

# Parametric imaging of dual-time window [<sup>18</sup>F]flutemetamol and [<sup>18</sup>F]florbetaben scans

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## Introduction

- Accurate quantitative measures of amyloid beta (Aβ) plaques are needed to identify individuals with subthreshold Aβ levels or for measuring small changes over time.<sup>1</sup>
- Aβ pathology might not follow anatomical boundaries, and more spatial information can be extracted from voxel-wise (parametric) approaches.
- Optimal parametric models for quantifying Aβ burden using both [<sup>18</sup>F]flutemetamol and [<sup>18</sup>F]florbetaben have not been evaluated for dual-time window scans.

### Purpose

To evaluate the performance of parametric methods for dual-time window scans using [<sup>18</sup>F]flutemetamol and [<sup>18</sup>F]florbetaben

## Methods

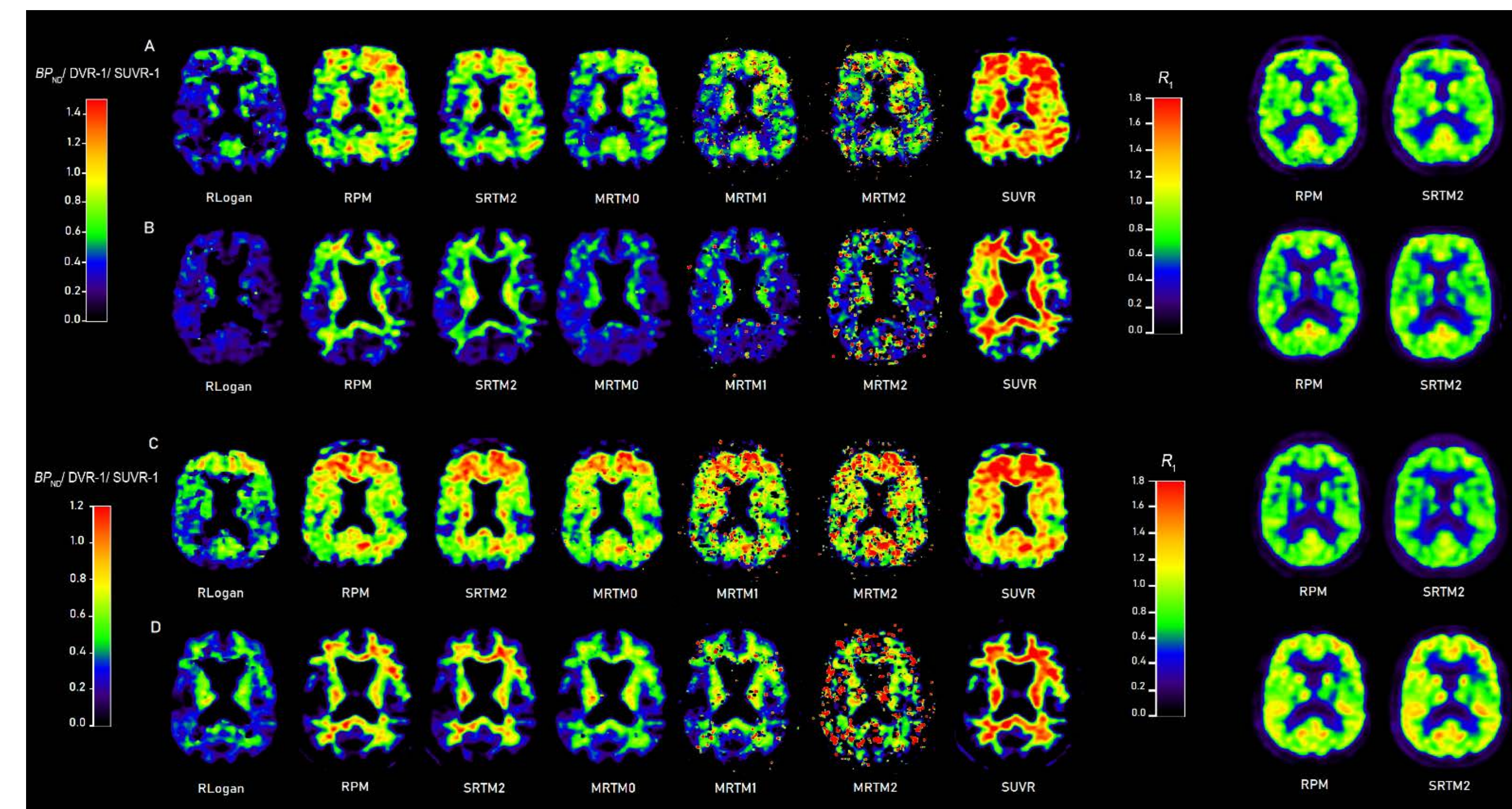
- Subjects & Image acquisition**
  - N=46 from the AMYPAD PNHS<sup>2</sup>
  - Dual-time window (0-30,90-110) [<sup>18</sup>F]flutemetamol or [<sup>18</sup>F]florbetaben PET and T1 MR scans<sup>3</sup>
- Image processing and analysis**
  - Regional standard: Reference Logan (Rlogan)
  - Parametric methods: SUVR (90-110), Parametric Rlogan, MRTM0,1,2, RPM and SRTM2 (all with cerebellar grey matter reference region) to derive DVR,  $BP_{ND}$  and  $R_1$  values
- Statistics**

Evaluate all parametric methods based on:

  - visual assessment of parametric images
  - ability to differentiate between Aβ-positive and Aβ-negative scans, and
  - quantitative accuracy and precision with respect to a reference method.
  - Visual assessment parametric images and quantitatively define extreme outliers.
  - ANOVA and AUC (from ROC analyses) for discriminating between Aβ-positive and Aβ-negative scans.
  - Linear regression and Bland-Altman analysis to assess correlations with the regional standard, (proportional) bias and variability.

## Results

- [1] Visual and quantitative evaluation of parametric images showed that, for both tracers, most image artefacts caused by outliers were present for MRTM2 and MRTM1 (Figure 1).
- High uptake in grey and white matter regions for SUVR (↑ risk false positives), RLogan images showed clearest underestimation of the Aβ burden (↑ risk false negatives)



**Figure 1. Parametric amyloid and relative perfusion images**  
 Parametric images of each of the methods for A) an Aβ-positive and B) an Aβ-negative [<sup>18</sup>F]flutemetamol scan, and for C) an Aβ-positive and D) an Aβ-negative [<sup>18</sup>F]florbetaben scan.

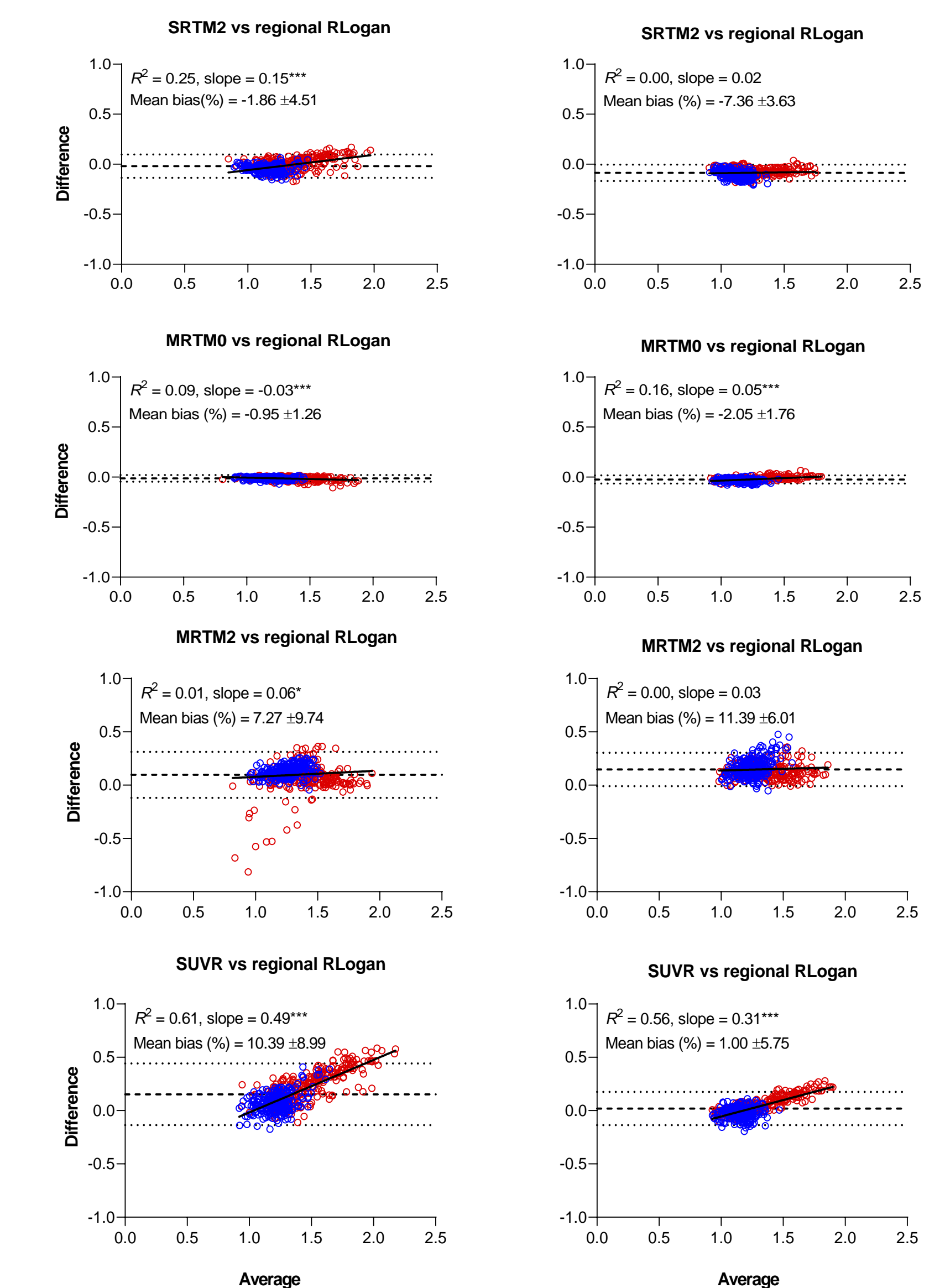
- [2] All methods could detect significant differences between Aβ-positive and Aβ-negative scans ( $p < 0.05$ )
- RPM, SRTM2 and SUVR provided highest AUC values, making these preferred methods for detecting subtle differences in Aβ burden, followed by MRTM0 and MRTM1

**TABLE 1. AUC: Models' ability to correctly classify Aβ-positive and Aβ-negative scans**

	[ <sup>18</sup> F]flutemetamol	[ <sup>18</sup> F]florbetaben
RRLogan DVR	0.94	0.79
RLogan DVR	0.88	0.77
RPM DVR	0.97	0.85
SRTM2 DVR	0.96	0.84
MRTM0 DVR	0.94	0.80
MRTM1 DVR	0.95	0.80
MRTM2 DVR	0.81	0.79
SUVR	0.96	0.83
RPM $R_1$	0.54	0.45
SRTM2 $R_1$	0.49	0.45

RRLogan corresponds to the regional implementation of reference Logan (regional standard). Values correspond to the Area Under the Curve (AUC) from ROC analyses

- [3] Very high correlations were observed for all methods  $R^2 > 0.85$ , except for MRTM2.
- MRTM0 and MRTM1 showed both minimal and constant bias (<5%), while all other methods showed a larger and/or proportional bias to a certain degree. (Figure 2)
- Lowest variability was observed for MRTM0 and MRTM1, followed by parametric RLogan, SRTM2 and RPM, in case of [<sup>18</sup>F]florbetaben (Figure 2)



**Figure 2. Bland-Altman plots showing the agreement between outcome measures of all parametric methods and the regional standard for [<sup>18</sup>F]flutemetamol and [<sup>18</sup>F]florbetaben**

## Conclusion

- ✓ The best overall compromise was provided by MRTM0, followed closely by SRTM2. SRTM2 is the preferred method because, in addition to its good performance, it has the advantage of providing a measure of relative perfusion ( $R_1$ ), which is useful for measuring disease progression.

1. Lammertsma AA (2017) *J Nucl Med* 58:1019–1024.2. Lopes Alves. (2020) *Alzheimer's Dement.* 3. Heeman et al. (2019) *EJNMMI Research* 9:32

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