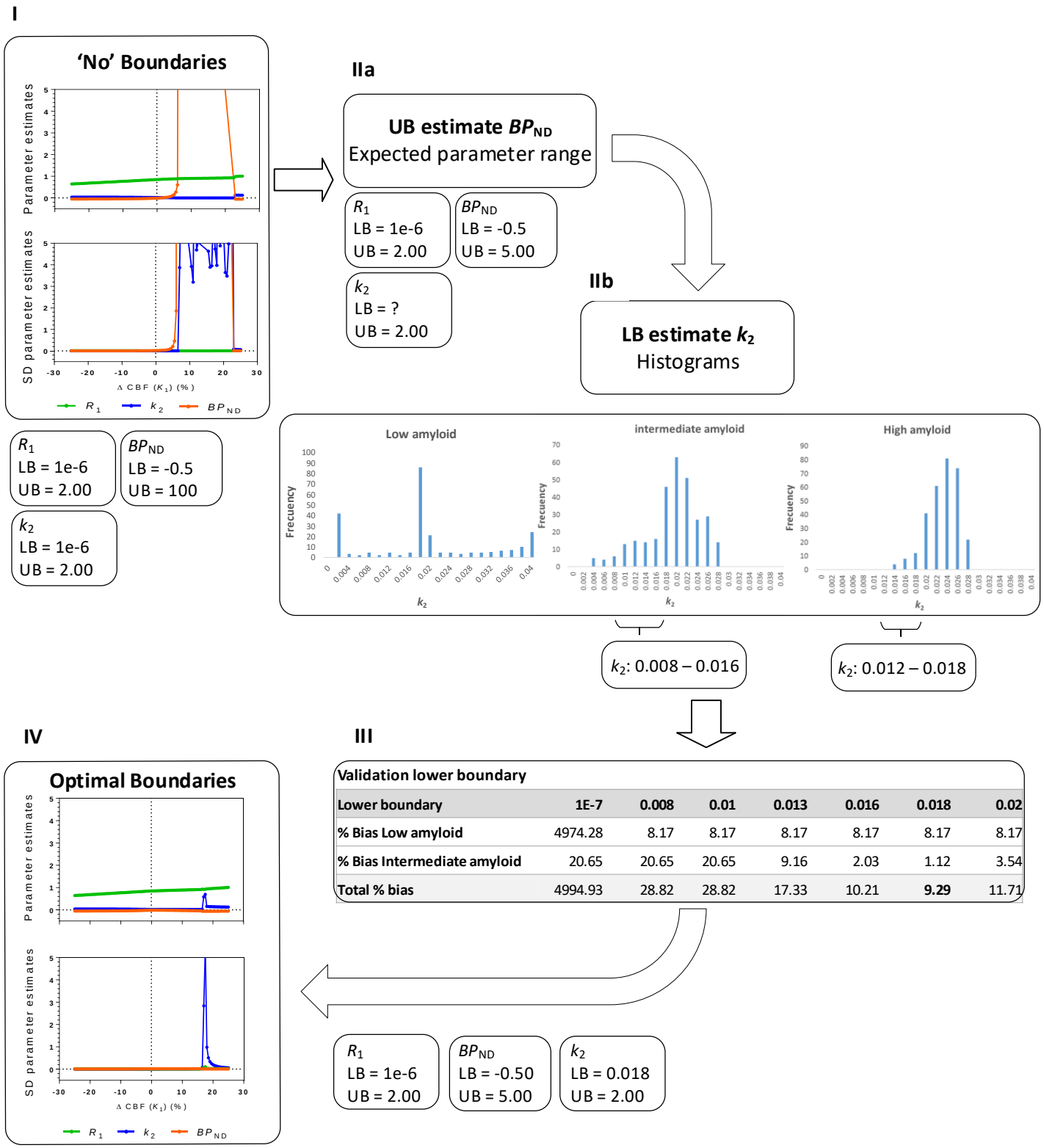
Supplementary Materials

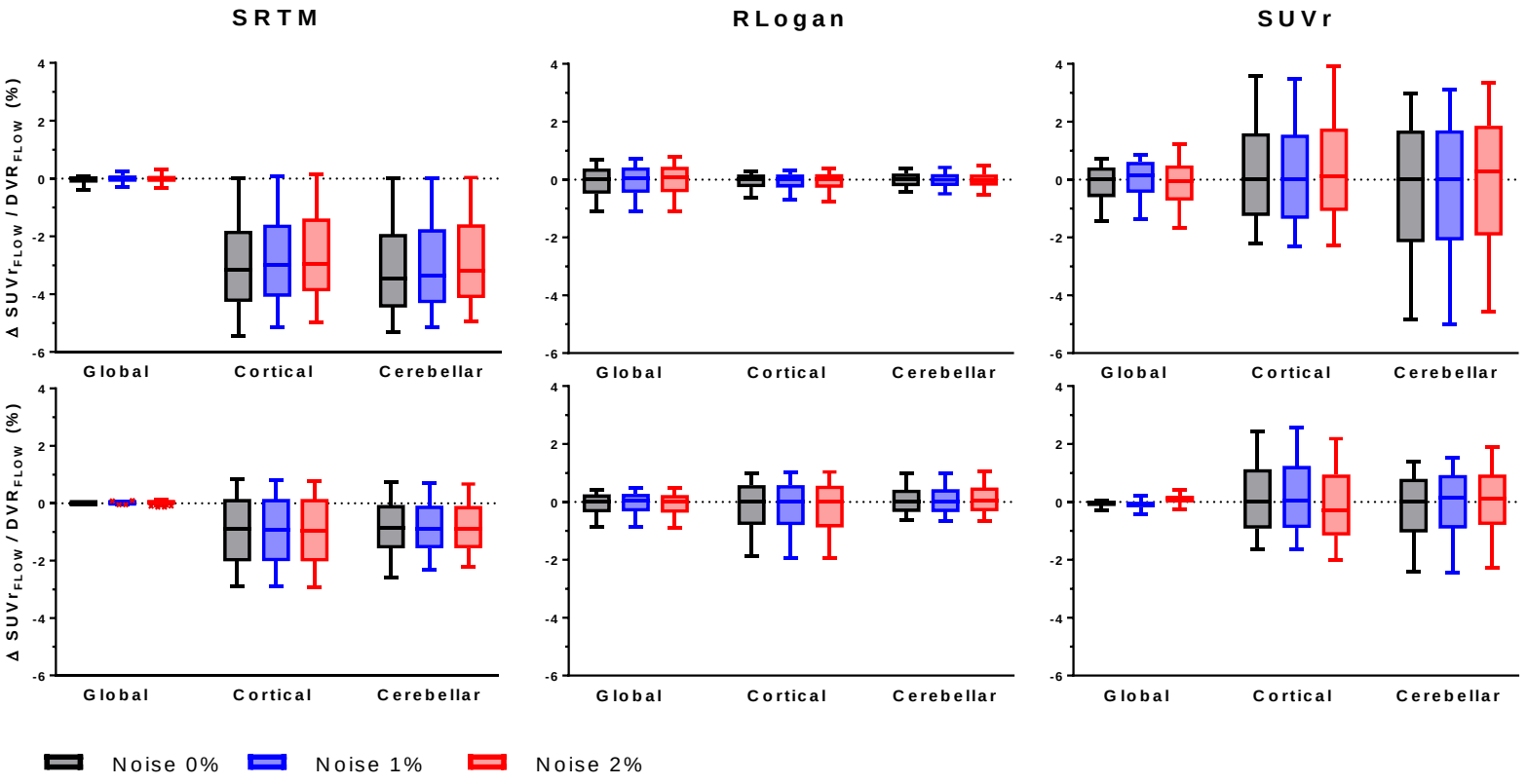


Validation lower boundary

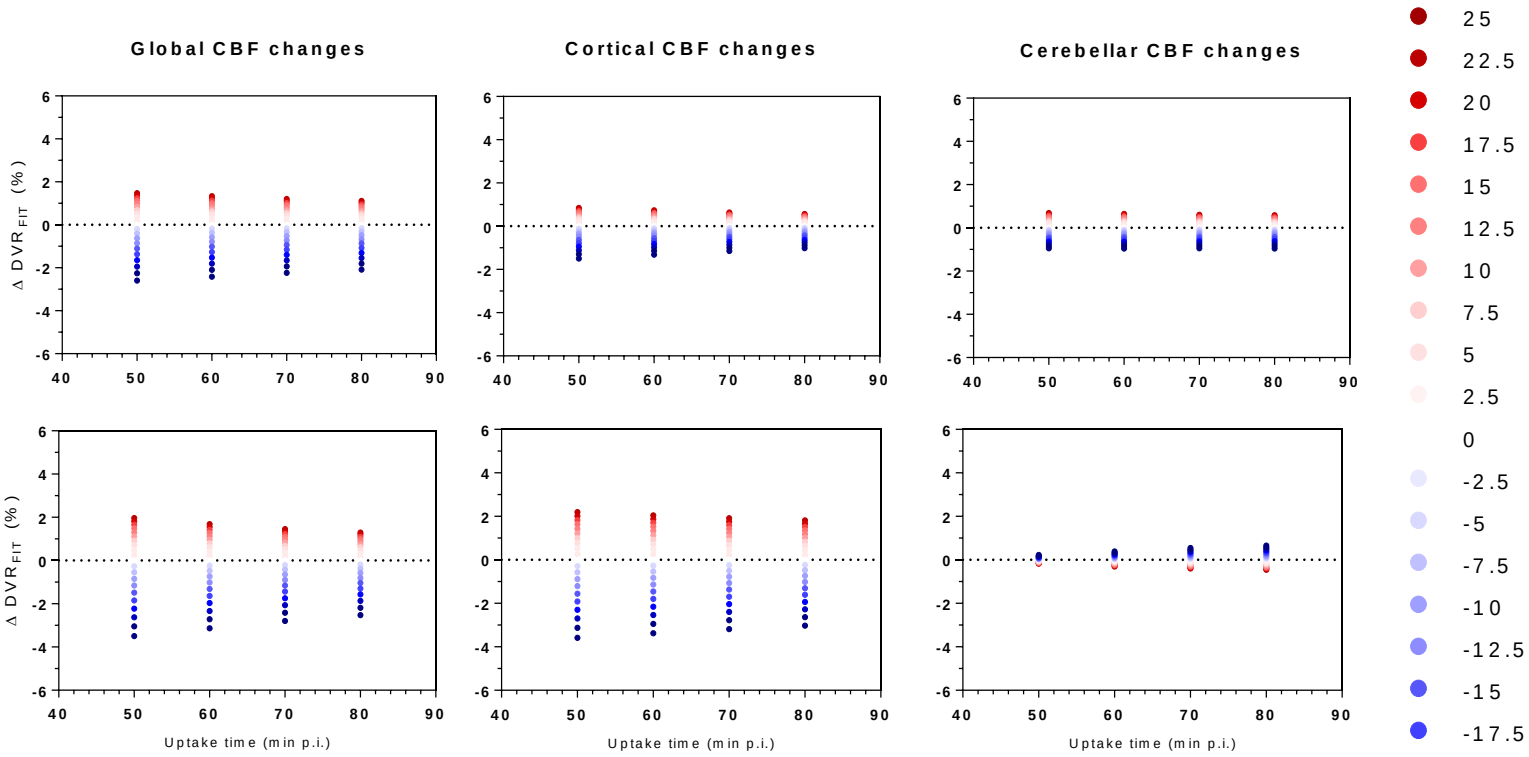
Lower boundary	1E-7	0.008	0.01	0.013	0.016	0.018	0.02
% Bias Low amyloid	4974.28	8.17	8.17	8.17	8.17	8.17	8.17
% Bias Intermediate amyloid	20.65	20.65	20.65	9.16	2.03	1.12	3.54
Total % bias	4994.93	28.82	28.82	17.33	10.21	**9.29**	11.71

Supplementary Figure 1. Boundary validation I. Example of SRTM derived parameters for noiseless full TACs with cortical CBF changes, corresponding to low amyloid. The fitting routine required implementation of boundaries (zero or infinite values not possible), therefore the following start-parameters were used: R_1(1e-6; 2), k_2(1e-6; 2), BP_{ND}(-0.5; 100). II. BP_{ND} and k_2 were poorly determined; BP_{ND} values were enormous while k_2 values approached zero. a) BP_{ND} upper boundary estimates were adjusted based upon the simulated parameter range and b) k_2 lower boundaries were adjusted based upon parameter histograms across binding levels. III. Lower boundary values were fine-tuned until the lowest overall bias (calculated from the simulated BP_{ND}+1) was obtained. IV. Same data as in 1. with new boundaries.

Note: All example values/graphs correspond to the [^{18}F]flutemetamol tracer, for [^{18}F]florbetaben the exact same procedure was carried out.



Supplementary Figure 2. The effect of noise on sensitivity to CBF changes across methods. Upper row is [^{18}F]flutemetamol and bottom row is [^{18}F]florbetaben. Note: plots correspond to the lowest level of amyloid load (DVR=1.022, DVR=1.026, for both tracers, respectively. Whiskers were defined according to the Tukey method and outliers are depicted as red crosses.



Supplementary Figure 3. The effect of linearization start-time on sensitivity to CBF changes for RLogan. Upper row is [^{18}F]flutemetamol and bottom row is [^{18}F]florbetaben. Results correspond to an intermediate level of amyloid (DVR=1.400 and DVR=1.538 for both tracers respectively) Red dots resemble CBF increases and blue dots CBF decreases.