In Defense of Quantitative PET Techniques

TO THE EDITOR: We are roused to rebut Di Chiro and Brooks' editorial in the September *J Nucl Med* (*1*). To suggest—as do Di Chiro and Brooks—that positron emission tomography's (PET's) limited impact on clinical practice is a direct consequence of "pitfalls in quantitation" is, in our opinion, to disinform the reader. To be sure, high-quality quantitative PET studies are technically demanding, and their interpretation requires a careful consideration of the relevant signals and sources of error. Yet two quite different approaches have recently made considerable progress in identifying and quantifying cognitively and neurobehaviorally relevant signals from normal (*2*) and diseased (*3*) brains by de-emphasizing absolute accuracy and by carefully extracting a small component of the regional PET count rate.

We believe that some of PET's problems stem from the descriptive nature of most PET studies, and we agree with Di Chiro and Brooks that statistical analyses used to confer validity on descriptive studies cannot replace scientific intuition. However, to be useful, such intuition must be clearly expressed as testable hypotheses—and then tested, a process that typically requires statistical analysis. We disagree with the view that if no difference is seen visually or graphically in a raw-count image, "it either does not exist, or is too small compared to methodological error to have great significance." Moreover, we find it inconsistent that Di Chiro and Brooks are comfortable with the sophisticated mathematics of tomographic reconstruction, a form of mathematic modeling, but are noticeably uncomfortable with postreconstruction data analysis.

The authors speak against "the veil of mathematics and models", which, in their view, obscures the "real world of clinical imaging", and they prefer "the trained human eye", which "once again triumph[s] over computers". However, the "remarkable consistency ... between PET-FDG and histology, with no false-negative and only four false positive results [in 100 studies]" reported by Di Chiro (*4*) has not been confirmed by other investigators. Tyler et al. (*5,6*) reported "variable, but low values of glucose metabolism in tumors, irrespective of grade"; more than 70% of their high-grade tumors had metabolic rates less than or equal to normal control white matter values.

It appears that Di Chiro and Brooks believe that the greatest challenge for the physician engaged in analyzing FDG/PET images of primary brain tumors "is to recognize the difference between hot tumor and normal gray-matter structures" (*4*). Once we learn their rules, viz., [1] that "visual diagnosis is not easy"; [2] that "the appearance of the tumor ... depends on its location"; [3] that "hot tumors that invade the cortex may easily be confused with normal structures" and [4] that visualization of hot tumors may be hampered by the limited spatial resolution of the scanner, then the rest is easy. But what do these so-called rules really mean? Can anyone apply them in an objective fashion? Only a blinded prospective study of untreated glioma patients scanned immediately prior to excisional biopsy will settle this issue to the satisfaction of the scientific community. And no such study has yet been attempted.

Until such a study confirms the optimistic predictions of Di Chiro and Brooks, we must remain skeptical of their enthusiasm. It may be that "the visual appearance of the tumor is a better guide to tumor grade than the absolute metabolic rate" (*4*) and that "PET metabolic studies should be considered at least on a par with, if not more important than 'static' histologic findings" (*7*). But the evidence does not yet compel us to free ourselves from "the burden of blood sampling and ... quantitation" in the application of PET techniques to the study of human brain tumors, and there is also no convincing evidence to support qualitative approaches to the study of epilepsy and dementia using FDG/PET.

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The Best Radionuclide Venography

TO THE EDITOR: We interpret the paper of Leclerc et al. (*1*) as showing unfavorable results in technetium-99m red blood cell venography. Because the diluted-continuous flow radionuclide venography imaging technique, pioneered by Sy et al. (*2,3*) is so popular in our hospital, we have little experience with the labeled red cell method. The diluted-continuous flow technique is not free of difficulties, and the use of tourniquets varies from institution to institution (*2*); however, it would appear to have obvious advantages over the labeled red cell technique. These advantages include: direct visualization of the venous channels, easy visualization of collateral circulation, better visualization of the vena cava, utility in the upper half of the body, less interference from the arterial system, and more efficient patient handling. Therefore, we promote the use of the more successful radionuclide technique.

We also agree with the recent concept that ultrasound venography may be the new "gold standard" (*4,5*). Combinations of radionuclide venography, ultrasound venography, and impedence plethysmography have virtually eliminated

the procedure of contrast venography at our hospital. Of the three procedures, the radionuclide method is the one that visualizes the venous system most completely.

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