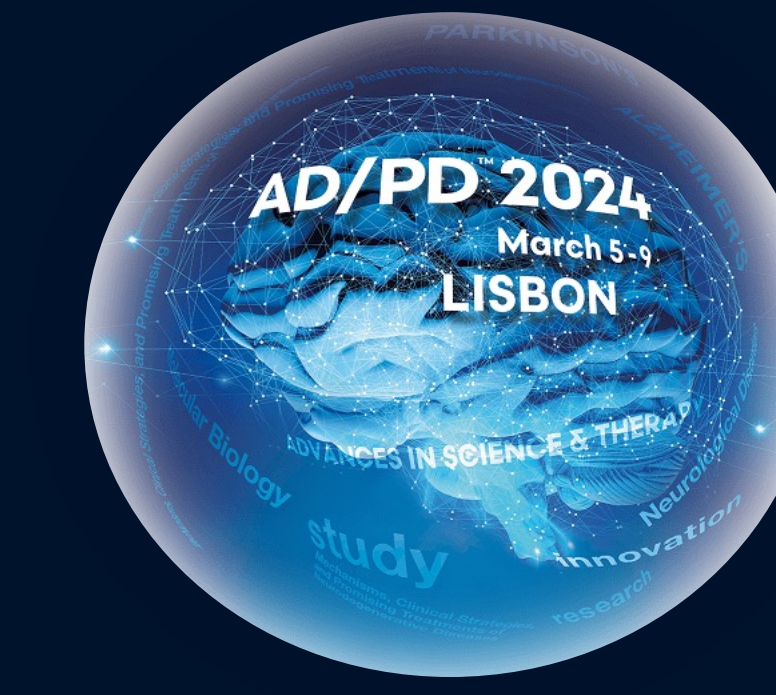


AN AUTOMATED PIPELINE FOR CENTILOID QUANTIFICATION OF AMYLOID- β USING MULTIPLE ^{11}C -PIB-PET AND ^{18}F -PET TRACERS

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AD/PD 2024
ADVANCES IN SCIENCE & THERAPY
March 5 - 9, 2024 | Lisbon, Portugal + Hybrid



BACKGROUND

Quantitative measures of amyloid- β (A β) pathology using positron emission tomography (PET) imaging are sensitive to identify pathological changes, even at the earliest stages of Alzheimer's disease (AD). However, the quantification values vary considerably between tracers and acquisitions, making comparisons across studies and clinical trials findings problematic.

The Centiloid scale aims to standardize these in vivo amyloid quantifications to a 100-point scale, where an average value of zero signifies high certainty of amyloid negativity and 100 identifies average typical AD A β -pathology load¹. A fully automated Centiloid quantification pipeline supporting multiple available amyloid-PET tracers would be valuable for improving the efficacy and comparability of PET-based analyses across study sites.

OBJECTIVES

To develop and validate Qyscore[®]'s single fully automated Centiloid quantification pipeline for multiple amyloid PET tracers.

METHODS

Qyscore[®]'s fully automated pipeline was validated on ^{11}C -PiB-PET and ^{18}F -PET images from the Centiloid project (<https://www.gaain.org/centiloid-project>):

- 34 young controls [age=31.5 \pm 6.3 years] and 45 AD patients [age=67.5 \pm 10.5 years; CDR= 0.5–1].

^{18}F tracers included Florbetapir² (FBP, $n = 46$), Forbetaben³ (FBB, $n = 35$), Flutemetamol⁴ (FTM, $n = 74$) and NAV4694⁵ (NAV, $n = 55$). PET/MR image pairs were both co-registered and normalized in the MNI template space (**Figure 1**).

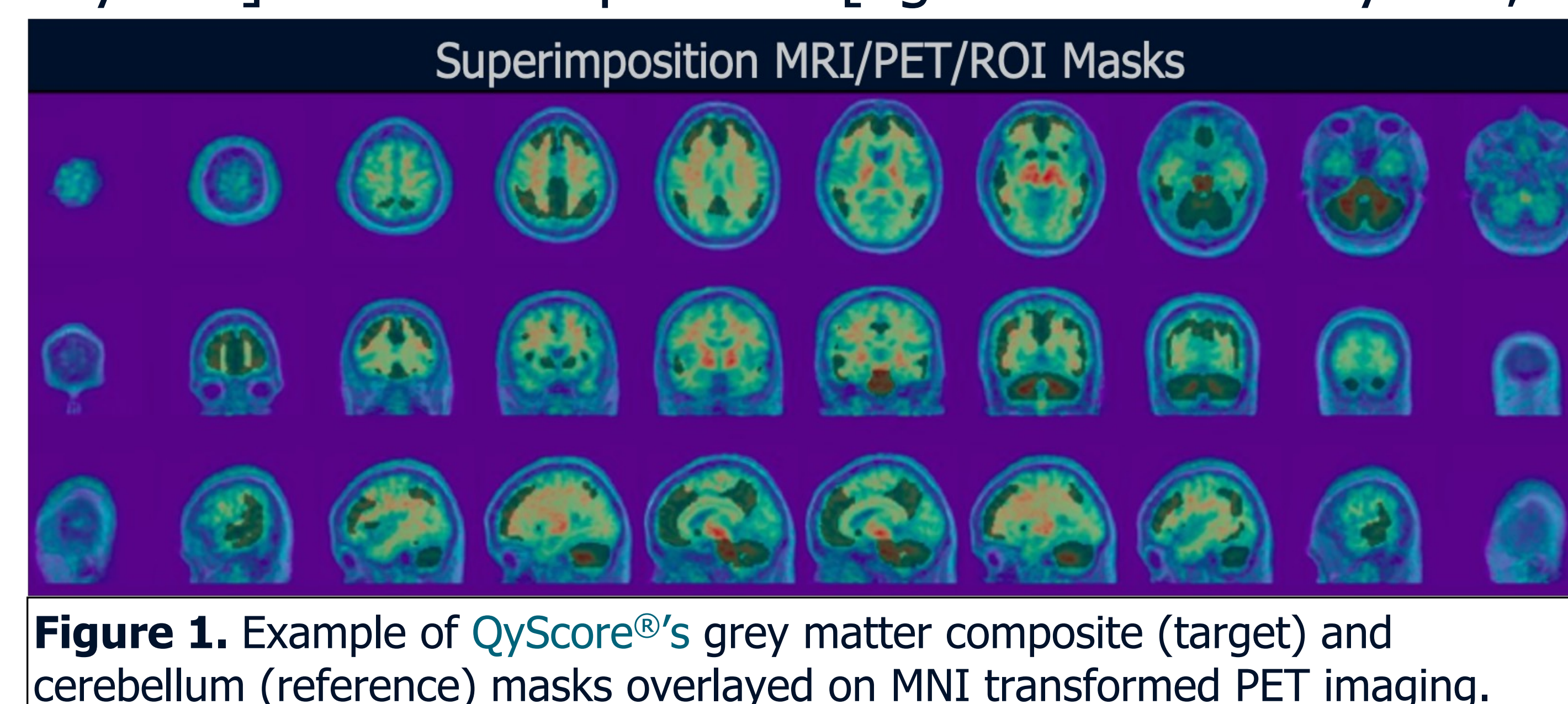


Figure 1. Example of Qyscore[®]'s grey matter composite (target) and cerebellum (reference) masks overlayed on MNI transformed PET imaging.

The fully automated segmentation from Qyscore[®], a CE-marked and FDA-cleared neuroimaging medical device, parcellated the regional masks of the grey matter tissue (target region of interest).

Standardized uptake value ratio (SUVr) was computed as the ratio of the mean signal in the target region compared to that in the cerebellum (reference) (**Figure 1**)¹.

Correlations of (^{11}C -PiB and ^{18}F) SUVr values with published SUVr data were computed^[2-5].

Further, correlations between ^{18}F SUVr and paired ^{11}C -PiB SUVr were computed. Correlation coefficients (R^2) > 0.7 were required to consider the Centiloid calibration valid.

Equations for converting ^{18}F -SUVr values to Centiloid (CL) standardized values were then derived from the Centiloid project recommended validation process¹.

RESULTS

Qyscore[®]'s fully automated quantitative pipeline produced SUVr values well within the bounds defined by the Centiloid method

- SUVr_**AD-100** = **2.08** +/- 0.2 and SUVr_**YC-0** = **1.01** +/- 0.05, $R^2 = 0.99$; slope = 1.00; intercept = -0.44).

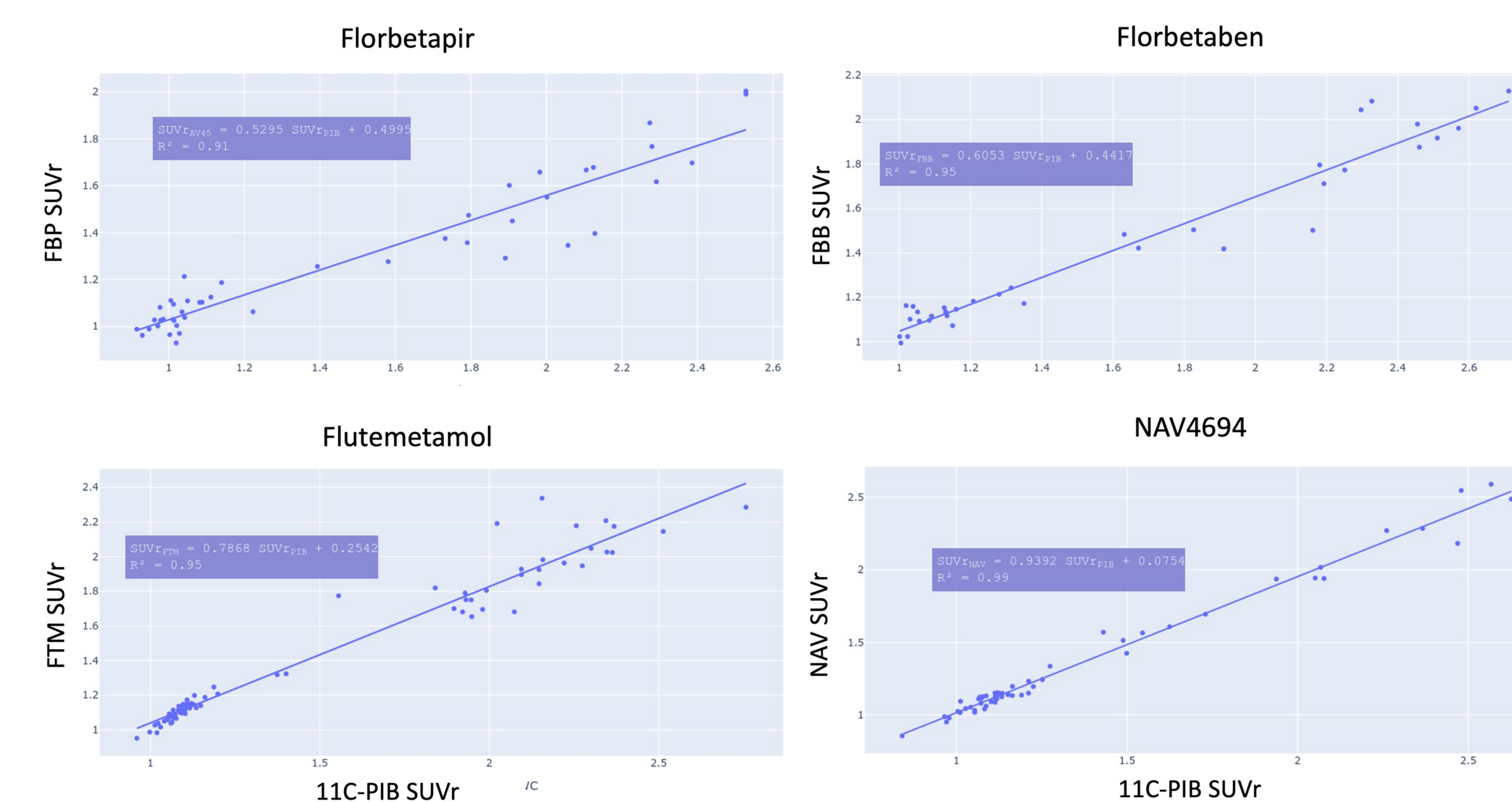


Figure 2. Correlation between each ^{18}F tracer and paired ^{11}C -PiB SUVr produced using Qyscore[®]'s fully automated quantitative PET pipeline

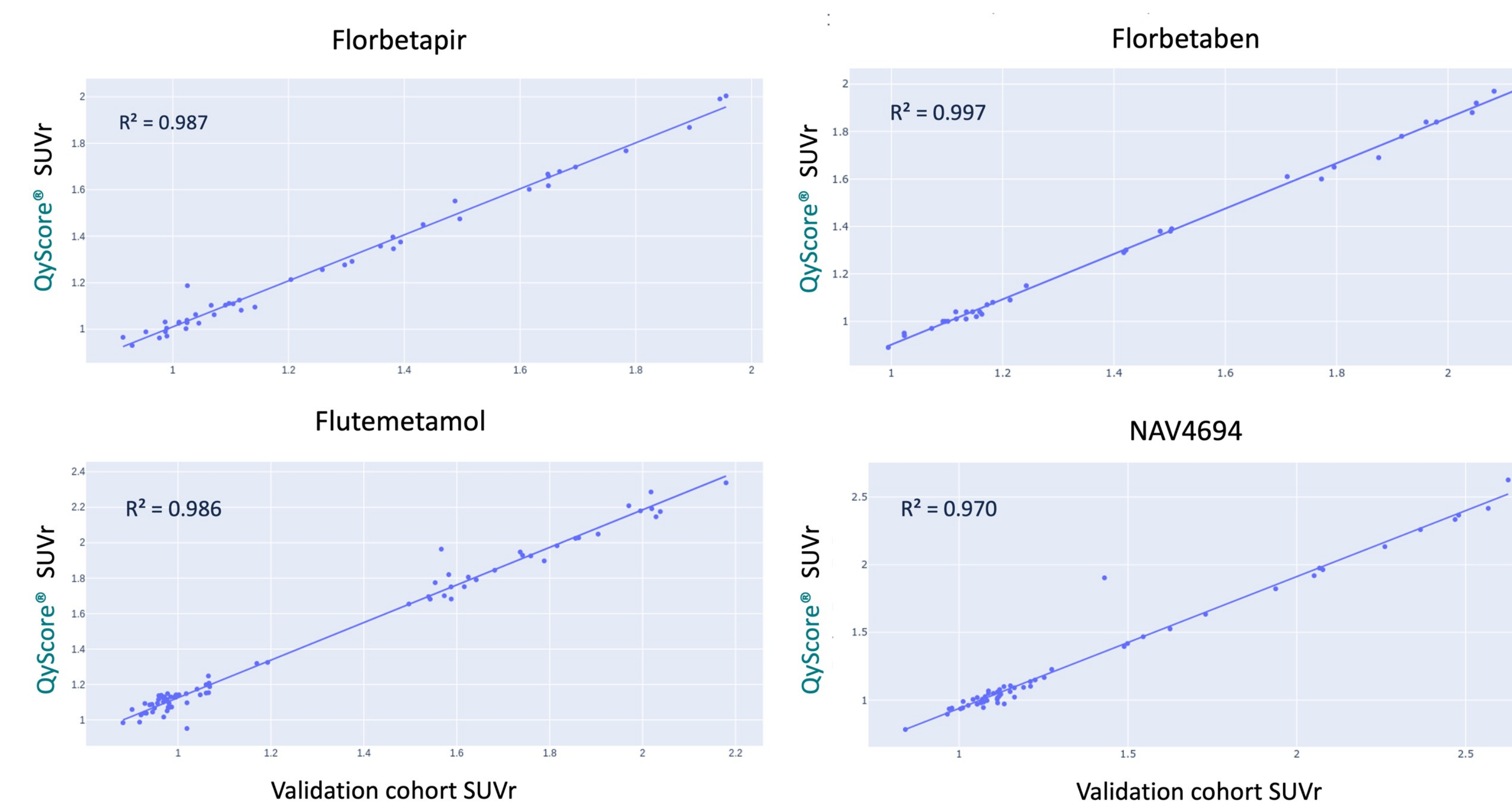


Figure 3. Correlation between Qyscore[®]'s ^{18}F tracer SUVr with the Centiloid GAIA validation gold-standard SUVr

Correlation coefficients of Qyscore[®]'s ^{11}C -PiB SUVr and ^{18}F tracer SUVr's were: 0.91 for Florbetapir, 0.95 for Forbetaben, 0.95 for Flutemetamol, 0.99 for NAV4694 (**Figure 2**).

Qyscore[®]'s ^{11}C -PiB and ^{18}F SUVr correlation coefficients with published values were above 0.98 (**Figure 3**).

Equations for converting Qyscore[®]'s automated SUVr to Centiloid were as follows:

Florbetapir: CL = **233.39** * FBP_SUVr – 243.48

Forbetaben: CL = **160.57** * FBB_SUVr – 183.35

Flutemetamol: CL = **136.94** * FTM_SUVr – 156.18

NAV4694: CL = **94.67** * NAV_SUVr – 98.72

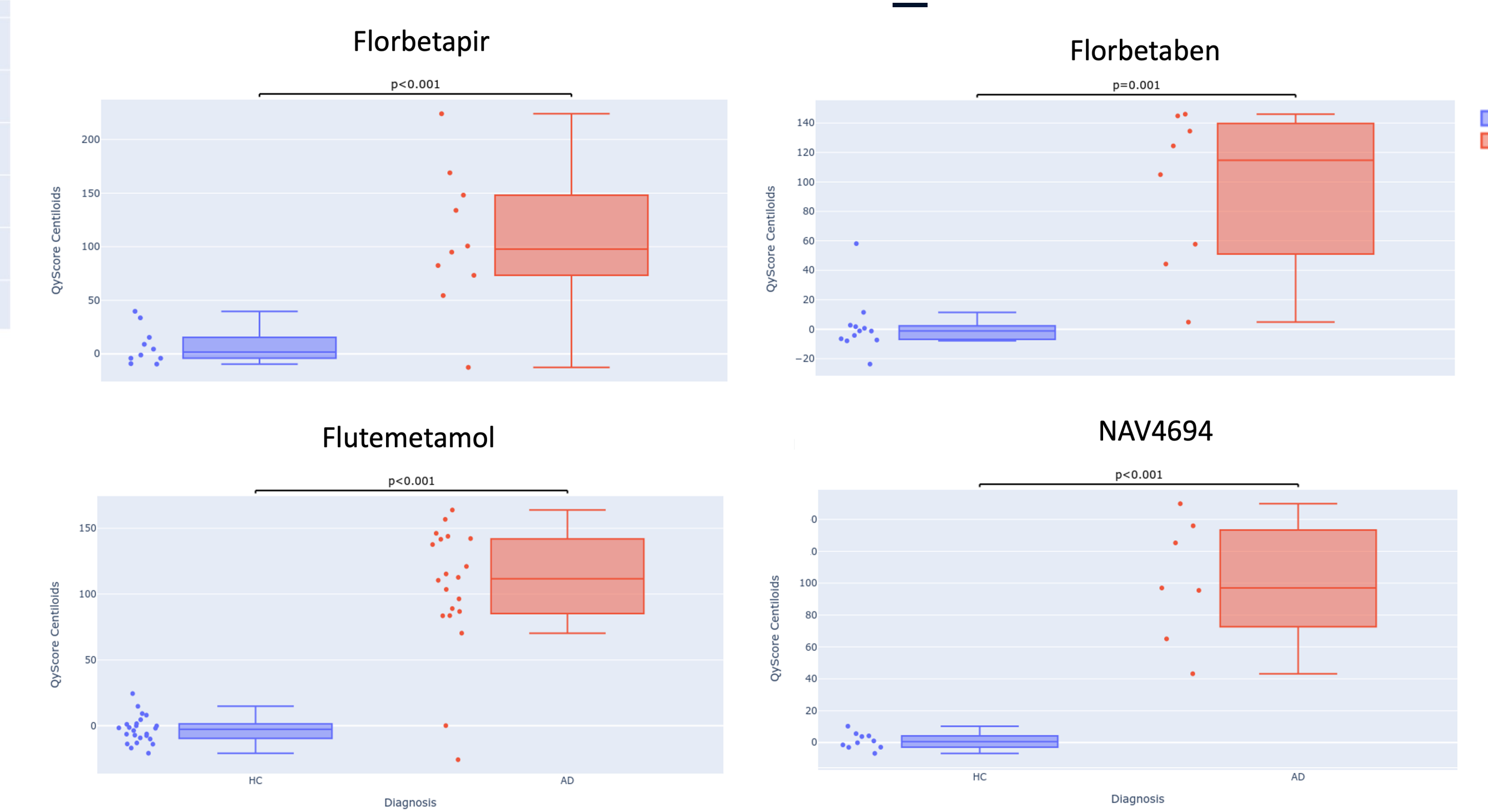


Figure 4. Qyscore[®]'s converted Centiloid results for Healthy Controls (HC) and Alzheimer's Disease (AD) patient amyloid-PET quantification across all four ^{18}F tracer validation datasets

Qyscore[®]'s Centiloid conversions showed significant differentiation between AD and healthy controls across all tracers (**Figure 4**).

CONCLUSIONS

We demonstrate the feasibility and reliability of Qyscore[®]'s fully automated amyloid PET pipeline for multiple amyloid-PET compounds (PiB and ^{18}F) suitable for implementation in multi-site, multi-tracer clinical trials.