Simulation Studies of Nuclear Medicine Instrumentation

A. G. Schulz

L. G. Knowles

L. C. Kohlenstein

ABOUT FIVE YEARS AGO A GROUP at the Applied Physics Laboratory began a study of the design of instrumentation systems for use in nuclear medicine under the guidance of Professor H. N. Wagner, Jr., of The Johns Hopkins Medical Institutions. A critical goal of these nuclear medicine systems is to produce an image of a soft organ within the body, such as the liver or brain, with the objective of detecting tumors or organ dysfunction.[1] The images are characterized by high noise levels and poor spatial resolution which make interpretation difficult. Improving the interpretability of these images through increased system performance is thus highly desirable. Attempts to develop a quantitative science for evaluating system performance have been hampered by the tedious and time consuming efforts necessary to conduct suitable experiments with clinical equipment. It appeared that all significant elements of the medical problem and the instrumentation could be simulated and "experiments" could be conducted on variations of the system with ease, using digital simulation techniques familiar to those with experience in the development of large systems. In the following sections a brief intro-

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1 H. N. Wagner, Jr., *Principles of Nuclear Medicine*, W. B. Saunders Company, Philadelphia, 1968.

A digital simulation of the radionuclide scanning process has been developed to aid in the quantitative evaluation of the clinical significance of instrumentation techniques and operational parameters associated with these systems. The impact of equipment design changes, radiopharmaceutical characteristics, and data processing on the ability of physicians to detect lesions in scan images has been evaluated. The simulation provides the capability to generate large numbers of scans in a relatively short time. This minimizes the problems of working with statistically noisy images which are typical in the science of nuclear medicine.

duction to nuclear medicine and its problems is followed by a discussion of these simulations and the results that have been obtained.

Nuclear Medicine

One of the most common procedures in the clinical repertoire is that of investigating thyroid structure and function. A salt containing a minute amount of radio-iodine is taken orally by the patient and the iodine normally begins to collect in the patient's thyroid gland. Within a few hours as much as 10% of the iodine is deposited in this small gland, and at 24 hours one-fourth of the iodine has been taken up by the thyroid. Often the nuclide administered is the isotope of iodine with atomic mass number 131 (^{131}I). The time history of the accumulation by the gland may be followed with a detector placed to view the patient's neck. This instrument detects the 364 keV gamma ray emitted by the decaying ^{131}I atoms. If the detector is shielded from receiving the radiation from regions other than the location of the thyroid, the measured gamma ray count may be compared to a count associated with the original administered dose to provide a percentage thyroid uptake as indicated above. The measured uptake may be compared to values determined over many years for normal patients to provide an indication of thyroid activity above or below the normal range. This information is then combined with the results of other tests to build up a diagnostic picture for a particular patient.

If a more sophisticated detecting instrument known as a gamma-ray scanner or a gamma-ray camera is used to measure the activity, the result is a visual image of the projected distribution of ^{131}I in the thyroid (Fig. 1). Instead of an average value of the iodine uptake for the entire gland, the projected image made with the gamma-ray "glow" emanating from the gland reveals the detailed uptake of individual portions of the gland. Such an image may show discrete areas of low activity within the gland where the tissue is not absorbing normal amounts of iodine or the image may show abnormal shape or regions of abnormally high activity. This visual presentation of the spatial distribution of the absorbed iodine thus adds another dimension to the diagnostic data since the presence of tumors and other lesions revealed in the picture can occur when the overall

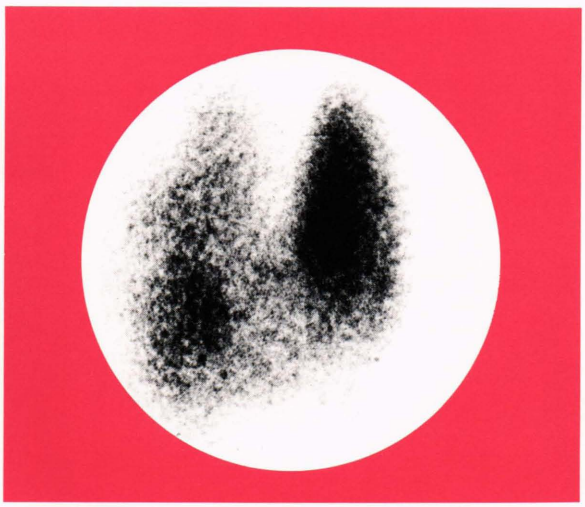

Fig. 1—A gamma camera image of a thyroid gland using ^{131}I as the radiopharmaceutical.

uptake measured by a simple detector is within the normal range. By using radioactive elements or compounds which are confined or absorbed by other organs or lesions of the body, the presence of abnormal function or shape can be studied for these structures in the same way.

This application of radioactive chemicals to the diagnosis and treatment of patients and to the study of the nature of human disease is the emerging clinical science of nuclear medicine. In many areas of diagnostic medicine such as the detection of tumors in soft organs like the brain, liver, and kidney, and in the detection of vascular

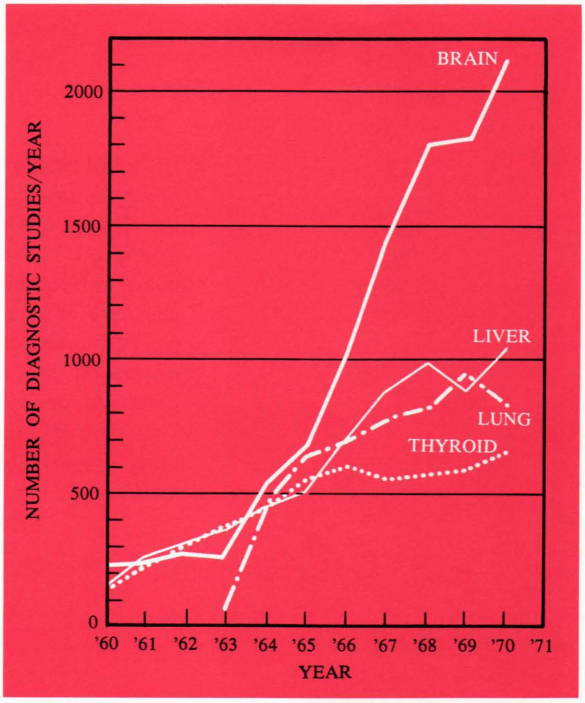

Fig. 2—Growth in the number of nuclear medicine examinations made annually at The Johns Hopkins Medical Institutions.

diseases such as pulmonary embolism, nuclear medicine is playing an increasingly important role. The clinical growth in the number of examinations at The Johns Hopkins Medical Institutions is presented in Fig. 2. The number of diagnostic brain, lung, liver, and thyroid studies per year for the last decade are shown in the figure. Brain examination was one of the first imaging applications of radioactive tracers and is the most frequently used technique, with over 5000 examinations made at Hopkins last year. Each examination involves five or more independent images of the patient's head taken from different directions. A brain scan view taken from the side is shown in Fig. 3.

Clinical use of diagnostic radionuclide imaging in the medical examination of the lung began to appear as a significant procedure in 1963 when new techniques were introduced by Professor Wagner and others which provided high effectiveness in detecting lung cancer, pulmonary embolism, and other lung defects.

The images of the thyroid and the brain illustrate the high noise level and lack of definition in the typical nuclear medicine image. The noise in these images arises from the poor predictabil-

ity in the decay of individual radioactive atoms. Since the decay of any given atom can only be predicted on a probabilistic basis, the decay activity from a group of atoms is characterized by random fluctuations. If counting experiments are conducted with equal intervals of time, the count will vary from one interval to the next. As the intervals are shortened, so that on the average fewer counts are received in the interval, the relative fluctuation from the mean will be larger. For instance, if the average count in an interval is one, the probability in a particular experiment of obtaining a zero count is equal to the probability of obtaining one count and the probability of obtaining two counts is half that of obtaining zero or unity. At very low count rates the chance of obtaining a measurement deviating from the "true" rate by 50% or 100% just due to statistical fluctuations is quite high. If we are doing an experiment in which the count rate is as high as 100 for the experiment interval, the probability of a statistical fluctuation error as large as 10% would be approximately 0.32. If the expected count were 1000, the probability of a 10% fluctuation error would be well under 0.01. To see how this characteristic of radioactivity is a primary underlying cause for the poor resolution as well as the noise in these images, we must examine more closely the technique for producing the image.

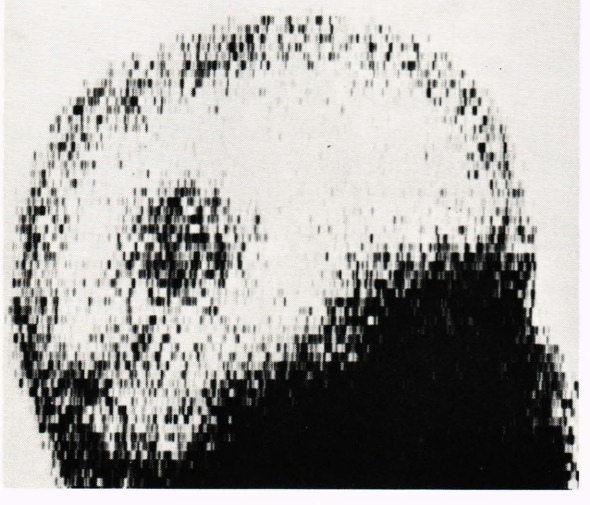

Fig. 3—A lateral brain scan of a patient with a brain tumor taken with a rectilinear scanner. The dark areas indicate detected radiation from the radioactive element ^{99}Tc administered to the patient and distributed in his blood.

Formation of the Nuclear Medicine Scan Image

The basic equipment and operations involved in forming a nuclear medicine image using a rectilinear scanner are indicated in Fig. 4. Gamma rays are emanating in all directions from the kidney which has collected the radiopharmaceutical administered to the patient. Gamma rays emerging from the body in a direction which passes through the narrow cylindrical channel in the lead collimator reach the sodium iodide detector crystal and are counted. Unlike visible light rays, gamma rays are so energetic that they cannot be focused to form an image. Although an arriving ray may

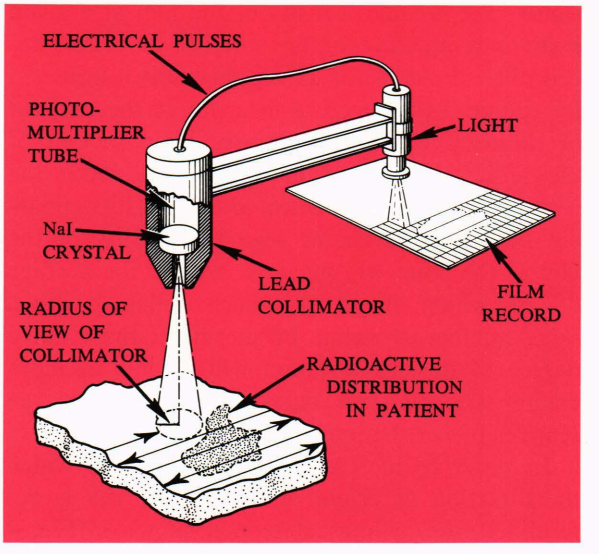

Fig. 4—Diagram of a typical rectilinear scanning instrument.

have been deflected into the detector channel by an accidental collision with an electron, in the normal case they reach the detector crystal along a straight line from the decayed parent atom. Hence, to a first approximation a gamma ray received at the detector is assumed to have originated in the narrow cylindrical section of the kidney shown in Fig. 4. The extent of the response volume from which gamma rays may pass through the collimator is characterized by the radius of the cylindrical section of the depth of interest. This quantity is referred to as the *radius of view*. In order to map the radionuclide concentration throughout the kidney, the detector is moved over the kidney area in a field-plowing pattern. This systematic survey of the area is referred to

as scanning, and nuclear medicine images made with either stationary "cameras"* or moving rectilinear instruments have been commonly referred to as radioisotope scans.

The scan image is generated by a photorecorder which projects a rectangular pulse of light onto an X-ray film each time a gamma ray falling within some predetermined energy range is counted. In order to portray the position of the source of the gamma rays, the projector in the photorecorder is moved over the film in a pattern identical in form and size to the pattern being traced out by the gamma-ray detector. At the end of the scan the developed X-ray film provides a full size image of the counts received by the detector. The relative density of the film at a given point is a measure of the number of counts received by the detector during the time it transited this point, and, hence, a measure of the amount of radioactivity in the corresponding section of the kidney. Recalling the discussion about the random fluctuation in detected counts, it is apparent that in a particular scan the density of the film at the point will fluctuate around the average density which would have been obtained with a large number of scans. Furthermore, the relative degree of density variation will be less as more counts are received during the time that the scanner passes the point.

In order to increase the precision with which the direction of origin of the gamma ray is determined, the cylindrical section shown in Fig. 4 may be made smaller in cross section (decreasing the radius of view) by increasing the length of the collimator hole or by making the hole diameter smaller. The effect is to better define the most probable source of the gamma ray to smaller regions around the axis of the collimator hole, but, unfortunately, *no data are obtained on the depth of the originating atom.* Since the face of the collimator cannot be brought closer to the organ because of the patient's body, any lengthening of the collimator or decrease in the size of the collimator hole introduced to *improve resolution* will result in a *reduced count rate.* The volume of radioactive material in the field of view of the detector crystal is correspondingly decreased. The net result is that the total number of counts in a given scan will vary approximately as the square of the radius of view of the collimator.

We now see why in practice the noise and the resolution in a scan image are controlled by the statistical fluctuations of radioactive decay. The resolution characteristics of existing collimators have been set by experience at a point which appears to give the most information. This point is a compromise which sacrifices achievable resolution to attain decreased fluctuation noise. Characteristically, scanning collimators have the capability for resolving distances of the order of one centimeter. This is to be compared to X-ray techniques where resolutions of tenths of millimeters are obtained and normal photographic techniques which go down to hundredths of a millimeter. On the basis of simple intuitive experiments and general clinical experience, scanning system designers had found that the reduced count densities obtained with higher resolution collimators had limited the visual information in the image because of statistical fluctuation noise. On the other hand, when lower resolution collimators were used, the lack of visual definition became the limiting factor even though the corresponding high count rates reduced fluctuation noise.

Scanning System Simulation

This problem of selecting the resolution of the collimator is a typical example of the state of design and application of nuclear medical instrumentation. Variations over extreme ranges in simple experiments had served to indicate approximate operating ranges, but no real design data existed which would permit quantitative estimation of expected performance of a particular design or what relative change in performance would result from a given design change. More counts in a scan must represent an improvement, but how much? We could double the administered dose of radioactivity with a small increase in risk to the patient. We could double the length of time devoted to a scan by buying more scanning instrumentation systems to accommodate the same patient load. We could increase the counting sensitivity of the scanners by designing them with larger and more expensive detector crystals. What

*Stationary detecting instruments, often called cameras, chart the emission pattern in all areas within the field of view simultaneously. Multiple detectors are arranged in such a way that the direction of the source of photons can be determined electronically. The camera is especially useful when investigating relatively fast physiological processes.

additional information would we obtain? What size lesions are we detecting now and how would this performance be changed? In principle these questions could be studied for existing systems by straightforward experiments. Analog organ and lesion phantoms could be filled with appropriate radioactive and inert materials to simulate the clinical problem and a scan could be taken with a clinical instrument. In order to obtain results which are independent of the statistical fluctuations in the image, a large number of such scans would be required for each experimental condition. The time and effort required to carry out these experiments is so formidable that only a few investigators had attempted them and only fragmentary results existed for a long time.

To deal with this problem, a digital simulation was set up which included as variable parameters the geometrical and chemical uptake properties of the organ and lesions, the physical properties of the radioisotope and its interaction with matter, and the characteristics of the scanning instrumentation system.[2] The system is programmed to compute the interaction of the radioisotope distribution in the lesion and organ with the scan detector to generate a precise equivalent of a clinical scan, including the fluctuation noise appropriate to the count density at each point.

Once a given organ/scanning system/radionuclide combination has been read into the computer, the generation of individual scans with varied lesion sizes and locations takes about 20 seconds. This is to be compared with times of the order of 20 to 30 minutes to take comparably varied scans with clinical scanners and analog phantom organs simulations. Analog phantoms are hollow plastic containers shaped like the organ being simulated which may be filled with a radioactive fluid to simulate a "hot" organ. A plastic sphere filled with nonradioactive water placed inside the liquid-filled organ would then represent a "cold" tumor. This combination of a "cold" tumor in a "hot" organ is representative of two types of problem studied most extensively in our work, namely, a liver or kidney in which the radiopharmaceutical was selected to be one which would accumulate in healthy organ tissue but would not be taken up by tumor tissue.

After the simulation computation is completed, the scan is shown on a special display developed for this application which stores and refreshes the image on a 20 by 25 cm cathode ray tube.[3] Sixty-four linear levels of light intensity are available in the display image.

Quantitative Study of Scanning Systems

According to the description of our simulation capability up to this point, we are in a position to vary the important parameters of the clinical scanning system problem and to generate and display statistically independent scans at a rapid rate. What kind of experiments can we run which will really develop quantitative design relationships between these parameters and system performance?

Since a critical diagnostic goal of the scan is the discovery of previously undetected lesions, the study of lesion detection in the neighborhood of the perception threshold should provide the kind of insight and functional relationships we seek. The basic experimental approach is to generate a series of scans which contain a particular size lesion at random unknown positions in the organ. In these scans the parameter of the nuclear medicine process or instrument to be studied is varied over the range of interest and a group of observers attempt to locate the lesions in each scan. The probability that the lesion will be detected is plotted as a function of the parameter studied. The process may be repeated for other lesion sizes or for other procedures or instrument characteristics. From these basic data the performance value of a given design feature or operating point may be determined, or conversely the performance to be expected for a given problem and diagnostic configuration may be predicted.

For almost all of our studies the observer is part of the experiment in a manner analogous to the physician being part of the diagnostic process. Our experiments consist of generating approximately 100 scans with a fixed set of design conditions in which lesions of various sizes are placed in the organ at random positions unknown to the observer. The observers are asked to ob-

2 A. G. Schulz, L. G. Knowles, L. C. Kohlenstein, R. F. Mucci, and W. A. Yates, "Quantitative Assessment of Scanning System Parameters", *J. Nucl. Med.* **11**, No. 2, Feb. 1970, 61–68.

3 L. G. Knowles and W. A. Yates, "The Flexicon", *APL Technical Digest* 7, No. 3, Jan.-Feb. 1968, 10–13.

serve the sequence of 100 scans in a test setting. For each scan the observer decides whether he detects the presence of a lesion and mentally notes its location. He notes via a push-button terminal connected to the computer that he believes *no lesion* to be present, or that he *suspects* the presence of a lesion at a particular location. After all observers have responded, the same simulated scan is presented with a small box indicating the center of the lesion, if one is present. The observers communicate to the computer the correctness of their observation of no lesion or of a correctly located lesion. On subsequent tests the parameter being explored is varied until the desired range is determined with adequate statistics.

Approximately 15 to 20% of these scans do not contain a lesion, and therefore the observers do not automatically "shoot" at anything that looks suspicious. In order to maintain conservative false positive rates (the erroneous detection of a lesion when none is present at the hypothesized location), the observers must exercise constraint and not guess at the existence of lesions in every frame. In our tests the observers had average false positive rates of about 20% of the total number of images observed.

Studies of System Parameters

A series of experiments was designed to determine the effects of variations in clinical operating procedures and instrument settings on the detection of lesions. Measurements of the detection performance of observers over a range of image count densities provide decision data on the length of time devoted to a scan (and hence on scan speed settings), on the amount of radioactivity administered to the patient, and on scan instrument characteristics such as detector sizes. Separate studies were made to determine the best settings for the instrument controls for raster line spacing, count rate smoothing using a time constant integrating circuit, and gamma energy window settings.

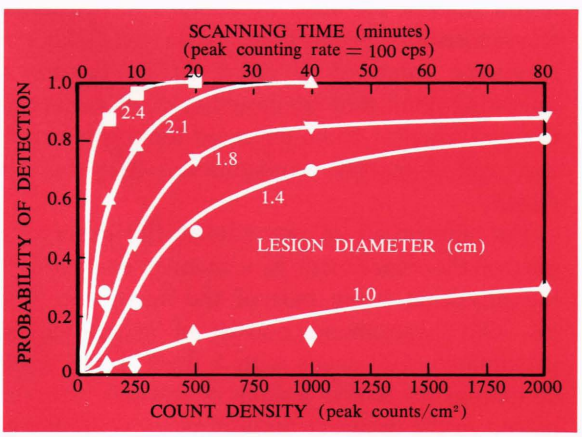

Fig. 5—Probability of detection of lesions of various diameters as a function of count density. The additional abscissa scale at the top relates scan time to detectability.

Count Density—The first studies run with the scanning procedure simulation determined the effect of image count density on the detectability of spherical lesions in a kidney. Several parameters of the instrumentation system and scanning procedures determine the density of counts in the visual image which in turn determines the fluctuation noise. The density of counts is directly proportional to the amount of radiopharmaceutical activity administered to the patient, to the duration of time the detector is scanning the organ, and to the area of the detector crystal. All of these factors affect the cost as well as the effectiveness of a diagnostic examination. Frequently, pharmaceuticals that can be administered in doses of higher activity are more expensive. If more time is devoted to each view of a scan examination, more instruments and staff are required to handle a given case load. The scanner with a detector having a large crystal costs more than one with a small crystal. These studies would provide a quantitative measure of performance improvement with which to compare such economic trade-off factors.

In these count density studies the lesion diameters varied from 0.7 cm to 2.8 cm. The scanner resolution corresponded to a 0.95 cm radius of view. The count densities ranged from 125 to 2000 counts/cm^2. Clinical experience for kidney scanning with a rectilinear scanner is characterized by count densities of the order of 250 to 500 counts/cm^2 depending on the scan instrument and radiopharmaceutical used. The results of this study are shown in Fig. 5. The probability of detection for various lesion sizes is plotted as a function of count density for all detections correctly evaluated by the observers. For the kidney these curves show that lesions of the order of 2 cm in diameter are fairly easily detected at present clinical count densities. As the lesion diameter approaches one

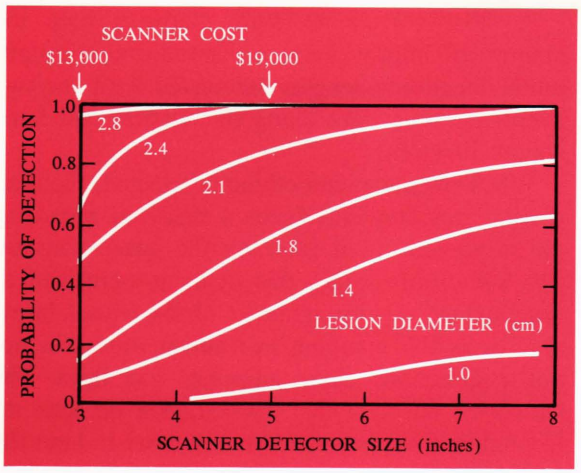

Fig. 6—Probability of detection of lesions as a function of scanner detector (crystal) size.

centimeter, the detectability falls significantly. For the larger lesions the improvement in detectability is quite marked between 250 and 750 counts/cm^2.

Rectilinear scanners have been made with detector crystal diameters ranging typically from three to five inches with occasional models having crystals as large as eight inches. The data in Fig. 6 would permit a physician interested in the diagnosis of kidney lesions to assess the difference in performance of the higher priced detectors. He would see that under the conditions of administered dose and scan time assumed in the study, the probability of detecting a 1.4 cm lesion in the patient's kidney would increase from less than 10% with a 3-inch-diameter crystal detector to better than 60% with an 8-inch-diameter detector.

The same data may be used to compare the use of pharmaceuticals labeled with different radionuclides. The differing decay schemes of the radionuclides lead to differing permissible administered doses of activity. This variation in administered activity coupled with the different tissue penetration and scattering characteristics associated with different gamma energies gives rise to significant changes in performance between radiopharmaceuticals. Figure 7 provides a comparison between ^{99}Tc and ^{131}I. The performance of a particular scanning system employing a five-inch-diameter crystal in detecting lesions of three different diameters is shown for ^{99}Tc and ^{131}I. This difference is entirely due to the higher activity that may be administered using the short half-life radionuclide ^{99}Tc. For comparison the performance that would be expected from a scanner with a three-inch-diameter crystal using ^{99}Tc as the radionuclide is plotted on the diagram and is seen to be superior to the five-inch crystal with ^{131}I. These kinds of comparative data may be used by physicians to assess the performance factor to be associated with economic factors in the trade-off between systems and pharmaceuticals.

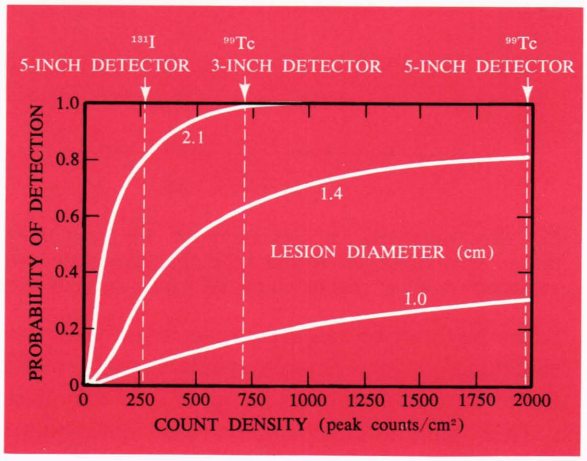

Fig. 7—Probability of detection of lesions as a function of count density. The scale at the top indicates the improvement to be expected as radiopharmaceutical and/or crystal size is changed allowing the same scan time in each case.

Effect of Line Space and Ratemeter Smoothing—One of the more important equipment settings that must be decided on before a scan can be taken is the distance the scan head is indexed between passes across the body. That is, given a certain amount of time dedicated to a specific scanning task, the clinician has the option of scanning at a relatively high linear speed and then indexing a small amount, or alternatively, choosing a somewhat slower speed and selecting a correspondingly larger distance between rows. Increasing the line spacing in this manner is essentially equivalent to simple spatial averaging in the direction perpendicular to the scan path. Averaging reduces the statistical noise but also tends to reduce the lesion contrast. A test series designed to systematically investigate the effectiveness of these several options was developed.[4]

[4] L. G. Knowles, E. F. Hart and A. G. Schulz, "Effect of Line Spacing and Time Smoothing on Lesion Detectability in Scanning", *J. Nucl. Med.* **11**, No. 6, June 1970, 336–337.

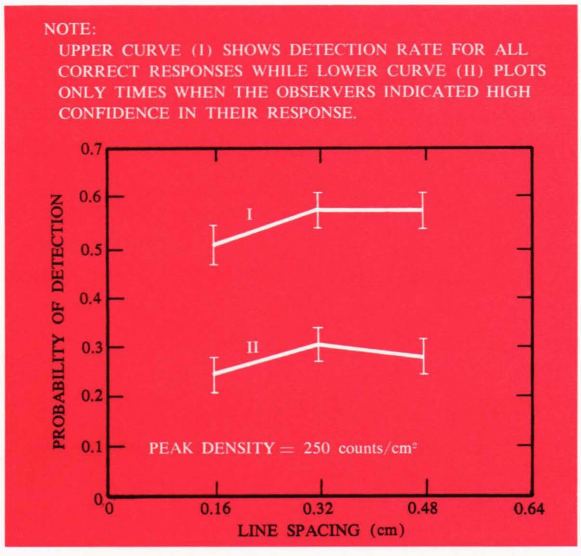

Fig. 8—Probability of detection of 1.6-cm-diameter lesion as a function of line spacing. Scan speed was adjusted in all cases to allow 10 minutes scan time.

Scans having two representative lesion sizes were generated at two different peak count densities. It was found that a line spacing of 0.32 cm offered a 15% gain in detectability over that obtained with 0.16 cm spacing. These data are shown in Fig. 8. It can be further noted that little additional gain is achieved by further increasing the index step size.

An averaging operation along the path of the scan is also available to the clinician. This on-line data processing option is called ratemeter smoothing and complements the line spacing technique of averaging perpendicular to the scan path. Ratemeter smoothing was introduced into the simulation by averaging the effect of a series of exponentially decreasing fractions of the preceding count history. This effect was then translated into a visual image that was equivalent to that which would have been produced if the output of an analog ratemeter with time constant τ had controlled the film density at every point in the scan. The data presented in Fig. 9 indicate that this type of smoothing can yield an additional 10 to 15% improvement over that already gained by scanning with the optimum line spacing. Improvement is noted as the space constant—a compound factor of time constant and scan speed—is increased from 0 to 0.25 cm. Further integration tends to decrease the lesion contrast faster than it decreases the noise so detection levels begin to fall off.

A close correlation exists between both the amount of improvement measured and the optimum integration lengths associated with the two averaging operations along the vertical and horizontal directions.

When ratemeter smoothing is selected, the integration function introduces a delay in recording the measured count rate. As the space constant gets sufficiently large, this delay is perceived as "scalloping," a misalignment of the visual information as the scanning instrument moves in opposite directions along adjacent scan lines. The "adverse" effect of this phenomenon on scan interpretation has persuaded many users to limit the space constant to a very small value. Little quantitative data has been published, however, on the degree of confusion larger amounts of "scalloping" might produce. Without contradictory evidence, one might postulate that some net gain in detectability of lesions may be made by increasing the space constant and accepting the fact that "scalloping" is noticeable.

In order to test this hypothesis, that is, to determine how ratemeter smoothing would affect detectability if scalloping were eliminated, an additional study was performed. A series of unidirectional scans was simulated where detection was inhibited while the detector indexed and rapidly retraced to begin scanning the next line in the same direction as in preceding lines. When the observer detection data were compared for both

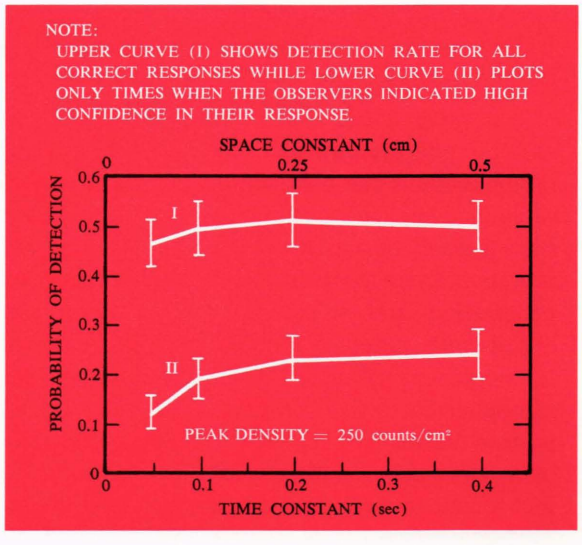

Fig. 9—Probability of detection of 1.6-cm-diameter lesion as a function of time constant selected. Scan speed was set at 1.25 cm/sec.

bidirectional and unidirectional scans under the same conditions reported in Fig. 9, there was essentially no difference between the two modes of scanning. Unexpectedly, "scalloping" apparently has little impact in this class of clinical problems.

Pulse Height Selection—When a gamma ray is scattered by collision with an atomic electron before it passes through the detector collimation system, it is no longer possible to associate the count with the location of the radioactive parent atom which emitted the gamma ray. It is only possible to conclude that the scattering atom is within the field of view of the detector, but this information is of no value. The counts from such collisions represent an additional background noise. Since the collision process causes the gamma rays involved to lose energy, the energy pulse transmitted to the crystal by these photons is smaller than for photons which had not been scattered en route from the parent atom. Most scanners use this energy differential or energy "window" to provide partial discrimination against counting scattered photons. The voltage pulse from the detector-crystal/electron-photomultiplier combination is proportional *on the average* to the energy of the gamma ray entering the crystal. Pulses corresponding to a much lower or much higher energy are not counted. In addition, the process provides only partial discrimination because the energy resolution in a typical sodium iodide detector is only about 20%. This spread of pulse heights for each gamma energy prevents complete discrimination between gamma rays differing by small amounts of energy.

The effects of this filtering by pulse height (energy) discrimination on the ability of observers to detect lesions was studied by simulating scans of a radioactive rectangular pseudo organ containing cold lesions.[5] This effect was determined experimentally by measuring the counts in a series of adjacent narrow energy intervals covering the range of interest and then simulating scans corresponding to various energy windows. The pulse height discrimination is referred back to the energy corresponding *on the average* to a particular pulse height. The upper edge of the energy window does not introduce any particularly

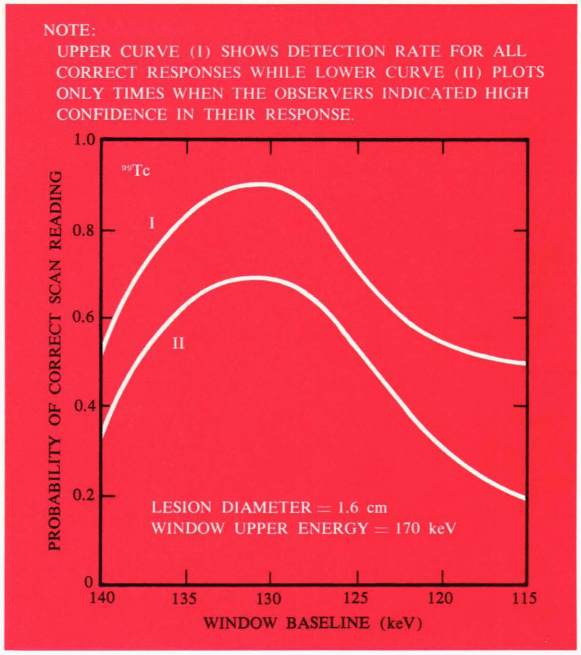

Fig. 10—Probability of correct scan reading as a function of energy window baseline for ^{99}Tc radiopharmaceutical.

interesting effects so the data are presented with a constant upper energy boundary and with the lower energy bound as the independent variable. The results obtained with the radionuclide ^{99}Tc are shown in Fig. 10 where the probability of detection of a 1.6-cm-diameter lesion is plotted as a function of the setting of the lower edge of the energy window which is referred to as the energy window baseline. The probability of detection increases rapidly as the window baseline is lowered from the center of the unscattered gamma-ray photopeak which is approximately 140 keV. The interpretation of this sharp increase is that more unscattered photons are being included in the final image. As mentioned previously, the crystal has poor energy resolution and many unscattered photons are falsely reported as having lost energy owing to scatter. Beyond about 130 keV, the increasing number of scattered photons carrying no information about the lesion depresses the capability to observe lesions by decreasing contrast and increasing fluctuation noise.

These experiments provided for the first time a quantitative measure of the effect of the gamma ray energy window setting on diagnostic capability to detect lesions. It now becomes possible to operate at the point of maximum effectiveness and to tell what is lost by operating at other points.

5 F. D. Rollo and A. G. Schulz, "The Effect of Pulse Height Selection on Lesion Detection Performance", to be published, *J. Nucl. Med.* **12**, No. 10, Oct. 1971.

TABLE 1

COMPARISON OF DETECTABILITY OF LESIONS IN SIMULATED SCANS VS CLINICAL SYSTEMS SCANS; NONMEDICAL OBSERVERS; CATHODE RAY TUBE (CRT) DISPLAY

Source of Scans	*Count Density (counts/cm²)*	*Lesion Diameter (cm)*	*Number of Observations*	*Detection Rate*
Clinical Scanner	550	1.8	1288	0.74 ± 0.02
Simulation	550	1.8	≈215	0.78 ± 0.06
Clinical Scanner	410	1.28	588	0.30 ± 0.04
Simulation	410	1.28	≈215	0.34 ± 0.08

Verification of the Simulation

Although great care was taken in its development, there is always the inherent danger that the simulation might not accurately model the scanning system. With this in mind, the initial simulation studies were designed to facilitate the evaluation of the functional accuracy of the simulation. Our scanning system evaluation studies using the simulation differ from clinical studies in several respects: (a) the studies are based on scans of phantom organs and lesions rather than using actual patients; (b) the phantom scans are generated on a computer rather than being obtained from clinical instrumentation; (c) the observers are engineers and physicists with a continuing involvement in nuclear medicine rather than medically trained personnel; and (d) a cathode-ray tube display is used to provide the image rather than the usual film photorecord.

The use of phantom organs and lesions is unavoidable. It is necessary to maintain precise control over the dose levels, uptake ratios, and the size, shape, and location of abnormalities. Obviously that degree of control cannot be accomplished with live patients. Although it is probable that there would be a slight variation in the absolute levels of detection between actual clinical experience and the simulation results for a specific problem, the main thrust of these investigations is to determine the relative effectiveness — either plus or minus—of the several parametric changes.

A deeper concern was felt for the remaining three important differences between the simulated scans and "the real world." A test series was developed to determine whether phantom scans obtained with clinical equipment produced the same results as computer-generated scans.

The simulation was designed to model a rectilinear scanner that is in regular clinical use at The Johns Hopkins Medical Institutions.[6] Likewise, a kidney phantom used at the same facility was incorporated into the computer simulation. Consequently, it was possible to run experiments using simulated and clinical scans of the same clinical problem. The validity experiment proceeded by first scanning the kidney phantom with the actual clinical instrument and recording the data both on the conventional film photorecorder and with a specially developed digital tape recording device. One hundred sixty scans were obtained with lesions of two different sizes placed at random positions in the phantom. The position and size of the lesions were recorded for each scan. When the scans were viewed later, the position of the lesion was unknown to the observers. Approximately 15% of the scans contained no lesion. Over a period of time the observers were asked to evaluate each of the scans several times. A similar experiment was conducted using simulated scans with the same size lesions and count densities.

The results of the evaluations of the computer simulation are shown in Table 1. The comparison is between: (a) scans simulated on the computer and (b) scans made with clinical equipment but with the data recorded on tape and then played back through the same CRT display that is used in the simulation system. The agreement in performance is remarkably good for both sets of conditions and for all observer confidence levels. These data confirm the basic validity of the computer simulation.

Using the scans made of the analog phantom with the clinical scanner, it was possible to compare the detection performance of medical observers to the nonmedical observers using both the normal photorecords and the CRT display. The results of this comparison are shown in Table 2.

For the nonmedical observers the similarity between the results of recorded scans displayed on the CRT and with photorecords is striking. This

[6] L. C. Kohlenstein, L. G. Knowles, and A. G. Schulz, "Comparison of the Detectability of Kidney Lesions as a Function of Count Density in Phantom Scans and Computer Simulated Phantom Scans", *J. Nucl. Med.* **10**, No. 6, June 1969, 415.

TABLE 2

COMPARISON OF MEDICALLY-TRAINED AND NONMEDICALLY-TRAINED OBSERVERS EMPLOYING CRT DISPLAY AND PHOTORECORDER

Type of Observers	*Count Density (counts/cm²)*	*Lesion Diameter (cm)*	*Number of Observations*		*Detection Rate*	
			Photorecord	*CRT*	*Photorecord*	*CRT*
Medically Trained	550	1.8	168	795	0.92 ± 0.08	0.80 ± 0.04
Nonmedically Trained			656	1288	0.82 ± 0.04	0.74 ± 0.02
Medically Trained	410	1.28	360	528	0.33 ± 0.07	0.15 ± 0.04
Nonmedically Trained			337	558	0.21 ± 0.06	0.30 ± 0.04

implies, at least, that no great gain (or loss) should be expected from the use of a linear TV-like presentation over the use of a carefully adjusted photorecord technique, once observers are comfortable using either system.

The medical observers were consistently better using the photorecord rather than the CRT display. This is reasonable since the physicians had far more experience with the photorecord technique. In this study the more experienced medical personnel, using the photorecords, had a somewhat better detection performance than did the engineers and physicists. While this difference might lead to a slight shift in absolute detection rates, it would not significantly effect system intercomparisons.

Summary

Although much empirical progress had been made in the evolution of nuclear medicine imaging systems, no design or performance equations existed that would permit quantitative optimization or performance prediction for the important procedure of tumor detection. Because of the statistical nature of the problem and the unmeasured subjectiveness of the physician's interpretation, the development of these relationships requires that thousands of independent experimental scans be generated and interpreted. The generation of these scans with clinical equipment and techniques is prohibitive in terms of time and money. Using techniques and digital computing facilities developed at the Laboratory for complex systems simulation, it was possible to generate and display highly realistic scans containing thousands of statistically independent images. With a combination of measured functions, such as organ geometry and detector spatial response in a scattering medium, a digital simulation was carried out which permits independent control and variation of all essential parameters of the clinical problem. These parameters include the radioactive label, the scanning instrument, and any desired real-time or post-scan data processing.

The simulation has been used in observer experiments to determine the capability of the instrument and the physician to detect lesions and how this capability changes as the physician varies his procedures and the settings of his scan instruments. The simulation permits the prediction of performance of proposed systems without carrying them to a complete hardware stage.

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