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Abstract

As the method for the diagnosis of metastasis of breast cancer to internal mammary nodes, ^{198}Au colloid was used in parasternal scintigram. In the internal mammary nodes, the rate of correct diagnosis was 90% in the cases where diagnosis of positive metastasis was obtained, 44.5% in whom metastasis was suspected, and 100% in whom diagnosis of negative metastasis was made. In the subclavian nodes, corresponding values were 69.0%, 34.5%, and 100% indicating poorer diagnostic rate. Examination on the relationship between metastasis to the lymph nodes and scintigram revealed more intense spots in the lymph nodes with very small metastasis than on normal side. As the metastatic portion increases in size, spots become less intense until finally the spots are cold as the whole lymph nodes are occupied by the cancer tissue. As the site of the tumor not only the medial side but also lateral side are involved in Stage I in a high rate of lymph node metastasis. Need of complete removal of internal mammary nodes was urgently suggested.

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**STUDIES ON THE METASTASIS OF BREAST CANCER
TO LYMPH NODES
II. DIAGNOSIS OF METASTASIS TO INTERNAL
MAMMARY NODES USING RADIACOLLOID**

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Abstract: As the method for the diagnosis of metastasis of breast cancer to internal mammary nodes, ^{198}Au colloid was used in parasternal scintigram. In the internal mammary nodes, the rate of correct diagnosis was 90% in the cases where diagnosis of positive metastasis was obtained, 44.5% in whom metastasis was suspected, and 100% in whom diagnosis of negative metastasis was made. In the subclavian nodes, corresponding values were 69.0%, 34.5%, and 100% indicating poorer diagnostic rate. Examination on the relationship between metastasis to the lymph nodes and scintigram revealed more intense spots in the lymph nodes with very small metastasis than on normal side. As the metastatic portion increases in size, spots become less intense until finally the spots are cold as the whole lymph nodes are occupied by the cancer tissue. As the site of the tumor not only the medial side but also lateral side are involved in Stage I in a high rate of lymph node metastasis. Need of complete removal of internal mammary nodes was urgently suggested.

In the previous paper, high possibility of metastasis of breast cancer to the internal mammary nodes and the need for complete removal regardless of the site occupied by the tumor were pointed out. In cases where diagnosis of positive or negative metastasis is preoperatively possible, more radical operative method might be selected.

Since current method of diagnosis on the metastasis to the internal mammary nodes is an indirect one based on angiography of the internal mammary artery and vein, detection is difficult unless the lymph nodes with metastasis reach certain size.

Recently, SCHENCK (1) reported on parasternal scintigram. Through a modification of this method, we conducted parasternal scintigraphy on the subclavian lymph nodes in addition to the internal mammary nodes.

Diagnosis of metastasis to lymph nodes was thus carried out to compare with histological metastasis and the method of evaluation of the result of diagnosis was studied.

EXPERIMENTAL METHODS

Materials: Among the cases of breast cancer admitted to our Department of Surgery, Okayama University Medical School between January 1969 and December 1971, preoperative parasternal scintigraphy was followed by radical operation and histological examination of the removed lymph nodes in 106 cases. According to TNM classification, 52 belonged to Stage I, 22 to Stage II, 25 to Stage III and seven to Stage IV.

Method of examination:

1) *Parasternal scintigram:*

Mixture of 100 μ Ci of ^{198}Au colloid and 200 units of hyaluronidase was injected into the intercostal muscle of both sides of the lower end of the sternum. Scintillation scan was carried out 48 hours after injection. Conditions for scanning; Scintillator: 5' ϕ \times 2' \times 2, Collimator: 85 holes, low: ten cm, superior and inferior confrontation system (constant sensitivity). PHA: 412 \pm 100 KeV. Rate down: 1/3. Running speed: 40 cm/min. Pitch size: four mm. Color level: Radioactivity at the third and fourth intercostal spaces was set at 100%.

2) *Histological examination of the lymph nodes:*

Removed lymph nodes were fixed in ten % formalin and embedded in paraffin. Three specimens were prepared from the upper one fourth, center and the lower one fourth. After HE stain, microscopy was carried out to see the presence or absence of cancer metastasis. By means of gold staining (2), gold uptake by the lymph nodes was studied. Iron staining (3) was also carried out.

Evaluation of the scintigram: Diagnosis of metastasis on the scintigram was based on the difference in spots between the healthy and diseased sites, assuming that the healthy side is always normal. When the spots on the diseased side are cold, positive metastasis is considered to be present. Weaker or stronger changes on the diseased side are evaluated as suspicious of metastasis. The lack of difference from the healthy side is considered to represent negative metastasis.

RESULTS

The following results were obtained: Based on parasternal scintigram of 106 cases of patients with cancer of the breast (Table 1).

TABLE 1 DIAGNOSIS OF PARASTERNAL SCINTIGRAM

pathological scintigraphic diagnosis	internal mammary node			subclavicular node		
	metastasis positive	metastasis negative	diagnostic rate	metastasis positive	metastasis negative	diagnostic rate
positive	18	2	18/20 (90.0)	20	9	20/29 (69.0)
suspicious	15	18	15/33 (45.5)	10	19	10/29 (34.5)
negative	0	53	53/53 (100)	0	48	48/48 (100)
total	33	73		30	76	

() = %

- 1) Positive metastasis to the internal mammary nodes was found in 20 cases, metastasis was suspected in 33 cases, and negative in 53 cases.
- 2) Positive metastasis to the subclavicular lymph nodes was found in 29 cases, it was suspected in 29, and negative in 48. Table 1 compares these results with those of histological examination of the lymph nodes.
- 3) In 18 of 20 cases with scintigraphic findings suggesting positive metastasis, which was demonstrated histologically. Among 33 cases with suspicion of metastasis in the scintigram, histological metastasis was found in 15. In none of the 53 cases with negative scintigraphic finding of metastasis, not any histological findings of metastasis were found.
- 4) In 20 of 29 cases with scintigraphic findings of positive metastasis to the subclavian lymph nodes, and in ten of 29 cases suspected of metastasis, histological evidence of metastasis was found. No metastasis was found in any of the 48 cases with normal scintigram (Figs. 1, 2, 3, 4, 5, 6, 7).

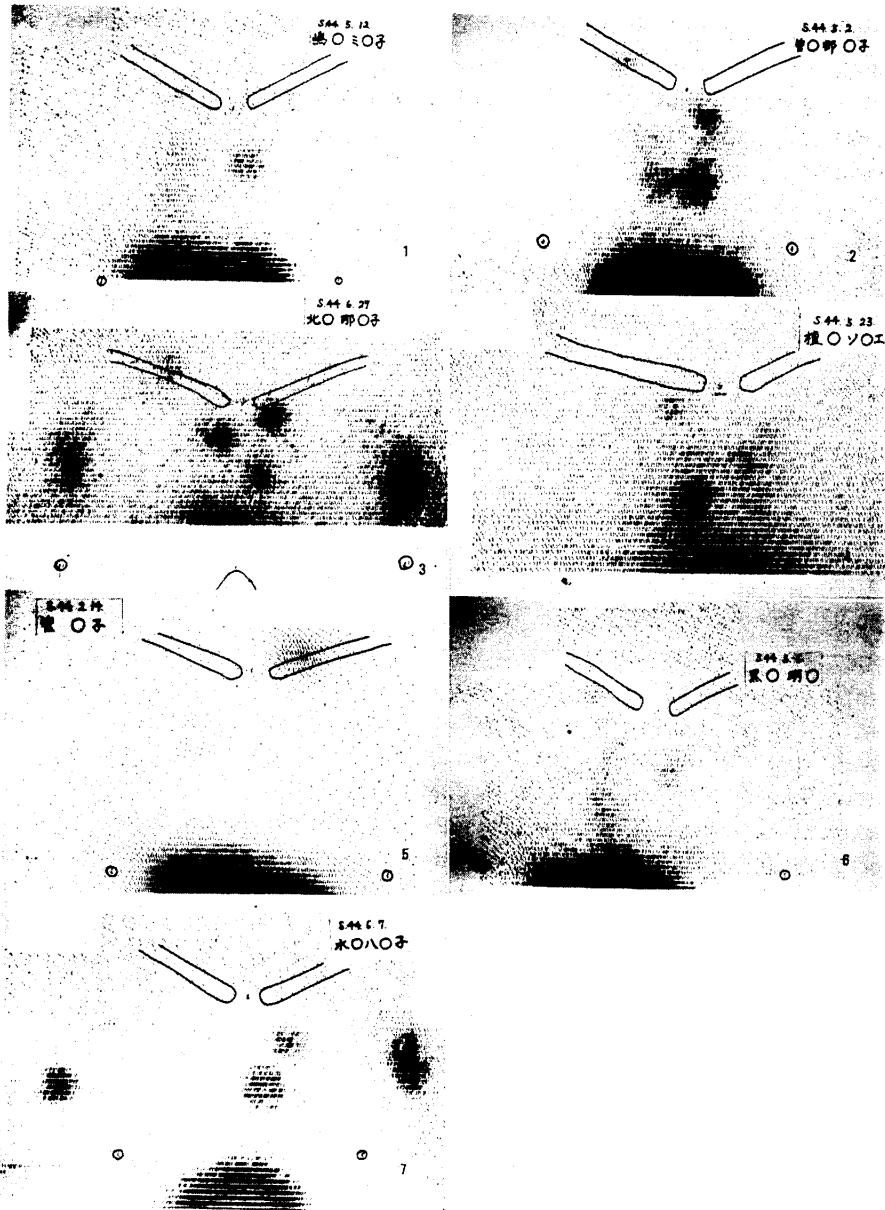
DISCUSSIONS

Many studies and reports are available on the lymph stream and metastasis to lymph nodes in the cases of breast cancer. In the previous paper, ^{198}Au colloid was used to study the lymph stream through the chest wall. As the results, abundant lymph flow was noted from the breast tissue to the axillary lymph node group. Regardless of the site of injection of ^{198}Au colloid into the breast tissue, a considerably abundant lymph flow was found towards the internal mammary nodes. Site of these lymph nodes did not appear to have so wide individual variation.

In the examination described in this paper, lymph stream was not studied but the lymph nodes were examined as to metastasis. The internal mammary nodes from a series along the lymphatic tract were distributed approximately symmetrically between the right and left intercostal spaces. Besides these, however, several small lymph nodes are found in the suprapleural fat tissue and adhering to the lateral, inferior edge of the sternum like oysters. While it is not clear to which system these lymph nodes belong, wide variation is present according to the reports of STIBBE (4), JU (5) and ARAO (6) and subsequent studies. Assuming that similar findings are found on the left and right, with lymph nodes of same size, function and position, spots on the diseased side were evaluated assuming the healthy side to be normal, but this is not without a risk of erroneous conclusion. However, the internal mammary nodes, unlike the axillary or inguinal nodes, are always well protected from the outside of the body, hence changes would rarely occur. Changes due to metastasis can, therefore, be relatively accurately assessed. In the subclavian lymph nodes simultaneously studied, the rate of correct diagnosis

probably was low due to the difference in the lymph stream between the left and right, variations in the lymphatic tract, and insufficient protection from the outside.

When metastasis involves only a small part of the lymph node, limit of



- Fig. 1. T_1N_1 1s A+C
 scintigraphic finding
 suspected of internal mammary and subclavicular node metastasis.
 pathological diagnosis
 breast tumor : papillotubular carcinoma.
 internal mammary node : reticulosis.
 subclavicular node : free of metastasis.
- Fig. 2. T_1N_1 1s C
 scintigraphic finding
 suspected of internal mammary node metastasis; positive metastasis to subclavicular node.
 pathological diagnosis
 breast tumor : papillotubular carcinoma.
 internal mammary node : reticulosis.
 subclavicular node : free of metastasis.
- Fig. 3. T_1N_1 1s C+D
 scintigraphic finding
 suspected of internal mammary node metastasis; positive metastasis to subclavicular node.
 pathological diagnosis
 breast tumor : papillotubular carcinoma.
 internal mammary node : reticulosis.
 subclavicular node : free of metastasis.
- Fig. 4. T_2N_0 1s A
 scintigraphic finding
 suspected of internal mammary node metastasis; positive metastasis to subclavicular node.
 pathological diagnosis
 breast tumor : papillotubular carcinoma.
 internal mammary node : positive metastasis.
 subclavicular node : positive metastasis.
- Fig. 5. T_2N_2 rs C+D
 scintigraphic finding
 suspected of internal mammary node, subclavicular and supraclavicular node metastasis.
 pathological diagnosis
 breast tumor : scirrhou carcinoma.
 internal mammary node : positive metastasis.
 subclavicular node and supraclavicular node : positive metastasis.
- Fig. 6. T_2N_0 1s C
 scintigraphic finding
 positive metastasis to internal mammary node and subclavicular node.
 pathological diagnosis
 breast tumor : scirrhou carcinoma.
 internal mammary node : positive metastasis.
 subclavicular node : positive metastasis.
- Fig. 7. T_3N_0 rs C
 scintigraphic finding
 positive metastasis to internal mammary node.
 pathological diagnosis
 breast tumor : scirrhou carcinoma.
 internal mammary node : positive metastasis.

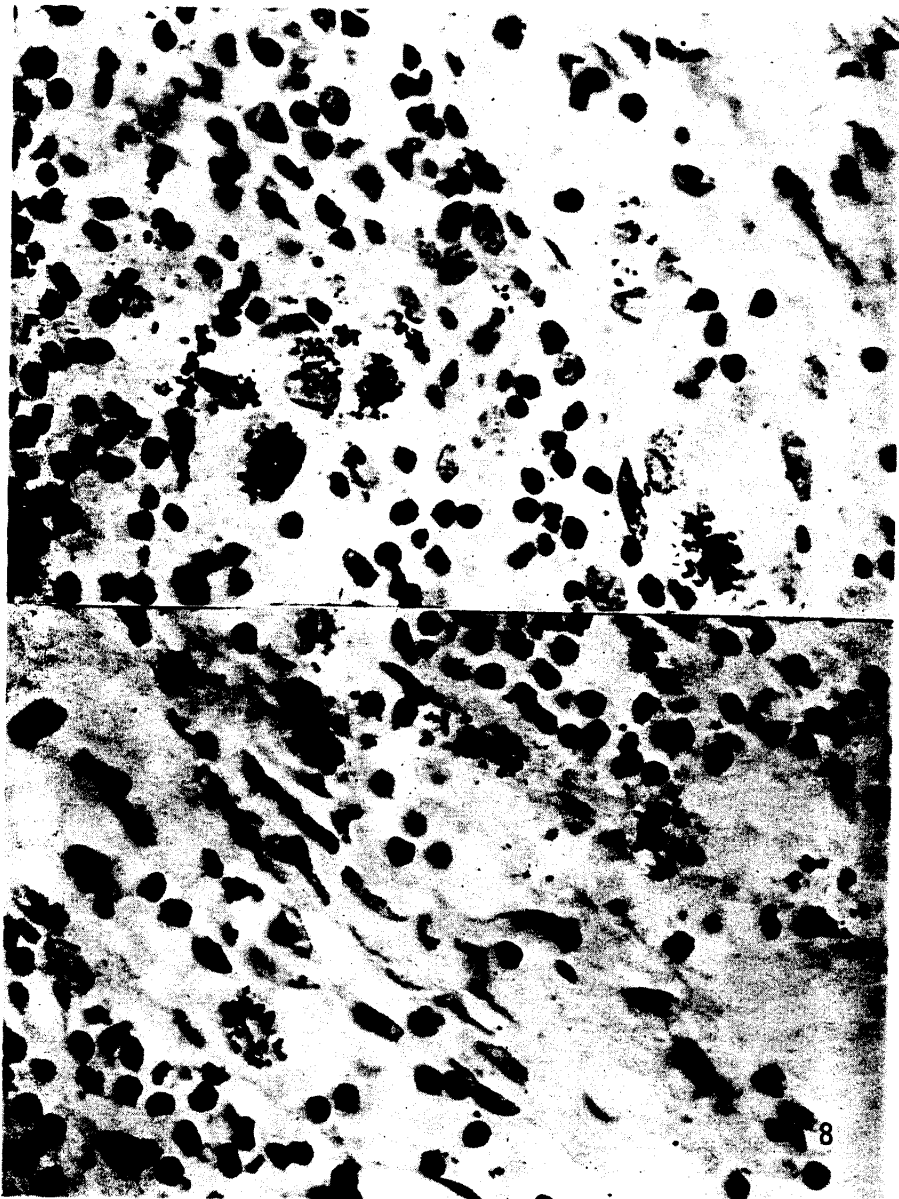


Fig. 8. Histologic picture of a lymph node. Picture shows gold particles in reticulum cell and histiocytes of lymph node as revealed by gold staining.

the diagnostic accuracy presents a problem. Reaction of lymph nodes to cancer metastasis would become the basis for diagnosis. Though the reaction of the lymph nodes at the time of entrance of cancer cells into the lymph

nodes via the lymphatic tract is unknown, some reaction probably occurs at the time of beginning of proliferation of cancer cells following embedding.

Some of the cancer cells do not settle in the lymph nodes after passing

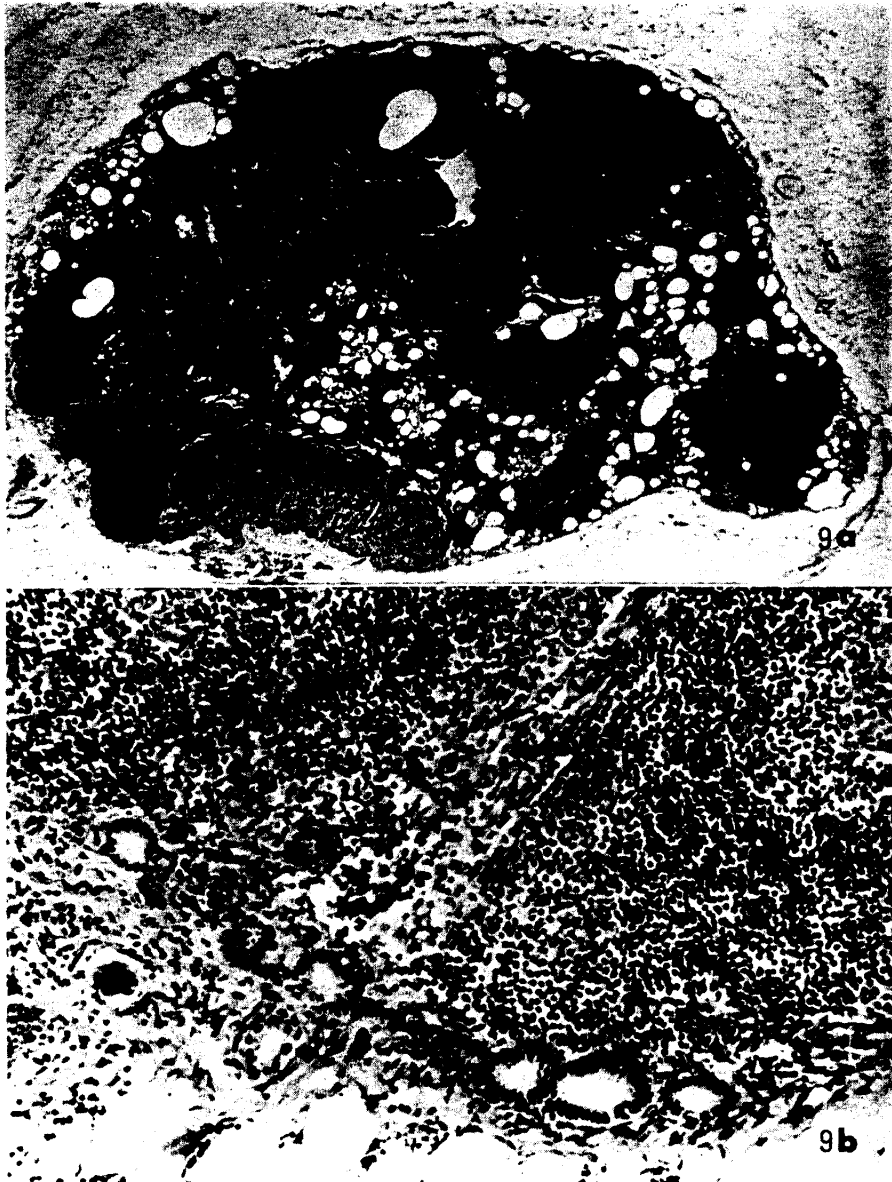


Fig. 9. Pictures of histologic sections of an internal mammary lymph node which was taken from the area showing a heavy shadow in scintigram (a). It has small metastatic foci of adenocarcinoma (b).

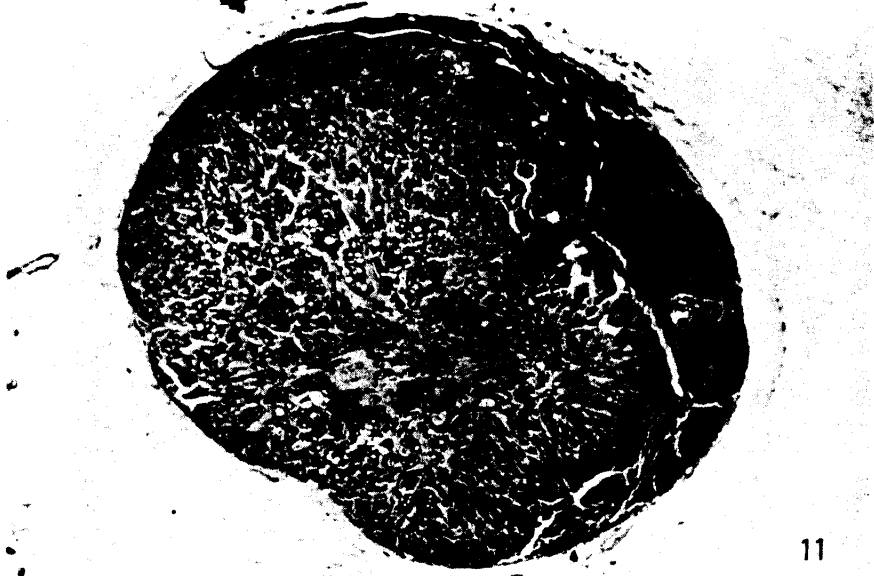
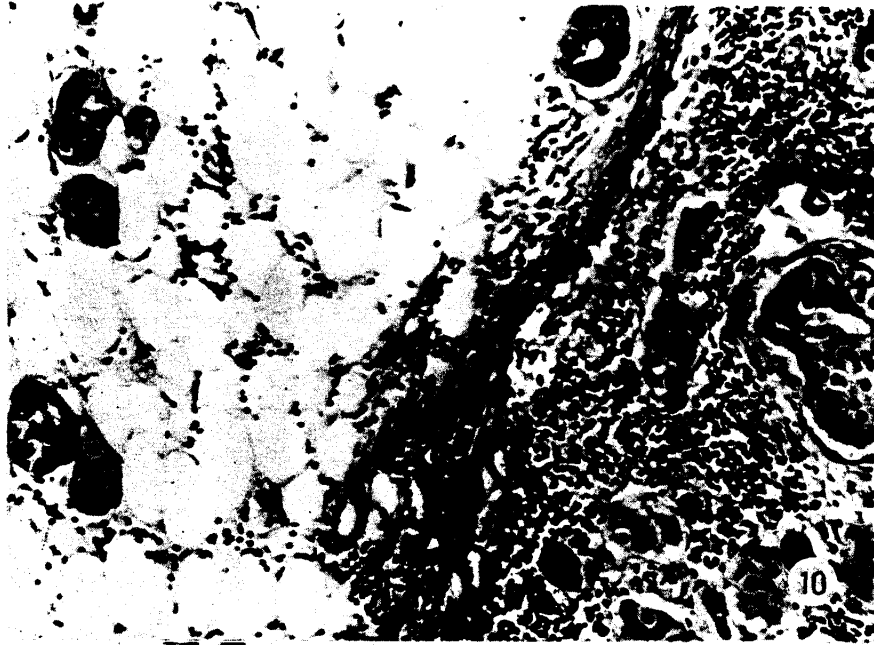


Fig. 10. A histologic picture of an internal mammary lymph node taken from the area shows a slight shadow in scintigram, and it reveals metastatic cancer nests both in lymph node and in fatty tissue surrounding of the lymph node.

Fig. 11. A section of internal mammary lymph node from the area showing cold scintigram, and reveals a big cancer nest occupying a large part of the lymph node.



Fig. 12. A histologic picture of internal mammary lymph node taken from the area showing hot scintigram and shows no cancer metastasis, but a marked follicular hyperplasia.

through the lymphatic vessel, while Indian ink and gold particles are always uniformly taken up depending upon the function of phagocytosis. This is the very difference between cancer cells and gold particles, simultaneously providing significant data in the present experiment.

In the present experiment, slices of lymph nodes stained for gold revealed uptake of gold particles by reticulum cells and histiocytes (Fig. 8). The presence of phagocytes within the lymph nodes and their function probably control the intensity of the spots on the scintigram.

In the lymph nodes with metastasis to a very limited part, intense reticulosis was found, and intense spots with uptake of gold colloid were noted, suggesting hyperfunction of phagocytes. As the proportion occupied by the metastasis becomes greater, the spots become less intense and the spot grows cold when most of the lymph node is replaced by cancer cells. Such differences are probably responsible for the variation in the intensity of the spot. In the cases subjected to exploratory excision of the breast tissue before test, some changes might have occurred in the regional lymph nodes (Figs. 9, 10, 11, 12).

In the diagnosis of changes of the internal mammary nodes, metastasis was erroneously suspected in 18 cases due to the presence of intense spots.

In five of these cases, the test was carried out within a week of exploratory excision, leading to the appearance of intense spots. In the subclavian lymph nodes, the exploratory excision was carried out in 12 of 19 cases suspected of metastasis in the scintigram and negative histological findings. In four of nine cases in which scintigram suggested positive metastasis but histological finding was negative, exploratory excision was carried out preoperatively. Such an error is probably due to the change of the lymph nodes in response to the stimulation to the breast tissue before test. This method always disclosed changes of lymph nodes as the changes of spots in the scintigram. The results so far gave some false positive but never false negative findings. This indicates a great diagnostic value.

Since ^{198}Au has a short half life of 64 or 75 hours, repeated test is possible, and the technique is simple without inflicting much discomfort to the patient, being more useful than other indirect methods. Through injecting ^{198}Au colloid subcutaneously on the medial surface of the upper arm, pictures of the axillary lymph nodes, the subclavian lymph nodes, and the supraclavicular lymph nodes may be obtained. With the use of this method, diagnosis of metastasis is possible even without lymphangiography of the upper extremity to an advantage.

In 33 cases with metastasis to the internal mammary nodes in histological examination, frequency of each stage was measured in TNM classification. Such cases were found in nine of 52 cases of Stage I (17.3%), six of 22 cases of Stage II (27.3%), and 11 of 25 cases of Stage III (44.0%). As to the sites occupied by these tumors, A (upper inner zone) was found in eight of 18 (44.4%), B (lower inner zone) in two of 12 cases (16.7%), C (upper outer zone) in 15 of 47 cases (31.9%), D (lower outer zone) in four of 15 cases (26.7%), and E (central zone) in four of 14 cases (28.6%) (Table 2).

TABLE 2 DISTRIBUTION OF INTERNAL MAMMARY METASTASIS AND STAGE

position	A	B	C	D	E	total
Stage I	3/12 (25.0)	1/9 (11.1)	3/16 (18.8)	0/7 (0)	2/8 (25.0)	9/52 (17.3)
II	2/2 (100)	0/2 (0)	3/11 (27.3)	1/4 (25.0)	0/3 (0)	6/22 (27.3)
III	3/4 (75.0)	0	5/16 (31.3)	2/3 (66.7)	1/2 (50.0)	11/25 (44.0)
IV	0	1/1 (100)	4/4 (100)	1/1 (100)	1/1 (100)	7/7 (100)
total	8/18 (44.4)	2/12 (16.7)	15/47 (31.9)	4/15 (26.7)	4/14 (28.6)	33/106 (31.1)

() = %

These facts are in an excellent agreement with the results described in the study on lymphatic stream through the chest wall. In the cases of Stage I, complete removal of the internal mammary nodes appears to be important regardless of the site occupied by the tumor.

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REFERENCES

1. SCHENCK, P.: Szintigraphische Darstellung des parasternalen Lymphsystems. *Strahlentherapien* 130, 504-508, 1966
2. ROBERTS, W. J.: Recherche de l'or dans les tissus animaux par la méthode du développement. *Physique. Bull. histol. appl.* 12, 344-361, 1935
3. KANEKO, H.: Soshiki-Hyohon, p.63, Igaku-shoin, Tokyo, 1970 (in Japanese)
4. STIBBE, E. P.: The internal mammary lymphatic glands. *J. Anat.* 52, 257, 1918
5. JU, D.: From Diseases of the Breast edited by Haagensen, C. D. p. 44-45, 1971
6. ARAO, A. and ABRAO, A.: Estudo anatomico da cadeia ganglionar mamária interna em 100 casos. *Rev. paulista de Med.* 45, 317, 1954 (referred from Diseases of the Breast edited by Haagensen, C. D., p.45, 1971)