$$F(x,y) = Af(x,y) +$$

$$B \nabla^2 f(x,y) + C \nabla^4 f(x,y) + \cdots \qquad (1)$$

where

$$\nabla^2 = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2}.$$

Restricting further their attention to the case where only the first two terms of Eq. 1 are kept, they stated that the isotropic operation is realized by averaging scan data in four directions along two orthogonal axes. Under these assumptions their process will be isotropic.

Our concern is, however, with a more sophisticated two-dimensional process to meet requirements in the recent progress on scintigraphic image processing. The generalized linear and shift-invariant process is expressed by

$$F(x,y) = f(x,y) * g(x,y) \qquad (2)$$

where $g(x,y)$ is the certain filter function and the symbol * denotes the two-dimensional convolution operation. When $g(x,y)$ is circularly symmetric, i.e., $g(x,y) = g'(\sqrt{x^2 + y^2}) = g'(r)$, the process should be called "isotropic" in our sense. The isotropic process in our sense is realized by the omnidirectional scan but not by the four-directional scan without rotation.

We believe that omnidirectional scanning is particularly important for the process of scintigraphic image because the images are generally associated with statistical noise, the spatial frequency of which extends to a much higher frequency region than that of the signal, and accordingly a derivative or Laplacian operation is not practical due to excess enhancement of noise. Even in the case where F can be determined from f in a small region around point (x,y) in the process such as smoothing or deblurring (resolution enhancement), omnidirectional scanning will yield a better signal-to-noise ratio in the obtained image due to the averaging effect for noise in all directions.

As to the last comment on the amount of smoothing in "deblurring operation," we should like to record the following. Suitable filter response for deblurring, including smoothing, has been discussed by several authors and summarized by Kirch and Brown (5). The typical response has a peak at a suitable frequency with sharp cutoff at the high-frequency side. Such a response can be approximately realized by, in our system, the combination of a high-frequency enhancer (electronic filter) and a low-pass filter (defocusing the beam of the flying spot tube) having sufficiently sharper cutoff characteristics than the response of the enhancer. The cutoff frequency of the low-pass filter has to be appropriately higher than the turnover frequency of the enhancer. Adjustment of the overall response is made both by tuning the turnover frequency and gain of the electronic enhancer and by suitable defocusing of the beam such as looking at the processed image on a cathode-ray tube.

NORIMASA NOHARA
EIICHI TANAKA
National Institute of Radiological Sciences
Chiba-shi
Japan

REFERENCES

1. NOHARA N, TOMITANI T, TANAKA E: Analog image processing in two dimensions by omnidirectional scanning. J Nucl Med 15: 844–847, 1974

2. GREGG EC: Analog techniques for processing image data. In Quantitative Organ Visualization in Nuclear Medicine, Kenny PJ, Smith EM, eds, Miami, Fla, University of Miami Press, 1971, pp 417–429

3. KOVASZNAY LSG, JOSEPH JM: Image processing. Proc IRE 43: 560–570, 1955

4. BRAINARD RW, ORNSTEIN GN: Image Quality Enhancement. Report No AMRL-TR-65-28, Aerospace Medical Research Laboratories, Wright Patterson AFB, Dayton, Ohio, 1965

5. KIRCH DL, BROWN DW: Recent advances in digital processing static and dynamic scintigraphic data. In Proceedings of Second Symposium on Sharing of Computer Programs and Technology in Nuclear Medicine, CONF-720430, Oak Ridge, Tenn, 1972, pp 27–54

REPLACEMENT FOR ^{131}I ROSE BENGAL. IS IT REALLY?

The July 1974 issue of the Journal of Nuclear Medicine carried an article by Lin and associates (1) entitled "A ^{99m}Tc-labeled replacement for ^{131}I-rose bengal in liver and biliary tract studies." Their data are presented in three figures. The first figure shows ^{131}I-rose bengal and ^{99m}Tc-labeled mercaptoisobutyric acid-stannous chloride complex (Hepatobiliary Scintigraphin) blood clearance in one dog. The second shows the body tissue distribution of ^{99m}Tc-mercaptoisobutyric acid-stannous chloride complex in rats. The third shows scintigraphy of the liver and gallbladder in a dog. The authors do not list any references. The article appears to give the reader the impression that ^{99m}Tc-mercaptoisobutyric acid-stannous chloride complex is the first ^{99m}Tc-labeled compound that is concentrated by the liver and gall-

bladder. These authors neglect to mention how their product differs from previously described ^{99m}Tc-labeled compounds that concentrate in the liver and gallbladder. We reported in 1972 that ^{99m}Tc-labeled penicillamine is concentrated by the liver and gallbladder, both in experimental animals and in man (2,3). Technetium-99m-penicillamine has been used in man to evaluate gallbladder function and has been shown to compare favorably with contrast cholecystography (4). Dugal, et al (5) have labeled a bile acid analog (dihydrothioctic acid) with ^{99m}Tc and have shown that this agent can be used in dogs for quantitative analysis of gallbladder contraction using an image display-analysis system. This group has also shown that their agent preceded by cholecystokinin injection can be used effectively for the diagnosis of acute cholecystitis in man (6).

Lin and his colleagues have neglected to mention how their new compound differs from these previously reported ^{99m}Tc-labeled agents and, on the basis of animal studies, claim that their compound is a replacement for ^{131}I-rose bengal. Since their data show only that ^{99m}Tc-mercaptoisobutyric acid-stannous chloride complex is concentrated in rat and dog gallbladders, we feel that they should not imply that their agent is a replacement for ^{131}I-rose bengal studies in man. It is surprising that the reviewers who suggested a revision of the original manuscript did not note that in their article, Lin and his associates failed to refer to other previously reported ^{99m}Tc-labeled agents available for hepatobiliary studies. We question the implications of the title of their article and suggest that at this stage of development of ^{99m}Tc compounds for biliary tract studies that ^{131}I-rose bengal still has a role to play in human studies.

G. T. KRISHNAMURTHY
M. TUBIS
W. H. BLAHD
VA Wadsworth Hospital Center;
University of California at Los Angeles
(UCLA) School of Medicine; and
University of Southern California (USC)
School of Pharmacy
Los Angeles, California

REFERENCES

1. LIN TH, KHENTIGAN A, WINCHELL HS: A ^{99m}Tc-labeled replacement for ^{131}I rose bengal in liver and biliary tract studies. J Nucl Med 15: 613–615, 1974
2. TUBIS M, KRISHNAMURTHY GT, ENDOW JS, et al: ^{99m}Tc-penicillamine. A new cholescintigraphic agent. J Nucl Med 13: 652–654, 1972
3. KRISHNAMURTHY GT, TUBIS M, ENDOW JS, et al: ^{99m}Tc-penicillamine. A new radiopharmaceutical for cholecystography. J Nucl Med 13: 447, 1972
4. KRISHNAMURTHY GT, ENDOW JS, TUBIS M, et al: ^{99m}Tc-penicillamine cholescintigraphy: Comparison with oral cholecystography. J Nucl Med 14: 418–419, 1973
5. DUGAL P, EIKMAN EA, NATARAJAN TK, et al: A quantitative test of gallbladder function. J Nucl Med 13: 428, 1972
6. EIKMAN EA, CAMERON JL, COLMAN M, et al: Radioactive tracer technique in the diagnosis of acute cholecystitis. J Nucl Med 14: 393, 1973

THE AUTHOR'S REPLY

Krishnamurthy, Tubis, and Blahd are quite correct in pointing out that significant publications exist that are related to ^{99m}Tc-labeled agents for gallbladder scintigraphy. Since our paper on this subject was merely intended to be a concise report of our initial evaluation of a single new agent, we made no effort at either review of prior art or evaluation of relative merits of similar agents. We regret that our manner of presentation was found offensive.

It should be noted, however, that our choice of Sn(II) mercaptoisobutyrate for ^{99m}Tc-labeling in cholescintigraphy is neither arbitrary nor capricious. We have been developing and evaluating agents for this purpose for many years, and, indeed, we have extensive data in animals comparing a variety of agents. The agents we studied included those mentioned by Blahd, Tubis, and Krishnamurthy, and our animal data convinced us that our ^{99m}Tc-labeled Sn(II) mercaptoisobutyrate showed the most rapid and complete concentration in the liver with the least amount of concentration and excretion by the kidneys of all of the agents we evaluated. We thought that little would be gained by publishing such comparisons, however, since, in the final analysis, the relative clinical utility of the various agents becomes the only criterion of relative merits.

With regard to the disclaimer that the agent is a substitute for ^{131}I-rose bengal, our argument is simply that ^{99m}Tc has physical properties superior to those of ^{131}I with regard to use with existing imaging devices and that plasma clearance and hepatic concentration of ^{99m}Tc-Sn(II) mercaptoisobutyrate is more rapid and complete than that found with ^{131}I-rose bengal in experimental animals. Our conclusion that ^{99m}Tc-Sn(II) mercaptoisobutyrate is a substitute for ^{131}I-rose bengal in hepatobiliary studies is thus a result of the apparent superior physical and biologic properties of the former agent in comparison with the latter, at least in animal studies.

H. S. WINCHELL
Medi-Physics, Inc.
Emeryville, California