

Validation of cardiac image derived input functions for functional PET quantification

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Supplementary Material

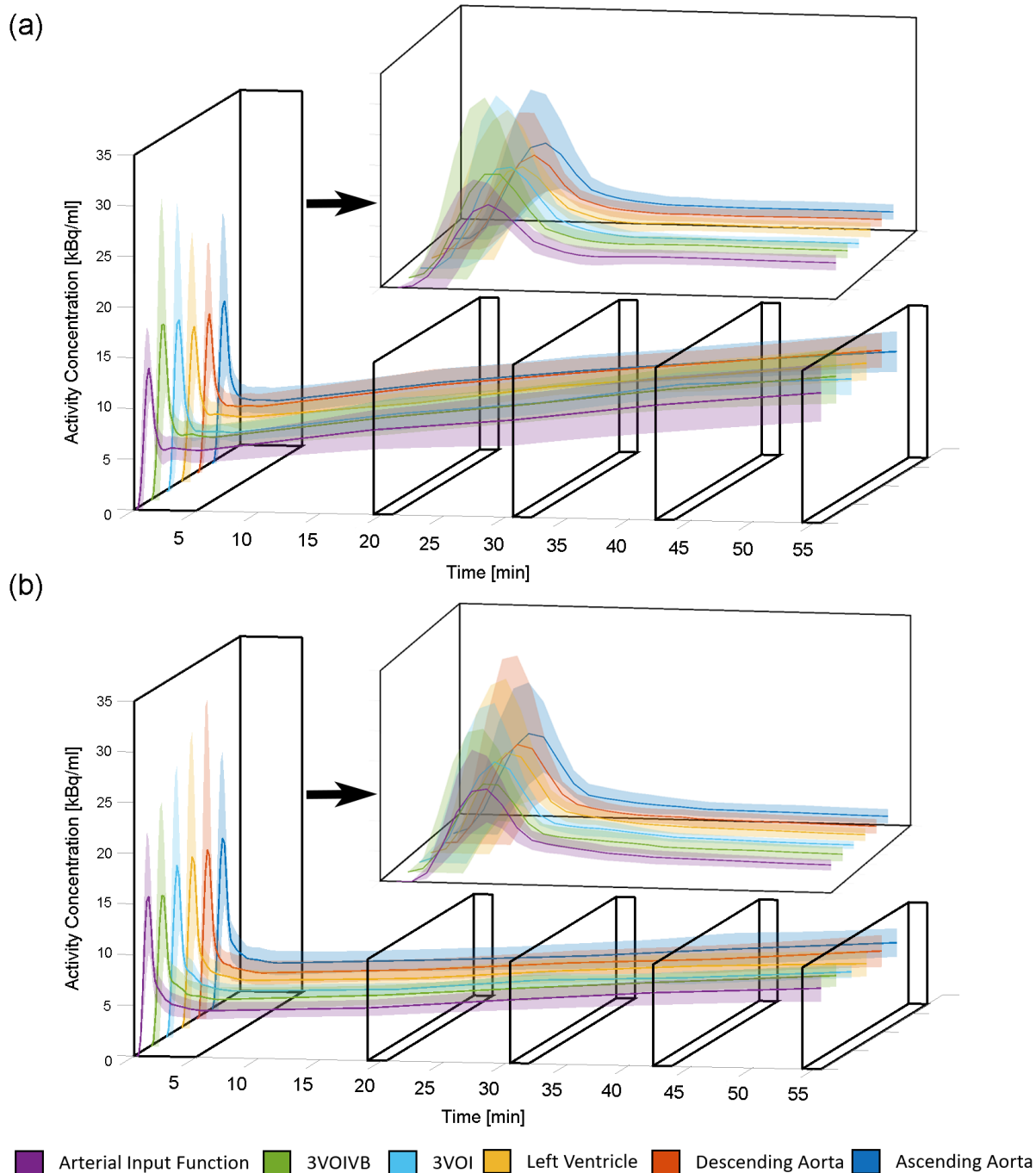
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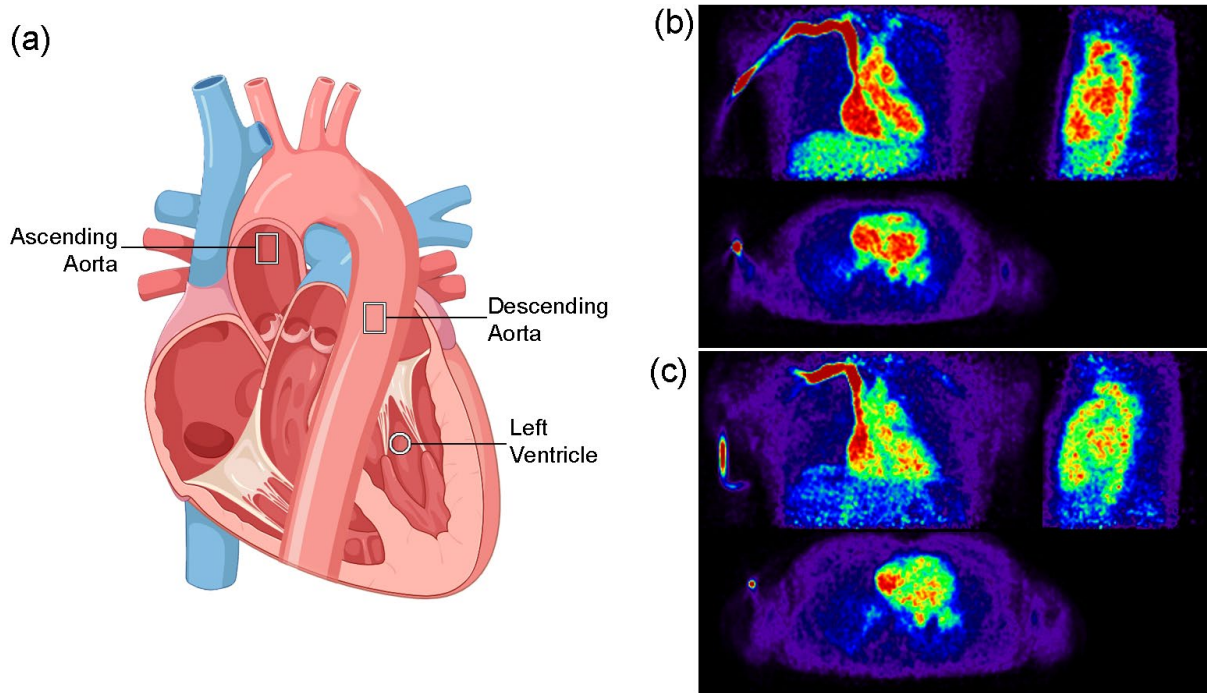
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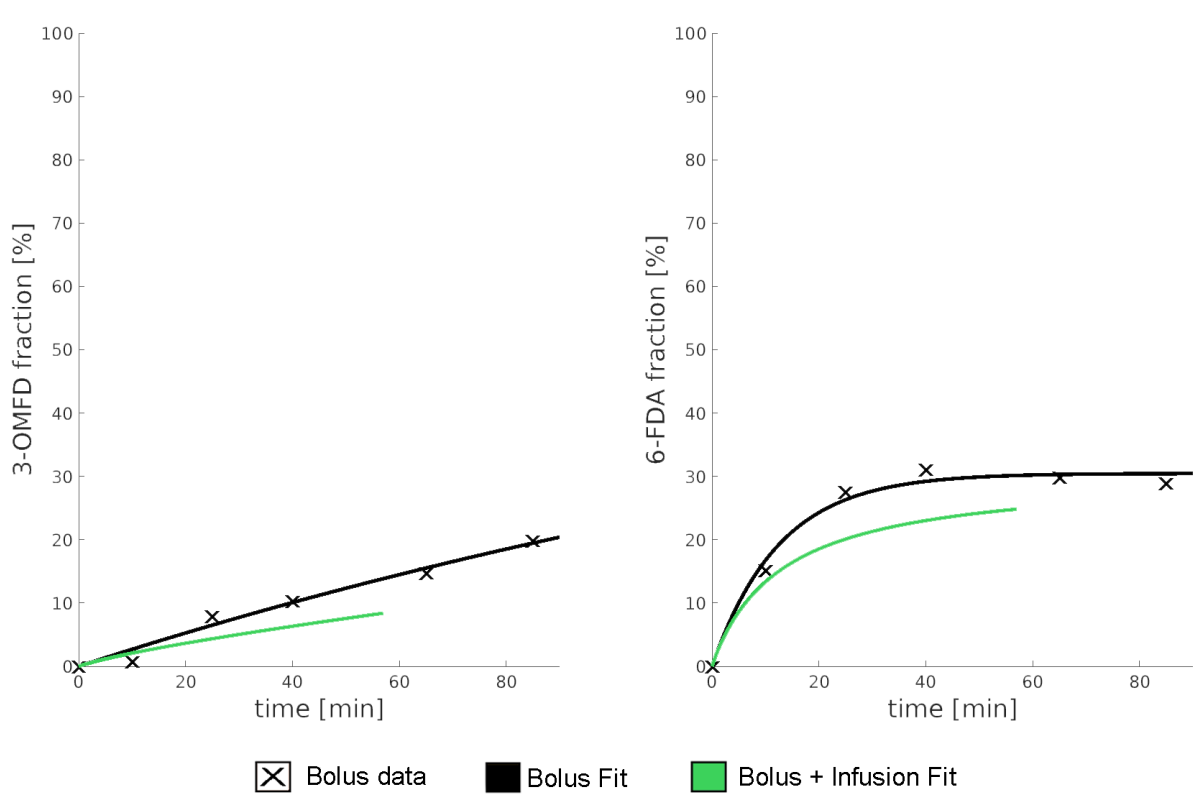
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Supplementary Figure 1: Graphical overview of all input functions extracted using the larger VOIs. The mean and standard deviation of each input function's time course for the $[^{18}\text{F}]\text{FDG}$ (a) and $6\text{-}[^{18}\text{F}]\text{FDOPA}$ cohort (b). The top right inlay represents the first 5 minutes of the entire time course. The boxes indicate the times when the FOV was shuttled from the brain to the thorax to record the image-derived input function. All input functions display a similar peak. The arterial input function (AIF) peaks later than all image-derived input functions. Finally, both the 3VOI and 3VOIVB display the highest similarity to the AIF.



Supplementary Figure 2: (a) Illustrates the intended anatomical positioning of each volume of interest for extracting each image-derived input function. Here the center point was selected and the volume of interest was extracted programmatically. (b) Displays the summed PET thorax image of a single participant in the $[^{18}\text{F}]\text{FDG}$ cohort, while (c) exhibits the summed image of a participant in the 6- $[^{18}\text{F}]\text{FDOPA}$ cohort.



Supplementary Figure 3: The metabolite fractions (3-OMFD) and (6-FDA) were extracted from previous studies ^{1,2} and ³, respectively (black crosses). These data points were then fitted with a single exponential function (black line) and adapted to match the bolus + infusion protocol (green line), showing the reduced metabolism with this protocol. The estimated bolus + infusion 6-FDA fraction data was combined with the individually measured plasma-to-whole-blood ratio to obtain the corrected arterial and image derived input functions. No corrections for the 3-OMFD fraction were done as participants received 150mg Carbidopa and 400mg Entacapone approximately 1 hour prior to tracer application to block the majority of the peripheral metabolism of 6-¹⁸F]FDOPA. Population based data extracted from ³.

Tracer			[18F]FDG					[18F]FDOPA				
Input Function			Asc Aorta	Desc Aorta	LV	3VOI	3VOIVB	Asc Aorta	Desc Aorta	LV	3VOI	3VOIVB
Brain Regions	Accumbens	r	0.952	0.988	0.989	0.995	0.997	0.706	0.969	0.955	0.968	0.955
		Slope	2.22	1.11	1.38	1.03	0.99	0.74	1.17	1.01	1.06	1.13
		Intercept	-2.14	0.15	-0.44	0.30	0.26	<0.00	<0.00	<0.00	<0.00	<0.00
	Caudate	r	0.913	0.982	0.975	0.991	0.995	0.734	0.964	0.950	0.964	0.948
		Slope	1.67	1.17	1.30	1.10	1.05	0.79	1.17	1.01	1.00	1.07
		Intercept	-0.18	0.01	-0.05	0.02	0.02	<0.00	<0.00	<0.00	<0.00	<0.00
	Putamen	r	0.865	0.952	0.946	0.977	0.987	0.846	0.974	0.971	0.977	0.968
		Slope	2.05	1.16	1.39	1.06	1.03	0.85	1.17	1.03	1.01	1.07
		Intercept	-0.25	-0.01	-0.07	0.03	0.02	<0.00	<0.00	<0.00	<0.00	<0.00
	Oldham*	r	0.975	0.985	0.988	0.995	0.997	-	-	-	-	-
		Slope	1.44	1.11	1.19	1.08	1.06	-	-	-	-	-
		Intercept	-0.23	0.06	-0.03	0.07	0.03	-	-	-	-	-

Supplementary Table 1: Pearson correlation and regression analysis of task-induced [18F]FDG CMRGlu and 6-[18F]FDOPA Ki over all participants between the larger image-derived and arterial input functions. *Cortical regions extracted from the Oldham meta-analysis of the monetary incentive delay task⁴. Bold values represent the best correlation for each tracer and region.

Tracer	Input Function	Brain Regions				
		Cohen's d	Caudate	Putamen	Accumbens	Oldham*
[18F]FDG	Asc Aorta	0.19	0.369	0.097	0.084	0.219
	Desc Aorta	0.18	0.089	<0.009	<0.002	0.091
	Left Ventricle	0.114	0.407	0.023	<0.007	0.131
	3VOIF	0.151	0.025	<0.001	<0.000	0.021
	3VOIFVB	0.930	0.012	<0.003	<0.000	0.040
[18F]FDOPA	Asc Aorta	0.55	0.303	0.140	0.104	N/A
	Desc Aorta	0.54	0.064	<0.002	<0.001	N/A
	Left Ventricle	0.59	0.045	0.060	0.014	N/A
	3VOIF	0.690	<0.003	<0.001	<0.000	N/A
	3VOIFVB	0.480	<0.000	<0.000	<0.000	N/A

Supplementary Table 2: Overview of equivalency test results estimated for regional task-induced net influx rates (K_i) quantified using each image derived-input function extracted from the larger VOIs and arterial input function (significance indicates equivalence). Cohen's d represents the standardized mean difference between the AIF and each IDIF. *Cortical regions extracted from the Oldham meta-analysis of the monetary incentive delay task ⁴.

Tracer	Input Function	Cohen's d	Brain Regions							
			Caudate		Putamen		Accumbens		Oldham*	
			p-value(1)	p-value(2)	p-value(1)	p-value(2)	p-value(1)	p-value(2)	p-value(1)	p-value(2)
[18F]FDG	Asc Aorta	0.19	0.22	0.05	0.19	<0.00	0.16	<0.00	0.07	0.17
	Desc Aorta	0.18	0.04	<0.00	0.01	<0.00	<0.00	<0.00	0.39	0.37
	Left Ventricle	0.11	0.04	0.01	0.05	<0.00	0.02	<0.00	0.26	0.31
	3VOIF	0.33	<0.00	<0.00	<0.00	<0.00	<0.00	<0.00	0.09	0.06
	3VOIFVB	0.22	<0.00	<0.00	0.01	<0.00	<0.00	<0.00	0.12	0.09
[18F]FDOPA	Asc Aorta	0.55	0.09	0.23	0.47	0.41	0.46	0.36	N/A	N/A
	Desc Aorta	0.54	0.08	0.04	<0.00	<0.00	<0.00	<0.00	N/A	N/A
	Left Ventricle	0.59	0.33	0.31	0.01	<0.00	0.01	<0.00	N/A	N/A
	3VOIF	0.69	0.30	0.27	<0.00	<0.00	<0.00	<0.00	N/A	N/A
	3VOIFVB	0.05	0.26	0.21	<0.00	<0.00	<0.00	<0.00	N/A	N/A

Supplementary Table 1: Overview of equivalency test results estimated for task-specific CMRglu ($[^{18}\text{F}]\text{FDG}$) or regional net influx rates (Ki , 6- $[^{18}\text{F}]\text{FDOPA}$) quantified using each image derived-input function and arterial input function (significance of both p-value(1) and p-value(2) indicates equivalence). Cohen's d represents the standardized mean difference between the AIF and each IDIF. The p-value(1) and p-value(2) represent the left and right one-sided t-test significance values from the two one-sided t-tests (TOST) for each region, respectively. Bold IDIFs show equivalence for all regions of interest. *Cortical regions extracted from the Oldham meta-analysis of the monetary incentive delay task ⁴.

References

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