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Dependence of Distribution of Short-Lived Tracers on Decay. A Noncompartmental Approach

In the paper by Modell and Graham (*1*) it was shown that the single-compartment, well-mixed model is a not good predictor of Kr-81m behavior in the lung. The authors tried to explain the differences between the experimental data and theoretical curves generated from a single-compartment, well-mixed model by the inhomogeneity of Kr-81m distribution and its dependence on factors such as combinations of tidal volume and frequency and inspiratory time, but dependence of Kr-81m distribution on decay was not discussed. To assess the dependence of Kr-81m distribution on decay only, one can simplify the problem by considering a system of fixed volume V, where the input concentration is denoted by $I_{in}(t)$, the output concentration by $I_{out}(t)$, the amount of tracer in the system by I(t), constant flow by F, and decay constant by λ. Then

$$I(t) = F \cdot \int_0^t H(t-t')I_{in}(t') \exp[-\lambda(t-t')]dt' \quad (1)$$

$$I_{out}(t) = \int_0^t h(t-t')I_{in}(t') \exp[-\lambda(t-t')]dt' \quad (2)$$

$$(I_{in}(t) = 0 \text{ for } t < 0)$$

Where H(t) is the impulse response function and h(t) is the spectrum of transit times. Equations (1) and (2) may be reduced to the well-known equation

$$\frac{dI(t)}{dt} = F[I_{in}(t) - I_{out}(t)] - \lambda I(t). \quad (3)$$

This, assuming thorough mixing, i.e.:

$$V = \frac{I(t)}{I_{out}(t)}, \quad (4)$$

has been used as a starting point for almost all studies with short-lived tracers. In the case of constant infusion (I_{in} is constant) and the steady state defined by $\dot{I}(t) = 0$, one can combine Eqs. (3) and (4) to write:

$$I = \frac{F}{\frac{F}{V} + \lambda} I_{in}. \quad (5)$$

That is the result for a well-mixed, single-compartment model, as pointed out by Fazio and Jones (*2*). Using a noncompartmental approach [Eqs. (1) and (2)], the ratio between I(t) and $I_{out}(t)$ should be found to obtain a corrected version of Eq. (5),

$$I = \frac{F}{A + \lambda} I_{in}, \quad (6)$$

where,

$$A = \frac{\int_0^\infty e^{-\lambda t}h(t)dt}{\int_0^\infty e^{-\lambda t}H(t)dt}. \quad (7)$$

For long-lived radionuclides ($\lambda = 0$), A^{-1} reduces to

$$A^{-1} = \bar{t} = \frac{V}{F}, \quad (8)$$

where $\bar{t}$ is the mean transit time. In that case Eqs. (4) and (8) are the same, showing that the assumption of thorough mixing is strictly appropriate only in the steady state and with negligible decay. That is, only in such a case is the volume of the system is equal to the volume of distribution of the tracers, which is defined by Eq. (4). For short-lived emitters such as Kr-81m, A may be approximated by $\exp(-\lambda t)$ and the contribution of A may be negligible if λ is large. Hence from Eq. (6) we obtain the approximate relation:

$$I \sim \frac{F}{\lambda} I_{in}, \quad (9)$$

indicating a more nearly linear relationship between the amount of tracer (or concentration at fixed volume) in the organ and the flow for a short-lived tracer than the single-compartment, well-mixed model does.

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Reply

The noncompartmental analysis by Knešaurek represents an alternative mathematical approach to explain our observation that Kr-81m activity compared with ventilation is more nearly linear than is predicted using a well-mixed, single-compartment model. The major differences are in the impulse response function and the spectrum of transit times that are introduced in Knešaurek's Equations (1) and (2). The most reasonable impulse response function for Kr-81m activity in the lung is a simple step function. This would reduce to 1.0 for $t > 0$ and thus would essentially cancel out of Eq. (1). The spectrum of transit times, however, is likely to be a broad function correlating with the general inhomogeneity of ventilation, which, we felt, explained the discrepancy between our data and the single-compartment analysis. This may represent a starting point for a better quantitative approach to the analyses of ventilation inhomogeneity.

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Abnormal Perfusion Scan Due to Intrathoracic Stomach and Colon

There have been previous reports in the literature of perfusion lung scan defects caused by intrathoracic stomach (*1*) and

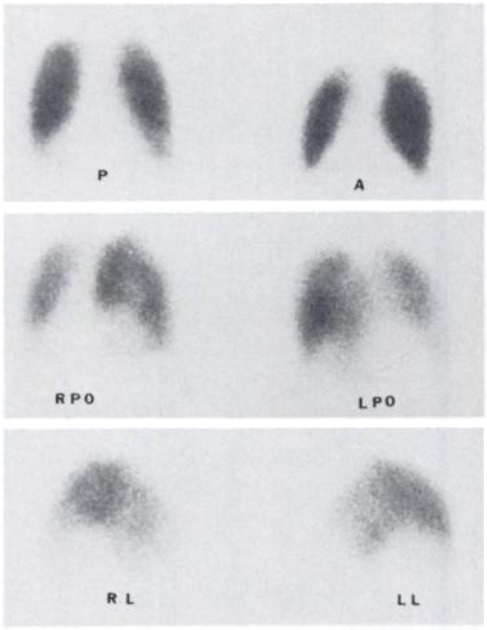

FIG. 1. Perfusion lung scan showing large perfusion defects in both bases seen on lateral and oblique views.

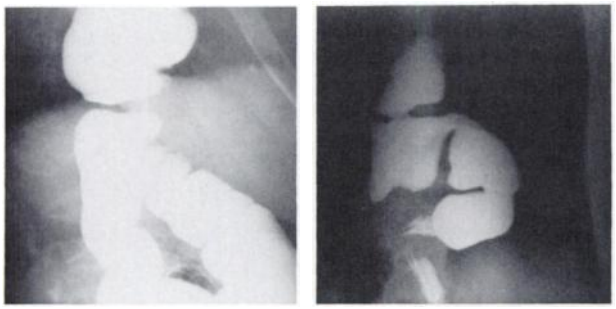

FIG. 2. Lateral view of barium enema showing mid portion of transverse colon in chest (left); Upper GI series demonstrating entire stomach and duodenal bulb in chest cavity (right).

esophageal hiatus hernia (*2*). We present a case of ventilation-perfusion mismatch secondary to intrathoracic stomach and colon.

A 68-yr-old white female was admitted for evaluation of anemia and fever. Her past medical history was remarkable for a left mastectomy for infiltrating ductal carcinoma. Physical examination revealed a temperature of 100.4°, a regular pulse of 80, and respirations of 16. The lungs were clear to auscultation. On cardiac examination a grade II/VI systolic ejection murmur was noted. The abdomen was negative. A chest radiograph showed evidence of old granulomatous disease and intrathoracic stomach.

During the patient's hospital course, she developed shortness of breath and chest pain, and a pulmonary embolism was suspected. A perfusion lung scan using 3 mCi of Tc-99m MAA demonstrated a large defect in both pulmonary bases (Fig. 1). The defects corresponded in location to a large hiatal hernia/intrathoracic stomach observed on chest roentgenogram. No segmental or subsegmental defects were noted, and the ventilation scan did not show a matched defect. Subsequently the patient demonstrated angina pectoris. As part of the evaluation of her anemia, a barium enema and upper gastrointestinal series (Fig. 2) were performed, and an intrathoracic stomach and colon were seen corresponding to the area of the perfusion defect on the lung scan.

Many causes of perfusion defects on lung scans have been described (*1*), and the above case illustrates two possible nonembolic etiologies.

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Re: Concerning the Labeling of DTPA-Coupled Proteins with Tc-99m

In their contribution describing the labeling of DTPA-coupled antibodies and fibrinogen with Tc-99m, Khaw et al. (*1*) do not claim that the label is attached to the DTPA moities, although this could be inferred since DTPA-coupled protiens were used in their study. In this respect, the article may be misleading. In our attempts to label free DTPA in the presence of proteins, including antibodies and fibrinogen, we find that Tc-99m normally attaches primarily to the proteins. Following a faithful reproduction of the dithionite method described by Khaw et al., we were unable to label free DTPA with Tc-99m even in the absence of antibody, and at much higher DTPA concentrations (up to 1 mg/ml).

It is unlikely that a Tc-99m labeling method that successfully chelates the DTPA groups on proteins would result in colloids such as that described by Khaw et al., nor would we expect the rapid blood clearance and large liver accumulation. It is surprising that the authors have not compared the in vitro and in vivo behavior of the Tc-99m-labeled proteins with and without the attached DTPA groups.

Although we feel that the attached DTPA groups are not involved, we agree that proteins are labeled with Tc-99m by the described method. Furthermore, there is little question that this and other reported methods provide a protein label that is stable during in vitro analysis by gel chromatography, affinity chromatography, etc. It is the stability of the label in vivo that is not adequately established. In studies such as these, it would be helpful if the biodistribution of the Tc-99m-labeled proteins were compared with that of the same protein labeled by alternative methods such as radioiodination or, in the case of DTPA-coupled proteins, with In-111. It might then be possible to distinguish liver activity due to the uptake of labeled proteins from that due to the accumulation of colloids and other Tc-99m species of low molecular weight.

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