COMPUTER SCIENCES

Myocardial Perfusion Imaging Using Thallium-201: A New Algorithm for Calculation of Background Activity

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A method is presented for calculating a background image to be subtracted from Tl-201 myocardial perfusion images. The method was derived from experimental measurements of background components in which hearts of animals injected with Tl-201 were replaced with hearts from nonradioactive animals. The algorithm generates a background image that accounts for Tl-201 activity in surrounding tissues and within the cardiac chamber. Comparison of the computer-generated background images with background images of the experimental models showed a mean difference of about 3% (range 1-6%). Clinical images using this method of background generation and subtraction are presented.

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Thallium-201 chloride is the most commonly used radiopharmaceutical for assessing myocardial perfusion. Studies using radioactive microspheres and contrast coronary angiography have demonstrated the ability of Tl-201 to detect regions of myocardial ischemia (*1–4*). Myocardial perfusion scans using Tl-201 have proven useful in the early detection of myocardial infarction (*5,6*), evaluation of results of coronary artery revascularization surgery, (*7*), and the assessment of regional ischemia of the myocardium during exercise stress testing (*8,9*).

A significant technical limitation in interpreting the Tl-201 myocardial scintigram is the relatively high background radioactivity in structures adjacent to the heart (*10*). The relatively low heart-to-background ratio of radioactivity (2:1 at rest) contributes to poor image quality and thus to difficulty with assessing myocardial perfusion. Although exercise increases the heart-to-background ratio and thus image quality, certain patients are able to achieve only modest levels of exercise. Image interpretation is further complicated by the requirement for imaging promptly after exercise to minimize the effects of Tl-201 redistribution (*11*).

With image data processing, some form of background subtraction may be used to diminish the interference of background activity in myocardial images. Goris et al. (*12*) described an interpolative method of generating background activity in the myocardial region. By use of an experimentally determined "true background" image, Narahara et al. (*13*) showed that the Goris method subtracted an excessive amount of true myocardial activity. Narahara et al. recommended the use of a constant 20% subtraction of background activity rather than calculation of true background activity.

This report describes a computer algorithm for calculating a background image based on experimentally determined (true) background components.

METHODS

The background contribution to the myocardial Tl-201 image was determined using an animal model. Studies were carried out in mongrel dogs weighing about 17 kg. Two dogs (six pairs) of similar size and weight were used for each study. Thallium-201, (thallous chloride) 1–2 mCi, was injected intravenously via leg vein in one animal in the resting state. The second animal did not receive the radiopharmaceutical. Fifteen minutes

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after Tl-201 injection, the first dog was anesthetized with secobarbital and cardiac fibrillation induced with i.v. potassium chloride. The second dog was killed in the same manner. Immediately after fibrillation scintigrams of the heart were obtained using a standard-field gamma camera with high-resolution collimator. The 43% energy window was centered on the 72.6-keV spectral peak. The camera was interfaced to a computer system* that allowed acquisition of data in a 64 × 64 frame buffer and storage on disk and tape. Images were obtained in anterior, 45° LAO, and left lateral positions by recording 500,000 counts.

A median sternotomy was then performed and all vessels entering and leaving the pericardium doubly ligated and severed. Extreme care was taken to maintain the anatomy of the surrounding lungs and vasculature and to ensure negligible blood loss from the heart and pericardial structures. The heart of the nonradioactive dog was removed in a similar manner. The volumes of the hearts were adjusted to equality using a volumetric beaker and catheters inserted into each ventricular chamber. The nonradioactive heart was then placed in the radioactive dog and the radioactive heart in the nonradioactive dog. Correct orientation of the donor heart was accomplished using sutures attached to each lateral wall and apex region of the heart before removal. The lungs were reinflated to fill the thoracic cavity and to stabilize the transplanted heart further. The thoracic cage was then closed. Gamma images were obtained in the original projections following replacement of the heart.

The contribution of the cardiac blood pool was assessed by removal of the heart from a Tl-201-injected dog by the technique described above, and the heart imaged in multiple projections. Through the cannulae placed in each ventricular chamber, the blood was then removed and replaced with normal saline. The heart was imaged again and pooled blood activity was determined under conditions identical to those of cardiac imaging. With a well counter, the activity per milliliter was determined in a 10-ml blood sample obtained 15 min after Tl-201 injection from the same dog. The cardiac blood-pool activity was calculated from the known volume of blood in the heart.

The relative distribution of background activity was determined from profile curves generated by an area three-channels wide (1.2 cm) over the center of the heart in a horizontal plane (*14*). The background consists of activity from adjacent organs, surrounding tissue, and the blood pool. The relative distribution of background activity was determined by the profiles and formed the basis for comparison between the true background and the computer-generated background. Figure 1 is a schematic of representative profiles.

From the experimental results, a background image construction algorithm was developed and is summarized as follows. First, starting with a digitized Tl-201 image, smoothed by weighted nine-point averaging, an elliptical region encompassing the heart image is defined. Second, within this region a "reference plane" (Fig. 1), an interpolated set of new pixel values, is generated as in the method of Goris (*12*). Third, the region is given a final content, calculated by subtraction of a fraction, f, of the difference, Δ, between the original image and the reference plane, from the reference plane itself.

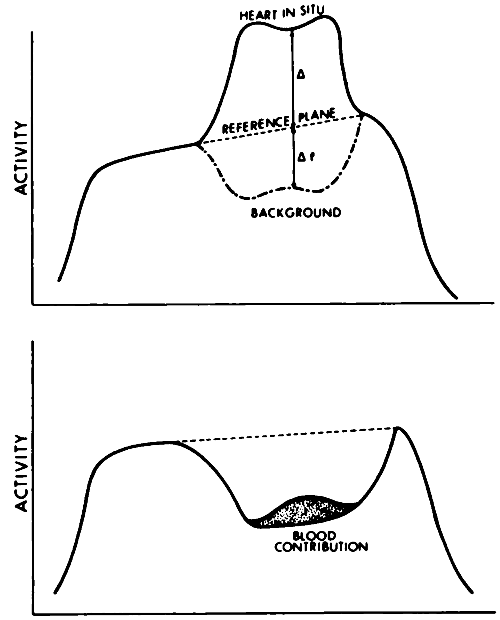

FIG. 1. Schematic representation of profiles of average background components. Top: profiles showing relationship between image data with heart in situ, reference plane, and background. Background = reference plane −Δf. Bottom: modification of background profile to show contribution to background caused by blood in cardiac chambers.

The background image, then, has new values inside the heart region and original values outside that region. (Actually generation of the final background image proceeds totally pixel-by-pixel—as indicated in the flow chart in the Appendix—rather than by the separated steps above, to achieve higher running speed.)

RESULTS

Figure 2 illustrates representative unprocessed Tl-201 scintigrams of the heart obtained in the anterior, LAO, and left lateral projections. At the right are the activity profiles for the sections between the horizontal lines. The unprocessed scintigrams show significant activity in the juxtacardial structures. Initial studies, in which the radioactive hearts were replaced by nonradioactive hearts, demonstrated that (a) the noncardiac or background activity within the heart outline was significantly less than (b) background activity surrounding the heart. The gross images (Fig. 4) are like those described by Narahara et al. (*13*), in which the radioactive hearts were

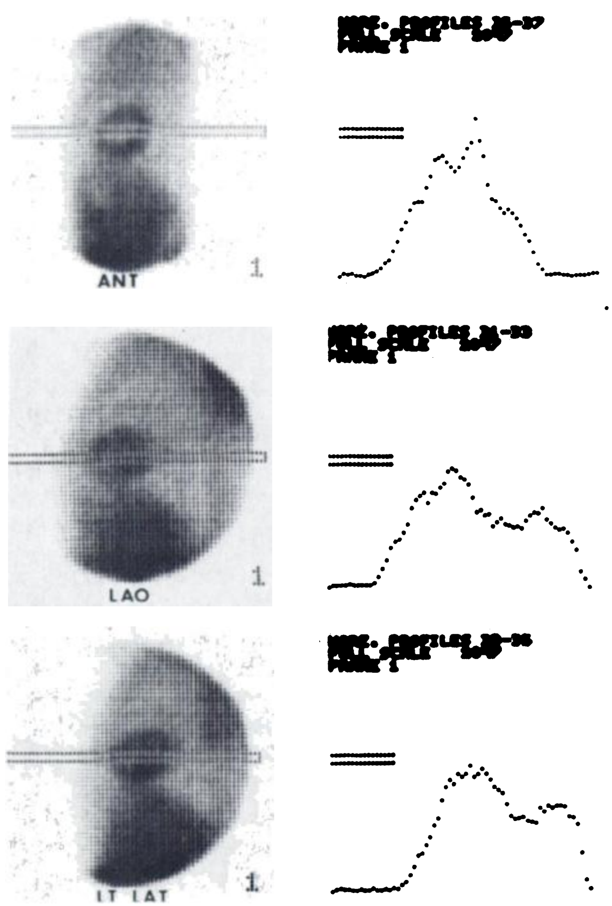

FIG. 2. Unprocessed Tl-201 images in anterior (Ant), left anterior oblique (LAO), and lateral (LAT) projections are illustrated at left. At right are profiles of counts between horizontal lines.

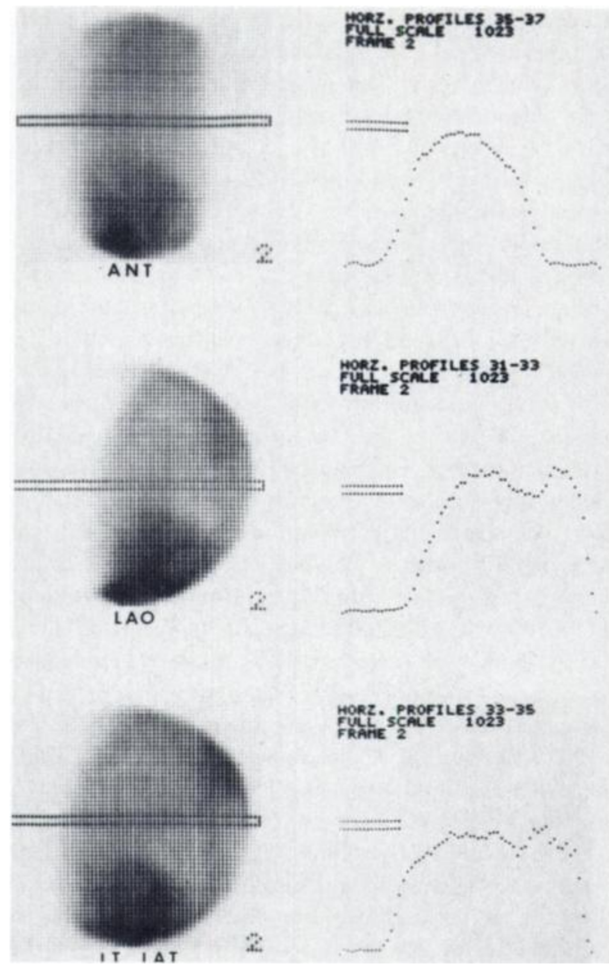

FIG. 3. Background images (within elliptical regions) computed from images in Fig. 1 using linear interpolated techniques described by Goris (*12*).

replaced by water-filled balloons. In Fig. 1 the continuous lines represent an activity profile with the heart in situ. The broken line, labeled background, represents the activity within the heart outline after replacement of the radioactive heart with a nonradioactive heart. It is clear that background activity surrounding the heart exceeds that within the heart outline and thus does not accurately reflect "cardiac background." Subtraction of a background based on activity surrounding the heart shadow from the myocardial image will result in excessive background subtraction. Figure 3 illustrates the computed background image using the linear interpolated technique described by Goris (*12*), based on radioactivity surrounding the heart. This technique overestimates the true cardiac background.

In the present study a computer algorithm was written to determine whether true heart background (Fig. 4) could be calculated as a fraction of radioactivity in the myocardial region relative to the activity level of a reference plane. The reference plane (Fig. 1) is generated by placing an ellipse around the heart outline so that organs adjacent to the heart are excluded, and then averaging two intersecting linearly interpolated values computed for every point within the ellipse.

A proportionality constant, f, was determined from experimental data in five dogs by integration of activity within the elliptical markers. The value of f is the ratio of activity contributed by myocardium below an interpolated reference plane to that above the reference plane, as illustrated in the following equation:

$$f = \frac{\int \text{reference plane} - \int \text{true background}}{\int \text{heart in situ} - \int \text{reference plane}}$$

The mean value of f was 0.64 ± s.d. 0.06. This was obtained from the anterior views.

The proportionality constant, f, was then used to calculate the background activity in each dog using images recorded before removal of the radioactive hearts. This was done as in the Goris method, modified by f times the difference between the original image and the reference plane. The computed background (Fig. 5) was then compared with the true background (Fig. 4) recorded after replacement of the radioactive hearts with

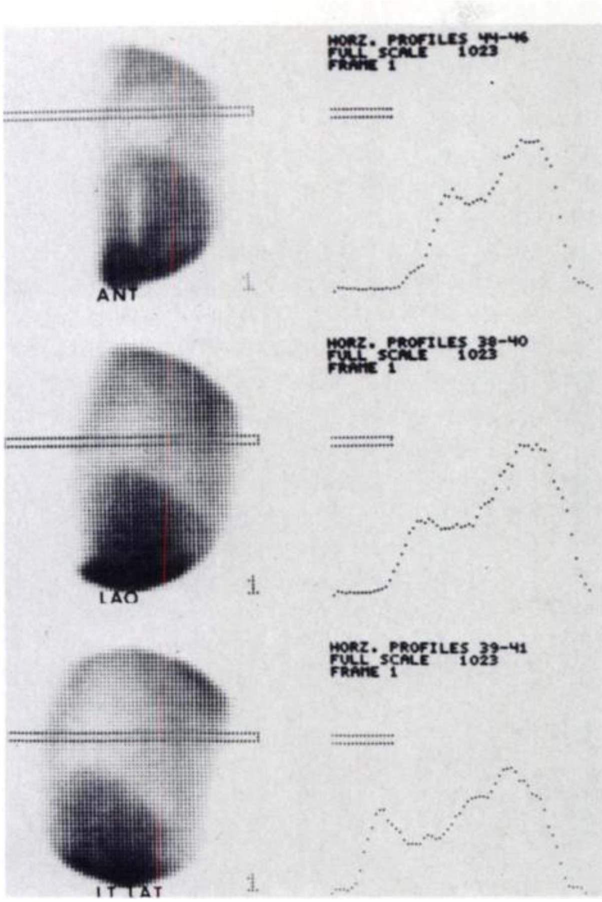

FIG. 4. Unprocessed images and associated profiles after radioactive heart has been replaced by nonradioactive heart. Images illustrate true background activity in heart region.

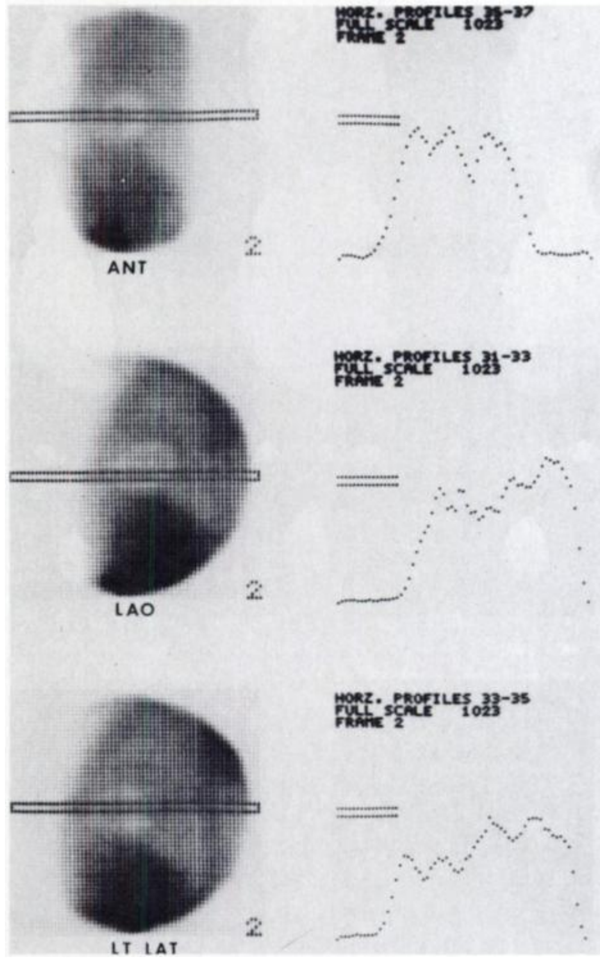

FIG. 5. Background images computed from image in Fig. 2 using new algorithm.

nonradioactive hearts. The two images are closely alike, the mean difference being 3% (range 1–6%).

Figure 6 illustrates the application of the technique in a patient. The top images, obtained at rest, are unprocessed. Those in the center are the computed background images using the new algorithm, and those at the bottom are the difference images obtained by subtracting the computed background image from the unprocessed image.

In certain views the part of the profile corresponding to the center of the heart is slightly greater than that of the true background. This was traced to activity in the intracardiac blood pool. The blood-pool activity, as a percentage of the total heart activity, was determined to be 24%, as has previously been reported (*4*) (see Table 1). This component of background is considered by the computation.

The computer algorithm developed from these data is included in the appendix.

DISCUSSION

Thallium-201 chloride localizes in organs surrounding the heart as well as in the myocardium. When injected with the subject at rest, heart activity is only about twice that in adjacent organs; this low target-to-nontarget ratio makes evaluation of the myocardial image difficult. Several methods have been proposed to improve image interpretability, including subtraction of a threshold value from all points in the image, and contrast enhancement achieved by display nonlinearities.

Goris et al. (*12*) developed an interpolative method of generating a background image of the myocardial region for subtraction, based on circumcardiac activity. Narahara et al. (*13*), using experimental animals, observed that when a radioactive heart was replaced by a water-filled balloon, the activity in the heart region was less than that in the surrounding tissues. Narahara et al. (*13*) reasoned that this high circumcardiac activity caused the Goris method to subtract an excessive number of counts that were myocardial in origin. Rather than attempting to calculate background activity, it was suggested that a constant background of about 20% should be subtracted.

The animal studies by Narahara, demonstrating that true background activity in the myocardial region was

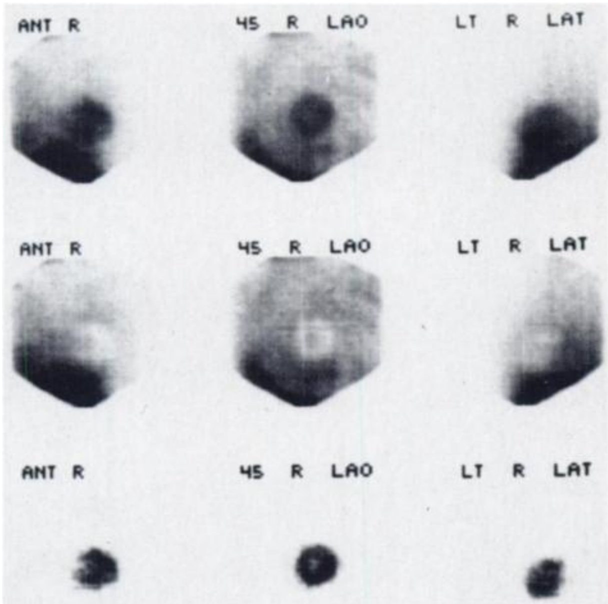

FIG. 6. Tl-201 heart images in normal patient at rest. Top: unprocessed images. Center: computed background images. Bottom: net difference images obtained by subtracting computed background images from unprocessed images.

less than that in the surrounding tissue, stimulated the present attempt to determine whether an algorithm could approximate true background activity in a clinical study. In the present study careful replacement of the radioactive hearts with nonradioactive hearts demonstrated that background activity in the myocardial regions was significantly less than activity in the circumcardiac regions. These images were similar to those described by Narahara et al.

The present study describes a computer algorithm that estimates background in the myocardial region as a fraction of the radioactivity in the myocardial region relative to a reference plane. The computer algorithm uses a proportionality constant derived from five dogs before and after replacement of radioactive hearts with nonradioactive hearts, an extension of Goris's procedure for background estimation. There was a close relationship between the actual and computed background images, the mean difference being 3%. The proportionality constant was derived from radioactivity localized in the myocardial region of dogs during the resting state. During exercise, the radioactivity in the heart would increase relative to background activity. Since the algorithm uses the radioactivity in the heart relative to a reference plane, the use of the computer-generated background to analyze exercise images will result in underestimation of true background activity. The degree of underestimation will be proportional to the increase in activity in the heart. Exercise favorably influences the target-to-nontarget ratio, so that difficulties with interpreting the exercise image with minimal background subtraction are not as great as they are in the rest images or in images of patients with severe disease who can achieve only modest physical activity before onset of symptoms of ischemia. The algorithm derived in the present study would err on the side of subtracting less than true background activity, and thus should minimize production of artifactual deficits as a consequence of removing myocardial counts.

The present study indicates that threshold subtraction of background activity and/or the use of interpolative techniques based on activity surrounding the heart, did not appropriately consider background elements contributing to the myocardial scintigrams. We feel the present technique is at least based on experimental data that more appropriately consider correction of background components. The proportionality constant derived in the dogs may be different from that suitable for man. There is no way to measure directly a proportionality constant in man. In the final analysis, the application of the technique will not rest on whether or not the algorithm correctly calculates background, but whether the application of the technique will improve its clinical utility.

The specific questions to be asked include: "Does the background correction clarify perfusion deficits that are not present or are equivocal in unprocessed scintigrams, without producing artifactual deficits?" "Does this background-correction technique reduce reader variability and/or facilitate the reading of thallium myocardial images?" These questions can be addressed by comparing unprocessed to processed images in patients with and without cardiac disease verified by cardiac catheterization.

TABLE 1. RELATIVE DISTRIBUTION OF ACTIVITY FOR HEART AND BLOOD DETERMINED BY IN VITRO COUNTING

	Counts per 100 sec (Imaged)
Heart and blood	124,000
Heart	88,000
Blood (100 ml)	35,200
Activity per ml (well counter)	366

APPENDIX

The thallium background program can be described basically by three steps. First, the heart is enclosed by an ellipse. Second, a reference plane is calculated. Third, background activity is calculated by subtraction of a fraction of (a) the difference between the original image and the reference plane from (b) the reference plane. The details are described below.

The empirical equation for an ellipse is expressed as:

$$\frac{(x - H)^2}{A^2} + \frac{(y - K)^2}{B^2} = 1 \qquad (1)$$

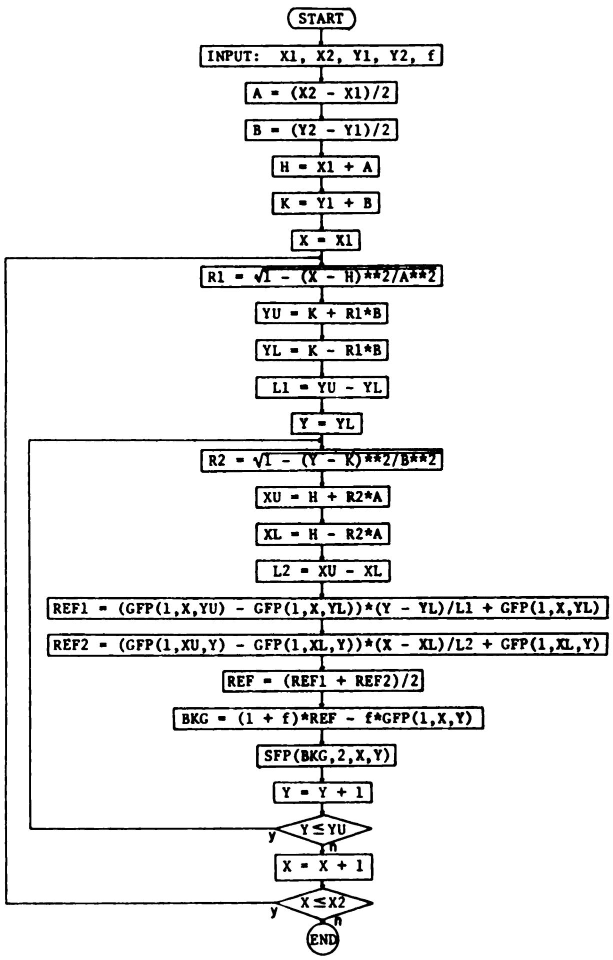

FIG. 7. Background algorithm.

where (x,y) = coordinate of elliptical boundary, (H,K) = coordinate of ellipse center, and (A and B) = semi-axes of the ellipse. For computational purposes, Eq. 1 is written in terms of an independent variable, x, and a dependent variable, y. Thus, Eq. 1 takes the form:

$$y = K \pm B^* \sqrt{1 - \frac{(x - H)^2}{A^2}} \quad (2)$$

or, conversely

$$x = H \pm A^* \sqrt{1 - \frac{(y - K)^2}{B^2}} \quad (3)$$

The reference plane is computed by averaging two intersecting linearly interpolated values for each point within the elliptical markers. This is quite similar to the Goris algorithm using box markers. The background can be computed by the expression:

$$BKG = REF - f^*(ORIG - REF) \quad (4)$$

where REF = reference plane, ORIG = original image, and f = 0.64 (determined experimentally). The above calculation is performed for every point within the elliptical boundary. For computational simplicity, Eq. 4 can be written in the form:

$$BKG = (1 + f)^*REF - f^*ORIG \quad (5)$$

The DO Loop parameters depicted in the flow chart (Fig. 7) restrict all calculations to within the elliptical boundary. Thus, the range of x values extends from the left marker setting to the right marker setting. The range of y values extends from the bottom of the ellipse to its top for each value of x, according to Eq. 2. Equation 3 is used in determining the elliptical boundary as a function of y only for the purpose of linear interpolation.

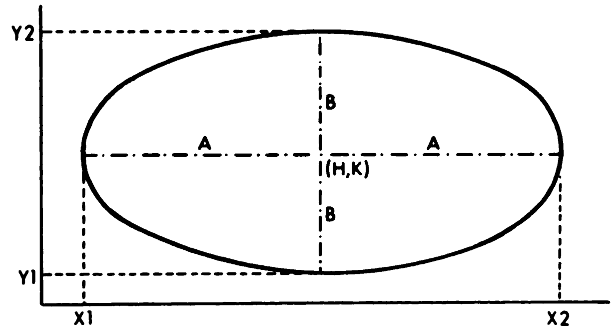

FIG. 8. Description of parameters.

Description of Parameters: The input variables X1, X2, Y1, and Y2 represent points on the ellipse as illustrated in Fig. 8., where the semi-axes are represented by A and B and the center is depicted by (H, K). The input variable f is determined experimentally to be 0.64 (±.06).

FOOTNOTE

* GE Med II,

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