Current ADNI PET Data

**Florbetapir**

1011 Baseline scans (910 Processed)
174 Follow-up scans (all processed)
39 “early frame” datasets

**FDG (N = 2920)**

<table>
<thead>
<tr>
<th></th>
<th>AD</th>
<th>EMCI</th>
<th>LMCI</th>
<th>N</th>
<th>SMC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>225</td>
<td>308</td>
<td>396</td>
<td>318</td>
<td>29</td>
</tr>
<tr>
<td>6 month</td>
<td>88</td>
<td></td>
<td>186</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>12 month</td>
<td>76</td>
<td>64</td>
<td>202</td>
<td>130</td>
<td></td>
</tr>
<tr>
<td>18 month</td>
<td></td>
<td></td>
<td>153</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 month</td>
<td>62</td>
<td>4</td>
<td>149</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>36 month</td>
<td></td>
<td></td>
<td>111</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>48 month</td>
<td></td>
<td></td>
<td>58</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>60 month</td>
<td></td>
<td></td>
<td>14</td>
<td>24</td>
<td></td>
</tr>
</tbody>
</table>
Florbetapir Frequency Distribution

51% Florbetapir+

910 Subjects
263 Normals
289 EMCI
212 LMCI
146 AD
Florbetapir Threshold in Normals

1.11
ADNI Florbetapir summary March 2013

N=910

Florbetapir-  Florbetapir+

28%

Normal
N=263

47%

Early MCI
N=289

63%

Late MCI
N=212

86%

AD
N=146

Florbetapir SUVR (Whole Cerebellum Normalization)
ADNI Florbetapir distribution stratified by ApoE4 status

- **ApoE4-**
  - 23% of ApoE4- are florbetapir+
  - 32% of ApoE4- are florbetapir+
  - 39% of ApoE4- are florbetapir+
  - 56% of ApoE4- are florbetapir+

- **ApoE4+**
  - 45% of ApoE4+ are florbetapir+
  - 67% of ApoE4+ are florbetapir+
  - 88% of ApoE4+ are florbetapir+
  - 98% of ApoE4+ are florbetapir+

- Total N=895

- N=260
- N=284
- N=210
- N=141
ApoE4+ Aβ40 Aβ42

**ApoE4-**

- (15/52) 29% of ApoE4- are CSF Aβ+
- (22/54) 41% of ApoE4- are CSF Aβ+
- (25/49) 51% of ApoE4- are CSF Aβ+
- (16/22) 73% of ApoE4- are CSF Aβ+

**ApoE4+**

- (11/25) 44% of ApoE4+ are CSF Aβ+
- (33/50) 66% of ApoE4+ are CSF Aβ+
- (54/56) 96% of ApoE4+ are CSF Aβ+
- (58/59) 98% of ApoE4+ are CSF Aβ+

*Total N=367*
Florbetapir and CSF Aβ agreement

Total N=378

Baseline florbetapir (whole cerebellum norm)

Kappa = 0.79
(previous = 0.72)

(Previous = 374)
CSF change by florbetapir status

Total N=94

CSF Aβ+

CSF Aβ-

Florbetapir -

Florbetapir +

Time relative to florbetapir scan
CSF change by florbetapir and APOE4 status

Total N=93

- CSF Aβ-
- CSF Aβ+

Time relative to florbetapir scan

ApoE4 -
ApoE4 +
ApoE4 -
ApoE4 +
New Initiative: “Early Frames” Add on

Initial uptake and clearance of highly permeable tracers reflect perfusion

Florbetapir data from injection to 50 min are not captured

Would Florbetapir data from 0-50 min provide functional information?

Compare early frame data to FDG-PET in a wide range of dementia severity/stages
Early PiB Frames vs FDG-PET

Minutes 1-8 after $[^{11}C]PiB$ injection summed

Correlations between FDG and PiB data computed for 12 ROIs

Mean Pearson $R = 0.91$

(72 cases of AD or FTLD)
Study Design

Approximately 20 sites
must be capable of dynamic scanning and simultaneous injection/scan start

100 subjects: Normal, EMCI, LMCI, AD

Data collection 0-20 min, then back in scanner for the standard 50-70 min

All data treated identically to all other ADNI data
The “Centiloid’ Project

An effort to standardize the numerical reporting of PET amyloid tracer retention

Goal: A numerical value reflects the same thing (ie, Aβ-, slightly Aβ+, very Aβ+, borderline) regardless of tracer

Participants: Bill Klunk, Mike Devous, Bill Jagust, Keith Johnson, Bob Koeppe, Chet Mathis, Mark Mintun, Mike Pontecorvo, Julie Price, Chris Rowe, Dan Skovronsky
Examples of Different Scales

BP
PIB

SUVR
AV-45

DVR
PIB

Typical AD Range

“Positive” threshold

Normals

0.0  0.5  1.0  1.5  2.0  2.5

0.0  0.5  1.0  1.5  2.0  2.5

0.0  0.5  1.0  1.5  2.0  2.5
The Centiloid Scale is meant to:
Help standardize reporting across labs and tracers
Clearly define thresholds for amyloid positivity
Define range from “borderline” to “AD-like”
Consistent representation of longitudinal change

The Centiloid Scale is not meant to:
Solve all problems related to standardization
Represent an “industry standard” requirement
Constrain laboratories in how data are analyzed or reported

Ultimately, the amyloid imaging investigators will decide if this is a useful approach
A Brief Explanation of How it Works

Step 1: Standardization

\[^{11}\text{C}]\text{PIB 50-70 min SUVR as the standard anchor: Young Subjects (median)}

100 anchor: Probable AD patients (median)

Standard data analysis method

Conversion of SUVR to Centiloid (y = mx + b)

\[ y = 68.214x - 81.768 \]

\[ R^2 = 1 \]
Step 2: Calibrate new Tracer (or method)

Collect PIB 50-70 SUVR data with new tracer data in same subjects (including young and AD)

Verification that standard analysis method works by downloading and analyzing the standard dataset

Convert newly acquired PIB data to Centiloids

Convert new tracer data to Centiloids
Next Up: Tau Imaging

[18F]-T807 PET (80-100 min p.i.)

HC (56y)  MCI (MMSE=26)  AD (MMSE=21)  AD (MMSE=7)

Chien et al, J Alz Disease 2012
Acknowledgements

Susan Landau, Suzanne Baker, Bob Koeppe, Eric Reiman, Kewei Chen, Norman Foster
Core Leaders
Site PIs
Participants