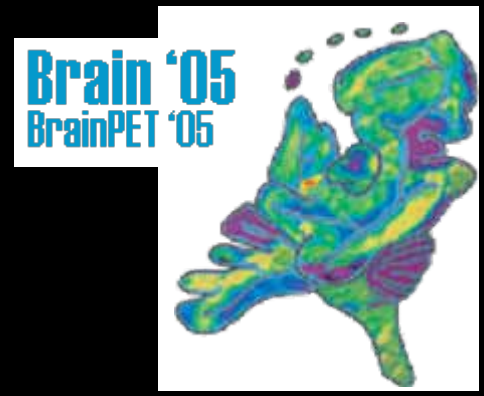
Parametric Imaging of [^{11}C]PIB Studies Using Spectral Analysis

Rainer Hinz[1], Gunnar Blomquist[2], Paul Edison[3], David J. Brooks[1,3]

[1] *Hammersmith Imanet Ltd., London, UK*
[2] *Uppsala Imanet AB,Uppsala, Sweden*
[3] *MRC Clinical Sciences Centre, London, UK*



Hammersmith Imanet | GE Healthcare | Uppsala Imanet

MRC Clinical Sciences Centre

Introduction

- [^{11}C]PIB has previously been shown to be a marker of amyloid deposits in brain of Alzheimer's disease (AD) patients.
- Clinical question: Is a differential diagnosis of early dementia with imaging techniques possible?
- PET study design which is able to reliably distinguish between amyloid load in normal elderly, AD and other types of dementia is required.
- Because of the scattered occurance of focal amyloid deposits in AD, exploratory interrogation of parametric binding images with statistical parametric mapping (SPM) may be more appropriate than an *a priori* defined region-of-interest based analysis.

Focus of this presentation

Comparison between different methods of quantification using arterial plasma input function with a view on the generation of parametric images.

Hammersmith Imanet GE Healthcare Uppsala Imanet
MRC Clinical Sciences Centre

Methods

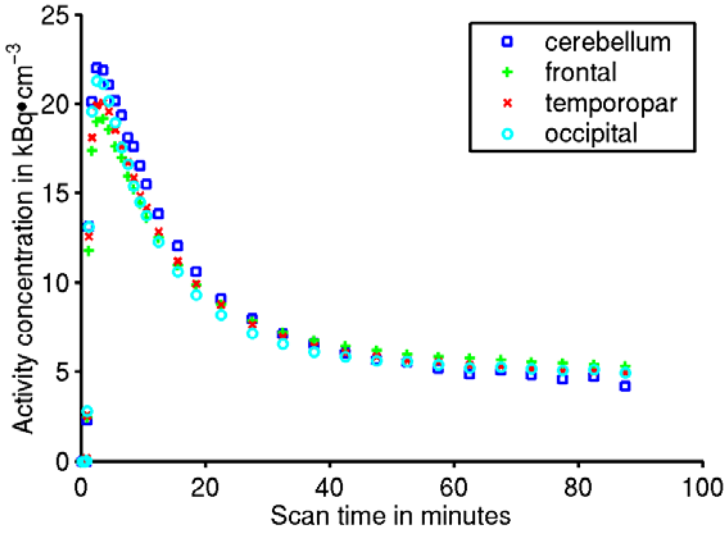
- Intravenous bolus administration of 370 MBq [^{11}C]PIB.
- 3D dynamic PET data acquired for 90 min, ECAT EXACT HR+ scanner.
- Metabolite corrected arterial plasma input function using online blood detector and discrete arterial samples, metabolite analysis on HPLC system.
- Regions of interest (ROIs) were defined on T_1 weighted MR images coregistered with the PET images summed from 10 min to 90 min.
- Graphical analyses of reversible binding (Logan plot) and of irreversible binding (Patlak plot), assuming a fractional blood volume of 5 % and defining the linear part of the plot from 35 min onwards. Outcome measures:
  * the total volume of distribution from the Logan plot: **VD**,
  * the net accumulation rate constant from the Patlak plot: $\mathbf{K_{acc}}$.
- Spectral analysis with functions logarithmically spaced between β_{min}= 0.0008 s^{-1} ($\log_{10}\beta_{min}$= -3.0969) and β_{max}= 0.1 s^{-1} ($\log_{10}\beta_{max}$= -1). From the obtained set of n peaks in the spectra (peak position β_i, peak height α_i), the following expressions were calculated:
  * the impulse response function (corrected for radioactive decay): $\mathbf{IRF(t)} = \sum_{i=1}^{n} \alpha_i \cdot e^{-(\beta_i - \lambda)\cdot t}$
  * the volume of distribution (area under the curve of the IRF): $\mathbf{VD} = \sum_{i=1}^{n-1} \frac{\alpha_i}{\beta_i - \lambda}$ (excluding the blood volume peak).

Hammersmith Imanet GE Healthcare Uppsala Imanet

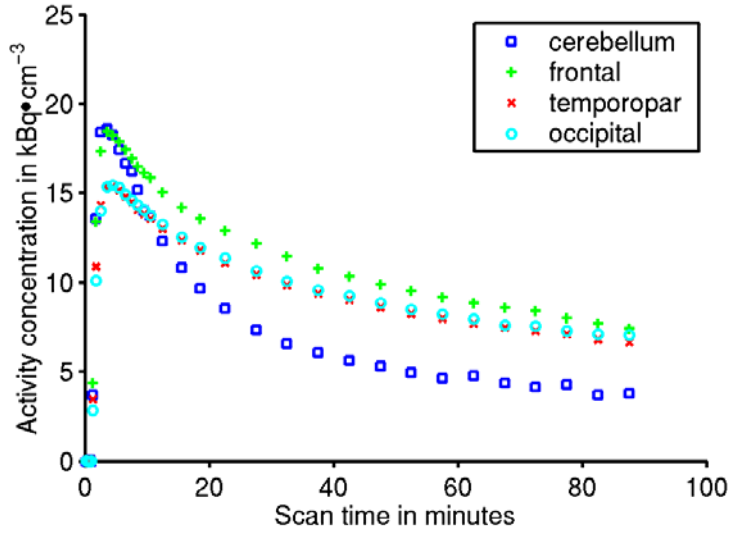
MRC Clinical Sciences Centre

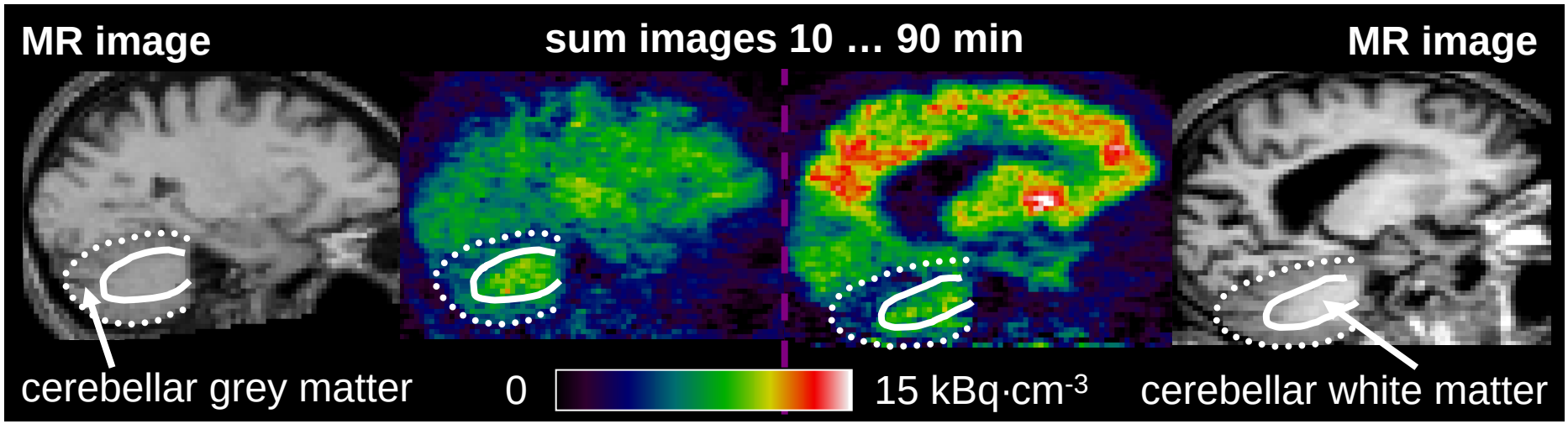
Results: tissue time-activity curves

Control subject



Alzheimer's patient





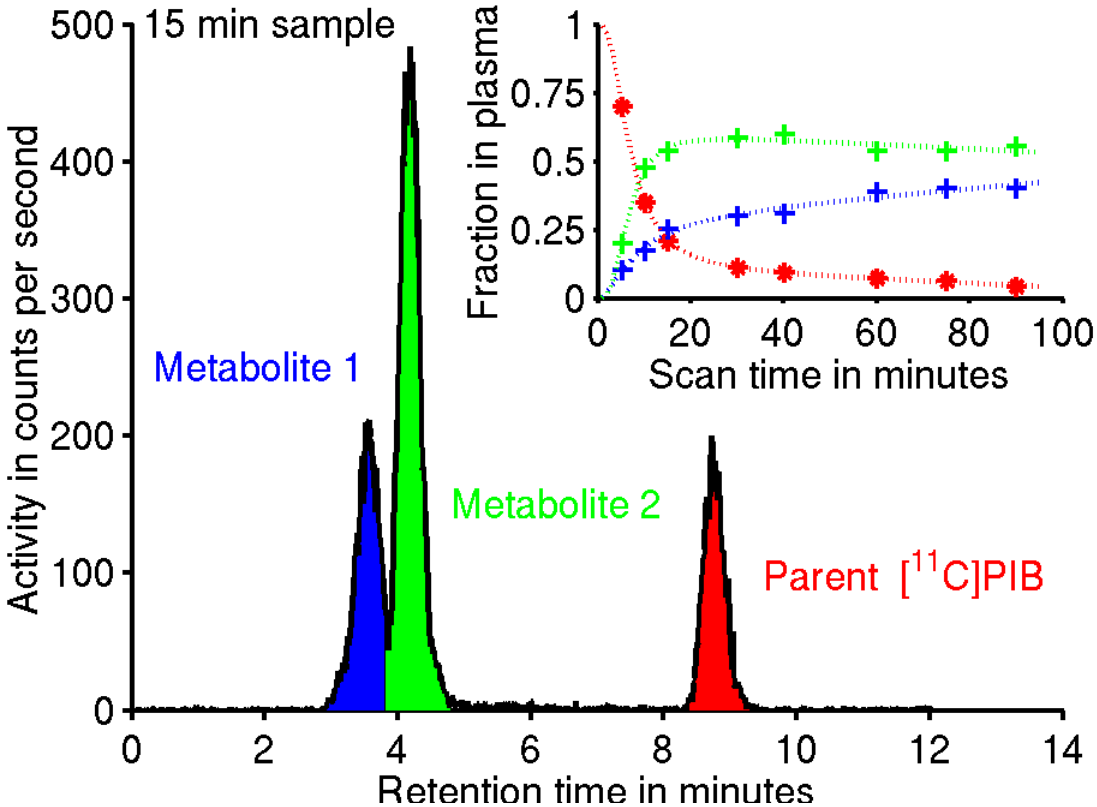
Hammersmith Imanet

GE Healthcare

Uppsala Imanet

MRC Clinical Sciences Centre

Results: plasma input function



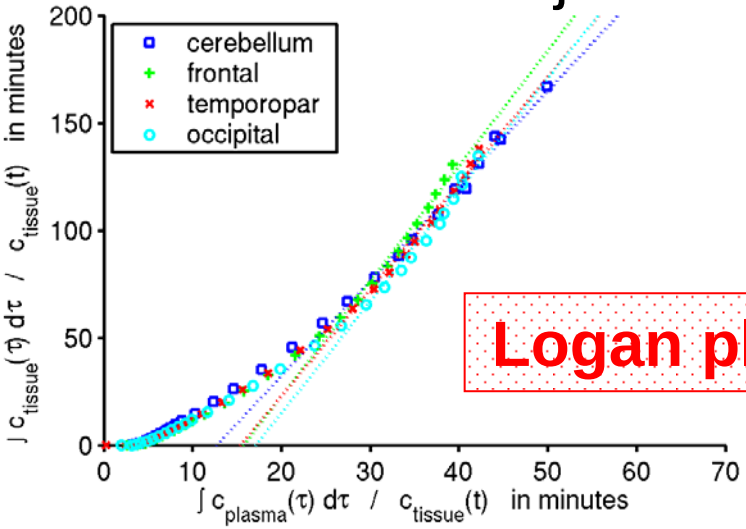
- No lipophilic metabolites were detected in the HPLC trace.
- The two metabolites 1 (blue) and 2 (green) have a considerably shorter retention time on the column than [^{11}C]PIB and overlap partially.
- The parent [^{11}C]PIB (red) is relatively rapidly metabolised.

Hammersmith Imanet GE Healthcare Uppsala Imanet

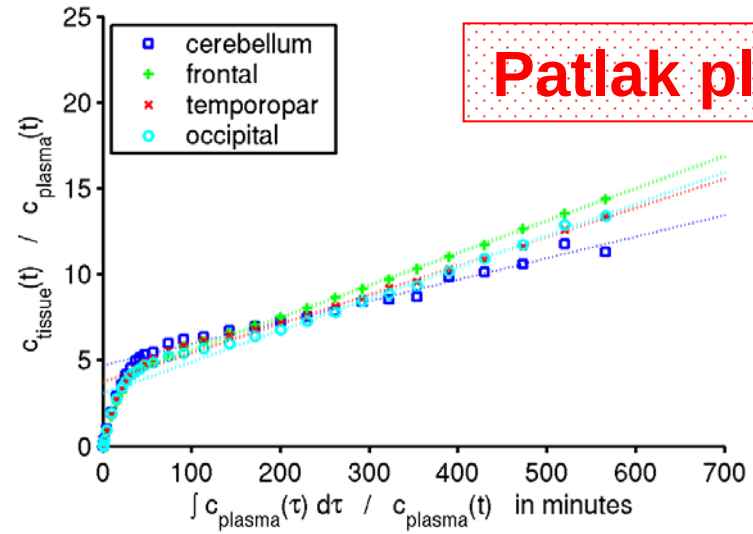
MRC Clinical Sciences Centre

Results: graphical analyses

Control subject

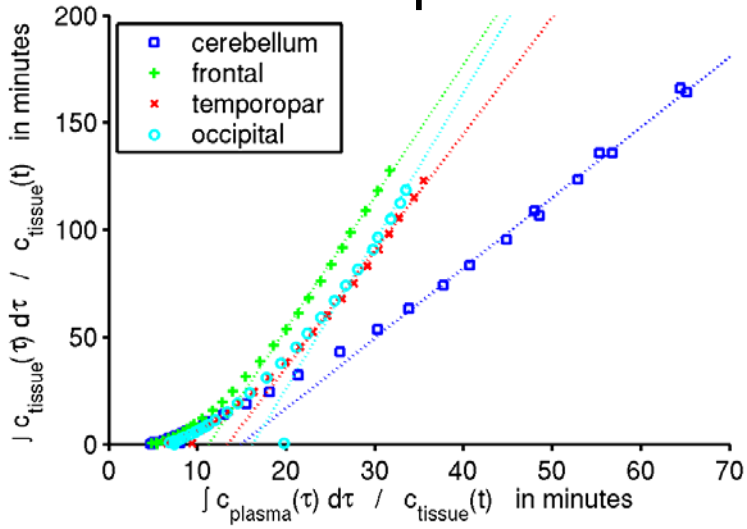


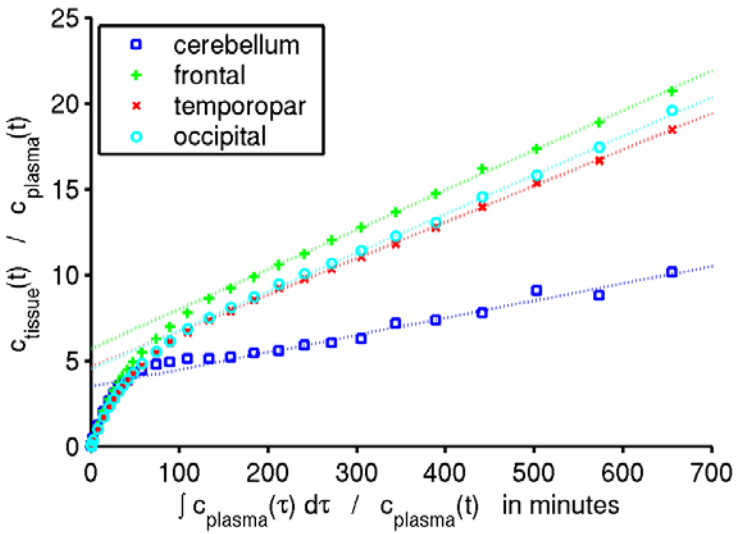
Logan plots



Patlak plots

Alzheimer's patient





Hammersmith Imanet

GE Healthcare

Uppsala Imanet

MRC Clinical Sciences Centre

Results: graphical analyses

	Logan plot				Patlak plot			
Region	control		AD subject		control		AD subject	
para-meter	slope VD	ratio	slope VD	ratio	slope K_{acc}	ratio	slope K_{acc}	ratio
unit	ml·ml^{-1}		ml·ml^{-1}		min^{-1}		min^{-1}	
cerebellum	4.43		3.28		0.0125		0.0100	
frontal	5.35	1.21	6.17	1.88	0.0188	1.50	0.0232	2.32
temporopar	4.95	1.12	5.43	1.66	0.0169	1.35	0.0211	2.11
occipital	5.18	1.17	6.90	2.10	0.0184	1.47	0.0227	2.27
mean		**1.17**		**1.88**		**1.44**		**2.23**

61 % increase

55 % increase

Hammersmith Imanet

GE Healthcare

Uppsala Imanet

MRC Clinical Sciences Centre

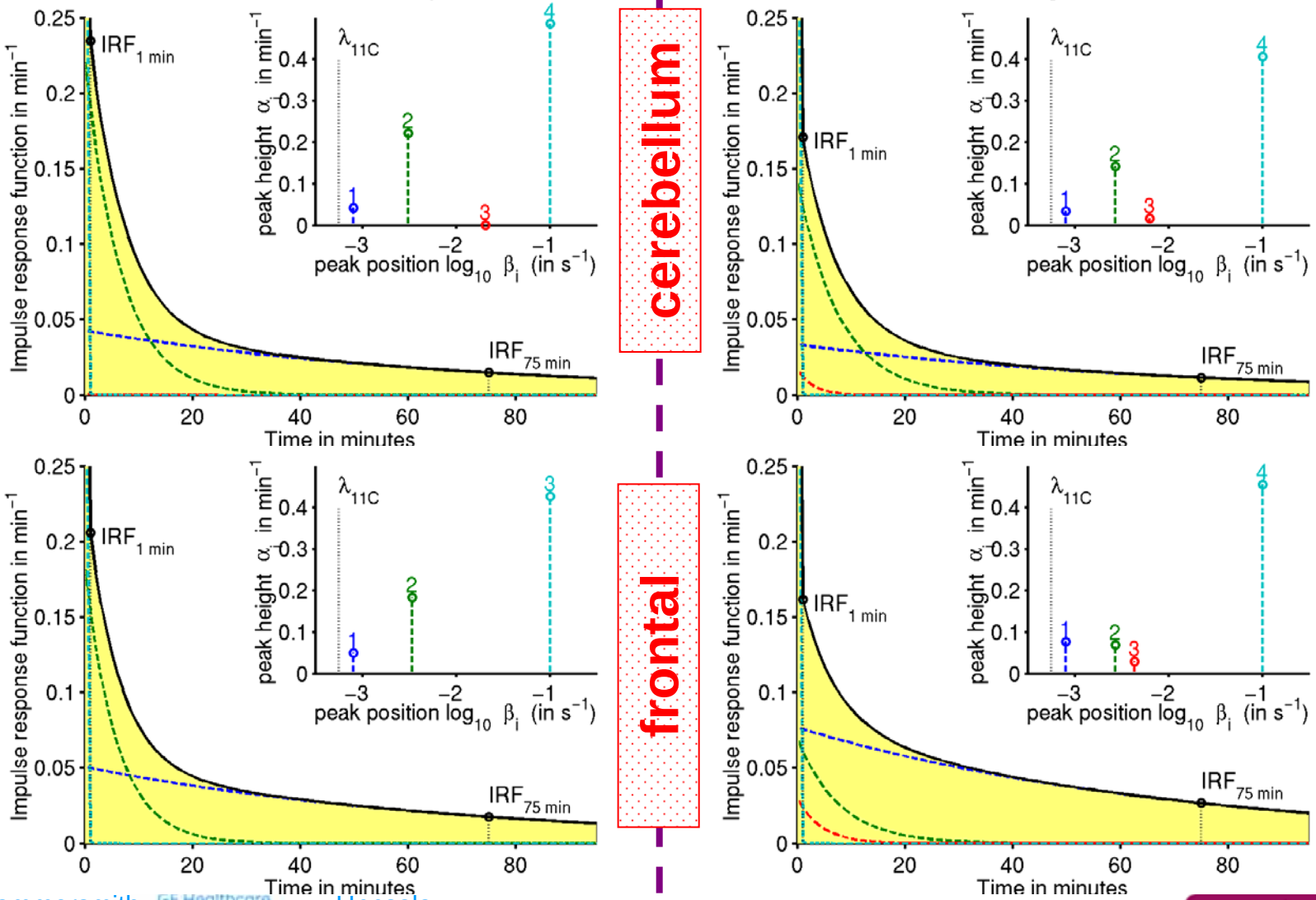
Results: spectral analysis

Control subject

Alzheimer's patient

cerebellum

frontal



Hammersmith Imanet

GE Healthcare

Uppsala Imanet

MRC Clinical Sciences Centre

Results: spectral analysis

	Spectral analysis					
Region	control		AD subject		contr.	AD
para-meter	IRF_{75}	ratio	IRF_{75}	ratio	VD	VD
unit	min^{-1}		min^{-1}		$ml \cdot ml^{-1}$	$ml \cdot ml^{-1}$
cerebellum	0.0150		0.0117		4.53	3.54
frontal	0.0177	1.18	0.0268	2.28	4.70	6.14
temporopar	0.0161	1.08	0.0234	1.99	4.52	5.32
occipital	0.0156	1.04	0.0241	2.06	4.38	5.52
mean		**1.11**		**2.11**		

90 % increase

spectral analysis VDs are in agreement with Logan plot VDs

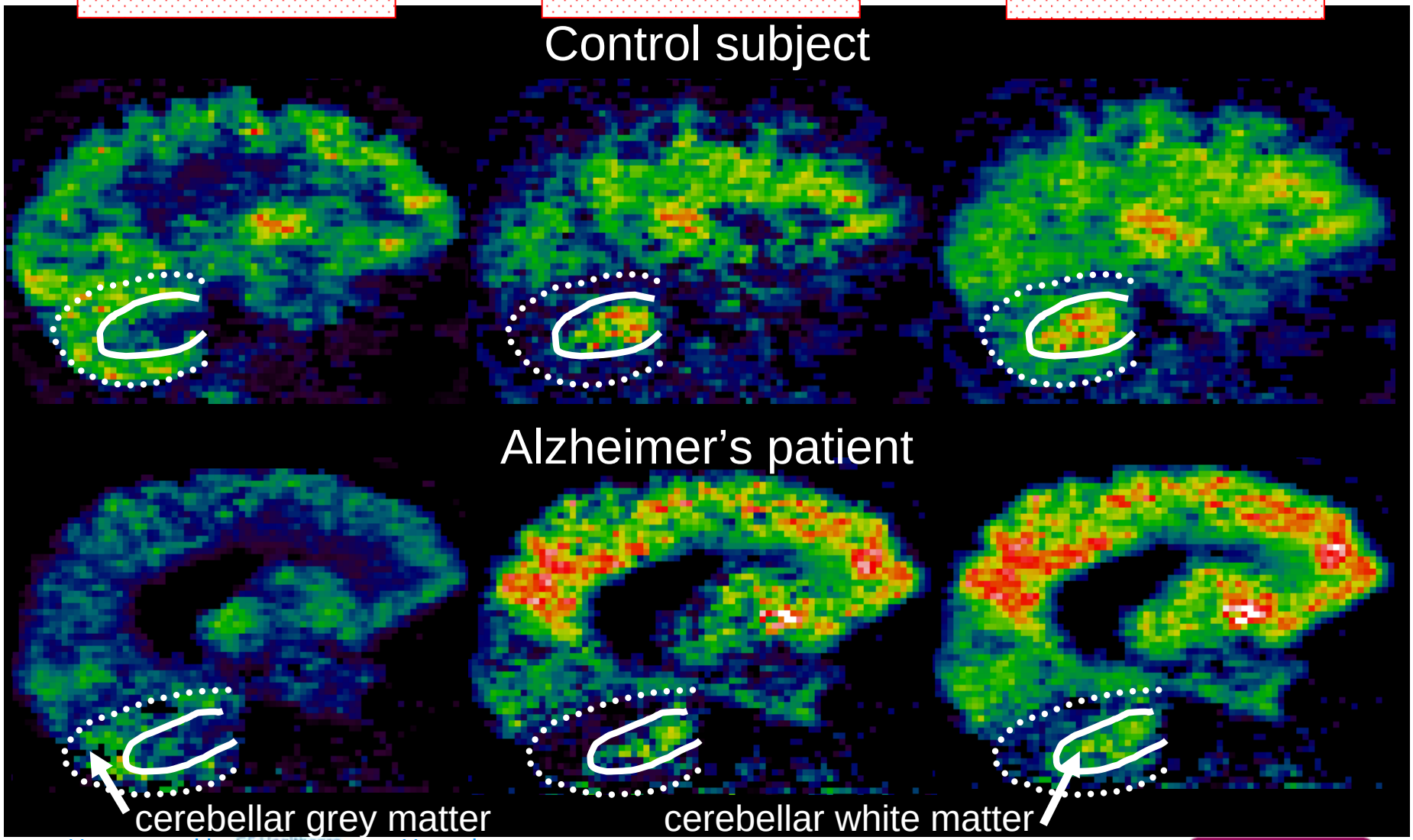
Hammersmith Imanet

GE Healthcare

Uppsala Imanet

MRC Clinical Sciences Centre

Results: parametric images



Hammersmith Imanet

GE Healthcare

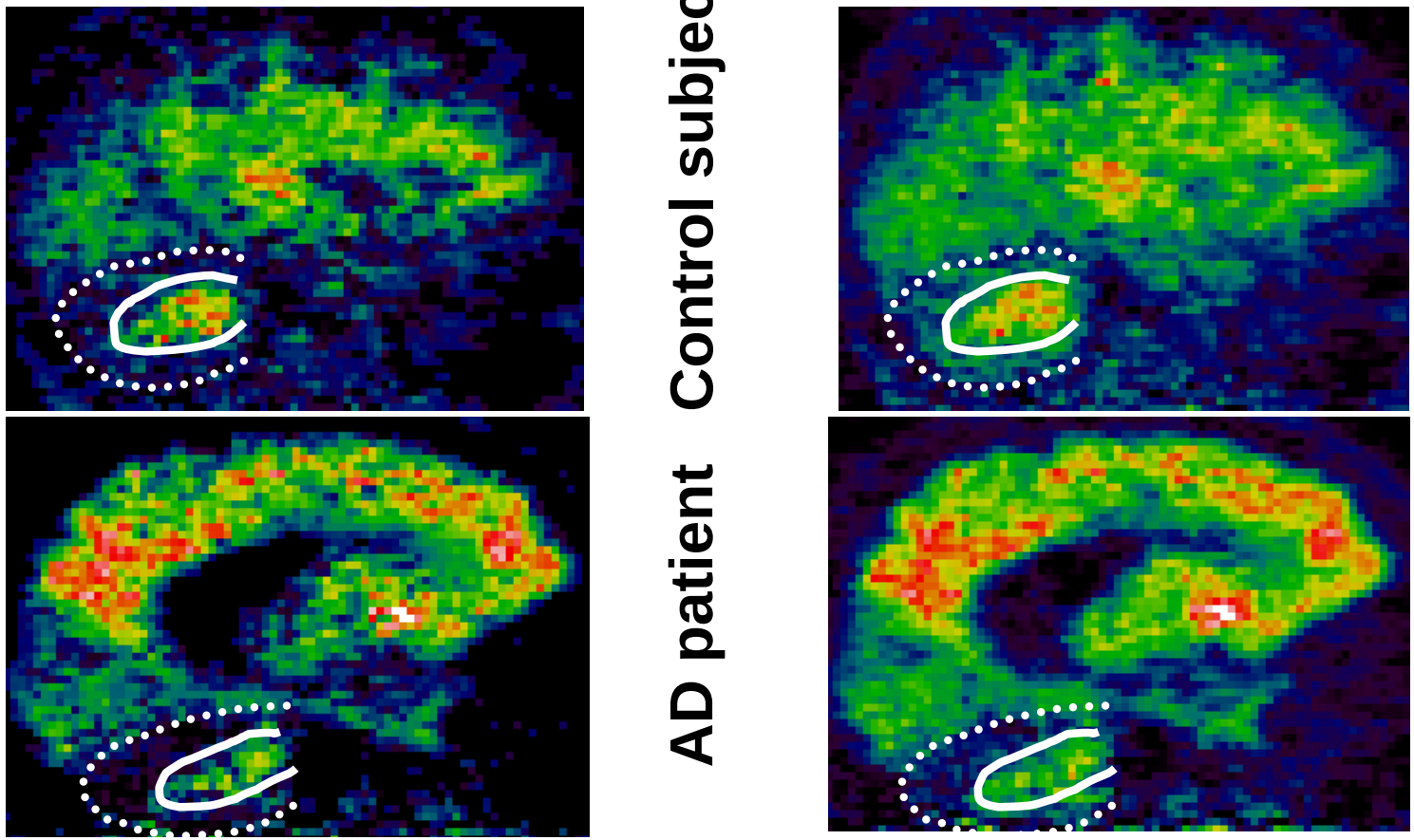
Uppsala Imanet

MRC Clinical Sciences Centre

Results: parametric images

IRF 75 min

$$K_{acc} = \frac{K_1 \cdot k_3}{k_2 + k_3}$$



See poster presentation BP-84: G. Blomquist et al.
“Different patterns of PIB uptake in AD patients.”

Hammersmith Imanet GE Healthcare Uppsala Imanet

MRC Clinical Sciences Centre

Conclusions

- Spectral analysis is a powerful tool for the generation of parametric images from [^{11}C]PIB studies. It separates the tissue response function into the early, blood flow dependent signal component and the later signal component indicative of [^{11}C]PIB retention to amyloid plaques.
- Imaging the IRF at late time produces a higher contrast than the VD image.
- The use of spectral analysis does, however, require the measurement of the plasma input function.
- Further work will include comparisons of reference tissue methods and whether shorter scan times are feasible.