Plausibility of Using [18F]NOS as a PET Radiotracer for Imaging Smoking-Induced Inflammation in the Aorta

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Introduction

- Smoking: strongest risk factor for the development of Aortic Abdominal Aneurysms (AAAs).
- Atherosclerosis: inflammatory vascular disease, known precursor of AAAs. Also correlated with smoking.
- Electronic Nicotine Delivery Systems (ENDS): may generate **similar** adverse effects to those caused by combustible cigarettes (American Heart Association, 2022)
- Inducible Nitric Oxide Synthase (iNOS): plays a key role in mediating the body's inflammatory response, increased iNOS expression is associated with inflammatory disease
- [18F]NOS: iNOS analog, may be well suited for imaging vascular inflammation.

Methodology

12 healthy controls (HC)
11 nicotine vapers (V)

PennPET Explorer with Spectral CT
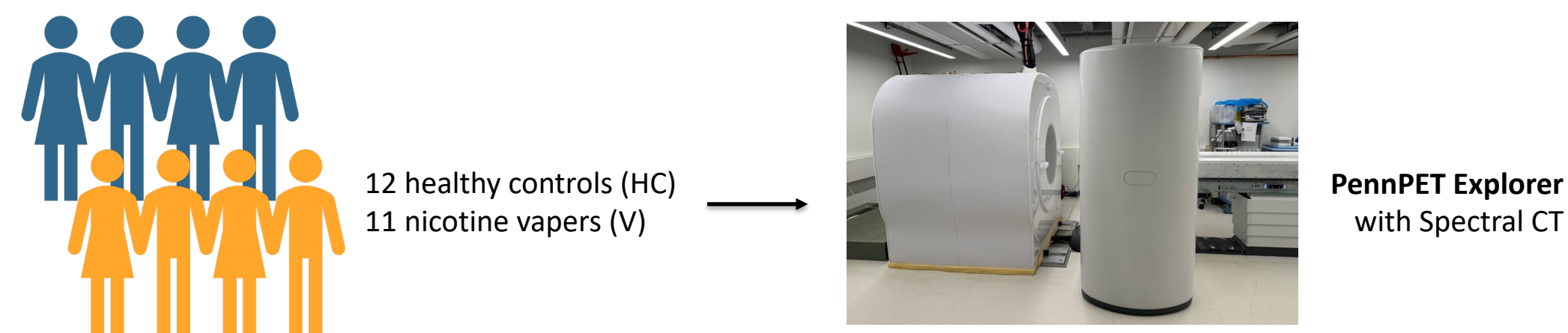
Figure 1. 23 subjects were initially included in the study; they underwent an (approximately) one-hour, dynamic PET scan.

- 3 HCs and 2 Vs excluded due to irregularities in the blood corrections.

Volumes of Interest (VOIs):
- Vessel walls of the Ascending Aorta (Asc. Aorta) and the Descending Aorta (Desc. Aorta) were segmented at the level of the carina.
- Vessel wall of the Abdominal Aorta (AA) was segmented between L1 and L3.
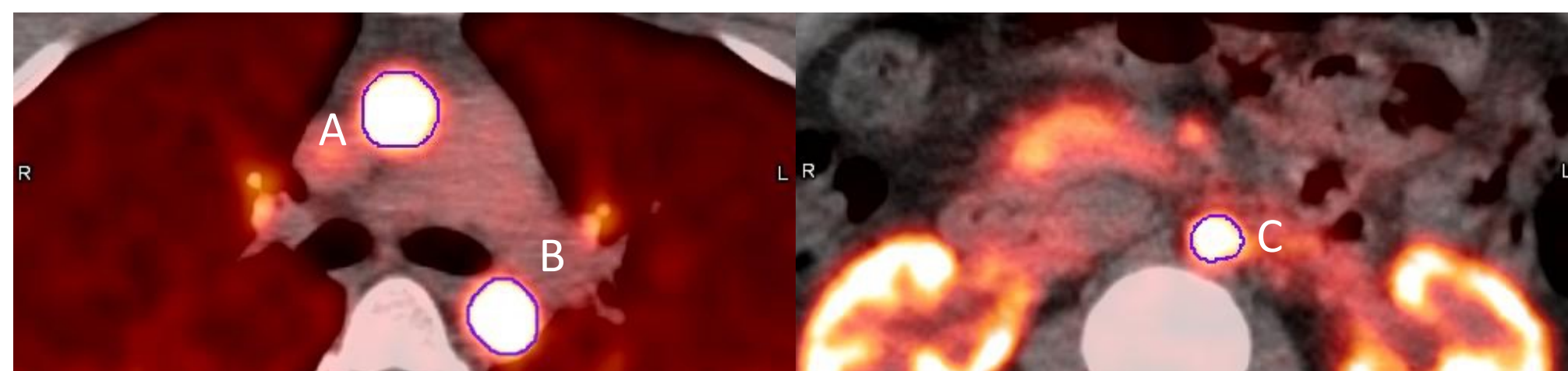
Figure 2. Sample segmentation of VOIs for IDIFs. A: ascending aorta. B: descending aorta. C: abdominal aorta.

The vessel walls were segmented on MIM; the difference between the inner and outer diameter was set between 2.0 mm and 3.0 mm in accordance with the normal width of the aortic wall.

Methodology
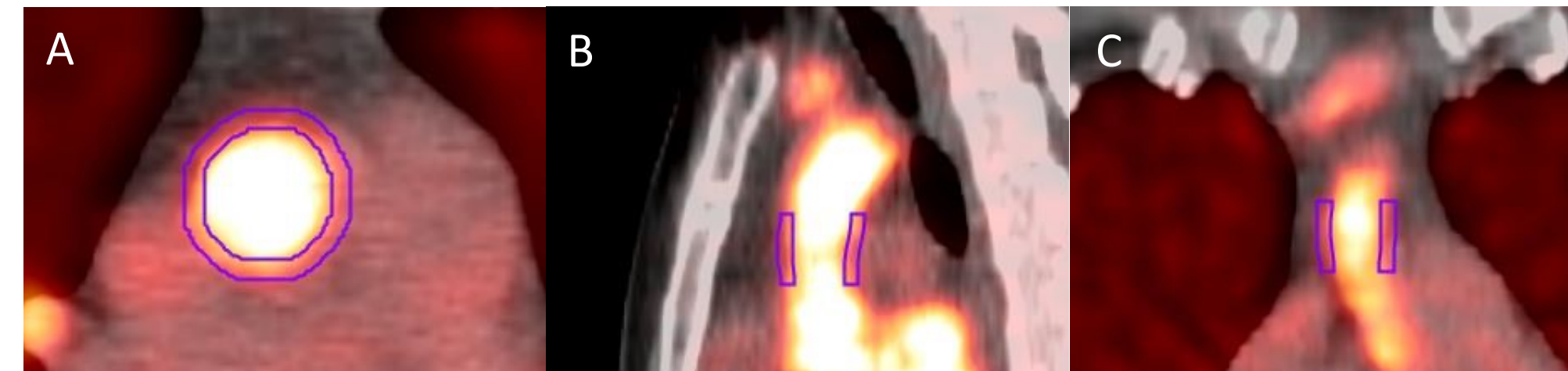
Figure 3. Sample segmentation of the vessel wall in the ascending aorta. A: axial view. B: sagittal view. C: coronal view.
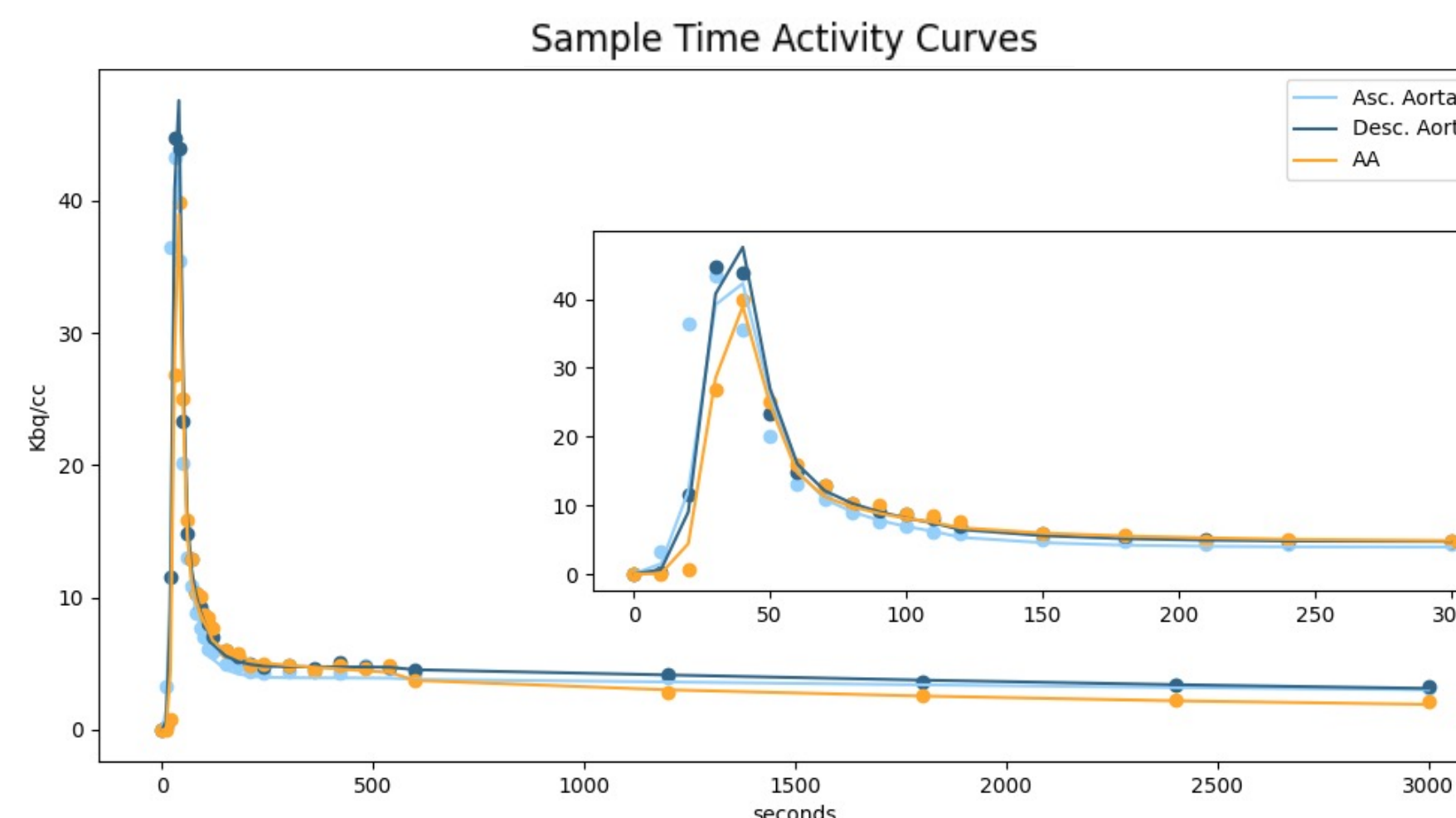
Kinetic Modeling:
- One-Tissue Compartment (1TC) and Two-Tissue Compartment (2TC) models as well as a Logan Plots were fit on PMOD.
- Image Derived Input Functions (IDIFs) were used for the kinetic modeling.

Metrics:
- Volume of Distribution (V_T), 2TC Binding Potential (BP_{nd}), Area Under the Curve (AUC)
- Akaike Information Criterion (AIC) for model selection.
- P-values were computed using a Mann-Whitney U Test ($\alpha = 0.05$)

Results

Figure 4. Sample TACs after kinetic modeling. Curves shown for Asc. and Desc. Aorta are 1TC models; curve shown for AA is a 2TC model. Inset shows first 300 seconds of TACs.
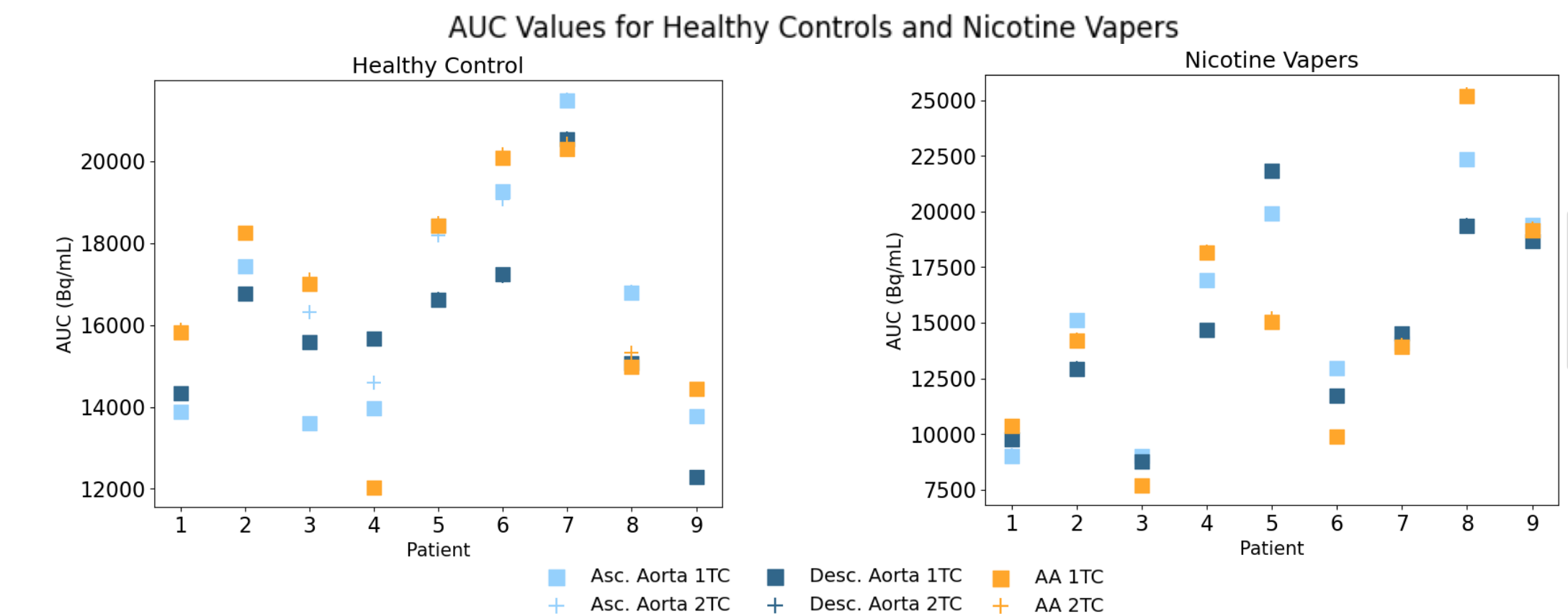
	Asc. Aorta		Desc. Aorta		AA	
	HC	V	HC	V	HC	V
1TC	1.41 ± 0.51	1.38 ± 0.58	0.96 ± 0.23	1.08 ± 0.49	1.91 ± 0.47	1.70 ± 0.97
2TC	3.16 ± 4.33	1.76 ± 0.85	1.48 ± 0.35	1.64 ± 0.67	3.08 ± 0.63	2.70 ± 0.97
Logan Plot	2.42 ± 0.29	2.35 ± 0.44	2.26 ± 0.23	2.28 ± 0.55	2.53 ± 0.40	2.41 ± 0.62

Table 1. Mean ± SD V_T values for 1TC, 2TC and Logan Plot.

	Healthy Control			Nicotine Vaper		
	1TC	2TC	Logan Plot	1TC	2TC	Logan Plot
Asc. Aorta vs. Desc. Aorta	0.022*	0.724	0.185	0.112	1.000	0.791
	0.078	0.022*	0.427	0.158	0.034*	0.930
Asc. Aorta vs. AA	0.078	0.022*	0.427	0.158	0.034*	0.930
Desc. Aorta vs. AA	0.001**	0.001**	0.042*	0.034*	0.027*	0.659

Table 2. p-values from Mann-Whitney U Test of V_T across regions of interest; * = p < 0.05, ** = p < 0.01.

Results

Figure 5. AUC for control and experimental groups. Squares and plus signs are 1TC and 2TC models, respectively.
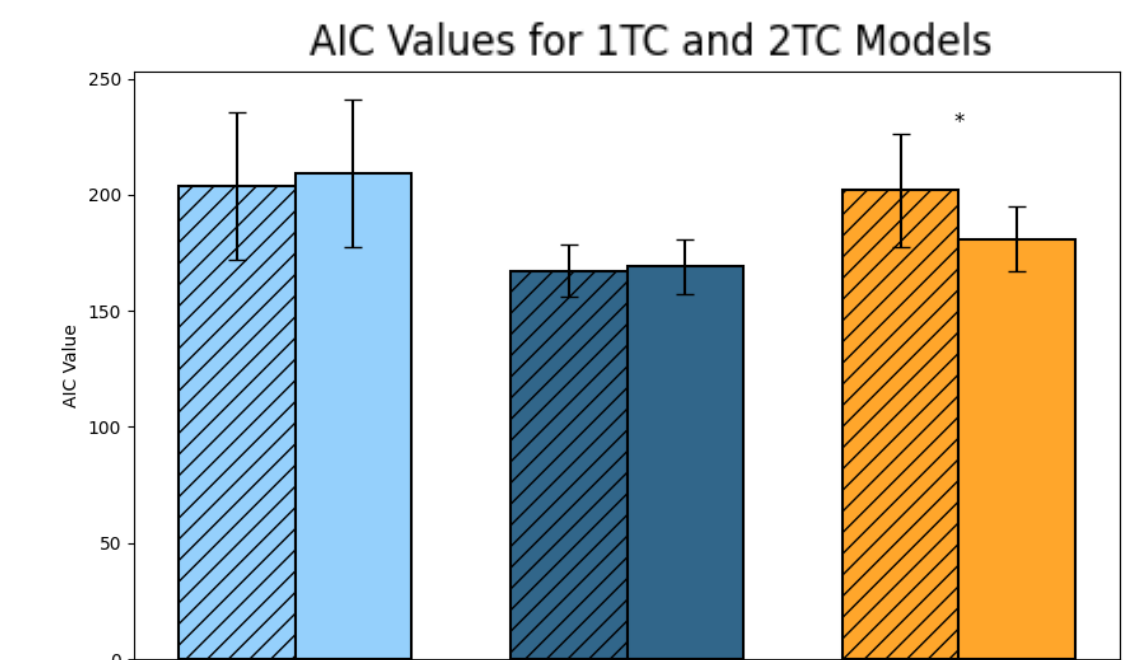
Asc. Aorta		
HC*	V	p
1.32 ± 1.74	2.05 ± 2.88	0.93

Desc. Aorta		
HC **	V	p
1.45 ± 1.04	2.68 ± 2.35	0.19

AA		
HC *,**	V	p
4.74 ± 2.27	3.16 ± 1.32	0.13

Table 3. Mean ± SD BP_{nd} values. Significant differences were found between Asc. Aorta and AA (p < 0.05) and Desc. Aorta and AA (p < 0.01) in HCs.

Figure 6. AIC values for 1TC (stripes) and 2TC (solid) models. Asc. Aorta in light blue, Desc. Aorta in teal, AA in yellow.

Conclusions and Future Directions

- V_T trend across regions: AA > Asc. Aorta > Desc. Aorta (for 1TC, 2TC and Logan Plot)
- BP_{nd} trend across regions: AA > Desc. Aorta > Asc. Aorta.
- Validation of segmentation methodology using FDG scans.
- Kinetic modeling of left ventricle (LV) to use as a reference tissue.
- Repeat kinetic modelling using an IDIF from LV or eroding the edges of the corresponding IDIFs to account for differences in spillover between models.

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References

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