BUILDING A PRACTICE IN FUNCTIONAL BRAIN IMAGING
Functional Brain Imaging
Key Elements in Practice Building

• Provide a technology that answers a question accurately at a reasonable cost that is easy for the patient to endure
  • Should not approach root canal status
  • Is more accurate than tea leaves
  • Should cost less than botox or collagen

• Become “expert” at all facets of the technology
  • Definition of an expert? (more than attaining a certificate for a 2-day course).
  • Courses available (CME desirable)
  • Review of quality literature
  • Experience
Functional Brain Imaging
Key Elements in Practice Building

• Have a quality facility
  • Multi-detector SPECT (SPECT-CT)
  • New generation PET (PET-CT)
  • Helps to have more than a one room structure attached to the neighborhood Starbucks

• Hire quality personnel
  • Technologists
  • Nurses
  • Receptionists (phone communications often more important than all of the above)

• Provide excellent service
  • Personal case review (doctor-doctor)
  • Rapid turnaround time (includes scheduling patients - issuing final report)
Functional Brain Imaging
Key Elements in Practice Building

• Marketing
  • More than a glossy brochure
  • Attend relevant scientific functions
    • Neurology conferences
    • Psychiatry conferences
    • Neurosurgical conferences
  • Develop a regional reputation for understanding the utility of Functional Brain Imaging in diagnosis and treatment of CNS disorders
    • Make intelligent comments as opposed to “members of the hospital administration need a PET-CT of the brain”.
    • Offer to provide lecture support at hospital functions or community gatherings (i.e. Alzheimer’s support group)
  • Work with your neuroradiologists to help carry the banner of functional brain imaging (this often requires continuing education)
Functional Brain Imaging
Key Elements in Practice Building

• Research Opportunities
  • Joint research projects with medical subgroups often define clinical opportunities
    • Memory disorders
    • Neurosurgical applications
    • Rheumatology
    • other

• Develop a high degree of self-confidence
  • If you don’t believe in the technology, you will fail
  • Know how functional brain imaging will improve medical care
What is Functional Brain Imaging?

- SPECT
- PET
- Radiopharmaceutical tumor imaging
- MRA
- MRS
- FMRI
- MEG
- Psychics analysis
- Wife’s or girlfriend’s intuition
- All of above
Is Functional Brain Imaging a Clinically Useful test?

What characteristics would you want in a test to be considered clinically useful?
Characteristics of a Clinically Useful Test

- Acceptable error rate
  - Sensitivity, specificity, accuracy
- Unique information
  - Pathophysiologic information different than other testing modalities
- Influences decision making
  - Management role
- Cost effective
- Any other thoughts?
“Expert Test”: What does this stand for?

S.P.E.C.T.
Single Photon Emission Computed Tomography
S.P.E.C.T.
PET / CT
What is PET?
What is PET?

Positron Emission Tomography

Congratulations!
Now, you are on your way to being an expert in Functional Brain Imaging

Remember, most of the lay population and by far, the majority of physicians have no idea what SPECT or PET means
FDG-PET

AF
Basic Components of PET and SPECT Studies

- Pre acquisition preparation
- Data acquisition
- Data processing
- Data display
- Data interpretation
- Reporting
Single Detector SPECT
Multi Detector PET
SPECT vs. PET

- Both give functional images
- Radiotracers differ
- SPECT tracers
  - Perfusion
  - Metabolism
- PET (FDG)
  - Metabolism
**Functional Brain Imaging**

**Common Indications**

- **Society of Nuclear Medicine**
  - Dementia
  - Epilepsy
  - Cerebral Vascular Disease
- **American Academy of Neurology**
  - Dementia of Alzheimer’s type
  - Temporal lobe epilepsy
  - Stroke
- **European Association of Nuclear Medicine**
  - Epilepsy
  - Dementing disorders
  - Neuro Oncology
    - Differential diagnosis of cerebral lumps
    - Detection of viable tumor tissue
    - Non-Invasive grading
Assessment of Brain SPECT *

Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology
<table>
<thead>
<tr>
<th>Application</th>
<th>Rating</th>
<th>Quality of evidence</th>
<th>Strength of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stroke</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detection of acute ischemia</td>
<td>Established</td>
<td>Class II</td>
<td>Type B</td>
</tr>
<tr>
<td>Determination of stroke subtypes</td>
<td>Promising</td>
<td>Class II</td>
<td>Type C</td>
</tr>
<tr>
<td>Vasospasm following SAH</td>
<td>Promising</td>
<td>Class II*</td>
<td>Type B</td>
</tr>
<tr>
<td>Prognosis/recovery from stroke</td>
<td>Investigational</td>
<td>Class II</td>
<td>Type C</td>
</tr>
<tr>
<td>Monitoring therapies</td>
<td>Investigational</td>
<td>Class III</td>
<td>Type C</td>
</tr>
<tr>
<td>Diagnosis of TIA</td>
<td>Investigational</td>
<td>Class III</td>
<td>Type C</td>
</tr>
<tr>
<td>Prognosis of TIA</td>
<td>Investigational</td>
<td>Class II</td>
<td>Type C</td>
</tr>
<tr>
<td><strong>Neoplasm</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grading of gliomas</td>
<td>Investigational</td>
<td>Class III</td>
<td>Type C</td>
</tr>
<tr>
<td>Differentiating radiation necrosis from tumor recurrence</td>
<td>Investigational</td>
<td>Class II</td>
<td>Type B</td>
</tr>
<tr>
<td><strong>HIV encephalopathy</strong></td>
<td>Investigational</td>
<td>Class II</td>
<td>Type B</td>
</tr>
<tr>
<td><strong>Head trauma</strong></td>
<td>Investigational</td>
<td>Class II</td>
<td>Type C</td>
</tr>
<tr>
<td><strong>Epilepsy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presurgical ictal detection of seizure focus</td>
<td>Established</td>
<td>Class II</td>
<td>Type B</td>
</tr>
<tr>
<td>Localization of seizure focus</td>
<td>Promising</td>
<td>Class II</td>
<td>Type C</td>
</tr>
<tr>
<td>Differential diagnosis of ictus</td>
<td>Investigational</td>
<td>Class III</td>
<td>Type C</td>
</tr>
<tr>
<td>Interictal detection of seizure focus</td>
<td>Investigational</td>
<td>Class III</td>
<td>Type C</td>
</tr>
<tr>
<td>Determination of seizure subtypes</td>
<td>Investigational</td>
<td>Class III</td>
<td>Type C</td>
</tr>
<tr>
<td>Receptor studies</td>
<td>Investigational</td>
<td>Class III</td>
<td>Type C</td>
</tr>
<tr>
<td>Monitoring therapy</td>
<td>Doubtful</td>
<td>Class III</td>
<td>Type D</td>
</tr>
<tr>
<td><strong>Alzheimer's disease</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>To support clinical diagnosis</td>
<td>Established</td>
<td>Class II</td>
<td>Type B</td>
</tr>
<tr>
<td><strong>Huntington's chorea</strong></td>
<td>Investigational</td>
<td>Class III</td>
<td>Type C</td>
</tr>
<tr>
<td><strong>Persistent vegetative state</strong></td>
<td>Investigational</td>
<td>Class III</td>
<td>Type C</td>
</tr>
<tr>
<td><strong>Brain death</strong></td>
<td>Promising</td>
<td>Class III</td>
<td>Type C</td>
</tr>
</tbody>
</table>

SAH = subarachnoid hemorrhage; TIA = transient ischemic attack; HIV = human immunodeficiency virus.
Dementia Diagnosis

Estimate of Need

- 50% of population > 80 will be demented
- 75% of population > 90 will be demented
- The remaining population when they misplace their keys or sunglasses or don’t remember their driver’s license number will think they’re demented
- Need for an accurate, cost effective diagnostic tool is self evident
Dementia Diagnosis
Current Methods

• History and physical examination
  • Neurologist (Sens. = 50-80%)
  • Neuropsychologist / Neuropsychiatrist
• Neuropsychological testing
• MRI / CT
• Blood testing
• Functional Neuro imaging (SPECT/ PET) (Sens.=80-90%)
Functional Brain Imaging in Dementia

- Differentiation of dementias
- Severity of dementia
- Progression
Functional Brain Imaging
Surface Rendered Images

Normal Brain

Alzheimer’s Disease
CD-ROM with viewer great for Marketing
FDG-PET
Color Also a Great Marketing Aid
FDG-PET
Quiz: Is the patient (a) comatose (b) reading war & peace, (c) in a nursing home, (d) none of the above
Answer: Living at home with help from his wife. He is trying to run a small business.
Emerging population needing a diagnosis

- Baby boomers with “memory hiccups”
- Adults with concerns that their memory “ain’t what it used to be” (remember that’s only the first thing to go)
- Physicians who can’t remember what SPECT and PET stand for after you have explained it twice
Emerging population needing a diagnosis

- MCI
- What is MCI?
Quiz
MCI Definition

1. Microwave Communication Inc.
2. Media Control Interface
3. Mild Cognitive Impairment
4. None of the above
5. All of the above
MCI Definition

1. Microwave Communication Inc.
2. Media Control Interface
3. Mild Cognitive Impairment
4. None of the above
5. All of the above
MCI Definition
(referring to possible brain dysfunction)

- General term to describe a subtle but measurable memory disorder (amnestic)
  - Memory problems greater than normally expected with aging
- Other functions such as language, attention, and visual spatial skills (non-amnestic)
MCI Population

- Prevalence estimates as high as 20% of non-demented subjects over 65
- Approximately 1/3 have amnestic variety linked to Alzheimer’s disease
- Conversion of amnestic type is approximately 10-15% / year
MCI Conversion

Time to dementia in MCI patients

A = MCI-amnestic
B = MCI-multiple cognitive domains

Cumulative Survival

Time in Months

0  12  24  36  48  60  72  84  96  108  120  132  144

0.0  0.2  0.4  0.6  0.8  1.0  1.2

S DeKosky, MD
MCI? Early Alzheimer’s Disease
Mild Cognitive Impairment (MCI)
Moderately Advanced Alzheimer’s Disease
Severely Advanced Alzheimer’s Disease
Error Rate of PET/ SPECT in the Diagnosis of Alzheimer’s Disease *

• Variable sensitivity and specificity for different stages
  • Advanced = Sensitivity > 90%; Specificity > 65% **
  • Early = Sensitivity 70–85%; Specificity > 80% **

* PET > SPECT in comparison studies
** Multiple publications with varying study design
Table 2. A comparison of functional brain imaging data applied to the separation of dementia from normal controls. See text for detailed explanation of each measure.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Diagnostic standard</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical assessment: probable AD</td>
<td>Histopathology</td>
<td>63</td>
<td>100</td>
<td>[23]</td>
</tr>
<tr>
<td>Clinical assessment: probable and possible AD</td>
<td>Histopathology</td>
<td>75</td>
<td>100</td>
<td>[23]</td>
</tr>
<tr>
<td>Clinical assessment: probable AD</td>
<td>Histopathology</td>
<td>59</td>
<td>95</td>
<td>[24]</td>
</tr>
<tr>
<td>Clinical assessment: probable and possible AD</td>
<td>Histopathology</td>
<td>93</td>
<td>88</td>
<td>[24]</td>
</tr>
<tr>
<td>Clinical assessment: probable AD</td>
<td>Histopathology</td>
<td>71</td>
<td>73</td>
<td>[31]</td>
</tr>
<tr>
<td>Community clinical assessment</td>
<td>Histopathology</td>
<td>50</td>
<td>Not specified</td>
<td>[8]</td>
</tr>
<tr>
<td>MRI hippocampal volume</td>
<td>Probable AD</td>
<td>79</td>
<td>69</td>
<td>[12]</td>
</tr>
<tr>
<td>MRI hippocampal volume</td>
<td>Probable AD</td>
<td>82</td>
<td>80</td>
<td>[13]</td>
</tr>
<tr>
<td>MRI hippocampal volume: mild AD</td>
<td>Probable AD</td>
<td>78</td>
<td>80</td>
<td>[13]</td>
</tr>
<tr>
<td>FDG PET: multicenter</td>
<td>Histopathology</td>
<td>94</td>
<td>73</td>
<td>[22]</td>
</tr>
<tr>
<td>FDG PET</td>
<td>Histopathology</td>
<td>93</td>
<td>63</td>
<td>[23]</td>
</tr>
<tr>
<td>FDG PET (publication review)</td>
<td>Clinical assessment</td>
<td>93</td>
<td>58</td>
<td>[16]</td>
</tr>
<tr>
<td>FDG PET</td>
<td>Histopathology</td>
<td>92</td>
<td>71</td>
<td>[31]</td>
</tr>
<tr>
<td>HMPAO SPET (low resolution)</td>
<td>Histopathology</td>
<td>63</td>
<td>93</td>
<td>[24]</td>
</tr>
<tr>
<td>$^{133}$Xe and HMPAO SPET (low resolution)</td>
<td>Histopathology</td>
<td>86</td>
<td>73</td>
<td>[25]</td>
</tr>
<tr>
<td>HMPAO SPET (discriminant function)</td>
<td>Probable AD</td>
<td>91</td>
<td>86</td>
<td>[28]</td>
</tr>
<tr>
<td>FDG PET: mild AD (avg. MMSE =26)</td>
<td>Probable AD</td>
<td>88</td>
<td>Not specified</td>
<td>[52]</td>
</tr>
<tr>
<td>FDG PET: mild AD (MMSE &gt;21)</td>
<td>Probable AD</td>
<td>87</td>
<td>Not specified</td>
<td>[17]</td>
</tr>
<tr>
<td>FDG PET (progressive vs nonprogressive MCI)</td>
<td>Probable AD</td>
<td>93</td>
<td>74</td>
<td>[51]</td>
</tr>
<tr>
<td>HMPAO SPET (progressive vs nonprogressive MCI)</td>
<td>Probable AD</td>
<td>78</td>
<td>71</td>
<td>[50]</td>
</tr>
<tr>
<td>Tau protein/FDG ratio (progressive vs nonprogressive MCI)</td>
<td>Probable AD</td>
<td>89</td>
<td>90</td>
<td>[56]</td>
</tr>
</tbody>
</table>

AD, Alzheimer’s disease; MCI, mild cognitive impairment
Alzheimer’s is a Progressive Disease

• Progression rate is variable
• Apolipoprotein-E (APOE) involved
• Progression rate accurately measured by PET/SPECT
Rapidly Progressing Alzheimer’s Disease Baseline
Rapidly Progressing Alzheimer’s Disease
22 Months Post Baseline
Rapidly Progressive Alzheimer’s

Baseline

22 months post Baseline

155
Progressive Alzheimer’s Disease

Baseline
Progressive Alzheimer’s Disease

26 months post Baseline
### Serial SPECT Studies in Dementia

<table>
<thead>
<tr>
<th>Clinical Group</th>
<th>Worse</th>
<th>Improved</th>
<th>Unchanged</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDD</td>
<td>17</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>MID</td>
<td>2</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>1</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>

* Golan, Kremer, Freedman, Ichise
Frontal Temporal Dementia

- Manifestations
  - Cognitive decline
  - Altered behavior

- Types
  - Pick’s disease
  - Non Pick’s FTD
  - Others

- Pathology
  - Tau protein disorder
Frontal Temporal Dementia
Frontal Temporal Dementia

Baseline

24 Months Post Baseline
Normal Pressure Hydrocephalus
Normal Pressure Hydrocephalus
Normal Pressure Hydrocephalus

IN-111 DTPA
CISTERNOCGRAM
6HRS POST INJ.
Normal Pressure Hydrocephalus

ANT 48HR

POST 48HR

FLAT 48HR

LLAT 48HR

ANT ABD

POST ABD

48HR CISTERNOGRAM
Quiz: Dementia
What is the etiology?
Quiz: Dementia
What is the etiology?

1. Alzheimer’s Disease
2. Progressive Supranuclear Palsy (PSP)
3. Lewy Body Disease
4. Huntington’s Disease
5. Multi System Atrophy (MSA)
Quiz: Dementia
What is the etiology?

1. Alzheimer’s Disease
2. Progressive Supranuclear Palsy (PSP)
3. Lewy Body Disease
4. Huntington’s Disease
5. Multi System Atrophy (MSA)
Comparison of PET with SPECT
History

- 85 year old female with progressive memory loss and known prior infarct
- CT demonstrated right parietal infarction and moderate atrophy
Alzheimer’s + Infarct
FDG-PET
Alzheimer’s + Infarct
FDG-PET
Alzheimer’s + Infarct
ECD  SPECT
Alzheimer’s + Infarct
ECD SPECT
Alzheimer’s + Infarct
Comparison of PET and SPECT
Functional Brain Imaging in the Dementias

Recommended Reading

- Michael D. Devous, Sr, Eur JNM, Vol.29, No.12, Dec 2002
- Daniel HS Silverman, JNM, Vol.45:594-607, April 2004
Epilepsy

- **Ictal SPECT**
  - Injection time post seizure onset is critical ( < 30 seconds)
  - Correlation with outcomes is excellent

- **Interictal PET**
  - Excellent for temporal lobe epilepsy
Epilepsy

Interictal

Ictal

360
Epilepsy
Ictal SPECT
Seizure Disorder Interictal FDG-PET
FDG-PET

What is the Diagnosis?
Temporal Lobe Epilepsy
What side is abnormal?

1. Right
2. Left
What side is abnormal?

1. Right
2. Left
Is the study Ictal or Interictal?

1. Ictal
2. Interictal
Is the study Ictal or Interictal?

1. Ictal
2. Interictal
Second Chance if you blew the first Epilepsy case
Epilepsy second chance
Side and Status

1. Interictal, Left
2. Ictal, Left
3. Interictal, Right
4. Ictal, Right
Interictal FDG-PET
Left Temporal Lobe Epilepsy
Interventional Perfusion Studies

- Acetazolamide (Diamox) Vasodilatory challenge
Indications for Vasodilatory Challenge

- Cerebrovascular reserve in TIA
- Distinguish vascular dementia from Neuronal
What is the diagnosis?

Baseline

Post Diamox
Moderately Advanced Alzheimer’s Disease

Baseline

Post Diamox
Functional Brain Imaging in Oncology

- **FDG-PET**
  - Tumor Grading
  - Radiation Necrosis vs. Tumor
  - Therapy assessment

- **Thallium – 201**
  - Tumor Grading
  - Radiation Necrosis vs. Tumor
  - Therapy assessment

- **Tc-99m MIBI**
  - Predict chemotherapy effectiveness (MDR p-glycoprotein system)
FDG-PET
Brain Lymphoma
Radiation Necrosis vs. Tumor
Radiation Necrosis vs. Tumor
Severe Radiation Necrosis

Thallium

MIBI

FDG
Rheumatology

• Systemic Lupus Erythematosus (SLE)
  – Small infarcts
  – Prominent watershed deficits
Watershed Regions

Outer surface of cerebral hemisphere, showing areas supplied by cerebral arteries. Frontal watershed area, is the region between the red and blue area at the Superior Frontal Gyrus.

Red – Middle Cerebral Artery (MCA)
Blue – Anterior Cerebral Artery (ACA)
Yellow – Posterior Cerebral Artery (PCA)

Normal Subject – threshold setting at 60%
Subject A - SLE, threshold setting at 60%.
Subject B – SLE pt with threshold at 60.
Z-score comparisons between normal subjects and SLE subjects with cognitive/neuropsychiatric symptoms.
39 y/o female with mild memory impairment and a “fog” like sensorium
ECD SPECT Baseline
Mild Cognitive Impairment
ECD SPECT 7 years
Progressive Cognitive Impairment (Moderate)
ECD SPECT  7 years
Progressive Cognitive Impairment (Moderate)
Subsequent diagnosis of SLE with high antibody titers
Future Directions

• Direct imaging of specific molecules
  • Beta amyloid (PIB, FDDNP)
• Receptor imaging
• Quantification
• Fusion imaging
• Movement disorders (F-Dopa, DAT imaging)
PIB Scan

Alzheimer’s Disease

Normal Subject

Courtesy of University of Pittsburg Medical Center
FDG-PET / CT Fusion
3D-SSP FMZ PET DISPLAY

Neurostat
3D-SSP Display of C-11 Flumazenil PET with Abnormal Right Cerebral Hemispheric lesions c/w site of seizure onset
Movement Disorders
DAT Agents

Trodat
Summary
Requirements for building a growing practice of functional brain imaging

- A patient population requiring a diagnosis for a specific problem
- A clinicians perspective that a diagnosis is needed to optimize patient care
- Management decisions will be made based upon an accurate diagnosis (medical, psychosocial, legal, estate planning…)
- Diagnostic facility has credibility
  - Quality service
  - Excellent equipment
  - Knowledgeable physicians
  - Physician participation in educational programs
Summary
Requirements for building a growing practice of functional brain imaging

- Physicians and facility personnel need to understand the basics of SPECT and PET brain imaging
  - SNM Procedure Guidelines a good start
- Physicians need continuing education and experience
  - The more expert the interpreting physician, the greater opportunity for growth
- Technologist expertise is critical
  - Quality studies distinguish a facility
- Presenting critical images for viewing by referring physicians important for marketing
  - Surface rendered images
  - Appropriate quantitative displays
Summary
Requirements for building a growing practice of functional brain imaging

• Most important factor in practice building is **YOU!!!**
  • Knowledge of subject
  • Networking and “people” skills
  • Service Service Service