Computer Analysis of Thallium-201/Technetium-99m Parathyroid Images

Jennifer L. Prekeges, Brian Eisenberg, G. Glenn Coates, John A. Ryan and Faye T. Lee

Departments of Radiology and Surgery, Virginia Mason Medical Center, Seattle, Washington

Objective: There is a lack of concensus regarding the analysis of ^{201}Tl/^{99m}Tc dual-isotope subtraction parathyroid images. We retrospectively evaluated two computer subtraction methods for the ability to increase the certainty of localization of parathyroid adenomas when compared to camera images only.
Methods: We evaluated 20 parathyroid studies using three sets of images: digital camera images (Tl survey, Tl pinhole and Tc pinhole of 100K counts each); a simple subtraction image of the Tc pinhole from the Tl pinhole without background subtraction or normalization; and multiple subtractions of 60, 80, 100, 120 and 140% of the background-subtracted Tc pinhole image from the background-subtracted, normalized Tl pinhole image.
Results: Simple subtraction decreased the certainty of adenoma localization as often as it increased it. Multiple subtractions increased the certainty in three cases and never decreased it. The sensitivities of the three techniques were calculated to be 84% for both camera images and simple subtraction and 90% for multiple subtraction.
Conclusion: If computer subtraction is desired to increase the certainty of diagnosis, it should be performed with multiple subtractions of the Tc pinhole image from the Tl pinhole image, as described in this paper.
Key Words: thallium-201/technetium-99m subtraction; computer subtraction methods; parathyroid images

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The inclusion of blood calcium levels in many automated blood assays has led to the increased detection of asymptomatic parathyroid adenomas. Parathyroid adenomas produce above-normal levels of parathormone, which can cause potentially life-threatening renal disease and bone loss. It is necessary to identify, and in many cases remove, parathyroid adenomas. Various imaging modalities have been used for localization of parathyroid adenomas; ultrasound and nuclear medicine techniques have generally proven the most useful.

For correspondence and reprints contact: Jennifer L. Prekeges, Nuclear Medicine, C5-NM, Virginia Mason Medical Center, P.O. Box 900, Seattle, WA 98111.

The technique for scintigraphic localization of parathyroid adenomas, originally proposed by Ferlin et al. in 1983 (*1*), uses both ^{201}Tl as thallous chloride and ^{99m}Tc as sodium pertechnetate. Since Tl is taken up by both the thyroid and parathyroid glands, while Tc is trapped only by the thyroid gland, some sort of implicit or explicit subtraction must be performed to identify parathyroid adenomas. The need for two radionuclides has produced a wide variety of techniques (*2–5*):

- Tl first versus Tc first
- Static versus dynamic imaging
- Parallel hole versus pinhole versus converging collimation
- 64 × 64 versus 128 × 128 matrix size
- Normalization versus no normalization
- Simple subtraction image versus multiple subtraction images versus specialized color schemes.

This variability in technique is one factor leading to the wide range of reported sensitivities for Tl/Tc parathyroid imaging (*3,6–8*).

The original article on parathyroid imaging in this journal (*9*), published in 1986, was from our institution. It recommended imaging with Tl using both a parallel-hole and a pinhole collimator, followed by injection of Tc and pinhole imaging 5–10 min postinjection. It also suggested direct subtraction of the Tc pinhole image from the Tl pinhole image without background subtraction or normalization. We undertook the present study to re-evaluate the latter advice.

MATERIALS AND METHODS

Images from 20 Tl/Tc parathyroid studies were retrospectively manipulated and analyzed. The patient group included 12 women and 8 men, ranging in age from 25 to 82 yr, with a mean age of 54 yr. The procedure for image acquisition was the same in all cases. Following explanation of the procedure, an indwelling catheter was placed and 3.0 mCi Tl injected. After allowing 1–2 min for distribution of the Tl, an anterior survey image (unzoomed) of the neck and chest was obtained using a low-energy all-purpose collimator (full field of view) and digital camera system. The patient was then

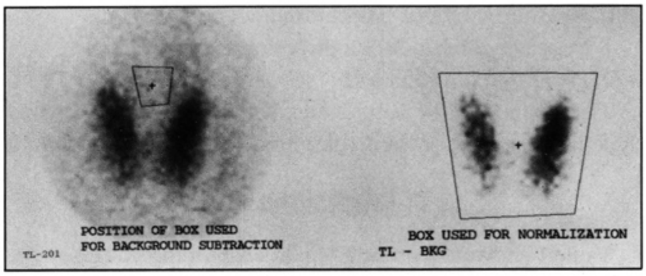


FIGURE 1. Thallium pinhole image (100K counts): the image on the left shows the ROI used for determination of background. The image on the right shows the ROI used to determine the total counts in the thyroid region in the Tl and Tc images. These values are used to generate a normalization factor that is applied to the Tl image.

instructed to lie still and tape was used to secure the head. The pinhole collimator was then installed and the patient's neck imaged in the anterior projection. Following this image, 10.0 mCi Tc were injected, and the neck imaged again 5–10 min later (based on adequate clearance of Tc from the bloodstream as observed on the persistence scope). All images were acquired for 100K counts. The two pinhole views were magnified 1.75 times to match the pinhole field of view to the camera screen size. The matrix size for all cameras was 256 × 256. Additionally, all three images were acquired on computer in a 64 × 64 matrix. The first two thallium images were acquired with energy photopeaks of 167 and 77 keV (20 and 15% windows, respectively) and the third Tc image at 140 keV (15% window). No downscatter image was generated or used.

The computer images were manipulated in two ways. In the first manipulation, direct subtraction of the Tc pinhole image from the Tl pinhole image produced a simple subtraction image. The second manipulation involved both background subtraction and normalization, and is modified from the procedure described by Blue et al. (*10*). The principles of this subtraction technique were originally described by Tuscan et al. (*11*). Our procedure is as follows:

1. A "background box" is drawn above and between the upper lobes of the thyroid gland, using the Tl pinhole image (Fig. 1). Average counts per pixel in the background box are determined for the Tl pinhole and Tc pinhole images, and these values are used to subtract background counts from their respective images.
2. A "thyroid box" which includes the whole thyroid is then drawn on the background-subtracted Tl pinhole image (Fig. 1). Any areas of Tl uptake that are entirely separated from the thyroid are excluded. Total counts within the thyroid box are determined from the background-subtracted Tl and Tc pinhole images.
3. A normalization factor (Tc total counts divided by Tl total counts) is calculated. The background-subtracted Tl pinhole image is multiplied by the normalization factor to get a normalized Tl pinhole image.
4. The background-subtracted Tc pinhole image is multiplied by the five weighting factors (0.6, 0.8, 1.0, 1.2 and 1.4)

TABLE 1
Results of Twenty Sets of Tl/Tc Parathyroid Studies

Case	Location	Camera Images	Simple Subtraction	Multiple Subtraction	Surgery Results
1	LUP	0	2	2	RMid
2	RLP	1	1	1	No surgery
3	LLP	0	1	1	LLP
4	LLP	2	2	2	LLP
5	RLP, LLP	2, 2	2, 2	2, 2	RLP, LLP
6	LLP	2	2	2	LLP
7	RLP	2	2	2	RLP
8	LUP	1	2	1	LUP
9	LUP, LLP	1, 0	1, 0	1, 1	LUP, lymph node
10	LLP	2	2	2	LLP
11	LLP	2	2	2	LLP
12	RLP	1	1	1	LUP, RLP thyroid neoplasm
13	LLP	1	2	1	LLP
14	RLP	2	2	2	RLP
15	RLP	2	1	2	RLP
16	RLP	2	0	2	RLP
17	LMid	1	0	1	No surgery
18	LLP	2	2	2	LLP
19	RMid	2	2	2	RMid
20	LMid	2	2	2	LMid

LUP = left upper pole; RUP = right upper pole; LLP = left lower pole; RLP = right lower pole; LMid = left middle lobe; RMid = right middle lobe.

TABLE 2
Analysis of Camera, Simple Subtraction and Multiple Subtraction Images for Parathyroid Adenoma Localization

	Camera Images	Simple Subtraction	Multiple Subtraction
True Positives	16	16	17
True Negatives	2	1	0
False Positives	1	2	3
False Negatives	3	3	2
Sensitivity	84%	84%	90%

used by Blue et al. (*10*). The resulting five images are each subtracted from the normalized Tl pinhole image to produce multiple subtraction images, all five of which are photographed on a single film.

Two radiologists evaluated the three sets of images (camera images, simple subtraction and multiple subtraction) according to the following grading system:

0 Not suggestive of parathyroid adenoma
1 Suggestive but not definitive for adenoma
2 Definitive for adenoma.

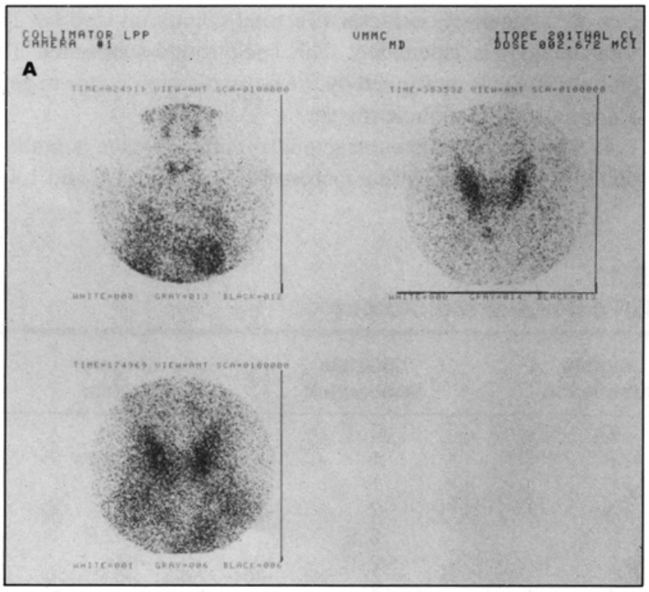
The location of the suspected adenoma was also specified. Results of surgical neck exploration were also obtained.

RESULTS

Table 1 shows the grade given to each of the images, along with surgical correlation. A total of 22 potential adenomas were identified by at least one set of images; 17 adenomas were found at surgery. Table 2 analyzes the three sets of images relative to surgical findings (excluding the two cases where surgery was not performed). A set of images was graded true positive if it received either a 1 or a 2 grade and correctly identified the adenoma location relative to the thyroid. The sensitivity (true positives divided by the total number of adenomas found) of the multiple subtraction technique is greater than either camera images or simple subtraction. Specificity is not quoted due to the very low incidence of true negatives in our study group. There is a high pretest likelihood of parathyroid adenoma in our patient population and therefore very few patients are found at surgery not to have an adenoma.

Table 2 shows that simple and multiple subtraction techniques both have the same effect as most other analysis techniques in nuclear medicine. They increase the numbers of both true positives and false positives. Two of the false positives in this series are known nonparathyroid sources of Tl/Tc mismatch (*10*): a lymph node (Case 9) and a thyroid neoplasm (Case 12). The third false positive (Case 1) suggested a left-sided mismatch, but a right-sided adenoma was found at surgery. The surgeon's report did not indicate whether any abnormality was found on the left side.

The primary use of parathyroid imaging in our institution is localization of the parathyroid adenoma. Therefore it is desirable that additional computer processing not decrease



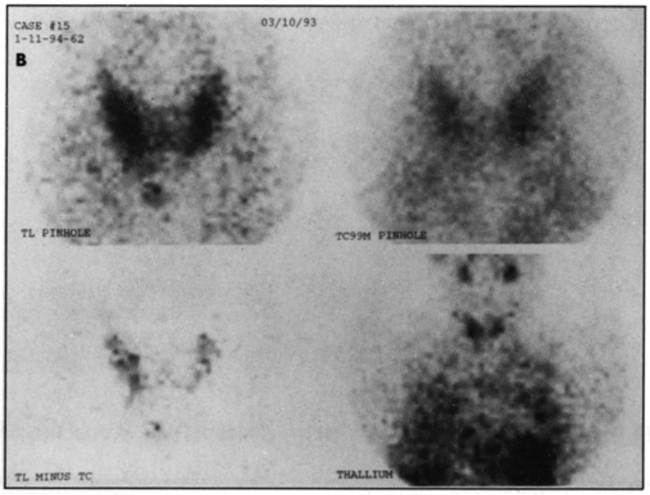
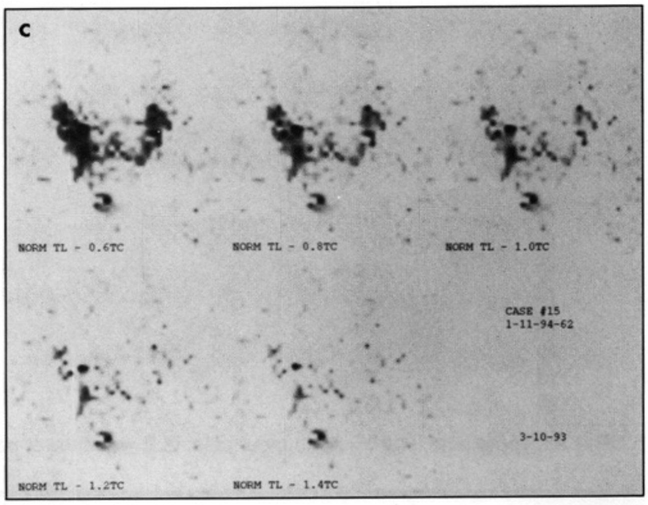
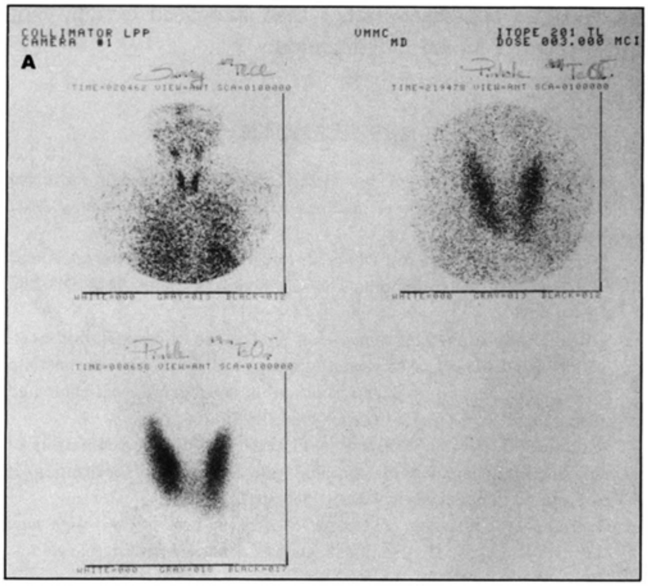
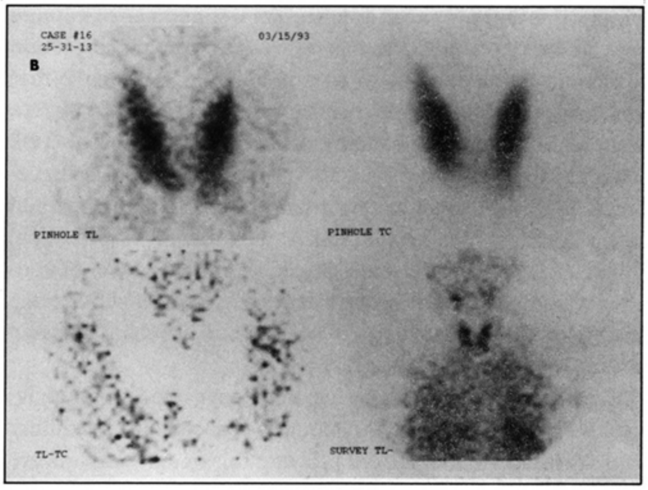


FIGURE 2. Case 15 demonstrates the importance of multiple subtractions. Fig. 2A shows the camera images; 2B the simple subtraction images; and 2C the multiple subtraction images.







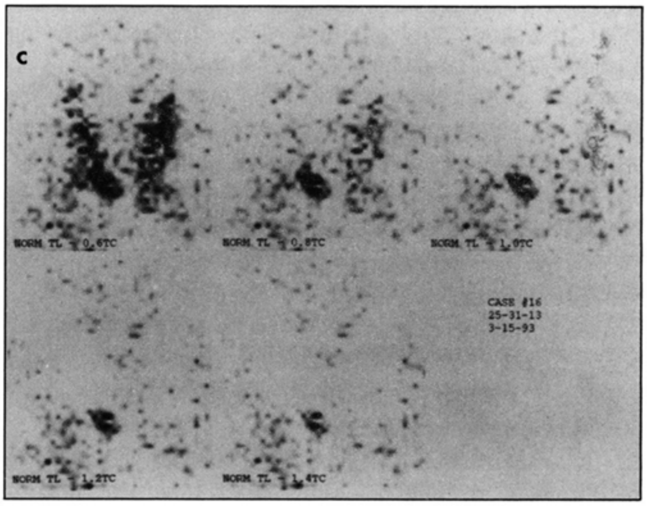


FIGURE 3. Case 16 demonstrates the importance of normalization prior to subtraction. 3A shows the camera images; 3B the simple subtraction images; and 3C the multiple subtraction images.

the certainty of localization as determined by camera images. In our series, 16 of the 17 parathyroid adenomas were localized correctly by camera images alone. Did computer analysis help? Multiple subtraction increased the grade in three cases, but never decreased it, whereas simple subtraction decreased the grade almost as often as it increased it (four cases versus three). We believe that this is due to careful attention to background subtraction and normalization in the multiple subtraction series, as well as the presentation of a series of images with different subtraction levels. Cases 15 and 16 provide two examples.

Case 15 (Fig. 2) shows relatively little localization of Tc in the thyroid gland, with correspondingly high background. This finding can be seen in patients with poor thyroid function, as well as when the delay after Tc injection is not adequate. The parathyroid adenoma was readily localized by camera images alone (Fig. 2A). However, simple subtraction without normalization (Fig. 2B) led to visualization of the thyroid gland as well as the parathyroid adenoma, which caused the physicians to question whether the adenoma might actually be normal thyroid tissue. Multiple subtractions following normalization (Fig. 2C) show the activity in the area of the thyroid becoming less obvious at higher multiplications, while the adenoma becomes more obvious. These images increased the physicians' certainty about the presence of the adenoma.

In Case 16, the location of the parathyroid adenoma was identified from the camera images (Fig. 3A) as being in the right lower pole. Simple subtraction without normalization (Fig. 3B) resulted in a complete loss of all counts in the thyroid region, including the area of the adenoma. This kind of subtraction image is obtained when the counts in the subtrahend (the Tc image) are much greater than the counts in the minuend (the Tl image). Normalization of the two images in the multiple subtraction series (Fig. 3C) makes the adenoma stand out clearly.

DISCUSSION

Initial surgery for parathyroid adenomas is successful about 90 to 95% of the time, without any preoperative localization studies (*12*). In our institution, preoperative localization by ultrasonography and nuclear medicine techniques is used to precisely identify the adenoma location, thus hopefully decreasing total surgery time and precluding the need for re-operation. Both techniques are necessary to localize all types of adenomas: ultrasonography for the small (<1.5 cm in diameter) adenomas that are below the limits of resolution of modern gamma cameras, and nuclear medicine for adenomas located in the retroesophageal (posterior) or mediastinal (inferior) regions where ultrasound is nondiagnostic. Using both techniques, we are able to localize 97% of all parathyroid adenomas preoperatively.

Since the need is for correct localization of the parathyroid adenoma, there is little need to distinguish between grade 1 (suggestive) and grade 2 (definitive). It is more important that any additional analysis of these images should not cause the interpreting physician to question the findings of camera images. We have noted in this paper that simple subtraction can be detrimental as often as it is helpful. We believe that this is primarily due to differences between Tl and Tc uptake in the thyroid. It is in the nature of subtraction images to look coarse and pixelly; normalization and background subtraction will prevent a statistical variation from being interpreted as a real adenoma. In addition, the availability of multiple subtraction images gives the physician a higher level of confidence that an area of increased activity on the subtraction images is truly an adenoma. These points are demonstrated in the two cases shown in this paper.

Recently ^{99m}Tc-sestamibi has been suggested as an imaging agent for parathyroid adenomas, with sensitivity similar to that for Tl/Tc imaging (*13*). Using this agent, patients are imaged immediately after injection and again in several hours. Both thyroid and parathyroid are seen in the initial image, and parathyroid only in the delayed image, following washout of ^{99m}Tc-sestamibi from the thyroid. Once again subtraction, either implicit or explicit, must be applied. We believe the same principles of computer subtraction demonstrated in this paper should be applied in the use of ^{99m}Tc-sestamibi for parathyroid adenoma localization. Difficult cases will be difficult with either sestamibi or Tl/Tc, and it is these cases that require careful attention to computer subtraction techniques.

CONCLUSION

We conclude that in most cases, camera images alone are sufficient to identify and localize parathyroid adenomas. If computer subtraction is desired to increase the certainty of the diagnosis, it should be performed with multiple subtractions of the Tc pinhole image from the normalized Tl pinhole image. Simple subtraction without these additional steps may lead to decreased rather than increased certainty of parathyroid adenoma identification.

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