

Impact of Reduced Injected Dose for In Vivo Quantification of Aβ Pathology Using [18F]flutemetamol



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Background

- Previous research has demonstrated that the injected dose in PET examinations can be reduced without effect on quantitative outcomes
- These reductions can lead to a lower radiation burden for subjects, reduced costs for institutions, and potential for additional research scans of the same subject
- Here, we investigated the effect of reduced injected doses of [18F]Flutemetamol on standardised uptake value ratios (SUVRs) and associated outcomes using a cohort of Aβ-positive and Aβ-negative individuals

Method

- Subjects were recruited from the AMYPAD consortium in Geneva (see table 1 for details)
- Images were manipulated to simulate injected doses of 70, 50, 40, 30, and 20% of the original injected dose
- List-mode data were edited to reduce counts and noise in images to represent the simulated injected doses
- Whole cerebellum was used as a reference region to compute SUVRs in a region of interest (ROI) corresponding to the GAAIN cortical composite
- Mean SUVRs were calculated for each injected dose level as well as group separation using the equation below:

$$Cohen's D = \frac{\text{mean}(A\beta+) - \text{mean}(A\beta-)}{0.5 \sqrt{SD_{A+}^2 + SD_{A-}^2}}$$

Tracer	Flutemetamol
Cohort	AMYPAD (100)
Aβ Status (+/-)	56/44
Age (y)	73
Sex (M/F)	52/48
Diagnosis	SCI=20 MCI=55 AD=18 Other=7
Scanner	Siemens Biograph mCT flow
Scan length	20 minutes (90 minutes p.i.)
Mean Injected Dose	~170MBq
Acquisition Type	List-mode
Reconstruction	OSEM, ToF

Table 1: Demographics and acquisition parameters for subject cohorts

AMYPAD: Amyloid imaging to prevent Alzheimer's disease, SCI: Subjective cognitive impairment MCI: mild cognitive impairment, AD: Alzheimer's disease

Results

- Figure 1 shows scans of a representative Aβ-positive individual derived from true and different simulated reduced injected doses
- Mean whole cortical SUVRs changed by a maximum of 0.01 (<1% change) in both Aβ-positive and -negative individuals (table 2)
- No meaningful change was measured in group separation between original and reduced injected doses
- Bland-Altman analysis (figure 2) demonstrates <3% change over all scans between the original injected dose and 20% of injected dose

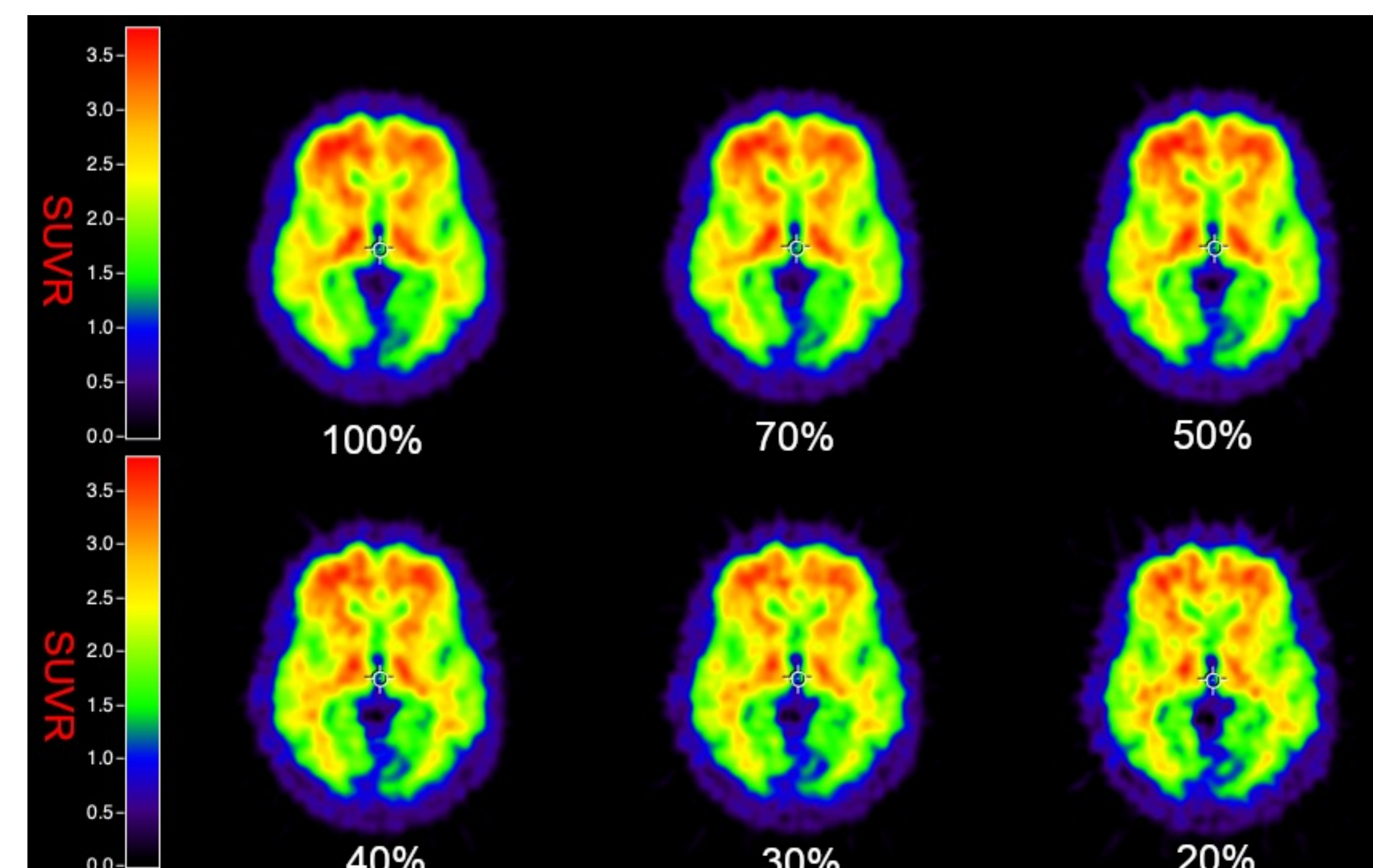


Figure 1 – Generated reduced injected dose in an amyloid-positive individual

Dose (%)	Aβ-		Aβ+		Group Separation
	Mean	SD	Mean	SD	
100	1.03	0.09	1.66	0.26	4.67
70	1.03	0.09	1.65	0.25	4.70
50	1.03	0.09	1.65	0.25	4.68
40	1.03	0.09	1.65	0.25	4.67
30	1.03	0.09	1.66	0.25	4.67
20	1.03	0.09	1.66	0.25	4.68

Table 2 – Application of simulation results to the clinical cohort

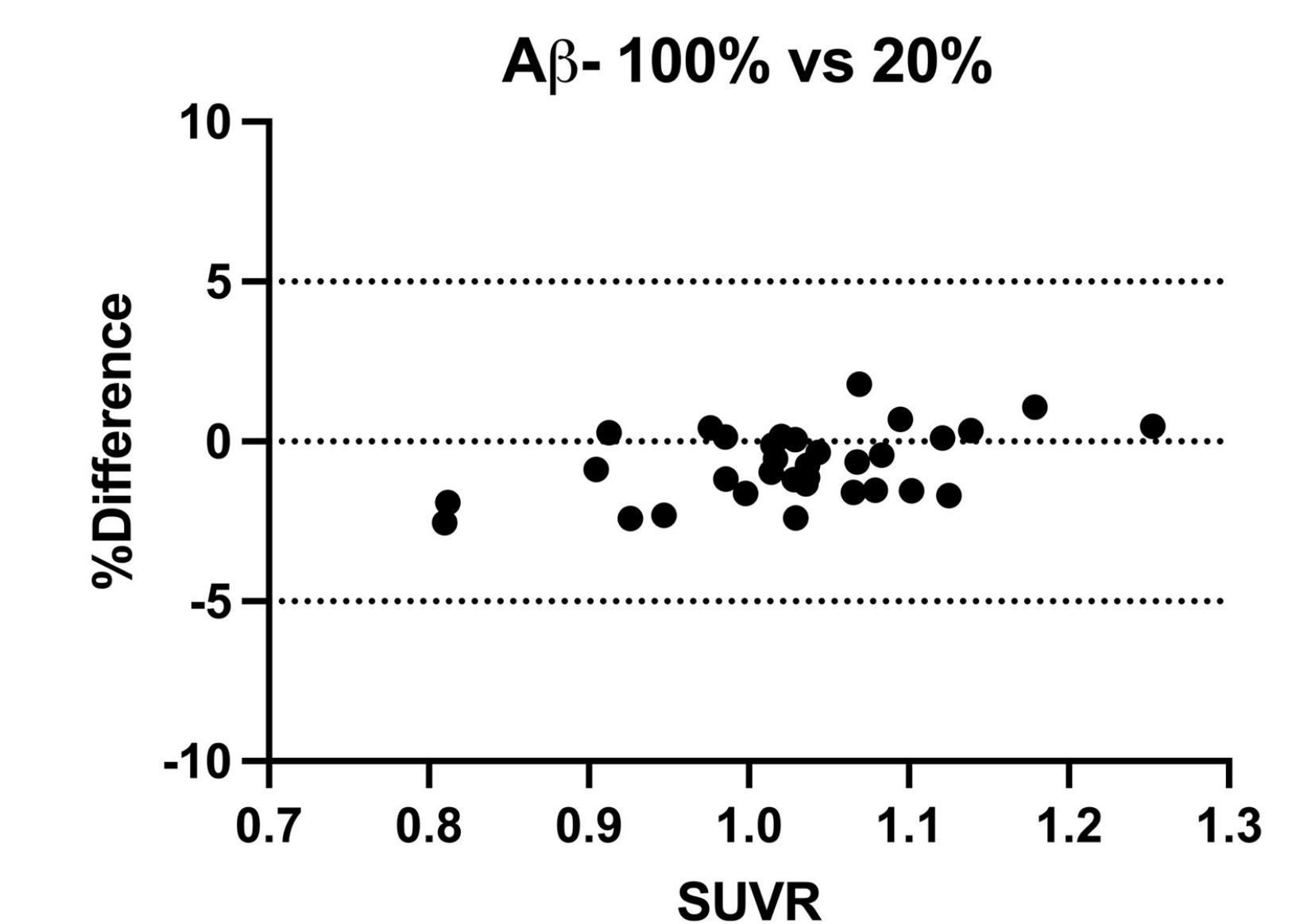
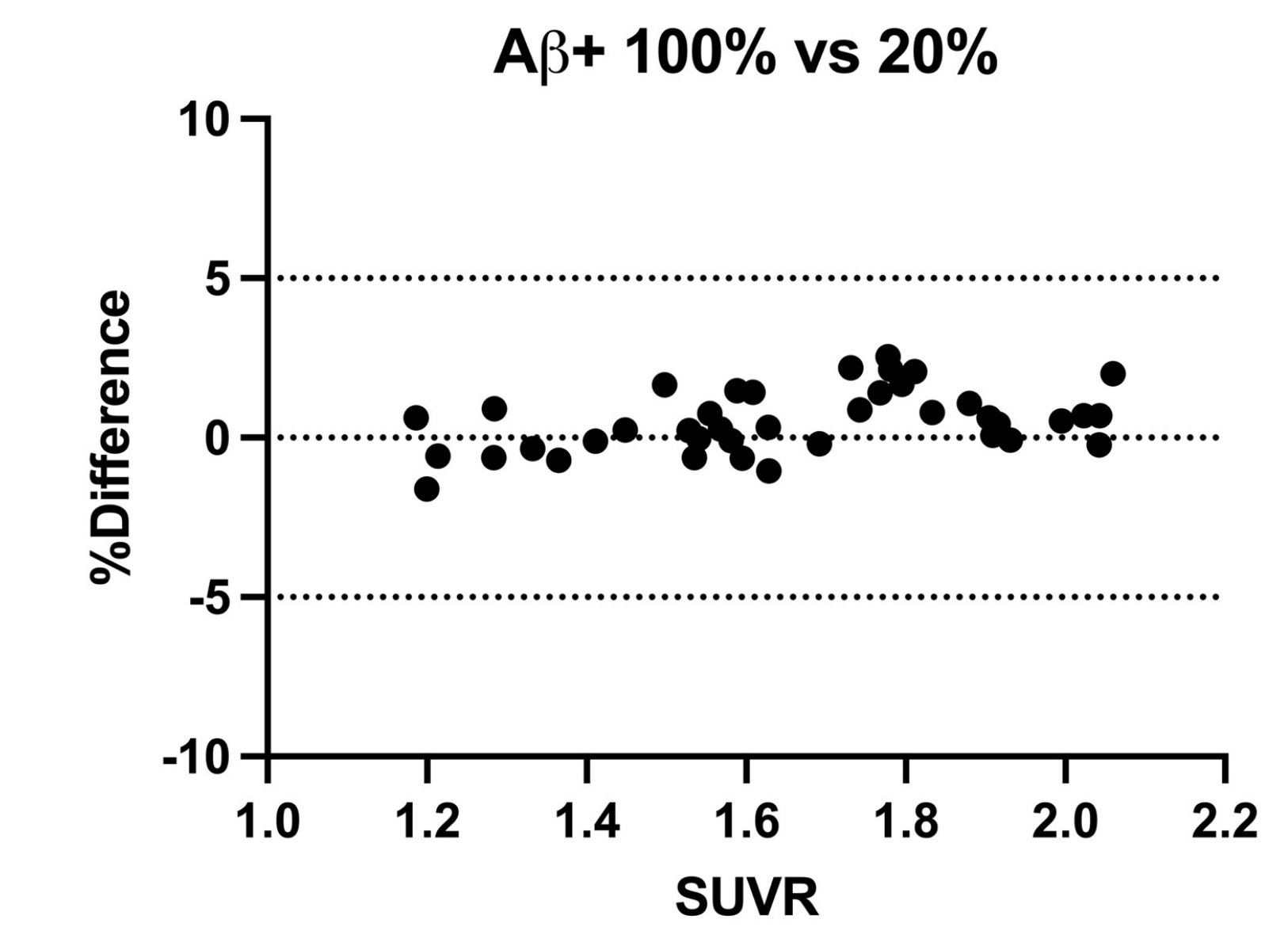


Figure 2 – Bland-Altman plots of Aβ+ and Aβ- subjects comparing SUVRs in whole cortical ROI at original injected dose and 20% injected dose

Conclusion

- Quantitative analysis suggests that lower injected tracer doses for [18F]flutemetamol yield robust SNRs and SUVRs at injected doses as low as 20% of the original dose
- Group separation does not meaningfully change and measured variance is <3% across all injected dose levels, this is close to previously measured test-retest rates of ~2%
- Further datasets from the AMYPAD consortium will be included that will add [18F]florbetapir and [18F]florbetaben as well as centiloid scaling applied
- Visual reads will be included for all tracers, assessing the ability of a reader to determine positive, negative, and equivocal cases at lower injected doses

Summary

[18F]flutemetamol scans remain clinically useful with carefully selected reductions in injected dose

(1)Battle MR, Pillay LC, Lowe VJ, Knopman D, Kemp B, Rowe CC, et al. Centiloid scaling for quantification of brain amyloid with [18F]flutemetamol using multiple processing methods. EJNMMI Res 2018;8:107. <https://doi.org/10.1186/s13550-018-0456-7>.
 (2)Klunk WE, Koeppe RA, Price JC, Benzinger TL, Devous MD, Jagust WJ, et al. The Centiloid Project: Standardizing quantitative amyloid plaque estimation by PET. Alzheimers Dement 2015;11:1-15.e4. <https://doi.org/10.1016/j.jalz.2014.07.003>.