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NONSTATIONARY AND NONLINEAR SCINTIGRAM PROCESSING

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I. INTRODUCTION

A considerable portion of the work done in digital scintigram processing until recently has been directed toward investigation of what can generally be called "filtering" techniques, in which the raw scintigram data is either convolved with some fixed "processing point spread function" to produce a processed image or, equivalently, transformed using a Fast Fourier Transform (FFT) algorithm, each sinusoidal coefficient multiplied by some factor, (the "filter" factor at each frequency) and the result inverse transformed to produce the processed image. Every processing procedure in which the final image at any point is derived from original data in the neighborhood of the point by one or more linear combinations independent of position can be shown to correspond to an equivalent filtering operation. The filter approach is restrictive, however, in that operations must be independent of position in the image plane ("isoplanatic" or "stationary") and must be linear.

It is the purpose of this paper to describe a number of nonlinear and nonstationary scintigram processing procedures and to encourage exploration of other such techniques. While the degree to which nonlinear and nonstationary techniques may be superior to the filtering approach is not yet clear, results do show improvement in some cases, and the essentially endless possibilities opened up by abandoning the restrictions of filtering unquestionably demand further exploration.

I.A. Rationale for scintigram processing

In this paper we define scintigram processing as manipulation of raw image data to produce a modified image which will then be interpreted by a human observer, in contrast to scintigram analysis, in which raw or

processed image data is interpreted, either wholly or in part, by machine. Noise smoothing and resolution enhancement are examples of image processing; extraction of organ function parameters in dynamic studies and computer identification of abnormalities in a static image are examples of image analysis.

The ultimate goal for scintigram processing in nuclear medicine is increased diagnostic usefulness of the image. To this end, processing procedures must make diagnostically relevant features of the radionuclide distribution more confidently detectable and/or recognizable by the human observer, and image quality must be evaluated in terms of empirical usefulness of the image.

One must recognize that meaningful empirical evaluation of scintigram processing techniques can be made only after observers' interpretive skills have been developed for the techniques in question. In our experience, observers trained to interpret unprocessed images often react negatively at first to processed images, which "look different" and must be interpreted differently. Resolution enhancement procedures, for example, tend to emphasize both real structure and noise artifacts; this tendency must be taken into account when interpreting the images. Similarly, different image processing techniques may produce results of rather different appearance, and comparisons can be made only after adequate observer training for each technique.

I. B. Parameters of image quality

Image quality depends in a complex way upon the techniques employed for data collection, processing and display, as well as on the human perceptual system. In an effort to understand the effect of various imaging procedures, we can think of image quality as being a function of at least three broad parameters: resolution, noise magnitude, and noise character.

Though choice of display techniques is of unquestionable importance in influencing overall image quality, it seems useful conceptually to separate effects of the display system, as well as the human perceptual system, from effects of data collection and processing techniques. In particular, nonlinear point-by-point ("zero memory") display transformations can often be varied quite flexibly by electronic means. If necessary, display transformations may be thought of as implicit image processing steps following the explicit processing and preceding an ideal display system which produces no change in transmitting data visually to the human observer, who in turn transforms the image.

I.B.1. Resolution

The term "resolution" is often used in a rather imprecise way to describe the ability of a system to render distinguishable small input details. In this paper we will use the term "resolution" to denote geometrical "sharpness" or "fidelity" of an image in the absence of noise. Although systems with poor resolution generally tend both to reduce contrast of small details and to blur edges, it is important to recognize that these two effects need not be always strictly related. Penetration of high energy photons through detector collimator septa, for example, can seriously degrade contrast without appreciably blurring edges, while background subtraction from a noiseless image can markedly increase contrast without changing edginess or separation of small details from each other.

In analysis of a stage of stationary linear image transfer (e.g. imaging or processing), resolution of the stage can be specified completely by either the stage point spread function or its Fourier transform (the stage transfer function), since any output can then be predicted by superposition of appropriately weighted responses to unit point inputs. Thus,

"resolution" depends only upon characteristics of the transfer stage.

The overall resolution of a system made up of a sequence of stationary linear image transfer stages can be described either by the point spread function which is the convolution of the individual point spread functions or by the product of the individual transfer functions.

The resolution of a nonstationary but linear stage can be described by a set of point spread or transfer functions.

Unfortunately, objective specification of resolution in cases involving nonlinear transformations is very much more difficult since superposition of inputs can no longer be used to predict system response. Resolution of a particular nonlinear transfer stage usually must be evaluated empirically for the class of inputs in question, and generalization to predict effects for other inputs is not usually possible. Resolution may be influenced in different ways for different inputs and does not depend on characteristics of the transfer stage alone.

I.B.2 Noise magnitude

In discussing image noise it is important to distinguish between noise magnitude -- the "intensity" or "height" of statistical fluctuations -- and noise character -- the "shape" or "texture" of the fluctuations. It is important to note that both noise magnitude and noise character in processed and unprocessed scintigraphic images depend in general upon expected count density and hence upon position in the image, since unprocessed scan data obeys the laws of Poisson statistics. That is, the noise is nonstationary.

Noise magnitude in unprocessed and linearly processed scintigraphic images can be described essentially completely in terms of the standard deviation σ of fluctuations about the "expected" or "noiseless" image at any point in the image, since unprocessed image statistics obey the Poisson

distribution and linearly processed image statistics tend strongly toward the Gaussian distribution due to the central limit theorem. In these cases, noise standard deviation can be expressed quite simply in terms of the expected image and the stationary or nonstationary spread function employed (Metz, 1969, pp. 66-70,95), and can be interpreted in the conventional way as denoting approximately 0.68 probability of fluctuations within $\pm 1\sigma$ of the mean, 0.95 probability of fluctuations within $\pm 2\sigma$ of the mean, etc.

Description and prediction of noise magnitude after one or more nonlinear transformations is much more difficult. Since nonlinear transformations of Poisson or Gaussian random variables are not (usually even approximately) Gaussian distributed and in fact tend to produce asymmetric noise probability distributions, the conventional interpretation of noise standard deviation in terms of the normal model is no longer applicable.

Unless the transformed probability distribution can be calculated directly, which is unfortunately often prohibitively difficult, one must resort to some approximate and incomplete interpretation of nonlinearly transformed noise magnitude. Possibilities include (1) calculation of the mean and central moments of the transformed random variables (Papoulis, 1965, pp. 151,152 and p.212; Metz, 1969, pp. 307-321) in terms of central moments of the Poisson distribution (Haight, 1967) or Gaussian distribution, to estimate both width and asymmetry of the transformed probability distribution, and (2) calculation of the output values when mean $\pm n\sigma$ are inputs, which (for transformations with single valued inverses) yields outcome boundaries within which probabilities of outcomes are 0.68, 0.95, etc., and which can also be used to estimate output asymmetries.

I.B.3 Noise character

The "character" or "texture" of noise in an image can be loosely described as ragged or smooth. It is a function of the way in which statistical outcomes of noise at one point in the image tend to be related to outcomes at nearby points and depends upon the type of processing to which the image has been subjected. Since visibility of source structures can depend on the texture of noise in the image, one must consider the effects of various processing methods upon noise character as well as upon magnitude and resolution.

Noise character can be described mathematically in terms of noise "autocovariance" -- the expected product of deviations from the mean at two adjacent points -- and to the extent that noise statistics in the processed image are approximately Gaussian, this description is approximately complete. Generally speaking, a noise autocovariance function which in magnitude drops rapidly to zero as the distance between points increases indicates "sharp" noise, with noise outcomes essentially unrelated except at small distances, while an autocovariance function which falls slowly to zero as distance between points increases indicates the presence of noise undulations, with noise outcomes at neighboring points highly correlated. Positive values of the autocovariance function at some separation distance indicate that noise outcomes tend to be of the same sign at that separation, so if the autocovariance function is positive up to a given separation distance, at the scale of that separation the noise will tend to be smooth. Negative autocovariance values indicate expected noise outcomes of opposite sign, tending to cause the noise to appear "ragged", with somewhat regular changes from positive to negative deviations.

Since unprocessed scintigraphic image data tend to follow the Poisson distribution, noise character in processed scintigrams depends, in general, upon local count density and hence upon position in the image plane. However,

autocovariance functions normalized to unity at zero separation tend to be approximately independent of position in the image plane, especially in locally uniform regions, and appear to provide a useful if not exact measure of noise character. It should be noted that since scintigram image noise is nonstationary, conventional "Wiener" or "power" spectra (Blackman and Tukey, 1959; Papoulis, 1965, Chap. 10) cannot be used to describe noise character, except qualitatively to the extent that normalized autocovariance functions are approximately shift-invariant.

Noise autocovariance in linearly processed scintigrams can be predicted rather simply in terms of the expected count density distribution and the processing point spread function (or functions, for the case of nonstationary linear processing) employed (Metz, 1969, pp. 70-72,94). Prediction of noise character after one or more nonlinear transformations is usually difficult, but can sometimes be approximated in terms of joint central moments of the input statistics.

Although prediction of effects of nonlinear processing techniques on noise character is often difficult, the importance of noise character in determining final image quality must be kept in mind in investigating new procedures.

I.C. Interdependence among image quality parameters

The degree to which image quality depends upon resolution, noise magnitude, and noise character seems to depend in a complex way both upon the source distribution and upon the information which is sought from the image. If the activity distribution is inherently unsharp, for example, then high spatial resolution in data acquisition and processing may be of little importance, and usefulness of the image will depend primarily upon

noise magnitude and noise character in the final result. If the source structure of interest is small, however, or if distinction of edges or boundaries is critical, then good resolution may be demanded. If a processing procedure results in noise of a certain texture, then usefulness of the method will depend on whether or not that noise texture can be confused with possibly real source structure; "mottled" noise might be interpreted as diffuse metastases or cirrhosis in a scintigram of the liver, for example, but possibly not as real structure in a scintigram of the brain.

I.C.1 Data accumulation

Design of radiation detection devices for scintigraphy inevitably requires that some compromise be made between achievement of high spatial resolution and high sensitivity (and hence statistical accuracy, for a given imaging time). Since ionizing x- and γ -ray photons cannot be focused by a lens, spatial resolution must be achieved by restricting the field of view of the detector, which reduces the number of photons which will reach the detector per unit time. In designing collimators for moving-detector devices of fixed area, for example, attainable counting rate is approximately proportional to the square of spread function full-width at half-maximum. A broad view of detection system design has been given by Beck (1964, 1968) and by Brownell et al. (1967).

Spatial resolution in unprocessed scintigraphic image data is usually determined primarily by geometrical field of view of the collimator employed, ability to reject scattered or collimator-penetrating photons originating outside the geometrical field of view, and, for stationary detector devices, intrinsic spatial resolution of the detector.

Since statistical fluctuations in unprocessed scintigraphic image data are usually due primarily to the Poisson statistical fluctuations of nuclear

decay, noise magnitude in unprocessed images depends upon source activity, imaging time, and detection system sensitivity. Assuming Poisson statistics, the standard deviation in the number of counts recorded in any small image area (N) will be proportional to $\sqrt{N}$.

Unprocessed image noise is essentially "white" in character, with uncorrelated statistical fluctuations from the means in any two distinct image areas (Metz, 1969, pp. 60-63).

I.C.2 Data processing

Very little research has been done to obtain the function of resolution, noise magnitude, noise character, source distribution characteristics, and information sought which describes the quality of an image. It is hard to overemphasize the usefulness such a function would have; the design of scintigram processing methods could become an explicit problem of the optimization of this quality measure.

The importance of such a quality measure is particularly great because processing methods generally affect all the image quality parameters in such a way that some parameters change in a direction that by itself would result in improvement of image quality and others in a direction that by itself would result in image degradation. Thus, without such a function it is very difficult to predict the usefulness of a processing method except empirically, and it is very easy to fall into a trap of trying to improve one image quality parameter while forgetting that the processing will degrade other parameters.

Vetter and Pizer (1970, 1971) have produced a quality measure for unprocessed scintigrams in which the individual dots are clearly distinguishable. This measure, which has been successfully used in practice in a number of different situations, combines the image quality parameters by showing

that the image noise can be characterized as an equivalent resolution degradation and this statistical resolution measure can be combined with the normal resolution measure as with any two cascaded sources of resolution degradation. However, this measure is not directly extendible to processed images.

Several generalizations concerning interdependence of image quality parameters after processing can be made.

Stationary and nonstationary linear noise-smoothing procedures involving convolution of the image data with a matrix (or matrices) of non-negative weights must degrade resolution to some extent, must reduce the relative RMS noise magnitude, and must increase positive correlation of noise outcomes from point to point. Stationary and nonstationary linear noise smoothing procedures which "cut off" high frequency content more sharply than Gaussian frequency response must involve use of some negative weights in the processing spread function matrix (or matrices), causing output autocovariance to be negative at some separation distances and thus imposing some degree of regular positive-to-negative "sawtoothed" character upon output image noise. Sharp cutoff low-pass filters can also cause the overall point spread response to "ring"--oscillate, taking on negative values at some distances--which can increase apparent resolution of properly spaced structures.

Stationary and nonstationary linear techniques for enhancement of resolution must involve convolution of the image data with a matrix (or matrices) containing some negative weights, again causing output autocovariance to be negative at some separation distances, and imposing some degree of positive-to-negative regularity upon processed image noise. Though partial resolution enhancement procedures can be designed to reduce

noise magnitude, noise magnitude must increase as the amount of resolution enhancement is increased, and strong resolution enhancement must ultimately increase noise magnitude.

Nonlinear point-by-point transformations can change contrast of both image structures and noise. Both resolution, in a sense, and noise magnitude can thus be increased or decreased together, though resolution cannot usually be increased in the sense of increased definition of small adjacent structures.

Interdependence of effects of general nonlinear procedures is difficult to predict because of the complex way in which structure and noise interact under such transformations. This complexity is, however, the basis upon which the possible usefulness of such procedures rests.

II. STATIONARY LINEAR PROCESSING

Stationary linear image processing techniques are, by definition, those methods for which output count density at any point in the image can be expressed as a fixed linear combination of input count densities in the neighborhood of the point.

Such methods can always be expressed either by convolution of a single appropriate processing point spread function with the input data or, equivalently, by Fourier transformation of the input data, multiplication of each sinusoidal coefficient by an appropriate "filter" factor (the Fourier transform of the corresponding processing point spread function), and inverse Fourier transformation. It is important to realize that equivalent processing spread functions and filters can be derived for any stationary linear procedure, including stationary linear iterative techniques and differential methods (Metz, 1969).

II. A. Implementation

In stationary linear image processing by digital computer, a single convolution of an $N \times N$ element image matrix with an $M \times M$ processing spread function matrix requires approximately $M^2 N^2$ real multiplications and the same number of real additions, while application of the frequency space filtering approach using an FFT algorithm (Cooley and Tukey, 1965; Cochran et al., 1967; Fisher, 1970; Gold and Rader, 1970, Chapter 6), requires approximately $4N^2 \log_2 N$ real multiplications and $6N^2 \log_2 N$ real additions. Although the relative speed of implementing the two approaches depends upon the two matrix sizes and the possible use of special techniques to improve efficiency of the basic FFT algorithm (Brown and Weaver, 1971; Markel, 1971), one can say that used intelligently the FFT approach is faster unless the processing spread function matrix is smaller than about 5×5 , and the FFT approach becomes considerably faster than direct convolution with processing spread functions larger than about 10×10 . Stationary linear methods which must be implemented iteratively in the spatial domain with at least one convolution operation at each iteration (Iinuma and Nagai, 1967; Metz, 1969, pp. 374-386), can be accomplished in a single step using the FFT and equivalent filter approach in the frequency domain (Metz, 1969, pp. 364-373 and pp. 379-384), with tremendous savings in computational effort.

Stationary linear techniques have been discussed by Sprau, Tauxe, and Chaapel (1966), Iinuma and Nagai (1967), Hart and Farrell (1968), Metz (1969), Nagai, Iinuma, and Fukuda (1969), Hunt et al (1970), Metz (1970), Tanaka and Iinuma (1970), Brown, Kirch, et al (1971), and Kirch and Brown (1972).

II. B. Effects on resolution and noise

Effects of stationary linear image processing techniques on image resolution and noise can be predicted rather simply (Metz, 1969, pp. 66-95 and pp. 197-241).

If b_{ij} represents the input unprocessed Poisson-distributed image matrix value at position (i,j) and if $\{t_{ij}\}$ represents the processing point spread function matrix, then the expected output matrix $\{E[c_{ij}]\}$ is given by the convolution of the expected input with the spread function:

$$E[c_{ij}] = \sum_{k,l=1}^N E[b_{kl}] t_{i-k,j-l}.$$

Variance (i.e., square of the standard deviation) of the output matrix is given by the convolution of the expected input with the square of the spread function:

$$\begin{aligned} \text{Var } [c_{ij}] &\equiv E[(c_{ij} - E[c_{ij}])^2] \\ &= \sum_{k,l=1}^N E[b_{kl}] (t_{i-k,j-l})^2. \end{aligned}$$

In locally uniform or linearly varying regions of the expected input image, output variance is given approximately by:

$$\begin{aligned} \text{Var } [c_{ij}] &= E[b_{ij}] \sum_{k,l=1}^N (t_{kl})^2 \\ &= E[b_{ij}] \cdot \frac{1}{N^2} \sum_{k,l=1}^N |T_{kl}|^2 \end{aligned}$$

where T_{kl} is the filter factor applied to the (k,l) coefficient of the FFT of $\{b_{ij}\}$ (i.e., the (k,l) coefficient of the FFT of the equivalent processing

point spread matrix $\{t_{ij}\}$ expanded to $N \times N$ by filling zeroes*).

Output image autocovariance is given by the convolution of the expected input with the product of the spread function matrix and the spread function matrix shifted appropriately:

$$\begin{aligned} C_{c:}(i,j;i+m,j+n) &\equiv \text{Covar}[c_{:ij}, c_{:i+m,j+n}] \\ &\equiv E[(c_{:ij} - E[c_{:ij}])(c_{:i+m,j+n} - E[c_{:i+m,j+n}])] \\ &= \sum_{k,l=1}^N E[b_{:kl}] t_{i-k,j-l} t_{i-k+m,j-l+n}. \end{aligned}$$

Note that $C_{c:}(i,j;i,j) = \text{Var}[c_{:ij}]$. In locally uniform regions of the expected input image, output autocovariance is given approximately by:

$$C_{c:}(i,j;i+m,j+n) = E[b_{:ij}] \sum_{k,l=1}^N t_{k,l} t_{k+m,l+n},$$

in which the second factor on the right represents convolution of the processing spread function with a version of itself reflected about its origin.

The normalized autocovariance function is defined as $C_{c:}(i,j;i+m,j+n)/\text{Var}[c_{:ij}]$ and essentially separates description of noise character from that of noise magnitude.

If originally Poisson-distributed image data are processed by a sequence of

*The factor $(1/N^2)$ may or may not be required in the last expression, depending upon definition of the FFT.

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stationary linear operations, then $\{t_{ij}\}$ and $\{T_{kl}\}$ in the above expressions represent the joint convolution of the individual processing spread functions and the joint product of the individual filter functions, respectively.

II. C. Discussion

Stationary linear image processing techniques can be implemented quite flexibly and efficiently using a digital computer and an FFT algorithm, and their effects on resolution and noise can be predicted quite simply. Thus, the only difficulty in designing an optimal filter is the complex way in which image quality depends upon the combination of resolution, noise magnitude, noise character, source structure, and information sought from the image.

However, optimal filtering may not be optimal processing, for the following two reasons. First, in all stationary linear methods both the signal and noise content at any particular frequency are multiplied by the same factor. Improvement in image quality can be made only by suppressing (or de-emphasizing) frequency components which are, in some sense, primarily responsible for perceived noise, and passing (or emphasizing) frequency components which are primarily responsible for transmission of diagnostically relevant signal information.

Second, since stationary linear methods inherently process data in all parts of the image plane in the same way, a filter (or equivalent processing point spread function) which is optimal in one part of the image plane may not be optimal in another part, either because the noise level may be different there due to non-uniform expected count density, or because the nature of source structures there may be quite different.

In view of these limitations of stationary linear processing methods, we turn to nonlinear and nonstationary methods.

III. LINEAR NONSTATIONARY PROCESSING

Linear nonstationary processing techniques are, by definition, those techniques in which output image count density at any point is given by a linear combination of neighborhood input count densities, with the linear combination varying from point to point in the image plane, and can be thought of as convolution of the input data with a processing spread function which changes from point to point.

Change in the processing spread function is usually governed by some property (or properties) of the local observed count distribution, such as estimated local count density, causing the processing spread function to "adapt itself" to local conditions. Since any estimate of local conditions must be made on the basis of noisy data, adaptation must, of course, be imperfect. Essentially all linear non-stationary processing methods proposed to date are based upon estimates of local count density, with the processing spread function adjusted appropriately to reflect the smaller relative standard deviation of count densities present in high count density regions, due to the Poisson nature of counting statistics.

III. A. Variable averaging

Pizer and Vetter (1966, 1969) and Pizer (1967, 1971) have developed noise smoothing methods in which the processing spread function is broadened in regions of lower count density and narrowed in regions of higher count density in such a way that relative standard deviation is made approximately constant over the output image plane. Relatively little smoothing is done and resolution is essentially preserved in high count density regions having good statistics, while noise is smoothed more heavily at the expense of some resolution loss in regions of lower count density and consequently poorer statistics.

In Pizer and Vetter's description of "variable averaging", the processing spread function is a uniformly weighted approximately circular region of variable size. For each element in the input image matrix, a circular region about the element in question is increased in size until some fixed number of counts, N , is included in the region; the output image element corresponding to the center of the circle is then assigned the value $(N-1)/A$, where A is the area required to enclose N counts. Relative standard deviation in all elements of the output image is then approximately equal to $(N-2)^{-1/2}$. Output noise autocovariance is difficult to predict exactly, but it decreases approximately linearly ^{to zero} as a function of separation distance until a separation of about $[(N-1)/\pi\rho]^{1/2}$ is achieved between image elements, where ρ represents local expected element count density.

Several modifications to variable averaging have been suggested:

1. Since conventional "fixed averaging" (a stationary convolution) keeps resolution constant but results in variable statistical accuracy over the image while variable averaging keeps statistical accuracy constant but results in variable resolution, and since image quality seems to depend upon some compromise between resolution and statistical accuracy, Vetter (personal communication, 1970) and Gustafsson and Todd-Pokropek (1972) have suggested letting the number of counts N to be included in the averaging area increase with count density according to an empirically specified scheme.
2. Gustafsson and Todd-Pokropek (1972) have developed a method of non-circular search which accepts an input image element into the running sum only if the number of counts in that element is within some statistically defined range about the present element density estimate. Such a procedure results in use of a spread function of variable shape,

adapted to the data, and avoids averaging across sharp boundaries in the scan, thus avoiding some of the blurring of boundaries present with circular variable averaging. The method has been shown to yield significant improvement in clinical scintigrams by Gustafsson and Todd-Pokropek (1972).

3. Variable averaging can be generalized so that the element values over which the averaging is done for any output position are weighted by a function of the position of the element in question relative to the output position. As with stationary weighted averaging (convolution) the weights can be chosen to suit the source distribution and the information desired.

III. B. Variable smearing

Smearing consists of replacing each raw image element by an intensity distribution (spot) centered at the element and with total intensity proportional to the value of the raw image element. That is, each element has its value smeared over the surrounding region and the smeared results are added up. Linear stationary convolution can be implemented as a smearing or as an averaging. In smearing one conceptually moves input element by input element, smearing out each. In averaging one conceptually moves output element by output element, collecting all the contributions of surrounding elements.

Variable smearing (Pizer and Vetter, 1966) consists of smearing where the width of the intensity distribution (spot) replacing an element varies over the image. The shape of the distribution remains constant (usually Gaussian), but the width is chosen to be inversely proportional to the square root of estimated local density. In order that the variation in shape be not too sensitive to statistical fluctuations in the raw image, the local density estimate must be produced by a preprocessing which is a smoothing of the raw image.

Because of the need for preprocessing, variable smearing is computationally less efficient than variable averaging. Furthermore, only if the preprocessing is a full variable averaging is the variation in variable smearing as stable as it is in variable averaging, in which the variation depends on the output result (the running sum), not on an estimate given by preprocessing. Therefore, variable smearing only gives as good results as variable averaging if it requires twice as much work, and thus variable smearing is never used.

III. C. Variable resolution recovery

Chesler (1969) and Pizer (1971) have described a method of resolution recovery somewhat analogous to weighted variable averaging in which a processing spread function comprised of a positive central region surrounded by a negative ring of equal area is used rather than an entirely positive smoothing spread function. Relative weights of the central spot and negative ring are chosen to approximate low-frequency correction for the original imaging system transfer function, and the size of the processing spread function is varied by a criterion on the signal to noise ratio of the output, to reduce higher frequency enhancement in regions of lower statistical accuracy.

This method produces a local filter of ^{highly} very prescribed shape, and more flexible but more complicated methods can be devised. However, the greater the number of variable parameters, the more time-consuming is the choice of their values for each position at which the processing spread function must be chosen, causing the methods to be very inefficient.

III. D. Combinations of stationary and nonstationary linear methods

In an attempt to combine the computational efficiency and theoretical convenience of stationary resolution recovery methods implemented using the

FFT approach with the desirable adaptive noise-control properties of variable spatial averaging (the most efficient of the nonstationary techniques), these two methods can be used successively to produce a final processed image (Metz, 1969, pp. 415-418). Since stationary and nonstationary methods are not generally commutative, results depend on the order in which the techniques are applied. Gustafsson and Todd-Pokropek (1972) have achieved nonstationary resolution recovery by following variable averaging with application of a stationary linear resolution recovery filter.

III. E. Implementation

Since variable averaging, variable smearing, and variable resolution recovery are equivalent to convolution of the image data with a spread function which varies from point to point (and hence must be recomputed at each point in the image), and since straightforward application of these methods must be made in the spatial domain because conventional filtering operations in the frequency domain are equivalent to stationary convolution operations, variable operations can be more time consuming than stationary filtering operations, especially variable smearing and variable resolution recovery. Results indicate that the variable techniques produce better pictures in at least some situations, however, and may be worth the increased cost.

Approximations to the variable processing approach can be made which take advantage of the efficiency of frequency domain operations yet retain some of the desirable adaptive properties of conventional variable techniques. These approximate methods are generally slower than stationary filtering operations but can be considerably more efficient than the standard variable techniques, though less sensitively adaptive. Both of the methods described

here consist essentially of dividing the image data up into subunits within which count density (or possibly source structure) is confined to some relatively narrow range, implementation of stationary filtering procedures appropriate to each subunit by frequency domain operations, and then recombination of the subunits to produce the final result. It should be pointed out that both of these methods are simply ideas at this point and, although they seem promising, have not yet been attempted.

In the first method, the original image matrix (128×128 , for example) is divided into smaller overlapping rectangular or square subunits. To avoid production of artifacts near the subunit boundaries after the filtering operations, each subunit must overlap adjacent subunits by a distance equivalent to the "significant" half-width of the processing spread function equivalent to the filtering operation to be implemented in the subunit in question. If, for example, each subunit is to be filtered to effect convolution with a Gaussian function of a width suited to the subunit count density (variable smearing), then each subunit must overlap adjacent subunits by several standard deviations of the Gaussian processing spread function for that subunit. Overlapping is required because Fast Fourier transformations implicitly "assume" that input data is periodic, so each subunit must be larger than that actually desired in the result to prevent the values at one edge of a subunit from seriously affecting the result at the opposite edge.

After the original data is divided into overlapping subunits (for example from an originally 128×128 image, into $64 \times 32 \times 32$ subunits with 16×16 central portions for which the results are actually used, which provides the possibility of 64 locally adapted spread functions up to 17×17 in significant size), each subunit is filtered in the frequency domain after a Fast Fourier Transformation, using a filter chosen on the basis of estimated

count density in the central portions of each subunit, and the subunits are inverse transformed individually. Non-overlapping central portions of the subunits are then pieced together to produce the final result.

For the example considered above, this approach requires approximately $64 \times 4 \times (32)^2 \times \log_2(32)$ multiplications versus $4 \times (128)^2 \times \log_2(128)$ multiplications for a stationary filtering and so is about 3 times slower, but the approach should be considerably faster than straightforward variable smearing and faster than the form of variable resolution recovery described in section IIIC.

In the second method, the original image matrix (say 128×128) is divided up into a number of 128×128 matrices (say 10), each of which consists of those elements from the original matrix with values falling into a specified range and with the other elements replaced by zeroes. The width of the count density ranges of the subunits need not be equal and possibly should be chosen inversely proportional to the square root of the value at the middle of the range. Each component 128×128 matrix is Fast Fourier Transformed and filtered using a filter appropriate for its count density range. The transformed and filtered component matrices are then added together and inverse Fast Fourier Transformed to produce the final result. If filters for adjacent count density ranges are not too different, overlapping of subunits will probably not be required using this method, and results can be added together before inverse transforming (thus reducing the number of transformations required), since the period of each subunit is equal to that of the original image matrix. Boundaries of subunits in the final results should not be noticeable since

- 1) "spillover" out of the non-zero portion of one subunit will be roughly compensated by spillover into that region from the subunit with adjacent range, and
- 2) noise in the original data matrix will cause boundaries of non-zero data in each subunit to be indistinct, preventing noticeably sudden changes in noise character and resolution across boundaries.

If the filters for adjacent count density ranges are quite different or if the effects of spillover are more troublesome than we suspect, overlapping regions can be used and the results pieced together in the space domain, at the expense of approximately a factor of two in processing time.

Assuming no overlapping is required and 10 count density ranges are used, this method requires approximately $(10 + 1) \times 2 \times (128)^2 \times \log_2(128)$ ^{multiplications} ~~operations~~ versus $4 \times (128)^2 \times \log_2(128)$ ~~operations~~ for stationary filtering and so is about $5\frac{1}{2}$ times slower. This method might be made relatively faster, however, by modifying the FFT algorithm to bypass multiplications and additions by zeroes, since each of the component subunit 128×128 matrices will be quite sparse.

One should note that although for the examples given here the first method allows 64 choices of processing spread function and the second allows only 10, choices using the first method are made for 64 positions while those using the second method are made for 10 count density ranges. In using the first method, many of the 64 spread function choices will be made approximately equal at different positions, so the flexibility afforded by the two methods is much more nearly comparable than might be apparent at first glance.

IV. NONLINEAR PROCESSING

The nonstationary linear techniques discussed in the previous section are linear in the sense that each output count density is determined by a linear (though variable) combination of local neighborhood count densities. These methods are, of course, nonlinear in the sense that if the number of counts in the image is doubled, then decisions on the processing spread function at each point are changed, and the expected output is not then simply twice the original expected output. Given any decision on a spread function at any point in the image, however, these methods are no longer nonlinear and are only nonstationary.

Other processing techniques exist which are much more basically nonlinear in that output count densities are determined by a nonlinear combination of input count densities involving divisions, products, square roots, and/or logarithms, for example. These nonlinear methods, however, can be conceived as nonstationary linear methods. One can think of the output at a point as a weighted sum of the values of surrounding elements, where the weights are a function of these element values. For example, if the result at position i, j is given by $\sum_{m,n} t_{mn} b_{i-m, j-n}^2$, where b is the raw image matrix and t is a constant matrix, the result can be rewritten as $\sum_{m,n} (t_{mn} b_{i-m, j-n}) b_{i-m, j-n}$, a weighted sum with weights which are a function of the local values of the raw image b .

Since nonlinear processing methods are not equivalent to a simple multiplicative operation in frequency space, they do not have the restriction of linear stationary methods that any method must multiply signal and noise at any frequency by the same filter factors. Thus the possibility exists that with nonlinear methods signal components can be "drawn out" from noise components in some sense.

Unfortunately, as we have seen in part I, effects of nonlinear methods are in general very difficult to predict, so formulation of nonlinear methods often becomes a matter of cut-and-try guided by educated guesswork.

Some promising nonlinear methods appropriate to scintigram processing are outlined in this section. Many more remain to be investigated and explored.

IV. A. Dot shifting and density shifting

Dot shifting and density shifting (Pizer and Vetter, 1966; Pizer, 1967; Metz, 1969, pp. 419-423; Pizer and Vetter, 1969) are essentially equivalent procedures in which counts are moved from their detected positions to positions which are a posteriori more likely, given knowledge of the detection system

point spread function and the observed image data. Specifically, each count (in dot shifting) or the count value of each image matrix element (in density shifting) is moved to its expected origin computed using Bayes' theorem, reflecting the increased probability that a count observed near a high-density region originated from within that region. If the observed location of a count or group of counts is indicated by position vector $\underline{r}$, if $s(\underline{r})$ represents the detection system point spread function, and if $b:(\underline{r})$ represents the observed (possibly smoothed) count density distribution, then an a posteriori estimate of the expected origin $\underline{r}'$ of the count or counts is given by (Metz, 1969, pp. 419-423):

$$\underline{r}' = \underline{r} - \frac{\iint \underline{u} s(\underline{u}) b:(\underline{r} - \underline{u}) d\underline{u}}{\iint s(\underline{u}) b:(\underline{r} - \underline{u}) d\underline{u}}$$

or in discrete notation:

$$i' = i - \frac{\sum_{m,n} m \cdot s_{mn} b:i-m,j-n}{\sum_{m,n} s_{mn} b:i-m,j-n}$$

and

$$j' = j - \frac{\sum_{m,n} n \cdot s_{mn} b:i-m,j-n}{\sum_{m,n} s_{mn} b:i-m,j-n}$$

Some smoothing operation is usually required in conjunction with dot shifting or density shifting, and somewhat different results are obtained depending upon the sequence of the operations, since nonlinear operations are generally not commutative with other operations.

One disadvantage of dot shifting and density shifting as they were originally formulated lies in their rigidity; only the smoothing parameters can be adjusted to adjust the method to reflect the statistical quality or structural nature of the original data. Another disadvantage, related to the first, lies in the fact that they do not produce the source distribution even in the absence of statistical fluctuations in the data, and cannot be used iteratively (without modification) to converge to the source distribution.

IV. B. Iterative Biased Smearing

In an effort to overcome some of the disadvantages of density shifting, we have developed a new method based on a similar theoretical approach. This new method is quite flexible and can be shown to converge to the source distribution when applied iteratively to noiseless data, at least in those special cases which we have been able to investigate up to this time. General convergence analysis is, unfortunately, very difficult.

IV. B. 1. Rationale

This new technique, which we call "iterative biased smearing", in its most elementary form consists of smearing out the contents of each image element in proportion to the best estimate of a posteriori Bayesian probability that the element contents originated in various other matrix elements, instead of shifting the entire contents of the element to its a posteriori expected origin as in density shifting. If $\{s_{ij}\}$ represents the detection system point spread function matrix, and if $\{b_{ij}\}$ represents the original (possibly smoothed) image data matrix, then an $(N+1)$ st estimate is calculated using the algorithm:

$$c_{ij}^{(N+1)} = c_{ij}^{(N)} \left\{ \sum_{m,n} s_{m-i,n-j} \left[\frac{b_{mn}}{\sum_{k,l} s_{m-k,n-l} c_{kl}^{(N)}} \right] \right\}$$

with $c_{ij}^{(0)} = b_{ij}$. Note that if after the N^{th} iteration the method achieves the source distribution, then in the absence of noise the quantity in square brackets

is unity, and further iterations effect no change; the source distribution is a fixed point of the method. One problem with the technique as it stands here is that in the presence of noise the fixed point becomes the inverse convolution of the noisy data, which is prohibitively noisy. We would prefer an only partially corrected distribution as a fixed point when applying the method to noisy data.

IV. B. 2 Modification

A remarkable property of this method is that the detector spread function matrix can apparently be replaced by two different rather arbitrarily chosen spread functions to increase flexibility of the method without adversely affecting its convergence in the absence of noise. In modified form, the algorithm becomes

$$c_{ij}^{(N+1)} = c_{ij}^{(N)} \left\{ \sum_{m,n} t_{m-i,n-j} \left[\frac{b_{mn}}{\sum_{k,l} u_{m-k,n-l} c_{kl}^{(N)}} \right] \right\},$$

where t and u are arbitrary processing spread function matrices.

In this form, the fixed point becomes that distribution which when convolved with u yields the observed count distribution. Thus by choosing u to be "narrower" than the detector spread function but of finite width, the fixed point can be adjusted to a partially corrected distribution.

The processing spread function t determines the rate at which the procedure changes the data; if t is chosen to be a very broad smoothing spread function, each iteration produces little change, while if t is a narrow or a resolution-correcting processing spread function--which is reasonable, as we show below--then each iteration produces a larger change. The spread function t also determines the degree to which noise is enhanced; the more t "smooths noise", the less each iteration enhances noise. One should note

in passing that total counts in the image is conserved at each iteration for any input image b : if and only if $t = u$; the significance of this property is not yet clear.

IV. B. 3. Convergence

One can show that in general the method corrects resolution--and enhances noise--more slowly in low contrast than in high contrast situations, since the term in square brackets approaches unity in low contrast regions of an image. This behavior is desirable in situations where features of equal amplitude are superimposed on different background levels in the same image, since signal to noise ratio is then lower in the low contrast region, and in this sense the method is adaptive even though stationary convolutions are used.

Analysis of convergence of the method and of effects on resolution, noise magnitude, and noise character for the general case is very difficult.

For the case of very low contrast image features superimposed on a uniform background, however, the method becomes approximately linear and can be shown to correspond to a stationary filtering operation using a filter with response

$$[1 - T_{kl}^* U_{kl}]^N + \frac{1 - [1 - T_{kl}^* U_{kl}]^N}{U_{kl}},$$

in which T and U are the discrete Fourier transforms of the equivalent processing spread function matrices padded with zeroes to the image matrix dimensions and $*$ indicates complex conjugate. For this case, the method converges in the absence of noise to that matrix which yields the observed distribution when convolved with u if and only if $|1 - T_{kl}^* U_{kl}| < 2$ at all frequencies (i.e., for all k and l). Thus the method can converge to a smoothed version of the source distribution, at least in the low contrast case, even if the matrix u is a smoothing matrix and t is a resolution-correcting or smoothing matrix, as long as the above condition is satisfied.

Note that for finite N , frequency response rises from unity, peaks, drops rather quickly toward unity, and approaches unity at high frequencies. Thus some form of additional rather sharp cut off filtering would seem to be desirable for noise control, at least in this case. One should note that for the general case, which apparently cannot be analyzed in detail, different results would be expected depending on whether the high frequency noise filtering is done before or after applying this method, since the procedures are not commutative. Note also that the closer T_{kl}^* approximates $1/U_{kl}$, the more the method approximates filtering by a $1/U_{kl}$ transfer function for any given N , and thus the more noise is enhanced.

One other special case which we have been able to analyze up to this time in the absence of noise is that of a Gaussian source distribution s imaged by a Gaussian detection system spread function s , and corrected using equal Gaussian functions for t and u . Convergence and at least partial resolution correction are guaranteed for this case if t and u are at least as narrow as s , and full correction is approached rather quickly if t and u are equal to s .

IV. B. 4. Implementation

Iterative biased smearing is not a quick technique, though its implementation can be made fairly efficient by using FFT methods. Each iteration requires, in order, a convolution, an element-by-element division, another convolution, and an element-by-element multiplication; when using an FFT algorithm to effect the convolution operations, four one-way transforms plus three element-by-element multiplications (two complex) and one element-by-element division are required, somewhat more than twice the operations required for a single stationary filtering. Although this computational load is not prohibitive when using a large, fast computer and a moderate number of iterations,

we do not yet know whether the performance and apparent flexibility of the technique will justify the cost of its implementation.

One additional possible modification is replacement of one or both of the convolutions by nonstationary procedures. Although these changes seem theoretically attractive, the additional cost in computational load would be high. We have not yet explored this possibility and do not know how much improvement over the above method using stationary filtering operations might be realized.

IV. C. Combination of Linear Techniques with Point-by-point (Zero Memory)

Nonlinear Transformations

A broad class of image processing techniques consists of applying some nonlinear point-by-point (zero memory) transformation to the original image data (i.e., nonlinear transformation of each image matrix value independently according to some rule), applying a linear processing technique (e.g., stationary filtering, variable averaging, or variable resolution recovery) to the transformed data, and then applying another, generally different, point-by-point nonlinear transformation to produce the final result. This general procedure (sometimes called "homomorphic filtering") can be written generally as:

$$c_{ij} = \phi_2[L[\phi_1[b_{ij}]]],$$

where ϕ_1 and ϕ_2 represent point-to-point nonlinear transformations and L represents a stationary or nonstationary linear processing operation. The transformation ϕ_2 is often chosen as the inverse of ϕ_1 .

The potential usefulness of these procedures lies in the possibility of "drawing out" a feature of interest from the noise (or separating several features of interest) in some sense by the first nonlinear transformation, selectively enhancing the feature(s) or suppressing the noise by the linear

operation, and then returning the enhanced image to a perceptually useful scale by the second nonlinear transformation.

Perhaps the best known example of this class of techniques is the case in which ϕ_1 is a natural logarithmic transformation, L is a stationary filtering operation, and ϕ_2 is exponentiation to the base "e". This method has been used with some success by Oppenheim, Schafer, and Stockham (1968) to process optical photographs and by Kirch and Brown (1972) to process scintigrams.

Because of the large number of nonlinear transformations which can be attempted, because their effects on features of interest and noise individually are not usually easy to predict, and because choice of the best linear operation to be used between transformations is not usually apparent, little work has been done using this approach up to the present time. The approach can be computationally quite efficient, however; especially if FFT methods are used to implement the stationary linear operation, and the flexibility afforded by the general technique suggests that it should be explored further.

V. SUMMARY

We have attempted to outline in this paper a number of nonstationary and nonlinear scintigram processing procedures, some of which have already been proved encouraging and some of which are still being developed.

Two basic advantages of stationary linear processing methods are their computational efficiency (when implemented in the frequency domain) and their theoretical convenience (in that measures of their effects on resolution, noise magnitude, and noise character can be predicted rather simply). A major disadvantage of stationary linear techniques, however, is their inability to respond selectively to the different balance between signal and noise in different parts of an image.

Nonstationary and nonlinear processing methods are often computationally less efficient than stationary linear techniques and are often difficult to analyze theoretically, but they are usually more flexible and can be made to adapt to local conditions of signal structure and noise. The vast number of conceivable nonstationary and nonlinear operations suggests that much work remains to be done in exploring these methods and in objectively evaluating results of their use.

References

- Beck, R. N.: Collimators for radioisotope scanning systems, In Medical Radioisotope Scanning. (Vienna: IAEA), Vol. 1, 1964, p. 211.
- Beck, R. N.: Collimation of gamma rays. In Fundamental Problems in Scanning. A. Gottschalk and R. N. Beck, eds. (Springfield, Ill: Charles C. Thomas), 1968, p. 71.
- Blackman, R. B. and Tukey, J. W.: Measurement of Power Spectra. (New York: Dover), 1959.
- Brown, D. W.; Kirch, D. L.; Ryerson, R. W.; Throckmorton, A. J.; Kilbourn, A. L.; and Brenner, N. B.: Computer processing of scans using Fourier and other transformations. J. Nuc. Med., 12: 287, 1971.
- Brown, N. J. and Weaver, H. J.: Two-dimensional Finite Fourier Transform Techniques. (Livermore, Calif.: Lawrence Radiation Lab.), Report UCRL-51046, 1971.
- Brownell, G. L., Aronow, S. and Hine, G. J.: Radioisotope scanning. In Instrumentation in Nuclear Medicine, Vol. 1, Hine, G. J. and Orvis, A., eds. (New York, Academic Press), 1967, pp. 381-428.
- Chesler, D. A.: Resolution enhancement by variable filtering. Internal report, Physics Research Laboratory, Massachusetts General Hospital, January, 1969.
- Cochran, W. T.; Cooley, J. W.; Favin, D. L.; Helms, H. D.; Kaenel, R. A.; Lang, W. W.; Maling, G. C. Jr.; Nelson, D. E.; Rader, C. M.; and Welch, P. D.: What is the fast Fourier transform? Proc. IEEE, 55, 1664, 1967.
- Cooley, J. W. and Tukey, J. W.: An algorithm for the machine calculation of complex Fourier series. Math. of Comput., 19: 297, 1965.
- Fisher, J. R.: Fortran Program for Fast Fourier Transform. (Washington, D. C.: Naval Research Lab.) Report 7041, 1970.
- Gold, B. and Rader, C. M.: Digital Processing of Signals, (New York, McGraw-Hill), 1969.
- Gustafsson, T. and Todd-Pokropek, A.: Filters with variable shape in radioisotope image processing. This volume, 1972.
- Haight, F. A.: Handbook of the Poisson Distribution. (New York, London: John Wiley and Sons), 1967, pp. 5-7.
- Hart, R. W. and Farrell, R. A.: Imaging distribution of radioactivity within the human body. I. Theoretical considerations in optimum data processing. Invest. Radiol., 3: 199, 1968.

- Hunt, W. A.; Lorenz, W. J.; Meder, H. G.; Luig, H.; Pistor, P.; Schmidlin, P.; Walch, G.; and Schmitt, H. G.: Digital Processing of Scintigraphic Images, (Wissenschaftliches Zentrum Heidelberg, IBM Germany), Tech. Rept. #70.03.001, 1970.
- Iinuma, T. A. and Nagai, T.: Image restoration in radioisotope imaging systems, Phys. Med. Biol., 12: 501, 1967.
- Kirch, D. L. and Brown, D. W.: Recent advances in digital processing static and dynamic scintigraphic data. In Proceedings of 2nd Oak Ridge Symposium on Sharing of Computer Programs and Technology in Nuclear Medicine, April 20-21, 1972. USAEC Conf. Series (Springfield, Va.: Nat. Tech. Info. Service, U.S. Dept. Commerce), 1972.
- Markel, J. D.: FFT pruning. IEEE Trans. Audio, AU-19: 305, 1971.
- Metz, C. E.: A Mathematical Investigation of Radioisotope Scan Image Processing. Doctoral thesis, Univ. of Pennsylvania. (Ann Arbor, Mich.: University Microfilms), Pub. (#70-16,186), 1969.
- Metz, C. E.: On the differential method of image focusing, J. Nuc. Med., 11: 142, 1970.
- Nagai, T., Fukuda, N. and Iinuma, T. A.: Computer focusing using an appropriate Gaussian function. J. Nuc. Med., 10: 209, 1968.
- Oppenheim, A. V., Schafer, R. W. and Stockham, T. G. Jr.: Nonlinear filtering of multiplied and convolved signals. Proc. IEEE, 56: 1264, 1968.
- Papoulis, A.: Probability, Random Variables, and Stochastic Processes, (New York and London: McGraw-Hill), 1965.
- Pizer, S. M. and Vetter, H. G.: The problem of display in the visualization of radioisotope distributions. J. Nuc. Med., 7: 733, 1966.
- Pizer, S. M.: Production and Processing of Radioisotope Scans, Doctoral Thesis, Harvard University, 1967.
- Pizer, S. M. and Vetter, H. G.: Processing radioisotope scans, J. Nuc. Med., 10: 151, 1969.
- Pizer, S. M.: Digital spatial filtering and its variations. In Quantitative Organ Visualization in Nuclear Medicine, P. J. Kenny and E. M. Smith, eds, (Coral Gables, Fla.: U. of Miami Press), 1971.
- Sprau, A. C., Tauxe, W. N. and Chaapel, D. W.: A computerized radioisotope scan-data filter based on a system response to a point source. Mayo Clinic Proc., 41: 585, 1966.
- Tanaka, E. and Iinuma, T. A.: Approaches to optimal data processing in radioisotope imaging. Phys. Med. Biol., 15: 683, 1970.

Vetter, H. G. and Pizer, S. M.: Perception of Quantum Limited Images,
Photogrammetric Engin., Nov. 1970, pp. 1179-1188.

Vetter, H. G. and Pizer, S. M.: A measure for radioisotope scan image quality.
J. Nucl. Med., 12: 526, 1971.