

SPAP and Avid florbetapir Analysis Methods

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Summary

Semi-automated quantification of florbetapir PET images was performed using syngo.PET Amyloid Plaque (sPAP) in a large clinical population downloaded from ADNI. sPAP performs automatic registration of each subject's florbetapir PET image to MNI (Montreal Neurological Institute) atlas space then computes the cortex-to-cerebellum regional count ratio (SUVr) for a set of six target regions of interest. We compared the mean cortical SUVrs calculated using sPAP with those calculated using Avid semi-automatic method described in Clark et.al¹ and Joshi et.al². Both methods are described in more detail below.

Method

Acquisition of florbetapir data from ADNI

Florbetapir PET data for 604 subjects clinically diagnosed (using the closest diagnosis to the florbetapir scan date) as normal subjects (NL, N= 200), early mild cognitively impaired (EMCI, N=215), mild cognitively impaired (MCI, N=163) and Alzheimer's diseases (AD, N=26). This data was downloaded (as per August 2012) from LONI in the most fully post reconstruction processed format (series description in LONI Advanced Search: AV45 Coreg, AVG, Std Img. and Vox Siz, Uniform Resolution).

Calculation of SUVr using Avid Semi-Automated Method

Florbetapir PET images were spatially normalized using SPM (version 2, University College London)³ to standard stereotactic atlas co-ordinates with reference to a Florbetapir PET template (in MNI space); this method was referred to as fit1. The spatial normalization results were visually checked for alignment of the patient brain to the template brain. Cases with unacceptable results from fit1 were spatially normalized using a weighting factor such as template brain mask; this method was referred to as fit2. Cases with unacceptable results from fit2 were spatially normalized using fit3 which includes de-skulling the patient image, fitting the de-skulled image and applying transformation to the original/non-de-skulled patient PET image. Cases with acceptable spatial normalization results were used for SUVr calculation.

SUVr values were calculated as a ratio of mean uptake value in six predefined anatomically relevant cortical regions of interest (medial orbital frontal, parietal, temporal, precuneus, posterior cingulate and anterior cingulate) with respect to the mean uptake in the entire cerebellum as a reference region. SUVrs for individual regions were also calculated.

Calculation of SUVR using Syngo.PET Amyloid Plaque

The semi-automatic method in sPAP is based on the method to compute the cortex-to-cerebellum SUVR described above and in Clark et.al¹ and Joshi et. al². Florbetapir PET images were spatially normalized using automatic affine registration to a synthetic florbetapir PET template in MNI atlas space. Registration results were visually examined by comparing alignment of the patient's PET brain to the template brain and alignment of the patient cerebellum to the template cerebellum outline. For cases requiring an improvement to the automatic registration results, manual registration adjustments were applied using 12 parameter manual adjustments, which includes translation, scaling, rotation and shearing.

Once registration results were acceptable after visual examination, mean and regional cortex-to-cerebellum SUVRs were calculated from the six anatomically relevant cortical regions of interest as described above. sPAP regions of interest were based on those presented in Fleisher et. al⁴.

Results

All 604 subjects were successfully registered to the template using both methods. Using Avid analysis method 589/604 cases were spatially normalized using fit1 method, 10/604 cases using fit2 and 5 cases using fit3 (Table 1). Using sPAP 590/604 cases were spatially normalized using automatic registration. 2.3% (14/604) of the total cases were registered using manual adjustment (Table 2). Mean cortical SUVR values calculated using both methods correlated highly ($r=0.99$, Figure 1). Based on the pre-specified cut-point for Avid method, $SUVR > 1.10$ (Joshi et.al².) was considered as florbetapir positive. Using the regression analysis ($y=0.04264+0.9782*x$) Avid threshold of 1.10 SUVR units can be compared to $SUVR = 1.1186$ in sPAP analysis.

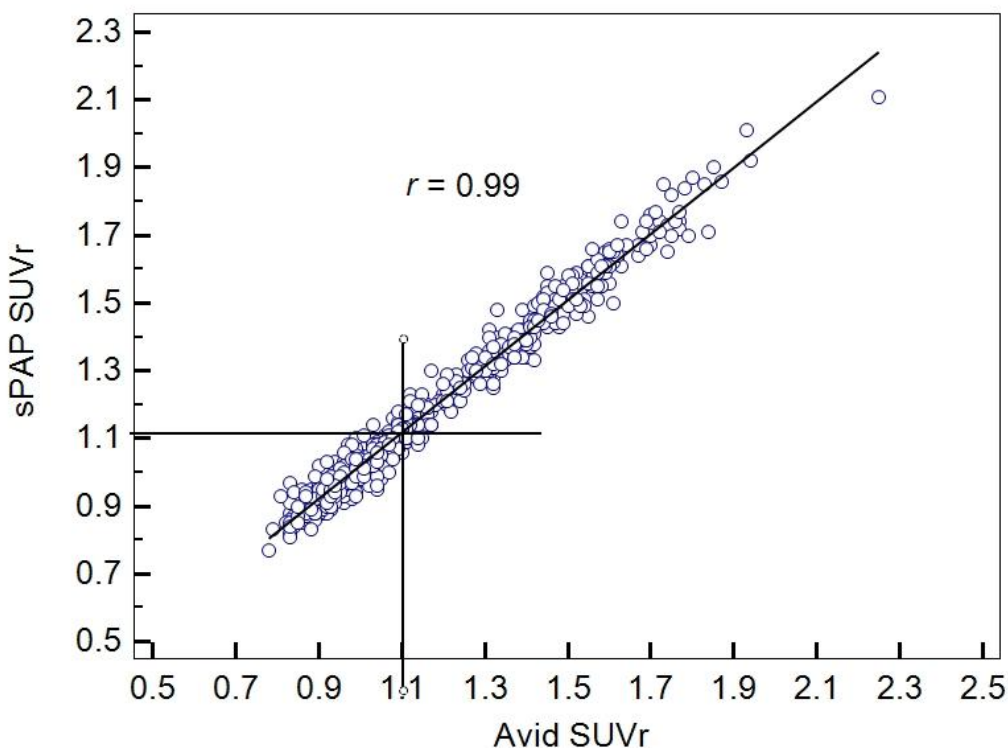
Table 1- List of cases that requires advance registration option such as using brain mask (referred as fit2) and de-skulling (referred as fit3) in Avid analysis method

RID	Subject ID	Fit method
1280	002_S_1280	Fit2
2010	002_S_2010	Fit3
1074	003_S_1074	Fit2
2180	018_S_2180	Fit2
118	027_S_0118	Fit2
1169	032_S_1169	Fit2
2074	035_S_2074	Fit2
127	068_S_0127	Fit2
2027	072_S_2027	Fit2
2191	073_S_2191	Fit2
2099	082_S_2099	Fit3
2278	109_S_2278	Fit3
225	128_S_0225	Fit3
1052	141_S_1052	Fit3
2210	141_S_2210	Fit3

Table 2-Cases requiring manual registration adjustments in sPAP

RID	Subject ID	sPAP SUVR Global	Avid Global SUVR
4136	003_S_4136	1.59	1.45
4288	003_S_4288	1.09	1.09
572	005_S_0572	1.87	1.8
4449	006_S_4449	1.04	1.03
4093	014_S_4093	1.09	1.04
702	016_S_0702	1.74	1.72
61	023_S_0061	1.48	1.33
845	029_S_0845	1.24	1.25
2018	031_S_2018	0.96	1.02
214	032_S_0214	2.18	2.25
1123	051_S_1123	1.66	1.56
896	098_S_0896	1.04	1.04
2347	129_S_2347	1.03	0.98
2210	141_S_2210	1.08	1.14

Figure 1-Correlation ($r=0.99$) between SUVR values calculated using Avid analysis method and sPAP software.



Dataset Information

This methods document applies to the following dataset(s) available from the ADNI repository:

Dataset Name	Date Submitted
sPAP_Florbetapir_Analysis_Data_5.xlsx	
Avid_analysis_ADNI_florbetapir_4.xlsx	

References

1. Clark CM, Pontecorvo MJ, Skovronsky DM, et. al. Cerebral PET with florbetapir compared with neuropathology at autopsy for detection of neuritic amyloid- β plaques: a prospective cohort study. *Lancet Neurol.* 2012; 11 (8):669-678.
2. Joshi AD, Pontecorvo MJ, Clark CM, et. al. Performance characteristics of amyloid PET with florbetapir F 18 in patients with alzheimer's disease and cognitively normal subjects. *J Nucl Med.* 2012; 53(3):378-384.
3. Friston KJF, Ashburner JT, Kiebel SJ, et. al. *Statistical Parametric Mapping: the Analysis of Functional Brain Images.* London, U.K.: Academic Press; 2007
4. Fleisher AS, Chen K, Liu X, et al. Using positron emission tomography and Florbetapir F 18 to image cortical amyloid in patients with mild cognitive impairment or dementia due to Alzheimer disease. *Archive of Neurology.* 2011; (doi:10.1001/archneurol.2011.150)

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