

Supplemental Table 1. "True" values (for each parameter) based on clinical data determined for each condition for the simulations. All micro/macro-parameters were estimated using simplified reference tissue model. SCD = subjective cognitive decline. AD = Alzheimer's disease. BP_{ND} = binding potential.

	BP_{ND}	k_2	R_1
SCD: almost no binding	0.05	0.05	0.91
AD: low binding	0.11	0.04	0.89
AD: medium binding	0.21	0.03	0.85
AD: high binding	0.32	0.08	0.88

Supplemental Table 2. [^{18}F]flortaucipir DVR, SUVR and R_1 values for amyloid negative (A-) SCD subjects. Mean \pm SD are provided. SCD = subjective cognitive decline. AD = Alzheimer's disease. DVR = distribution volume ratio (= binding potential (BP_{ND}) + 1). SUVR = standardized uptake value ratio.

A- SCD (n=26)	DVR			SUVR ₈₀₋₁₀₀			R_1		
	BL	FU	%change	BL	FU	%change	BL	FU	%change
Braak I/II	1.001 (0.083)	1.023 ^z (0.091)	2.26 (2.16)	1.084 ^a (0.116)	1.10 ^{ax} (0.111)	1.57 (2.74)	0.712 (0.045)	0.721 ^x (0.048)	1.24 (2.79)
Braak III/IV	1.015 (0.035)	1.037 ^z (0.032)	2.24 (1.73)	1.062 ^a (0.057)	1.082 ^{az} (0.051)	1.92 (2.38)	0.841 (0.038)	0.849 ^x (0.044)	0.92 (2.28)
Braak V/VI	1.020 (0.036)	1.036 ^z (0.030)	1.61 (2.03)	1.046 ^a (0.047)	1.060 ^{ax} (0.040)	1.39 (2.87)	0.936 (0.043)	0.939 (0.050)	0.35 (2.52)

DVR vs. SUVR: ^ap<0.001 | BL vs. FU: ^xp<0.05, ^yp<0.01, ^zp<0.001 | %change DVR vs. %change SUVR: n.s.

Supplemental Table 3. [¹⁸F]flortaucipir DVR, SUVR and R₁ values for amyloid positive (A+) SCD subjects. Mean ± SD are provided. SCD = subjective cognitive decline. AD = Alzheimer’s disease. DVR = distribution volume ratio (= binding potential (BP_{ND}) + 1). SUVR = standardized uptake value ratio.

A+ SCD (n=12)	DVR			SUVR ₈₀₋₁₀₀			R ₁		
	BL	FU	%change	BL	FU	%change	BL	FU	%change
Braak I/II	1.122 (0.151)	1.158 ^x (0.166)	3.22 (4.01)	1.243 ^a (0.189)	1.272 ^a (0.184)	2.45 (4.28)	0.700 (0.029)	0.698 (0.051)	-0.36 (5.76)
Braak III/IV	1.110 (0.095)	1.158 ^y (0.137)	4.08 (3.52)	1.189 ^a (0.128)	1.235 ^{ay} (0.154)	3.67 (2.87)	0.824 (0.030)	0.829 (0.041)	0.51 (3.66)
Braak V/VI	1.090 (0.066)	1.134 ^y (0.100)	3.90 (3.55)	1.140 ^a (0.091)	1.185 ^{ay} (0.118)	3.85 (3.62)	0.904 (0.035)	0.911 (0.042)	0.75 (3.07)

DVR vs. SUVR: ^ap<0.001 | BL vs. FU: ^xp<0.05, ^yp<0.01 | %change DVR vs. %change SUVR: n.s.

Supplemental Table 4. Percentage overestimation of SUVR₈₀₋₁₀₀ relative to DVR. Mean ± SD are provided. SCD = subjective cognitive decline. AD = Alzheimer’s disease. DVR = distribution volume ratio (= binding potential (BP_{ND}) + 1). SUVR = standardized uptake value ratio.

	SCD		AD	
	BL	FU	BL	FU
Braak I/II	8.95 (3.92)	8.16 (3.39)	11.49 (3.46)	11.18 (3.21)
Braak III/IV	5.34 (3.02)	4.97 (2.67)	8.59 (3.04)	9.47 (3.29)
Braak V/VI	3.19 (2.35)	3.00 (1.98)	7.08 (3.59)	7.97 (3.47)

Supplemental Table 5. Annualized %change for [¹⁸F]flortaucipir DVR and SUVR₈₀₋₁₀₀ in SCD subjects. Mean ± SD are provided. SCD = subjective cognitive decline. AD = Alzheimer's disease. DVR = distribution volume ratio (= binding potential (BP_{ND}) + 1). SUVR = standardized uptake value ratio.

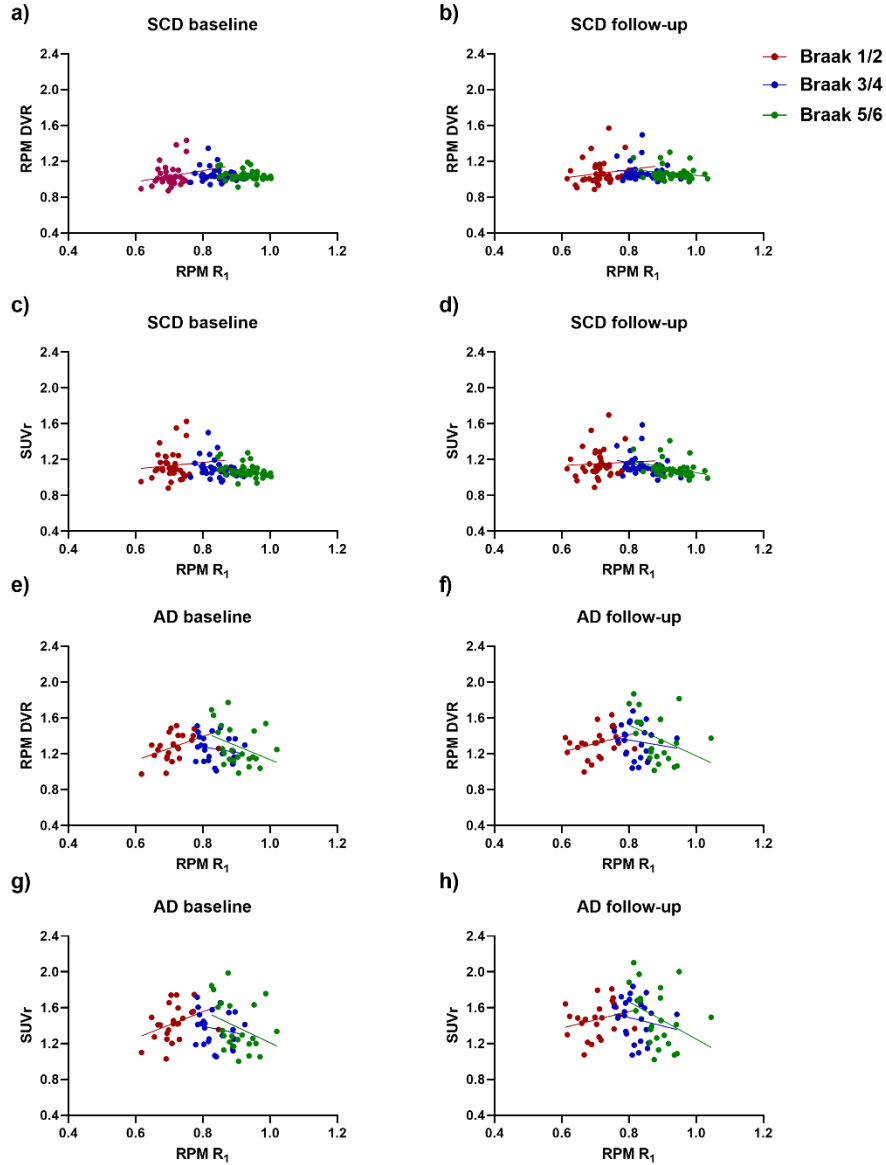
SCD (n=38)	Annualized %change DVR	Annualized %change SUVR₈₀₋₁₀₀
Braak I/II	1.27 (1.44)	0.92 (1.62)
Braak III/IV	1.41 (1.31)	1.23 (1.32)
Braak V/VI	1.16 (1.38)	1.08 (1.61)

Supplemental Table 6. Annualized %change for [¹⁸F]flortaucipir DVR and SUVR₈₀₋₁₀₀ values in AD patients. Mean ± SD are provided. SCD = subjective cognitive decline. AD = Alzheimer's disease. DVR = distribution volume ratio (= binding potential (BP_{ND}) + 1). SUVR = standardized uptake value ratio.

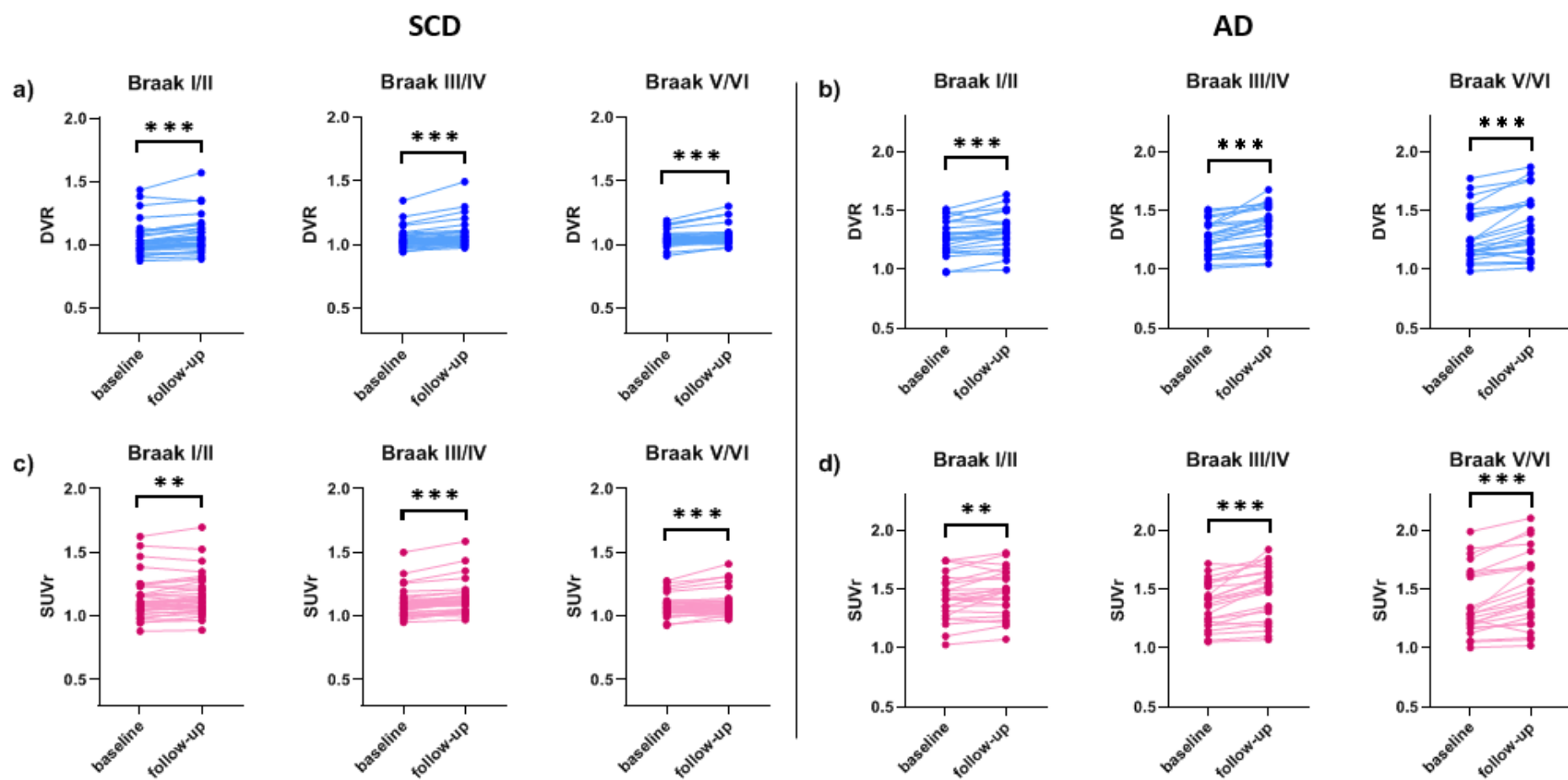
AD (n=24)	Annualized %change DVR	Annualized %change SUVR₈₀₋₁₀₀
Braak I/II	1.54 (1.77)	1.42 (2.35)
Braak III/IV	2.86 (2.13)	3.23 (2.51)
Braak V/VI	3.15 (2.65)	3.53 (3.01)

Supplemental Table 7. Required sample sizes (n) for [¹⁸F]flortaucipir for different effect sizes. The differences between two dependent means (matched pairs) was calculated, with an α (error probability) of 0.05 and a power (1- β error probability) of 0.80. To adhere to the typical duration of clinical trials in AD we calculated percentage change over an 18 month period and used those standard deviations as input for the sample size calculations. Calculations were performed using GPower v3.1.9.7. SCD = subjective cognitive decline. AD = Alzheimer's disease. DVR = distribution volume ratio. SUVr = standardized uptake value ratio.

SCD												
Expected change	0.5%	1%	2%	3%	4%	5%	6%	7%	8%	9%	10%	
DVR	Braak I/II	141	37	11	7	5	4	4	3	3	3	3
	Braak III/IV	117	31	10	6	5	4	4	3	3	3	3
	Braak V/VI	131	34	11	6	5	4	4	3	3	3	3
SUVr ₈₀₋₁₀₀	Braak I/II	180	47	14	8	6	5	4	4	3	3	3
	Braak III/IV	119	32	10	6	5	4	4	3	3	3	3
	Braak V/VI	177	46	13	8	5	5	4	4	3	3	3
AD												
Expected change	0.5%	1%	2%	3%	4%	5%	6%	7%	8%	9%	10%	
DVR	Braak I/II	223	58	16	9	6	5	4	4	4	3	3
	Braak III/IV	324	83	23	12	8	6	5	4	4	4	4
	Braak V/VI	497	126	33	16	10	8	6	5	5	4	4
SUVr ₈₀₋₁₀₀	Braak I/II	391	100	27	13	9	7	5	5	4	4	4
	Braak III/IV	446	113	30	15	10	7	6	5	5	4	4
	Braak V/VI	641	162	42	20	13	9	7	6	5	5	4



Supplemental Figure 1. Correlation plots for [¹⁸F]flortaucipir DVR/SUVr and R₁. No significant correlation between [¹⁸F]flortaucipir DVR or SUVr and R₁ was observed in both SCD and AD groups, at both timepoints, in all regions. SCD = subjective cognitive decline. AD = Alzheimer's disease. RPM = receptor parametric mapping. DVR = distribution volume ratio (= binding potential (BP_{ND}) + 1). SUVr = standardized uptake value ratio.



Supplemental Figure 2. Spaghetti plots of regional DVR in **(a)** SCD and **(b)** AD. Spaghetti plots of regional $SUVR_{80-100}$ in **(c)** SCD and **(d)** AD. SCD = subjective cognitive decline. AD = Alzheimer's disease. DVR = distribution volume ratio (= binding potential (BP_{ND}) + 1). SUVR = standardized uptake value ratio. ** $p < 0.01$, *** $p < 0.001$