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.

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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

solution obtained from the fillable phantom, which was measured with a dose calibrator. The performance of this dose calibrator was evaluated using ^{137}Cs (280.1 μCi on October 1, 1984, Medi + Physics/Amersham CDCV1, Arlington Heights, IL) and ^{133}Ba (277.0 μCi on October 27, 1983, DuPont NEN #3581083A-26, Boston MA) calibration sources which bracket the 0.511 MeV annihilation photon energy.

Based on the routine calibration procedure described above, we found the PET measured activity concentration of the fillable phantom is consistently 11% less than the concentration determined using the dose calibrator. We attribute this mainly to two factors:

1. Approximately 40% of this 11% error was attributable to slight differences in the results that occur when measured or calculated attenuation correction data are used.
2. The true distribution volume of $^{68}Ge/^{68}Ga$ in the sealed phantom is less than the assumed distribution volume.

In particular, transverse and longitudinal CT scans of the sealed phantom revealed the internal height of the phantom is actually 19.6 cm, slightly smaller than the 20.0 cm assumed value. These scans also revealed that there were air gaps in the gel, which prevents the gel from completely filling the phantom interior. From the CT data, we estimated that the difference between the actual and assumed distribution volume of $^{68}Ge/^{68}Ga$ is sufficient to explain the remaining 6.5% of the calibration error.

We do not believe any significant component of the error is due to dose calibrator measurements. Using the calibration sources, the dose calibrator was found to have the following precision and accuracy: The maximum error was $< 0.5\%$ and the s.d. was $< 0.3\%$.

Although the manufacturer suggests the phantom should be replaced yearly, it may not be practical because of costs. When accuracy of absolute PET quantitation is required, we recommend that a camera calibration using a fillable phantom be periodically performed to determine if the adjustment to camera calibrations obtained using a gel phantom is necessary. After the cross-calibration, we recommend that the sealed gel phantom be used for routine calibration measurements for reasons of convenience and precision.

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