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.

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FOOTNOTES

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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.

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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*).

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