as patient-specific bladder volume, bladder residence time and filling and emptying rates can easily account for a factor of two difference in the dosimetry estimates. Furthermore, the calculated doses are being used as surrogates for risk. The uncertainty associated with these risk estimates (i.e., weighting factors) is at least as large as the uncertainty associated with the doses. Given all these uncertainties, small differences ($<\pm 50\%$) in estimates of dose are not very meaningful.

Despite the uncertainties, the Guidelines and Communications Committee listed effective dose or effective dose equivalent in dosimetry tables to provide a simple way to compare the magnitude of doses for a variety of nuclear medicine procedures. Important limitations of using these dose estimates as a surrogate for risk have been pointed out by the SNM's Medical Internal Radiation Dose committee (*7*) as well as the ICRP itself (*4*). For example, the weighting factors used are derived from age-weighted populations that have normal life expectancy. Application of these weighting factors to a specific age population that may not have a normal life expectancy may diminish the value of effective dose or effective dose equivalent as a simple surrogate for risk.

Any questions, comments or corrections to the SNM Procedure Guidelines should be directed to the SNM Guidelines and Communications Committee.

REFERENCES

1. Mandell GA, Eggli DF, Gilday DL, et al. Procedure guideline for radionuclide cystography in children. *J Nucl Med.* 1997;38:1650–1654.
2. Society of Nuclear Medicine. Procedure guideline for radionuclide cystography in children. In: Society of Nuclear Medicine Guidelines and Communications Committee. *Society of Nuclear Medicine Procedure Guidelines Manual 1999.* Reston, VA: Society of Nuclear Medicine; 1999:145–150.
3. International Commission on Radiological Protection. *Recommendations of the International Commission on Radiological Protection.* ICRP publication 26. Stockholm, Sweden: ICRP; 1977.
4. International Commission on Radiological Protection. *Radiation Dose to Patients from Radiopharmaceuticals.* ICRP publication 53. Stockholm, Sweden: ICRP; 1988.
5. International Commission on Radiological Protection. *Recommendations of the International Commission on Radiological Protection.* ICRP publication 60. Stockholm, Sweden: ICRP; 1991.
6. International Commission on Radiological Protection. *Radiological Protection in Biomedical Research.* ICRP publication 62. Stockholm, Sweden: ICRP; 1993.
7. Poston JW for the MIRD Committee. Application of the effective dose equivalent to nuclear medicine patients. *J Nucl Med.* 1993;34:714–716.

Henry D. Royal
Past Chair
Guidelines and Communications Committee
Mallinckrodt Institute of Radiology
St. Louis, Missouri

Kevin Donohoe
Chair
Guidelines and Communications Committee
Beth Israel Deaconess Medical Center
Boston, Massachusetts

Photodegraded Nifedipine Augmented Tumor Cell Uptake of Gallium

TO THE EDITOR: The recent article by Luttropp et al. (*1*) on the use of photodegraded nifedipine to promote the uptake of gallium into tumor cells is interesting and opens up several possibilities. The authors mention that the greatly augmented transferrin-independent gallium uptake into cultured tumor cells "may offer a way to improve the use of ^{67}Ga for tumor imaging." The 1000-fold increase in the transferrin-independent gallium uptake pathway made this 50-fold greater than in the transferrin-dependent pathway. As well as raising the possibility of usefulness in diagnostic imaging, this immediately raises the possibility of radiotherapy with gallium. In 1953, Andrews et al. (*2*) used ^{72}Ga to treat bone tumors but were unsuccessful because of the unfavorable radiation dosimetry. The use of photodegraded nifedipine may revive that method of therapy, especially in such tumors as lymphomas, which already often show good transferrin-dependent gallium uptake.

The other possibilities raised include strongly influencing uptake at various sites in the body for other radiopharmaceuticals, both in physiologic processes and in pathology. There may be many modifiers other than photodegraded nifedipine that can accomplish this. There have already been reports on such use with less dramatic results than with photodegraded nifedipine. Retinoic acid has been used to increase radioiodine uptake by causing redifferentiation in some dedifferentiated thyroid cancers (*3*). Accumulation of damaging ^{131}I in salivary glands during therapy for thyroid cancer has been reduced using amifostine (*4*). Such techniques would be ideally suited for nuclear medicine because of the inherent biochemical nature of nuclear medicine diagnosis and therapy.

REFERENCES

1. Luttropp CA, Vu C, Morton KA. Photodegraded nifedipine promotes transferrin-independent gallium uptake by cultured tumor cells. *J Nucl Med.* 1999;40:159–165.
2. Andrews GA, Root SW, Kerman MD. VI. Clinical studies with gallium-67. *Radiology.* 1953;61:570–588.
3. Grünwald F, Menzel C, Bender H, et al. Redifferentiation therapy-induced radioiodine uptake in thyroid cancer. *J Nucl Med.* 1998;39:1903–1906.
4. Bohuslavizki KH, Brenner W, Klutmann S, et al. Radioprotection of salivary glands by amifostine in high-dose radioiodine therapy. *J Nucl Med.* 1998;39:1237–1242.

Izzie Boxen
University of Toronto
Toronto, Ontario, Canada

Variability of Quantitative Scintigraphic Salivary Indices in Healthy Subjects

TO THE EDITOR: Salivary glands are assuming greater significance in recent days. Multiple and varied roles have been attributed to salivary contents and secretions. Apart from the widely known role in bolus formation, secretion of digestive enzymes and maintenance of oral hygiene, the reduction in the buffering capacity of saliva is being increasingly implicated in occurrence of gastroesophageal reflux disease and esophagitis. Absence of neutralizing capacity of salivary bicarbonates and other bases potentiates the acid reflux-based esophageal damage, as has been recently reported (*1*). Apart from the secretion of salivary immunoglobulins such as IgG, IgA and IgM, it has been speculated that the salivary glands may have a role in neuroimmunomodulation. In laboratory rodents, factors extracted from salivary gland have been shown to stimulate lymphocyte proliferation, to affect the weight of the thymus, spleen and lymph nodes, and also to induce immunosuppression in several in vivo animal models. The endocrine functions of the salivary gland include production and secretion of epidermal growth factor, nerve growth factor and vasoactive intestinal peptides, among others. In this context, the ability to quantify salivary function assumes greater importance.

Various quantitative parameters for estimation of salivary function using radioisotopic means have been suggested. Wide variability of the quantifiable parameters has been reported (*2*). Hermann et al. (*2*) discussed the noncentrality and dispersion of quantitative indices of salivary function. We believe that two crucial points need to be considered in arriving at a conclusion.

1. Dependability of quantified parameters: The partition percentage (PP) proposed as an index to identify composite function of individual salivary glands becomes inappropriate when its computation is extended up to 45min. By this time significant portions of salivary contents are lost on account of unstimulated salivary secretion. It is for this reason that the authors reported a PP of 66% for parotid glands and 34% for submandibular glands. These findings are discordant with the well-known finding that approximately 70% of salivary secretions are contributed from the submandibular glands. Of the total salivary secretion of approximately 1500 mL/day, it is known that the submandibular gland contributes approximately 1000 mL.

   Considering the episodic discharge pattern seen, the computation of net uptake ratio (NUR) as maximum counts of the glandular time-activity curve divided by initial postinjection counts (in short, salivary gland-to-background ratio) becomes unreliable. This argument is supported by the fact that the authors did observe a wide range of NURs for submandibular glands reaching 11-fold differences, whereas the range was narrower for parotid glands. The PP or any such index of salivary uptake may work if it is restricted to the first 3–5 min as done by Vigh et al. (*3*).
2. Selection and grouping of patients: The age group in the study of Hermann et al. ranged from 18 to 91 y; 25 of 31 subjects were women. In healthy subjects too, the salivary function varies with age and menstrual status. Mucin content and the concentration of the IgG and IgM decrease with age. Recently, a study of the patients selected from the 'Baltimore Longitudinal Study of Aging' has shown that premenopausal women had higher unstimulated submandibular secretions than postmenopausal women (*4*). Smoking, masticating and chewing habits too are known to modify salivary function. The authors (*2*) did observe weak relationship between age and functional indices, but, due to small numbers, the scatter was great.

The weakness of the quantitative parameters obtained should not be misconstrued as the inherent weakness of quantitative salivary scintigraphy.

The findings of Hermann et al. supplement our findings regarding the high frequency of unstimulated submandibular secretions (*5*). They have reviewed 32 salivary publications between 1971 and 1997 and surmise that the mean frame rate of dynamic salivary study was 231 s (range 30–1200 s). It appears that our study (*5*) was not noticed. We wish to point out that we used a frame rate of 5 s/frame and were able to segregate the so-called "episodic discharge" from the submandibular gland into various patterns. It varied from a sawtooth pattern (ripple pattern) to a slow and continuous discharge without any external stimuli. It would be interesting to know whether Hermann et al. noted such patterns in their 31 subjects. The authors (*2*) are right in pointing out that the submandibular glands contributed primarily to the oral pool activity before stimulation but state that about half the parotid glands showed multiple episodes of spontaneous nonstimulated excretion. We feel the incidence of parotid discharge reported is too high. Were the pattern and magnitude of parotid secretion similar to and coincident with submandibular secretion?

In conclusion, we agree that the indices proposed and evaluated by Hermann et al. are unlikely to be of use in decision making. A broader physiologic model for parametrizing such organ function has been proposed previously (*6*). We recently evaluated its application in salivary scintigraphy (*7*). The tracer input-output model has helped us in quantifying unstimulated secretion of salivary secretions, which we believe can be a major tool to evaluate xerostomia.

REFERENCES

1. Sarosiek J, Scheurich CJ, Marcinkiewicz M, McCallum RW. Enhancement of salivary esophagoprotection: rationale for a physiological approach to gastroesophageal reflux disease. *Gastroenterology.* 1996;110:675–681.
2. Hermann GA, Vivino FB, Shnier D, Krumm RP, Mayrin V, Shore JB. Variability of quantitative scintigraphic salivary indices in normal subjects. *J Nucl Med.* 1998;39:1260–1262.
3. Vigh L, Carlsen O, Hartling OJ. Uptake indexes and stimulated salivary gland response in $^{99m}TcO_4^-$ salivary gland scintigraphy in normal subjects. *Nucl Med Commun.* 1997;18:363–366.
4. Streckfus CF, Baur U, Brown LJ, Bacal C, Metter J, Nick T. Effects of estrogen status and aging on salivary flow rates in healthy caucasian women. *Gerontology.* 1998;44:32–39.
5. Malpani BL, Samuel AM, Ray S. Differential kinetics of parotid and submandibular gland function as demonstrated by scintigraphic means and its possible implications. *Nucl Med Commun.* 1995;16:706–709.
6. Rutland MD. Tracer flow in difficult organs. *Nucl Med Commun.* 1995;16:31–37.
7. Malpani BL, Jaiswar RK, Samuel AM. Noninvasive method to quantify unstimulated secretion from individual salivary glands. *Auris Nasus Larynx.* 1999;26:453–456.

Basant L. Malpani
Rajnath K. Jaiswar
Aban M. Samuel
Bhabha Atomic Research Centre
Mumbai, India

"N of 1": A Respectable Pedigree

TO THE EDITOR: With all due respect to and best wishes for success to our new Editor-in-Chief, it is disheartening to see that one of his first official acts was to pronounce the death sentence on the venerable single-case study (*1*). I do not agree with Dr. Martin Sandler, however, that discontinuing publication of case reports "...to concentrate on more substantive, multicase studies" will *improve* the *Journal of Nuclear Medicine*. I would argue the opposite.

Dr. Sandler's motives and qualifications are not in question. He acts in the best interests of nuclear medicine in these uncertain and turbulent times, and his position is not particularly enviable. But his action represents a wrong-headed vision of science, one which holds that the skillfully told single event or occurrence is inferior to the so-called "more substantive, multicase studies." It violates an inate logic which understands that every beach begins as a single grain of sand.

Case studies—the medical equivalent of the historically revered narrative of the raconteur—have a critical place both in clinical medicine and in science. Science that disregards the importance of single observations is a truncated version of that branch of