An Operator-Independent Method for Background Subtraction in Adrenal-Uptake Measurements: Concise Communication

Kenneth F. Koral and Salil D. Sarkar

University of Michigan Medical Center, Ann Arbor, Michigan

A new computer program for adrenal-uptake measurements is presented in which the algorithm identifies the adrenal and background regions automatically after being given a starting point in the image. Adrenal uptakes and results of reproducibility tests are given for patients injected with [^{131}I] 6β-iodomethyl-19-norcholesterol. The data to date indicate no overlap in the percent-of-dose uptakes for normal patients and patients with Cushing's disease and Cushing's syndrome.

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The accurate subtraction of background in adrenal images is a difficult problem that limits the usefulness of quantitative uptake measurements. In 1972, Morita et al. described a method for quantitative determination of [^{131}I] 19-iodocholesterol uptake by using a standard curve and a lateral view to correct for "tissue" attenuation (*1*). The standard curve was determined from measurements on a rice phantom. The background in the adrenal count was estimated by the number of counts in one or more nearby regions, which were not to include bowel, bladder, or liver activity. Moses et al. (*2*) modified the preceding method of background estimation by summing all horizontal slices through an area of radioactivity including the adrenal, and then drawing a baseline under the resultant adrenal peak to give the background curve.

Both of these methods for estimating background were time consuming and had the disadvantage of allowing the operator considerable freedom in choosing a baseline or flagging areas of interest. In the series by Moses et al. (*2*), the average combined percent-of-dose uptake for both adrenals in 18 normal patients was 0.23 ± 0.11 (1 s.d.) and five out of eight patients with Cushing's disease had values that were within 2 s.d. of the normal mean.

In an effort to improve the accuracy of adrenal-uptake values, we have developed a new computer program that chooses the adrenal and background regions automatically after being given a starting point.

This paper describes the algorithm and presents adrenal uptakes and results of redroducibility tests in patients injected with [^{131}I] 6β-iodomethyl-19- norcholesterol, NP-59 (*3–5*). The preliminary clinical results indicate that these uptakes can differentiate between normals and those with hypercortisolism due to adrenocortical adenomas or hyperplasia.

MATERIALS AND METHODS

Algorithm. The basic assumption of the algorithm is that for every patient a fixed number of matrix points in the image will adequately encompass the radioactivity concentration in either adrenal. Empirically it has been found that 108 points (approximately a 4-cm × 4-cm area) is a good choice.

The computer algorithm starts with a point chosen by the operator near the adrenal center and repeatedly searches an expanding region for matrix points with maximum counts. Once the entire adrenal area has been mapped out, the algorithm surrounds this area by a narrow band of matrix points (approximately 2 matrix points in width) which are

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For reprints contact: Kenneth F. Koral, R-3054 Kresge II, University of Michigan Medical Center, Ann Arbor, MI 48109.

used to estimate the background in the adrenal count. The adrenal uptake in counts, U, is then given by:

$$U = A - \frac{108}{N} \cdot B,$$

where A is the number of counts in the adrenal region and B and N are the number of counts and the number of points, respectively, in the background region.

In detail, the procedure is as follows. The algorithm assigns the operator-selected point to a region that can be called the adrenal "center." It then "draws" a square around this point and tentatively assigns all eight nearest-neighbor matrix points to a region that can be called adrenal "edge." Next, it searches all adrenal edge points for the one or more points having the highest count value. These "hottest" points are reassigned to the adrenal center and any unassigned nearest neighbors to these points are again tentatively made adrenal edge. The search-and-assign procedure is continuously repeated until the center plus edge includes 108 matrix points. The algorithm then surveys all edge points and establishes unassigned points within two nearest-neighbor distances on a square matrix as background points.

A typical adrenal image is shown in Fig. 1a. In Fig. 1b the region that has been selected for the left adrenal is shown outlined in black. The black outline itself covers the region chosen to estimate the background. Figure 1c shows that the final result is not sensitive to the operator's choice of the adrenal center. Any one of the matrix points highlighted may be chosen as the center without producing a difference in the results.

Patients. Twenty-minute posterior and 10-min lateral images were obtained with an Anger scintillation camera from 4 to 14 days after intravenous injection of 2 mCi/1.7 m^2 of [^{131}I] 6β-iodomethyl-19-norcholesterol and stored on the magnetic disk of a minicomputer. The uptake in counts was determined as outlined above, and the uptake as a percentage of administered dose was computed from a phantom standard curve as in Morita et al. (*1*). For the scintillation camera with a 1,000-hole medium-energy collimator, the computer scale factor was 0.36 cm per matrix element and the exponential attenuation constant was 0.10 cm^{-1}. The percent-of-dose uptakes were obtained for five patients with no evidence of adrenal disease, for four patients with ACTH-excess bilateral adrenocortical hyperplasia, and for three patients with adenoma-induced Cushing's syndrome.

Test of reproducibility. The reproducibility of results was studied in five instances by dividing the normal 20-min imaging time for the patient into two 10-min subsets. The percent difference in the uptakes for the two images thus obtained was compared with the average percent standard deviation expected from statistical error alone.

RESULTS

Typical time dependence of the results obtained for the left adrenal of a normal patient is presented in Fig. 2. At the top the counts in the adrenal region, the weighted background, and the net uptake in

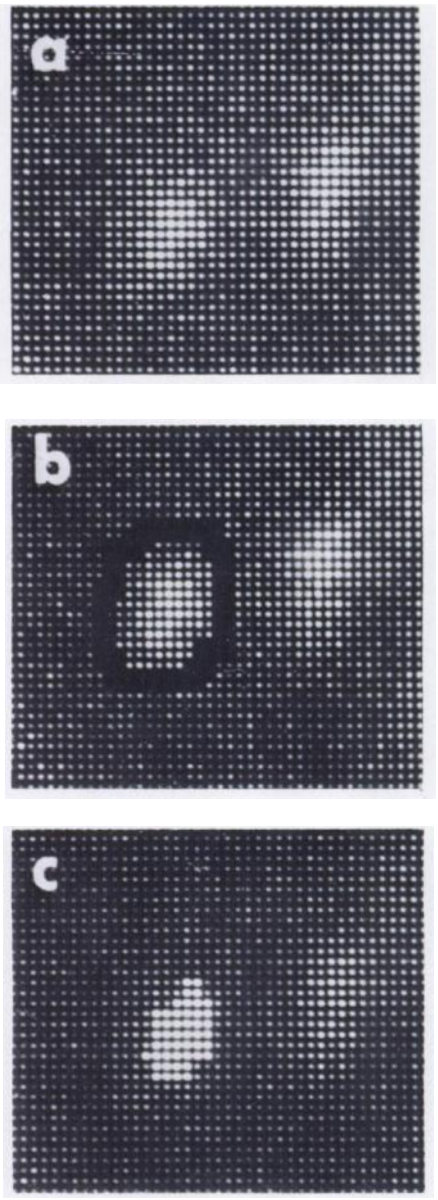

FIG. 1. (a) Typical 20-min posterior adrenal image. (b) Outline of left adrenal as chosen by computer algorithm. Outline in black itself covers region selected to estimate background adding to adrenal count. (c) Image showing all possible starting points that could be chosen by operator without changing region selection shown in (b).

counts are plotted against the number of days after injection. The expected uptake error, due to statistics alone, is ±7% (1 percent s.d.) on Day 7. This percent standard deviation, Σ, was computed as:

$$\Sigma = \frac{\sqrt{(\sigma_A^2 + \sigma_B^2)}}{U} \times 100,$$

where σ_A is the standard deviation for the counts in the adrenal region and σ_B is the standard deviation for the weighted background.

The lower graph shows percent-of-dose uptake plotted against days after injection. This uptake was computed using a depth determination (distance from the center of the adrenal gland to a cobalt-56 strip lying on the patient's back) of 9.9 cm made from a right lateral image on Day 8. For each millimeter of uncertainty in the depth determination there is an additional error of ±1% in these values.

Table 1 presents a list of the percent-of-dose uptake for each adrenal in normals (patients without detectable adrenal disease) and patients with various known adrenal disorders. In five normal patients the average combined percent-of-dose uptake for both adrenal glands 5–7 days after injection inclusive was 0.42 ± 0.05 (1 s.d.). The same uptake in the case of four patients with ACTH-excess Cushing's disease was 1.04 ± 0.17. The uptake for a single adrenal was 0.21 ± 0.03 in normals and was 1.11 ± 0.70 in three patients with Cushing's adenoma.

The reproducibility of results for the patients tested was only slightly less than the reproducibility that would be expected from statistical error alone. The percent difference in uptake between the two 10-min images and the average percent standard deviation for the 2 images, $\bar{\Sigma}$, was computed for an adrenal in ten cases. The percent difference fell within 1 $\bar{\Sigma}$ in four of ten cases and within 2 $\bar{\Sigma}$ in all ten.

TABLE 1. PERCENT-OF-DOSE UPTAKE VS DAYS AFTER INJECTION FOR THREE CLASSES OF PATIENTS

Pt. No.	Adrenal	Days 4	5	6	7	8	14
		No evidence of adrenal disease					
1	L			0.21		0.21	
	R			0.21		0.21	
2	L		0.23	0.26			
	R		0.23	0.22			
3	L		0.20		0.20		
	R		0.23		0.23		
4	L		0.18			0.20	
	R		0.17			0.18	
5	L		0.23		0.15		
	R		0.23		0.21		
		ACTH-excess Cushing's disease					
6	L		0.40		0.56		
	R		0.41		0.58		
7	L		0.59		0.55		
	R		0.57		0.57		
8	L		0.40				
	R		0.41				
9	L	0.48			0.56		
	R	0.58			0.61		
		Cushing's syndrome (due to adenoma)					
10	L			—			—
	R			1.13			0.86
11	L		—				
	R		1.80				
12	L		—				
	R		0.41				

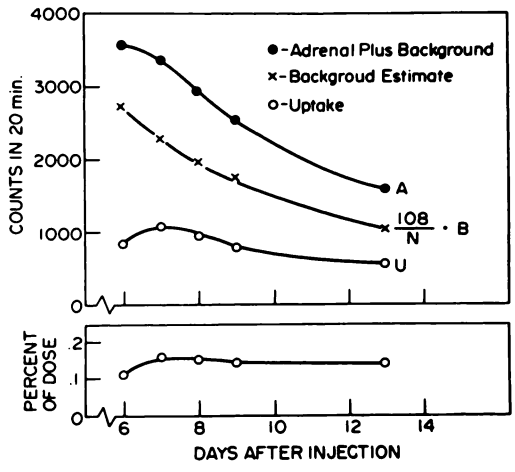

FIG. 2. Results for left adrenal of a normal patient, given 1.3 mCi of radiopharmaceutical, as a function of days after injection. At each day, adrenal uptake in counts, U, is difference between counts in adrenal region, A, and the counts in background region, multiplied by number of points in adrenal region over that in background region, (108/N) B. Adrenal uptake as a percentage of dose is derived from U taking into account tissue attenuation and administered dose corrected for radioactive decay to day of measurement.

DISCUSSION

The usefulness of adrenal imaging could be enhanced if a reliable quantitative uptake measurement were available. Only tomographic imaging could rule out the possibility of error due to background lying directly in front of or behind an adrenal. However, our new method for background subtraction provides a simpler and, probably, a more accurate method than has been available. Only two decisions are required of an operator:

1. He must determine the x,y coordinate of the center of the adrenal. The result is *not* sensitive to this selection.
2. He must decide if the algorithm has failed to find a reasonable adrenal region upon being presented with the background and

adrenal display (Fig. 1b). This failure occurs when the target-to-nontarget ratio drops below that needed to resolve the adrenal from the background and the liver. (The problem would be more frequent if the fixed number of matrix points to be included as adrenal by the algorithm were increased.) In practice, the operator's decision is usually easy, since failure involves inclusion of a region that is obviously not part of the adrenal.

Preliminary data show no overlap in the percent-of-dose uptake between normal patients and those with hypercortisolism due to bilateral adrenocortical hyperplasia or unilateral adenoma.

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