theless, some estimates of the effect on resolution in an imaging system can be made by considering typical values of the width of the angular distribution. Stewart (*5*) measured this width for positrons annihilating in 34 different elements and found a mean FWHM of about 0.5° with a range of 0.2–0.7°.

The effect of these angular distributions, as discussed by Muehllehner, is to add additional width to the best resolution attainable with annihilation coincidence detection. This width is directly proportional to the separation distance of the pair of coincident detectors (*2*). If one takes 0.5° to be the mean angular distribution around 180°, then this produces a line spread distribution with a FWHM of 4.8 mm and 2.7 mm for detector separation distances of 111 cm [e.g., PETT III (*6–9*)] and 62 cm [e.g., Cho et al. (*10*)], respectively. In support of Muehllehner's conclusions, this effect is typically greater than that of β^+ range and, whereas these effects place some limits on the highest resolution possible with annihilation coincidence detection, they do not pose significant problems with the realistic system resolutions of 8–10 mm. Depending on the particular detector separation distance, system design, and radionuclides employed, the combination of positron range and angulation error will typically contribute 1–3 mm FWHM to the total system resolution. Since the several factors that affect resolution are not simply added together, but are convoluted together, a slower changing loss in resolution is obtained than the simple sum would (incorrectly) indicate.

It is important to point out that this discussion and that of Muehllehner are in reference to only two factors affecting spatial resolution. There are obviously many other factors (which are, in fact, typically more important) that determine the overall system resolution: statistics, depth-dependence and resolution of collimated detector response, sampling frequency, detection efficiency, photon attenuation, scattered radiation, random coincidence rate, object motion, display resolution, etc. All of these physical considerations must be carefully analyzed before a system can be optimally designed, since there are many trade-offs among these factors. For example, as the detector separation distance is increased, one achieves more uniform detection efficiency and resolution, better scatter coincidence rejection, and other improvements that are beyond the scope of this letter (*6–12*). On the other hand, this is done at the expense of an increase in the annihilation angulation errors, lower efficiency (although effective design can remove this to a major degree), and the need for more or larger detectors to cover the field of view of the object. Discussions of the above design considerations are given in Refs. *2* and *6–12*.

Lastly, one must contain one's scientific enthusiasm by making some effort to include cost-effective constraints in the design.

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Reply No. 2

Dr. Muehllehner's letter "Resolution Limit of Positron Cameras" seems to be an interesting observation. Measuring the finite spread of the 180° back-to-back radiation has been a classical physics problem in the nuclear physics community. In addition to the "finite range" of the positron, the angular uncertainty deserves mention in any discussion of expected improvements in resolution in future positron cameras.

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Measurement of Unbound ^{99m}Tc in ^{99m}Tc-Labeled Human Serum Albumin

In a paper by Lamson et al. (*1*), a rapid method was reported for the estimation of unbound ^{99m}Tc in preparations of ^{99m}Tc-labeled human serum albumin (^{99m}Tc-HSA). Their method was based on protein precipitation using trichloroacetic acid (TCA), followed by filtration through a 0.22-μm disposable membrane filter. Their main problem was the retention of unbound reduced ^{99m}Tc on the filter membrane.

We wish to report an alternative method, namely, centrifugation, for the separation of the precipitated protein from its supernatant. The ^{99m}Tc-HSA is added to a centrifuge tube containing 0.1 ml of HSA carrier solution (7.5 mg/ml).

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,