reliably and efficiently characterize the intrinsic performance of a PET device . . . ." We couldn't agree more. That is why we do not believe that the PET manufacturers should design and build anatomically detailed brain and body phantoms for standardized tests. This is incompatible with Bice and Miyaoka's and our stated goal to characterize the intrinsic performance of a PET device using basic and well-established parameters, such as spatial resolution, sensitivity, scatter and count rate capability.

Drs. Bice and Miyaoka are also puzzled by "the number of tests that required the user to choose acquisition parameters . . . as they would be set for a patient study." It seems obvious to us that a BGO system requires a wider energy window than a NaI (Tl) system, and a system with fixed septa cannot be tested with a large axial acceptance angle, to give two examples. No single set of parameters can be fairly applied to all PET scanner configurations. These parameters are optimized by the manufacturer, but they will depend on the particular scanner. It is important to keep the parameters fixed for all tests, but it is not possible to fix them for all scanners.

Another confusing suggestion is to eliminate the test of scatter fraction but retain the test of scatter correction. A system with 5% scatter is clearly preferable to one with 95% scatter, since scatter correction only subtracts the estimated scatter contribution but not the noise associated with the scatter. Also, knowledge of the scatter fraction allows one to calculate the true sensitivity and true count rate as a function of activity. While the phantom selected has no "physical significance," it is not so unrealistic as to preclude comparisons between scanners. The value measured for intrinsic scatter fraction may change with a more realistic phantom, but the relative values between scanners are unlikely to change.

We were somewhat dismayed at the reference to the measurement of the accuracy of scatter correction as "weak" without a suggestion as to how to make it better. As the proposed measurements come into routine use on a variety of scanners, especially those newer systems whose specifications are not yet known, specific ideas as to improvements to these measurements will be welcomed.

Finally, we disagree with Bice and Miyaoka that purchasers of PET devices will "rely less on phantom data as information on the clinical performance of a current generation machine" becomes available. Clinical PET studies will always be evolving, as will PET scanners, while the performance measurements were designed to serve as standards for a substantial period of time. Both the intrinsic performance and the clinical experience will be important considerations to potential purchasers of PET scanners.

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Patterns of Dementia in Alzheimer's Disease

TO THE EDITOR: We have read with a great interest Holman et al.'s article in the February issue of the *Journal* (*1*). This paper points out the wide variety of patterns observed in dementia, particularly in Alzheimer's disease (AD).

They confirmed previously published results obtained with [^{123}I]IMP (*2*) or the ^{133}Xe noninhalation method (*3*). Unfortunately, the statistics were undoubtedly incorrect, and Holman and coworkers failed to calculate the predictive values (PV) of the HMPAO tomograms. By using the author's method and the same notation (Q_i: pattern $_i$; AD + or AD− for the presence or no presence of AD) we can emphasize that the meaning of P (Q_B/AD+) as it appears in the Results section is wrong. Indeed, P (Q_B/AD+) does not represent the probability for the patient to have AD if Q_B is present, but exactly the opposite: the probability to encounter the Q_B pattern if AD exists. This is the Bayesian notation corresponding to the sensitivity of the test. By using Holman's results, sensitivity is equal to 27% (14/52).

Moreover, Holman and coworkers said that the positive predictive value (PPV) for Q_B patterns is 82% (Table 1; summary). This is incorrect. Indeed, the PPV corresponds to P (AD+/Q_B). This value (the negative PV) can be calculated only if the sample represents the probability of the distribution in all populations. Clearly, it is not true here since the prevalence, p, of AD can be assumed to be equal to 5% (for individuals older than 65 yr, no comment is made) and in Holman's study p is nearly equal to 50% (52/113)!

PPV can be obtained using Bayes' theorem, which results in the following relationship:

$$PPV = p \times \text{sensitivity}/(p \times \text{sensitivity}) + (1 - p)(1 - Sp),$$

where Sp is the specificity: P (Q_B−/AD−).

Holman's data, (sensitivity = 27%; specificity = 95%) and assuming p = 5%, results in a PPV of only 21% and not 82%, the result obtained by Holman et al. With a similar calculation, the negative predictive value (NPV) is 50%. We agree with Holman that Q_B is one of the most probable patterns of AD (but only 14/52), but it is not pathognomonic. What is true for Q_B is even more true for other patterns. In a previous study using the cerebellum as reference (*4*), we showed that the best cutoff value to discriminate AD from normals was 0.8, with a sensitivity and specificity of 0.6 and 1, respectively. Thus, the NPV (P(AD−/Q_B−)) was equal to 100%. The main goal of Holman and coworkers' paper was to provide interesting raw data for several diseases according to their different patterns. This leads to the conclusion that HMPAO brain tomograms are of very low value in determining diagnostic causes of memory or cognitive complaints, or both. Holman et al. also provided for calculations of predictive values for each pattern, but a correct application of the Bayes' theorem was needed.

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REPLY: Steinling and Leys correctly point out that the probability notation used by the authors is incorrect: test result and diagnosis have mistakenly been inverted. For example, what is notated as $P(Q_B/AD+)$ in the article should read $P(AD+/Q_B)$ and refers to the probability that patients with a B pattern on the HMPAO SPECT study have Alzheimer's disease (AD). Although the probability notation is incorrect, the percentages presented in the Results section and Table 1 correctly enumerate what is described in the text and table legend respectively.

As was pointed out in the discussion of the article, the hospital where this study was performed is a tertiary center. Therefore, a high prior probability of AD can be expected which will increase the predictive value. In order to use the results from this study in another setting, one should apply Bayes' theorem to calculate the predictive value (or posterior probability) of AD. However, we strongly disagree with Steinling and Leys that a prior probability of the disease among the general population should be used in applying Bayes' theorem. Instead, a prior probability should be used based on the information available at the time the patient is studied and will depend on information such as the regional prevalence of the disease, referral patterns to the imaging center, as well as the patient's age, gender, race, history and clinical findings. Clearly this will vary from center to center and from patient to patient.

Furthermore, in applying Bayes' theorem, Steinling and Leys have assumed a dichotomous test result, i.e., either B or non-B. In doing so, information is lost for the non-B test results. It is preferable to calculate predicted values for each test result according to Bayes' theorem in the following form:

Q_i = the SPECT pattern i
$P(AD+)$ = the prior probability of AD
$P(Q_i/AD+)$ = the true positive rate of test result Q_i
= the probability of test result Q_i among patients with AD
$P(Q_i/AD-)$ = the false positive rate of test result Q_i
= the probability of test result Q_i among patients without AD
$P(AD+/Q_i)$ = the predictive value (or posterior probability) of AD given Q_i

$$P(AD+ \mid Q_i) = \frac{P(AD+)\cdot P(Q_i \mid AD+)}{P(AD+)\cdot P(Q_i \mid AD+) + (1 - P(AD+))\cdot P(Q_i \mid AD-)}$$

Figure 1 gives the posterior probability as a function of the prior probability for all seven SPECT patterns.

Finally, in calculating the negative predictive values for a negative test result $P(AD-/Q_{nonB})$ (assuming a dichotomous test), for both the results from our center and their own results, Steinling and Leys apply Bayes' formula incorrectly. With a sensitivity of 0.269, a specificity of 0.951 and a prior probability of AD of 0.05, the negative predictive value for a negative test (the predicted probability of *not* having Alzheimer's disease given a non-B SPECT pattern) is:

$$(0.95 \times 0.951)/(0.95 \times 0.951 + 0.05 \times (1 - 0.269)) = 0.961 \text{ (not } 0.50)$$

Similarly, with a sensitivity of 0.6, a specificity of 1.0 and a prior probability of 0.05, the negative predictive value is:

$$(0.95 \times 1.0)/(0.95 \times 1.0 + 0.05 \times (1 - 0.6)) = 0.979 \text{ (not } 1.0).$$

We are delighted, incidentally, that Drs. Steinling and Leys were able to confirm our previously published quantitative comparisons of AD patients and normal subjects using the cortical-to-cerebellar activity ratio (*1–4*). As one would expect, we had a somewhat higher sensitivity by using a lower threshold value but at the expense of specificity.

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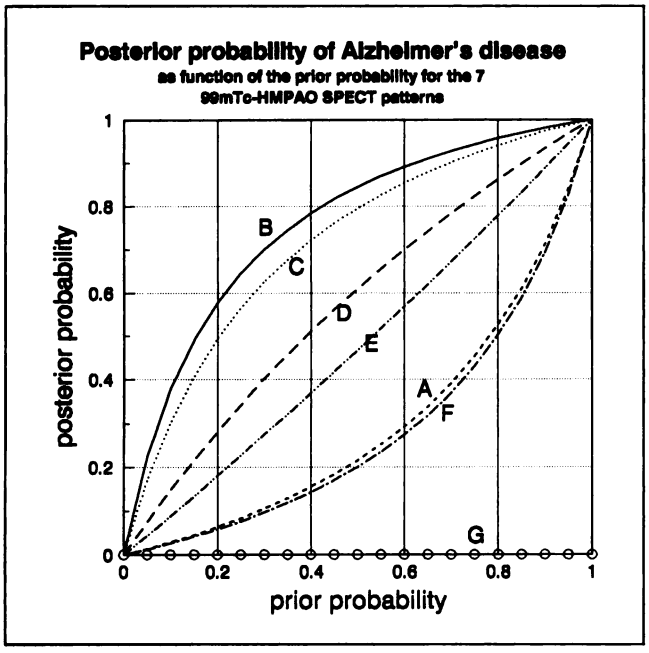

FIGURE 1. The posterior probability as a function of the prior probability for all seven SPECT patterns.

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