Nontarget Activities: Can We Correct for Them?

The term background or background activity should be reserved for events detected in the absence of an object. Electronic noise, cosmic radiation, and activity originating from the detector location are background. Background activity can easily be measured and correction determined for it. As used in the paper by Beck et al. (*1*) in this issue, however, background is really *tissue crosstalk:* it originates from real activity in real structures. Crosstalk activity does not differ from "target" activity, except intentionally. During myocardial perfusion studies, all activities that are detected but originate from nonmyocardial tissues are tissue crosstalk activities. Unlike real background, crosstalk cannot be measured in the absence of the target, except in extreme experimental designs like the one discussed here. Correction is therefore not trivial.

In most clinical scintigraphic applications, the count-rate density (cpm/cm^2) in the projection area of the target is higher than in the projection areas where all counts are due to tissue crosstalk. To the extent that this is true, crosstalk can be handled by thresholding.

The reason for thresholding images should be well understood: thresholding restores the dynamic range in the pictorial representation. Indeed, if the maximum count rate over the target is (T + B), where T is the target activity proper and B is crosstalk activity at that point, the useful fraction of a dynamic range from zero to (T + B) is only $T/(T + B) < 1$. If, by thresholding, the dynamic range is restricted to T alone, the useful fraction is $T/T = 1$.

The restoration of the dynamic range is not a purely esthetic matter; nor can one necessarily compensate for the loss of the useful fraction by refining the scale (making the scale 16-bit rather than 4-bit) or redistributing the scale (*2*). The problem resides in comparison or standardization. If B is included in the scale, the contrast between two parts of the target is also a function of the proportion between B and T, instead of only a function of the relative difference in count-rate density. Thresholding is therefore of particular importance when the crosstalk fraction is known to differ between two studies.

The methods and thresholding criteria vary, and some are controversial (*3*). Narahara (*4*) proposed a thresholding algorithm for thallium-201 myocardial perfusion studies based on empirical data from dog studies at rest. According to him, the threshold that corrects for tissue crosstalk is always a set fraction of (T_M + B), where B is tissue crosstalk and T_M is the maximum count rate density in the target. In dogs (at rest), $B = 0.2 (T_M + B)$, and the application of this rule to humans yielded acceptable results. The implications of this, if interpreted as paradigmatic, are most disturbing. We are asked to accept that the target concentration cannot vary independently of nontarget concentration, since the equation given above reduces to $T_M = 0.8B$. In general, however, the target has been selected because its size and function need to be determined. Both size (volume) and function (concentration) determine T_M, at least partially independently of the size and function of other tissues (B). Accordingly, one does not expect that the nontarget count-rate density can be derived from maximum count-rate density in all cases. The tissue crosstalk, or the threshold, B, needs to be evaluated independently of the still-unknown net maximum count-rate density, T_M, or the maximum total count-rate density (T_M + B). The most widespread method consists in sampling for B in a region of the image close to the target but where no target activity is present. It is worth noting that historically this approach became popular when quantitation became necessary—i.e., with the introduction of the scintigraphic evaluation of ejection fractions (*5*). On the other hand, scaling B as a function of (T_M + B) was (and is) widely used in scanner-type imaging devices (*6*).

There is another assumption hidden in the conclusion reached by Narahara: Tissue crosstalk is

taken to be homogeneously distributed. Few of us will agree that this is true, and we will note that most digital devices that include a thresholding algorithm include a suppression for negative values—the reason being, of course, that the subtraction of a constant across the image will yield negative values in those regions where the tissue crosstalk yields lower count-rate densities. It is true that a single value is used in emission cardiology, and with apparent success, for the determination of ejection fractions. However, the threshold is subtracted as a single number from a single number (total end-diastolic count rate) and not necessarily on a point-by-point basis. Moreover, the importance attached to the size, position, and shape of the sampling region is a reflection of the heterogeneity of tissue crosstalk.

The Goris algorithm (*3*) attempted to take the inhomogeneity of nontarget activity into account by continuous sampling around the target. Basically the same approach is used in the paper by Beck et al.

The difference with the Narahara approach is twofold: The threshold is measured by sampling regions with assumed zero value for T; and B is not expected to be constant across the detector field. For this reason we construct (in the terminology of the present paper) a reference plane that is not horizontal (constant) or even planar. This plane cannot be believed to represent true nontarget tissue crosstalk, as Narahara and the present author demonstrated more than adequately using the dog model. The reference-plane method overlooks the fact that the presence of the target organ decreases the amount of nontarget activity present. The demonstration by Narahara is crucial because it underscores the independent influence of volumes. It is probably with this in mind that Dr. Thomas Budinger stated in 1969 (personal communication) that the problem of "background" would be solved only to the extent that tridimensional reconstruction of emission images becomes possible, and he was correct. The reference plane, in contrast, is meant only to recovery the dynamic range—i.e., to restrict the scale to the target activity, as much as possible. Even in this it fails. Indeed, the reference-plane method assumes that the total count-rate density is $(T_1 + T_2 + B')$, in which B′ is crosstalk from off-target structures, T_2 is due to target concentrations that do not differ from nontarget concentrations, and T_1 is the activity due to the higher (specific) target concentration. (For this discussion I have assumed a constant nontarget concentration, C_2, and a target concentration, C. The excess concentration in the target is $C - C_2 = C_1$.) The dynamic range is recovered for T_1 only.

The present paper attempts to recover T_2 also. The starting point is correct. The reference plane is given by $REF = T_2 + B'$. The contribution of T_2 to REF could be derived if one knew the volume occupied by the target. But this volume is not known. One could derive the volume from T_1 if the specific target concentration, C_1, were constant, since $T_1 = C_1 \times V$. In the same way, to the extent that the nonspecific concentration is constant, we have $T_2 = C_2 \times V$, or $T_2 = (C_2/C_1)T_1$. It is easy to see that in this paper $C_2/C_1 = f$, the empirically defined factor.

The presented approach, however, is circuitous and adds no information beyond that present in the reference-plane method. Proof of this rash statement is easily found. Using the symbols and definitions from the text (Appendix), we find that the final value is given by NET = ORIG − BKG, and that the term BKG is defined as BKG = (1 + f)*REF − f*ORIG.

By substitution, we obtain NET = ORIG − (1 + f)REF + f*ORIG, and by recombination NET = (1 + f)*ORIG − (1 + f)*REF, which simplifies to NET = (1 + f)*(ORIG − REF).

Therefore, the resulting value is simply the original counts (ORIG) minus the reference-plane value (REF), both scaled by a factor (1 + f). This is the same result as with the Goris method. The lack of new information yielded by the computation stems from the uncritical substitution of count-rate densities for volumes. The concordance between computed and empirical results from the correlation of count-rates and volumes in normal subjects.

Like Narahara before them, the authors used a normal (invariant) situation that suited their purpose, and in which C_1 and C_2 were constant. But this is not necessarily so in abnormal situations. If Narahara had exercised his dogs, he might have found that B is not always 0.2 $(T_M + B)$. In the same circumstances, the authors of the present paper would not have found f always to be 0.64; and had they used a heart ischemic in one of its segments, the concordance between computed and actual crosstalk would have been less convincing.

Budinger was right: True crosstalk correction requires three-dimensional reconstruction (independent knowledge of volumes). In the meantime we should not forget what we do: We threshold to restore the useful dynamic range of the final image—the best we can do, no better.

MICHAEL L. GORIS
Stanford Medical Center
Stanford, California

REFERENCES

1. BECK JW, TATUM JL, COBB FR, et al: Myocardial perfusion imaging using thallium-201: a new algorithm for calculation of background activity. *J Nucl Med* 20: 1294-1300, 1979
2. GORIS ML, SCHEIBE PO, KRISS JP: A method to optimise the use of gray-shade scale in nuclear medicine images. *Comput Biomed Res* 9: 571-577, 1976
3. GORIS ML, DASPIT SG, MCLAUGHLIN P, et al: Interpolative background subtraction. *J Nucl Med* 17: 744-747, 1976
4. NARAHARA KA, HAMILTON AW, WILLIAMS DL, et al: Myocardial imaging with thallium-201: an experimental model for analysis of the true myocardial and background image components. *J Nucl Med* 18: 781-786, 1977
5. WACKERS FJTH, BERGER HJ, JOHNSTON DE, et al: Multiple gated cardiac blood pool imaging for left ventricular ejection fraction: validation of the technique and assessment of variability. *Am J Cardiol* 43: 1159-1166, 1979
6. MALLARD J: The radionuclide imaging process and factors influencing the choice of an instrument for brain scanning. *Prog Nucl Med* 1: 1-114; Karger, Barel and University Park Press, Baltimore, 1972