Simplified Calculation of MRglcUsing PET

TO THE EDITOR: Measurement of metabolic rates for glucose (MRglc) in the brain and other organs using PET and [^{18}F]2-fluoro-2-deoxy-D-glucose (FDG) has diagnostic value in monitoring the effects of therapy, for example, in oncology (*1*) and in basic research on brain function (*2–4*). Some applications do not require absolute quantification since relative values of MRglc are sufficient. Quantification is essential, however, for comparisons between repeated measurements (*5*) or between results from different laboratories. The standard technique for quantifying MRglc, as described by Sokoloff et al. (*6*) and Huang et al. (*7*), requires many samples of arterial plasma.

On the basis of plasma curves from 119 PET acquisitions in human subjects administered FDG, we showed high correlation between the concentration of radiotracer in arterial plasma at a fixed time and values of the plasma integrals $C_1(T)$ and $C_2(T)$, where T is the time of measurement of radioactivity in tissue, C_1 is the concentration of radioactivity in the compartment directly coupled to plasma and governed by facilitated transport of the radiotracer in tissue and C_2 is the concentration in the compartment containing labeled phosphorylated metabolite (2-[^{18}F]fluoro-2-deoxy-D-glucose-6-phosphate) (*8*). This correlation implies that any technique that uses a single estimate of the concentration of radiotracer in arterial plasma to calculate MRglc could show some degree of agreement with values of MRglc calculated using the conventional technique. During the past few years, several methods for simplifying the measurement of MRglc using PET and FDG have been introduced (*8–12*). These procedures, which require either only one sample or none at all, produce MRglc values that are, as our results predict, highly correlated with those obtained using conventional techniques.

The problem with analyses based on a single sample or a fixed plasma curve shape, however, is that they ignore variances that could come from one of several sources, including standard deviations of up to 10% in the concentrations of glucose and FDG in plasma. Thus, a method that uses only one sample will produce results that vary from those of the full numeric integral by 5–10% because of statistical noise alone. In addition, systematic errors (e.g., due to differences in rates of clearance of radiotracer from the body) can affect comparisons between subjects and between repeated measures on the same subject. Methods that assume a fixed clearance, rather than allowing the shape of the plasma curve to vary between assays, ignore this type of error. We observed a range of differences of ±10% when we compared two calculations using a single scan method: those calculations obtained using a full, numerically integrated plasma curve and those obtained using a fixed function fitted to one sample of plasma. In contrast, the difference is less than 3% when a variable curve shape is used (*8*). Similarly, Hunter et al. (*11*) obtained a mean percentage difference of nearly 16% (range = −60% to +10%) between values of MRglc obtained using dynamic, rather than static, analysis with a full blood curve and those calculated using a simplified kinetic model in static PET analysis. Thus, their data supports our observations of a difference of about ±10% between values obtained using methods that rely on a fixed curve shape (as do all techniques based on zero or one sample and most two sample methods) whether the shape is derived from a population-averaged curve, a mathematical model, or an ad hoc parameterization.

The reported success of the various methods of calculating MRglc shows that a canonical form for the input function is likely to be a very useful tool. Selection of the method must be guided by the precision required. If precision on the order of 10% is acceptable (e.g., for diagnosis of tumors), any one of several methods, based on a single sample of plasma, is likely to provide acceptable accuracy and precision. If greater precision is needed, at least 6–10 samples of plasma and a model that can account for differing rates of radiotracer clearance are required. In particular, for research studies where quantification is important, a multiple-sample technique is recommended.

REFERENCES

1. Di Chiro G. PET using [^{18}F]fluorodeoxyglucose in brain tumors: a powerful diagnostic and prognostic tool. *Invest Radiol* 1987;22:360–371.
2. Loessner A, Alavi A, Lewandrowski KU, Mozley D, Souder E, Gur RE. Regional cerebral function determined by FDG-PET in healthy volunteers: normal patterns and changes with age. *J Nucl Med* 1995;36:1141–1149.
3. Swartz BE, Halgren E, Simpkins F, et al. Primary or working memory in frontal lobe epilepsy: an [^{18}F]FDG-PET study of dysfunctional zones. *Neurology* 1996;46:737–747.
4. Stapleton JM, Morgan MJ, Phillips RL, et al. Cerebral glucose utilization in polysubstance abuse. *Neuropsychopharmacology* 1995;13:21–31.
5. London ED, Broussolle EPM, Links JM, et al. Morphine-induced metabolic changes in human brain. Studies with PET and [^{18}F]FDG. *Arch Gen Psychiatry* 1990;47:73–81.
6. Sokoloff L, Reivich M, Kennedy C, et al. The [^{14}C]deoxyglucose method for the measurement of local cerebral glucose utilization: theory, procedure and normal values in the conscious and anesthetized albino rat. *J Neurochem* 1977;28:897–916.
7. Huang S-C, Phelps ME, Hoffman EJ, Sideris K, Selin CJ, Kuhl DE. Noninvasive determination of local cerebral metabolic rate of glucose in man. *Am J Physiol* 1980;238:E69–E82.
8. Phillips RL, Chen CY, Wong DF, London ED. An improved method to calculate metabolic rates for glucose using PET. *J Nucl Med* 1995;36:1668–1679.
9. Huang SC, Phelps ME, Hoffman EJ, Kuhl DE. Error sensitivity of fluordeoxyglucose method for measurement of cerebral metabolic rate of glucose. *J Cereb Blood Flow Metab* 1981;1:391–401.
10. Takikawa S, Dhawan V, Spetsieris P, et al. Noninvasive quantitative fluorodeoxyglucose PET studies with an estimated input function derived from a population-based arterial blood curve. *Radiology* 1993;188:131–136.
11. Hunter GJ, Hamberg LM, Alpert NM. Simplified measurement of deoxyglucose utilization rate. *J Nucl Med* 1996;37:950–955.
12. Tamaki N, Yonekura Y, Kawamoto M, et al. Simple quantification of regional myocardial uptake on fluorine-18-deoxyglucose in the fasting condition. *J Nucl Med* 1991;32:2152–2157.

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Bias in PET Quantitation Due to Camera Calibration Procedures

TO THE EDITOR: Accurate absolute quantitation of radiopharmaceutical activity in vivo is important for numerous clinical and research PET applications. In our laboratory, we found a consistent 11% underestimation of PET radioactivity concentration that resulted from routine performance of established scanner calibration methodologies.

We calibrate our ECAT EXACT (CTI, Knoxville, TN) PET scanner using the manufacturer supplied protocol. An emission scan is performed on a permanently sealed cylindrical phantom measuring 20 cm i.d. × 22.6 cm long and filled with a known activity of ^{68}Ge/^{68}Ga dissolved in a gel (2.62 mCi measured by the manufacturer on September 24, 1993). A calculated transmission scan is used for attenuation correction. The scanner calibration is calculated by dividing the total radioactivity by the internal volume of the cylinder and the coincidences per second within the phantom. The total radioactivity and the internal volume of the cylinder were obtained based on the data provided by the manufacturer. We then used this calibration data to quantify the radioactivity concentration in a fillable 20-cm diameter phantom which was loaded with an aqueous solution of ^{18}F. Images were reconstructed using measured transmission data and compensated for the branching ratio effect so the activity concentrations reported in the image included all nuclear disintegrations and not just positron annihilations. We compared the PET measurement of radioactivity concentration to the concentration of an aliquot of the ^{18}F