Optimized coffee-break protocols for quantitative [^{18}F]flutemetamol and [^{18}F]florbetaben studies

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Introduction

[^{18}F]flutemetamol and [^{18}F]florbetaben are PET tracers used for imaging amyloid-β plaques in the brain. For both tracers, a static scan (90-110 min) has been approved for diagnostic purposes. For monitoring disease progression and treatment response, however, quantification based on a dynamic scanning protocol (0-110 min), providing a measure of binding potential (BP), may be required[1]. As long scanning times may cause discomfort to patients, the purpose of the present study was to define the optimal dual time window (coffee-break) protocol, (scanning time vs accuracy of BP measurement) in which patients are scanned only during the early and late phases after tracer injection.

The aim of this simulation study was to define the optimal trade-off between quantitative accuracy and scanning time for [^{18}F]flutemetamol and [^{18}F]florbetaben using a coffee-break protocol

Methods

- Clinical input data[2,3]
  - Representative plasma input curves (Fig. 1) and kinetic parameters from dynamic time activity curves (TACs, 110 min)
- Simulated TACs (Fig. 2)
  - Reference tissue TAC (GM cerebellum) using plasma input
  - Target region TACs (global cortex) for a full range of clinically observed BP_{ND} values using SRTM (Table 1)
  - Several noise levels added to TACs (COV 0 – 15%)
  - Various coffee-break intervals removed from TACs (i.e. 0 min break = full scan, 80 min break = interval from 10-90 min)
- TACs fitted using SRTM (simplified reference tissue model)
- Error assessment
  - % outliers
  - Resulting coffee-break BP_{ND} and R_1 were compared to the simulated BP_{ND} and R_1

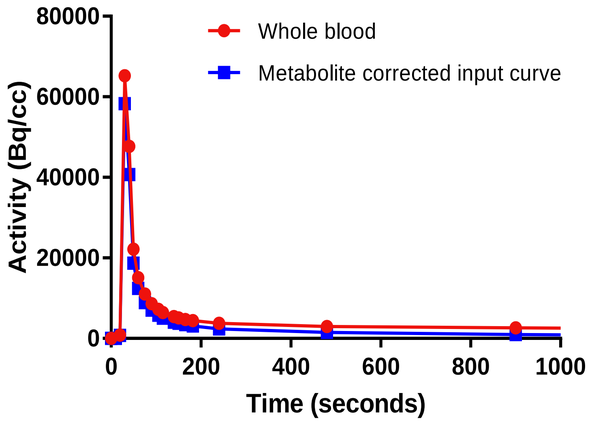


Figure 1 Input Curves [^{18}F]flutemetamol

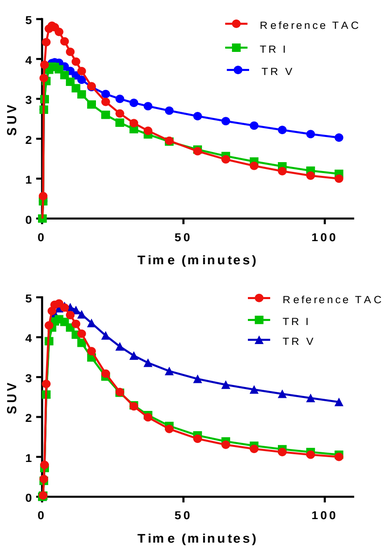


Figure 2 Simulated TACs [^{18}F]flutemetamol (top) and [^{18}F]florbetaben (bottom)

Table 1. Kinetic parameters for simulations

Region	FLUT BP_{ND}	FBB BP_{ND}
TR_I	0.003	0.0051
TR_II	0.107	0.3978
TR_III	0.211	0.7905
TR_IV	0.315	1.1786
TR_V	0.453	1.5713

TR = target region, FLUT = [^{18}F]flutemetamol, FBB = [^{18}F]florbetaben
FLUT: R_1 = 0.827, k_2 = 0.08, FBB: R_1 = 0.769, k_2 = 0.075

Results

- Outliers: As expected, more outliers were found for longer coffee-break intervals and at higher noise levels for both tracers
- Bias: Both longer coffee-break intervals and higher noise levels showed larger errors and different trends in SRTM derived BP_{ND} and R_1 errors, especially for the 10-90 and to a lesser extend for the 20-90 interval (Fig. 3)

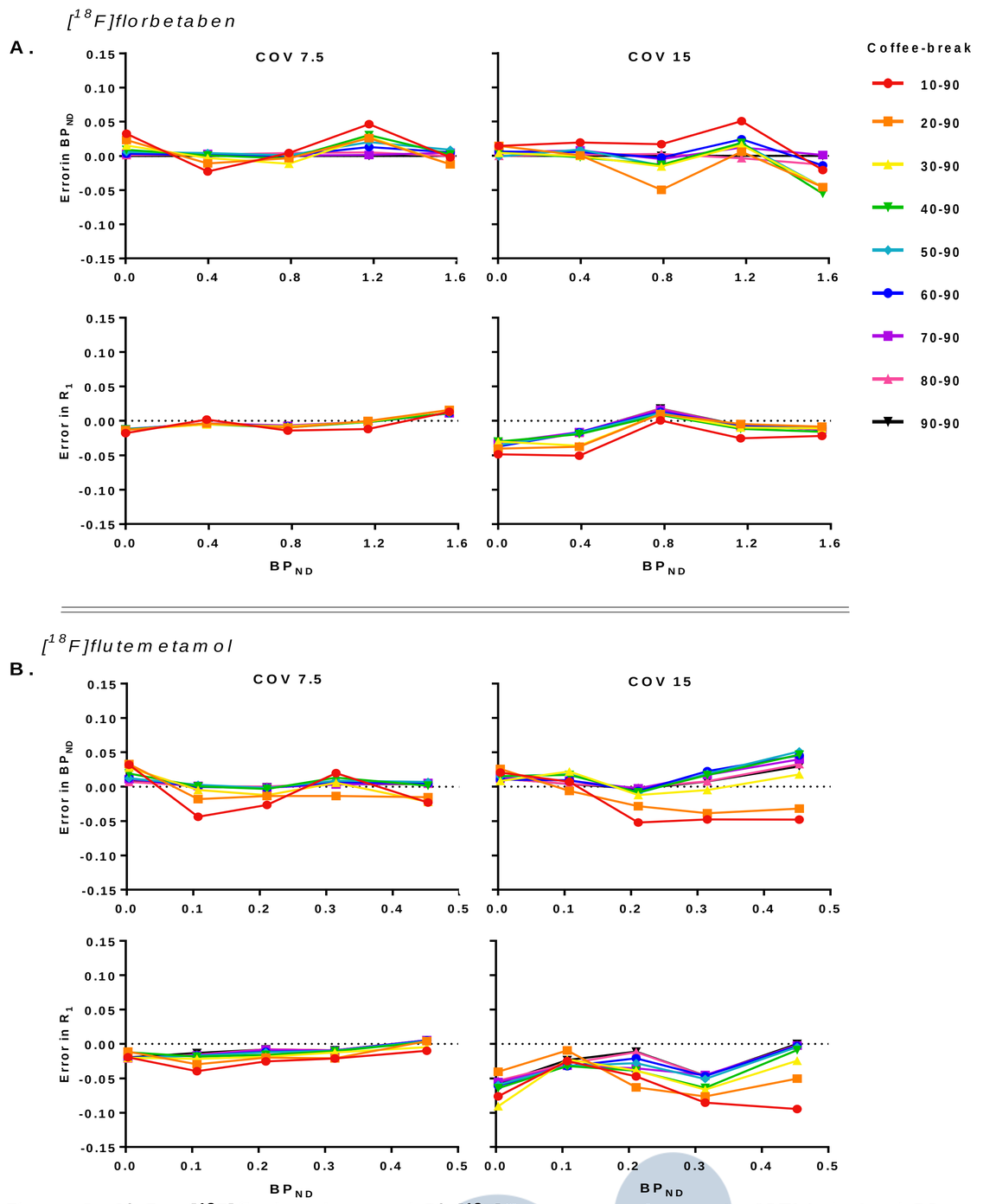
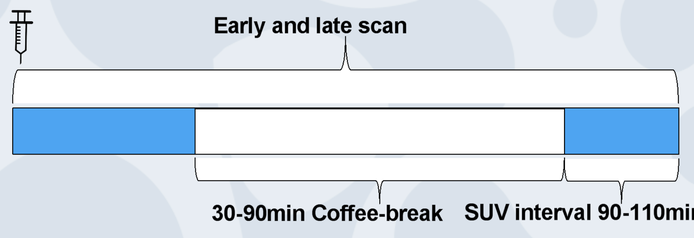


Figure 3. A) For [^{18}F]florbetaben and B) [^{18}F]flutemetamol error in SRTM derived BP_{ND} from simulated BP_{ND} (left) and SRTM derived R_1 from simulated R_1 (right) for TACs simulated with various coffee-break protocols. COV = Coefficient of variation (noise)

Conclusion

✓ **The optimal trade-off between quantitative accuracy and scanning time corresponded to a coffee-break interval of 60 minutes or smaller. The 60 minutes interval would also allow for interleaved scanning, increasing patient throughput and efficient tracer batch utilisation.**



1. Van Berckel et al. (2013) J Nucl Med 54(9) 1570-1576, 2. Heurling et al. (2015) Neuroimage 121: 184-192, 3. Becker et al. (2013) J Nucl Med 54: 723-731

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