the amount of time one will have to spend scanning, or the amount of radioactivity that one will have to administer, it relates more to radiation dose considerations than to biologic considerations. The authors have excluded the radiation dose considerations from their rating system. Therefore, this parameter should be excluded as well.

Because of these drawbacks, it is difficult to imagine what, if anything at all, their rating system represents. To prove my point, let us consider two hypothetical agents, A and B, with the following experimental data for the four components used in their rating system:

Agent	% ad. dose per gram	Tumor-to-brain	Tumor-to-blood	Tumor-to-skin
A	2	10	10	1
B	3	3	3	2

According to their rating system, both agents should be rated equal, whereas with such high tumor-to-brain and tumor-to-blood ratios, and with only slightly inferior % administered dose/g and tumor-to-skin ratios, Agent A will be a far better choice than Agent B.

This fundamental weakness of their rating system is also evident in their radiopharmaceutical rankings. I am reproducing experimental data for the 4th ranked (one of the best) and 15th ranked (one of the worst) radiopharmaceuticals from Table 1 of their first paper (*1*).

	% ad. dose per gram	Tumor-to-brain	Tumor-to-blood	Tumor-to-skin
4th rank	3.04	6.8	0.25	1.13
15th rank	2.80	6.6	0.21	0.56

A glance at the data makes it clear that there is not a large difference between a good and a bad agent. The differences in the first three pairs of numbers are probably statistically insignificant. The only numbers that seem different are the tumor-to-skin ratios, which alone have pushed one to 4th place and the other to 15th place. Incidentally, when these authors used their experimental results in the rating system, they completely ignored the statistical significance of the differences between the measurements. Consequently, a tumor-to-blood ratio of 0.21 rated better than one of 0.19. Due to the want of the standard deviation data in their papers, I am unable to make a definite statement as to whether these two numbers are statistically different, but, from my own experience, it seems highly unlikely.

In conclusion, I feel there is a vital need for a suitable biologic parameter (figure of merit) with which to compare different radiopharmaceuticals in an experimental model system for brain scanning. I do not think, however, that the parameter used by Haynie et al. meets the desired need.

RAMESH CHANDRA
New York University Medical Center
New York, New York

REFERENCES

1. KONIKOWSKI T, JAHNS MF, HAYNIE TP, et al: Brain tumor-scanning agents compared in an animal model. *J Nucl Med* 16: 200–207, 1975

2. HAYNIE TP, KONIKOWSKI T, GLENN HJ: Technetium-99m stannous citrate brain-tumor uptake in mice: Concise communication. *J Nucl Med* 18: 915–918, 1977

3. EDWARDS AL: *Statistical Analysis.* New York, Rinehart and Company Inc, 1958, p 12

Reply

The letter of Dr. Chandra concerning "Rating of Radiopharmaceuticals for Brain Imaging" is acknowledged with thanks, since it stresses problems encountered by every investigator who attempts to study tumor-localizing agents. We respond not to justify the defects in our rating system but rather to emphasize again our previous admonition that these data should not be translated into the clinical sphere without due caution.

Point 1 in Dr. Chandra's letter is well taken. The rating system does not provide an index of how agents differ or how much they differ. From inspection it is apparent that some are quite close, others quite different in their values. In our previous papers we have provided figures for statistical significance. We did not think it appropriate in the rating system, which was more an attempt at "optimization" than at judging differences.

With regard to point 2, we cannot agree with Dr. Chandra that the percentage administered dose per gram of tumor does not belong in the rating system. It certainly is a measure of the avidity of the tumor for the substance. Limitations on available scanning time and radioactivity that can be administered also make this of importance. We do recognize that some rapidly excreted agents may achieve good ratios with low percentage uptake per gram. It is for this reason that we now also use percentage *retained* dose/g tumor as an alternate means of evaluation (*1,2*). We agree that tumor-to-skin ratios are not an entirely satisfactory substitute for "calvarial" contribution, but technical difficulty with this model confined us to this. The proximity of the calvarium to the detector, however, leads us to believe that its contribution to count rate makes it of considerable importance. Dr. Chandra's hypothetical case will be of importance if we ever encounter an agent with the bizarre characteristics that he postulates.

Among our suggestions for future developments has been the need for comparisons between existing tumor models and the results obtained in humans, in order to understand better the relationship between animal and human tumors (*3*). It should be our goal in laboratory research with tumor models to indicate to clinicians those trends and phenomena that can be observed repeatedly and that may be applicable to a better understanding of malignant disease in man. As Dr. Chandra points out, we have a long way to go.

THOMAS P. HAYNIE
HOWARD J. GLENN
The University of Texas System Cancer Center
Houston, Texas

REFERENCES

1. HAYNIE TP, KONIKOWSKI T, GLENN HJ: Technetium-99m stannous citrate brain-tumor uptake in mice: Concise communication. *J Nucl Med* 18: 915–918, 1977

2. GLENN HJ, KONIKOWSKI T, HAYNIE TP: Retained doses in brain-tumor scanning. *Appl Rad/Nucl Med* 6: 182–184, 204, 1977

3. HAYNIE TP, KONIKOWSKI T, GLENN HJ: Experimental models for evaluation of radioactive tumor-localizing agents. *Sem Nucl Med* 6: 347–369, 1976

Dry Aerosol Delivery System Compared with Ultrasonic Nebulizer

We have previously described a compressed-air system to