# INSTRUMENTATION

# Minimum Detectable Gray-Scale Differences in Nuclear Medicine Images

Frank R. Whitehead

*Searle Diagnostics Incorporated, Des Plaines, Illinois*

***An analysis of the effects of display-system characteristics upon the image from a nuclear medicine imaging system is presented. Simple, quantitative relationships are developed for calculation of contrast values for a minimum detectable lesion and maximum useful image count densities, from the slope of the D-log E characteristic curves of different films. The results provide a practical aid in the selection of films for various nuclear medicine imaging procedures.***

**J Nucl Med 19: 87–93, 1978**

A common complaint of nuclear medicine physicians is that standard specifications for imaging-system performance, such as resolution and sensitivity, do not adequately explain poor lesion visibility in clinical images. It is intuitively clear, for example, that diagnostic image quality should be affected in some way by the characteristics of the photographic film used for image recording. Thus knowledge of an imaging system's modulation transfer function and point-source sensitivity provides only a partial description of its important imaging characteristics.

The complete specification of low contrast lesion visibility in a gamma image can be obtained by describing the imaging system in the manner shown in Fig. 1. The basic imaging system, which consists of the collimator, scintillation detector, and pulse-counting electronics, creates an electronic count-density image that can never be viewed directly by an observer. This count-density image is used as the input to some display system, such as a persistence CRT or photographic film, to provide the final observable image. As a result, the characteristics of the final image depend not only upon the modulation transfer function and point-source sensitivity of the basic imaging system, but also upon the dynamic range and contrast amplification from the gray-scale transfer function of the display system. Whenever an image is to be viewed by a human observer, the appropriate gray-scale transfer function of the display system is a log-log plot of its input-output response, such as the familiar D-log E characteristic curve for photographic film. Even though the logarithmic function is nonlinear, the fact that the human visual system's psychophysical response function is also logarithmic (*1*) means that the analysis of an imaging system's gray-scale properties can still be done by the use of linear systems theory, if the analysis is done in terms of *ratios* instead of absolute signal levels. While this is a rather subtle distinction, it is extremely important, as is illustrated by the following example.

**Relationship between perceived gray-scale values and numerical contrast ratios.** Consider the common test of a computerized display system in which a step wedge is used to test the system's gray-scale response. Often this is done by starting with a certain minimum signal increment and then increasing the value of the input signal in staircase fashion, each step being an additional increment of signal over the previous one. Thus the tenth step has ten times the signal level of the first, the eleventh step has eleven times, etc. When one looks at such a display, the first few levels are easily distinguishable as separate gray-scale levels, but levels near the top tend to blend together. Although this problem can result from saturating the CRT display, this is usually not the case. Instead, the effect is exactly the visual response to be expected. In order to make all steps appear to be equal steps in gray-scale value to an observer, the input

Received Apr. 28, 1977; revision accepted Aug. 11, 1977.

For reprints contact: F. R. Whitehead, Searle Diagnostics, Inc., 2000 Nuclear Dr., Des Plaines, IL 60018.

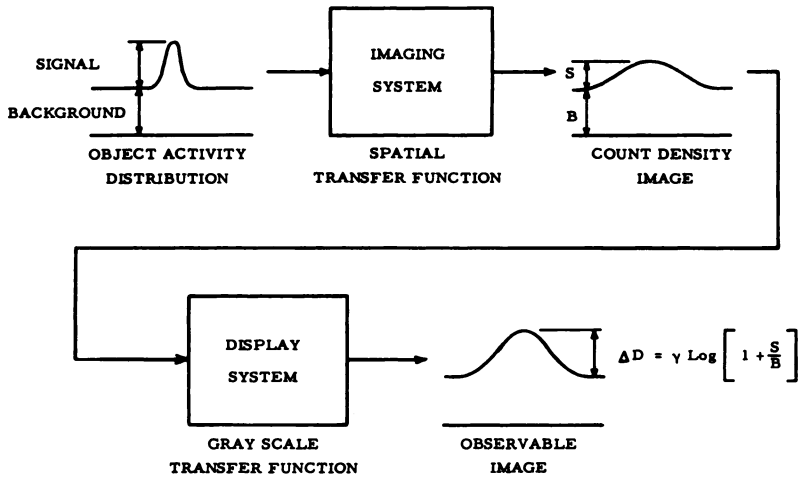


**FIG. 1.** Description of a nuclear medicine imaging system with a linear system model. Final image density difference may be related to the object signal-to-background ratio by means of appropriate transfer functions for imaging and display systems (Ref. 5).

steps should *not be equal increments* of signal level, *but equal ratios* of signal level. For example, if each input step is 20% greater than the previous step (i.e., the ratio of adjacent steps is 1.2:1), the resulting display will appear to have uniform steps in gray scale at both the high and low ends of the scale, provided the CRT response is linear on a log-log plot over the range of the input signal.

Because of the logarithmic response of the human visual system, the visually perceived gray-scale difference between adjacent steps in the display can be expressed mathematically by the equation

$$\Delta D = \gamma \log\left[\frac{\text{Step A}}{\text{Step B}}\right], \qquad (1)$$

where $\Delta D$ is the perceived gray-scale value expressed as an optical density change, and $\gamma$ is the slope of a log-log plot of the CRT brightness response function. Step A and Step B are the input signal levels for two adjacent steps.

The usual meaning of the term "gamma correction" is that the electronics for the CRT have been compensated for variations in the response function of the CRT so that the overall display system response has a gamma of unity over the largest dynamic range possible. Under this condition, the 20% steps in the example above will yield density differences of 0.08 units between adjacent steps.

For nuclear medicine images recorded on film, the perceived gray-scale difference between a lesion and its surrounding background can be determined in a similar manner. In this case, one has

$$\Delta D = \gamma \log\left[1 + \frac{S}{B}\right], \qquad (2)$$

where $\Delta D$ is again the perceived gray-scale value expressed as an optical density change, $\gamma$ is now the slope of the D-log E curve for the film, S is the incremental increase or decrease (for —S) in image counts per unit area caused by the lesion, and B is the average number of background counts per unit area in the image.

Note specifically that the signal-to-background ratio, S/B, is just the numerical contrast value of the lesion in the electronic image data formed by the scanner or scintillation camera. Thus if an image contains 500 counts per resolution element in the background area adjacent to a lesion that produces an extra 100 counts per resolution element, the lesion contrast value is 20%, and the density difference between the lesion and background will be found to be 0.08 units times the gamma of the film used for image recording. For example, the Polaroid films commonly used with nuclear medicine cameras have a gamma of about 1.3 (*2*), so that the final image density difference between lesion and background in this case will be about 0.1 units.

Observe that the perceived gray-scale difference for a given value of lesion contrast is directly proportional to the gamma of the film used for image recording. This is why high-gamma films produce high-contrast images, and vice versa. Also, if one wishes to copy a given image—for example one being displayed on a CRT monitor—without changing the perceived gray-scale values, it must be done by using a film with a gamma of one. As mentioned above, Polaroid film Types 084 and 667 have a gamma of approximately 1.3, so that attempts to copy images displayed on a CRT, using these films, are usually unsatisfactory unless one either desires the resulting increase in image contrast, or adjusts the original CRT display for a relatively "flat" appearance.

**Threshold gray-scale value for the human visual system.** As one would expect, there is a minimum detectable gray-scale value, or density difference, for the human visual system. As a practical matter, establishing a numerical value for this threshold density difference is difficult because it depends upon

several parameters, such as object size and shape, and the absolute brightness level of the image. We have found, however, that a reasonable value for nuclear medicine images of spherical lesions in a uniform background distribution is a density difference of approximately ±0.07 units (positive sign for hot lesions, negative sign for cold), when using the typical three-lens camera and Polaroid film display with lesions of 2- to 4-cm in diameter. Although this is obviously a "best guess" type of estimate, we will show that it leads to a straightforward explanation for the clinical practice of collecting approximately 1,000 counts per square centimeter in gamma images displayed on Polaroid film. Before we can do this, however, we must develop a method of quantifying the effects of random noise in an image.

**Effect of quantum noise on lesion perception.** Several qualitative effects of quantum noise in an image are well known to practitioners of nuclear medicine. First, there is the obvious fact that random fluctuations present in the images tend to obscure changes due to a true variation in an object's activity distribution. Second, as more and more counts are collected in an image in order to minimize these random deviations, diagnostic image quality improves, but only up to a certain level. There is nothing to be gained, for example, by collecting more than about 1200 c/cm$^2$ (plus or minus a couple hundred) of object area when the image is recorded on Polaroid film. Finally, many physicians have long maintained that use of standard radiographic transparency films for image recording (in a 70-mm format, for example) provides significantly improved image quality compared with Polaroid film. This is especially striking if more counts are collected in the images than would be useful with the Polaroid film. All these effects can be quantitatively explained from a surprisingly simple analysis of the statistical properties of a quantum-noise-limited image. This analysis, first given by Rose (*3*) on standard television images, is paraphrased here in terms of a nuclear medicine image.

One asks the question: "What is the possibility that a variation in counts equal to, or greater than, that caused by the presence of the lesion occurs somewhere in the image simply as a random accident in the background distribution?" The answer to this question is the probability of obtaining a false-positive lesion in the image. For example, suppose the difference in counting rate between a lesion and its adjacent background is 15%. If an average of 500 counts per resolution element is collected in the image, the difference between a resolution element containing the lesion and one that does not is 15% of 500, or 75 counts. For Poisson-distributed noise, the probability that a random accident would cause a count deviation of 75 or more counts in a resolution element that does not contain the lesion is approximately 0.0008. Standard nuclear medicine cameras with a 10-in. field of view have about 500 resolution elements, so that the average number of errors in a single image is 500 × 0.0008, or 0.4. Using a table (*4*) of the summed Poisson probability function, we then find that there is a 33% chance that any given image will have one or more statistical variations in the background level that are equal to, or greater than, the count difference caused by the presence of the lesion. Obviously, no observer will be able to make a reliable statement about the presence or absence of a 15% contrast lesion in such an image, because there is a high probability that any 15% variation between different resolution elements is merely a random deviation in the background level.

Note that it is necessary to consider the problem based on a single resolution element, because there is no *a priori* way to know that the lesion is larger than this, and even if it is, we still wish to know that the image represents an accurate representation of its size and shape. Therefore, we must be confident that each resolution element appearing to contain a lesion actually does so, rather than merely containing a random change in the background distribution. Thus the calculation for a false positive is based on the total number of resolution elements in the image, rather than the number of areas in the image equal to the size of the lesion.

For an average count density of 500 counts per resolution element, the RMS variation in count density is 22 counts per resolution element. The lesion variation of 75 counts per resolution element is approximately three times this RMS value, so that in effect one has a signal-to-*noise* ratio of 3 to 1 in the example considered. (From this point on the reader must note carefully the distinction between signal-to-*noise* ratio and signal-to-*background* ratio.) The above calculation of the probability of an error has shown that this is inadequate for reliable detection of the lesion, and from a similar calculation (*4,5*) it is possible to show that a signal-to-noise ratio of between 4 and 4.5 to 1 does provide reliable detection of the lesion. A signal-to-noise ratio of 4 to 1 results in an error rate from random variations in the background of 1.5% for a nuclear medicine image from a camera with a 10-in. field of view. For 15-in. fields of view it is necessary to approach a signal-to-noise ratio of 4.25 to 1 in order to maintain this error rate, simply because there are approximately twice as many resolution elements in the larger field.

In addition to random variations on the background, the signal also has random variations. As pointed out by Rose (*3*), this means that any given signal-to-noise ratio represents only an average value, and the actual value for a particular image is less than this value 50% of the time. Obviously, this will increase the probability of an error and, in fact, numerical integration with a digital computer shows that the error is approximately doubled. To return to an overall error rate of less than 2%, it is necessary to increase the average value of the signal-to-noise ratio to 4.25 to 1 for cameras with a 10-in. field of view, and to 4.5 to 1 with a 15-in. field of view.

*In short, the minimum detectable lesion contrast or signal-to-background ratio is between 4 and 4.5 times the RMS noise level divided by the average background level.*

**The minimum detectable gray-scale value in a nuclear medicine image.** The results of the above analysis for quantum noise effects in a nuclear medicine image, and the relationship between lesion contrast and image gray-scale values, given by Eqn 2, can be combined to develop an expression for the minimum density difference that will be statistically reliable in any nuclear medicine image. With a background level of N counts per resolution element and a signal-to-noise ratio of k, the statistically reliable signal level is given by

$$S = k\sqrt{N}, \tag{3}$$

so that the signal-to-background ratio is

$$\frac{S}{B} = \frac{k}{\sqrt{N}}. \tag{4}$$

Substitution of this expression into Eqn 2 yields the density difference produced by this minimum detectable lesion contrast value. Thus,

$$\Delta D = \gamma \log\left[1 + \frac{k}{\sqrt{N}}\right]. \tag{5}$$

Equation 5 gives the statistically reliable photographic density difference or minimum detectable gray-scale value, for an image containing N counts per resolution element. The statistical reliability of this density difference is determined by the value chosen for k, the signal-to-noise ratio, whereas the numerical value of the density difference is determined by the number of counts per resolution element in the image, N, and the gamma of the film chosen for image recording. This minimum detectable gray-scale value is reduced in magnitude as more counts are collected in the image, so that smaller differences between lesion and background radionuclide uptake are observed at higher count densities. Obviously, with a sufficient number of counts, the minimum detectable gray-scale value can be made equal to the threshold of detection for the visual system. *At this point, accumulation of more counts in the image is simply a waste of time, because no perceptible increase in image quality will occur.* Even though lower-contrast lesions will be displayed with statistically significant density differences as the number of counts increases, these lesions will not be detected by the observer because their density differences will be below visual threshold. Thus, there is a maximum useful count density for a nuclear medicine image, and its value depends upon the visual system's detection threshold, the signal-to-noise ratio needed to obtain a desirably low probability of a false-positive lesion in the image, and the gamma of the gray-scale transfer function of the film or CRT system used for image display. Note, also, that this maximum useful count-density value is the point where random fluctuations between *different resolution elements* in the image are no longer perceived by the observer. Thus the image becomes subjectively pleasing at this point, in the sense that it no longer appears "noisy."

**Maximum useful count densities and minimum detectable contrast values for different films.** From the preceding analysis, it is relatively straightforward to compute the maximum useful count density and minimum detectable lesion contrast value for nuclear medicine images displayed on different types of film. The difficult part of this calculation is determining the precise signal-to-noise ratio needed to obtain a specified probability for a false-positive lesion. We will choose a signal-to-noise ratio of 4.25 to 1, which corresponds to an approximate 2% probability of a false-positive lesion at threshold contrast on Polaroid film. More detailed formulae for determining the false-positive rates with other values of signal-to-noise ratio and lesion contrast are given in another publication (*5*).

Numerical values for the maximum useful image count density, for any given film and selected value of signal-to-noise ratio, may be calculated by rearranging Eqn 5 to obtain

$$N = \frac{k^2}{[10^{\Delta D/\gamma} - 1]^2} \tag{6}$$

where k is the required signal-to-noise ratio, $\Delta D$ is the threshold of visibility for the human visual system, $\gamma$ is the slope of the D-log E curve for the film, and N is in counts per resolution element.

Now let us calculate the maximum useful count densities for images of hot and cold lesions displayed on Polaroid film, which has a gamma of approximately 1.3 (*2*). For hot lesions we use the visual

threshold value of +0.07 density units and obtain a maximum useful count-density value of 1036 counts per resolution element. For cold lesions we use −0.07 density units for the visual threshold value and obtain a corresponding maximum usable count density value of 1328 counts per resolution element. Most nuclear medicine cameras have a resolution element approximately 1 $cm^2$ in area, so these values correspond to the maximum useful number of counts per $cm^2$ in the image. Although both of these numbers appear to be consistent with standard clinical practice, we emphasize that they are dependent upon an arbitrarily accepted false-positive rate and visual threshold value. Other values of false-positive rate obtained by choosing a slightly higher or lower value for the signal-to-noise ratio will vary the calculated count-density values by 10–20%. Also, differences in the observer's visual threshold, because of complex background structure, or variations in viewing conditions, will cause significant changes in the calculated maximum useful count-density value. Thus the importance of this result is not its numerical accuracy, but the relatively simple and straightforward relationship between the human visual system threshold, photographic film characteristics, imaging system resolution, and the number of counts needed in a nuclear medicine image.

If the count-density values calculated from Eqn 6 are used in Eqn 4, we can obtain the minimum detectable *lesion contrast value* for any given film. Thus with Polaroid film the minimum detectable lesion contrast values are 13% for hot lesions and 11% for cold lesions. Note that the lower contrast requirement for detection of cold lesions results from the logarithmic relationship between optical density difference and contrast ratios. This difference in the minimum detectable contrast ratio for black-on-white against white-on-black is often a confusing and controversial observation in psychophysical experiments. It is important to recognize the simple "mathematical difference" between black-on-white against white-on-black in order to avoid confusing it with more complex phenomena such as changes in the visual system's gray-scale response characteristics with variations in average light level. This latter phenomenon also produces variations in the visual system's contrast detection threshold between white-on-black against black-on-white. In this case, however, there is an actual change in the visual system's response characteristic. We note also that the "mathematical difference" in contrast detection for black-on-white against white-on-black does not imply an inherent advantage for viewing a positive against a negative image or vice versa. The effect we are discussing results from a change of algebraic sign inside the brackets of Eqn 5. Positive and negative images result from changing the algebraic sign for the film gamma (which is outside the log function) and this produces no alteration in contrast perception.

As a second example, let us calculate the maximum useful count density and minimum detectable lesion contrast values for a high-contrast transparency film such as Kodak nuclear medicine film type SO-179. This film has a gamma of approximately 2, so that for a signal-to-noise ratio of 4.25 to 1 and a visual threshold value of ±0.07 density units, the maximum usable count densities for hot and cold lesions are approximately 2,500 and 3,000 counts per resolution element, respectively. Applying Eqn 4 we find that the minimum detectable contrast value for hot lesions is approximately 8.5%, whereas the value for cold lesions is about 7.75%. Again, we emphasize that these numerical values result from an arbitrary tolerance on false-positive rate in the image and therefore are meant to be benchmark values only. The numerical difference from Polaroid film is definitely significant, however, since the same values for visual threshold and signal-to-noise ratio were used for both films. The higher gamma of the SO-179 film allows a significant improvement in minimum detectable lesion contrast and maximum useful count density. Although use of films with even higher values of gamma would theoretically offer further improvement, problems with patient comfort and motion blur, due to the long study times required, probably make impractical the use of films with gamma values greater than 2.5 or 3.

Since the use of a high-contrast film (gamma greater than 2) will always increase the visibility of image gray-scale values, even when high count densities are not used, it may appear that one should simply use such a film for all image recording. Note, however, that if a high-contrast transparency film, such as SO-179, is used with a count density appropriate for Polaroid film, the image will contain distinctly visible quantum mottle. The presence of this quantum mottle will then give the appearance of a complex background structure to the image, and this *may* have the effect of increasing the observer's visual threshold, thereby decreasing his diagnostic accuracy. Also, nuclear medicine physicians have commented that the visibility of quantum mottle in a liver scan, for example, can make it difficult to determine the presence of diffuse liver disease. Thus we caution that selection of the appropriate film for any particular procedure involves other factors that are not considered in the simple analysis presented above.

**Minimum detectable target-to-nontarget ratios for**

**spherical lesions.** In order to estimate the potential clinical significance of the use of different films for image recording, the minimum detectable target-to-nontarget ratios for various-sized spherical lesions were calculated for two hypothetical imaging problems with a high-quality gamma camera. The detailed procedure for such calculations is given in another publication (*5*). Results for the first problem, meant to simulate detection of a brain lesion are shown in Fig. 2, and the results for the second, meant to simulate detection of a lesion in a liver, are shown in Fig. 3. Both figures compare lesion detectability using Polaroid film with that obtained using higher-contrast Kodak SO-179 transparency film.

The predicted improvement in performance with the higher-contrast film is quite significant and was actually unexpected by the author before doing the numerical calculations. With hindsight, however, it is easy to see that such a large variation in minimum detectable contrast ratio is reasonable, because the film's gamma enters the equations as an exponent. Small changes in the numerical value of an exponent can easily cause significant changes in the results from a power-law relationship such as the one for photographic image contrast.

For those interested in the experimental comparison of these films, we caution that all films must be properly exposed and the developed images viewed with the proper illumination. For example, the approximate midrange of the D-log E curve for SO-179 film is at the relatively high density value of 1.5. When viewed on a standard radiographic illuminator, such films appear to be much too dark unless both background room illumination and any uncovered portions of the view box are blocked out. It is impossible to view a properly exposed SO-179 film in the same room as a Polaroid print, because the dynamic range of the human visual system is not sufficient for the differences in light levels. In addition to proper exposure and viewing procedures, it is also advisable to make quantitative measurements of the gamma for the SO-179 film in order to maintain quality control of the development equipment. Reasonable control over the Polaroid print films can be maintained by strict adherence to the manufacturer's instructions regarding development time and room temperature.

## CONCLUSION

Analysis of the relationship between photographic film characteristics and diagnostic image quality leads to several important conclusions for nuclear medicine images. First, even for the ideal case of a noise-free image, the minimum detectable value of lesion contrast is determined by the choice of film used for image display. This is because the film is actually

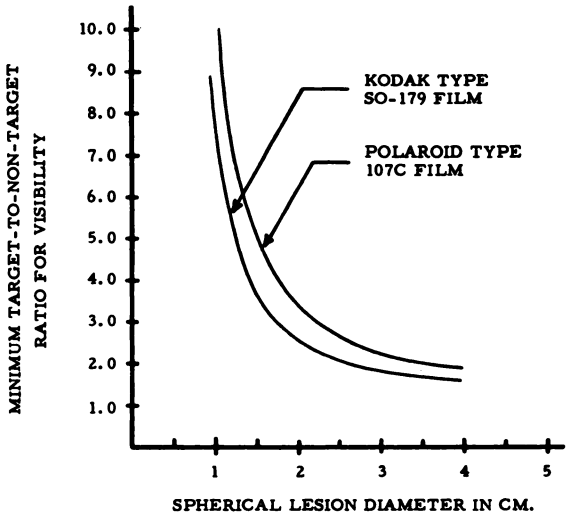


**FIG. 2.** Minimum detectable uptake ratios for various-size hot spherical lesions. Lesions are 5 cm deep, in 15-cm-thick background. Imaging system uses a parallel-hole collimator, has 10-mm FWHM line-spread function, and 30% energy window. Required count densities are 1,300 counts per $cm^2$ for Polaroid film, and 3000 counts per $cm^2$ for SO-179 film. Note that combinations of lesion size and activity ratio that lie *above* the line for each film will be visible in final image (Ref. 5).

an important subsystem of the overall imaging device, and as such it can be used to increase or decrease the value of lesion contrast presented to the observer. Second, the film's gamma determines the visibility of random noise in clinical images, and, therefore, the maximum useful count density for any given film. Accumulation of image count densities higher than this maximum useful value cannot improve diagnostic image quality, because lower-

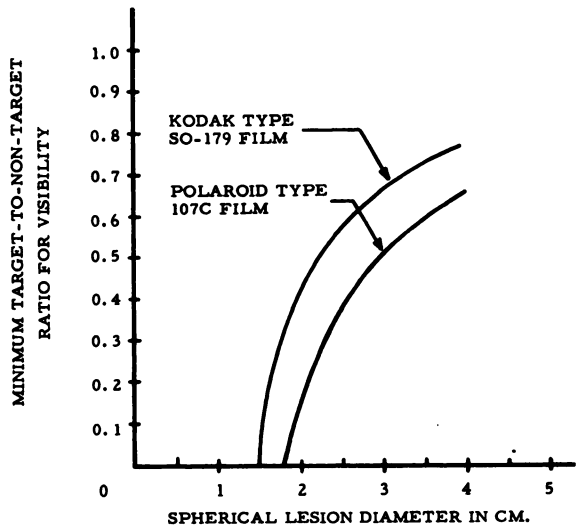


**FIG. 3.** Minimum detectable uptake ratios for various-size cold spherical lesions. Lesions are 2.5 cm deep, in 8-cm-thick background. All other parameters are same as for Fig. 2. Note that combinations of lesion size and activity ratio that lie *below* the line for each film will be visible in final image (Ref. 5).

contrast lesions will still not be seen by the observer. If one accepts the validity of this analysis, it follows that the correlation of theoretically calculated image count densities with empirical values, chosen by trained observers, implies that the visibility of statistical noise is an important factor in establishing an observer's subjective impression of diagnostic image quality. (Of course, there are other factors such as patient comfort, motion blur, or instrumentation limitations which may preclude the accumulation of the maximum useful count density.) It also follows that digital image processing *for contrast enhancement* can offer only limited benefits with nuclear medicine images, because unless image count densities higher than those currently selected for most imaging procedures are used, all statistically reliable gray-scale values can be seen by trained observers viewing the unprocessed image.

Quantitative relationships for all these effects are given in equations (2), (5), and (6) as a function of (a) the observer's visual threshold, (b) the signal-to-noise ratio in the image, and (c) the gamma of the film used for image display. With these equations, one can quickly calculate the image count density needed for a particular combination of film, lesion contrast, and desired value of signal-to-noise ratio in the image. The signal-to-noise ratio determines the probability of a false positive in the image, and as a rule-of-thumb, error rates of 10%, 5%, and 2% for a full field-of-view image from a 10-in.-diam. camera, are obtained with signal-to-noise ratios of 3.75, 4, and 4.25, respectively. For cameras with 15-in. fields of view, the error rates for a given value of signal-to-noise ratio are approximately double the values for 10-in. cameras because there are nearly twice as many resolution elements. Thus, it is relatively easy to determine the image quality due to random variations, and weigh this against other important considerations such as patient comfort, motion blur, and other specific instrumentation limitations.

Finally, when the analysis for the effects of photographic film on lesion contrast is combined with well-established theories (*6,7*) on the effects of imaging-system resolution and gamma-ray scattering on lesion contrast, it is possible to calculate the minimum detectable uptake ratio for various-size spherical lesions in a uniform distribution of background activity. Such calculations are quite useful because specification of imaging-system performance in terms of spherical-lesion detectability should be more easily related to clinical experience than measurements and predictions of performance based on bar-phantom studies.

ACKNOWLEDGMENTS

Preparation of this paper would not have been possible without help and stimulation from many colleagues and friends. I gratefully thank R. Jaszczak, G. Muehllehner, and R. McKeighen for valuable data and discussions; D. Huard for computer expertise; M. Groch for technical criticism and other assistance; and J. Wolff for discussions on the characteristics of photographic film. Typing and illustrative talent were patiently contributed by Linda Walker and Anton Smudde. Outside help and encouragement were freely provided by Robert Beck of the University of Chicago, and David Turner of Rush-Presbyterian-St. Luke's Medical Center.

REFERENCES

*1.* CORNSWEET TN: *Visual Perception.* New York, Academic Press, 1970, p 249

*2.* POLAROID: *Technical Publication T570-1.* August, 1976

*3.* ROSE A: *Vision Human and Electronic.* New York, Plenum Press, 1973, Chp 1

*4. Handbook of Tables for Probability and Statistics,* 2nd ed. Cleveland, CRC Press, 1968, p 213

*5.* WHITEHEAD FR: Quantitative analysis of minimum detectable lesion-to-background uptake ratios for nuclear medicine imaging systems. *Medical Radionuclide Imaging* 1: Vienna, IAEA, 1977, 409–434

*6.* BECK RN: The scanning system as a whole General considerations. In *Fundamental Problems in Scanning.* Gottschalk A and Beck R, eds. Springfield, Ill., Charles C. Thomas, 1968, Chp 3

*7.* BECK RN, et al: Effects of scattered radiation on scintillation detector response. *Medical Radioisotope Scintigraphy* 1: Vienna, IAEA, 1969, 595–616