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Introduction

- Reference tissue approaches for AB quantification circumvent arterial sampling, reduce patient burden and facilitate large-scale clinical trials.
- For the Aβ-radiotracer [¹¹C]PiB, the standard reference region (RR) is the cerebellar grey matter (GMCB)¹, however segmentation may be difficult and the GMCB may be compromised in late disease stages².
- Few alternative RRs have been properly validated.

Purpose To evaluate the use of alternative RRs by comparing them to full quantification using the cerebellar grey matter for [¹¹C]PiB.

Methods

- Subjects & Data
 - 13 from a test-retest study³ and 30 from a longitudinal study⁴ (13 CU, 13 MCI, 17 AD), Table 1
 - Dynamic [¹¹C]PiB PET 90 minutes and T1 MR scans
- Target & Reference ROIs
 - Target: Hammers atlas grey matter ROIs
 - Reference: GMCB, whole cerebellum (WCB), white matter brainstem/pons (WMBS), whole brainstem (WBS), eroded subcortical white matter (WMES).
- Amyloid load estimation:
 - Plasma input model with GMCB (DVR_{2T4k Vb GMCB})⁵, reference Logan (RLogan)⁶, simplified reference tissue model (SRTM)⁷, SUV, SUV ratios (40-60 and 60-90 minutes p.i.).⁵
- Statistics
 - Variability and agreement between test and retest scan
 - Correlations with DVR_{2T4k} Vb GMCB, annual % Aβ change

TRT	CU (<i>N=</i> 6)	MCI (<i>N=</i> 1)	AD (<i>N=</i> 6)
Age	64.3 ±5.7	71.0	61.0 ±3.0
Females (%)	50%	100%	17%
MMSE	29.7 ±0.5	28.0	20.7 ±2.0
Longitudinal	CU (<i>N=</i> 11)	MCI (<i>N</i> =12)	AD (<i>N</i> =7)
Age	66.4 ± 7.3	67.4 ±6.7	60.4 ± 5.4
Females (%)	27%	33%	14%
MMSE	29.4 ± 0.5	27.2 ±2.5	25.3 ±2.3

Table 1 Subject demographics

Values depicted as average (%) ±SD, MMSE= mini mental state examination

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^{[11}C]PiB Amyloid Quantification and Choice of Reference Region

Results (1)

- WCB showed the lowest test-retest variability (maximum 2.8%), except for the 2T4k_V_b (*Table 2*), and good agreement between test and retest outcome measures (maximum difference ≤1.5%) (*Fig.1*).
- Outcome measures of all methods and RRs showed good correlation with those of DVR_{2T4k Vb GMCB} (r>0.80) and cerebellar RRs showed least bias.

Table 2 Test-retest variability (%) across RRs and methods

	DVR _{2T4k_Vb}	DVRRLOGAN	DVR _{SRTM}	SUVr ₄₀₋₆₀	SUVr ₆₀₋₉₀
GM Cerebellum	12.4	2.8	2.9	3.5	5.1
Whole Cerebellum	8.5	1.4	2.0	2.2	2.8
WM Brainstem /Pons	1.9	2.4	3.3	2.3	3.7
Whole Brainstem	2.2	2.1	3.8	2.2	3.1
Subcortical Eroded WM	7.5	2.4	2.7	3.7	3.9





- window).
- opposed to a linear shape) for all methods (*Fig.2*).

✓ Although, across reference tissue approaches, all RRs showed good test-retest variability and high correlations with the DVR_{2T4k} vb GMCB whole cerebellum is the RR of choice for measuring longitudinal amyloid accumulation using [¹¹C]PiB PET.





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Results (2)

Cerebellar and WMES Aβ measurement remained unaltered across a 2-4 year period, in contrast to the A β measurement of the WBS and WMBS regions (for the 60-90 min acquisition

For cerebellar RRs, the relationship between baseline amyloid and annual amyloid accumulation showed an inverted u-shape (as

Conclusion