

## LETTERS TO THE EDITOR

### Technetium-Thallium Subtraction Images for Location of Parathyroid Adenomata

Ferlin et al. (1) and Young et al. (2) have recently described the successful utilization of combined technetium-99m and thallium-201 imaging for the localization of parathyroid adenomata in patients with primary hyperparathyroidism. Both groups have obtained the technetium image first, followed by the thallium study. Winzelberg and Hydovitz (3) have commented on the advantages, from a technical point of view, of injecting thallium first. If technetium is given first, significant Compton scatter will occur at about 80 keV, and this may obscure small thallium-avid adenomas. A scatter image can be obtained (2), but this prolongs the period of immobility required of patients who may be frail, and degrades count statistics in the thallium image.

We have recently reported our experiences with an imaging protocol that uses shorter acquisition time and in which thallium is injected first (4). Five minutes after injection of 1.5–2 mCi (60–80 MBq) Tl-201 we obtain and store on computer 15 1-min frames of the neck and upper thorax using the 80-keV photopeak. Technetium-99m (1 mCi) is then injected and, using the 140-keV photopeak, 10 more 1-min images are obtained. The individual images are checked for movement, any frames in which serious motion has occurred are discarded, and minor changes in position are corrected by a digital move routine. All Tl-201 images are summed, and the last five Tc-99m images are also summed. The summed images are scaled for intrathyroidal activity, and the summed Tc-99m image is subtracted from the summed Tl-201 image. Residual focal activity is considered to represent an adenoma.

We have correlated the image findings so far in a consecutive series of 16 patients who also underwent neck exploration. The position of the adenoma was correctly predicted in 10 of 11 patients with primary hyperparathyroidism. Two false-positive images occurred in patients with thyroid nodules. The scintigram was negative in one patient with recurrent parathyroid carcinoma and in one patient with parathyroid hyperplasia. In a second patient with hyperplasia, two out of four enlarged glands were detected by scintigram.

Our results confirm the findings of Ferlin et al. (1) and Young et al. (2), who found that the subtraction image allows accurate localization of parathyroid adenomata but is less successful in patients with parathyroid hyperplasia. We have also demonstrated that satisfactory results are obtained, with shorter imaging times, when Tl-201 is given first, followed by Tc-99m. Injection of Tc-99m first does cause problems with Compton scatter, and we can see no compensating advantages.

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### Re: Mucociliary Clearance Mechanism in Smoking and Nonsmoking Normal Subjects

In a recent *Journal* paper by Isawa et al. (1), the authors observe that both overall and peripheral lung retention ratios of inhaled radioaerosol particles are significantly lower in smoking subjects than in nonsmokers. Their conclusion is that this represented accelerated mucociliary clearance due to more proximal particle deposition.

Physiologically, the disappearance of an inhaled substance from the pulmonary system may be due to mechanisms other than mucociliary clearance. It may not be feasible to use external gamma imaging to differentiate these mechanisms from each other with certainty, as a decrease in count rate will occur whenever the radiolabel disappears from the lung field being imaged. The substance under investigation can leave the lung field by mucociliary clearance, or it can move across the pulmonary epithelium and leave the region of interest by way of lymphatic or blood flow. The translocation of solute across the epithelium can occur through active mechanisms (ionic pumps, saturable carrier-mediated mechanisms, or pinocytosis) or by passive diffusion transcellularly or through the paracellular shunt pathways. The passive movement across the epithelium is dependent, in turn, on the molecular size and lipophilicity of the substance and the state of health of the epithelium.

It is possible that problems in the use of Tc-99m human serum albumin (HSA) in this study might have contributed to the findings of Isawa et al. First, despite its widespread use as a blood-pool agent, the binding efficiency, radiochemical purity, and biodistribution of Tc-99m HSA preparations have been shown to be variable (2–6). Second, in vivo degradation or modification of Tc-99m HSA molecules could have occurred, resulting in either leaching of the radiolabel or the formation of smaller molecules containing the label. It is conceivable that the airway and/or alveolar lining fluid might contain substances such as proteolytic enzymes capable of causing in vivo modification of HSA, and that smokers and nonsmokers may have different types or amounts of these substances in their pulmonary lining fluid. Third, increased pulmonary permeability to small solutes such as Tc-99m DTPA

has been reported in smokers (7,8). Further, in animals, cigarette smoke has been shown to cause airway epithelium to become permeable to even large molecules (such as horseradish peroxidase) that have molecular weights similar to that of HSA (9).

In the study of Isawa et al., one of the main objectives is to investigate mucociliary clearance. It is clear that the ideal substance for such an investigation should have most of the following properties. First, it should be inert to the pulmonary epithelium in order to avoid ambiguity during measurement of mucociliary function. Second, it should retain its radiolabel during the course of the study. Third, it should be of sufficient size so that its residence in the airway would not be shortened by a change in the permeability characteristics of the epithelium, or influenced by either active or passive mechanisms known to exist in the pulmonary epithelium. While no ideal marker has been found, it seems to us that Tc-99m sulfur colloid has distinct advantages over Tc-99m HSA in this type of study.

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## Reply

We appreciate the interest and comments of Logus and Man regarding our findings of a seemingly faster clearance of inhaled aerosol from the lungs in healthy smokers than in nonsmokers (1).

We have used Tc-99m albumin aerosol for more than 15 years now as an "inert and nonpermeable" substance to the pulmonary epithelium to investigate not only the ventilatory status or the space of aeration in the lungs (1-3), but also to study their mucociliary clearance mechanisms (1,5,6). We have never been bothered by increased background activity due to poor tagging of albumin.

We have been aware of the reports regarding increased per-

meability of the pulmonary epithelium in smokers when DTPA aerosol is inhaled (7-9). This is a very interesting finding, but the molecular sizes of DTPA and albumin are so different that it is hard for us to accept the factor of increased epithelial permeability to explain the seemingly faster clearance of inhaled radioactivity in the normal smokers. The fact that DTPA diffuses through the lung epithelium was first reported in 1968 (10). Actually when airway clearance efficiency is calculated, there is no difference between smokers and nonsmokers, and net clearance is not accelerated even in the smokers.

As we stated in the text (1), we believe that the increased mucus production and subclinical bronchoconstriction in smokers might be the main cause of this phenomenon.

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### Re: Quantitative Evaluation of Cerebrospinal Fluid Shunt Flow

The meticulous laboratory and clinical evaluation of cerebrospinal fluid flow in Rickham-Holter ventriculoperitoneal or ventriculocardiac shunts described by Chervu et al. (1), while clearly