PPMI Imaging Core Update

2 May 2012
Imaging Technical Sites Visited

Northwestern
IND- New Haven
Johns Hopkins
Federico II - Naples
Parkinson’s Institute- Sunnyvale
Univ Pennsylvania
Univ Rochester
APDC- Sun City, Az
Baylor
London
Univ Cincinnati

Univ Alabama-Birmingham
Boston University
Portland
Innsbruck
Marburg
Tübingen
Univ Washington
Tampa
Emory Univ
San Diego
Cleveland Clinic
Boca Raton
Sydney
PPMI DAT Imaging Studies In-house at IND Core Lab

Scans received: controls = 186  PD baseline = 217

SWEDDs = 39 (about 15%), 25 enrolled for follow-up

PD Year 1 scans = 55

DATScans uploaded to LONI = 275

Healthy volunteers with abnormal scans = 6
Percent of SWEDDs Decreases With Disease Duration

Example Healthy with Abnormal Scan
DAT SPECT Quantitative Analysis

1. Core lab reconstruction from raw projection data, including attenuation correction based on phantoms from site visit
2. Spatial normalization of image creates consistent orientation
3. Apply standard volume of interest template on caudate, putamen, occipital regions
4. Extract count densities and calculate Striatal Binding Ratios (SBR)
5. 57Co Phantom correction of SBRs (?)
DAT SPECT Striatal Binding Ratios-Baseline Scans

**PPMI Avg SBR**

PD n=197  HV n= 129  SW n=25

**PPMI lowest putamen**

PD n=197  HV n= 129  SW n=25
SBR signal loss is 6.2% per Decade in Healthy Volunteers

N = 129
SBR signal in PD is poorly correlated with age

N = 197
SBR signal loss is 4.7% per decade in SWEDDs

N = 25
PD “outlier” scan
Longitudinal Assessment of Striatal Binding Ratio in PD

N = 47
Percent change over one year (n=47)

Mean reduction = 12.4%  (COV= 131%)
DAT Imaging in PPMI

• SWEDDs rate about as expected (15%) in de novo PD, SBR outcomes similar to controls, but limited data

• Normal aging is associated with about 6% signal loss per decade (0.6%/year)

• First longitudinal data suggests SBR reductions over one year approximately 20 times the rate of signal loss seen in normal aging
Presentations

• Society of Nuclear Medicine Annual Meeting, June 12, 2012. Miami, Florida

• The MDS 16th International Congress of Parkinson's Disease and Movement Disorders June 19, 2012. Dublin, Ireland
New DEA 222 Procedure

• GE will no longer accept “open-ended” DEA 222 forms after May 7, 2012
• Those sites using paper 222 forms will need to submit a 222 for each order
• Solution is to obtain digital certificate and order vials electronically from CSOS
• A GE representative can help sort through process of registering for the digital certificate
DTI Subproject Processing & Analysis

K. Wu, S. Buckley, D. Tosun, F. Ezekiel and N. Schuff

VA and UCSF, San Francisco
May 2012
## Processing Status

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Baseline (Year 1)</th>
<th>Follow-up (Year 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received</td>
<td>112</td>
<td>6</td>
</tr>
<tr>
<td>Processed</td>
<td>85</td>
<td>2</td>
</tr>
<tr>
<td>LONI Uploaded</td>
<td>71</td>
<td>0</td>
</tr>
</tbody>
</table>

As of April 27, 2012.

Note: the number of processed images is almost twice as large, since most subjects have two DTI scans in a single session and we process both sets.
# Subject Demographics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control</th>
<th>PD</th>
<th>SWEDD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 52)</td>
<td>(n = 54)</td>
<td>(n = 6)</td>
</tr>
<tr>
<td>Age (year)</td>
<td>58.5 (11.1)</td>
<td>61.7 (9.1)</td>
<td>57.0 (14.1)</td>
</tr>
<tr>
<td>Gender: M/F</td>
<td>31 / 21</td>
<td>38 / 16</td>
<td>3 / 3</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>NA</td>
<td>1.4 (0.8)</td>
<td>1.0 (0.5)</td>
</tr>
</tbody>
</table>

As of April 10, 2012.
Results are presented as: mean (standard deviation).
n, number; NA, not applicable;
DTI Sites

- As of March 6, 2012:
  - 9 active sites
    - Baylor, Parkinson’s Institute, John Hopkins, Emory, Northwestern, Mellen Center, Tubingen, Paracelsus-Elena, and Innsbruck

<table>
<thead>
<tr>
<th>Site</th>
<th>Subjects</th>
<th>DTI sets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baylor</td>
<td>14</td>
<td>27</td>
</tr>
<tr>
<td>Parkinson’s Institute</td>
<td>14</td>
<td>28</td>
</tr>
<tr>
<td>John Hopkins</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>Emory</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>Northwestern</td>
<td>17</td>
<td>33</td>
</tr>
<tr>
<td>Mellen Center</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Tubingen</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>Paracelsus-Elena</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>Innsbruck</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100</strong></td>
<td><strong>197</strong></td>
</tr>
</tbody>
</table>
1 Year DTI Stability Across Sites
(Signal-To-Noise Ratio)
Minimum qualification is SNR > 30

Special headcoil used

SNR

Time


007 Baylor 012 Parkinson's Institute 028 John Hopkins
032 Emory 088 Northwestern 120 Mellen Center Cleaveland
289 Tubingen 290 Paracelsus-Elena 291 Innsbruck
Representative FA Maps

Group Averaged FA

Control

PD
Regional DTI Abnormalities In PD

In Relation to:

Increased Movement Deficits

Substantia nigra
[3,5] Lateral frontal lobe
[1,2] Lateral Temporal lobe

Diminished Dopamine Uptake

Key regions:
[1] Supplementary Motor Area
[2] Insular region
Representative Maps With Markings For Evaluating DTI In The Nigra

T2

FA

Directional Diffusion Map
Preliminary Results: FA Variations In The Nigra
Conclusions

• DTI may have clinical value for the assessment of Parkinson’s disease.

• Moreover, DTI provides complementary information to DAT imaging, especially with respect to quantification of severity of symptoms.

• DTI is feasible in a multicenter setting
Publications

1. *Distribution of diminished brain microstructure in Parkinson’s disease:
   Abstract AAN, New Orleans

2. Associations between brain microstructural and dopaminergic integrity in Parkinson’s disease: A joint diffusion tensor and DAT imaging study:
   Abstract MDS meeting, Dublin

* Selected for AAN Scientific Program Highlights Plenary Session.
Plans

1. Repeat analyses with a larger sample size, especially ROI analysis of FA in substantia nigra
2. Processing and analysis of 1 yr follow-up DTIs
3. Implementation of tractography and tract-based analysis
4. Joint analysis of DTI and structural MRI
5. Joint analyses of DTI, clinical data and biomarkers (with guidance from Christopher)
New Development: Probabilistic Fiber Tracking*

* TRACULA
by Anastasia Yendiki
MGH