EDITORIAL

The Influence of Positioning on Accuracy and Precision in Emission Tomography

Fundamentally, all medical imaging involves comparisons. When used for diagnosis, images are frequently compared with mental images of normality and different disease states. For prognosis or treatment monitoring, comparisons often focus on changes in serial studies in the same patient. Whenever comparisons are made, it is important to understand both the accuracy *and* precision (variability or reproducibility) of *each individual observation.*

While comparisons are frequently qualitative in nature, quantitative data also play an important role. This is particularly true in clinical and research settings which utilize a combination of positron emission tomography (PET) and tracer kinetic modeling. Such studies often involve a test-retest paradigm; for example, to assess the effects of a pharmacologic intervention. A long-term goal in PET research is thus to identify the sources of variation in measurements made both serially in the same subject and between subjects. It is clear that such sources include both technical factors (e.g., statistical noise, tomograph fluctuations, and subject positioning errors) and biologic factors (e.g., normal variations in the physiologic parameter of interest over time within a subject and across subjects) (*1*). It is interesting to note that disagreement exists regarding the nature of biologic variables, such as global changes, as intrinsically interesting "signal" or confounding "noise." In this regard, many investigators favor normalizing serial data for global changes in order to better discover regional effects (*2*).

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In this issue of the *Journal*, Pate and coworkers describe the reproducibility of PET-based striatal uptake measurements in monkeys (*3*). The investigators found that back-to-back scanning on the same day, compared with scanning on two occasions separated by 2 wk or more, reduced the scan-to-scan variation from 34% to 14% (coefficient of variation). They believe that this reduction was primarily due to elimination of (the 1–2 mm) repositioning error, although at least some of the observed higher variation in the separate-days protocol could have come from true biologic fluctuations.

Positioning can strongly influence *both* the accuracy and precision of SPECT and PET measurements. Since current SPECT and PET systems offer multiple simultaneously-acquired slices, it is tempting to think that all areas within the tomograph's field are equally "viewed," and that subjects can be initially positioned without a priori knowledge of the locations of structures of interest. The best PET tomographs have approximately 4–6-mm "thick" slices, limited by the tomograph's axial resolution; the best dedicated SPECT tomographs have approximately 8–12-mm slices, limited in practice by axial resolution (and theoretically in rotating-camera SPECT by the size of each pixel). Axial profiles are not square wave in shape, nor typically constant throughout each imaging plane (*4*); adjacent slices are almost never truly "contiguous," nor is axial coverage uniform or "complete." Thus, in practice, slices frequently do not pass through the centers of small structures, reducing quantitative recovery. A 1–2-mm change in the axial position of a slice with respect to the center of small brain structures, like the monkey striata featured in Pate's report, can change the observed counts by 10%–20% or more. The magnitude of such a change will depend on the relationship between the size of the structure and the axial response profile of the tomograph, but even relatively "thick" slices, such as those produced by the PETT VI tomograph Pate and coworkers used, with a 14-mm axial FWHM, can produce such effects, as we and others have shown (*4–6*). It is sobering to realize that a 1–2-mm change represents axial mispositioning *within* one pixel in rotating-camera SPECT. Thus, accurate *initial* positioning is important for accurate quantification; accurate *repositioning* is important for reproducible quantification.

In Pate's approach, the influence of initial positioning on quantification appeared to be minimized by the use of a rigorous scheme to first identify the slice-of-interest, followed by accurate positioning and head immobilization. As should be obvious from the preceding paragraph, we strongly support the type of approach the investigators chose, which emphasizes a priori selection of scan slice and verification during PET scanning (the investigators used the transmission scan). In this regard, we endorse the use of custom headholders or masks that can be affixed to both CT/MRI and SPECT/PET tomographs (*7–9*), permitting both the transfer of slice location data and adequate immobilization during scanning.

Pate's specific protocol could not, of course, be designed to completely control technical and biologic variation. The positioning of regions of interest in the images was less controlled; Pate's approach did not incorporate MRI data, in spite of its

availability. Use of co-planar CT/MRI data is becoming popular in both SPECT and PET, as methods for both a priori and a posteriori multi-modality image registration are developed and validated (*10*). As in most PET neuroreceptor imaging, image noise was probably high; the influence of this noise on mathematical model-based parameter estimation was not discussed. Other technical factors that may have played a role include any variation in specific activity or total mass of tracer injected and errors in correcting the second scan (in the single-day study) for residual activity from the first scan.

Pate's protocol directly compared back-to-back (same-day) variation with that from separate-days scanning. In my mind, the two largest potential sources of such variation are positioning and biologic fluctuations. Unfortunately, no explicit attempt was made to separate these two sources. For example, it might have been helpful to perform additional experiments in which the monkey was either intentionally moved 1–2 mm, or completely removed from the tomograph and then repositioned, *on the same day.* In spite of any limitations to the study, Pate's conclusion that the reduction in variability was primarily due to repositioning error (even in the face of rigorous attempts to control this factor) is extremely important, in that it argues for same-day imaging paradigms. Such a setting would, of course, also control any (normal) biologic fluctuations that occur over time. In this regard, the recent report by Devous and coworkers of *simultaneous* dual-tracer SPECT imaging in a test-retest paradigm is particularly noteworthy (*11*).

Ultimately, we should require of ourselves an estimate of the reproducibility or variability of an observation, be it qualitative or quantitative, before we begin comparing that observation with others. For quantitative PET studies, reports such as that from Pate and coworkers provide the information we need both to understand the sources and magnitude of this variation, and to point the way to techniques to reduce it when desirable.

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REFERENCES

1. Tyler JL, Strother SC, Zatorre RJ, et al. Stability of regional cerebral glucose metabolism in the normal brain measured by positron emission tomography. *J Nucl Med* 1988;29:631–642.
2. Friston KJ, Frith CD, Liddle PF, et al. The relationship between global and local changes in PET scans. *J Cereb Blood Flow Metab* 1990;10:458–466.
3. Pate BD, Snow BJ, Hewitt KA, et al. The reproducibility of striatal uptake data obtained with positron emission tomography and F-18 L-6-fluorodopa tracer in non-human primates. *J Nucl Med* 1991;32:1246–1251.
4. Hoffman EJ, Huang SC, Plummer D, Phelps ME. Quantitation in positron emission computed tomography. 6. Effect of nonuniform resolution. *J Comput Assist Tomogr* 1982; 6:987–999.
5. Wong DF, Links JM, Molliver ME, et al. An anatomically realistic brain phantom for quantification with positron tomography [Abstract]. *J Nucl Med* 1984;25:P108.
6. Mintun MA, Fox PT, Raichle ME. A highly accurate method of localizing regions of neuronal activation in the human brain with positron emission tomography. *J Comput Assist Tomogr* 1989;9:96–103.
7. Bergstrom M, Boethius J, Eriksson L, et al. Head fixation device for reproducible position alignment in transmission CT and positron emission tomography. *J Comput Assist Tomogr* 1981;5:136–141.
8. Mazziotta JC, Phelps ME, Meadors AK, et al. Anatomical localization schemes for use in positron computed tomography using a specially designed headholder. *J Comput Assist Tomogr* 1982;6:848–853.
9. Meltzer CC, Bryan RN, Holcomb HH, et al. Anatomical localization for PET using MR imaging. *J Comput Assist Tomogr* 1990; 14:418–426.
10. Correia JA. Editorial. Registration of nuclear medicine images. *J Nucl Med* 1990;31:1227–1229.
11. Devous MD, Gassaway SK. Simultaneous SPECT imaging of Tc-99m- and I-123-labeled brain agents in patients using the Prism• scanner [Abstract]. *J Nucl Med* 1990;31:877.