not those expected in light of the patient's diagnosis.

2. The time sequence and the symptoms are similar to those of other patients who have had adverse reactions to the radiopharmaceutical.
3. Further quality-control tests indicate a possible fault in the radiopharmaceutical.
4. Other patients exhibit similar symptoms. *It is often the case that increasing volumes of the radiopharmaceutical are administered as the radioactive tracer decays. In such cases, if there is a progressive increase in symptoms, such as fever, as the volume administered increases, this is strong evidence that the radiopharmaceutical is at fault.*
5. The patient's febrile response follows that expected in a pyrogen reaction. *Intravenous pyrogens cause, in man, headache and an elevation in body temperature beginning no sooner than ½-hr postinjection peaking 2–3 hr postinjection. Intrathecal pyrogens in doses too low to cause a reaction when injected intravenously may cause, in man, an elevated temperature peaking 4–8 hr postinjection. Pyrogens may also cause aseptic meningitis which is manifested by an elevation in cerebrospinal fluid cell count, headache, and neck stiffness in addition to fever.*
6. The nuclear medicine procedure was the only significant event that might have resulted in an adverse reaction, *e.g., the patient has not been started on any new drug regimen.*

B. The investigation should include:
   1. Interviewing all technicians, nurses, and staff involved with the patient to document the time sequence, symptoms, and possible causes.
   2. Identifying the vial which contains the suspected radiopharmaceutical.
   3. Instituting any quality-control tests such as pyrogen and sterility tests which seem appropriate.
   4. Checking other patients who received the same radiopharmaceutical.
   5. Identifying other possible causes of the reaction.
   6. Deciding to continue or discontinue the investigation using criteria listed above.

VI. If the radiopharmaceutical remains suspected, the following steps are taken.
   A. The manufacturer is notified, giving:
      1. the agent, lot number, dose, date of administration
      2. sequence of symptoms
      3. estimation of probability that the radiopharmaceutical is at fault.
   B. The patient's clinical course is monitored over the next few days with accumulation of additional quality-control data and data from the manufacturer.
   C. A case report is prepared and reviewed with the physician in charge of the patient and physician in charge of the nuclear medicine clinic.
   D. A report is sent to the manufacturer who in turn reports to regulatory agencies, i.e. AEC, and the Food and Drug Administration, and to the Adverse Reaction Registry of the Society of Nuclear Medicine.

We welcome comments and further discussion of this subject.

BUCK A. RHODES
HENRY N. WAGNER, JR.
Johns Hopkins Medical Institutions
Baltimore, Maryland

COMMENT ON "FRESNEL ZONE PLATE IMAGING IN NUCLEAR MEDICINE"

Barrett and others (*1,2*) recently proposed a method which permits a considerable increase in collection efficiency and sensitivity of gamma cameras, all other characteristics remaining unchanged. This method roughly consists of spatially coding the gamma beam by a Fresnel zone plate aperture and in decoding the picture by handling it as a hologram. It is very similar in its principle to methods of coding employed in fields as different as radar detection (*3*), infrared spectrometry (*4*), neutronic diffraction (*5*), or x- and gamma-ray astronomy (*6*). The success of these methods lies in the fact that they permit an increase of the signal without increasing the part of the noise which is independent from the signal (detector noise for instance) and without losing resolution. They thus permit, when the main noise is independent from the signal, a gain in signal-to-noise ratio (SNR) over the classical methods.

When the main noise is linked with signal (photon noise) as in nuclear medicine or in x- and gamma-ray

astronomy, the gain in SNR is not so clear. It depends for each point on the image of the ratio (σ) between the intensity of the signal in this point and the average intensity in the image. It is also a function of a parameter which corresponds in nuclear medicine to the transparency of the collimator (equal to one-half for a Fresnel zone plate).

Figure 1, drawn from a study on the application of these methods in neutronic diffraction (statistical chopper), gives an idea of the gain in SNR which we can hope to obtain. Thus the gain in SNR will be significant only for the points of the image presenting an intensity far superior to the average of the image (hence the interest for astronomy). For all other points, the gain will be either poor or a loss. A very simplified analysis will enable us to have a more thorough view of the problem.

If we do not take the geometrical problems into account, and if we consider a one-dimensional object and grid described by the functions f(x) and g(x), then the detector will record the convoluted image of the object by the grid, which is described by:

$$\int f(\tau)\, g(x-\tau)\, d\tau = f(x) * g(x)$$

The decoding consists roughly in convoluting the image once again by the grid-function. We then obtain:

$$h(x) = [f(x) * g(x)] * g(x) = f(x)\,[g(x) * g(x)]$$

For grids such as FZP, we have approximately:

$$g(x) * g(x) = \frac{1}{2}\,\delta(x) + \frac{1}{2},$$

the constant being due to the fact that the grid can only absorb gamma rays. Hence:

$$h(x) = \frac{1}{2}\,[f(x) + \int f(x)dx]$$

On the final image a background thus appears whose average equal to:

$$\frac{1}{2}\int f(x)dx$$

can be eliminated but whose statistical deviation from the average cannot be and entails a noise equal to:

$$\sqrt{\frac{1}{2}\int f(x)dx}.$$

The SNR in this method is then in every point:

$$(SNR)_{FZP}(x) = \frac{1}{\sqrt{2}}\,\frac{f(x)}{\sqrt{\int f(x)dx}}.$$

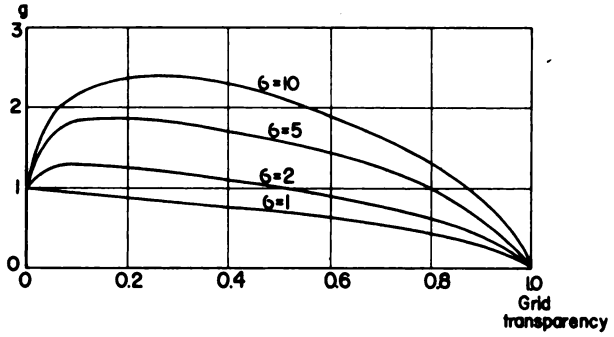

FIG. 1. Gain in accuracy of one-dimensional coding method compared to conventional one vs the grid transparency. Arranged from (Ref. 5), with permission.

In the classical method (pinhole), every point is imaged separately but collimator lets through approximately N times less photons, where N is the number of points to be imaged. The SNR is then:

$$(SNR)_{pinhole}(x) = \sqrt{\frac{f(x)}{N}}.$$

The gain g is then:

$$g(x) = \left[\frac{SNR_{FZP}}{SNR_{pinhole}}\right]^2 = \frac{1}{2}\,\frac{f(x)}{\frac{1}{N}\int f(x)dx} = \frac{1}{2}\,\frac{f(x)}{\mu} = \frac{1}{2}\,\sigma(x)$$

where $\mu = \frac{1}{N}\int f(x)dx$ is the average intensity of the image.

As a conclusion, the nature of the image and the origin of noise in nuclear medicine does not generally enable us to use the advantages those methods have proved to have in other fields. Nevertheless these methods enable us to obtain a tomographic effect and it would be very interesting to study their effective advantages in this field.

GILLES LEVY
Commissariat a L'Energie Atomique
Grenoble, France

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