Technique for Locating Homogeneous Regions within CT Brain Slices

H. T. Thaler,[1] H. C. Lu, and D. A. Rottenberg

Accurate estimates of the CT numbers of cerebral spinal fluid, white matter, gray matter, and bone are difficult to obtain from transaxial CT brain slices using a manually controlled joy stick/cursor and standard region of interest/statistics software. Careful manual surveys of anatomically homogeneous regions of interest [1] are tedious and may be subject to unconscious observer bias. The use of an interactive minimum variance computer program to select small, homogeneous areas within larger, user-defined regions of interest greatly facilitates the estimation of characteristic tissue CT numbers by reducing observer bias, excluding volume-averaged voxels, and graphically delimiting the homogeneous areas on a video screen image.

Materials and Methods

Within a given region of interest, the CT numbers of individual voxels may be considered as random noise superimposed upon a measure of the true density of circumscribed brain tissue(s). Let X_{ij} denote the observed CT number for a voxel in row i, column j of the image grid. Then $X_{ij} = \mu_{ij} + e_{ij}$, where μ_{ij} designates the expected (true) value for the measured CT density at location ij and e_{ij} designates random noise (measurement error) with mean = 0 and variance (standard deviation squared) = σ_{ij}^2.

The sensitivity of the measurement may vary with density, i.e., σ_{ij}^2 may be a function of μ_{ij}. But in most available CT scanners, σ^2 is a relatively slowly changing function of μ, and we simply assume that σ_{ij}^2 is nearly constant over the range of CT numbers of interest. The average CT number for voxels in a square region of interest centered at ij in the grid may be written as the sample mean,

$$\bar{X}_{ij} = \left(\sum_m \sum_n X_{mn}\right) \Big/ N,$$

and the variance for the same region of interest may be written as the sample variance,

$$s_{ij}^2 = \left(\sum_m \sum_n X_{mn}^2 - N\,\bar{X}_{ij}^2\right) \Big/ (N-1),$$

where the summations are from $m = i - d$ to $i + d$, and from $n = j - d$ to $j + d$. The square has $2d + 1$ voxels on a side so that $N = (2d + 1)^2$.

The expected value of the sample mean is:

$$E(\bar{X}_{ij}) = \bar{\mu}_{ij} = \sum_m \sum_n \mu_{mn}/N.$$

If the measurement errors e_{ij} are uncorrelated, then the expected variance is:

$$E(s_{ij}^2) = \sum_m \sum_n (\mu_{mn} - \bar{\mu}_{ij})^2 \Big/ (N-1) + \sum_m \sum_n \sigma_{ij}^2 \Big/ N$$

The first term, $\sum_m \sum_n (\mu_{mn} - \bar{\mu}_{ij})^2/(N-1)$, is a nonnegative number representing the heterogeneity of voxels in the region of interest and goes to zero when all voxels have the same CT density. Thus, on the average (apart from any inherent measurement error), the smaller s^2, the greater the homogeneity.

In practice, a large rectangular region of interest may be covered with small, overlapping squares with, for example, 3, 5, or 7 voxels on a side. If the square with the smallest s^2 value is selected out, its corresponding $\bar{X}$ value provides an estimate of the mean CT number of a homogeneous, "pure" tissue within the region of interest. Based on these considerations, a FORTRAN/graphics program has been written to facilitate the interactive determination of the mean CT numbers of various brain tissues (e.g., cerebral spinal fluid, white matter, gray matter, and bone) from standard CT brain slices (figs. 1 and 2). This program locates and displays the most homogeneous square of specified dimensions within a larger region of interest and prints the corresponding $\bar{X}$ and s^2 value to the right of the video screen image. Upper and lower threshold CT numbers may be input so as to exclude those squares with mean values outside of a predetermined range. This option permits the localization of homogeneous bone regions, for example, within a region of interest containing air and gray matter (fig. 2), although the bone (skull) may be inherently more heterogeneous than air or brain and scanner measurement error is greatest for bone.

Discussion

The FORTRAN/graphics program has been used to estimate the CT density of metrizamide-containing cerebral spinal fluid (fig. 1) and to obtain $\bar{X}$ and s^2 values for "pure" cerebral spinal fluid, white matter, and gray matter. Estimates of the CT density of metrizamide-containing cerebrospinal fluid are required for measuring ventricular volume

Received November 19, 1979; accepted after revision March 26, 1980.

This work was supported in part by a National Cancer Institute grant CA08748 to H. T. Thaler. D. A. Rottenberg received Teacher Investigator award 1-KO7 NS 00286 from the National Institute of Neurological and Communicative Diseases and Stroke.

[1]All authors: Biostatistics Laboratory and Department of Neurology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10021. Address reprint requests to D. A. Rottenberg.

 0195-6108/80/0104-0475 $00.00 © American Roentgen Ray Society

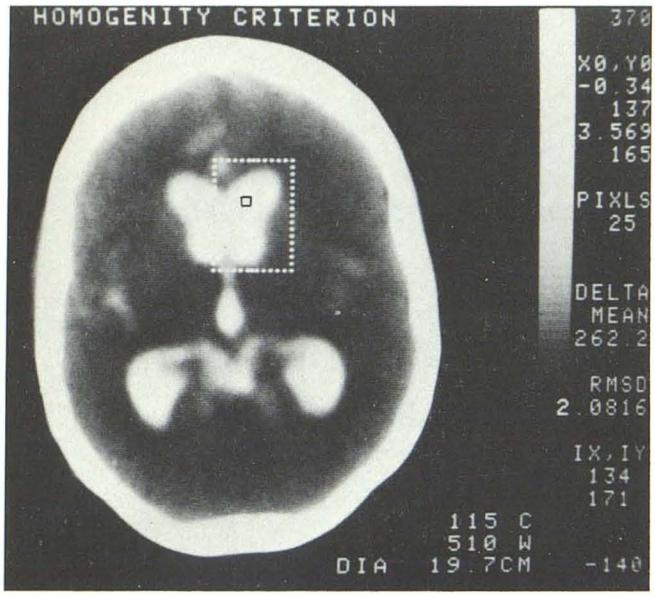

Fig. 1.—Determination of lateral ventricular metrizamide concentration using minimum variance computer program. Rectangular region of interest (dotted lines) is superimposed on CT image and encompasses part of right lateral ventricle. *X* and *Y* coordinates at center of region of interest (*XO*, *YO*) are at upper right. 5 × 5 pixel cursor (area 25 pixels) systematically surveys region of interest, and 25 pixel square with the smallest variance (root mean square 2.0816) is automatically selected as defining most homogeneous region within metrizamide-filled ventricular contour (threshold $150 < \bar{X} < 350$ Delta units). Mean CT number of square is 262.2 Delta units. 25 pixel square is outlined in black on image; location of square is specified by coordinates *IX*, *IY*.

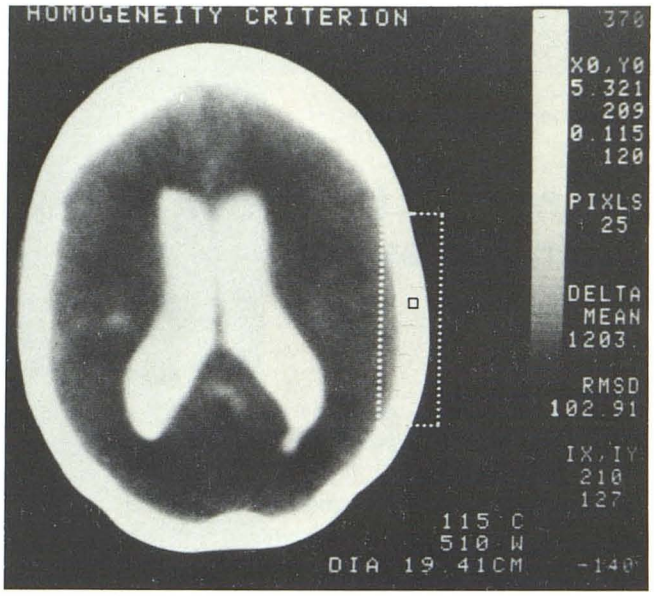

Fig. 2.—Homogeneity criterion applied to calvarial bone. Within user-defined rectangular region of interest, 25 pixel square with $500 < \bar{X} < 1500$ Delta units and smallest variance is outlined in black (root mean square 102.91, CT number 1203 Delta units).

using partial volume analysis [2] and for assessing lateral [1, 3] and third-ventricular contributions to total cerebral spinal fluid bulk flow. $\bar{X}$ and s^2 values for the cerebrospinal fluid, white matter, and gray matter are required input to a published algorithm for estimating the relative proportions of these three substances in CT brain slices [4].

Our algorithm may be further refined by standardizing the observed variances, which, as noted, may increase slightly with CT number. If the relationshiip between σ^2 (the variance) and μ (the mean CT number) is expressed as a mathematical function (f), so that $\sigma^2 = f(\mu)$, then a correction factor may be empirically determined for any tomograph by scanning phantoms containing homogeneous substances with characteristic CT numbers spanning the range of interest. So long as the change in σ^2 is small relative to the difference in the observed mean CT numbers (i.e., $f'(\mu) \ll 1$), the bias introduced by not using a correction factor will be negligible. The very nature of the algorithm introduces a negative bias into the selected s^2, since s^2 is deliberately minimized and tends to underestimate σ^2 in homogeneous regions.

The minimum variance method may be used to survey anatomically defined regions of interest and to obtain characteristic mean CT numbers for "pure" brain tissues and calvarial bone. Our FORTRAN/graphics program will facilitate the study of age-related changes in the mean CT numbers of anatomically defined white- and gray-matter structures and provide quantitative information about the progression of symptomatic leukodystrophy [5], drug-induced leukoencephalopathy [6], and cerebral edema.

REFERENCES

1. Rottenberg DA, Deck MDF, Allen JC. Metrizamide washout as a measure of CSF bulk flow. *Neuroradiology* **1978;** 16:203–206
2. Rottenberg DA, Pentlow KS, Deck MDF, Allen JC. Determination of ventricular volume following metrizamide CT ventriculography. *Neuroradiolgy* **1978;** 16:136–139
3. Rottenberg DA, Howieson J, Deck MDF. The rate of CSF formation in man: preliminary observations on metrizamide washout as a measure of CSF bulk flow. *Ann Neurol* **1977;** 2: 503–510
4. Thaler HT, Ferber PW, Rottenberg DA. A statistical method for determining the proportions of gray matter, white matter, and CSF using computed tomography. *Neuroradiology* **1978;** 16: 133–135
5. Arimitsu T, Di Chiro G, Brooks RA, Smith PB. White-gray matter differentiation in computed tomography. *J Comput Assist Tomogr* **1977;** 1:437–442
6. Allen JC, Thaler HT, Deck MDF, Rottenberg DA. Leukoencephalopathy following high-dose intravenous methotrexate chemotherapy: quantitative assessment of white matter attenuation using computed tomography. *Neuroradiology* **1978;** 16: 44–47