that these other ligands (e.g., phosphate ion) may form different species with the main compound to be labeled, and/or may form an independent chelate with reduced form of technetium-99m. The labeling of the necrotic myocardium by Tc-99m heparin might be due to a combination of these factors. Further work is needed to identify the chemical nature of the species formed in the heparin kit with phosphate buffer medium. Our previous work shows that necrotic myocardium can be labeled and successfully imaged with phosphate-free Tc-99m heparin when blood flow is provided by reperfusion (*4*).

Further studies are needed to explore the structure and activity relationships among tagged heparin compounds as used in myocardial imaging and thromboembolic studies.

PADMAKAR V. KULKARNI
ROBERT W. PARKEY
JAMES E. WILSON III
SAMUEL E. LEWIS
L. MAXIMILIAN BUJA
FREDERICK J. BONTE
JAMES T. WILLERSON
University of Texas Health Science Center
Dallas, Texas

FOOTNOTES

* Abbott Laboratories.
† Upjohn Company.

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Re: Modified Technetium-99m Heparin for Imaging Acute Experimental Myocardial Infarcts

I read the paper from Kulkarni et al.(*1*) with interest and make the following comments regarding some factors that may influence the interpretation of the results. A lyophilized kit, such as that used by the Texas group, is composed of 150-200 IU heparin, 80 μg, Sn^{++}, and orthophosphate (2.34 mg phosphorous) per vial. The fact that phosphate is present during labeling must indicate that a Tc-99m phosphate label could be and probably is formed during the preparation of the Tc-99m heparin. If this be true, then caution is in order when myocardial infarcts are interpreted from images obtained using this method of preparation of the radionuclide. In point of fact we have been interested in the use of Tc-99m monophosphate as a myocardial infarct imaging agent, since the uptake in bone is lower than that with Tc-99m pyrophosphate.

TERENCE I. HALE
Nuklearmedizin
Kantonsspital
Schaffhausen
CH-8200 Switzerland

REFERENCE

1. KULKARNI PV, PARKEY RW, WILSON JE, et al: Modified technetium-99m heparin for the imaging of acute experimental myocardial infarcts. *J Nucl Med* 21: 117-121, 1980

Reply

We appreciate the comments by Dr. Hale. It is logical to ask the question that when there is more than one ligand present during the Tc-99m labeling process (in this case orthophosphate in heparin kit), how can one be certain that only a single ligand is labeled. The interpretation of the biological tissue distribution pattern of such a preparation requires careful consideration. In the Tc-99m heparin preparation (in the presence of Sn^{++} and orthophosphate) it is possible to have at least three species: (a) Tc-99m heparin complex, (b) a Tc-99m heparin phosphate complex, (c) a Tc-99m phosphate complex, assuming that there are no other radiochemical impurities, such as hydrolyzed reduced (unbound) Tc-99m and [^{99m}Tc] pertechnetate (free Tc). The exact quantity of the various possible species in our final labeled preparation is difficult to determine with certainty, and further radiochemical studies will be required to clarify this point. We have asked the manufacturer to provide any data that will assist in the identification of the Tc-99m species formed when the lyophilized material is reconstituted.

As pointed out by Dr. Hale, it would be interesting to evaluate Tc-99m monophosphate as a myocardial infarct imaging agent. We have done preliminary studies (in three dogs) with a preparation containing 80 μg Sn^{++} and orthophosphate (2.34 mg phosphorous per vial) without heparin. In the infarcted regions of dog myocardium after 48 hr fixed LAD coronary artery ligations, this preparation showed mildly increased uptake. Tissue concentrations of the radioactivity in the subepicardial and subendocardial regions of the infarct periphery were 5.9 to 7.7 times that in normal myocardium, and 2.8 times that in the subendocardium of the infarcts. Although the number of animals studied was small, the data indicate a trend that one might expect with this type of agent. These uptake values in the myocardial infarct are lower than the values reported in our study when we used Tc-99m heparin (orthophosphate buffer) (*1*). In infarcts this preparation had concentrations as great as 20 times that in normal myocardium at 48 hr after permanent LAD coronary artery occlusion in dogs. In addition, we avoided the presence of any phosphate ions in our earlier preparations of Tc-99m heparin (*2*). Our preparation also had an affinity for infarcted canine myocardium and could be successfully used for in vivo imaging of experimental myocardial infarcts when reflow was provided (*2*).

Further studies are required to evaluate the potential advantages of the Tc-99m heparin agents for imaging myocardial infarcts, identifying damaged myocardial vessels, thrombi, etc. It is clear, however, that labeled heparin *per se* has an affinity for damaged canine myocardium (*1,2*).

PADMAKAR V. KULKARNI
ROBERT W. PARKEY
JAMES E. WILSON III
SAMUEL E. LEWIS
L. MAXIMILIAN BUJA
FREDERICK J. BONTE

JAMES T. WILLERSON
University of Texas Health Science Center
Dallas, Texas

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Re: Ventilation-Perfusion Studies and the Diagnosis of Pulmonary Embolism: Concise Communication

An article in this *Journal* (*1*) linking the scintigraphic results and clinical findings in patients suspected of pulmonary embolism suggests that the information provides the referring physician with a rational basis for patient management. Other recent reports on the role of nuclear medicine in the diagnosis of pulmonary embolism have provided sophisticated analyses of their data, and the most commonly used perfusion scan parameters include: the size of the largest perfusion lesion, the degree of involvement of individual segments, and the correlation of the perfusion defects with radiographic and ventilation scan abnormalities (*2-4*). One important pattern recognition feature of perfusion images has been ignored, however, and we believe that knowledge of the frequency distribution pattern of segmental defects would be helpful as a diagnostic criterion of pulmonary embolic disease. Furthermore, this pattern may explain some of the reported advantages of different imaging techniques.

We reviewed our recent experience of six-view perfusion lung scans in patients suspected of having pulmonary embolic disease. Twenty-two patients with the typical scan findings were treated for pulmonary embolism. The frequency distribution of the 121 segmental perfusion defects is shown in Table 1, with some liberties taken in grouping various bronchopulmonary segments. The average number of perfusion defects per patient was 5.5; 67% were located in the lower lobes, 15% in the right middle lobe or lingulae of the left upper lobe, and 18% in the upper lobes.

TABLE 1. FREQUENCY DISTRIBUTION OF SEGMENTAL PERFUSION DEFECTS. TABULATION OF THE OBLIQUE OR LATERAL VIEW IN WHICH A DEFECT IS BETTER VISUALIZED

Segment*	Total defects	Oblique better visualizes defect	Lateral better visualizes defect
Posterobasal	25	12	—
Medial and/or anterobasal	20	10	—
Lateral basal	17	11	—
Superior	19	7	6
Medial/inf. lingula†	5	1	2
Lateral/sup. lingula†	12	—	—
Apical and/or posterior	13	—	2
Anterior	9	—	1
Total	120	41	11

* Individual or groups of bronchopulmonary segments.
† The right middle lobe and the lingular segments of the left upper lobe are grouped together.

The posterior oblique views were compared with the lateral views to determine which resulted in better lesion definition. As seen in Table 1, if lower-zone defects are better visualized in any one view, then the posterior oblique view is superior, whereas in the upper zones the lateral view is superior. In the middle zone of either lung field no one view was found to be superior. Fifty-two (43%) of all segmental defects were better visualized in one view, and in 41 (79%) the oblique view gave superior results.

Table 1 indicates that the superiority in visualization by the oblique view, a similar finding in other studies (*5*), is directly related to the distribution of these perfusion defects. Since the majority of perfusion defects are located in the lower lung zones and are better defined in the posterior oblique views, this view is more productive for visualizing defects. These data indicate, however, that when the perfusion abnormality is in the middle or upper lung zone (superior segment of lower lobes, middle lobe or upper lobes), then the posterior oblique view may not be the view to best define the lesion.

In summary, we believe that the frequency distribution of segmental defects is an important feature of pattern recognition of the scan findings in pulmonary embolism and should be included among the diagnostic criteria currently used. Based on our findings this distribution pattern explains the superiority of posterior oblique views in defining scan lesions in pulmonary embolism.

MICHAEL A. WILSON
BEHRAM PASTAKIA
ROBERT E. POLCYN
LINDELL GENTRY
University of Wisconsin
Madison, Wisconsin

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Reply

Dr. Wilson and his colleagues are right in indicating that patterns of perfusion defects may be helpful as diagnostic criteria in pulmonary embolic diseases. I am not sure, however, that the data in their table are useful for this purpose. First, such data would be useful only if the relative frequency of perfusion defects in various bronchial pulmonary segments was known for patients with pulmonary embolism *as well as* for patients without pulmonary em-