STUDY OF NORMAL MAMMARY LYMPHATIC DRAINAGE USING RADIOACTIVE ISOTOPES

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The use of radioactive tracers for the study of the normal mammary lymphatic drainage with indirect lymphoscintigraphy began with Hahn, et al (*1*) in 1946. Isotopic lymphoscintigraphy started in 1960 with Sherman, et al (*2*) who showed that ^{198}Au-colloidal gold injected into the female rabbit's parametrium is retained by regional nodes.

In 1962 Rossi, et al (*3*) studied the lymphatic drainage of mammary glands with scintigraphy. The images obtained were somewhat unclear; later on, during the years 1965–1968, studies were made chiefly to perfect the scintigraphic visualization of the internal mammary chain nodes using variants of the original technique, related either to the method of administration of the radioactive tracer [Rossi, et al (*4*), Schenk (*5*), Buchwald, et al (*6*), Capdevila (*7*)], or to the radionuclide which was used [Schenk, et al (*8*)]. Our aim is to present the data from a systematic study of the lymphatic drainage within the several areas of normal mammary glands using scintigraphy with radioactive gold injected into the mammary tissue.

MATERIALS AND METHODS

Two hundred fifty indirect mammary lymphoscintigraphies, performed in physiological conditions, were distributed as follows: (A) 50 scintigraphies after injection in the upper inner quadrant, (B) 50 scintigraphies after injection in the lower inner quadrant, (C) 50 scintigraphies after injection in the upper outer quadrant, (D) 50 scintigraphies after injection in the lower outer quadrant, and (E) 50 scintigraphies after injection in the subareolar area.

The isotope used in all the cases has been ^{198}Au in colloidal suspension. Its chief properties are particle size, 35 Å mean diameter; dose, 200 μCi; and volume of injection, from 0.3 to 0.5 cc.

Because of the colloidal state of the suspension and of the particle size, the resorption of ^{198}Au is carried out exclusively by the lymphatics. Afterwards it is phagocytosed by the reticuloendothelial cells of lymphatic nodes so that it is confined within the nodes (*9*).

We have not used hyaluronidase added to the diluting substance because we are convinced that this enzyme increases the local diffusion without improving the lymphatic resorption. By examining our scintigraphies, it can be seen that excellent images are obtained without recourse to hyaluronidase. We have not added any local anesthetic because the injection of ^{198}Au-colloidal suspension is painless.

We have usually employed insulin syringes because they offer the advantage of a precise measurement of the volume to be injected.

The injection technique used in the intraparenchymal administration is different from that used in the injections into the subareolar area.

Intraparenchymal technique. When the patient is supine, the operator grasps the mammary gland with the left hand, retracting it from the thoracic layer. Thus the puncture is simpler, and the needle does not transfix the gland and reach the retromammary muscular layer. The puncture is performed with the syringe held vertically. After perforating the skin, the needle traverses the subcutaneous layer with little resistance, until the operator feels the resistance of the mammary gland. With a slight increase of pressure on the syringe, the needle penetrates about 1–1.5 cm into the mammary parenchyma. The syringe contents are injected with gentle pressure. The syringe and needle are removed with a quick movement with slight pressure on the puncture spot to avoid liquid reflux.

Subareolar injection. The puncture is performed at the areolar edge while holding the syringe at an angle about 20 deg to the horizontal plane. Once the subcutaneous layer is reached, the needle is pushed 0.5–1 cm deeper in the direction of the nipple in the subcutaneous layer. We have always performed two injections, one in each side of the areola, to prevent the isotope from being injected totally either

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outside or inside the nipple because we are interested in revealing the drainage of the subareolar area and not only that of half the area.

We carried out the lymphoscintigraphies at variable intervals after the injection: 6, 12, 24, and 48 hr. The best results were obtained at 24 hr after the injection, although we believe that good results may be obtained between 12 and 48 hr after the injection time, and Sage, et al (*10*) affirm that good pictures may be obtained during the first 7 days.

In the 24-hr interval between the injection and the scintigraphy, patients are allowed to follow their usual routine because their movements are sufficient to obtain an effective lymphatic drainage. It is not necessary to practice local massage.

In our studies we have used a conventional scanner fitted with a 5-in. NaI(Tl) scintillation crystal and a color paper printing system. Simultaneously, we have obtained in all cases a picture on radiographic film.

A 3-in. focusing collimator is used for the lymphoscintigraphies. This collimation pattern is adequate to identify the lowest activity nodes with some loss of definition.

Scanning parameters were adjusted by centering the collimator upon the maximal activity area. To achieve this, a lead hood was placed on the mammary gland. Background suppression was adjusted to 10% of the maximal activity.

RESULTS

The indirect lymphoscintigraphy is a procedure which reproduces physiological conditions almost ideally. Although interstitial injection of radioactive material brings about changes in local pressures and the lymphatic flow related to them, the quantity of injected fluid (0.3–0.5 cc) cannot change the direction of the lymphatic flow. Slight modification in the lymphatic resorption speed is possible, but the direction of the lymphatic flow is not altered. Moreover, the technique is harmless, nontraumatic, and easy. The only alteration observed has been the appearance in two cases of a small gray spot, 2 cm in diam, in the injection site. We have observed (*11*) that the nodes which take up the ^{198}Au do not remain blocked because the repetition of scintigraphy 2 months afterwards shows drainage pictures equal to those of the first scintigraphy (Fig. 1).

Images of isolated nodes, even if they were small (Fig. 2), were obtained. Nevertheless, it is not pos-

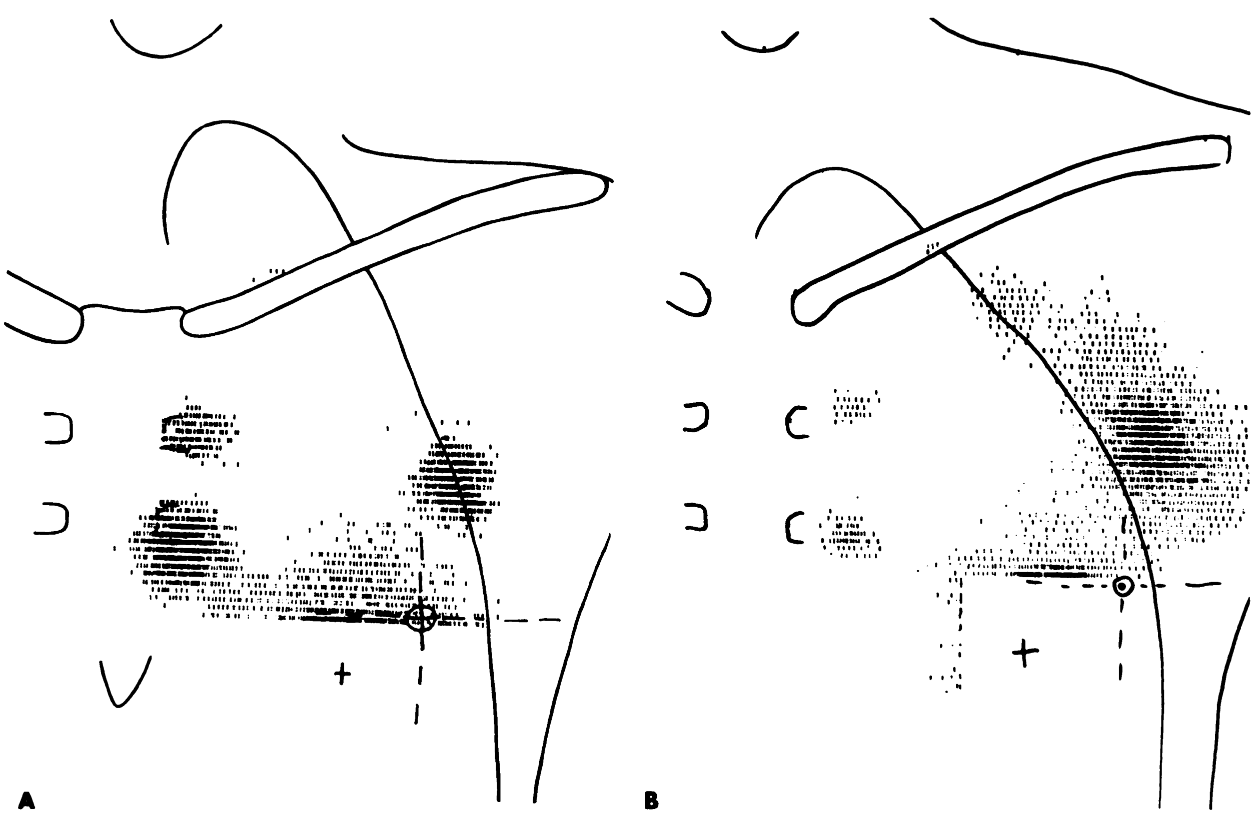

FIG. 1. (A) Lymphoscintigraphy (Nov. 2, 1967) revealing lower axillary nodes and internal mammary nodes of second and third intercostal spaces. Injection site of tracer substance is indicated by +. (B) Lymphoscintigraphy performed in same patient 2½ months later (Jan. 19, 1968). Activity is revealed in upper and lower axillary nodes and in internal mammary nodes of second and third intercostal spaces. Distribution is similar in A and B, suggesting first exploration did not block nodes receiving ^{198}Au.

sible to distinguish the different nodes of the same group, so that they appear as a single round image or, more frequently, as a polycyclical one (Fig. 3). The imaging does not have the sharpness of direct radiological lymphography.

The ganglionar picture usually appears clearly distinct from the diffuse image of the injection area, but in some cases both images merge so that they superimpose to some degree. On occasion the nodes appear side by side, thereby tracing out a path which enables one to observe the direction followed by the lymph flow (Fig. 4).

All the nodes revealed by the lymphoscintigraphy take part in the drainage of the mammary area into which ^{198}Au has been previously injected. However, some of the radionuclide may travel to other nodes which are not detected because of their low radioactivity. This means that the injected area drains *at least* into the nodes revealed by lymphoscintigraphy although there is no assurance that it does not likewise do so in small quantities into other nodes.

In Tables 1 and 2 we show in percentages the results obtained in our series. The most significant data are the following: The upper inner quadrant drains into axillary nodes in almost all the cases and into the internal mammary chain nodes in two-thirds of the cases. The lower inner quadrant drains into axillary nodes in two-thirds of the cases and to the internal mammary chain nodes in 85% of the cases. The upper outer quadrant drains into axillary nodes in practically all the cases and to the internal mammary chain nodes in one-third of the cases. The lower outer quadrant drains into axillary nodes in 90% of the cases and to the internal mammary chain nodes in two-thirds of the cases. Lastly, the subareolar area drains into axillary nodes in all the cases and to the internal mammary chain nodes in 20% of the cases.

DISCUSSION

Axillary nodes are the main drainage center of mammary lymph, except for the lower inner quadrant

TABLE 1. PERCENTAGES OF DRAINAGE IN BREAST LYMPHATICS FROM SEVERAL MAMMARY AREAS

Site of ^{198}Au injection	Axillary nodes (%)	Inner mammary nodes (%)	Supraclavicular nodes (%)	Other ganglia (%)
Upper inner quadrant	94	62	6	8
Lower inner quadrant	68	86	2	6
Upper outer quadrant	98	36	4	0
Lower outer quadrant	90	64	4	12
Subareolar region	100	20	0	2

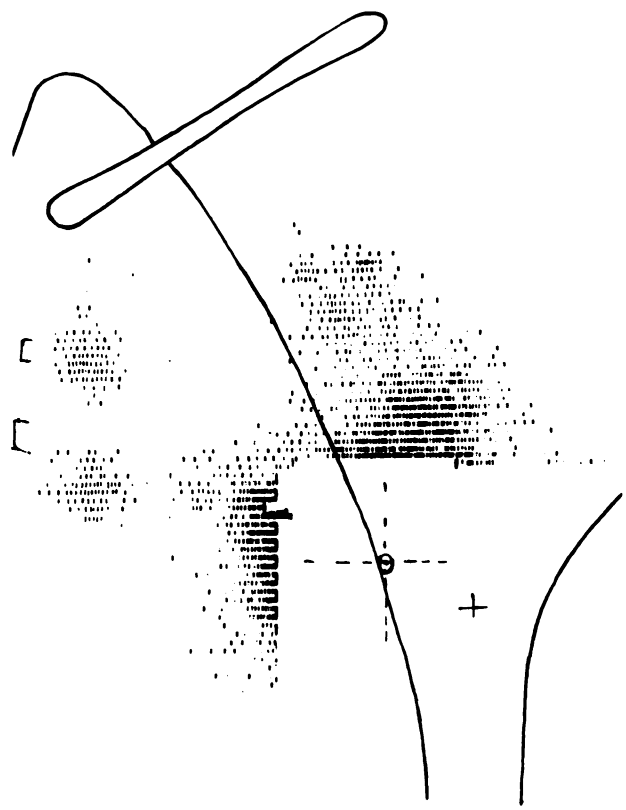

FIG. 2. Isolated internal mammary nodes. Injection site of tracer substance is indicated by +.

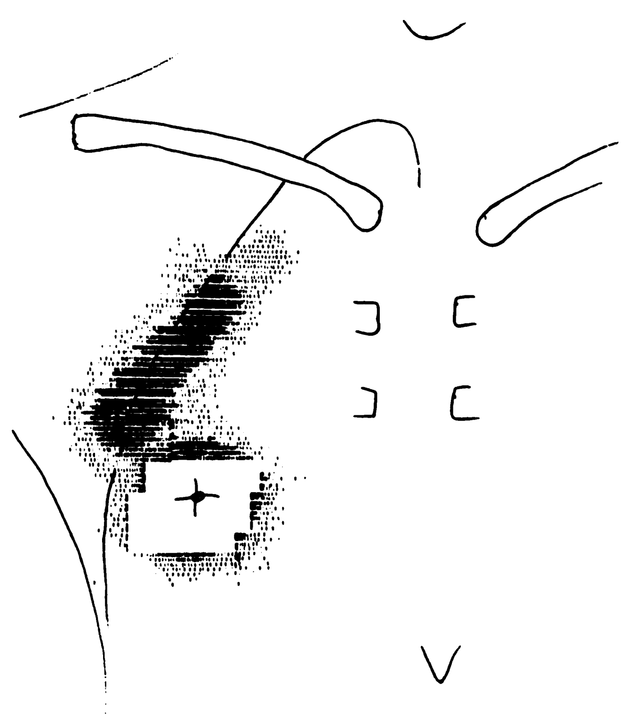

FIG. 3. Polycyclic margins of multiple axillary nodes, so-called "peanut image." Injection site of tracer substance is indicated by +.

TABLE 2. POSSIBLE WAYS OF LYMPHATIC DRAINAGE FROM DIFFERENT BREAST AREAS

Drainage station of ^{198}Au	Upper inner quadrant (%)	Lower inner quadrant (%)	Upper outer quadrant (%)	Lower outer quadrant (%)	Subareolar region (%)
Only to axillary nodes	38	14	64	36	80
Only to internal mammary nodes	6	30	2	10	0
To internal mammary and axillary nodes	50	54	30	50	20
To internal mammary, axillary, and supraclavicular nodes	6	2	4	4	0

where it has a greater tendency to flow into the internal mammary chain nodes and the axillary nodes contain radioactivity in only 68% of cases. The importance of axillary nodes observed in the present study is in agreement with previous studies (*12*).

On the other hand, our results show that the internal mammary chain nodes are of greater importance than is generally thought. In the lower inner quadrant, internal mammary chain nodes have been visualized on more occasions (86%) than the axillary groups (68%). In the other quadrants, the internal mammary chain nodes are found to be radioactive in a high percentage of cases. It is remarkable that the high radioactivity of the latter is not limited to the inner mammary half but that it is also important in the outer half, especially in the lower quadrant where there is drainage into the inner mammary chain nodes in 64% of the cases.

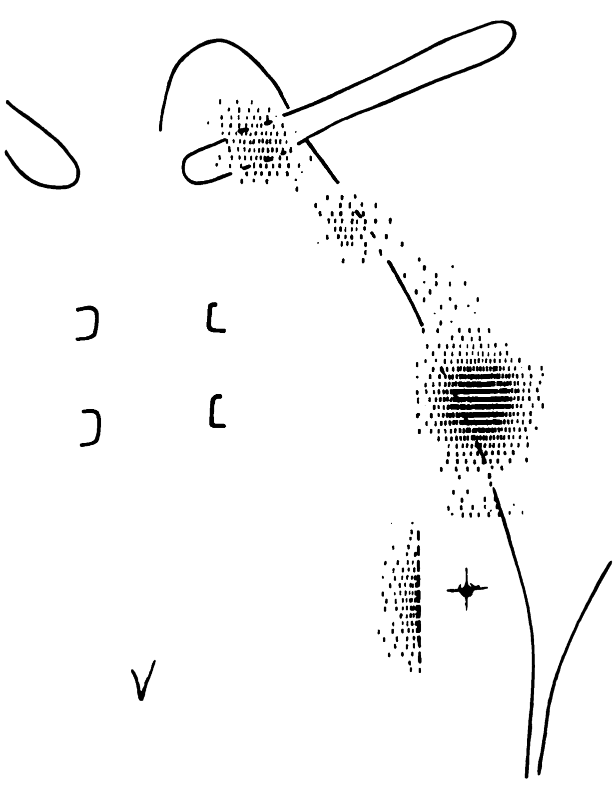

FIG. 4. Ganglionary groups disposed side by side, tracing radioactive path that reveals lymphatics. Injection site of tracer substance is indicated by +.

Our findings do not agree with those of others [Arandes (*13*) and Capdevila (*7*)] which suggest that the subareolar area drains exclusively into the axilla. Although we have proven that axillary nodes play their role in draining this region in 100% of the cases, we have also observed that, at the same time, there is a drainage into the inner mammary chain nodes in one-fifth of the cases.

Nevertheless, this proportion is clearly lower than that registered by intraparenchymal injections of radioactive gold, even in those carried out in the outer half of the mammary gland. We saw in one case that the subareolar injection drained only into the axillary nodes, but the intraparenchymal one performed in the outer half of the gland drained into the axillary groups and; likewise, into the internal mammary chain nodes in spite of the fact that the latter were farther away from the injection site.

Sometimes the internal mammary chain nodes distal to the point of the radioactive isotope injection tend to be filled, which leads us to suppose that, in certain cases, the lymphatic vessels which carry the lymph towards the internal mammary chain nodes take a slightly descending course.

We have visualized nodes situated behind the sternum in only five cases (2%). In four cases, the isotope injection had been performed in the inner half of the gland, two in the upper inner quadrant, and two in the lower inner quadrant. In only one case had the injection been made into the outer half of the gland.

In four cases the retrosternal nodes were located behind the sternal manubrium in accordance with the situation described by Sledziewski (*14*) who called them "retromanubrial nodes." In the remaining case there was a retromanubrial node and another node behind the sternum, although it was situated a little more caudally, at the level of the third rib cartilage.

In only two cases (0.8%) did the radioactivity cross the body midline. In one of them it filled the internal mammary chain nodes of the first intercostal

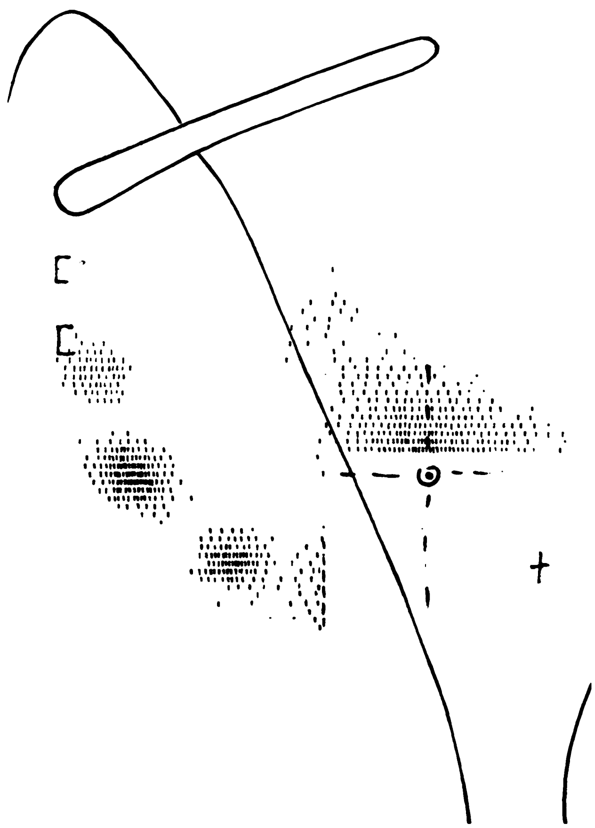

FIG. 5. Scintigraphy showing accessory node; by its position it corresponds most likely to Gerota's paramammary node. Several nodes are distributed along curved line, its concavity being on upper side, revealing lymph path. Injection site of tracer substance is indicated by +.

space and, in the other, those of the second intercostal space. The injections had been made in the upper inner quadrant and in the subareolar region, respectively.

Those results are in contradiction with the data obtained by Rossi, et al (*3*), who reported high percentages of contralateral radioactivity.

In seven cases (2.8%) we observed the node image in a position that had no correspondence either with that of the internal mammary chain or with that of the axillary nodes. Possibly, it was a Gerota's paramammarian node. We were surprised by the constancy of its position, because in all the cases it was located in the vertical line which begins in the union of the inner third and the two outer thirds of the clavicle (Fig. 5). This node apparently belongs to the internal mammary lymphatic trunks since in several cases we have observed a sequence of radioactive nodes in the course of which may be seen the accessory node and, further on, the inner mammary nodes, the whole path tracing a smooth arched line, concave on its upper side.

This accessory node has been found especially after the injection in the lower outer quadrant (five cases, 10%); the other two cases corresponded to the upper inner and lower inner quadrants, respectively.

The results of our work point to the significant role played by the internal mammary chain nodes in the lymphatic drainage of mammary glands. Its importance is not limited to the inner half of the gland, but it extends throughout the organ. Consequently, at the time of planning a therapeutic approach there is no point whatever in making a distinction between inner and outer carcinomas as many authors nowadays persist in doing. We believe that the criteria ought to be the same, regardless of the site of mammary carcinoma. The internal mammary chain nodes must always be included in the topographic area to be treated, irrespective of the mammary carcinoma location.

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