and, thus, the spatial resolution characteristics had to be selected on the basis of the available collimators.

By manufacturing a new optimal planar-concave collimator, it may be possible to remove most of the present nonisotropic blurring in SPECT. It should also be possible to design a collimator with curvature that better matches the thoracic and the abdominal regions of the body.

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Comparative Methods for Quantifying Thyroid Volume Using Planar Imaging and SPECT

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SPECT enables improved accuracy over planar imaging in the determination of the volume since it is derived from three-dimensional data rather than from a two-dimensional projection with a certain geometric assumption regarding the thyroid configuration. **Methods:** By using the phantoms of known volume, it was possible to estimate the accuracy of three different methods of determining thyroid volume from planar imaging used in clinical routine: the standard method used at Malmö General Hospital; a modified version of this standard method; and the method used in Lund Hospital in combination with different ways of defining the regions of interest (ROIs), and to assess the accuracy of the adaptive threshold or gray level histogram method based on SPECT imaging which determines a threshold that maximizes the separability of two classes (object and surround). **Results:** The correlation coefficient (r) and the regression equation between the true (x) and the calculated volume (y) were as follows: r = 0.99 and y = 0.98x + 3.6 using SPECT and the gray level histogram method for edge detection combined with attenuation and scatter corrections, while r = .97 and y = 0.67x + 3.2 using the standard method based on planar scintigraphy. The standard method as used in routine was found to produce large errors (24.8%). The error on the volume estimate was reduced to ~7% for volumes in the range 16-to-75 ml using SPECT. **Conclusion:** Compared with conventional scintigraphy, thyroid phantom volumes were most accurately determined with SPECT when attenuation and scatter corrections are performed, which allows accurate radiation dosimetry in humans without the need for assumptions on organ size or concentration.

Key Words: planar imaging; SPECT; volume estimation; thyroid

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The weight of the thyroid gland is an important factor entering into the determination of the activity of ^{131}I to be administered for the treatment of hyperthyroidism caused by Graves' disease (*1*). There is nearly 50 years of experience in the use of ^{131}I for the management of patients both with hyperthyroidism and thyroid cancer (*2*). As a result of this experience radioiodine therapy is now considered to be the treatment of choice, offering many advantages over surgery. There are still, however, controversies regarding the role and management of radioiodine therapy in the treatment of thyrotoxicosis. These controversies are due mainly to the difficulties in determining accurately the mass of the thyroid gland and hence the radiation dose delivered (*3*).

Scintigraphy of the thyroid gland is usually carried out taking a single frontal image. The volume of the gland is then calculated using an empirical formula for the correlation between the cross-sectional area of the gland in the frontal image and the volume. Thyroid volume can be indirectly determined from the anterior and lateral views of radionuclide images, but with a certain geometric assumption regarding the thyroid configuration. The obvious difficulty, however, of matching a geometric form to such a complex three-dimensional organ made it necessary to further develop the technique. Several formulas have been proposed (*4,5*) but these methods have been shown to produce large inherent inaccuracy. Rotating scintillation camera SPECT systems are ideal for such volumetric quantification because they are true three-dimensional volume imaging systems. The advantage of the ECT approach is its complete independence of thyroid shape, since no geometric assumption is necessary.

The work presented in this article was designed to study the errors induced by thyroid volume determination using different calculation methods based on planar imaging routinely being used at both the Malmö and Lund University Hospitals.

MATERIALS AND METHODS

Phantom Studies

The first step was to produce thyroid phantoms of different shapes and sizes. For this purpose, plastic ellipsoids and a MIRD thyroid phantom were constructed. Their volumes were carefully determined by weight after the phantoms were filled with water. The experimental MIRD thyroid phantom was designed to repre-

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sent the MIRD mathematical phantom described in the MIRD pamphlet No. 5 (*6*). Various combinations of ellipsoids representing the right and left lobes plus the MIRD phantom result in several thyroid phantoms with volumes ranging between 16 ml and 75 ml. These phantoms were placed in a solid, homogeneous perspex cylindrical phantom (diameter = 90 mm, height = 240 mm) filled with nonradioactive water at a depth approximately equal to the average gland depth in the patient neck. Each phantom was filled with an activity concentration of 74 kBq/ml (2 μCi/ml) of [^{99m}Tc]pertechnetate.

Planar Imaging

A SPECT camera fitted with a low-energy, high-resolution collimator was used for the measurements. The scintillation camera was interfaced to a data processor. A 20% energy window centred on the ^{99m}Tc photopeak was used for the acquisition of two static images, one anterior and one left lateral in a 256 × 256 matrix with a hardware zoom factor of 1.6. One pixel in zoom mode equals 0.8 mm. The acquisition time was set to 5 min per frame. Images were then smoothed using a nine-point smoothing filter in order to reduce statistical fluctuations.

The geometrical approximation used for volume estimation was to divide the thyroid up into two ellipsoids representing the right and left lobes on which the three main axes (a, b, and c) representing the longest craniocaudal axis, the medial lateral axis and posterior-anterior axis, respectively, were measured. Three different methods were compared in this work.

1. *Standard Method.* The standard method used in Malmö General Hospital for routine thyroid volume evaluation is based on the measurement of long and lateral axes (a, b) from anterior gamma camera scintigram (Fig. 1A). The thickness of the right and left lobes is empirically assumed to be equal to 0.75 times the lateral axis, b, of the corresponding lobe. Then the volume of each lobe is calculated using the following formula (Brämstang T, *personal communication*, 1968):

$$V = \text{area} \times 0.75 \times b, \qquad \text{Eq. 1}$$

   where the delimitation of the cross-sectional area boundary is estimated using a fixed threshold value of 10% of the maximum pixel count in each separate lobe if the shape of the lobes is well-defined (Fig. 1B), or a manually drawn computer ROI if the thyroid shape is irregular (e.g., presence of hyperfunctioning nodules which prevent automated thyroid gland edge detection). Images were examined visually to assess overall image quality and appropriate choice selected.

   In this study, we have also investigated the effect of different background subtraction levels (contour = 5%, 10%, and manual ROI) on thyroid volume determination. For operator-drawn boundaries, the operator outlined two thyroid lobes in each frontal image using a joystick. The operator was a trained nuclear medicine technician who was given several training sessions before the start of data processing.

2. *Modified Standard Method.* Equation 1 is a gross oversimplification ignoring the ellipsoidal shape of the thyroid lobes and assuming a relationship between the thickness and width of the thyroid lobes. We have modified the above described procedure by the use of the lateral scintigram in order to measure the average thickness, c, of the thyroid lobes. The volume is thus simply given by:

$$V = \text{area} \times c. \qquad \text{Eq. 2}$$

   The modified standard method is simple, fast and reproducible. Although, reservations about ignoring the ellipsoidal shape still stand.

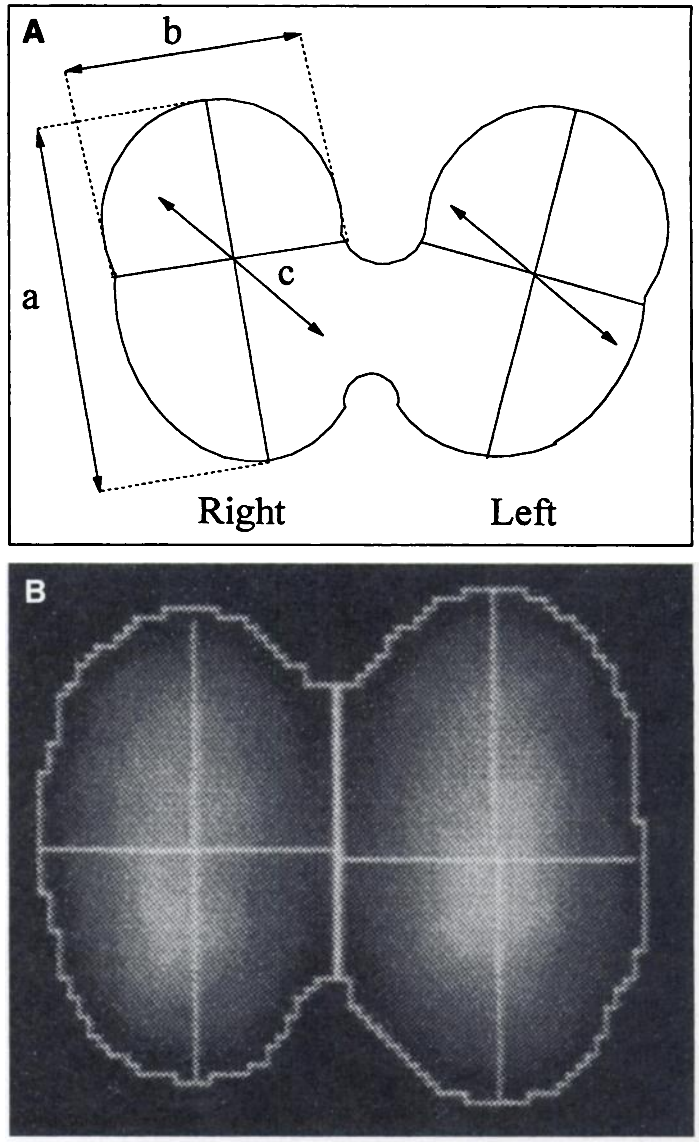

FIGURE 1. (A) Diagram shows measurements of the long (a) and short axes on the two lobes of the thyroid gland. c is the thickness of the lobe. (B) Illustration of the standard method shows an anterior scintigram on which two main axes of the right and left lobes are measured. The area is estimated using a 10% contour (isocount level) as used in clinical routine. The phantom being imaged consists of two ellipsoids separated by approximately 1 cm.

3. *Lund's Method.* The method used in routine for thyroid volume evaluation in Lund University Hospital is based on the exact formula for the calculation of the volume of an ellipsoid (*4*). An average thickness of thyroid lobes is measured using the lateral image which generally looks like an ellipsoid. It represents the short axis of this ellipsoid. The mean depth is drawn at the full extent perceived for the overlapped thyroid lobes, thus,

$$V = \frac{\pi}{6} \times a \times b \times c. \qquad \text{Eq. 3}$$

SPECT Imaging

SPECT imaging was performed using a commercial scintillation camera equipped with a low-energy general-purpose parallel-hole collimator. Sixty frames were acquired in step-and-shoot mode over 360° with an acquisition time of 30 sec per angle. Projection data were acquired using two pulse-height windows (127–153 keV, 92–125 keV) to include the photopeak and Compton scatter, respectively, and were corrected for radioactive decay. In each study, about six million counts in average were obtained in the photopeak as well as the scatter window. The radius of rotation used for phantom SPECT studies is 14 cm. The spatial resolution was measured as 12.1 mm FWHM using our acquisition and processing protocol. Transaxial images of one pixel thickness were reconstructed into 128 × 128 matrix using a filtered backprojection algorithm; a third order Butterworth filter was used having a cut-off frequency equal to 0.4 Nyquist. Measurement of pixel value yielded a value of 4 mm for the side length.

Images were obtained without any correction and with two correction methods: (a) attenuation correction was performed according to Chang (*7*), assuming uniform attenuation with an attenuation coefficient of 0.12 cm^{-1} (CAS1); (b) a combination of the scatter subtraction method proposed by Jaszczak et al. (*8*) using a scatter fraction of 0.42 and the previous attenuation correction method using an attenuation coefficient of 0.15 cm^{-1} was performed (CAS2). A slightly lower value of the attenuation coefficient (μ = 0.12 cm^{-1} rather than μ = 0.15 cm^{-1} for ^{99m}Tc) is used for the following reason (*9*). The full value of μ predicts how many photons will be removed from a single, narrow-beam of radiation due to the combined processes of absorption and scatter. It ignores the number of photons that can be scattered into the path from other directions. We used a Monte Carlo simulation of the SPECT system (*10*) to determine accurately the weighting factor k required for scatter correction using the same methodology described by Jaszczak et al. (*8*). The dimensions and characteristics of the SPECT system together with the phantom used for the measurements were used as input for the computer code (SIMIND) which resulted in a value of 0.42 for the weighting factor k for our gamma camera system and reconstruction algorithm.

Volume quantitation using SPECT was performed by summing up the volume elements (voxels) lying within the contour of the thyroid gland determined by the gray level histogram method in each reconstructed slice (*11*). A detailed description of the algorithm of gray level histogram method used has been given by Otsu (*12*). Briefly, the method works as follows: the operator has to define an ROI so that only the selected object is included. A gray-level histogram of the pixels in the selected ROI in all the slices is constructed. The method of maximizing the inter-class variance is then applied to obtain the threshold value that optimally separated pixels within and without the object. The functioning volume is equal to the total number of voxels in the SPECT images above the calculated adaptive threshold value multiplied by the volume of each voxel.

Patient Studies

Seven patients were chosen from those visiting the Nuclear Medicine Clinic of Malmö General Hospital for thyroid evaluation. Three patients had a diffuse goiter, while four were classified as hyperthyroid patients on basis of the scintigraphy. The patients received 200 MBq of [^{99m}Tc]pertechnetate. Informed consent was sought from each patient before the study. SPECT acquisition started just after the planar imaging study. The prime cause of the less-than optimal resolution performance of patient SPECT studies is the source-to-detector distance. For this reason, an elliptical orbit was used instead of a circular one. Reconstruction was done in a manner identical to that used for the phantom studies. Attenuation correction for the patient studies was performed according to Chang's algorithm with an effective linear attenuation coefficient of 0.12 cm^{-1} (CAS1).

RESULTS

Volume estimation results are shown in Figures 2–5. In each figure, the calculated volume is plotted on the ordinate axis with the true volume plotted on the abscissa. The dashed line indicates the line of identity between the true and the calculated volumes. The regression equation, the correlation coefficient (r), and the standard error of estimate (s.e.e.) are quoted.

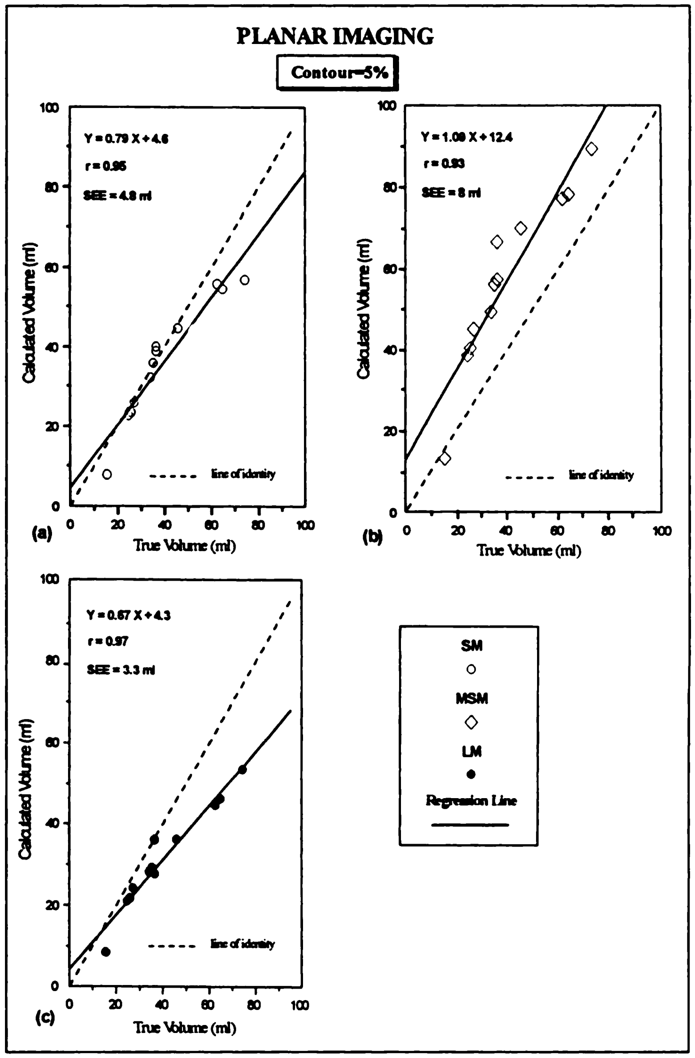

FIGURE 2. Plots of calculated versus true volume using a 5% fixed contour for: (a) standard method, (b) modified standard method and (c) Lund's method. The regression line is also shown.

The measured volumes for the different calculation methods based on planar imaging are illustrated in Figures 2, 3 (a–c) for a contour of 5% and 10%, respectively. The results for the operator-drawn boundaries are shown in Figure 4 (a–c). Figure 5 shows the correlation between the true and the calculated volumes for the gray level histogram method with and without the different correction methods (*13*). A comparison of the relative errors between the true and the calculated volumes for the different methods studied are summarized in Table 1. Table 2 compares the results of thyroid volume assessment for seven patients using the standard method used in routine and the gray level histogram method based on SPECT imaging combined with attenuation correction using an effective linear attenuation coefficient (CAS1).

DISCUSSION

As stated by many authors, functional volume measurements offer a great potential in every day nuclear medicine and a variety of clinical applications have been described (*14*). While thyroid uptake measurements using a single probe is a well-established and routine nuclear medicine procedure for determining the activity in the gland, there is no universal method widely accepted by the nuclear medicine community for assessment of the volume and hence the mass of the thyroid gland.

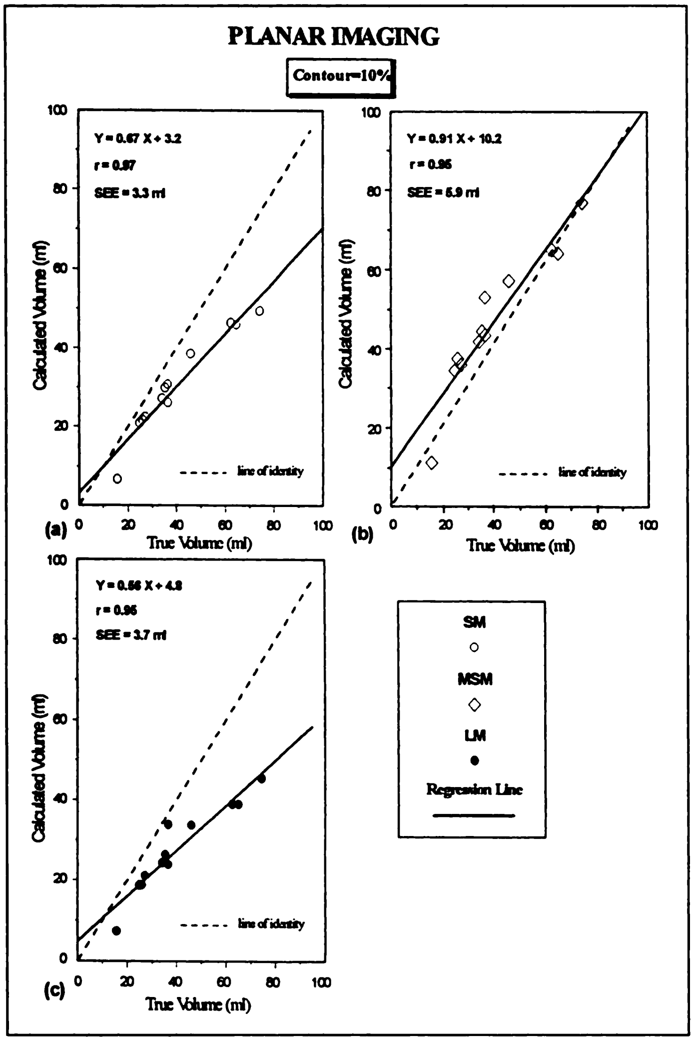

FIGURE 3. Plots of calculated versus true volume using a 10% fixed contour for: (a) standard method, (b) modified standard method and (c) Lund's method. The regression line is also shown.

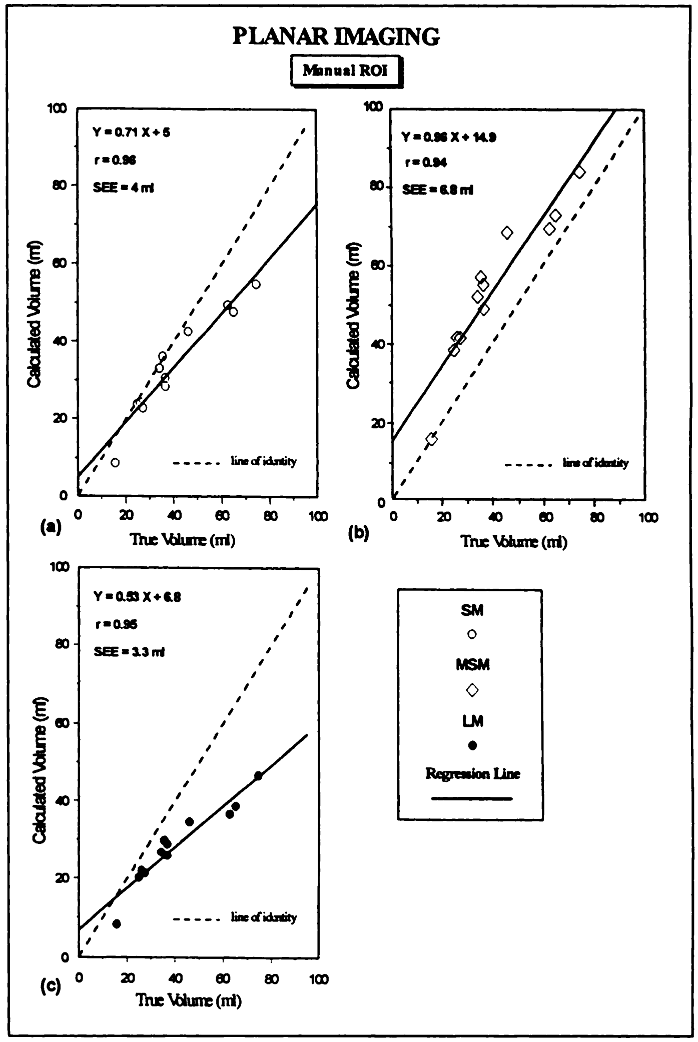

FIGURE 4. Plots of calculated versus true volume using a manually drawn ROI for: (a) standard method, (b) modified standard method and (c) Lund's method. The regression line is also shown.

Thyroid volume determination using planar imaging is a procedure often performed in routine nuclear medicine, but is hampered by several physical difficulties, in particular by structures which overlie or underlie the organ of interest (*15*). SPECT overcomes these difficulties since it is able to separate these structures in the reconstructed images and thus produces images with higher contrast than seen in planar images. Additionally, the images from SPECT show that the radionuclide distribution in some thyroid glands is nonuniform when the conventional imaging indicates otherwise.

Figures 2–5 show that much higher values of the correlation coefficient r are obtained for SPECT than for planar imaging. This is the consequence of the improved quantitative accuracy when using SPECT and thus the improved quantification. The volumes of thyroid phantoms were more commonly significantly underestimated using standard method with a 10% isocontour (Fig. 3a). The modified method for determining the thyroid volume is clearly an improvement over the usual calculation of volume from only the frontal cross-section (Fig. 3b). The results presented in Table 1 have shown the latter method to be inaccurate due to large variations in the ratio between thickness and width of the thyroid lobes. The modified standard method overcomes this problem by measuring a mean thickness for the two lobes since there is always overlap of the right and left lobe regions, as viewed on the gamma camera image, making exact size measurement of the thickness of each lobe separately difficult. In using modified standard method, the regression line approaches the line of identity compared with the case when using standard method. This method works fairly well for the smallest and largest phantoms. It is important to point out that when using a 10% isocontour, modified standard method is more accurate than the standard method applied in clinical routine (Table 1). Lund's method was found to produce a systematic underestimation of the thyroid phantom volumes which become worse with an increase in the size of the phantoms (Fig. 3c).

Planar imaging results were linear despite they were not along the line of identity. This is especially true of Lund's method which seemed particularly insensitive to isocount or manual borders. It is necessary to correct the measured thyroid gland volume because this method underestimated the gland volume. This underestimation could be compensated by the application of a linear regression as a postprocessing corrective measure. Regression methods, however, may be effective when the true object volumes are known as is the case in our study, but are of questionable value in cases in which there is no a priori knowledge of the size or shape of the objects being imaged (*14*).

The following observations were made in comparing the different methods of boundary delimitation for three different calculation methods. Comparisons were based on quantitative planar imaging with respect to their performance in accurately quantifying the volumes of the thyroid phantoms. The count-

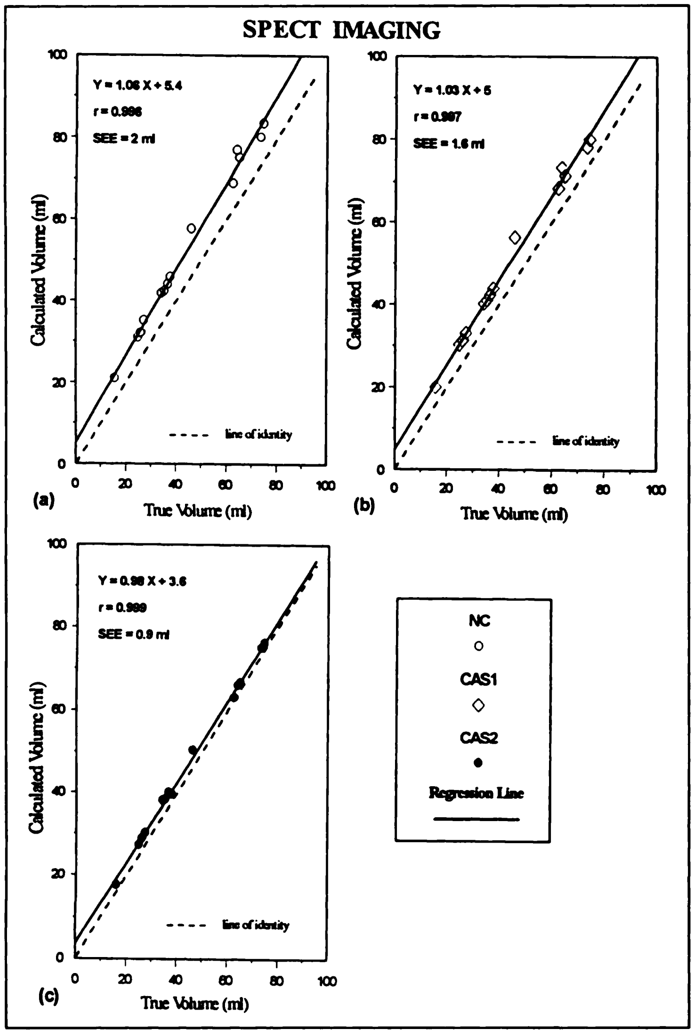

FIGURE 5. Correlation between the true and the calculated volume for the gray level histogram method. (a) Without attenuation correction (NC), (b) with attenuation correction (CAS1) and (c) with attenuation and scatter corrections (CAS2).

based method is fast and reproducible. Volume determination by means of operator drawn ROIs on frontal and/or lateral image is: (a) time-consuming; (b) biased by where the operator decides to draw the ROI on a blurred and noisy image; and (c) lacking in precision and reproducibility. According to the results presented in Figures 2–4 and Table 1, the standard method when used with a 5% isocontour produced the smallest relative error, but the regression line deviated from the line of identity. We believe that this method is the most useful among the other calculation methods based on conventional scintigraphy.

The first problem we deal with in SPECT imaging is the elimination of the Compton scatter. Although image quality is enhanced, improvements in image quantification are only minimal with the reduced μ method of scatter correction. This is because this method assumes that all locations in the image are affected by scatter to the same extent, however, scatter is object-dependent, and a correction method which does not take this fact into account may result in large quantification errors. In this study, the Compton scattering subtraction was carried out by a modified version of the dual window method. The main advantage to using the scatter-window subtraction is the speed with which this technique can be carried out. A difficulty in using the scatter-window technique, however, is in choosing the most appropriate value of k. Whatever the criterion for choosing

TABLE 1
Comparison of Relative Errors (%) between True and Calculated Volumes*

	Planar imaging		
	Contour = 5%	Contour = 10%	Manual ROI
Standard method	12.3 ± 3.7	24.8 ± 3.5	16.4 ± 3.7
Modified standard method	45.2 ± 5.9	23.8 ± 4.4	37.2 ± 6.3
Lund's method	21.4 ± 3.3	30.8 ± 3.3	28.1 ± 3.2
	SPECT imaging		
	Gray level histogram method		
NC	20.8 ± 1.8		
CAS1	16.4 ± 1.5		
CAS2	7.3 ± 1		

*Volumes are defined as the absolute values of the difference between the true and the calculated volumes divided by the true volume for the different calculation methods based on planar imaging and the gray level histogram method in case of SPECT imaging. Mean relative errors with standard error on the mean are shown with and without the different correction techniques.

k, the value will vary with the object being imaged and with the imaging conditions.

Mortelmans et al. (*11*) proposed a new thresholding method based on an automatic threshold selection method (*12*), which has the advantage of being automatic. This method is sensitive to both noise and contrast and produced significant errors in volume estimation unless correction for attenuation and scatter are included in the method. As shown in Figure 5, the correlation coefficients between the true and the calculated volumes were excellent in all cases, while the regression equations were different. This is considered to represent the difference of the power of attenuation and scatter corrections in improving the quantitative reliability of SPECT. The regression line agreed well with the line of identity and the relative error was minimal (Table 1) when using the gray level histogram method combined with attenuation and scatter correction techniques (CAS2), which is quite satisfactory compared to the results obtained with the other methods (*13*). The increase in accuracy may be due to the high contrast reached after scatter subtraction which allows better distinction between the thyroid phantoms and the surrounding medium in the gray-level histo-

TABLE 2
Comparison of Thyroid Volumes*

Patient no.	Sex	Age (yr)	Standard method (ml)	Gray level histogram method (ml)	% Diff
1	F	75	37	41.5	12.6
2	F	46	18.2	29.7	63
3	F	69	21.6	34.6	60.4
4	F	59	20.8	28	34.6
5	F	38	21.1	30.5	44.4
6	F	39	10.3	18.7	81.9
7	F	42	20.8	30.4	46.2

*Volumes are estimated by the standard method based on planar imaging using a 10% contour except the first patient where manual delineation of the lobes was used, and from SPECT and the gray level histogram method combined with attenuation correction (CAS1) for the seven patients studied.

gram, so that the statistical method could determine an optimal threshold. Although the use of a uniform attenuation coefficient for phantom and patient studies appear reasonable. The method will fail for smaller volumes where errors introduced by the partial volume effect are significant. So, meaningful and consistent results could not be obtained due to the small size of the object relative to the system spatial resolution.

In the patient studies (Table 2), SPECT volume quantitation gave results that were consistently higher than those obtained from the routine planar imaging method. From the phantom studies, it was determined that standard method tended to underestimate the volume when using a 10% threshold, while the gray level histogram method when combined with attenuation correction (CAS1) slightly overestimates the volume, however, this latter method was the most accurate one. Differences in volume estimation between the two methods of greater than 80% have been reported.

In this study, all the phantom acquisitions were performed without the presence of background activity (contrast 1:0). We expect a decrease in accuracy as the contrast decreases (*14*). Although this is a simple method for routine use, this technique may not be applicable to clinical situations where there are a poor contrast and a high background activity. Therefore, one factor making the technique of value is the high object contrast. This limitation is significant since it implies the need for extensive calibration (using a set of phantom data over the appropriate contrast range) before the technique can be applied to clinical studies. The dependence of the systematic error on contrast is not yet evaluated.

The use of sonography (US) for measuring the volume of the thyroid has been reported by other investigators (*16*). They used an ellipsoid method, identical to Lund's method except that the volume of the isthmus is also considered. More importantly, they also described a more accurate corrected ellipsoid method which uses the cross-sectional areas of the thyroid lobes in three orthogonal directions rather than the lengths of the three main axes. US-derived volumes, however, need not be necessarily the same as the volumes in which the radionuclide localise because the physiological uptake may not correspond exactly to the anatomical configuration of an organ.

CONCLUSION

Organ volume quantitation is best accomplished by quantitative SPECT technique based on an automatic threshold selection method combined with attenuation and scatter corrections. This allows accurate measurements in humans of absorbed radiation dose without the need for assumptions on organ concentration or size. Our data demonstrate the accuracy of this method when measuring a range of volumes which covers most situations that could be expected in a clinical setting. The method will fail for smaller volumes where errors introduced by the partial volume effect are significant. We believe that this method should replace the actual method used in clinical routine based on planar imaging.

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