Dynamic Imaging and Tracer Kinetic Modeling of ^{18}F-flutemetamol PET for Cardiac Amyloidosis Patients

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Purpose

Recent studies showed the promise of ^{18}F-flutemetamol PET imaging for detecting cardiac amyloidosis (CA) [1]. However, static PET data analysis methods for ^{18}F-flutemetamol are time sensitive due to patient-dependent tracer wash-out in the myocardium, as shown in Figure 1. In this study, we performed kinetic modeling on dynamic ^{18}F-flutemetamol PET images to obtain fully quantitative myocardial volume of distribution (V_T) for CA patients.

Methods

Six ATTR CA patients underwent 60 mins dynamic PET imaging on a GE Discovery 690 PET/CT after bolus ^{18}F-flutemetamol tracer injection. The acquired list-mode data were binned into a sequence of 34 frames (12×10 s; 13×1 min; 9×5 min) which were reconstructed into 34 dynamic images with attenuation, scatter, and decay corrections. Image-derived input functions (IDIF) and myocardium time activity curves (TAC) were generated from manually drawn left ventricle and myocardium volumes of interest on dynamic frames. Population-based whole blood-to-plasma ratio correction (PBPC) and population-based plasma metabolic correction (PMC) derived from a previous brain study [2] were applied to correct image-derived input functions. We investigated Patlak and Logan plots, and tested 1T, 2T reversible, and 2T irreversible compartmental models with blood volume estimation. Finally, parametric images of V_T, the equilibrium myocardium to plasma ratio, were generated for the six patients, voxel-by-voxel.

Results

The 2T reversible model had a lower Akaike criteria value (145.3 ± 24.4) than the 1T reversible model (195.0 ± 32.0, $P = 0.02$) and the 2T irreversible model (196.0 ± 36.5, $P = 0.01$) when using IDIF with both PMC and PBPC, as shown in Figure 2. As demonstrated in Figure 3, the Logan plot was more suitable than the Patlak plot for myocardial TACs, suggesting 2T reversible model in the myocardium. V_T values generated by the 2T reversible compartmental model were consistent with V_T values calculated by the Logan plot ($P = 0.99$). In 2T reversible compartmental model fitting, significant lower Akaike criteria value was achieved using image-

derived input functions after both PMC and PBPC (145.3 ± 24.4), than PMC only (178.2 ± 27.4, $P = 0.04$), PBPC only (225.8 ± 12.5, $P = 4.1\times10^{-5}$), or without any corrections (206.1 ± 11.77, $P = 4\times10^{-4}$), as illustrated in Figure 4. The mean V_T values of six CA patients was 2.61 ± 0.47 with PMC and PBPC, which was 118% ± 30% higher than those without corrections. V_T images of six CA patients are shown in Figure 5. In addition, we generated V_T images utilizing only 30 mins dynamic data as shown in Figure 6. The mean V_T values of the 30 mins data was 2.35 ± 0.32 ($P = 0.01$), which was 10.1% ± 5.5% lower than those generated from 60 mins data.

Conclusion

^{18}F-flutemetamol parametric V_T images in CA patients were generated for the first time and provided a fully quantitative measurement for clinical evaluation. ^{18}F-flutemetamol in the myocardium follows a 2T reversible compartmental model. Both PMC and PBPC are needed to correct the image-derived input function for accurate kinetic modeling of ^{18}F-flutemetamol. We will further investigate the feasibility of shortening image acquisition time from 60 mins to 30 mins.

References

1. Gallegos, C. and E.J. Miller, *Advances in PET-Based Cardiac Amyloid Radiotracers.* Curr Cardiol Rep, 2020. **22**(6): p. 40.
2. Heurling, K., et al., *Parametric imaging and quantitative analysis of the PET amyloid ligand [18F] flutemetamol.* Neuroimage, 2015. **121**: p. 184-192.

Figure

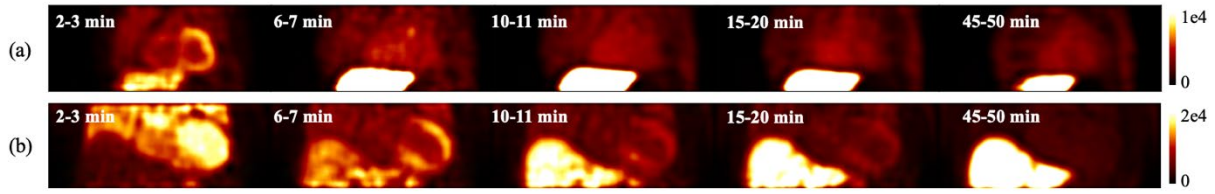

Figure 1. Sample dynamic images of ^{18}F-flutemetamol for two patients with different tracer wash-out properties. (a)^{18}F-flutemetamol tracer uptake in myocardium is unnoticeable after 5 mins post-injtection. (b) Myocardium tracer uptake is still evident after 20 mins post-injection.

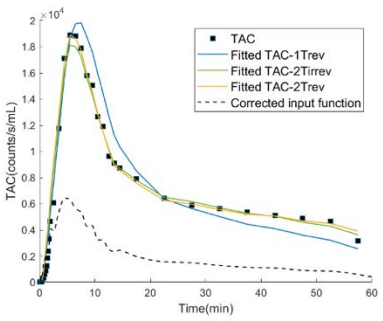

Figure 2. Sample myocardial TAC fitting results by 1T reversible, 2T reversible, and 2T irreversible models.

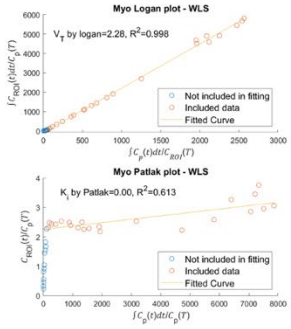

Figure 3. Sample Logan plot (upper) and Patlak plot (lower).

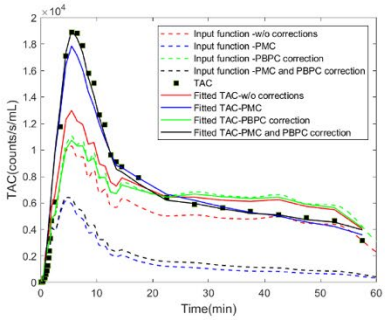

Figure 4. Sample Myocardial TAC fitting results without and with correction for the input function.

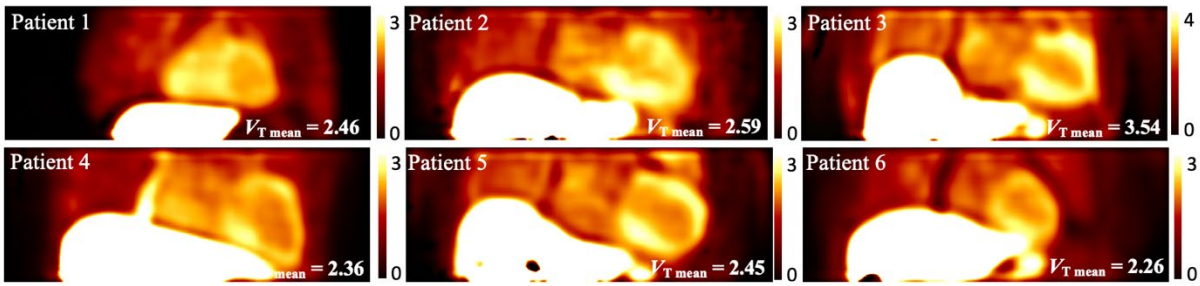

Figure 5. V_T images for 6 patients, generated from 2 mins to 60 mins dynamic data. Mean V_T values of myocardium are shown on the bottom right.

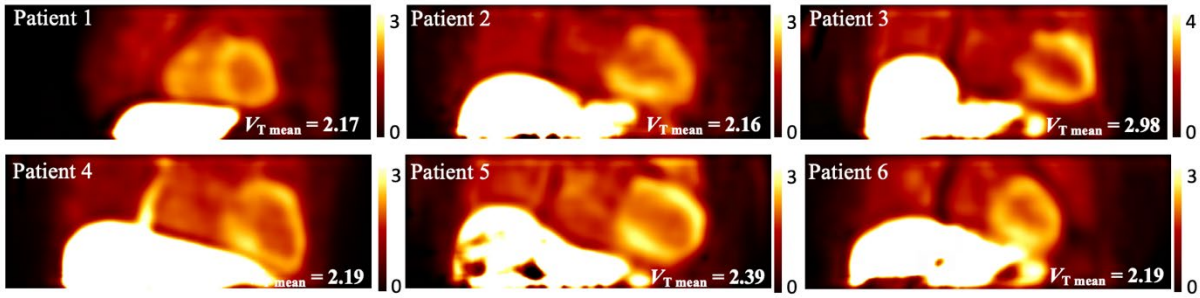

Figure 6. V_T images for 6 patients, generated from 2 mins to 30 mins dynamic images. Mean V_T values of myocardium are shown on the bottom right.