

infusion of tracer. Our simulations indicate that changing the tracer administration from a bolus to 30-second infusion results in a K1 bias reduction from 118% to 6%. The COV was reduced from 63% to 37.2%. This investigation demonstrates that sampling requirements must be optimized when planning a dynamic PET study.

No. 241

A METHOD FOR CORRECTING MYOCARDIUM TO BLOOD POOL SPILLOVER IN DYNAMIC CARDIAC PET FDG STUDIES
K.P. Lin, S.C. Huang, Y. Choi, R. Brunken, H. Schelbert, M. Phelps, Division of Nuclear Medicine, UCLA School of Medicine, CA

In dynamic cardiac PET FDG studies for measurement of myocardial metabolic rate of glucose (MMRGlc), the plasma FDG time activity curve (input function) is commonly obtained from the left ventricular (LV) region on the PET images. The input function is contaminated by the spillover of radioactivity in the surrounding myocardium and could cause significant error in the estimated MMRGlc. In this study, we have developed and investigated a method to correct this spillover of activity from the myocardium to LV blood pool. The method is based on a reformulation of the FDG model equation in terms of the spillover contaminated input function that included both the myocardium to blood pool and blood pool to myocardium spillover fractions as variable parameters (F_{bm} and F_{mb}). The reformulated model equation can be used to fit the global myocardial tissue activity curve to estimate F_{mb} and thus the uncontaminated input function.

The effectiveness of the method was evaluated using computer simulated data and human cardiac PET FDG data. In the computer simulation, the values of 0.10 and 0.25 were used for F_{bm} and F_{mb}, respectively. Various noise levels in the input function and tissue curve were simulated. Results from the simulation study show that F_{mb} could not be determined reliably from fitting the tissue curve alone, but if the true input function at 40 to 60 minute were included in the fitting, the estimated F_{mb} was found to be accurate (< 4.3% error) and the resulted input function had an average error of less than 0.5% for 12% noise level in the input function. The MMRGlc estimate with the corrected input function was within 97% of the true value (compared to 15% error for estimation using uncorrected input function). Dynamic PET FDG data were obtained in four normal volunteers and blood samples were obtained during the study. After applying the method, the corrected input function agreed well with those obtained directly from the blood samples. The F_{mb} was 0.05±0.03. As compared to the results with uncorrected input function, the estimates of MMRGlc was changed by 20±6% and that of k₄ by 47±20%.

In conclusion, the method is effective in correcting the F_{mb} spillover and lead to improved estimates of MMRGlc. The method also has the potential to allow larger region of interest be drawn over the LV in dynamic PET images to reduce the noise level in the input function.

No. 242

NEW ANALYSIS APPROACH FOR QUANTIFICATION OF MYOCARDIAL PERFUSION WITH PET USING CORRECTION FOR PATIENT MOTION AND AUTOMATED REGION DEFINITION
O. Muzik, R. Beanlands, M. Schwalger, E. Wolfe, G. Hutchins, University of Michigan, Ann Arbor, MI.

Dynamic PET imaging requires an integrated analysis approach, rapid data processing and correction of possible patient motion which may limit kinetic data analysis. The purpose of this study was to develop an algorithm, which includes correction for patient motion, an automated definition of multiple (96-120) regional myocardial time-activity curves and the application of a 3-compartment model to quantify myocardial blood flow. Using a SUN workstation, the multi-plane image data set was resliced in the short-axis view. In order to improve count statistics for the motion correction, image data were summed in the spatial (3 adjacent mid-ventricular planes) and the temporal (4x30s in first 2min) domain. The resulting dynamic sequence was filtered (1, median, 2, sobel, 3x3 filter) to sharply enhance the epicardial and endocardial edge information, from which x/y-offset factors were derived and subsequently applied to the original image sequence, thereby correcting for motion by in-plane translation. For the definition of time-activity curves twelve sectors per plane were automatically positioned based on averaged radial activity profiles. A threshold point at the inner profile flank was defined where the activity level reached a certain percentage of maximal activity. The radial borders of the sectors were then generated by preserving a constant inner and outer distance to this point. The effects of resolution distortions were accounted for by optimizing the radial position and width of individual sectors based on our previous studies (ROI blood volume fraction of 50-70%). Using this approach in 6 normal subjects, myocardial blood flow (ml/min/g) was 0.70±0.17 at rest and 3.24±0.85 after pharmacological vasodilation (coronary reserve=4.63±0.62). Homogeneity throughout individual polar maps as measured by relative dispersion (=SD/mean) significantly improved after application of motion correction and optimal sector definition from 22.3±13.2 to 17.6±6.8% (p<0.05).

This study demonstrates the importance of patient motion correction and automated definition of regions for the noninvasive quantification of myocardial blood flow in routine clinical studies.

No. 243

EFFECT OF INSTRUMENTAL ERRORS ON THE *IN VIVO* MEASUREMENT OF RECEPTOR CONCENTRATION IN THE HEART USING PET. B. Bendriem, J. Delforge, V. Frouin and A. Syrota. *Service Hosp. F. Joliot, C.E.A., Orsay, France.*

With the appropriate ligand, experimental protocol and mathematical model, it is possible, using Positron Emission Tomography (PET), to measure receptor concentration (B_{max}) in the heart (Delforge, 1990). In order to use this physiological parameter as a reliable index, one needs to assess its precision. We have characterized the precision of B_{max} estimates using simulated and experimental data obtained from the distribution of C11-MQNB in the dog heart. Effects of statistical fluctuations and systematic errors due to the limitations of the quantification of PET images have been analyzed.

Using the covariance matrix, which under certain conditions can reflect noise propagation in parameter estimation, it has been found that a 1% random error on PET data will translate in a 4% error on the value of B_{max}. This error can be reduced to 2% if the experimental protocol is complexified by multiple injections (thus providing more information). The effect of inaccurate measurements of the ligand concentration in tissue elements (which can be due to an incorrect value of the specific activity of the labeled ligand, inadequate PET data calibration or partial volume effect) has been simulated by multiplying the time activity curve by a constant. It has been verified that the estimation of B_{max} is multiplied by the same constant whereas K_{on} is divided by the latter. Thus the product K_{on}·B_{max} remains unchanged.

Another source of errors comes from the spill-over effect between the LV cavity and the myocardium, which modifies the shape of the myocardial time activity curve. In heart studies, this can be corrected for by estimating (rather than imposing) a vascular fraction (F_v) from the PET data. We have found that neglecting F_v will prevent the model from properly fitting the data and that a 5% error in the estimation of F_v will modify the estimated B_{max} value by 10%.

Neurology Basic II: Neuroreceptor Studies

3:30-5:00

Session 42

Room 503

No. 244

TRACER KINETIC ANALYSIS OF [C-11]N-METHYL-4-PIPERIDYL BENZILATE BINDING TO MUSCARINIC CHOLINERGIC RECEPTORS.
R.A. Koeppe, K.A. Frey, J.A. Zubieta, J.A. Fessler, G.K. Mulholland, M.R. Kilbourn, T.J. Mangner, D.E. Kuhl. Division of Nuclear Medicine, University of Michigan, Ann Arbor, MI

[C-11]N-methyl-4-piperidyl benzilate (NMPB) was examined as a new ligand for assessing muscarinic cholinergic receptor density. Previous PET studies of the muscarinic system in our laboratory have used [C-11]scopolamine and [C-11]tropanyl benzilate (TRB) with limited success due to high rates of binding relative to transport (k₃>k₁,k₂) and to low rates of dissociation (k₄). Thus, differences between regions of high receptor density cannot be detected reliably due to the flow-limited conditions, particularly for scopolamine. We have attempted to find a ligand with a lower ratio of binding to transport rates and a higher dissociation rate in order to be less flow limited and approach equilibrium more rapidly.

Five normal volunteers were studied following administration of 20-25 mCi NMPB. Dynamic data were acquired for 110 min and arterial samples were drawn and corrected for radiolabeled metabolites. Data were analyzed using models with 2 or 3 compartments. 2-compartment analysis yielded functional images of transport rate (K1) and receptor distribution volume (DV), while 3-compartment analysis provided an estimates of the binding rate, k₃.

Results show NMPB to have brain uptake rates over 4 times higher than scopolamine and 2.5 times higher than TRB. K1 values ranged from 0.38 ml/g/min in the cerebellum and pons to 0.46 in the occipital cortex and putamen. Coefficients of variation ranged from 7-14% across regions. Receptor DV values, using a 2-compartment model, ranged from 9.0±1.4 ml/g in the cerebellum to 69±15 in the basal ganglia, with intermediate values for pons, thalamus, and cortex (parietal) of 25±8, 41±9, and 57±10, respectively. Values for the binding parameter, k₃, using a constrained 3-compartment model, ranged from <0.1 min⁻¹ in the cerebellum to >1.0 in the basal ganglia. The quality of images for either DV or k₃ is superior to those produced with TRB. In conclusion, NMPB appears to be superior to our previous ligands for imaging and quantifying muscarinic cholinergic receptors in the human brain.