

SATURDAY, JULY 15, 2017
ALZHEIMER'S IMAGING CONSORTIUM
POSTER PRESENTATIONS
IC-P

IC-P-001 STUDIES ON THE USE OF MRI TO DETECT
 β -AMYLOID LOAD IN THE BRAINS OF
5XFAD ALZHEIMER'S MODEL MICE



Brian M. Austen, *St George's University of London, London, United Kingdom. Contact e-mail: sghk200@sgul.ac.uk*

Background: A rapid method capable of detecting early signs of Alzheimer's Disease would revolutionise diagnosis, treatment and outcome of this neurodegenerative disease. **Methods:** We have used the 5XFAD mice model of Alzheimer's Disease developed by Oakley et al (2006) to see if MRI can be used to detect changes. 5XFAD and wild-type mice were imaged in a 4.7 T Varian horizontal-bore MRI system to generate T1 quantitative maps using the spin-echo multi-slice sequence. **Results:** Scanning was followed by immunostaining for GFAP, Iba-1 and beta-amyloid, which showed that amyloidosis developed at 2.5 months in the FAD mouse, and gliosis at 5 months, but not in the wt mice. However, MRI T1 relaxation times were not significantly different to those of age-matched wt mice, indicating that MRI T1 alone would not be a sensitive method of detecting disease initiation or progression (Spencer et al., 2016). In attempts to enhance the MRI response in T1 or T2 node, we synthesised Gd-complexed beta-amyloid-binding contrast agents, comprising peptides from the b-amyloid sequence that were found to have high self-aggregating affinity for b-amyloid itself, covalently linked to DOTA, complexed to an atom of 157 gadolinium; biodistribution of 153 -Gd labelled analogue of the contrast agent was found to preferentially distribute to liver in mice, with very little adsorbed into brain, so focussed ultrasound and reagent co-injection with microbubbles was used to gain an enhance MRI T1 profile in the 5XFAD mice compared to WT mice (Matharu et al. 2015) **Conclusions:** MRI T1 was not sufficient to detect amyloidosis or gliosis in 5XFAD Alzheimer mice models. Uptake of a contrast agent could be a useful method to gain visualisation of beta-amyloid deposits at early stages of Alzheimer's Matharu B, Spencer N, Howe F, and Austen B (2015) Gadolinium-complexed Ab-binding contrast agents for MRI diagnosis of Alzheimer's Disease. *Neuropeptides* 53 <http://dx.doi.org/10.1016/j.npep.2015.07.001> Oakley H, et al (2006) *J Neurosci* 26(40): 10129-10140 Spencer NG, Lovell DP, Elderfield K, Austen B and Howe FA. (2016) Can MRI T1 be used to detect early changes in 5XFAD Alzheimer's mouse brain. *Magn Reson. Mater. Phys* <http://dx.doi.org/10.1007/s10334-016-0593-9>.

IC-P-002 EFFICACY OF [18F]FLUTEMETAMOL
10-MINUTE VERSUS 20-MINUTE
SUMMATION IMAGING METHOD: VISUAL
ASSESSMENT AND QUANTITATIVE
VALIDATION



Caterina Ghetti¹, Maura Scarlattei², Fulvio Lauretani³, **Giorgio Baldari**², Giulio Serreli⁴, Carla Cidda², Livia Ruffini², *Medical Physics Department, University Hospital of Parma, Parma, Italy;* ²*Nuclear Medicine Unit, University Hospital of Parma, Parma, Italy;* ³*Geriatric Rehabilitation Department, University Hospital of Parma, Parma, Italy;* ⁴*Medical Physics, University Hospital of Parma, Parma, Italy.*
Contact e-mail: gbaldari@ao.pr.it

Background: With progressive implementation of amyloid PET imaging in clinical settings, issues regarding elderly pts compliance during scan have been proposed. [18F]flutemetamol (Vizamyl™)

was recently approved to assess β -amyloid neuritic plaque density in cognitively impaired patients. The primary mean of assessing [18F]flutemetamol scans in clinical settings is by visual evaluation, using the late 20-min summation image, displayed using a rainbow colour scale. However, this acquisition time frequently appears too much long for people cognitively compromised. Aim of the study was to compare early 10-min (E-10min) to late 20-min (L-20min) summation images to assess potential use of the E-10min acquisition method in the clinical context. **Methods:** Ten patients with diagnosis of MCI and dementia syndrome, using the new NIA-NIH criteria, were submitted to [18F]flutemetamol PET scan. Neuropsychological battery (abstract reasoning, memory, attention, language, praxis and visuo-perceptive functions), Geriatric Depression Scale and Summary Performance Physical Battery were assessed. Hand-Grip strength was measured by manual dynamometer. All patients underwent brain MRI or CT scan in the previous 3 months. PET scan began 90 minutes after injection of 185 MBq [18F]flutemetamol. using a whole-body hybrid system Discovery IQ (GE Healthcare) operating in 3D detection mode. PET images were visually interpreted by 2 board-certified independent nuclear medicine physicians. To validate visual results, we performed quantitative assessment of [18F]flutemetamol uptake using CortexID Suite (GE Healthcare) software implemented in Advantage GE workstation. CortexID Suite produces a Z-score surface map that highlights areas and degree of beta amyloid tracer uptake. The severity is measured in standard deviations from normal controls. **Results:** Visual assessment didn't change in any patient comparing E-10min vs L-20min independently of the reference region (pons/cerebellum). Quantitative analysis confirm visual assessment conclusion, in fact assessing E-10min vs L-20min with a Pair T test using Bonferroni correction and $p=0.01$, results are not statistically different. This means that, comparing E-10min vs L-20min, we have the same data for all areas of the Cortex ID Suite. **Conclusions:** Our results show that acquisition time may be reduced to 10 min without decreasing diagnostic accuracy in the clinical context. Moreover, quantitative analysis confirm robustness of acquired data for research utilization.

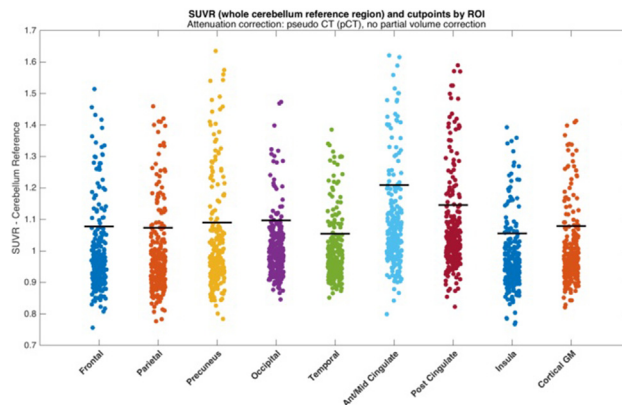
IC-P-003 DETERMINING THE UTILITY OF PMOD
IMAGE QUANTIFICATION SOFTWARE
FOR PROCESSING [11 C]PIB AND [18 F]
FLUTEMETAMOL IMAGES IN A PET-ONLY
PIPELINE TO GENERATE SUVR FOR
QUANTIFICATION ON THE CENTILOID
SCALE



Mark R. Battle¹, Chris J. Buckley¹, Adrian Smith¹, Val Lowe², ¹*GE Healthcare, Amersham, United Kingdom;* ²*Mayo Clinic College of Medicine, Rochester, MN, USA. Contact e-mail: mark.battle@ge.com*

Background: Utilising a standardised quantitative imaging analysis scale, Centiloid, for comparing β -amyloid imaging tracers in Alzheimer's disease (AD) has been promoted by the Global Alzheimer's Association Information Network (GAAIN), with established process pipelines reported (Rowe et al., 2016). We previously reported data confirming Centiloid pipeline implementation in PMOD Image Quantification Software produced results highly concordant with the GAAIN data. However, these pipelines require both PET and MRI images for processing. MRIs were not obtained for end-of-life subjects in GE Healthcare's pivotal registration studies for [18 F]Flutemetamol Injection. Therefore, for these subjects we evaluated the utility of PMOD for application in PET-only image analysis. **Methods:**

Using Centiloid Volume of Interest (VOI) regions, GAAIN [¹¹C] PiB images (YC-0, n=34; AD-100, n=45) were processed using a PET-only method. Standard Uptake Value ratios (SUVr's) and Centiloid values for the VOI regions were calculated, and compared with published values by way of validation (Klunk et al., 2015). The utility of PMOD's PET-only method was assessed by cross-compared to the PET/MRI method using the Centiloid standard CTX VOI. Subsequently, subjects from GE Healthcare's pivotal autopsy studies were evaluated using PMOD's PET-only method. Tissue-based autopsy measures were used in a Receiver Operating Characteristic (ROC) curve analysis to estimate the Centiloid value corresponding to boundaries used in CERAD pathology assessments in regards to AD classification. **Results:** For all subjects, we found the [¹¹C]PiB SUVr values were within recommended limits of the published set for the key reference region (whole cerebellum). When converted to Centiloid values, there was a high degree of correlation between the GAAIN data and values derived from PMOD. PET-only processing was applied to the autopsy-cohort [¹⁸F]flutemetamol images. Centiloid values were compared to the tissue based neuritic plaque assessments. ROC analysis determined the CERAD designation boundary's in Centiloid units. **Conclusions:** PET-only image processing, such as the one established using PMOD, provide an alternate method of Centiloid processing, and is suitable for assessing subjects without MRI. The SUVr and Centiloid values obtained from our autopsy cohort proved suitable for determining the CERAD pathological boundaries in Centiloids equivalent units, indicating that [¹⁸F]flutemetamol Centiloid values can be related to CERAD style stratification.



Andrew Wong¹⁰, Marcus Richards¹⁰, Nick C. Fox⁵, Sebastien Ourselin^{5,11}, Jonathan M. Schott¹, ¹Dementia Research Centre, Institute of Neurology, University College London, London, United Kingdom; ²Translational Imaging Group, Centre for Medical Image Computing, Department of Medical Physics and Biomedical Engineering, UCL, London, United Kingdom; ³Institute of Nuclear Medicine, UCL, London, United Kingdom; ⁴Translational Imaging Group, UCL Centre for Medical Image Computing, London, United Kingdom; ⁵UCL Institute of Neurology, London, United Kingdom; ⁶UCL Institute of Nuclear Medicine, London, United Kingdom; ⁷Neuroradiological Academic Unit, Department of Brain Repair and Rehabilitation, UCL Institute of Neurology, London, United Kingdom; ⁸Translational Imaging Group, Centre for Medical Image Computing, University College London, London, United Kingdom; ⁹CNR-MAJ / Rouen University Hospital, Rouen, France; ¹⁰MRC Unit for Lifelong Health and Ageing at UCL, London, United Kingdom; ¹¹Centre for Medical Image Computing, University College London, London, United Kingdom. Contact e-mail: d.cash@ucl.ac.uk

IC-P-004 A COMPARISON OF TECHNIQUES FOR QUANTIFYING AMYLOID BURDEN ON A COMBINED PET/MR SCANNER



David M. Cash¹, Ninon Burgos², Marc Modat², John Dickson³, Daniel Beasley², Pawel Markiewicz⁴, Christopher A. Lane⁵, Thomas Parker⁵, Anna Barnes⁶, David L. Thomas⁷, M. Jorge Cardoso⁸, Ian B. Malone⁵, Thomas Veale⁵, David Wallon⁹, Jana Klimova⁵, Kjell Erlandsson⁶,

Background: Amyloid-specific PET tracers provide quantitative measurements for determining amyloid load in vivo. Many cutpoints have been proposed to define amyloid positivity; those based on post-mortem pathology are highly specific, but may

Table
Mean cortical GM SUVr results, showing the mean and standard deviations of the two groups based on the defined cutpoints (99% of amyloid negative cluster). UTE=Ultrashort echo time method, the vendor-supplied method for attenuation correction. pCT=pseudo CT, the in-house method for attenuation correction that builds a synthetic CT image. PVC=Partial Volume Correction, performed using the Iterative Yang approach with a full-width half-maximum kernel of 6.8 mm and 10 iterations (Erlandsson, Phys. Med. Biol., 57(21): R119-159, 2012)

Reference ROI	Method	Amyloid Negative Mean (SD)	Amyloid Positive Mean (SD)	Cutpoint	% Amyloid Positive
Whole Cerebellum	pCT, no PVC	0.959 (0.053)	1.218 (0.100)	1.080	17.5%
	UTE, no PVC	0.996 (0.054)	1.255 (0.106)	1.120	18.5%
	pCT, with PVC	0.759 (0.059)	1.129 (0.183)	0.899	23.3%
	UTE, with PVC	0.784 (0.063)	1.153 (0.190)	0.917	24.5%
Cerebellar Grey Matter	pCT, no PVC	1.103 (0.077)	1.424 (0.113)	1.275	15.4%
	UTE, no PVC	1.156 (0.077)	1.485 (0.113)	1.326	14.7%
	pCT, with PVC	1.019 (0.109)	1.581 (0.267)	1.253	20.4%
	UTE, with PVC	1.053 (0.106)	1.574 (0.269)	1.260	24.1%
Pons	pCT, no PVC	0.575 (0.040)	0.754 (0.066)	0.664	15.8%
	UTE, no PVC	0.557 (0.037)	0.729 (0.058)	0.641	17.6%
	pCT, with PVC	0.462 (0.049)	0.729 (0.118)	0.574	18.8%
	UTE, with PVC	0.446 (0.046)	0.704 (0.105)	0.557	20.1%
Subcortical White Matter	pCT, no PVC	0.541 (0.036)	0.688 (0.053)	0.621	17.5%
	UTE, no PVC	0.535 (0.035)	0.677 (0.049)	0.611	16.8%
	pCT, with PVC	0.444 (0.055)	0.705 (0.105)	0.565	17.8%
	UTE, with PVC	0.443 (0.050)	0.739 (0.150)	0.558	19.5%