

COMPUTER-ASSISTED SCANNING IN EVALUATION OF

<sup>67</sup>Ga-CITRATE UPTAKE IN THYROID DISEASE

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*Fifty-two patients having thyroid nodules were investigated with <sup>67</sup>Ga-citrate in conjunction with scintillation scanning in order to assess its value for the preoperative diagnosis of malignancy. It was found that conventional images are equivocal and difficult to interpret. Therefore, a computer method was devised by means of which the uptake of various neck structures was expressed in terms of "body-background" counting rate thus producing an image of apparent target/nontarget ratios. By means of this method, it was demonstrated that radiogallium concentrates in a variety of normal and pathological neck structures, the range of ratios being roughly 1.5–2.5. The diagnostic power of the procedure was found to be low except in four patients with anaplastic carcinoma which invariably showed high concentrations of <sup>67</sup>Ga. The highest uptake of this agent was found in a case of Hashimoto's disease (5.2).*

Both <sup>75</sup>Se-methionine and <sup>67</sup>Ga-citrate have been reported to concentrate within some malignant tumors (1–4). Therefore, the two radiopharmaceuticals have been investigated and an attempt has been to determine their value for the preoperative diagnosis of thyroid pathology. The results obtained with <sup>75</sup>Se-methionine did not differ substantially from those found by others (1,2) and this paper deals only with our experience with <sup>67</sup>Ga-citrate.

MATERIAL AND METHODS

To the first group of 30 patients with solitary or multiple thyroid nodules, 2 mCi of carrier-free <sup>67</sup>Ga-citrate was administered intravenously. The images of the neck radioactivity were made 2 days later by

means of a rectilinear color-dot scintiscanner. No contrast was used for imaging.

The relative concentration of the radiopharmaceutical within the nodules was visually scored as higher (+), equal (+/–), or lower (–) than that of the adjacent normal thyroid tissue.

Since the overall target/nontarget ratios were low in most cases, the scoring of images was soon found to be equivocal in spite of the interpreters' reasonable amount of experience. In some instances also, a topographic correlation to the anatomical structures was found to be difficult. Therefore, a computer technique was devised for a better assessment of the quantity and topography of the radionuclide concentration within the normal and the pathological neck tissues.

Before the examination a second group of 22 patients with suspected or proven thyroid disease was given orally about 1 mCi of <sup>99m</sup>Tc-pertechnetate as the second tracer. A dual-analyzer digitalized scintiscanner was used for this study. For <sup>99m</sup>Tc the spectrometer was set at appropriate photopeaks. For <sup>67</sup>Ga, the lowest peak at 92 keV was ignored and only those at 182 and 206 keV were encompassed within the second counting window. Parallel to the color-dot imaging, counts from the two analyzers were fed into a CAMAC-type data acquisition system and punched into paper tape.

The tapes were processed off-line by a 6000 series CDC digital computer. After the formation of the two matrices within the computer core memory, the background counts for each matrix were assessed by averaging the activity of two adjacent transversal

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scanning lines with the lowest mean values. Then the "background" counts were subtracted and the remaining data smoothed. The images of the two radionuclide distributions were produced on a fast lineprinter using alphanumerical symbols corresponding to ten isocount levels. Blanks and overprints were employed to increase the legibility of the image.

The uptake of  $^{67}\text{Ga}$  within the neck structures as compared with the "background" neck radioactivity was visualized by an additional image of the count/background ratio, the ten printing levels being arbitrarily preset at a "maximum" of three times the background value. The highest count/background ratio and its coordinates were printed out also numerically.

In order to facilitate the topographic correlation, the contours of the functioning thyroid, represented by a half-maximum isocount line of the  $^{99\text{m}}\text{Tc}$  matrix established separately, were brought into the processed  $^{67}\text{Ga}$  matrix by using the dollar sign (\$).

In two cases of autonomous or toxic adenomas, the diagnosis was supported only by clinical, laboratory, and scintigraphic findings. The rest of the patients were operated upon. Surgical specimens were topographically oriented and histologically examined. The findings were topographically correlated with scintigrams.

#### RESULTS

The results obtained with conventional techniques are shown in Table 1. A remarkable concentration of  $^{67}\text{Ga}$ -citrate was found only in three cases of anaplastic carcinomas. The rest of the conditions showed slight or no uptake of the agent as compared with the normal thyroid tissue.

The results of "quantitative" computer-assisted scintigraphy are shown in Table 2. Radiogallium was moderately taken up by the sternal bone marrow, by normally functioning, and by hormonally suppressed thyroid tissue. In most thyroid conditions the apparent target/background ratio was roughly the same (1:5-2:5) whereas in nodular goiter with regression changes it was lower (1:0-1:6).

Well-differentiated thyroid carcinoma showed a moderate uptake of  $^{67}\text{Ga}$  visualized occasionally if the tumor was situated well outside the gland area. Among four patients examined, the highest ratio (2:3) was found in a case with follicular carcinoma showing dedifferentiated foci. In anaplastic cancer, however, the ratio was much higher (4:9).

The highest target/background ratio (5:2) was found in a case of Hashimoto's disease, the radiogallium being distributed more or less evenly throughout the whole gland. At re-examination after 2

**TABLE 1. UPTAKE OF  $^{67}\text{Ga}$ -CITRATE IN 30 PATIENTS WITH THYROID NODULES**

Histology	Patients (No.)	$^{67}\text{Ga}$ -citrate		
		-	+/-	+
Adenoma	6	4	2	-
Autonomous/toxic adenoma	2	2	-	-
Nodular goiter with regressive changes	15	14	1	-
Papillary/follicular carcinoma	4	3	1	-
Anaplastic carcinoma	3	-	-	3
<b>Total</b>	<b>30</b>	<b>23</b>	<b>4</b>	<b>3</b>

The uptake of  $^{67}\text{Ga}$  within the lesion was visually scored as higher (+), equal (+/-), or lower (-) than that within the normal thyroid tissue.

**TABLE 2. UPTAKE OF  $^{67}\text{Ga}$ -CITRATE IN NECK STRUCTURES: 45 OBSERVATIONS IN 22 PATIENTS**

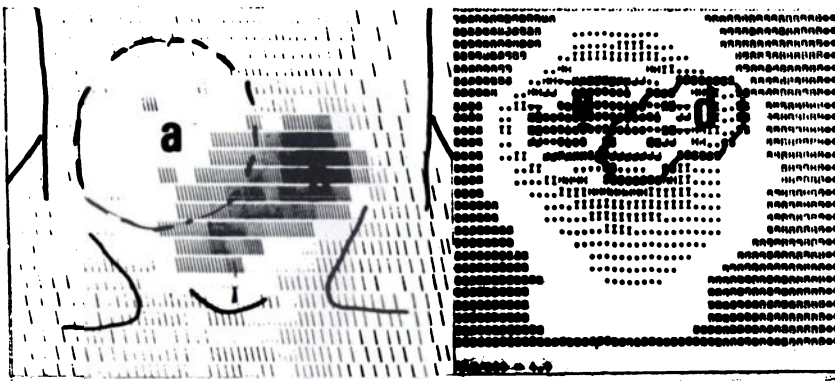
Structure	Observations (No.)	structure/bcg ratio	
		mean	range
Normal thyroid tissue	7	2.1	1.5-2.3
Suppressed thyroid tissue	2	1.7	1.7
Manubrium sterni	14	1.7	1.6-2.0
Autonomous/toxic adenoma	2	1.75	1.7-1.8
Thyroiditis chronica	4	3.1	1.3-5.2
Nodular goiter with regressive changes	9	1.4	1.0-1.8
Lymphadenitis tuberculosa	1	2.2	
Papillary/follicular carcinoma	4	1.7	1.2-2.3
Medullary carcinoma	1	2.0	
Anaplastic carcinoma	1	4.9	
<b>Total no. of observations</b>	<b>45</b>		

The structure/neck background ratios were determined by means of computer-processed images.

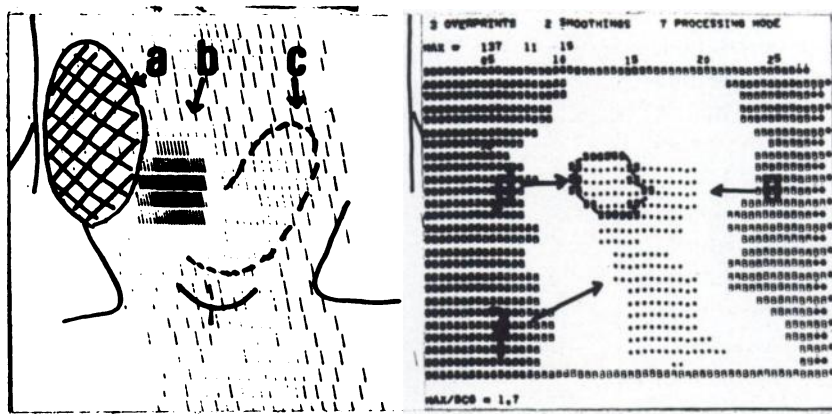
months of treatment with corticoid and thyroid hormones, this ratio was found decreased (4:6). In another patient with chronic fibroplastic thyroiditis, moderate ratios were found: 1:3 over most of the fibrotic gland and 2:0 over an area showing somewhat more pronounced inflammation with lymphocytic infiltration.

#### CASE REPORTS

Patient LA (Fig. 1) had a large lump on the right side of the neck (Fig. 1A) representing a histologically proven metastatic papillary thyroid carcinoma. In a  $^{99\text{m}}\text{Tc}/^{67}\text{Ga}$  study the pertechnetate was taken up only by an autonomous nodule of the right thyroid lobe (Fig. 1B). The computer-processed



**FIG. 1.**  $^{99m}\text{Tc}$ -pertechnetate/ $^{67}\text{Ga}$ -citrate study of large papillary thyroid carcinoma metastatic to right neck lymphnodes (A) in coincidence with autonomous adenoma of right thyroid lobe (B, D). Nodule, suppressed paranodal tissue, and sternal bone marrow show a certain degree of  $^{67}\text{Ga}$  (D, E, F) uptake but none within malignant mass.



**FIG. 2.**  $^{99m}\text{Tc}$ -pertechnetate/ $^{67}\text{Ga}$ -citrate study of fast-growing, anaplastic carcinoma of right thyroid lobe (A). In  $^{99m}\text{Tc}$  image growth is represented as cool nodule. Gallium-67 concentrated within nodule with apparent maximum target/nontarget ratio of 4:9 (C) and is printed with symbols for "maximum."

$^{67}\text{Ga}$  image showed that the nodule (Fig. 1D) as well as the silent paranodal thyroid tissue (Fig. 1E) had concentrated radiogallium uniformly but moderately, the maximum/background ratio having been 1:7. Some radiopharmaceutical was taken up by the sternal bone marrow (Fig. 1F) but none by the right lateral malignant mass. A second radiotechnetium dose administered after TSH stimulation demonstrated the formerly silent thyroid tissue (Fig. 1C).

Patient JF (Fig. 2) was admitted for a fast-growing right paramedian neck lump (Fig. 2A). A similar study as in the former case was performed. The  $^{99m}\text{Tc}$  image showed a normal thyroid uptake in the left lobe and isthmus (Fig. 2B), and the lump was scored as a "cool" nodule. The processed  $^{67}\text{Ga}$  image demonstrated a similar pattern in the thyroid tissue and a high uptake of radiogallium within the "cool" nodule, the maximum/background ratio having been 4:9. Counts in most of the nodule area (Fig. 2C) exceeded the three times background limit and were printed with the symbols for maximum (Fig. 2D). The frozen sections made during the operation were negative but after the examination of the entire surgical specimen the histological report was anaplastic carcinoma.

**DISCUSSION AND CONCLUSIONS**

Scintillation scanning of the neck by means of  $^{67}\text{Ga}$ -citrate was investigated for its potential value in preoperative diagnosis particularly in cases suspicious of a malignant disease. When the target/nontarget concentration ratios are low, visual interpretation of the conventional images is difficult, unreliable, and highly dependent on the technical quality of the image. It is possible to devise a computer-assisted image-processing method permitting a certain quantitation of the concentrations thus facilitating the interpretation of the image with an inherently low contrast. The diagnostic power of radiogallium was found to be disappointingly low save in cases of anaplastic carcinomas and Hashimoto's disease, which seem to concentrate this agent to a clinically useful degree.

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