TABLE 1. MEASUREMENT OF $^{99m}TcO_4^-$ AND REDUCED ^{99m}Tc IN ^{99m}Tc-HSA BY VARIOUS ANALYTIC TECHNIQUES

Analytic technique	Material measured	Amount detected (%)	No. of analyses
Paper chromatography with 85% methanol	$^{99m}TcO_4^-$	1.5 ± 0.6	5
HSA-saturated paper chromatography with 0.15 M NaCl	Reduced ^{99m}Tc	1.4 ± 0.8	17
ITLC (Gelman silica gel) with 85% methanol	$^{99m}TcO_4^-$	2.3 ± 1.5	25
TCA precipitation	$^{99m}TcO_4^-$ + reduced ^{99m}Tc	3.7 ± 0.8	12

The protein is precipitated with 1 ml of 10% TCA solution and separated by centrifuging for 20 min. The radioactive content of the supernatant, determined by comparing the count rate with that of a reference sample, indicates the total unbound ^{99m}Tc activity (both $^{99m}TcO_4^-$ and reduced ^{99m}Tc).

As shown in Table 1, our results with this technique agree favorably with those obtained using conventional techniques, such as paper or instant thin-layer chromatography and 85% methanol for the detection of $^{99m}TcO_4^-$ (*2*) and paper chromatography (in which the paper has been saturated with HSA) and nitrogen-purged saline for the detection of reduced ^{99m}Tc (*3*). The analyses were performed on numerous ^{99m}Tc-HSA samples prepared from several vials of the same HSA kit (lot No. SA-2314, Diagnostic Isotopes, Upper Saddle River, N.J.) The $Na^{99m}TcO_4$ was eluted from a New England Nuclear generator (Boston, Mass.).

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Reply

McLean and Welsh have suggested an alternative method, i.e., TCA centrifugation, for analysis of preparations of ^{99m}Tc-human serum albumin. In our laboratory, the TCA filtration method (*1*) was chosen for this quality-control procedure because of its speed (5 min or less), ease of determination, and simplicity of equipment required. These factors permit the assay of individual batches immediately prior to patient administration, an important factor when using ^{99m}Tc-HSA (*2*). Although the procedure described by McLean and Welsh appears to provide adequate separation, the time required to perform the assay (20–30 min) is a definite disadvantage.

We have referred to the TCA filtration assay as an "index" of free activity rather than as an absolute determination in view of the potentially incomplete separation of non-albumin-bound reduced technetium from the labeled HSA. Although partial separation of the hydrolyzed fraction of technetium is a limitation of the TCA filtration procedure, this problem was thought to be of minor importance in our study since the electrolytic preparations used fail mainly by incomplete reduction of $^{99m}TcO_4^-$ (*3,4*).

This limitation of the TCA filtration procedure may be of greater significance in the assay of ^{99m}Tc-HSA prepared through the stannous reduction of $^{99m}TcO_4^-$, since the presence of non-albumin-bound reduced technetium is more troublesome with this method (*3*). The data presented by McLean and Welsh, however, do not compare their centrifugation technique with our filtration technique. Preliminary data from such a comparison in our laboratory (three duplicate determinations), using the electrolytic labeling method, suggest that there is no significant difference between the indices of unbound ^{99m}Tc obtained by the two methods. The filtration method has proven to be an effective index of unbound ^{99m}Tc activity in over 300 batches of ^{99m}Tc-HSA tested.

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The Difference Between $\bar{t}$ and $t_{1/2}$

In the Discussion section of their recent paper (*1*), Alpert et al. explain the difference between $\bar{t}$ and $t_{1/2}$ by noting that $t_{1/2}$ is computed on the basis of a single-exponential (and thus inexact) model. The actual difference between paired $\bar{t}$ and $t_{1/2}$ values cannot be found in the text, nor can it be deduced from first principles since, while $t_{1/2}$ is underestimated by the single-exponential analysis, $\bar{t}$ is also underestimated because the washout data are not collected until the counting rate is zero. It would not have disgraced this interesting paper, however, to point out that, barring those two types of error, if the data were truly single-exponential,

the difference would be that $\bar{t} = 1/\lambda$ while $t_{1/2} = 0.693/\lambda$, where λ is the initial slope of the exponential. The 15-sec difference would then correspond to an average value of 48.3 sec for $\bar{t}$ and 33 sec for $t_{1/2}$, corresponding grossly to the values plotted in their Fig. 6.

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REFERENCE

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Reply

As we stated in our paper, the $t_{1/2}$ index assumed a single-exponential model, while $\bar{t}$ is essentially model-independent. The paper does not state, nor should the reader infer, that one index is superior to the other. In fact, each uses a single parameter to characterize the complex data of tracer clearance. These indices appear sufficient to quantitate regional ventilation relevant to the diagnosis of pulmonary embolism, but they may not be satisfactory for analyzing more subtle ventilation abnormalities. Very long washout times are difficult to measure accurately with either method unless data are collected for extended periods.

Figure 6 of the text indicates that $\bar{t}$ was, on the average, about 15 sec greater than $t_{1/2}$. This trend could be predicted from first principles. Since the overall washout curve is not single-exponential, the first half-time emphasizes the early, more rapidly falling data. The second half-time would be greater than the first, and so on. Because the mean transit time uses all of the data and includes the effect of the more slowly clearing tracer, the fact that $\bar{t} > t_{1/2}$ is not surprising, but to be expected.

That the average values of $\bar{t}$ and $t_{1/2}$ computed for the single-exponential model agree with the data of Fig. 6 is interesting but fortuitous, since the data are clearly not well represented by a single-exponential curve over their entire range.

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