Optimised coffee-break protocol for quantitative [^{18}F]flutemetamol studies

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Introduction

- AMYPAD aims to improve understanding and diagnosis of Alzheimer's Disease using ß-amyloid PET
- [^{18}F]flutemetamol is a PET tracer used to image ß-amyloid in the brain for clinical and research purposes
- A static scan (90-110 min) can be used for diagnostic purposes, but a dynamic scan (110 min) may be required for monitoring disease progression and treatment response
- As a long scanning time may cause discomfort to patients, the purpose of the present study was to optimize a dual time window (coffee-break) protocol, in which a patient is scanned 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 using a coffee-break protocol

Methods

- Clinical input data[1]
  - Kinetic parameters from dynamic Time Activity Curves (TACs,110 min)
  - Plasma input curves (Fig.1)
- Simulated TACs
  - Reference tissue TAC (Fig.2)
  - Target region TACs (full range of clinically observed BP_{ND} values) using SRTM (Table 1)
  - Various noise levels (COV 0 – 15%)
  - Various coffee-breaks (i.e. 0 min break = full scan, 80 min break = interval between 10-90 min)
- TACs fitted using SRTM (simplified reference tissue model) and it's basis function approach: RPM (Receptor Parametric Mapping)
- Error assessment: BP_{ND} and R_1 were compared to the corresponding values of the full data set (90-90, no interval)
  - Visual analysis
  - Mean and variance
  - Clinical relevance: error BP_{ND} > 0.05 based on test-retest variability of BP_{ND}[2]

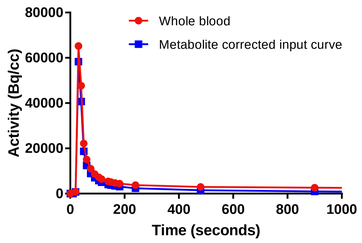

Figure 1 Input Curves

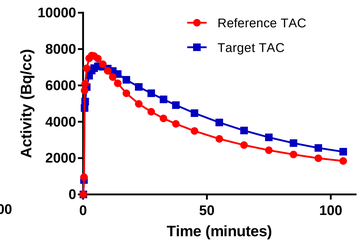

Figure 2 TACs

Table 1 Kinetic parameters for simulations

	R_1	k_2	BP_{ND}
TR_I	0.827	0.080	0.003
TR_II	0.827	0.080	0.107
TR_III	0.827	0.080	0.211
TR_IV	0.827	0.080	0.315
TR_V	0.827	0.080	0.453

TR = target region

Results

- Outliers: No extreme outliers (BP_{ND}>2) in RPM derived BP_{ND}. For SRTM, extreme outliers mostly present at higher noise levels, for the longest coffee-break intervals.
- Visual analysis: 10-90, 20-90 intervals show largest deviation for BP_{ND} and R_1, even when no noise is added (Fig.3)
- Mean and variance analysis: Majority of significant differences in mean found in 10-90, 20-90, fewer in 30-90,40-90 interval.
- Clinical relevance: errors predominantly in 10-90, 20-90 interval (Fig.4)

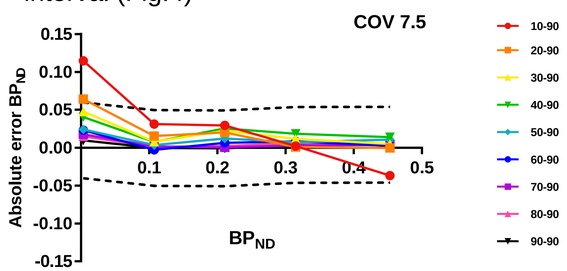

Figure 4 Dashed lines represent ±0.05 BP_{ND} differences with the 90-90 no interval estimates

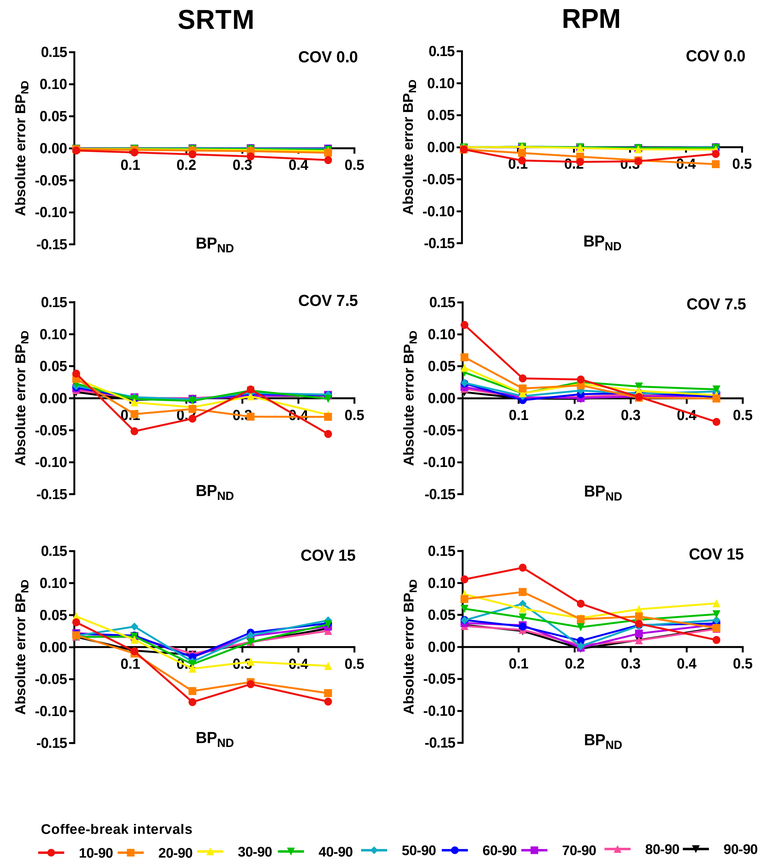

Figure 3 Absolute errors in BP_{ND}, COV=coefficient of variation (noise level)

Conclusion

✓ **For quantitative [^{18}F]flutemetamol studies, accurate BP_{ND} results can be achieved using coffee-break intervals of 60 minutes (30-90) or smaller**

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1. Heurling et al. (2015) *Neuroimage* 121: 184-192, 2. Yaqub et al. (2008) *Neuroimage* 42: 76-86

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