Visual assessment of [18F]flutemetamol PET images can detect early amyloid pathology and grade its extent

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Abstract:

Purpose: To investigate the sensitivity of visual read (VR) to detect early amyloid pathology and the overall utility of regional VR.

Methods: [18F]Flutemetamol PET images of 497 subjects (ALFA+ N = 352; ADC N = 145) were included. Scans were visually assessed according to product guidelines, recording the number of positive regions (0–5) and a final negative/positive classification. Scans were quantified using the standard and regional Centiloid (CL) method. The agreement between VR-based classification and published CL-based cut-offs for early (CL = 12) and established (CL = 30) pathology was determined. An optimal CL cut-off maximizing Youden's index was derived. Global and regional CL quantification was compared to VR. Finally, 28 post-mortem cases from the [18F]flutemetamol phase III trial were included to assess the percentage agreement between VR and neuropathological classification of neuritic plaque density.

Results: VR showed excellent agreement against CL = 12 (κ = .89, 95.2%) and CL = 30 (κ = .88, 95.4%) cut-offs. ROC analysis resulted in an optimal CL = 17 cut-off against VR (sensitivity = 97.9%, specificity = 97.8%). Each additional positive VR region corresponded to a clear increase in global CL. Regional VR was also associated with regional CL quantification. Compared to mCERADSOT-based classification (i.e., any region mCERADSOT > 1.5), VR was in agreement in 89.3% of cases, with 13 true negatives, 12 true positives, and 3 false positives (FP). Regional sparse-to-moderate neuritic and substantial diffuse Aβ plaque was observed in all FP cases. Regional VR was also associated with regional plaque density.

Conclusion: VR is an appropriate method for assessing early amyloid pathology and that grading the extent of visual amyloid positivity could present clinical value.

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