We have been using a commercially available test for this combination (Corning) for the last 4 mo and are fully satisfied about it.

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REFERENCE

1. CUARÓN ALFREDO, HAPPEÉ DE CUARÓN CHRISTINA: Tables to estimate total binding capacity of thyroxine-binding globulin from the in vivo thyroid function tests. *J Nucl Med* 20: 67-71, 1979

Reply

We completely agree with the opportune comments of Dr. Bakker and Dr. Terpstra. Actually, the units used on Tables 1 and 2B were mistaken: They should be micrograms (μg) for total serum thyroxine and for total TBG, and nanograms (ng) for serum free-thyroxine, as they are properly noted on Figs. 1 and 2.

We can only blame this unfortunate blunder to a lapsus dactili of our secretary during typing, at which it was added a lapsus cerebrii on our part at the time of proof reading.

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Re: Optimization of the Gray Scale for Photoscanners

I would like to comment on what I feel are some subtle, but important, technical issues in the article "Optimization of the Gray Scale for Photoscanners" (*1*).

The quantitative aspects of image gray scale are probably the most poorly understood topic I have encountered in my career as an optical physicist. The reason for this appears to be twofold: first, the gray-scale response (or transfer characteristic) of the most common imaging device—photographic film—is nonlinear; second, we humans observe the results of all imaging devices using one of the most complex and sophisticated of imaging systems that one could imagine. Our visual system not only has a nonlinear gray-scale response, but special features in its spatial response, or MTF. One of these—lateral inhibition—makes the visual system predominantly an edge detector, while another—independent spatial-frequency channels—produces some interesting characteristics in terms of the system's effective noise band width and threshold perception. From the standpoint of both qualitative understanding and quantitative analysis, these features are in themselves sufficiently difficult; however, the ultimate in sophistication appears to be present also, in the fact that the quantitative values for all these response functions seem to vary with a dynamic feedback mechanism controlled by the ambient light level. Thus there is ample opportunity for disagreement on both the propriety and interpretation of any experiment to determine the "optimum" gray-scale response for an imaging system.

With regard to the above-mentioned article I have two such disagreements. First, I will argue that one does *not* want equal gray-scale visualization for *equal count-rate changes*. I will grant that one can build a logical argument for either side of this issue, thus we must be content with subjective opinion as to which is the stronger case. Second, I contend that regardless of one's opinion on the first point, Chang and Blau were technically inconsistent and confusing in demonstrating their case. Because of the importance of correct definitions of terms, let us consider the technical inconsistencies first.

Optical density is, of course, a nonlinear function of the transmitted light level through film. Specifically, it is the logarithm of the *ratio* between the incident and transmitted light levels. The key word turns out to be ratio, because with a little algebra one can show that *constant contrast ratios* in input exposure level produce constant density differences in a photographic image. Within a reasonable dynamic range (perhaps even greater than 100:1) the human visual system appears to perceive equal density differences as equal gray-scale steps.

Chang and Blau begin their article by stating that ". . . the human eye . . . is intrinsically nonlinear with respect to the mathematically defined parameter, optical density (OD), over the . . . range (0.2-2.0 OD)." They and I disagree. It is not quite clear from their article, but I infer that their Fig. 3A demonstrates this nonlinear response of the human visual system with respect to optical density changes. This figure shows the resulting gray-scale steps "generated by using pulses of decreasing frequency in 10% steps." They state that "At the low end of the scale the 10% changes in count rate are readily perceived, but at the high end it is difficult to see any change in density even with 20% or 30% changes in count rate." Of course it is! *These are not equal optical-density differences*! For example, the optical-density change between 100% brightness and 90% brightness is $\Delta D = \log[1.0/0.9] = 0.046$ units, whereas the change between 30% brightness and 20% brightness is $\Delta D = \log(0.3/0.2) = 0.176$ units. *Note that a 10% difference in count rate is not a 10% ratio in count rate!* It takes equal *ratios* to produce equal density, or gray-scale steps. Thus I question the technical consistency of the article, because the stated problem of nonlinear density perception appears to be incorrectly defined and illustrated.

A completely separate issue is the question of whether equally perceived shades of gray should represent equal *ratios* (i.e., density differences) in count rate or equal *differences* in count rate. Chang and Blau state, both in the abstract and the text of the article, that equal *linear changes* in count rate should produce equally perceived steps in gray scale. There is no fundamental reason why one might not desire such a gray scale; however, it does not occur naturally in any imaging process that I know of, and, I submit, would provide a rather strange image if used to photograph one's children in the back yard, for example. Such a gray-scale response function could be obtained by letting image brightness = exp[object brightness], and a little algebra will show that this function would produce an image with its contrast proportional to object brightness. In other words, the bright (dark) portions of the image (negative image) would have higher contrast than the dark (light) portions. While such an image might appear "artistic," it would not satisfy the conditions found necessary for a subjectively pleasing photograph of a familiar scene (*2*). These conditions are that the photograph properly reproduce the luminance *ratios* of the original scene, and that the combination of its absolute brightness and ambient room illumination be such that the eye is placed in a state of adaptation where its contrast response reasonably approximates the response that would be obtained in viewing the original scene.

With medical images, of course, there is no "natural mental reference" of the object, so one is theoretically free to choose any desired gray-scale function consistent with optimum diagnostic interpretation of the image. While admitting that the arguments are now philosophical and subjective, I submit that there are two reasons for continuing to use a relationship demanding that equal ratios must produce equal gray-scale steps. First, use of a gray scale based upon differences instead of ratios

will change the noise characteristics of an image; and second, I believe observers are naturally inclined to interpret even medical images in terms of ratios.

With regard to image noise characteristics, we are all familiar with the fact that the percent RMS noise (a *ratio*) in a nuclear medical image *decreases* as the count level increases, because it is given by $1/\sqrt{N}$ where N is the number of counts per unit area in the image. Note that the actual noise fluctuation is $\sqrt{N}$, so that the *difference* in counts, produced by statistical variations, *increases* with increasing count level. A gray scale based upon equal visibility for equal *differences* would therefore produce images that are noisiest in the high-count-level areas. Admittedly the gray scale could always be adjusted so that the noise was not perceptible to the observer, but it is not obvious that this could always be easily and properly done. In any case, the statistical properties of the image would be altered significantly, and it has not been shown that this would be beneficial.

For the observer interpretation argument, one must first accept my contention that equal *ratios* of brightness level appear as equal gray-scale steps to the eye. If this is done, a 20%-contrast lesion in a high-count-level region of the image appears no more, nor less, prominent than a 20%-contrast lesion in a low-count-level region. (The *noise* level will of course be different.) The equal-differences gray-scale function, however, would make the high-count-level 20% contrast value *look* much more significant than the low-count-count level 20% contrast value, because 20% of a high level is a greater difference than 20% of a low level. I argued above that an observer apparently *interprets* a photograph of a familiar object, such as an outdoor scene, on the basis of its brightness *ratios*, and I have previously shown (*3*) that the gray-scale characteristics and study protocols for nuclear medical images can be objectively quantified if one makes this assumption for medical images as well. While there is no "intrinsic" reason why an observer could not interpret a medical image with a gray scale of differences, I submit that it would be difficult to train him to do so, after he has spent a lifetime learning to interpret visual data in terms of brightness ratios.

If nothing else, I hope it is clear that "Optimization of the Gray Scale for Photoscanners" is both a complex and a controversial problem. Finding a simple solution, if it exists, will require a combined effort between those of us who design imaging systems, and those who use them. I am glad to see some interest in the field.

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3. WHITEHEAD FR: Minimum detectable gray-scale differences in nuclear medicine images. *J Nucl Med* 19: 87-93, 1978

Reply

We are in complete agreement with the last paragraph of Dr. Whitehead's letter. After many years of attempting to stimulate some interest in the gray scale among the engineers engaged in the design of commercial photoscanners it is indeed pleasing to have elicited so strong a response with our concise communication. Our experimental design was deliberately chosen to avoid many of the effects cited, including the spatial-frequency response of the eye, edge effects, illumination levels, statistical fluctuations, etc.

The principal disagreement is on the question of what form the "optimum" gray scale should have. Clearly, the count-rate distribution to be imaged varies with the type of study being done and therefore the "optimum" gray scale is different for each organ. Increased activity (brain and bone tumors) is best visualized with a gray scale different from that for decreased (liver imaging); a decreased focal lesion of a given size in a thin organ (thyroid) requires a different "optimal" gray scale than the same size of lesion in a thick organ (liver), etc. It is therefore pointless to discuss the characteristics of the "optimum" gray scale without specifying the target distribution.

Out of a desire to keep our "concise communication" concise, we did not spell out in any detail the target distribution for which our "optimum" gray scale would provide the best imaging characteristics. What we had in mind was the problem of finding a given minimum tumor size with equal ease at any location in a large organ of varying thickness. This is precisely the situation in liver scanning. A 2-cm tumor, for example, would result in a *fixed* decrease in count rate (except for collimator response) no matter where it was located. Our experiment was designed to reproduce this by generating an "optimum" gray scale that makes *fixed* (not relative) changes in count rate equally perceptible. We chose the liver-scanning situation for optimization because it is the most difficult one in routine clinical practice. The effect of our suggested gray scale is to emphasize the dark end of the scale at the expense of the light end.

As we pointed out in our paper, the gray scales built into most commercial photoscanners are far from optimal. This problem goes beyond any of the subtle issues raised in Dr. Whitehead's letter. The instruments provided to us by the manufacturers have been inadequate. On some of them it is not even possible to tell whether the count rate is going up or down in the upper one-third of the scale. This is not the result of philosophical differences regarding the shape of the optimal gray scale but the result of deficient engineering. We recommend that all clinics generate gray scales with their scanners and their computer-cameras. The nature and magnitude of this problem will be readily apparent. Changing the gray scale is difficult on most scanners, but there can be no excuse for poor gray scales on computer-cameras, where software changes are simple.

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Radionuclide Left-Ventricular dV/dt and its Dependence on Cardiac Rate

In a recent article, Bianco et al. (*1*) reported on the changes induced in cardiac function by exercise. The population studied consisted of 20 patients with ischemic heart disease. Left-ventricle ejection fraction (LVEF) and the rate of change of left-ventricular volume (LV dV/dt) were calculated after EKG-gated gamma-camera data acquisition. It was shown that, during exercise, the LVEF and LV dV/dt parameters changed in opposite directions, the former decreased while the latter increased. Bianco et al. (*1*) could not determine a mechanism to rationalize this result, and used the unexplained behavior of LV dV/dt to justify its exclusion from a list of potentially valuable cardiac parameters (*2*). In the following we give a simplified explanation for their results as well as an argument for presenting LV histograms in a standard form.

We model the volume of the left ventricle as:

$$LV = V_0 + V_1 \cos(\omega t)$$