Lymphology 10 (1977) 107-114

Scintigraphy of Lymph Nodes

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Summary

The basic considerations, pharmacology, techniques, and clinical results of lymphoscintigraphy performed after the interstitial application of radiocolloids or after i.v. injection of radiogallium or radiobleomycin are described. The advantages and disadvantages are summarized, and the indications are given.

Scintigraphy of the lymphatics after radiopharmaceuticals have been subcutaneously applied provide information about the circulation within the lymphatic vessels and the phagocytic function of the lymph nodes. On the other hand, the metabolism of lymphatic tumors can be studied after intravenously injected ^{67}gallium citrate or radioactive labeled bleomycin.

By means of scintigraphy, the following topographic groups of lymph vessels and nodes can be studied after the subcutaneous application of radiocolloids:

1. Retroperitoneal lymphatics (21),
2. Axillary and infraclaviculary lymphatics (8),
3. Parasternal lymphatics (3, 15, 17),
4. Cervical lymphatics (18).

Pharmacology

The transport of subcutaneously applied radiocolloids through the lymphatic vessels (2, 6, 9, 14, 16, 24) is based on the particle size. Since the average particle size for radiocolloids is 3μm or more, they cannot diffuse through the blood capillaries. Up to 70% of the radiocolloids are removed from the point of interstitial injection. Lymphatic transport is proportional to the quantity applied, saturation is higher when more than 0,12 mg of colloidal gold is administered. Provided the lower extremities are moved actively, the velocity of lymphatic transport is about 10 cm per minute. Radiocolloids enter the blood circulation via the thoracic duct, and are deposited in the reticuloendothelial system of the liver.

Colloidal ^{198}aurum is a suitable radiopharmaceutical because of its small particle size (average: 5 μm) as well as its stable and reliable preparation. However, the physical half-life of 2.7 days is long and the radiation dose for the patient is rather high due to beta radiation. Substances labeled with ^{99m}technetium are important (10) because of the short half-life of 6 hours and the lack of beta radiation. Today kits containing sulphur microcolloids are available which can be labeled with ^{99m}Tc pertechnetate within a few minutes. The average particle size is 3 μm. In spite of these advantages, the labeling of ^{99m}Tc is less stable than that of radiogold colloid. ^{99m} technetium is often seen in the bladder after renal excretion.

Radioactive gallium and bleomycin are deposited in tumors and some inflammatory affections, as well as in inflammatory and neoplastic diseases of the lymph nodes (1, 4, 7, 13, 19). Noteworthy is the fact, that gallium is excreted or accumulated by liver, intestinal tract, kidneys, and bones; bleomycin is excreted by the kidneys.

Radiation Dose

Colloidal radiogold (150 μCi ^{198}Au per leg) will cause an average radiation dose of 0.7 rad to the ovaries, 30 rad to the lymph nodes, and about 1000 rad to the point of injection up to a distance of several millimeters (22). Due to the lack of beta radiation and the very short half-life, the radiation dose is considerably lower after the application of ^{99m}. technetium microcolloids; activities up to 10 mCi can be injected. The radiation dose in-

creases considerably in obstructed lymphatic circulation or lymphedema; this fact must be especially noted when colloidal radiogold is injected.

After 2 mCi ^{67}Ga citrate, the radiation dose to the whole body and to the gonads is 0.4 rad, to the bones 1.0 rad and to the liver 0.8 rad. After 1 mCi ^{57}Co bleomycin, the radiation dose to the whole body is 0.2 to 0.3 rad and to the kidneys 2 rad (7).

Techniques

For retroperitoneal lymphoscintigraphy, 150 μCi colloidal ^{198}Au with an average particle size of 5 μm are injected into the webs of each foot; no more than 0.5 ml should be injected. Movements of the lower extremities for 2 hours are required. Scintigraphy can be performed 2 hours after the injection at the earliest, but usually after 24 hours.

For axillary as well as for cervical lymphoscintigraphy, 100 μCi colloidal ^{198}gold is injected into the webs of each hand or subcutaneously in each retroauricular region. Scintigraphy is performed after 24 hours.

For parasternal lymphoscintigraphy, 100 μCi colloidal ^{198}Au is injected exactly 1 cm lateral the xiphoid process on each side. The material must be deposited below the xiphoid process. Scintigraphy is performed after 24 hours.

The application technique is the same for ^{99m}. technetium microcolloids. On each side, 0.5 to 10 mCi are injected; more than 0.5 ml should not be injected. Scintigraphy is performed after several hours or after 24 hours. In scintigraphy made 1 hour after the application, one has to consider that most of the activity is in the lymph vessels.

The area of resorption is increased when hyaluronidase is added to the activity. While this fact may be important for studies of lymphatic transport, we do not use this technique for imaging of lymph nodes. The addition of Novocain leads to delayed lymphatic transport.

For scintigraphy scanners or scintillation cameras can be used. The correct recording of paralumbar radioactivity with the scanner is difficult and requires the exact positioning of the focal plane in the ventral parts of the lumbar spine. The scintillation camera allows uncomplicated registration of the radioactivity in all retroperitoneal regions. The registration time is shorter and the resolution of the modern camera systems is superior to the scanner. For these reasons we have preferred the scintillation camera for some time now.

Results

Scans of patients with *normal lymphatics* show

1. In the retroperitoneal region: two symmetrical chains of inguinal and iliac nodes which fuse at the paralumbar nodes. Some radioactivty is found in the liver which corresponds to the transport through the thoracic duct. From here activity is transported to the venous system and deposited in the reticuloendothelial system of the liver (Fig. 1).

2. In the axillary-infraclavicular region: An accumulation of radioactivity in circumscribed

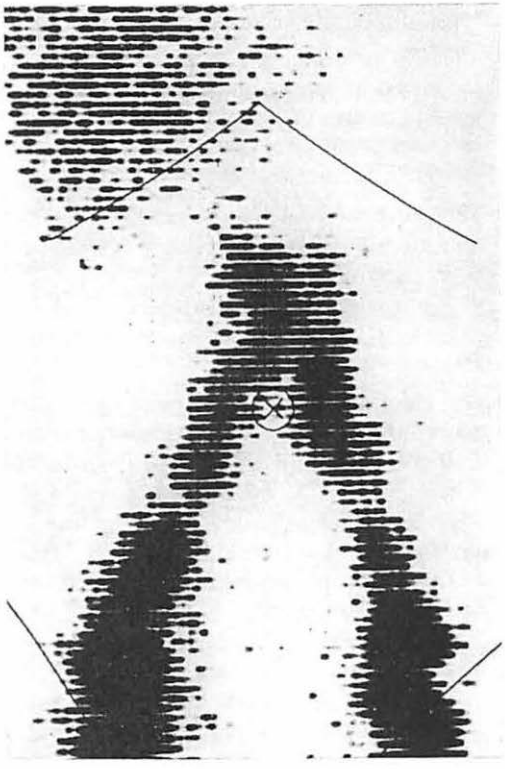

Fig. 1a (legend see next page, Fig. 1b).

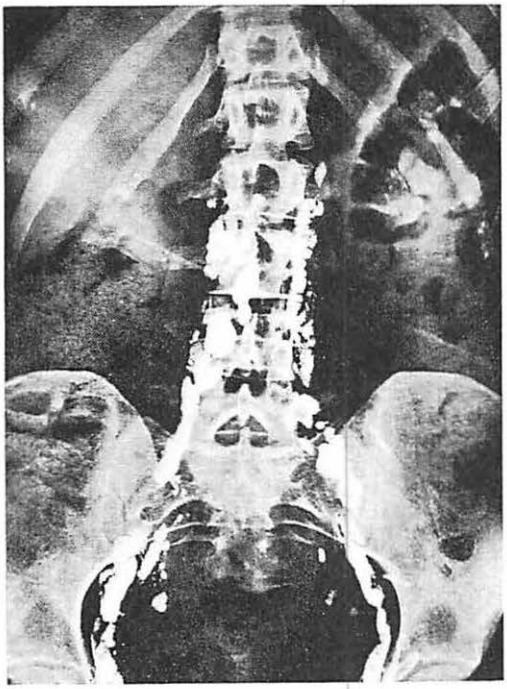

Fig. 1b. – Retroperitoneal lymphoscan 24 hours after application of 100 μCi ^{198}Au colloid together with 75 units hyaluronidase into the webs of each foot. Normal uptake and distribution like a chain of radioactivity in the inguinal, iliac, and paralumbar lymph nodes. Distinct liver activity. No differentiation of single lymph nodes. – Lymphadenogram of the same patient (5).

axillary, infraclavicular and supraclavicular lymph nodes (Fig. 2).

3. In the parasternal region: Usually single lymph nodes on each side in the first and second optionally in the fourth, fifth or sixth intercostal space (Fig. 3, page 105).

4. In the cervical region: A continuous, uniform chain of radioactivity beginning at the retroauricular point of injection down to the supraclavicular region (Fig. 4, page 105).

The uptake of radiocolloids in lymph nodes is:

1. Decreased by lymphadenitis, malignant lymphomas (Fig. 6, page 106), melanomas, and after irradiation (Fig. 7, page 106).
2. Increased by obstructed circulation of the lymphatics and sometimes in acute lymphadenitis;
3. Absent in metastases of solid tumors (Fig.5).

The uptake area of the lymphatics is:

1. Enlarged in hyperplasia and malignant lymphomas (Fig. 6);
2. Deplaced by obstructed circulation and collateral lymphatics (Fig. 7);
3. Ectopic when lymphedema inhibits lymphatic transport (Fig. 2).

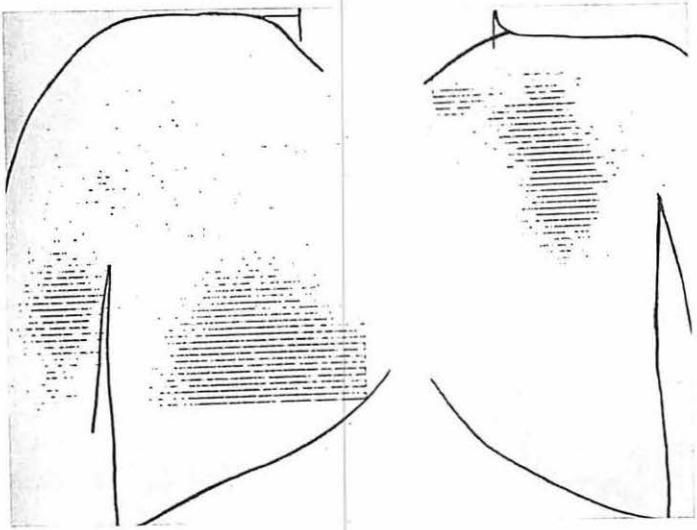

Fig. 2 Axillary-infraclavicular lymphoscan 24 hours after 100 μCi ^{198}Au colloid together with 75 units hyaluronidase into the webs of each hand in a patient with edema of the right upper arm following radical mastectomy and radiotherapy. Normal uptake in the axillary and infraclavicular lymph nodes of the left side. Retention of radioactivity in the lymphatic vessels of the right upper arm; no uptake in the right axillary region (5).

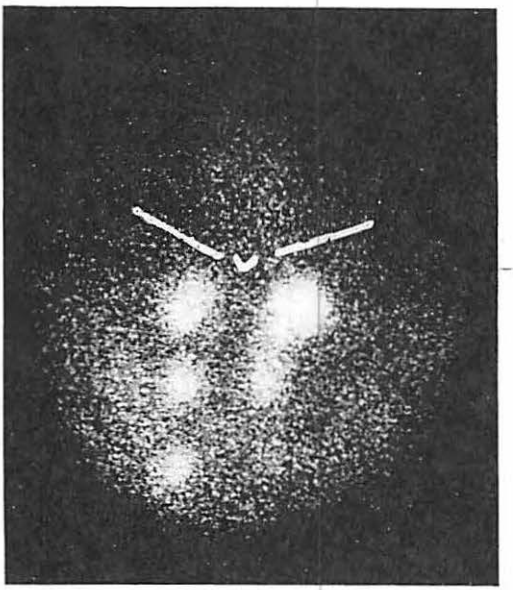

Fig. 3. Parasternal lymphoscintigraphy 24 hours after bilateral suxiphoidal application of colloidal radiogold. Normal uptake in the lymph nodes of the first, second, fourth intercostal space (5).

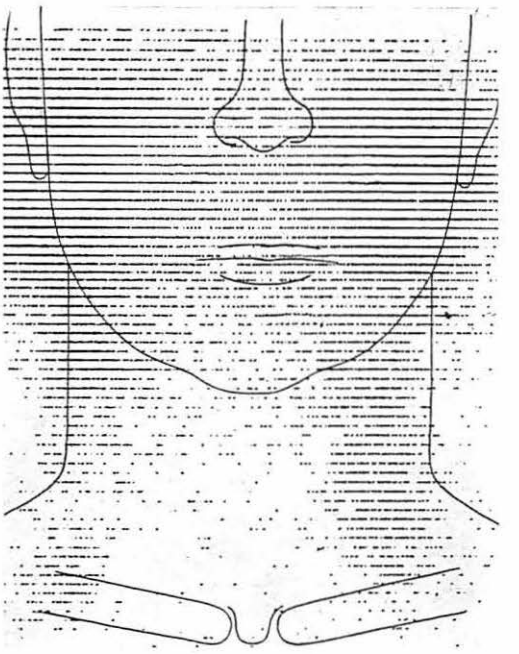

Fig. 4. Cervical lymphoscintigraphy 24 hours after retroauricular injection of colloidal radiogold in a patient with cervical lymph nodes destruction of the right side due to squamous cell carcinoma. Normal transport and uptake on the left side. Reduced transport and uptake on the right side (18).

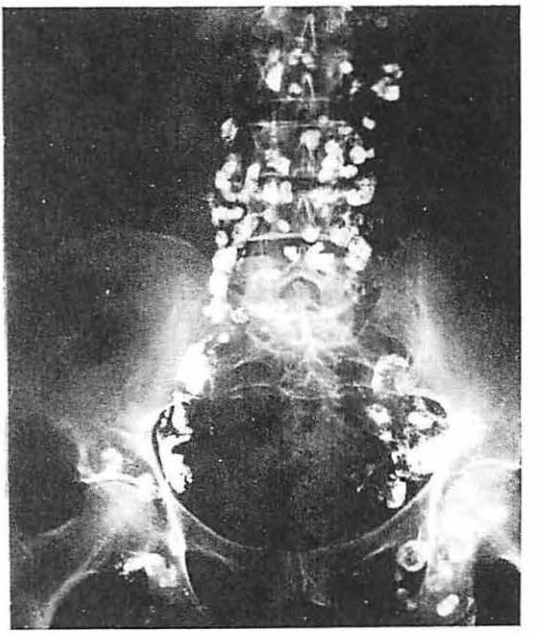

Fig. 5. Retroperitoneal lymphoscan and lymphadenogram in a patient with cancer of the cervix. Extended defect in the left common iliac lymph nodes. Lymphadenogram shows metastatic destruction in the same region.

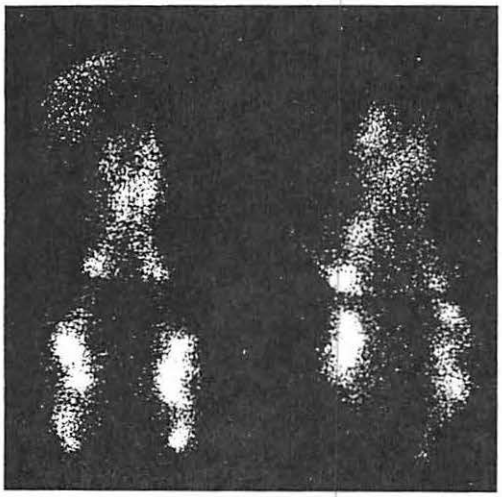

Fig. 6. Retroperitoneal scans in a patient with progressive lymphogranulomatosis. In the left scan, slight enlargement of the cranial portion of the paralumbar lymph nodes; the lymphadenogram was normal. The right scan, performed 8 months later, demonstrates distinct enlargement in the paralumbar region and defects in the left common iliac region together with lack of liver activity; repeated lymphography shows typical affections of the lymph nodes in the same regions.

To recognize *pathologic alterations* on should evaluate:

1. The continuity of the typical chain of radioactivity. This may be interrupted by physiological variants usually located in the iliac region, metastases of solid tumors (Figs. 5, 7), or after lymphadenectomy.

2. The width of the pelvic and paralumbar deposited radioactivity. This may be increased by inflammatory affections, malignant lymphomas (Fig. 6) or stasis of the radioactivity in the lymphatic vessels (Fig. 2) due to partial or total obstruction.

3. The intensity of accumulated radioactivity. This can be reduced by malignant lymphomas (Fig. 6), reactive hyperplasia, or increased in a few cases of acute lymphadenitis.

4. The topography of the accumulated radioactivity. This can be altered by metastases, collateral lymphatics (Fig. 7) or sometimes in lymphadenitis.

5. The radioactivity in the liver. This may be absent (Fig. 6) due to insufficient movement of legs or total obstruction of the lymphatic vessels.

It should be mentioned that, in the retroperitoneal and cervical region, single lymph nodes cannot be differentiated. Scintigraphy provides

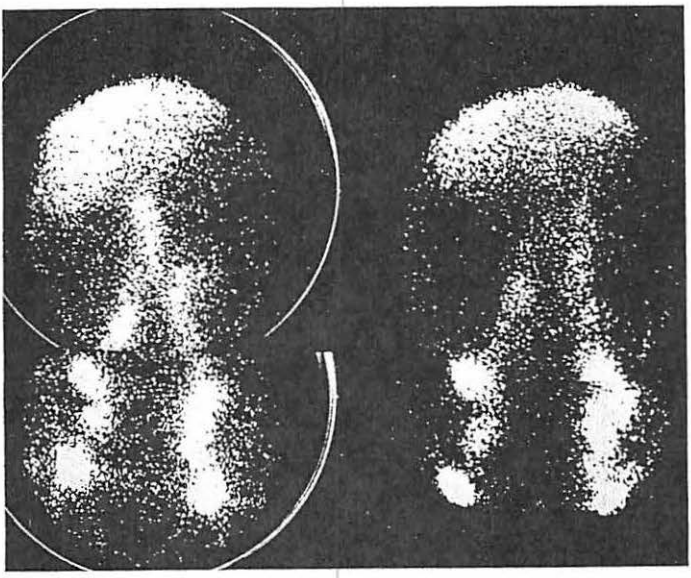

Fig. 7. Retroperitoneal scans in a patient with metastatic seminoma before and after radiotherapy with 4000 rad. Left scan before radiation demonstrates circumscribed, but distinct, defect of the left paralumbar region combined with displacement of the afferent lymphatics corresponding to collateral lymphatics. Right scan, after radiotherapy of the paralumbar region, shows diminished uptake of the lymph nodes in the irradiation field; the pattern of the colloidal radiogold, however, is now normal (5).

no information about the partial destruction of single lymph nodes or about micrometastases.

Tumors of the lymphatics show in the lymphoscintigram one or more of the following signs (Fig. 4, 5, 7):

1. Localized defects;
2. Extended defects, which often correspond to a blockade;
3. Enlargement with increased uptake corresponding to obstruction;
4. Enlargement with diminished uptake in lymphomas (Fig. 6);
5. Dislocation;
6. Collaterals;
7. Lack of liver activity corresponding to total blockade.

Malignant lymphomas (Fig. 6) are characterized by enlarged region of uptake and localized or more extended defects. Total blockades, collateral lymphatics, or displacements are seldom. Usually liver activity is also found in blockades due to the existence of lymphovenous shunts.

In *lymphedema* the radioactivity remains at the point of injection or in the afferent lymphatic vessels (Fig. 2); the activity in the regional lymph nodes is reduced. The lymphatic transport is undisturbed in patients with edema caused by cardiac, or renal, or thyroid insufficiency.

Irradiation causes decreased uptake (Fig. 7). Associated with lymphadenitis, the uptake is completely suspended. The same effects are seen in lymphatic fibrosis of the retroperitoneal space or following intensive treatment with cytostatic drugs. On the other hand, initial defects and collateral lymphatics can be normalized after irradiation (Fig. 7; 18, 22).

Comparison of lymphoscintigraphy and lymphography (Fig. 5; 11, 12, 20, 23) shows satisfactory agreement (Table 1) if the scan was found to be unequivocally normal or pathologic. Nearly 30 % of the scans, however, are uncertain; in such cases, lymphography is indicated.

Radiogallium is accumulated in many malignant lymphomas (Fig. 8) and some solid tumors of the lymphatics. Diagnosis must be cautious with abdominal lymphomas because of the mentioned excretion by liver and intestine. Moreover, one must consider that gallium and bleomycin can also be accumulated in acute and chronic lymphadenitis.

The recording of lymphatic affections with gallium or bleomycin depends on the quantity of accumulation. Affections with a diameter of more than 2 cm can be easily detected. A pathologic accumulation does not, however, permit the differentation between malignant lymphoma, solid tumor, or inflammation of the lymph node.

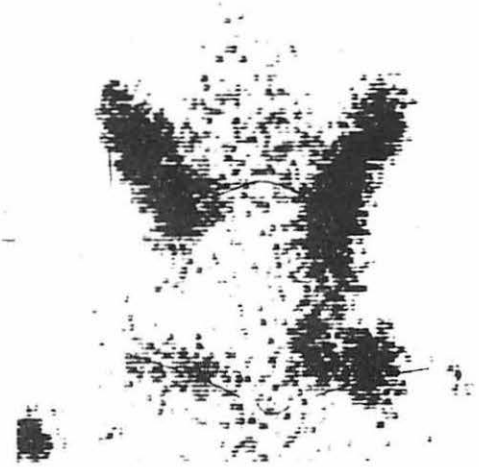

Fig. 8. Scan of the cervical and axillary regions in a patient with lymphogranulomatosis 3 days after 2 mCi ^{67}gallium citrate i.v. High uptake of radiogallium in affected lymph nodes of the bilateral cervical and supraclavicular regions as well as in axillary lymph nodes of the right side.

Table 1. Results of Lymphoscintigraphy and Lymphography (22)

X-Ray	Scintigraphy			
	Normal	Doubtful	Pathological	Total
normal	29	70	11	110
doubtful	4	12	28	44
pathological	3	43	261	307
total	36	125	300	461

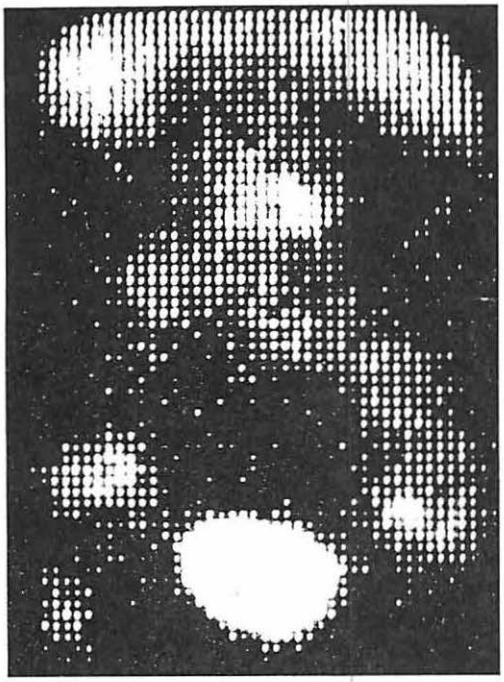

Fig. 9. Scan performed with the scintillation camera and data processing system in a 8-year-old girl with neuroblastoma 1 day after 1 mCi ^{57}Co bleomycin. Corresponding to the metastases high uptake was found in numerous paralumbar and iliac lymph nodes. Due to renal excretion, radioactivity was found in the kidneys and bladder (7).

Uptake of gallium in lymph nodes appears to be the most consistent; the accuracy of the scan for detecting lymphomas is 87% (1). The method can, therefore, be used for the localization and staging of lymphoma.

Gallium is accumulated in liver, bones, intestinal tract, lacrimal glands, mammary glands, and kidneys. Moreover, uptake is seen in sarcoidosis, pulmonary tuberculosis, amebic abscesses of the liver, pneumonia, bronchiolectasis, and silicosis. Increased accumulation in affected lymph nodes may disappear after radiotherapy or chemotherapy. Due to this fact, the method is suitable for controls after treatment.

Because of the lack of intestinal excretion bleomycin can be used for the scintigraphy of the abdominal region. (Fig. 9). The material is accumulated not only in tumors, but also in some inflammatory affections, postoperatively in scars, and in bones with increased metabolism such as after hip replacement.

Indications

Lymphoscintigraphy with radiocolloids is indicated for:

1. Search for lymphatic metastases of solid tumors or malignant lymphomas;
2. Control of lymphatics in patients with tumors of the pelvic region, of the gastrointestinal tract, of the pancreas, and of the liver for the appearance of metastases;
3. Control of surgical and radiological treatment of the lymphatics;
4. Examination of the lymphatic transport from the periphery;
5. Radiation treatment planning in patients with breast cancer (parasternal lymphatics);
6. Selection of patients suitable for endolymphatic therapy with radioactive substances. Our experience with 250 patients, especially those with melanoma or urologic tumors, indicates that endolymphatic therapy should be used only for patients with a normal lymphoscan.

Scintigraphy after the application of ^{67}gallium citrate or bleomycin is suitable for:

1. Search for affected lymph nodes in patients with proven malignant lymphomas or solid tumors;
2. Control of the efficiency of radiotherapy or chemotherapy;
3. Recognition of recurrences.

Evaluation

Lymphoscintigraphy has the following advantages:

1. Can be easily carried out, even for outpatients;
2. Techniques is noninvasive;
3. Short-term follow-up studies are possible;
4. Correct information about the lymphatics provided for nearly 70% of the cases (Table 1);
5. Patients suitable for endolymphatic therapy with radionuclides can be selected.

On the other hand, the method has the following disadvantages:

1. In comparison with lymphography, resolution is definitely reduced;
2. The morphological structure of the lymph nodes cannot be evaluated;
3. In 30% of the cases, additional lymphography is necessary in order to make a diagnosis.

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