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REPLY: The peripheral organ distribution volume (PODV) is indeed an old concept whose temporal behavior was seldom studied in the past (*1,2*).

More recently, it has been studied, as a function of the integrated-plasma-to-plasma concentration ratio, in unidirectional phenomena (*3*), its main advantage being the easy correction for activity in vascular and exchangeable compartments in the region of interest (ROI). Its interest, in metabolic studies with PET, has recently been reviewed by Gjedde and Wong (*4*).

In our first paper (*5*), we mainly were concerned with the kinetic behavior of PODV as a function of the time itself (instead of the integrated-plasma-to-plasma ratio), not only for irreversible but also for reversible processes.

From the study of more than 460 patients, we conclude that, with [^{99m}Tc]pertechnetate or ^{99m}Tc-DTPA, only two simple functions, linear for irreversible transfer or uniexponential for reversible exchange, are actually necessary and sufficient to represent the PODV time behavior, at least in the time limits of our investigations. This may not be valid for other tracers or for longer time intervals.

The second paper (*6*) illustrates a simple application of the PODV approach in a largely used clinical test.

Peters and Bell's first concern is the temporal behavior of PODV for bidirectional tracer exchange.

After the first minute (Figure 3 of reference 5), our ^{99m}Tc-DTPA data clearly show two characteristics, not found in Peters and Bell's Figure 3, but are constant in our DTPA data base: an equilibrium is practically reached at 20 min and the monoexponential fit fully describes the observed data. Figure 4 of reference 5 confirms a similar pattern in 85 thyroid and 166 interstitial fluid studies with pertechnetate.

During the first minute, we agree that a monoexponential fit does not follow the data. A biexponential function fits the whole interval, even the first minute (Fig. 1 and Table 1): the slow exponential component of the biexponential fit in the whole interval is practically identical to the single exponential component of the monoexponential fit limited to the 2–20-min interval.

Unfortunately, in their letter, Peters and Bell give no description of the function they used to fit their data and an accurate comparison with ours is not straightforward.

The second exponential term is very rapid (25 times faster

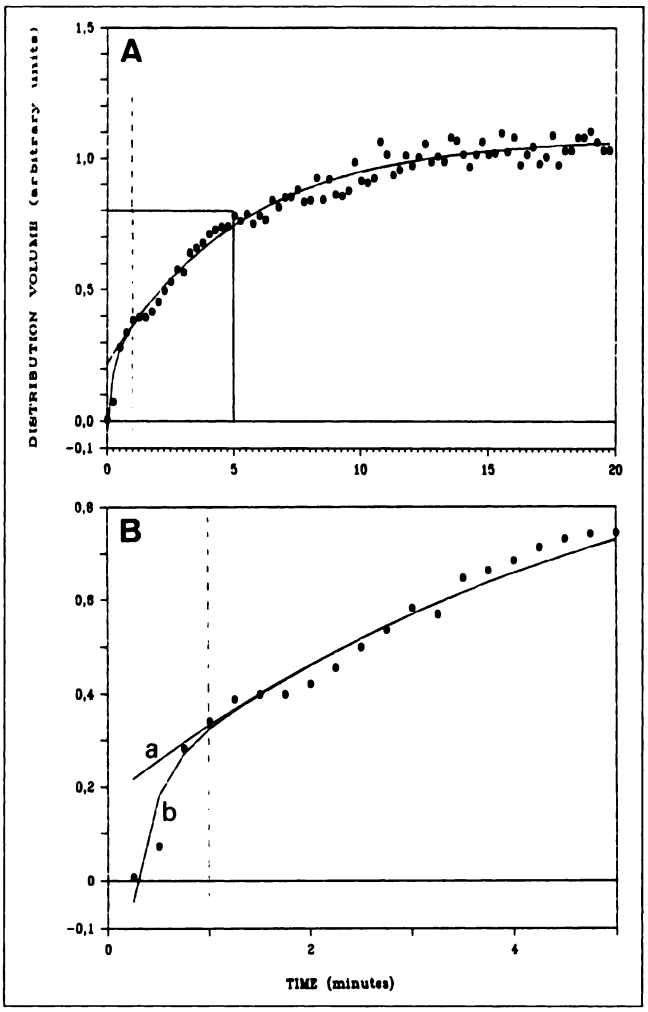

FIGURE 1. Mono-exponential versus bi-exponential fit of PODV in a subrenal ROI with ^{99m}Tc-DTPA. (A) Mono-exponential fit in the 2–20-min interval and bi-exponential fit in the whole interval. (B) Magnification of the first 5 min showing the difference between the fits to be no more significant after the 1st minute (a: mono- and b: bi-exponential).

TABLE 1
Comparison of PODV Monoexponential and Biexponential Fit for Reversible Bi-directional Exchange

Fit	Interval	Vo	V∞	k1	k2	r
Mono	5-80	0.1763	1.077	0.003169	—	0.981
Bi	1-80	−0.7327	1.076	0.003197	0.08354	0.987

Mono: $V(t) = V_o + (V_\infty - V_o)\cdot(1\text{-}e^{-k1t})$.
Bi: $V(t) = V_o + (V_\infty - V_o)\cdot(1 - \frac{1}{2}e^{-k1t} - \frac{1}{2}e^{-kt2})$.

than the slow component). It influences the early data fit only, leads to a lower initial PODV (Vo) estimate, and practically vanishes by the end of the first minute.

However, it is evident that the first minute of the externally recorded cardiac curve is not reliable and should not be used in any fit procedure. After intravenous injection, the right and left cardiac chambers are successively seen in the cardiac ROI and summed in the same first 15-sec frame (overestimating the plasma value). One minute is probably necessary before reasonable bolus mixing is reached. We thus never used the first minute data to fit the PODV curves.

The initial PODV, Vo, was introduced in the fit function for "automatic correction of the residual plasma component" (*7*), which always remains after classical background correction. As Vo estimation is largely dependent on the function used in the fitting procedure, its validation with monoexponential fit function is presented in the second paper (*6*). Indeed, Vo is estimated with the PODV decomposition algorithm in the renal (VoK) and background (VoBG) ROIs after ^{99m}Tc-DTPA injection and their ratio is shown to be, if not equal, very close to the renal (QK) to background (QBG) ROIs activity ratio in a blood-pool agent study with ^{99m}Tc-HSA.

It can be argued that if an identical percent error alters both VoK and VoBG, their ratio will not be affected. However, as VoK is estimated by an unequivocal linear PODV fit (our unpublished data show evidence that the integrated-plasma to plasma ratio is an unequivocal linear function of time with ^{99m}Tc-DTPA up to 20 min), a systematic 40% error in VoK is very unlikely.

The systematic 40% overestimation of VoBG suspected by Peters and Bell should therefore strongly affect the VoK/VoBG ratio, which then would not match the QK/QBG ratio. This is actually not the case.

The second point raised by Peters and Bell, i.e., the identification of the extravascular signal in the renal ROI, was already discussed in our second paper (*6*). The choice of our background ROI (BGROI) is justified by anatomical criteria only, assuming in addition that the virtually empty peritoneal cavity and the gastrointestinal tract seen together with muscles and fat tissue in BGROI have no significant contribution (i.e., no more significant than the 'large bag" seen in the kidney ROI).

We are aware that this assumption, as others, has its limitations and that the ideal solution is still to be found.

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Maximum-Likelihood Estimation: A Mathematical Model for Quantitation in Nuclear Medicine

TO THE EDITOR: As we are working on contrast detectability and quantitation in SPECT (*1*), we found great interest in the paper by Müller et al. (*2*). To understand the mathematical developments underlying the work, we consulted early published papers (*3–5*), where authors derive an expression for the noise power spectrum.

In all of these analyses, however, we found various errors, especially based on misuses of nonstationary process approximations to a stationary one which led to invalid results.

Indeed, if we assume that noise in projections is an uncorrelated process, its covariance function, γ, is defined by:

$$\gamma(1_1, \theta_1; 1_2, \theta_2) = \sigma^2(1_1,\theta_1)\, \delta(1_2 - 1_1, \theta_2 - \theta_1), \qquad \text{Eq. 1}$$

where $\sigma^2(1, \theta)$ represents the noise power density at point $(1, \theta)$ of the detector and δ is the DIRAC distribution.
If we denote the reconstruction filter W in the Fourier space as follows:

$$W(R) = |R|\, H(R), \qquad \text{Eq. 2}$$

where R is the radius and H(R) is the filtering function, with $H(0) > 0$, the noise power spectrum density Γ of the reconstructed image therefore is (*6*):

$$\Gamma(R_1, \theta_1; R_2, \theta_2) = S(R_1 - R_2, \theta_1)\, H(R_1)\, H^*(R_2)\, \delta(\theta_2 - \theta_1), \qquad \text{Eq. 3}$$

where $S(R, \theta)$ is the Fourier transform of $\sigma^2(1, \theta)$ along the 1-axis.

If, in order to study noise behavior, we use the approximation of the average power spectrum, M [APS] (*7*), we do not obtain:

$$M(R, \theta) = S(R, \theta)\, |R|\, |H(R)|^2 \qquad \text{Eq. 4}$$

as calculated in (*3–5*). In such a case, the value of the APS would be null at the origin of the Fourier space, and this condition results in the equality:

$$\int\int \sigma^2(1, \theta)\, d\theta\, dl = \theta \qquad \text{Eq. 5}$$

which implies

$$\sigma^2(1, \theta) = 0 \qquad \text{Eq. 6}$$

for all points of the detection space.

Thus, noise would be null, in the mean square sense over all projections. According to Poisson process properties, it would be null with probability one (*8*) (i.e., projections would be noiseless). Therefore the APS in tomography cannot behave as the ramp function for low frequencies, as mentioned in (*3–5*).