PB methodological protocol for the scintigrahic investigations of the <u>superficial</u> lymphatic system in patients with limb edemas

The rationales of our protocol

Based on the clinical conditions of edema occurrence, the images must be obtained in at least two conditions:

- In resting conditions, because lower limb edema, for instance, will appear only after the patient sits for several hours without moving or with limited movement
- After a period of normal activity in cases in which edema only appears after several hours of normal activity.

In practice, however, these two conditions can result in insufficiently detailed or in incomplete images of the studied lymphatic system, particularly considering the potential implications for treatment. In many cases, the solution is to obtain an intermediate image after a short period of standardized exercises.

In the 1980s, these previous considerations prompted us to develop a 3-phases protocol of lymphoscintigraphic investigation of the limbedemas. The protocol was then refined over time.

These three phases correspond to image acquisitions as follows:

a) Phase 1. Images are acquired during and after a resting period, with the patient lying on the examination table for 30 minutes.
b) Phase 2. With the patient lying on the examination table, the images are acquired during and after performing a standardized exercise (5 minutes of tiptoeing or 15 minutes of hand gripping).
c) Phase 3. Images are acquired after the patient performs normal activities for one hour. In cases with lower limb edema, the images should be acquired after walking, making sure that the patient does not remain sitting in the waiting room prior to imaging. In cases with upper limb edema, the images should be acquired after the patient performs movements with the fingers, hands, and limbs in ways that would be part of his-her normal daily activity. The images can be obtained after longer periods of normal activity, but normal values for the extractions of the tracer (see below) will have to be obtained. Note that one hour is usually convenient both for patients and for imaging scheduling at a nuclear medicine service. The images and the information they contain will then be representative of the response of the lymphatic system to the patient's lifestyle activities that precede the appearance of edema.

For the lower limb edemas… in summary

Our methodological protocol can be summarized as follows. 0.2 ml of 99mTc-labeled (74 MBq per injection) Human Serum Albumin nanosized colloids (0.05 mg per injection: Nanocoll ®) are injected subcutaneously (using tuberculin syringe) in the first interdigital space of each foot the patient lying on the table of examination and having been informed that he-she had not to move the toes and feet during the following 30 minutes. One picture of the injected sites was obtained directly after the injections and thereafter the camera head moved on the inguinal areas on which one dynamic imaging was performed in order to see the time to inguinal nodes appearance and to evaluate the possible asymmetry in the nodal accumulation of the tracer. One whole body imaging (WBS) (anterior and posterior views) is thereafter obtained (this is our "phase 1"). For the "phase 2", one dynamic imaging (lasting 15 minutes) is performed on the inguinal areas but with patient performing tip-toeing during the sixth to tenth minute of the acquisition (the patient still lying on the table of examination and with the same goals as for "phase 1" but also to have one higher activity in the lymphatic vessels of the limbs). One 2^{nd} WBS is thereafter obtained as well as one 3^{rd} after one hour of walking ("phase 3": the injected sites being also imaged in order to calculate the percent of radio-colloids extracted from the injected sites by the lymphatic system at the end of the investigation). The whole protocol is lasting at most 3 hours (and is limited so that the patient is busy for only half a day).

For the upper limb edemas… in summary

Our methodological protocol can be summarized as follows. 0.2 ml of 99mTc-labeled (74 MBq per injection) Human Serum Albumin nanosized colloids (0.05 mg per injection: Nanocoll ®) are injected subcutaneously (using tuberculin syringe) in the first interdigital space of each hand the patient lying on the table of examination and having been informed that he-she had not to move the fingers and hands during the following 30 minutes. One picture of the

injected sites is obtained directly after the injections and thereafter the camera head moved on the axillary areas on which one dynamic imaging is performed in order to see the time to axillary nodes appearance and to evaluate the possible asymmetry in the nodal accumulation of the tracer. One 1rst series of 3 static imagings (anterior and posterior views) are thereafter obtained on the wrists, forearms and elbows, elbows, arms and axillary areas (this is our "phase 1"). For the "phase 2", one dynamic imaging (lasting 15 minutes) is performed on the axillary areas but with patient performing hand-gripping during the 15 minutes of the acquisition (the patient still lying on the table of examination and with the same goals as for "phase 1" but also to have one higher activity in the lymphatic vessels of the limbs). One 2nd series of static imagings is thereafter obtained as well as one 3rd after one hour of activities with movements of the arms and hands performed by the patient mimicking what he-she is doing during his-her daily life ("phase 3": the injected sites being also imaged in order to calculate the percent of radio-colloids extracted from the injected sites by the lymphatic system at the end of the investigation). The whole protocol is lasting at most 3 hours (and was limited so that the patient was busy for only half a day).

The "phase 1" in patients with upper limb edema after axillary nodes dissection?

In women who are investigated for upper limb edema after axillary nodes dissection for breast cancer, we found that more than 90% had one insufficient lymphatic drainage in resting conditions at the level of their "normal" contralateral upper limb. This is in agreement with other data (genetic studies) that show that these women were in fact predisposed to the development of such edematous situations. We concluded that the phase 1 in these women might be avoided and their investigations so shortened.

However, the phase 1 remains relevant in all other situations with upper limb edema and has to be kept in the protocol!

Why such a protocol?

The protocol is long but it is robust and physiological.

The protocol was first developed for diagnostic purposes, not only to diagnose the secondary limbedemas but also and merely the primary ones and the functional lymphedemas.

Now, lymphoscintigraphy is mainly used in Belgium to define the patients who will benefit from the re-imbursement of physical treatments by the Belgian insurance system. This "focus" biased our medical point of view.

More and more physical therapists and surgeons also discover now the interest of the lympho-spect-ct evaluation of their patients with lymphedema to help them in their practice to treat their patients and to define the patients who will benefit from their intervention.

The specialists in Nuclear Medicine who will perform these lymphoscintigraphic investigations have now to work not only with the physicians who ask us "'Is it one lymphedema?" but also with these "therapists" (surgeons and physiotherapists) to answer to their questions!

The interpretation of the imagings after these 3 phases?

a) Phase 1:

After its subcutaneous injection in the first interdigital space of each limb with the patient at rest, the tracer should normally penetrate the initial lymphatic vessels and their collectors and be transported from the injection site by the superficial lymphatic vessels due to their normal intrinsic contractility to reach (at least) the first lymph nodes at the limb's root 30 minutes after injection.

These images (the anterior and posterior whole-body images from the head to the toes for the lower limbs or the anterior and posterior views of the upper limbs including the axillas) that are obtained after the 30 minutes of rest, give us morphological information about the status of the lymphatic system. All the images that show deviations from this expected result indicate an abnormal situation

Specifically, studying the arrival of the tracer at the first nodes allows one:
- to identify lymphatic system insufficiency in resting conditions (when the tracer has not reached the first lymph node at the root of the limb) or
- (when the tracer has reached the first lymph nodes at the root of the limb on both sides) analyzing the (time-activity curves derived from area of interest drawn on) dynamic imaging acquired on the lymph nodes at the root of the limb may (also) show functional asymmetry in lymphatic function between the edematous limb-site and its normal contralateral part.

b) Phase 2:

Either anterior and posterior whole-body imagings from head to toes, or anterior and posterior views of the upper limbs (including the axillas) are obtained after the patient (always lying on the table of exam) has been tiptoeing for 5 minutes (for lower limbedema) or after 15 minutes of fingers and hands movements (for upper limb edema). These exercises improve the penetration of the tracer in the initial lymphatics and collectors, and they also activate and stimulate the lymphatic vessels. The result should be a perfect image of the lymphatic vessels and increasing filling of the ending nodes.

This second phase is important. At rest (after phase 1), the amount of extracted tracer may in certain cases be insufficient to produce an acceptable image of the lymphatic vessels and, in other pathological cases that have important reflux, the normal lymphatic vessels can (after phase 3) be masked by the reflux. These phase 2 images may also show localized lymphatic lesions or suspended lymphatic reflux that may arise at any level in an early stage (that may be masked after phase 3 imaging).

The analysis of (time-activity curves derived from area of interest drawn on) dynamic imaging acquired on the lymph nodes at the root of the limb during exercise may show (as for phase 1) functional asymmetries.

c) Phase 3:

Either anterior and posterior whole-body imagings from head to toes, or anterior and posterior views of the upper limbs (including the axillas) are obtained after an hour of normal activity i.e. a one-hour walk (for lower limb edema) or an hour of normal activity using the upper limbs (for upper limb edema).

At this point, we should have 1) minimal extraction of the tracer out of the injection site; 2) an image of variable quality of the superficial lymphatic vessels of the limb plus the complete visualization of the lympho-nodal axis at the ends of the limb; 3) visualization of colloidal activity in the liver (and sometimes in the spleen and bone marrow); 4) after one lympho-scintigraphy of the lower limbs, visualization (in one-third of patients) of retro-supraclavicular left-sided lymph nodes (that normally end the ductus thoracicus). Here, too, images that are not as expected indicate an abnormal situation.

The readers will find further (see “For-The lympho-spect-ct definitions!”) the definitions of the lymphatic abnormalities they can observe and they are invited to use in their protocols.

Reasons for adapting the methodological approach

The specialist in Nuclear Medicine, however, will have to keep in mind that the dynamic and/or static acquisitions (and their consecutive results) will have sometimes to be adapted to answer specific questions as listed, but not limited to, in the followings:

- To study the Ductus Thoracicus, the thoracic duct
- To precisely determine the level of one lymphatic leakage (in the abdomen, in the thorax…)
- To demonstrate the patency-functionality of the lymphatico-venous anastomoses, of the node to vein anastomoses, of grafted lymphatic vessels (or veins: used to “bridge” the lymphatic “gap”, to reconstruct the lymphatic pathway, to switch the lymph flow from one side to the other), so that grafted lymph nodes remain functional and/or viable
- To study the effects of specific manual lymphatic drainage maneuvers, of pressotherapy systems, of wearing specific bandaging and/or elastic stockings, of drugs,..
- To investigate edema at the level of the face, of the breast, (limited to part) of the genitals,…

Anyway and in conclusion, any imaging protocol of the lymphatic system, once the injections made, should always specify:

- the clinical condition of the acquisitions: at rest, during or after a standardized exercise, after a period of “normal” activity for the patient,… but also
- the duration of the different clinical conditions imposed on the patient.

Our protocol in details

The preparation of the "tracer"… is the same for the upper and lower limbs

In one vial of Nanocoll, 20 mCi (740 MBq) of 99mTc04 are injected as well as one additional volume of physiologic saline so that the labeled particles are finally dispersed in 2.0 ml. After labelling and homogenization, 0.2 ml and 2.0 mCi (74 MBq) per tuberculin syringe can then be withdrawn from the vial.

The same vial can be so used for up to 3 patients with limb edemas (and/or for sentinel lymph node imagings) as well as for additional injection-s (if useful: see further).

10 mCi (370 MBq) are used for children.

The Type of Injection ("Intradermal"? "Subcutaneous"?) and their implications…

How the tracer is injected is of great importance. In case of edema at the level of the skin, two kinds of injections can be performed: either subcutaneous or intradermal. The latter will usually allow rapid entry of the tracer into the initial lymphatics, fast transport into the lymphatic vessels, and rapid arrival in the lymph nodes. The former is, however, more "physiological" and sensitive to the pathophysiological parameters underlying the observed edema. Removal of the injected tracer will indeed depend on the characteristics of the injected interstitial tissue and, more precisely, on the local density of the lymphatic vessels network, but more importantly on the local hydrostatic and oncotic pressures. Once in the lymphatic vessels, transport of the tracer will depend (in addition to some of the characteristics of the tracer itself) on the normal or abnormal contractility of these vessels and on the forces that eventually oppose the lymph flows. The choice of injection will depend on the type of information desired.

In practice, this means that both injections will allow the clinician to obtain morphological images of the studied lymphatic system, albeit in different ways. However, with intradermal injections, the observations may not be physiologically relevant.

We are performing intradermal injection (0.4 ml) in several well-defined circumstances and always after-with the informed consent of the patient (see further).

The (partly) intravenous injections?

Sometimes and especially in patients with known venous problems and/or multiple obvious varicosities, part of the tracer may be injected intravenously (even despite the fact that the technician-physician controlled that he had no blood backflow in the syringe and when they are injecting but removing the syringe at the same time). Such intravenous injection can be confirmed during-on the dynamic imagings following the injection by the observation of the venous transit at the root of the limb and/or by the uptake of the tracer in the liver, the spleen and the bone marrow. Such injections partly intravenous do not seem in our experience influence the calculations of extractions of the tracer. However, the activity remaining at the level of the injected site may sometimes be low and may imply to repeat the injection.

The site of injections!

One subcutaneous injection per limb is performed in the first interdigital space, in the subcutaneous space between the 1rst and 2nd toe-finger (not at the level of the dorsum of the foot-hand between the 1rst and 2nd metatarsal-metacarpal bones). We precise: at the level of the mid part of the interdigital space (see "the killing details"). In the framework of this diagnostic protocol, we are against multiple injections in the 1rst and/or 2ndand/or in the 3rd and/or in the 4rth interdigital spaces.

Most of the protocols used to investigate the superficial lymphatic system propose using one subcutaneous injection in the first interdigital space of the feet or hands. The anatomical lymphatic drainage of this site is well established. Consequently, in the case of lower limb edema, it is not normal to see popliteal lymph nodes, which are related to the deep lymphatic system. Visualization of the popliteal lymph nodes is a sign of functional insufficiency and/or overload of the superficial lymphatic system. On the other hand, a subcutaneous injection in a more external interdigital space, i.e. in the fourth interdigital space, normally leads to lymphatic drainage toward and into the popliteal lymph nodes. At the level of the upper limbs, it is not normal to see interosseous antebrachial or humeral lymph nodes after a single injection in the first interdigital space.

Two or more injections in different interdigital spaces will certainly give a more representative view of the entire edematous area compared to a single injection in the first interdigital space. However, multiple injections can lead to misdiagnoses of some pathological conditions that affect the superficial lymphatic system that would be diagnosed correctly if a single injection was made in the first interdigital space.

(The Deep Lymphatic System ?)

To date, relatively few scintigraphic studies have investigated the deep lymphatic system, although as early as quiet 50 years ago, the great "lymphologist", Prof. Tosatti, noted that "one attempt of the deep lymphatic system has to be searched when the edema is exclusively located to the foot and the retro-malleolar area or when exist one big foot tough to the touch". In our clinical practice, mounting evidence indicates that some edemas are not related to morphological or functional issues of the superficial lymphatic system; rather, they are related to the deep lymphatic system. More and more frequently, women are presenting who complain of edema of the ankle and associated pain and tension in the calves ("heavy limbs"). Sometimes the edema extends to the dorsum of the foot, but usually it does not involve the toes. In fact, this matches the symptoms of the patients described by Tosatti. Investigation of the superficial lymphatic system after subcutaneous injection of the tracer into the first interdigital space of such patients frequently shows normal findings. However, when there is unilateral edema, the investigation may also show a paradoxical functional asymmetry in which the superficial lymphatic system of the affected limb seems to work better than that on the non-edematous side. Investigation of the deep lymphatic system of both limbs in these women show that the deep lymphatic system of the edematous side is either absent or functionally insufficient compared to the normal side (for the methodology, the readers are invited to contact us).

The pictures at the level of the injected sites

These pictures (see next slide) are obtained after the injections and at the end of our protocol with the hands put on the belly (and with the syringes in the field of view wherein residual activities remain and is used to calculate the physical decay of the 99mTc due to the delay between these pictures).

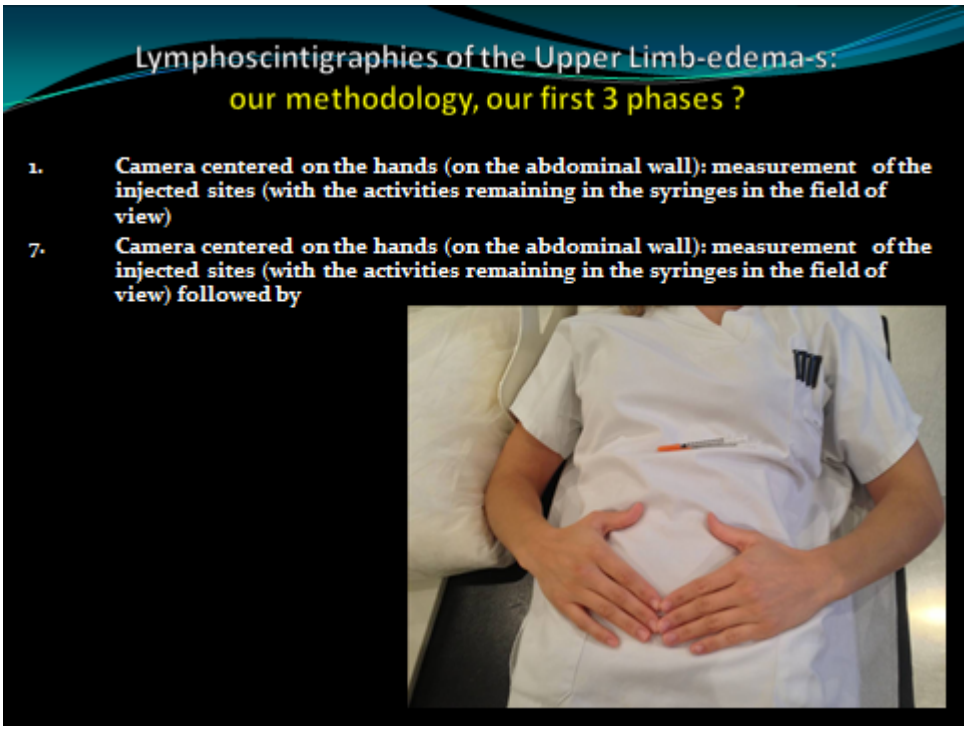
These pictures allow us to calculate the percentages of labeled colloids extracted by the lymphatic system at the end of our exam.

The normal values for these extractions are:

- At the level of the upper limb: = or > than 8%,
- At the level of the lower limb: = or > than 30%.

These values were established for-in one general "population" of healthy limbs. Slightly lowest values have been sometimes found in very old patients.

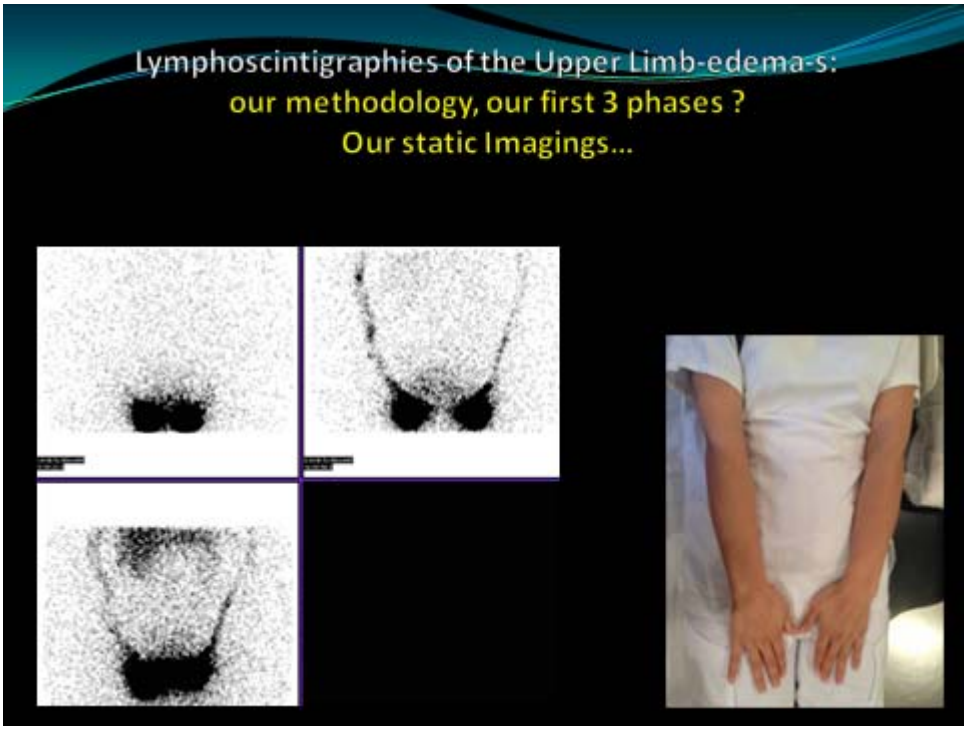
These pictures have to be well evaluated and analyzed. Sometimes, they allow indeed to identify dermal backflow or/and dermal progression of the tracer limited to the distal part of the foot or of the hand. However and with some cameras, the star-dust effect may be very marked and may hamper the identification of these situations.

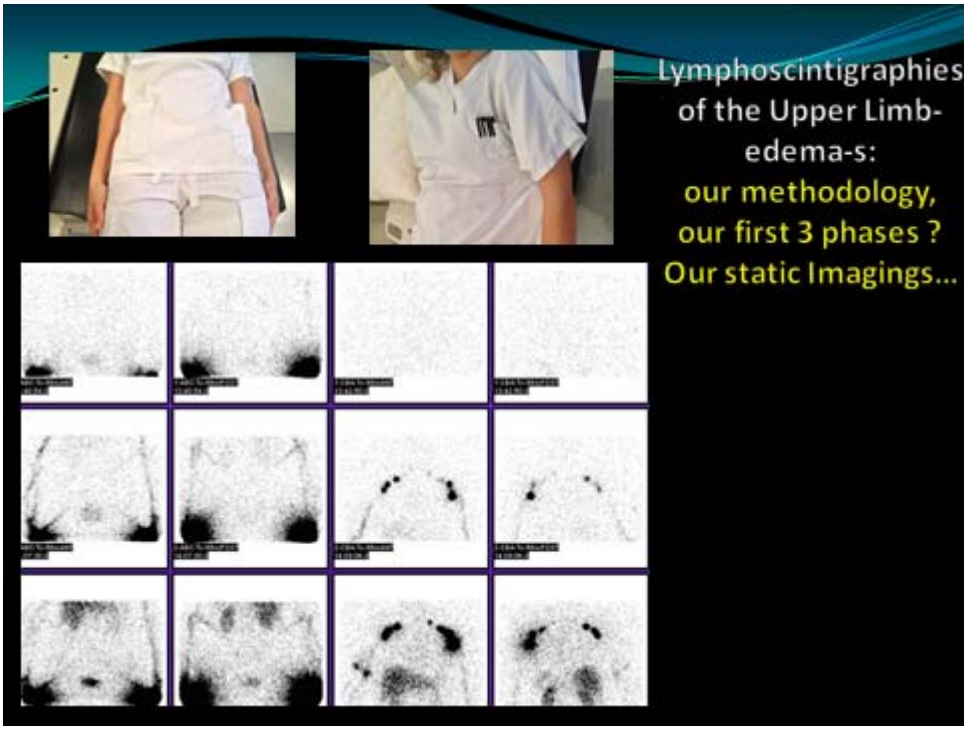


The pictures at the level of the upper limbs

We are performing three pictures at the level of the upper limb:

1) One anterior view including the injected sites, the wrists, forearms and elbows with arms out-stretched on the belly (see next slide) and with the hands put on the belly,
2) Anterior and posterior views from the wrists to the elbows with the arms along the body and with the hands put on the buttocks,
3) Anterior and posterior views from the elbows to the neck with the arms along the body and with the hands put on the buttocks.

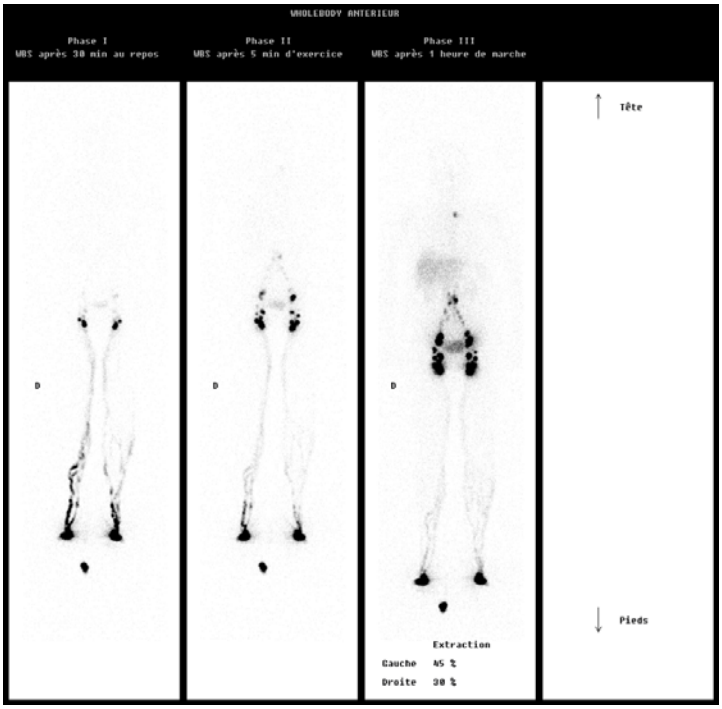



Lymphoscintigraphies
of the Upper Limb-
edema-s:
our methodology,
our first 3 phases ?
Our static Imagings...

Our iconographies… for the lower limb lymphoscintigraphies

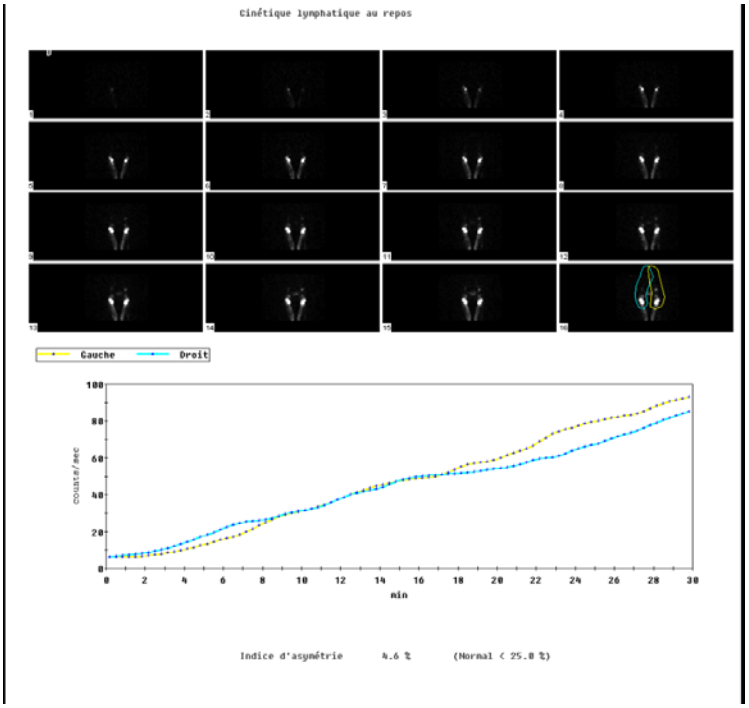
One normal patient with multiple lymphatic vessels at the level of the feet and calves (with internal and external lymphatic vessels at the level of the left limb), with extraction at the lowest limit on the left and with one left sided retro-clavicular LN terminating normally the Ductus Thoracicus

From your left to your right, anterior WBS (phase 1, 2 and 3)

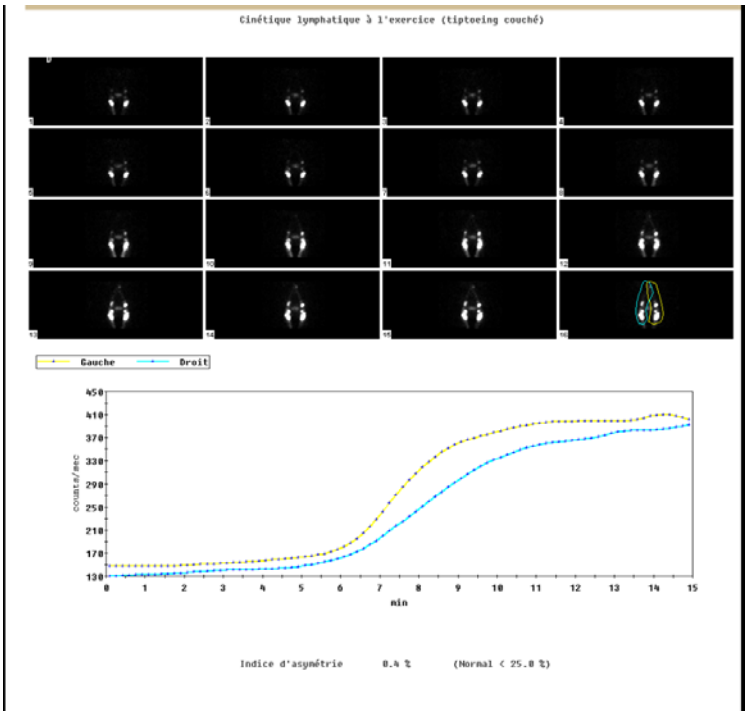


From your left to your right, posterior WBS (phase 1, 2 and 3)

First dynamic imaging centered on the inguinal areas during 30 minutes without any movement and the time-activity curves generated from area of interest drawn **on and including** all the visualized LN



2nd dynamic imaging centered on the inguinal areas during 15 minutes with tip-toeing from the 6th to the 10th minutes and the time-activity curves generated from area of interest drawn **on and including** all the visualized LN



For-The "lympho-SPECT-CT" investigations?

The contributions of SPECT-CT to investigations of the lymphatic system are the same as for other systems. That is, SPECT-CT can better define lymphatic-related activities, especially those of the deep lymphatic system, after the signals are corrected and enhanced. It can also correlate lymphatic-related activities with the corresponding and surrounding anatomical structures that are seen on the CT slices. These contributions are described in greater detail below:

- SPECT-CT allows better definition of the anatomical extent of dermal backflow than on planar images.
- Although some deep lymphatic structures may be recognized as such at the level of the limbs, such as the sural, popliteal, femoral, interosseous antebracchial, and humeral lymph nodes, a SPECT-CT approach allows definitive assessment of the deep (inter-muscular) structures versus superficial localization of these lymphatic structures.
- In the popliteal areas, at the roots of limbs, in the abdomen, and in the thorax, SPECT-CT can better identify the deep lymphatic structures, which can sometimes be superimposed on superficial structures on planar images (see figure 22-14 and 22-15).
- In patients with extensive dermal backflow which is better seen on delayed images, SPECT-CT highlights the activities of the underlying deep structures or normal lymphatic vessels and nodes, which can be masked by superficial signals on planar images and which may sometimes be missed when an ad hoc approach is not used.

We recently reviewed the results of abdominal and pelvic SPECT-CT imaging of 53 patients with secondary lower limb lymphedema and compared them to the results of their planar images. SPECT-CT imaging showed or confirmed lymph node localization, indicating the presence of collateral lymphatic pathways, in the following areas: intergluteal (12%; none were seen on planar images); anterior abdominal wall (8%; none were seen on planar images); suprailiac (11%; in half of the cases, these lymph nodes could not be seen on planar images); and thoraco-vertebral (11%; these were seen on planar images, but SPECT-CT allowed more precise localization). Thus, in one fourth of the patients, SPECT-CT showed lymphatic drainage pathways that could not be seen on the planar images.

For-The lympho-spect-ct definitions!

Based on SPECT-CT images, Baulieu et al. (8) proposed the following definitions for the lymphatic lesions and abnormalities seen during lymphoscintigraphic investigations:

- Lymphatic varicosis: tortuous lymphatic vessels,
- Lymphangiectasia: saccular dilatation of the main lymphatic vessels,
- Localized or diffuse lymphangioma: circumscribed dermal lesions with a cluster of large interconnected multiple spots or large lymph spaces that might extend into the dermis, muscles, and bones,
- Lymphatic saccular aneurysms: lymphatic collection connected to the surface of a lymphatic vessel by a thin neck,
- Lymphocele: accumulation of lymph outside the lymphatic system, resulting from an injury,
- Lymphorrhea: leakage of lymph from the skin due to communication between the lymphatic vessels and the epidermis,
- Lymph nodes: foci of activity that are usually spherical and that are found along the vascular pathways,
- Lymphatic dermal backflow: when the imaging agent flows back from the lymphatic nodes or vessels towards the superficial dermal collateralization lymphatic network or when it has reached this network. In lymphoscintigraphy, the imaging agents are radiolabeled molecules, but in other imaging techniques, the agents may be radiological contrast, gadolinium, free ICG, or ICG that is bound to fluorophores. Such dermal backflow is the result of either limited or extensive blockade of the lymphatic flow, with backflow of the tracer in collateral and smaller lymphatic vessels in which the propulsive pressure is lower than in the great vessels and in which, due to their dilatation, the valves become incompetent. The agent can then flow up to and into the superficial dermal collateralization lymphatic network. This is what I personally describe as vascular lymphatic backflow that results in re-routing of the lymph. Blockade of the lymphatic flow can be due to lymphatic vessel thrombosis, to massive lymph node invasion, or to lymph node aplasia, among other possibilities. In the framework of lymphoscintigraphic investigations, we have observed that this sometimes limited dermal backflow can finally collect in normal lymphatic vessels.

- Dermal collateralization of lymphatic flow or dermal lymphatic progression: from an injected site, the tracer is no longer collected in lymphatic vessels but rather flows only in the superficial dermal collateralization lymphatic network. In very severe cases, sometimes only diffusion of the signal in the subcutaneous tissues is observed i.e. lymphatic structures are no longer visible.

SPECT-CT sometimes allows the clinician to recognize that activities that appear on planar images are non-lymphatic. Two such situations (apart from their accumulation in the bone marrow) can be identified when 99mTc-labeled colloids are used:

- Activity in the urinary tract or superficial contamination by the urinary tract, which should not be confused with true lymphatic dermal backflow in the magna labia of women. Notably, backflow is usually more active. This is related to the presence of unlabeled reduced (non-anionic) technetium that is excreted by the kidneys. It is usually observed in the bladder within 30 minutes after the injection of the 99mTc-labeled HSA nanocolloids, even in patients in whom no lymphatic vascular drainage is seen.
- Activity in muscles that may be related to necrosis.

SPECT-CT in-for the therapeutic management of lymphedematous patients?

In general, SPECT-CT is of particular interest for the following situations:

- In patients with a past history of cancerous disease, SPECT-CT may allow the detection of a mass or lymph nodes, especially when the structures are not taking up the colloids. Sometimes the mass or lymph nodes may be unexpected at the time that the edema develops or worsens. This may suggest evolution of the cancerous disease and this must then be confirmed or excluded.

- For the microsurgical treatment of lymphedema or for planning surgical lipo-lymphosuction (55), SPECT-CT allows the precise localization of superficial or deep functional lymphatic vessels or lymph nodes that can be used for lymphatic-to-vein anastomosis. SPECT-CT can also show their relationships with the surrounding structures (as can also be seen on MRI).

- SPECT-CT visualization and localization of the superficial lymphatic vessels and collaterals can help guide physical therapists who perform manual maneuvers to stimulate the lymphatic vessels or to flush the contents of the lymphatic vessels or nodes. When superficial lymphatic vessels or nodes are shown to be deep at the root of the limbs within the fatty tissues of overweight patients, the manual maneuvers might have to be performed using higher pressure than that used on very superficial structures (which could be damaged with high pressure manoeuvers). When the lymphatic draining structures are demonstrated to be deep, i.e. intramuscular or sub-aponeurotic, for example, the physical therapist should question the use of light/soft superficial manual maneuvers and should consider using muscular exercises as a way to stimulate these lymphatic structures.

- For the patients themselves, SPECT-CT can demonstrate that some lymphatic draining vascular structures are very superficial. The images can show the patients that they should avoid positions that press on or that collapse these structures and that they should avoid wearing clothes that have localized elastic that might also collapse the draining lymphatic vessels or collaterals.

- As noted in the previous point, visualization of very superficial lymphatic draining vascular structures can guide physicians or bandagists to direct the patient to wear elastic stockings. For instance, sometimes pantyhose or elastic stockings that extend to the buttock and are fixed at the level of the abdomen should be worn rather than stockings that only extend to the root of the limb and are held up by elastic at that level.

SPECT-CT is also useful in these specific situations:

- In the patients with an oozing ulcers and in whom spect-ct identified lymphorrea, the localization of the lymph escape from the lymphatic vessel is a relevant abnormality that could guide local therapy,
- In patients with activity that is seen on planar images in unusual areas that are outside the classical lymphatic pathways,

- When the diagnosis of lymphangioma circumscriptum or extensive lymphangioma allows treatment options to be discussed,
- In patients with Gorham's disease, SPECT-CT clearly shows the lymph spaces, allowing the patients to avoid invasive biopsy

Indications for lympho-spect-ct?

Where SPECT-CT devices are available, lympho-SPECT-CT investigations should systematically plan for the following situations:

- Patients with limb lymphedema in whom the edema originates (descends) from the root of the limb or extends up to the root of the limb or involves the root of the limb and the neighboring areas,
- Patients with a past history of cancer in whom edema either appears suddenly or worsens despite appropriate physical treatment,
- Patients with proven or suspected evolution of cancer,
- Patients in whom lymphangiomatosis or lymphangiectasia or loss of lymph (chylothorax, chyloperitoneum, or protein-losing enteropathy, among others) are known or suspected,
- Patients with lymphedema that does not respond to appropriate physical treatment,
- Patients with syndromic lymphedema

For-The Additional Injection at the root of the limb!

In our clinical experience, one third of the patients (with upper and/or lower limb lymphedema) show none of the lymph nodes expected to be seen at the root of the limb, either in the axillary area or in the inguinal and/or iliac area. This outcome raised two possibilities: either the tracer injected peripherally was not transported up and into these lymph nodes (which are in fact present), or these lymph nodes are absent as either a normal variant, or a symptom of a lymphatic disease. This question can be addressed by the use of an additional injection.

In three fourths of upper limb lymphedemas, intradermal injection of 99mTc-labeled Human Serum Albumin (HSA) nanocolloids (twice what is injected into the hands) in the lateral part of the arm under the shoulder led either spontaneously or after massage to the lymphatic drainage of the tracer towards the homolateral axillary lymph nodes. In some cases, collateralization lymphatic pathways reaching lymph nodes in the ipsilateral supra and/or retro-clavicular area were also demonstrated (the Caplan's and Mascagni's pathways), as were the ipsilateral posterior scapular and/or cervical lymph nodes, the ipsilateral internal mammary, the ipsilateral posterior intercostal and/or paravertebral lymph nodes, and the contralateral parasternal and/or axillary lymph nodes.

In cases of lower limb lymphedemas, an intradermal injection at the level of the lateral part of the thigh in front of the great trochanter led (spontaneously or after massage) to direct lymphatic drainage of the tracer towards the homolateral inguinal lymph nodes and/or to the demonstration of collateralization lymphatic pathways reaching lymph nodes in the ipsilateral inguinal and/or iliac area in 90% of cases. Ipsilateral or contralateral posterior lumbo-aortic nodes were also demonstrated, as well as the opposite-contralateral inguinal lymph nodes (through lymphatic collaterals transiting in the prepubic area and/or through the genitals and rarely by transiting in the back of the patients), and more rarely, the ipsilateral axillary lymph nodes. Deep intergluteal lymphatic drainages and nodes could also be identified.

The results of additional injections are interesting in many respects:

- In case of lower limb lymphedemas, the demonstration of the presence of normal inguino-iliac lymph nodes (not reached by the tracer) excludes lymphadenodysplasia (associated with peripheral lymphangiodysplasia), which is associated with a worse prognosis for the lymphedema according to Kinmonth,
- These inguinal lymph nodes that we are able to be visualized with the help of the injection may be used by surgeons to perform lymph node-to-vein anastomoses.
- For physical therapists, these additional injections also show the collateralization pathways present in their patients, pathways that the therapists can target for pushing the fluid of the edema. This practice could be an improvement on attempting all of the possible collateralization pathways that physical therapists have learned but that are not systematically present in the treated patient.

For-The Additional Injection at the level of the pelvis and of the thoracic wall!

Some patients may also come with symptoms of edema at the level of:
- the breast and/or the lateral thoracic wall (sometimes after mammary reconstruction),
- the buttocks, the pelvis and/or the genitals organs.

In these patients, our 3 phase protocol and our additional injection at the level of the root of the limb may sometimes show that the lymph flows from the root of the limb towards these areas previously mentioned.

However and when it is not the case, it is interesting to perform one additional intradermal injection of (0.4 ml of) 99mTc-labeled Human Serum Albumin (HSA) nanocolloids in the edematous area.

The results of these injections are particularly interesting for the physiotherapists. Again, they show them the collateralization pathways present in their patients, pathways that the therapists can target for pushing the fluid of the edema. This practice could be an improvement on attempting all of the possible collateralization pathways that physical therapists have learned but that are not systematically present in the treated patient.

Teaching cases:

Evolution of one primary LL lymphedema (progressive lymphadenodysplasia?):

1n 1995, one year after the first event announcing her lymphatic disease, the WB lympho Scintigram shows vascular lymphatic reflux from the left inguinal nodes (and on the right side the presence of popliteal LN).
In 1998, the WB lympho Scintigram shows the reflux of the tracer into the superficial lymphatic collateralization network ("dermal backflow") of the buttock, of the superior two thirds of the left thigh and the disappearance of the left common iliac LN (and of the right popliteal LN).
In 2004, the tracer flows now back into the superficial lymphatic collateralization network ("dermal backflow") of the distal two thirds of the thigh and up to the level of the ankle. On the right side, some inguinal LN are no more seen and vascular lymphatic reflux towards the buttock and the upper inner part of the thigh can be observed.
In 2006, on the left side, the tracer is seen in the superficial lymphatic collateralization network from the ankle up to the distal part of the thigh but does not reach the inguinal LN.