Molecular Imaging – Emerging Techniques and Staging of Prostate Cancer

Michael Pacold, HMS III
Gillian Lieberman, MD
Non Nova... Sed Novae (Not New Things, but Things Done Newly)

- Molecular Imaging: defined as visualization of a unique process *in vivo*, using a specific probe and imaging modality

- Not a new field: same principle as Nuclear Medicine, but more specific

- May be viewed as a “Special Stain” for the Radiologist
Research application: Imaging a Plaque in the Brain

- Alzheimer’s disease: 4 million cases in US

- At present, no drugs to prevent or disrupt plaque formation

- Disease evaluation requires neuropathology

- *In vivo* plaque detection useful for drug development (would allow rapid detection of plaques in experimental animals)
An *In vivo* Congo Red

Congo Red

AOI-987

Modality: Optical (Near-Infrared Fluorescence)

Michael Pacold, HMS III
Gillian Lieberman, MD

Alzheimer’s plaques in a mouse

APP23 + AOI-987
(Fluorescence visible at 240 min.)

Wild Type + AOI-987
(no fluorescence at 240 min.)

APP23 + Saline
(no fluorescence)

Michael Pacold, HMS III
Gillian Lieberman, MD

Hintersteiner et al., Nat. Biotech 2005, 23, 577-583
Translational application: Imaging a Plaque in the Aorta

• Coronary Artery Disease: ~500,000 deaths/year

• Conventional imaging assesses calcification and degree of stenosis – but not risk of plaque rupture

• Vulnerable plaque cannot be imaged at present – but has high levels of inflammatory cell and protease activity that might be imaged
An active probe for Cathepsin B

Quenched

Fluorescent

Cy5 =

Chen et al., Circulation 2002, 105, 2766-2771
Cathepsin B activity – *in vivo*

MRI

Fluorescence-mediated tomography-shows active Cathepsin B

Michael Pacold, HMS III
Gillian Lieberman, MD

Chen et al., Circulation *2002*, 105, 2766-2771
Lymph Node Imaging for Prostate Cancer

• ~200,000 diagnoses/year; ~30,000 deaths
• Two principal avenues of therapy based on metastases
  – Local: Radical prostatectomy, radiotherapy, or watchful waiting
  – Locally advanced/metastatic: Androgen-deprivation therapy and radiation
• Current methods to detect metastases limited by node size
Superparamagnetic Iron Nanoparticles – a marker for the lymph system

**Electron Micrograph**

**Model of Nanoparticle coated with 10 kDa dextran**

**Modality: MRI** (lymphatics have low signal 24 hrs. post injection with nanoparticles)

Michael Pacold, HMS III

Gillian Lieberman, MD

Harisinghani et al., *NEJM* 2003, 348, 2491-2499
Imaging the Lymphatic System

Michael Pacold, HMS III
Gillian Lieberman, MD

Harisinghani et al., NEJM 2003, 348, 2491-2499
Metastases Visualized *in vivo*

Pathology post-excision

Pre-nanoparticle injection

Post nanoparticle injection

metastasis

Benign lymph node (dark)

Michael Pacold, HMS III
Gillian Lieberman, MD

Harisinghani *et al.*, *NEJM 2003*, 348, 2491-2499
# Lymph Node Metastasis Detection

<table>
<thead>
<tr>
<th></th>
<th>MRI</th>
<th>MRI+Probe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All sizes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>35.4</td>
<td>90.5*</td>
</tr>
<tr>
<td>Specificity</td>
<td>90.4</td>
<td>97.8</td>
</tr>
<tr>
<td><strong>5-10 mm</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>28.5</td>
<td>96.4*</td>
</tr>
<tr>
<td>Specificity</td>
<td>87.2</td>
<td>99.3</td>
</tr>
<tr>
<td><strong>&lt;5 mm</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0</td>
<td>41.1</td>
</tr>
<tr>
<td>Specificity</td>
<td>100</td>
<td>98.1</td>
</tr>
</tbody>
</table>

*P<0.001 Harisinghani et al., *NEJM* 2003, 348, 2491-2499

Michael Pacold, HMS III
Gillian Lieberman, MD
Conclusions

• Molecular imaging of specific biological processes enhances the diagnostic power of radiology

• At a basic research level, molecular imaging is useful for observing molecular events in living organisms and for evaluation of therapeutics

• The clinical applications of molecular imaging include earlier detection and more effective intervention and treatment
References

Acknowledgements

• Gillian Lieberman, MD
• Larry Barbaras
• Pamela Lepkowski