tissue-activity curves (TACs) generated for 29 brain regions (anatomically defined via MRI co-registration). Model-based receptor parameters used were the total distribution volume (V_T) and the distribution volume ratio (DVR) (reference: posterior corpus callosum). In addition the standardized uptake value ratio (SUVR) (50-70 min) as approximation of the DVR and the tissue-to-plasma concentration ratio (TTPR) (70-90 min) as approximation of V_T were used as non model-based receptor parameters.

Results: TACs of all 29 regions could be described adequately with the 1TCM and all kinetic parameters could be reliably estimated from 90 min PET data. V_T increased as expected with receptor density: corpus callosum (V_T: 5.68 ± 1.01), frontal cortex (9.18 ± 0.59), parietal cortex (9.10 ± 0.61), pons (11.10 ± 0.86), thalamus (25.03 ± 3.33). Mean TTPR values in frontal and parietal cortices were 2% higher than the corresponding V_T values but 7% lower in the thalamus. There was a strong linear correlation between the two sets of TTPR and V_T values ($r^2 = 0.98$, $p < 10^{-4}$) (Figure 1A). As V_T, DVR increased with receptor density. Frontal cortex (DVR: 1.66 ± 0.27), parietal cortex (1.64 ± 0.27), pons (2.01 ± 0.35), thalamus (4.52 ± 0.87). Mean SUVR values in frontal and parietal cortices were almost identical to mean DVR values (difference $< 0.1\%$) but $\sim 15\%$ lower in the

thalamus. Accordingly there was a strong linear correlation between the SUVR and DVR values ($r^2 = 0.97$, $p < 10^{-4}$) (Figure 1B).

Conclusions: For (-)-[^{18}F]-Flubatine the receptor parameters TTPR and SUVR in cortical regions are in excellent agreement with corresponding parameters computed by full kinetic modeling. For unbiased estimates of TTPR and SUVR in the thalamus the use of a bolus/infusion scheme for tracer application should be considered.

References

1. O Sabri, P Brust. Acetylcholine receptors in dementia and mild cognitive impairment. *Eur J Nucl Med Mol Imaging* 2008; 35(Suppl. 1):30-45.
2. K Kendziorra, O Sabri. Decreased cerebral α4ß2 nicotinic acetylcholine receptors in living patients with mild cognitive impairment and Alzheimer's disease assessed with positron emission tomography. Eur *J Nucl Med Mol Imaging* 2010; 38: 515-525.
3. P Brust, O Sabri. *In-vivo* measurement of nicotinic acetylcholine receptors with [^{18}F]norchloro-fluoro-homoepibatidine (NCFHEB). *Synapse* 2008; 62:205-218.

P150.   Development and validation of an integrative software for automatic MRI and [^{11}C]PiB dynamic PET image processing and parametric Imaging

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Background: Functional Positron Emission Tomography (PET) imaging is usually combined with high resolution Magnetic Resonance Imaging (MRI) in order to relate functional measures to anatomical structures. In light of emergent PET-MR imaging technology, it is important to use a combination of structural and functional images to obtain meaningful insight. Current image processing and analysis software for MRI and PET are separate and some steps are manual or semi-automatic. This practice places limitations on the size of studies and raises concerns over errors caused by rater variability. This paper describes the development of an automated pipeline of [^{11}C]PiB image processing integrating fully-automatic MR image processing tools with in-house PET image processing and kinetic modeling procedures.

Methods: The software was developed using Java Image Science Toolkit (JIST), a modular and cross-platform framework [1] developed for the Medical Image Processing, Analysis and Visualization (MIPAV) program [2]. The image processing involves the use of [^{11}C]PiB dynamic PET images and concurrent MR images collected for the same subject. The MR images underwent a skull stripping step using a brain extraction algorithm called SPECTRE [3]. These were then segmented using a topology preserving anatomy driven algorithm TOADS [4] to obtain the grey matter cerebellum (GM-CB) membership which was thresholded at 85% to avoid partial

volumes. The GM-CB region masks were binarized and co-registered to the dynamic mean of the PET data and used as the reference region for normalizing the [^{11}C]PiB retention in the whole brain. The time activity curves (TAC) obtained for the reference region were used as input to a parametric model [5] and distribution volume ratio (DVR) and R1 images were produced.

Results: The resulting parametric images and histograms from both automatic and manual methods are comparable to one another. The manual delineation produces a very limited number of slices of the reference region when compared to the automated process, which encompasses the entire reference region. The TAC for both the manual and automated process are noted to be similar. An additional reference region for the whole cerebellum (WCB) is also included, highlighting the ease of adding a new ROI.

Conclusions: The automated process allows the possibility to use different reference tissue regions and also for switching out parametric models. The dynamic range of the [^{11}C]PiB images can also be adjusted based on the timing of the study. The pipeline allows us to readily test different modifications in a repeatable and reliable manner. The modular nature of this process pipeline expands the opportunities to explore different multi-modal imaging techniques.

Figure Time Activity Curve for GM-CB mask (manual, auto) and WCB (auto).

References

[1] Lucas BC et al. *Neuroinformatics* 8:5-17 (2010).
[2] McAuliffe MJ et al. *IEEE-CBMS* 381-386 (2001).
[3] Carass A et al. *4th IEEE ISBI* 656–659 (2007).
[4] Bazin PL, Pham DL. *J Cogn Neurosci* 19:1498–1507 (2007).
[5] Zhou Y et al. *Neuroimage* 18:975-989 (2003).

P151. Kinetic modeling without a reference region

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Background: The two-tissue compartmental model is commonly used to describe the kinetic behavior of radiotracers in neuroreceptor mapping applications. Estimation of BP_F for each region of interest (ROI) or voxel generally requires estimating the four rate parameters using standard nonlinear regression techniques applied to each region's observed time-activity curve. However, these four rate parameters are not always identifiable and "direct" estimation of BP_F ($BP_F = K_1 k_3/(k_2 k_4 f_P)$) can be unstable. This can be overcome if it is possible to identify a "reference region", i.e., a region devoid of the receptor of interest. This can be done by estimating K_1 and k_2 for the reference region using a one-tissue model, then fitting each ROI/voxel separately using a two-tissue model while constraining the ratio K_1/k_2 to match the estimated K_1/k_2 ratio of the reference region. This reduces from four to three the number of free parameters that must be estimated for each ROI/voxel, and can greatly increase the stability of the estimation of BP_F. However for some radiotracers there is no true reference region, i.e., every region has at least some level of specific binding. In such a situation,
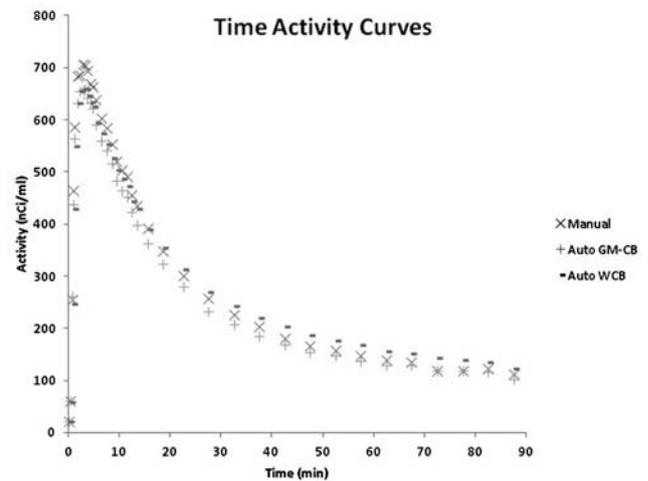
applying the constrained estimation procedure outlined above will result in biased estimation of BP_F for every region.

Methods: Even without a true reference region, if nondisplaceable binding is constant throughout the brain [3], it is possible to estimate BP_F for all regions by fitting multiple time-activity curves simultaneously. This can be accomplished by constraining K_1/k_2 to be the same for all regions and estimating the three other kinetic parameters specific to each ROI. In particular, the objective function is the (weighted) sum of squared residuals, summing across time and across regions, giving $3R + 1$ free parameters when applied to R regions. This greatly increases the dimensionality of the parameter space and thus the computational complexity required for optimization. Since standard nonlinear regression techniques will not be adequate, we instead must consider algorithms for estimation in high-dimensional parameter spaces such as simulated annealing. We take an approach similar to [1, 2], who applied simulating annealing to estimate an arterial input function, but simpler, since when the input function is observed, there is only one shared parameter. We note that the