

days. Since the radiation effect is time-dependent, none of the four showed any evidence of damage. (There was not the slightest hint in any patient of leakage into abdominal cavity.) Control of radiation exposure to the staff was not difficult. For beta-particle, and a layer of glass or plastics with certain thickness was enough to serve as effective shields. We would appreciate it if Ho et al. (2) could kindly inform us about the methods they use to protect their surgeons during intraoperative probing.

On most of the Bremsstrahlung images of our patients, the liver could be dimly seen behind the hot spot of the injected dose. We did not think that this implies leaching of the tracer because the liver was visualized so early (30 min after injection of highly insoluble 20–45- μ m particles), and the liver activity was too uniform. However, the mechanism of liver's "showing out" was not clear, but scatter of the higher energy Bremsstrahlung radiation might account for that.

We are concerned about the radioactivity shunted to lungs as Ho et al. (2) mentioned. Moreover, Ho et al. (2) kindly calculated the shunt index in six of our patients. However, we would like to point out that the most significant difference between their studies and ours lies in the incidence of the shunt [six patients in our study versus almost all patients in the Ho et al. (2) study (3,4)]. Just as Ho et al. (2) kindly indicated, the dose of ^{90}Y -GMS was much smaller in our study (less than 0.7–1.1 GBq for any patient), therefore, no patient received a lung dose higher than 0.07GBq (2). That is, in fact, one of our reasons for choosing interstitial instead of intra-arterial treatment for liver cancer.

We sincerely agree with Ho et al. (2) that the dose-calculation in our study is far from proper. However, it was our belief that the distribution of interstitial injected ^{90}Y -GMS in the liver was not as unpredictable as given intra-arterially. As Fox et al. (5) indicated, the heterogeneous distribution of ^{90}Y microsphere introduced intra-arterially was so unpredictable that it varied even at different parts of the liver in the same patient. The uncertainty resulted in an "inferred dose." By careful surgery with real-time guidance of ultrasound, GMS could be administered to almost any part one wanted inside the tumor. Besides, we did take into account the volume of source in our calculation, and it showed the size of source had little effect on the periphery dose as calculated in our study. As in our article, we think the radiation to that part of the tumor is the most important, since many investigators indicated that the most active, recurrence-potential part of a tumor is around the periphery (5,6). The Valley's method served the purpose well.

We thank Dr. Ho for mentioning some of our mistakes such as lesion sizes. We apologize that the biggest lesion (Patient 7, 10.7 \times 7.6 cm) was not included in our statistics when we prepared the first manuscript because the patient died early after his treatment. We did not see any relation between the second point given by Ho et al. As for collimators, we used a medium-energy collimator merely for fear of higher energy penetration degrading the already not-so-good image since Bremsstrahlung from ^{90}Y has a wide energy range (7). Finally, we realized the combination of alcohol and chemotherapy at the beginning of our study might cause doubt on the effectiveness of ^{90}Y -GMS treatment. Though it was not our intention to compare the different modalities, we had the impression, although not verified, that the alcohol and chemical agents used in our institute for interventional treatment of liver cancer was not as good as radionuclide therapy, since fewer patients could survive such a long time.

As we mentioned in our article and Dr. Ho agreed, the interstitial use of ^{90}Y -GMS is not ideal, but it provided certain possibilities that enable us to reach our common goal. Many factors need further exploration, and we like to have more options and interests in this field.

REFERENCES

1. Tian JH, Xu BX, Zhang JM, et al. Ultrasound guided internal radiotherapy using yttrium-90 glass microsphere for liver malignancies. *J Nucl Med* 1996;37:958–963.
2. Ho S, Lau WY, Leung WT, et al. Partition model for estimating radiation doses from yttrium-90 microsphere in treating hepatic tumor. *Eur J Nucl Med* 1996;23:947–952.
3. Leung WT, Lau WY, Ho S, et al. Radiation pneumonitis after selective internal radiation treatment with intra-arterial yttrium-90 microspheres for inoperable hepatic tumors. *Int J Radiat Biol Phys* 1995;33:919–924.
4. Goldberg JA, Bradnam MS, Kerr DJ, et al. Arteriovenous shunting of microspheres in

patients with colorectal liver metastases: errors in assessment due to free pertechnetate, and the effect of angiotensin II. *Nucl Med Commun* 1987;8:1033–1046.

5. Fox RA, Klemp PFB, Egan G, et al. Dose distribution following selective internal radiation therapy. *Int J Radiat Oncol Biol Phys* 1991;21:463–467.
6. Roberson PL, Buchsbaum DJ. Reconciliation of tumor dose response to external beam radiotherapy versus radioimmunotherapy with ^{131}I -labeled antibody for a colon cancer model. *Cancer Res* 1995;55(suppl):5811s–5816s.
7. Andrew JC, Walker SC, Ackermann RT, et al. Hepatic radioembolization with yttrium-90 containing glass microspheres: preliminary results and clinical follow-up. *J Nucl Med* 1994;35:1637–1644

Jia-he Tian

Bao-wei Dong

Bai-xuan Xu

Jin-ming Zhang

The Great Wall Hospital

Beijing, China

Technetium-99m-Sestamibi Cellular Uptake: Passive or Secondary Active Transport?

TO THE EDITOR: Since it has been demonstrated that the cellular accumulation of $^{99\text{m}}\text{Tc}$ -sestamibi is driven by the plasma and mitochondrial membrane potentials (1), this agent is commonly considered as being taken up by the cells through a mechanism of passive diffusion. However, in biochemistry, the difference between passive and active transport is based on the fact that in passive transport the solute moves down its concentration gradient, while in active transport the solute moves against this gradient. Active transport resembles passive transport in its overall mechanism and kinetics properties, the only difference being that it requires energy to move the solute up its concentration gradient. Depending on the nature of this energy, two kinds of active transport are defined (2). Primary active transport uses energy directly from ATP hydrolysis, light or electron transport. Examples of active transport proteins utilizing ATP and involving common radiopharmaceuticals are the $\text{Na}^+\text{-K}^+$ ATPase, which can transport ^{201}Tl (3), and the P-glycoprotein involved in the multidrug resistance, which accepts $^{99\text{m}}\text{Tc}$ -sestamibi as a substrate (4). Secondary active transport uses a formerly established gradient across the cell membrane to transport a molecule of interest up its concentration gradient. The gradient used as a source of energy can be either an ion concentration gradient or a transmembrane potential, both being a form of potential energy. Finally, since only transmembrane electrical potentials drive the $^{99\text{m}}\text{Tc}$ -sestamibi cellular accumulation, this agent should be recognized as undergoing a secondary active transport, not a passive distribution. This would not only be a more accurate classification but it would be in better accordance with the fact that this agent can be used clinically for the study of myocardial viability and of tumor malignancy, two situations characterized by the presence of active metabolic phenomena.

REFERENCES

1. Chiu ML, Kronauge JF, Piwnicka-Worms D. Effect of mitochondrial and plasma membrane potentials on accumulation of hexakis (2-methoxyisobutylisonitrile) technetium(I) in cultured mouse fibroblasts. *J Nucl Med* 1990;31:1646–1653.
2. Devlin TM. Biological membranes: structure and membrane transport. In: Devlin TM, ed. *Textbook of biochemistry with clinical correlations*, 3rd ed. New York: Wiley-Liss; 1992:226.
3. McCall D, Zimmer LJ, Katz AM. Kinetics of thallium exchange in cultured rat myocardial cells. *Circ Res* 1985;56:370–376.
4. Rao VV, Chiu ML, Kronauge JF, Piwnicka-Worms D. Expression of recombinant human multidrug resistance P-glycoprotein in insect cells confers decreased accumulation of technetium-99m-sestamibi. *J Nucl Med* 1994;35:510–515.

Jean Maublant

Centre Jean Perrin and Auvergne University

Clermont-Ferrand, France

James Baggott

Allegheny University

Philadelphia, Pennsylvania