IMAGING IN PULMONARY MEDICINE

PCCP/ESAP SEMINAR, AUGUST 7, 2014
CROWNE PLAZA GALLERIA
DIAGNOSIS THROUGH CONVENTIONAL RADIOGRAPHY HAS A LOW SENSITIVITY (60%) AND SPECIFICITY (50%)
Detection Range of Imaging Modalities

<table>
<thead>
<tr>
<th>Modality</th>
<th>Anatomy</th>
<th>Physiology</th>
<th>Metabolism</th>
<th>Molecular</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-Ray/CT</td>
<td><img src="image" alt="Bar" /></td>
<td><img src="image" alt="Bar" /></td>
<td><img src="image" alt="Bar" /></td>
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<tr>
<td>US</td>
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<td><img src="image" alt="Bar" /></td>
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<tr>
<td>MRI</td>
<td><img src="image" alt="Bar" /></td>
<td><img src="image" alt="Bar" /></td>
<td><img src="image" alt="Bar" /></td>
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<tr>
<td>Nuclear</td>
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<tr>
<td>Optical</td>
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</tr>
</tbody>
</table>

Weissleder, Radiology 1999; 212: 609–614
Molecular Imaging

Nanotechnology

Molecular Therapy
Molecular Imaging Modalities

- Magnetic Resonance Imaging
- Computed Tomography
- Positron Emission Tomography
- Optical Imaging

- Resolution
- Penetration Depth
- Sensitivity
- Information
- Clinical Use
DIAGNOSTIC INNOVATIONS APPLICABLE TO ONCOLOGY: SPECIFIC INDICATIONS

- Early detection of malignant disease
- Diagnosis and staging
- Imaging guided biopsy
- Guidance for tumoricidal techniques (RFA, embolotherapy, catheter derived therapy)
- Radiotherapy planning
- Monitoring of treatment response
- Disease follow up
- Clinical trials and specific demands
- Research in oncology
<table>
<thead>
<tr>
<th>Imaging modality</th>
<th>Form of energy used</th>
<th>Spatial resolution (millimeters)</th>
<th>Acquisition time per frame (seconds)</th>
<th>Molecular probe mass required (nano-grams)</th>
<th>Molecular sensitivity* (mole/liter)</th>
<th>Tissue penetration depth (millimeters)</th>
<th>Small animal or clinical?</th>
<th>Molecular signal quantification capabilities</th>
<th>Cost (equipment and usage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET</td>
<td>Annihilation photons</td>
<td>1-4 (animal) 6-10 (clinical)</td>
<td>1-300</td>
<td>1-100</td>
<td>$10^{-11}$-$10^{-12}$</td>
<td>$&gt;300$</td>
<td>Both</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>SPECT</td>
<td>Gamma rays</td>
<td>0.5-5 (animal) 7-15 (clinical)</td>
<td>60-2000</td>
<td>1-100</td>
<td>$10^{-10}$-$10^{-11}$</td>
<td>$&gt;300$</td>
<td>Both</td>
<td>Medium-High</td>
<td>Medium-High</td>
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<tr>
<td>BLI</td>
<td>Visible to infrared light</td>
<td>3-10</td>
<td>10-300</td>
<td>$10^3$-$10^6$</td>
<td>$10^{-13}$-$10^{-16}$*</td>
<td>1-10</td>
<td>Small animal</td>
<td>Low-Medium</td>
<td>Low</td>
</tr>
<tr>
<td>FLI</td>
<td>Visible to infrared light</td>
<td>2-10</td>
<td>10-2000</td>
<td>$10^3$-$10^6$</td>
<td>$10^{-9}$-$10^{-11}$*</td>
<td>1-20</td>
<td>Small animal</td>
<td>Low-Medium</td>
<td>Low</td>
</tr>
<tr>
<td>MRI</td>
<td>Radio frequency waves</td>
<td>0.025-0.1 (animal) 0.2-1 (clinical)</td>
<td>60-3000</td>
<td>$10^3$-$10^6$</td>
<td>$10^3$-$10^{-5}$</td>
<td>$&gt;300$</td>
<td>Both</td>
<td>Medium</td>
<td>High</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>High frequency sound waves</td>
<td>0.05-0.5 (animal) 0.1-1 (clinical)</td>
<td>0.1-100</td>
<td>$10^3$-$10^6$</td>
<td>*</td>
<td>1-200</td>
<td>Both</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>CT</td>
<td>X-rays</td>
<td>0.03-0.4 (animal) 0.5-1 (clinical)</td>
<td>1-300</td>
<td>N/A</td>
<td>*</td>
<td>$&gt;300$</td>
<td>Both</td>
<td>N/A</td>
<td>Medium-High</td>
</tr>
</tbody>
</table>

*Adapted from [37]. *Not well characterized yet. *The molecular probe, subject physiology and biology, as well as the imaging system’s signal (e.g. photon) sensitivity, spatial resolution, and contrast resolution work together to define a modality’s molecular sensitivity (the ability to visualize and quantify small concentrations of molecular signal). Here the molecular sensitivity is expressed as the limit of signal detection in
Table 1 – *In vivo* imaging techniques currently used in the context of biomedical research and/or medical diagnosis.

<table>
<thead>
<tr>
<th>Technique</th>
<th>Clinical imaging</th>
<th>Resolution</th>
<th>Animal imaging</th>
<th>Resolution and time scale</th>
<th>Application</th>
<th>Main characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPECT (low energy γ-rays)</td>
<td>yes</td>
<td>6-8 mm; s</td>
<td>yes</td>
<td>1-2 mm; min</td>
<td>Functional</td>
<td>Radioisotopes have longer half-lives than those used in PET; sensitivity 10 to 100 times smaller than PET</td>
</tr>
<tr>
<td>PET (high energy γ-rays)</td>
<td>yes</td>
<td>4 mm; s</td>
<td>yes</td>
<td>1-2 mm; min</td>
<td>Metabolic, functional, molecular</td>
<td>High sensitivity (picomolar concentrations); cyclotron needed</td>
</tr>
<tr>
<td>CT</td>
<td>yes</td>
<td>0.5 mm; s</td>
<td>yes</td>
<td>50-100 μm; min</td>
<td>Anatomical, functional</td>
<td>Poor soft tissue contrast</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>yes</td>
<td>300-500 μm; s</td>
<td>yes</td>
<td>50 μm; min</td>
<td>Anatomical, functional</td>
<td>Difficulties to image through bone or lungs; microbubbles used for contrast enhancement</td>
</tr>
<tr>
<td>MRI</td>
<td>yes</td>
<td>1 mm; s to min</td>
<td>yes</td>
<td>80-100 μm; s to h</td>
<td>Anatomical, functional</td>
<td>High spatial resolution and soft tissue contrast</td>
</tr>
<tr>
<td>Bioluminescence</td>
<td>no</td>
<td>–</td>
<td>yes</td>
<td>1-10 mm; s to min</td>
<td>Molecular</td>
<td>High sensitivity; transgene-based approach; light emission prone to attenuation with increased tissue depth</td>
</tr>
<tr>
<td>Optical imaging</td>
<td>no</td>
<td>–</td>
<td>yes</td>
<td>1-3 mm; s to min</td>
<td>Molecular</td>
<td>Excitation and emission light prone to attenuation with increased tissue depth</td>
</tr>
</tbody>
</table>
Window Settings

Lung Window

Mediastinal Window
What is Hounsfield unit?

A measure of density of a structure on CT

<table>
<thead>
<tr>
<th>Structure</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>0</td>
</tr>
<tr>
<td>Muscle &amp; ST</td>
<td>40</td>
</tr>
<tr>
<td>Air</td>
<td>-1000</td>
</tr>
<tr>
<td>Bone</td>
<td>1000</td>
</tr>
<tr>
<td>Fat</td>
<td>-60</td>
</tr>
<tr>
<td>CSF</td>
<td>10</td>
</tr>
<tr>
<td>Fresh clot</td>
<td>50</td>
</tr>
<tr>
<td>WM</td>
<td>30</td>
</tr>
<tr>
<td>GM</td>
<td>40</td>
</tr>
</tbody>
</table>
When to Request for Contrast Media

- Tumor or Nodule
- Staging of Cancer
- Metastasis
- Lesions near the hilus or intimately related to vascular structures (i.e. heart, vessels)
- Empyema or Abscesses
Common Indications of Chest CT Scan

Normal Chest Radiograph (Occult Disease)

1. Metastases
2. Hemoptysis
3. Suspected bronchiectasis
4. Myasthenia gravis (thymus)
5. Endocrine abnormalities (suspect lung tumor or mediastinal origin)
6. Unknown source of infection (immuno-compromised)
7. Suspected infiltrative lung disease
8. Suspected aortic dissection
Common Indications of Chest CT Scan

Abnormal Chest Radiograph

1. Staging bronchogenic carcinoma
2. Solitary nodule, mass, opacity
3. Infiltrative lung disease
4. Mediastinum widening, mass, other abnormality
5. Pleural abnormalities
6. Chest wall lesions
GROUND GLASS OPACITY NODULE
NODULE WITH BENIGN FEATURES
ASPERGILLOMA
RIGHT UPPER LUNG ATELECTASIS
LEFT UPPER LOBE BRONCHUS
CT SCAN ADVANTAGE

- Highly detailed and comprehensive
- **Non-invasive**, Painless and generally quick and convenient to patients
- Readily available
- Precise due to high spatial resolution (bone/lung)
- Real time imaging in intervention
- **Speed** of acquisition
- Fewer restrictions than MRI
- Wide field of view, hence, more information
- Ability to provide cross-sectional images
- Detection of subtle differences between tissues, 3D and crisper images
- Cost less than other imaging studies
Advantages of Multi-slice CT

- Same acquisition in shorter time
- Thin slices give better resolution
- Scan larger volumes in the same time
- Large volume can be scanned in a single breathhold
What is HRCT?

- High Resolution CT
- Use of thin collimation (thinnest is 1-1.5 mm)
- Image reconstruction with a high spatial frequency
- Increased kVP or mA technique
Clinical Uses of HRCT

- To detect morphologic lung disease in patients with respiratory disease, or abnormal pulmonary function tests who have normal chest radiographs.
- To characterize lung disease morphologically (i.e. reticular, nodular, honeycombing).
IDIOPATHIC PULMONARY FIBROSIS
MDCT 3-DIMENSIONAL RECONSTRUCTIVE IMAGING
Venous collaterals from SVC syndrome

Note subcutaneous edema from SVC obstruction

Near total occlusion SVC from mediastinal adenopathy
Mediastinal Window

1. trachea
2. esophagus
3. right brachiocephalic vein
4. left brachiocephalic vein
5. innominate art
6. left common carotid art
7. left subclavian art
8. thymus (left lobe)
Mediastinal Window
1. tracheal carina
2. ascending aorta
3. descending aorta
4. superior aspect left pulm art
5. superior pericardial recesses
6. thymus
7. superior vena cava
8. truncus ant (RUL art)
9. normal lymph node
10. esophagus
11. azygos vein
Mediastinal Window
1. ascending aorta
2. descending aorta
3. main pulm art
4. left pulm art
5. right pulm art
6. superior vena cava
7. left main bronchus
8. esophagus
9. normal subcarinal lymph node
10. superior pulm veins
11. azygos vein
12. hemiazygos vein branch
13. thymus
ADENOCARCINOMA

ABSCESS
RADIOFREQUENCY ABLATION
POST RADIOFREQUENCY ABLATION
CT SCAN LIMITATION/DISADVANTAGES

- Patient can not tolerate complete supine position
- Uncooperative patient
- Contrast hypersensitivity or allergy
- Huge patients that do not properly fit CT gantry
- Claustrophobic patients
- Limitation brought about by technology
- High radiation dose
- Misinterpretation
Need for contrast material for enhance soft tissues due to poor tissue contrast

Tissue non-specificity (no target specific imaging)

Cost concerns
ROLE OF NUCLEAR MEDICINE IN CHEST IMAGING

- **V/Q SCAN IN PULMONARY EMBOLISM**

- **SURGICAL PLANNING (QUANTIFICATION OF PERFUSION OR VENTILATION DEFICIENCY BY V/Q SCAN**

- **DIAGNOSE RECURRENT OR DIFFERENTIATE VIABLE TUMOR FROM POST THERAPEUTIC FIBROSIS**

- **BONE METASTASIS**

- **DIAGNOSIS OF INFLAMMATION OR INFECTION (i.e. SARCOIDOSIS, TB) AND SOME MALIGNANT NEOPLASM (i.e. LYMPHOMA, HEPATOCCELLULAR CA, ADENOCARCINOMA)**
SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT)

- Nuclear medicine imaging technique that uses gamma rays.
- Images primarily the biological process or function of organs rather than anatomical structures.
- Images processed and converted to 2-D images using CT technology.
- Multiple slices are obtained and stacked to form 3-D representations.
- To acquire the images, the gamma camera is rotated around the patient.
- A nuclide in a radiopharmaceutical is placed into the body by either injection, oral or inhalation. It consists of an emitting isotope.
SPECT V/Q SCAN FOR EMBOLISM
SPECT V/Q SCAN FOR COPD
INDICATIONS OF SPECT/CT

- HIGH SUSPICION FOR ACTIVE DISEASE OR KNOWN STRUCTURAL PATHOLOGY, AS IT MAY LOCALIZE MULTIPLE SITES AND DEFINE EXTENT OF DISEASE: HEART, BRAIN, RENAL, BONE, PARATHYROID PLANNING TREATMENT (MEDICAL, SURGICAL, RADIATION THERAPY)

- MONITORING RESPONSE OF TREATMENT

- ABNORMAL STRUCTURAL FINDINGS OF EQUIVOCAL FUNCTIONAL SIGNIFICANCE, EITHER AT DIAGNOSIS OR POST-TREATMENT

- ABSENCE OF OVERT STRUCTURAL PATHOLOGY IN THE PRESENCE OF A HIGH CLINICAL SUSPICION
ADVANTAGES OF SPECT CT SCAN

- Physical and functional imaging that is accurate and reliable for diagnostics
- 3-D images
- Good image contrast
- Cardiac gated acquisition are possible with SPECT
- High diagnostic ability for bone Scintigraphy compared to MRI
- More sensitive to brain injury than MRI or CT
- Useful for pre-surgical evaluation of medically controlled seizures
- Effects of CT based attenuation correction of SPECT image data sets and potential future applications
- Use of SPECT/CT data for estimating internal radiation dosimetry
- Radiation dose of CT from SPECT/CT
DISADVANTAGES OF SPECT

- POOR RESOLUTION
- TAKES LONG TIME SCANNING
- RADIATION EXPOSURE
- NOT SAFE FOR PREGNANT WOMEN
- BLEEDING, PAIN OR SWELLING CAN OCCUR AT THE INJECTION SITE
- SENSITIVE TO MOTION
- COSTLY
- NOT WIDELY AVAILABLE
IMPORTANT CANCER IMAGING TOOL BOTH FOR DIAGNOSIS AND STAGING

PROGNOSTIC INFORMATION BASED ON TREATMENT RESPONSE

GOLD STANDARD FOR EVALUATION OF INDETERMINATE SOLITARY PULMONARY NODULE OR MASS (\(^{90}\%\) SPECIFIC) BUT WITH LIMITED ROLE IN DIAGNOSIS OF PRIMARY TUMOR

EVALUATION OF METASTATIC SPREAD TO LOCOREGIONAL LYMPH NODES: PET IS SUPERIOR TO CT IN ASSESSMENT OF MEDIASTINAL AND HILAR NODE METASTASIS

USEFUL AS AN ADJUNCT TO THE CONVENTIONAL IMAGING

FDG-PET IS SUPERIOR TO CT SCAN IN DIFFERENTIATING BETWEEN MALIGNANT AND BENIGN TUMORS

FASTEST EMERGING MOLECULAR IMAGING
PET/SPECT ADVANTAGES

- CLINICAL TRANSLATION
- HIGH SENSIVITY WITH UNLIMITED DEPTH PENETRATION

PET DISADVANTAGES

- COST
PET SCANNING DETECTS MALIGNANCY IN PULMONARY LESIONS WITH SENSITIVITY OF 96%, SPECIFICITY OF 88% AND ACCURACY OF 94% IN LESIONS MORE THAN 10 MMS
<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>57%</td>
<td>82%</td>
</tr>
<tr>
<td>PET</td>
<td>84%</td>
<td>89%</td>
</tr>
<tr>
<td>EUS</td>
<td>78%</td>
<td>71%</td>
</tr>
<tr>
<td>EUS WITH FNAB</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>
NEGATIVE PREDICTIVE VALUE OF PET FOR N3 DISEASE IS IDENTICAL TO MEDIASTINOSCOPY
Enlarged lymph nodes on both sides of the mediastinum, as well anterior to the trachea.
ACCURACY OF CT FOR DIAGNOSING MEDIASTINAL INVASION RANGES FROM 67% TO 79% WITH A SENSITIVITY OF ABOUT 60% TO 79% (PET IS MORE SENSITIVE AND SPECIFIC (80-90%) IN DIAGNOSING MEDIASTINAL NODE METASTASIS)
PET AND CT STAGING IF USED IN CONJUNCTION INCREASES SENSITIVITY TO 93%, SPECIFICITY OF 97% AND ACCURACY OF 96%
This 55-year-old smoking man developed a new cough. PET/CT shows a large, active cancer (arrow) compressing the bronchus leading to the right lung.
PET IS MORE SENSITIVE AND SPECIFIC THAN BONE SCINTIGRAPHY AND HAVE 100% POSITIVE PREDICTIVE VALUE FOR PRESENCE OF ADRENAL DEPOSITS (vs CONVENTIONAL IMAGING; 43%)
PET HAS A 90% SENSITIVITY AND HIGHER SPECIFICITY (98%) AND ACCURACY (^96%) AND IS CONSIDERED SUPERIOR TO BONE SCINTIGRAPHY IN THE DETECTION OF BONE INVOLVEMENT
<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDG PET/CT</td>
<td>93.3%</td>
<td>94.1%</td>
<td>93.4%</td>
<td>75.7%</td>
<td>98.6%</td>
</tr>
<tr>
<td></td>
<td>(28/30)</td>
<td>(143/152)</td>
<td>(171/182)</td>
<td>(28/37)</td>
<td>(143/145)</td>
</tr>
<tr>
<td>Bone scan</td>
<td>93.3%</td>
<td>44.1%</td>
<td>52.2%</td>
<td>24.7%</td>
<td>97.1%</td>
</tr>
<tr>
<td></td>
<td>(28/30)</td>
<td>(67/152)</td>
<td>(95/182)</td>
<td>(28/113)</td>
<td>(67/69)</td>
</tr>
<tr>
<td>p</td>
<td>1.000</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum ALP</td>
<td>26.7%</td>
<td>94.1%</td>
<td>83.0%</td>
<td>47.1%</td>
<td>86.7%</td>
</tr>
<tr>
<td></td>
<td>(8/30)</td>
<td>(143/152)</td>
<td>(151/182)</td>
<td>(8/17)</td>
<td>(143/165)</td>
</tr>
<tr>
<td>Serum ALP + bone scan*</td>
<td>26.7%</td>
<td>97.3%</td>
<td>85.7%</td>
<td>66.7%</td>
<td>87.1%</td>
</tr>
<tr>
<td></td>
<td>(8/30)</td>
<td>(148/152)</td>
<td>(156/182)</td>
<td>(8/12)</td>
<td>(148/170)</td>
</tr>
</tbody>
</table>
FDG-PET IS NOT SUITED FOR DETECTION OF BRAIN METASTASIS DUE TO LOW SENSITIVITY (60%). CT AND MRI REMAINS THE METHOD OF CHOICE
PROGNOSTIC FOR TREATMENT RESPONSE
PROGNOSTIC FOR TREATMENT RESPONSE
Treatment response with PET FDG in non-small cell lung cancer

Baseline  2 weeks  6 weeks
Time after start of treatment
PET IS MORE ACCURATE IN DETECTING RECURRENT LUNG CANCER
THERE IS NO SINGLE SUPERIOR DIAGNOSTIC IMAGING. IT IS IMPORTANT TO KNOW WHAT YOU WANT TO KNOW, AVAILABILITY OF IMAGING TOOLS, THEIR STRENGTHS/LIMITATIONS, COMPETENCE OF READERS AND THE COST
THANK YOU AND GOOD DAY