# Effect of blood flow changes on quantification of [$^{18}$F]flutemetamol studies

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## Introduction

- Cerebral blood flow (CBF) decreases with age and additional reductions occur in patients suffering from Alzheimer's Disease (AD)
- Reductions in CBF of up to 30% have been reported[1,2]
- Longitudinal assessment of amyloid load may be biased because of sensitivity to changes in CBF[3]

### Purpose

**The purpose of this simulation study was to assess the effect of CBF reductions on quantification of [$^{18}$F]flutemetamol scans**

## Methods

- Clinical input[4]
  - Kinetic parameters for a range of amyloid load levels, based on dynamic 110 minutes time activity curves (TACs) validated previously (Table 1)
- Simulated CBF reductions
  - Tracer delivery reduction $K_1$ (0 to -25%, while keeping $K_1/k_2$ ratio constant)
  - Global: reduction in cortical (target) and cerebellar grey matter region (reference) (Fig.1)
  - Local: reduction in cortical region only
- Amyloid load estimation
  - SUVr (90-110 minutes post injection)
  - Simplified reference tissue model[5]: non displaceable binding potential ($BP_{ND}$=) and distribution volume ratio (DVR = $BP_{ND}$+1)

**Table 1** Pharmacokinetic parameters for simulating plasma TACs using reversible two-tissue compartment model

| Amyloid level | $BP_{ND}$ | DVR | $k_3$ | $V_B$ |
|---|---|---|---|---|
| I | 0.380 | 1.020 | 0.008 | 0.05 |
| II | 0.635 | 1.208 | 0.013 | 0.05 |
| III | 0.890 | 1.397 | 0.018 | 0.05 |
| IV | 1.145 | 1.585 | 0.023 | 0.05 |
| V | 1.400 | 1.774 | 0.028 | 0.05 |
| ***Reference*** | 0.350 | 1.000 | 0.018 | 0.05 |

*BP* = Binding potential of target tissue, DVR = Distribution Volume Ratio. [18F]flutemetamol target tissue: $K_1$=*0.248*, $k_2$=0.08, reference tissue: $K_1$=0.32, $k_2$=0.103.

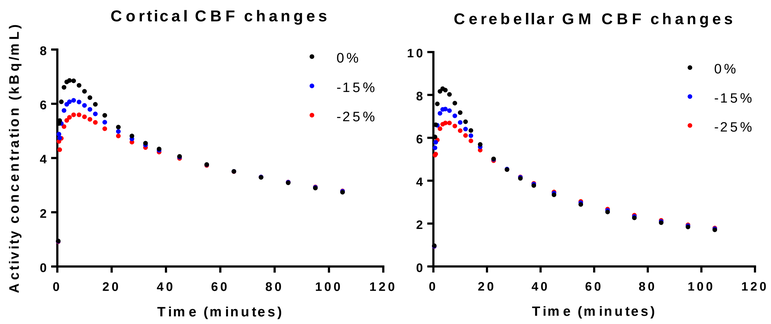


**Figure 1.** Example TACs showing reductions in tracer delivery ($K_1$) for **a)** the cortical region and **b)** the cerebellar grey matter region. $K_1/k_2$ ratio was kept constant for both regions.

## Results (1)

- Large global CBF reductions resulted in only a small bias in DVR (<3%) for all simulated amyloid levels (Fig. 2a)
- Bias in SUVr was larger (4-16%) and affected by the level of amyloid load (Fig. 2b)

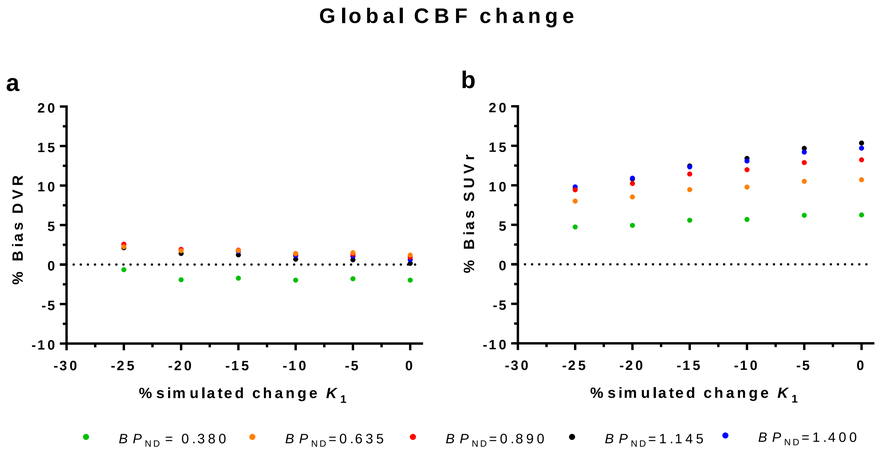


**Figure 2. a)** Percentage bias in DVR and **b)** SUVr, as a function of global CBF ($K_1$) for various levels of amyloid load ($BP_{ND}$).

## Results (2)

- Bias in DVR increased slightly for large local CBF reductions (Fig. 3a)
- A local CBF decline resulted in a relatively stable bias in SUVr, however strongly affected by level of amyloid load (Fig. 3b)

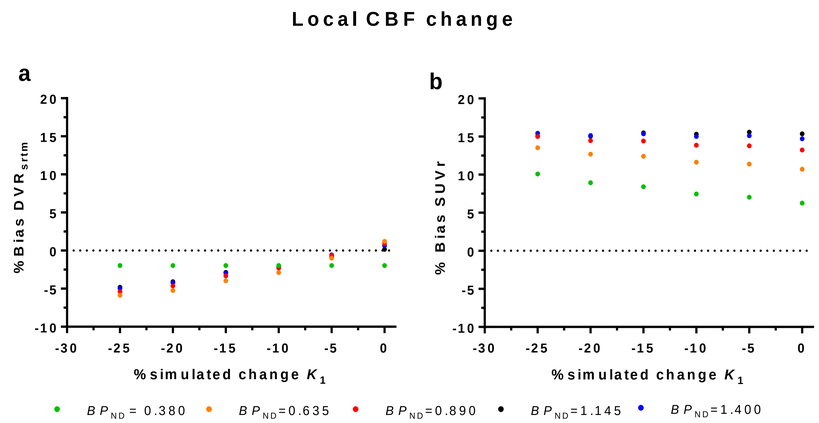


**Figure 3. a)** Percentage bias in DVR and **b)** SUVr, as a function of local CBF ($K_1$) for various levels of amyloid load ($BP_{ND}$).

## Conclusion

✓ **Changes in derived amyloid load may be affected by reductions in CBF when using SUVr. Hence, for more accurate amyloid load estimates, especially in a longitudinal setting, dynamic scans should be used.**

1. Frackowiak (1986) *Prog Brain Res.* 1986;70:69–85, 2. Bremmer et al. (2010) *Molecular Imaging and Biology*;13: 759–68. 3. van Berckel et al. *J Nucl Med* 54.9 (2013): 1570-1576. 4. Heurling et al. (2015) *Neuroimage* 121: 184-192, 5. Lammertsma & Hume (1996) *Neuroimage 4.3 (1996): 153-158.*

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