Data are given as means ± standard deviations.
* P values were obtained with the paired t test.
Reader 1: 40% necrotic
Reader 2: 50% necrotic
Reader 3: 60% necrotic

Reader 1: 80% necrotic
Reader 2: 80% necrotic
Reader 3: 80% necrotic
Why Diffusion Imaging?

- Diffusion imaging available across platforms
- Consensus methodology of DWI in abdominal/pelvic applications emerging
- Ease of implementation for technologists
- Minimal post-imaging processing
But...

- Are diffusion changes in tissue sufficient for improved detection or response assessment?

- Potential multi-site trials with DWI
  - Multi-modal prostate detection (post XRT?)
    - Combined with MRI/MRS/DCE-MRI
  - Liver DWI HCC post TACE and/or sorafenib
    - Comparison to gad T1W to quantify response
  - Whole body diffusion for tumor staging
    - Comparison to PET-CT
## Comparison Chart

<table>
<thead>
<tr>
<th></th>
<th>DCE-MRI</th>
<th>DW-MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse sequence</td>
<td>Standard</td>
<td>Emerging</td>
</tr>
<tr>
<td>Implementation</td>
<td>Complex</td>
<td>Simpler</td>
</tr>
<tr>
<td>Post-processing</td>
<td>Complex</td>
<td>Simpler</td>
</tr>
<tr>
<td>Dx sensitivity</td>
<td>Strong</td>
<td>Moderate?</td>
</tr>
<tr>
<td>Tx sensitivity</td>
<td>Strong</td>
<td>Moderate?</td>
</tr>
<tr>
<td>Quantitation</td>
<td>Complex</td>
<td>Simple</td>
</tr>
<tr>
<td>Whole body</td>
<td>No</td>
<td>Feasible</td>
</tr>
</tbody>
</table>
Conclusions

• Are DCE-MRI and DW-MRI methods ready for “prime-time” in multi-site trials in abd/pelvis?
  – No, but..

• Selected applications may be feasible
  – Primary site of disease > metastatic
  – Fixed locations > respiratory motion
  – Small studies in selected sites
    • Experimental Imaging Committee may be a more suitable target for developing DCE- and DW-MRI applications