Test-retest variability of relative tracer delivery rate as measured by [^{11}C]PiB

Fiona Heeman[1], Janine Hendriks[1], Isadora Lopes Alves[1], Nelleke Tolboom[2], Bart N.M. van Berckel[1], Maqsood Yaqub[1], Adriaan A. Lammertsma[1]

[1]Amsterdam UMC, Vrije Universiteit Amsterdam, Radiology & Nuclear Medicine, [2] Imaging Division, Department of Radiology, UMC Utrecht

Introduction

- Reductions in CBF are characteristic for Alzheimer's disease (AD) and could be used as proxy for disease severity or progression.[1,2]
- Moderate-to-high correlations have been reported between [^{11}C]PiB PET derived R_1 (relative tracer delivery rate) and [^{15}O]H_2O CBF, thus, it has been suggested that R_1 could be used as proxy for relative CBF[3]
- Longitudinal PET studies become more common in AD, therefore it is important to understand the variability of R_1 to determine what magnitude of change signifies an actual change.

Purpose

Assess precision of [^{11}C]PiB R_1 through retrospective analysis of a test-retest data-set

Methods

- **Subjects & Image acquisition**
  - 12 participants from a test-retest (TRT) study (Table 1)[4]
  - Dynamic [^{11}C]PiB PET 90 minutes and T1 MR scans
- **Image processing and analysis**
  - The simplified reference tissue with fixed k_2' (SRTM2) was used (with cerebellar gm reference region) to derive R_1 values for a global cortical and smaller cortical regions
- **Statistics**
  - Test-retest variability was calculated (equation 1) for all regions

$$TrT\ variability\ (\%) = \frac{|T-R|}{0.5 \cdot |T+R|} \cdot 100 \qquad (1)$$

  - Correlation, Linear Mixed Effects Models (LME) and Bland-Altman analysis were used to assess the correlations and variability between test and retest measures.

Results

TABLE 1. Subject demographics

	CU (*N*= 5)	MCI (*N*=1)	AD (*N*=6)
Age	64.6 ±6.4	71.0	61.0 ±3.0
Females	60%	100%	17%
VR positive	20%	0%	100%
MMSE	29.8 ±0.4	28.0	20.7 ±2.0

VR: Visual read, MMSE: Mini Mental State Examination, Values are depicted as Mean±SD, unless indicated otherwise

- Relative tracer delivery R_1 was significantly lower in AD dementia patients compared with cognitively unimpaired participants (p< 0.01), Table 2.
- TRT variability was low for a global cortical region (1.70%), while the range of regional TRT variability was slightly higher (1.5-5.8%).

TABLE 2. Relative tracer delivery values by diagnostic group

	SRTM2 derived- R_1	
Diagnostic groups	**Test**	**Retest**
CN (*N*=5)	0.93 ± 0.04	0.91 ± 0.03
MCI (*N*=1)	0.91	0.91
AD (*N*=6)	0.82 ± 0.04	0.82 ± 0.03

Values are depicted as Mean±SD

- Test and retest R_1 values were strongly correlated and the slope was not significantly different from 1 (R^2=0.92, slope=0.98 C.I.[0.94-1.01], p<0.001).
- Bland-Altman analysis showed a negligible bias (0.69±3.07%) between test and retest R_1 (Figure 1).

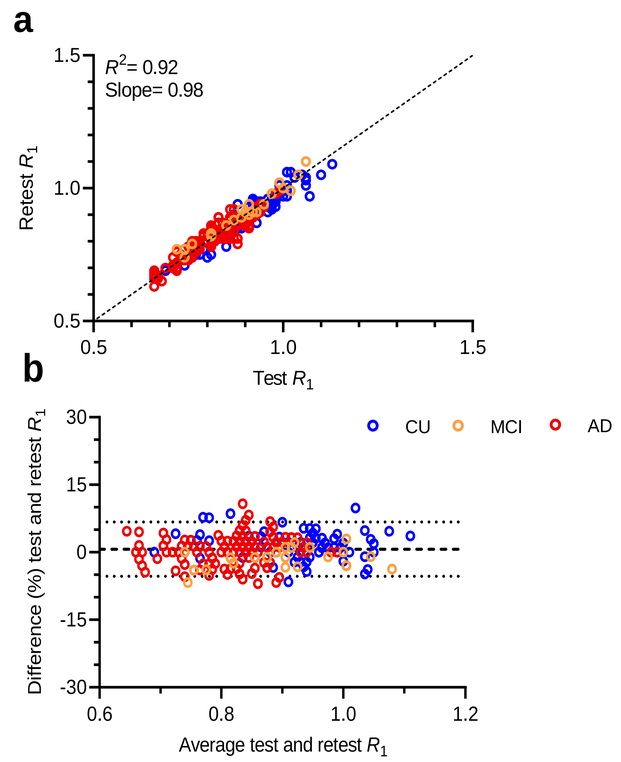

Figure 1. Relationship between SRTM2-derived test and retest R_1
(a) The correlation between R_1 test and retest measures, with R^2 and slope parameters corresponding to the LME analysis and (b) a Bland-Altman plot, which indicates the bias between the two measures.

Conclusion

✓ **[^{11}C]PiB relative tracer delivery rate R_1 showed high global and regional precision in participants covering the AD spectrum. Therefore, [^{11}C]PiB R_1 appears to be a stable parameter for measuring cross-sectional differences and longitudinal changes in relative CBF.**

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Contact: f.heeman@amsterdamumc.nl

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