Brain Perfusion SPECT in Cerebrovascular Disease

David H. Lewis, MD
Director, HMC Nuclear Medicine
Associate Professor, Department of Radiology
University of Washington School of Medicine
Cerebrovascular Disease

- 3rd Leading Cause of Death in USA
- 1st Leading Cause of Disability in USA
- 700,000 strokes per year (90% ischemic, 10% hemorrhagic)
- Time is Brain!
Brain Perfusion
Radiopharmaceuticals

- Tc-99m HMPAO (hexamethyl propylene amine oxime, Ceretec)
- Tc-99m ECD (ethyl cysteinate dimer, Neurolite)
- Lipophilic, cross intact BBB and enter cells. Undergo hydrophilic conversion and thus remain in cell (HMPAO glutathione; ECD esterase). Peak activity in brain approximately at 20 seconds after antecubital bolus injection.
- Differences: Luxury Perfusion (HMPAO shows uptake more commonly, ECD rare but possible)
CEREBRAL BLOOD FLOW TRACING

Gray Matter
- High Flow
- High Counts

White Matter
- Low Flow
- Low Counts

Intravenous Injection of Tracer

Tracer trapped in the brain
○ Tracer in blood stream
Hyperperfusion Defined
- Uptake exceeds other supratentorial gray matter including adjacent and contralateral homologous regions
- Uptake exceeds or approximates cerebellar activity

Hypoperfusion Defined
- Uptake is less than adjacent and contralateral homologous regions and is much less than cerebellar activity
CVD: Clinical Uses

- Subarachnoid Hemorrhage and Vasospasm
- Hemodynamic TIA/Stroke Evaluation
- Acute Stroke
SAH and Vasospasm

- Vasospasm 4-12 days after hemorrhage
- Baseline SPECT post aneurysm obliteration
- Transcranial Doppler Flow Velocities and Indices are recorded daily
- SPECT images all vascular beds simultaneously (ICA, MCA, ACA, PCA, VB)
- Combination Helps Direct Medical and Interventional Management of Vasospasm at HMC
SPECT and CT Image Fusion (Hermes)
Brain SPECT after Subarachnoid Hemorrhage

- Davis et al. Stroke 1992. Correlations between cerebral arterial velocities, blood flow and delayed ischemia after subarachnoid hemorrhage. “Concordant vasospasm and hypoperfusion were most often present in patients with delayed ischemia and lateralizing neurological deficits.”

Baseline

Vasospasm In Right MCA

Baseline

Vasospasm In Right MCA
Vasospasm in Vertebrobasilar arterial system
Improved luminal diameter after balloon angioplasty
Sagittal Axis SPECT images are best for viewing brainstem.
Baseline perfusion

Vasospasm in VB circulation
Posterior Circulation Vasospasm after aneurysmal Subarachnoid Hemorrhage

- High correlation between TCD and SPECT in vertebrobasilar vasospasm
- Other methods are less well suited to perfusion imaging in posterior fossa in this patient population
Baseline

Left thalamus hypoperfusion
Baseline

Left ICA and VB vasospasm
Brain Perfusion SPECT shows the Effect of Endovascular Treatment

Pre-angioplasty

Post-angioplasty
Effect of Interventional Endovascular Therapy in Vasospasm

- Lewis DH, et al. 1995, 1999 *Journal of Stroke and Cerebrovascular Diseases*
- Elliott P, et al. 1998 *Journal of Neurosurgery*
- Studies show that brain perfusion SPECT reliably images effect of endovascular treatment and that balloon angioplasty is most effective technique
Vasospasm in left MCA

Left occipital Infarct
Severe Vasospasm in Bilateral ACA territories
Severe Ischemia from Vasospasm: ACA territories

PERFUSION DEFECTS

<table>
<thead>
<tr>
<th>Size (%)</th>
<th>Voxels</th>
<th>Size (mL)</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-25</td>
<td>341</td>
<td>235-275</td>
<td>1-2</td>
</tr>
</tbody>
</table>
BRASS Quantification of Difference

<table>
<thead>
<tr>
<th></th>
<th>Size (%)</th>
<th>Voxels</th>
<th>Size (mL)</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>STUDY1</td>
<td>20.77</td>
<td>6441</td>
<td>236.7</td>
<td>4.4</td>
</tr>
<tr>
<td>STUDY2</td>
<td>6.86</td>
<td>2127</td>
<td>78.2</td>
<td>3.8</td>
</tr>
<tr>
<td>DIFFERENCE</td>
<td>20.808</td>
<td>6453</td>
<td>237.1</td>
<td></td>
</tr>
</tbody>
</table>
STUDY1: 21.06 Voxels 6530 Size (mL) 240.0 Severity 4.3
STUDY2: 11.01 Voxels 3415 Size (mL) 125.5 Severity 3.9
DIFFERENCE 14.078 Voxels 4366 Size (mL) 160.4

PERFUSION DEFECTS


- A multivariate logistic regression analysis identified SPECT measurements obtained during Days 7 to 14 after the SAH as the only independent predictor ($[\beta] = 0.042, P = 0.02$) for impaired perfusion after 1 year.

- “Serial SPECT measurements after aneurysmal SAH demonstrate that regional changes in cerebral perfusion follow a nonlinear time trend, and repeated measurements are necessary. This observation, as well as the low feasibility of SPECT, restricts the clinical value of such measurements.”

- **Low feasibility? My response “NOT”**
Cerebral Perfusion before and after endovascular or surgical treatment of acutely ruptured cerebral aneurysms: a 1-year prospective follow-up study

Koivisto et al. Neurosurgery 2002. Though no differences were perceived at 1 year on MRI between endovascular and surgical cases, SPECT showed more early defects in post-surgical group 1 week after treatment.
Brain Perfusion SPECT after Subarachnoid Hemorrhage

- Clinically Feasible
- Predictive of Outcome
- Helps in Management of Patients
- Requires Repeat Measures
- Comparison to TCD, angiography and anatomic imaging is essential
Hemodynamic Disease

- Moya moya
- Atherosclerotic
- Limb Shaking TIA
- Cerebrovascular Reserve
Vasoactive Challenge

- Diamox (acetazolamide)
- Carbon Dioxide
- Adenosine
- Cold Hands Test
Hemodynamic TIA

- Due to occlusive vascular disease or multiple and/or multilevel stenoses
- At Harborview the most common referral is moyamoya disease, but most common cause in USA is atherosclerosis
- Diamox Testing is used to assess vasodilatory reserve
- Carbon Dioxide Testing is used in those who are sulfa allergic
Vasodilatory Reserve Testing

- In adults, 1000 mg Diamox (acetazolamide) IV over 5 minutes with tracer injection 20 minutes after Diamox has been infused
- In children, pediatric Diamox dose is 14 mg/kg
- In sulfa allergic patients, carbon dioxide 5% is given by inhalation over 5 minutes with tracer injection at 1 to 2 minutes during inhalation
- Probable contra-indication in acute and subacute stroke
Moya
Moya
Disease
Diamox Stress Test

**Imaging parameters:**
- SPECT imaging 45 minute after Neurolite injection
- Triple-head camera
- Fanbeam collimators
Diamox Stress Test Example

Visual comparison of stress/rest images
Right ICA Occlusion
With Limb Shaking
TIA
Right ICA stenosis and bilateral MCA aneurysms, pre-operative risk assessment
MRI and Diamox SPECT Fusion (Hermes)
<table>
<thead>
<tr>
<th>Size (%)</th>
<th>Voxels</th>
<th>Size (mL)</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y1</td>
<td>11.60</td>
<td>3597</td>
<td>132.2</td>
</tr>
<tr>
<td>Y2</td>
<td>7.64</td>
<td>2363</td>
<td>86.8</td>
</tr>
<tr>
<td>REFERENCE</td>
<td>17.535</td>
<td>5438</td>
<td>199.8</td>
</tr>
</tbody>
</table>

PERFUSION DEFECTS
<table>
<thead>
<tr>
<th></th>
<th>Size (%)</th>
<th>Voxels</th>
<th>Size (mL)</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>STUDY1</td>
<td>11.60</td>
<td>3597</td>
<td>132.2</td>
<td>3.8</td>
</tr>
<tr>
<td>STUDY2</td>
<td>7.64</td>
<td>2363</td>
<td>86.8</td>
<td>3.7</td>
</tr>
<tr>
<td>DIFFERENCE</td>
<td>17.535</td>
<td>5438</td>
<td>199.8</td>
<td></td>
</tr>
</tbody>
</table>
MoyaMoya Disease
Where is the brain most at risk?
Diamox minus rest SPECT Fused with MRI: Neurostat
Acute Ischemic Stroke Evaluation and Treatment

Does Brain Perfusion SPECT have a role?
Why Image Perfusion During Stroke?


Case: 35 F, 4 hours

Pretreatment SPECT

Follow-up CT

R/CE ratio = 0.51
Asymmetry index = 1.35

Toshihiro Ueda, MD
Dept. of Neurosurgery, Ehime University, JAPAN
Case: 82 F, 6 hours

Pretreatment SPECT

Follow-up CT

R/CE ratio = 0.45
Asymmetry index = 1.25

Toshihiro Ueda, MD
Dept. of Neurosurgery, Ehime University, JAPAN
Case: 61 M, 3 hours
Pretreatment SPECT

R/CE ratio = 0.12
Asymmetry index = 1.71

Follow-up CT

Toshihiro Ueda, MD
Dept. of Neurosurgery, Ehime University, JAPAN
Outcome vs. Severity of Ischemia

R/CE ratio vs. Asymmetry index

Non-infarction
Infarction
Hemorrhage

Toshihiro Ueda, MD
Dept. of Neurosurgery
Ehime University, JAPAN
J Cereb Blood Flow Metab
1999;19:99-108
Outcome vs. Severity and Duration of Ischemia

- **Non-infarction**
- **Infarction**
- **Hemorrhage**

Toshihiro Ueda, MD
Dept. of Neurosurgery
Ehime University, JAPAN
J Cereb Blood Flow Metab
1999;19:99-108
81 year old female with R hemiparesis and transient dysphasia

L caudate and lentiform hypoperfusion
62 year old female with R hemiparesis and mild transient dysphasia

lentiform nucleus and posterior limb internal capsule infarct
Neurolite®

posterior limb
internal capsule

48 year old female
with R internal carotid
near occlusion and
left hemiplegic stroke

Patient #4
Right MCA Stroke

ECD uptake
### Left Cerebellar Diaschisis from Right MCA Stroke

<table>
<thead>
<tr>
<th>STUDY1</th>
<th>Size (%)</th>
<th>Voxels</th>
<th>Size (mL)</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>STUDY1</td>
<td>16.95</td>
<td>5243</td>
<td>192.7</td>
<td>5.1</td>
</tr>
</tbody>
</table>

**Perfusion Defects**

2006:08:02 Brain
Right ICA angiogram shows evidence of luxury perfusion
ECD on right shows infarct which matches MRI after 2 weeks
Vascular BRASS analysis shows extent of Right MCA stroke
CONCLUSIONS

NEUROLOGIC SPECT SCANNING, GENERAL
- Images brain function, based on tracer distribution
- Analogous to PET perfusion imaging at far lower cost
- FDA-approved tracers image cerebral perfusion

SPECT IN CEREBROVASCULAR DISEASE
- Delineates ischemic lesions before MRI or CT
- Potential stratification of stroke risk post-TIA
- Monitoring of perfusion before and after medical/surgical interventions
- Monitoring of subarachnoid hemorrhage patients for vasospasm
- Helps distinguish cortical from lacunar stroke