ACRIN 6702 Concept:
A Multi-Center Study Evaluating the Utility of Diffusion-Weighted Imaging for Detection and Diagnosis of Breast Cancer

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Breast MRI

- Current clinical indications include
  - High risk screening
  - Staging local extent of disease
- DCE-MRI provides high detection sensitivity
  - Moderate specificity, positive predictive value
- Need for improved specificity to reduce number of unnecessary biopsies
## Results from large MRI screening studies:

<table>
<thead>
<tr>
<th>Patient population</th>
<th>Number of Patients</th>
<th>Biopsies Prompted by MRI (n)</th>
<th>Number of Cancers</th>
<th>PPV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berg WA, AJR 2009</td>
<td>High Risk</td>
<td>4,485 (pooled from 9 studies)</td>
<td>350</td>
<td>141</td>
</tr>
<tr>
<td>Houssami N, JCO 2008</td>
<td>New Cancer Dx (affected breast)</td>
<td>2,610 (pooled from 19 studies)</td>
<td>602</td>
<td>371</td>
</tr>
<tr>
<td>Lehman CD, NEJM 2007</td>
<td>New Cancer Dx (opposite breast)</td>
<td>969</td>
<td>144</td>
<td>30</td>
</tr>
</tbody>
</table>

*Positive predictive value = Number cancers/Number biopsied
Diffusion-Weighted MRI (DWI)

- Short, non-contrast MRI sequence
- Measures the mobility of water diffusing in tissue, reflects tissue microstructure
- Sensitive to restriction of water motion
  - cell density/cellularity
  - membrane integrity, microstructure
- Reduced diffusion in solid tumors

DWI of the Breast

- Breast malignancies exhibit restricted diffusion on DWI [1, 2]
- Apparent Diffusion Coefficient (ADC) on DWI is significantly lower in malignant vs. normal breast tissue and benign breast lesions [1,2]
- ADC may improve diagnostic accuracy of conventional breast MRI [3,4]
- No standardized approach or consensus on how to incorporate into clinical assessments

1. Guo et al. JMRI 2000
2. Woodhams et al. 2005
3. Partridge et al. AJR 2009
Malignancies typically exhibit lower ADC values than benign lesions.
ADC for Differential Diagnosis

- Suspicious breast MRI lesions (BI-RADS 4,5)
  - ADC (malignancies) < ADC (benign), p < 0.001
  - Combined DWI, DCE improves diagnostic accuracy
- DWI may help reduce the number of false positives

Partridge S, et al. AJR 2009
Primary Aim:
To evaluate the performance of ADC measures in excluding benign lesions from suspicious lesions (BI-RADS 4 or 5) identified on DCE-MRI

Secondary Aims:
Multiple secondary aims will investigate factors influencing ADC, including imaging and histologic characteristics
A woman undergoes clinical breast DCE-MRI with DWI.

Recommended for biopsy based on DCE-MRI.

Participant enrolled to study.

Biopsy** of BI-RADS 4 or 5 lesion

Malignant

Benign

Lesion ADCs calculated and compared, ROC analysis (Primary Aim)

Comparison of ADC with histological characteristics

**Surgical excision for atypical findings on biopsy per standard of care.

Malignant = invasive and/or intraductal carcinoma and/or pleomorphic LCIS.

Subjects: BIRADS 4,5 lesions on standard DCE-MRI (n≈280)

DWI prior to biopsy (part of clinical MRI)

Approximately 10 institutions

1 year for accrual
Proposed DWI Protocol

- Standardized approach necessary to establish a useful diagnostic ADC threshold across systems
  - Multi b-value (0, 100, 600, 800, 1000 mm²/s)
  - Spatial resolution
- QC procedure will be performed for site qualification and ongoing, biannual QA
  - Already established for another ACRIN study (6698, Hylton N, PI)
  - Quantitative DWI phantom to assess system accuracy and stability
  - In vivo test cases reviewed for protocol compliance and image quality
Concept Status

• Presented to CTEP 10/16/2012
• CISC summary received 11/8/2012
• Revise protocol to address concerns
  – Exploratory vs. Phase II/III trial design
  – Timing of consent (before vs. after MRI)
  – Central vs. local ADC quantitation
  – Statistical approach
Thank You