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

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BACKGROUND

- Quantitative measures of amyloid-β (Aβ) 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 Aβ-pathology load[1]
- 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 site

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 ± 6.3 years] and 45 AD patients (age=67.5 ± 10.5 years; CDR= 0.5–1)
- ^{18}F tracers included Florbetapir[2] (FBP, *n* = 46), Forbetaben[3] (FBB, *n* = 35), Flutemetamol[4] (FTM, *n* = 74) and NAV4694[5] (NAV, *n* = 55).
- PET/MR image pairs were both co-registered and normalized in the MNI template space (Figure 1).
- 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) and of the cerebellum (reference) region (Figure 1)[1]

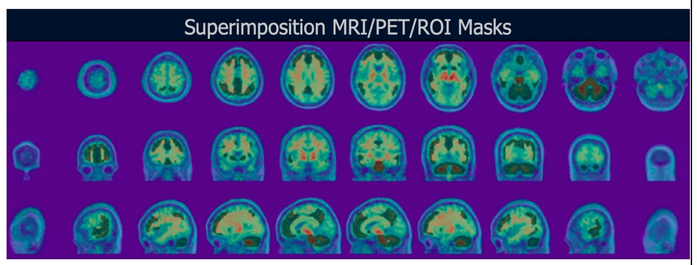

Figure 1. Example of QyScore®'s grey matter composite (target) and cerebellum (reference) masks overlayed onto the MNI transformed PET imaging

- The standardized uptake value ratio (SUVr) was computed as the ratio of the mean signal in both regions. 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 F18-SUVr values to CL were then derived.

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).

QyScore®'s ^{11}C-PiB SUVr correlation coefficients with published values were above 0.99.

Correlation coefficients of QyScore®'s ^{11}C-PiB SUVr and ^{18}F tracer SUVr's were :

- 0.91 for Florbetapir,
- 0.95 for Forbetaben,
- 0.96 for Flutemetamol,
- 0.99 for NAV4694 **(Figure 2.)**

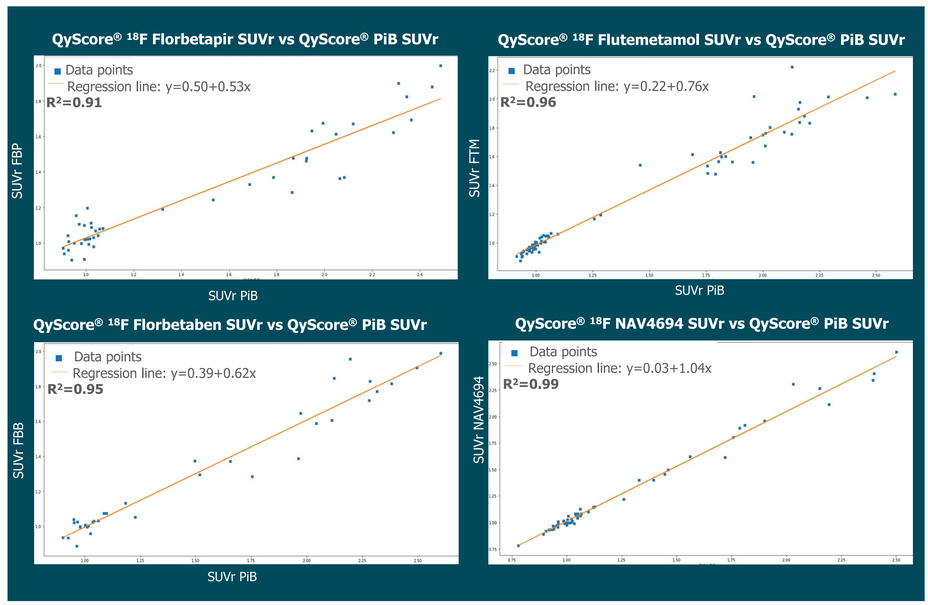

Figure 2. Linear regression comparing QyScore®'s automated SUVr for ^{11}C-PiB and the ^{18}F tracers

Equations for converting QyScore®'s automated SUVr to Centiloid were (Figure 3)

Florbetapir:
CL = **177.79** * FBP_SUVr - 183.56
Forbetaben:
CL = **153.08** * FBB_SUVr – 152.93
Flutemetamol:
CL = **122.39** * FTM_SUVr – 120.97
NAV4694:
CL = **90.20** * NAV_SUVr – 91.61

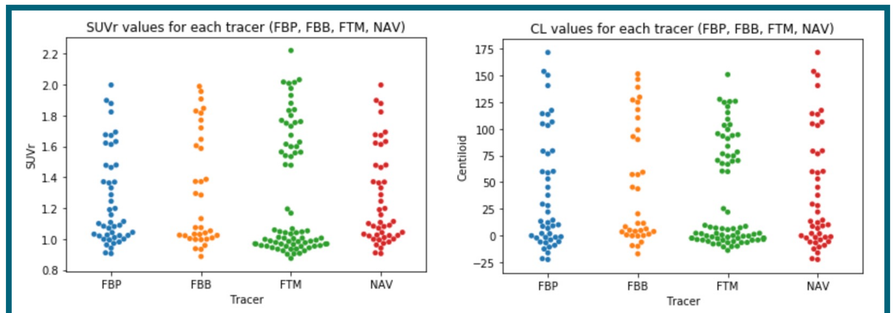

Figure 3. QyScore®'s automated SUVr and corresponding Centiloid values for each of the four ^{18}F tracers

References: [1]Klunk WE et al. 2015; [2]Navitsky M et al. 2018; [3]Rowe CC et al. 2017; [4]Battle MR et al. 2018; [5]Rowe CC et al. 2016

CONCLUSIONS

We demonstrate the feasibility and reliability of Qyscore®'s fully automated amyloid PET pipeline for multiple amyloid-PET compounds (PiB and ^{18}F) and transformation to standardized Centiloid quantifications, suitable for implementation in clinical trials.