Lymphoscintigraphy and Lymphedema of the Lower Extremities

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Lymphoscintigraphy, using technetium-99m-labeled sulphur microcolloid, was employed to study the flow and transport of lymph in the lower extremities of 39 consecutive patients in whom lymphedema of one or both legs was suspected clinically. Time-activity curves of four segments of each leg were evaluated for lymph capacity, flow and soft-tissue uptake, and compared with the results from film scintigraphy. Curve analysis provided quantitative evaluation of the extent of hypoplasia or aplasia in primary lymphedema and of lymphatic obstruction in secondary lymphedema, and is particularly suited to assess the involvement of lymphatics in chronic venous disease. Film scintigraphy, on the other hand, is preferable in cases in which the pattern of activity distribution in the affected extremity is diagnostic, such as in dermal back flow, traumatic lymphocele, or megalymphatics. Venography is most informative in cases of suspected underlying venous disease, but the role of lymphangiography, which shows only part of the lymphatic system and requires incision of the edematous tissues, is considered questionable.

J Nucl Med 1990; 31:990–998

Lymphedema is a result of an abnormal accumulation of interstitial fluid and hence is closely related to both lymphatic and venous pathology. It frequently presents complicated diagnostic and therapeutic problems. Edema of the extremities is called primary lymphedema if no causes extrinsic to the lymphatic system can be found for the occurrence of swelling of the soft tissue. It can present from birth or appear later in life. Secondary lymphedema is associated with lymphatic obstruction due to postinflammatory scarring, radical surgical procedures, postradiation fibrosis and spread of malignant tumor cells with obstruction of either the lymphatic channels or the nodes of drainage. Lymphedema secondary to venous pathology such as varicosity and deep vein thrombosis also plays a significant clinical role.

Differentiation between primary and secondary lymphedema usually presents no diagnostic problems, but lymphedema secondary to venous insufficiency and late-onset primary lymphedema cannot be distinguished easily (*1*,*2*). Ruling out venous pathology requires a venographic evaluation of the extremity whereas lymphangiography can visualize part of the lymphatic channels and provides information on caliber and structural abnormalities (*3*).

Lymphoscintigraphy using technetium-99m- (^{99m}Tc) labeled sulphur microcolloid is suitable for studying flow and transport of lymph through the extremity (*4–6*).

It is the purpose of this paper to show that information on the anatomical integrity or compromise of the lymphatic system as well as on the dynamics of lymph flow and transport can be obtained if the radioactivity is measured as a function of time in a number of segments of the lower extremities. To this end, time-activity (TA) plots were analyzed (AMR and RAJ) and the lymphatic involvement in four segments of the edematous legs was quantitatively assessed for each patient. Diagnoses were made with prior knowledge of the patients' histories and compared with diagnoses made (BYC) from the scintigrams recorded on transparent film at 3 hr after injection and subsequently reviewed in the presence of a series of scintigrams taken at different time intervals. The involvement of the lymphatic system in the edematous process can be evaluated directly in all cases whereas an additional venograph can provide necessary information in patients with underlying venous disease. This method has been applied to a series of consecutive patients referred for lymphoscintigraphic evaluation over a period of 30 mo.

MATERIALS AND METHODS

Patients

The study population comprised 39 patients with complaints of swelling of one or both lower extremities. They were referred to the nuclear medicine section of the Leiden Uni-

Received May 30, 1989; revision accepted Dec. 26, 1989.
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versity Hospital only when pathologic involvement of the lymphatics was suspected on clinical grounds. This method of selecting patients is obviously far from perfect. The ideal investigation into the value of quantitative lymphoscintigraphy of the lower extremities would involve flow and transport studies in all of an unselected group of patients in whom the diagnosis was confirmed or refuted by rigorous correlation with proof of lymphatic and venous status. This is clearly not feasible.

Thirty-five of the 39 patients were women in the 20–75 age group, averaging 42 yr. The ages of the men ranged from 28–35, averaging 32 yr.

Lymphoscintigraphy

The lymphoscintigraphic studies were performed by subcutaneously injecting 111 MBq (3 mCi) ^{99m}Tc-(Sn) sulphur microcolloid (Lymphoscint Solco, Nuclear Basle Ltd, Basel, Switzerland) of particle size <50 nm diameter, divided into four equal portions of 0.1 ml, into the webbed spaces between the first and second and the third and the fourth toes of both feet. The injection sites were massaged immediately after injection for ~30 sec; the patients then walked around for 5 min in order to further distribute the microcolloid within the interdigital soft tissues, thereby promoting lymphatic uptake. This protocol of injecting, massaging, and walking around was strictly adhered to so as to standardize the amount and the exposure of the terminal lymphatics to the microcolloid in all patients. Data were recorded for 3 hr while the patient remained supine and did not exercise during the remainder of the examination (*7*). Complete relaxation of the leg muscles during this part of the examination is required to guarantee reproducibility of colloid uptake and to avoid irregular and unassailable muscle pump action.

After the five minutes of exercise, radioactive markers were placed at the patient's ankles, knees, and thighs, and the patient was placed in a supine position under a large field of view Anger camera (Toshiba GCA 402, Tokyo Shibaura Electric Co. Ltd.) attached to a nuclear medicine minicomputer (ModuMed Trinary System, Medical Data Systems, Ann Arbor, MI). Two-minute images were recorded on film and by the computer immediately and 15, 30, 45, 60, 90, 120, and 180 min after injection; images were made of the feet and ankles, lower leg and knees, upper leg and groin in that order. At 3 hr, the pelvis and abdomen were imaged to look at the inguinal and aortic chain and at the liver and spleen. Six regions of interest, feet, ankles, lower legs, knees, upper legs and groin, were delineated on each leg by dividing the legs into sections based on the radioactive marker positions. The regions for the two legs were chosen by drawing a line across both legs; hence identical portions of each leg were considered. The region of interest count data were corrected for radioactive decay of ^{99m}Tc.

From the images, without benefit of the numerical data, one observer (BYC) made two diagnoses. This was accomplished first by looking at only the final image, and then by considering all the images together. The diagnostic categories ranged from normal, in which the lymph channels were few and were visible on all images at the earliest time, to aplasia in which no activity was visible in the leg during the time of the examination. In patients labeled hypoplastic, the density and apparent size of the channels were less than those characteristic for the normal examinations, but the counts were still apparent. In some of these patients, the flow appeared slower than in the normals, while in others only the amounts seemed diminished. In the megalymphatics, the lymph vessels were more obvious than they were in the normals. The lymphocele collected activity and did not lose it. Dermal backflow was diagnosed when the ankle and lower leg showed a blush which seemed especially obvious around the sides, where the column of tissue imaged is thicker (*8*).

On one occasion, it was obvious from the 3-hr abdominal image containing the liver and the spleen activity that a part of the dose had been injected into the venous system. There was no apparent diminution in the amount flowing through the lymph channels of this case in the curve analysis.

Venographic studies (*9*) were performed prior to the lymphoscintigraphic examination in 10 patients as indicated by history and physical examination.

X-ray contrast lymphangiography was not considered practical for reasons of incomplete visualization of the lymphatics, difficulties in cannulation of lymph vessels, and reluctance to perform minor surgery on the edematous tissues.

RESULTS

Normal Functional State

Both legs of one volunteer, one psychotic patient, and two patients with questionable left thigh pain, as well as the contralateral legs of thirteen patients with obvious unilateral involvement only, constituted our series of normal (16 patients, 20 legs).

The count data for the feet, ankles, lower legs, knees, and upper legs all showed exponentially decreasing activity with time immediately following the standardized exercise protocol (Fig. 1). By the end of the examination, only two to three percent of the injected colloid had left the injection site and, as a result, the useful data from the feet were superimposed on a high background and were rendered unreliable by activity fluctuations in the large remaining colloid collections. The data from the ankles were overwhelmed by the much greater activity in the feet due to imperfect collimation of gamma rays in the scintigraphic camera. For this reason, data from the feet and ankles were not further considered in our subsequent evaluations (*10*). The amount of tracer in the leg between the injection site and the groin is relatively small but adequate for purposes of visualization and data analysis.

The significance of complete relaxation of the leg musculature during data gathering is exemplified by the volunteer and illustrated in Figure 2. The patient consented to a repeat examination during which he walked around for 5 min after 60 min of data collection. A sharp increase in activity uptake is noted at 60 min, showing an exponential decrease with time identical to that observed during the first 60-min of immobilization. This finding suggested that repeated exercise in the course of such an examination would cause colloid to enter the lymphatics in an uncontrolled fashion that would defy any further quantitative analysis.

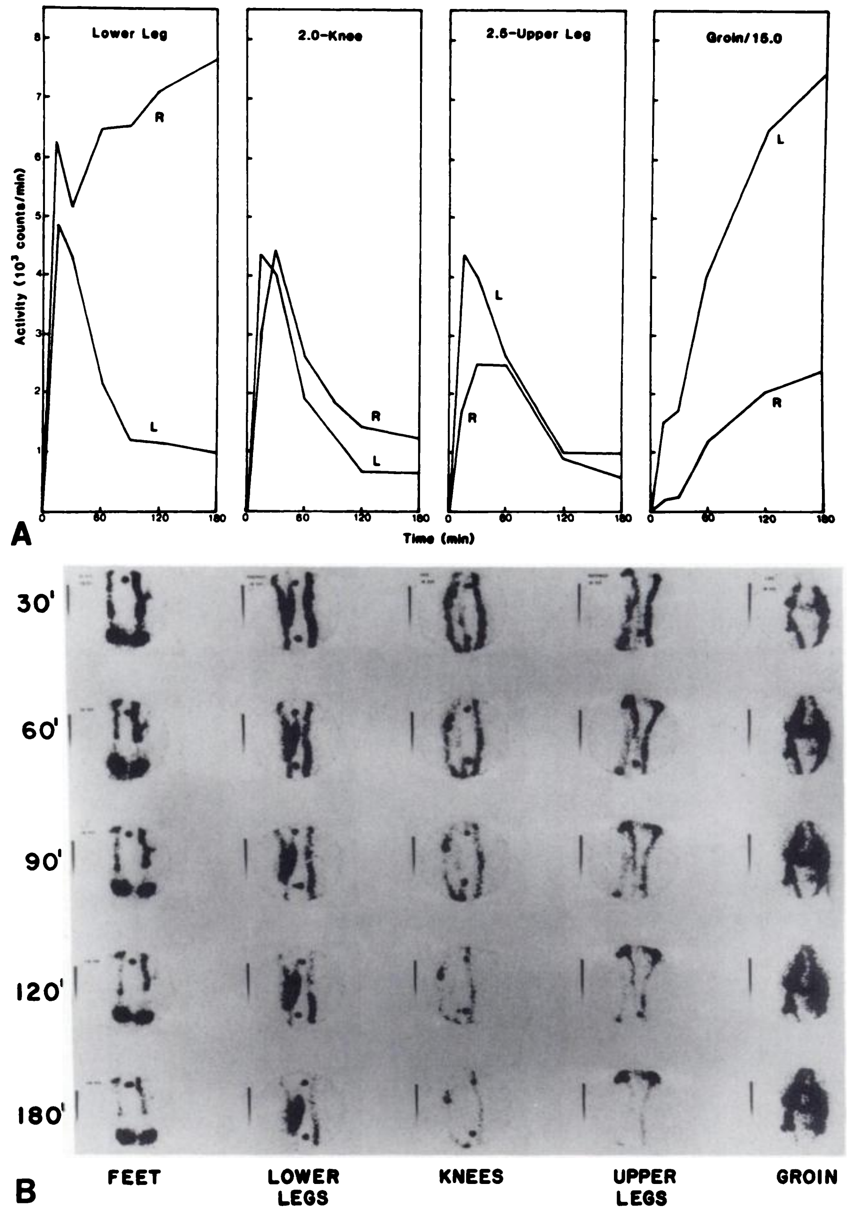

FIGURE 1
(A) Patient 11, Time-activity curves for lower leg, knee, upper leg, and groin. Left leg shows normal patterns. Right leg shows normal flow in knee and upper leg, but abnormal accumulation of tracer in lower leg and concomitant decreased accumulation in the groin. Patient with traumatic lymphocele in right lower leg. (B) Film scintigrams of lower extremity segments with midline markers. Anterior view. Same patient as in 1A showing normal pattern in left leg and tracer accumulation in lymphocele in the right lower leg.

For a number of normal and abnormal studies, the activity did not level off to zero by the end of the examination as a result of tracer collections in soft tissues other than the lymphatic system. This activity is seen to decrease with time, but its biologic half-life is too large to be determined from these studies. Appropriate corrections for soft-tissue accumulation in each leg segment and in the groin were made in the quantitative analysis of the data.

The data for lymph drainage in a normal leg is exemplified by Patient 11 (Fig. 1). Time-activity curves for the normal left lower leg, knee, and upper leg all show a similar pattern with the activity of the knee about one-half and that of the upper leg about two-fifths that of the lower leg. The data for all three segments of the left leg with differing activity scales to adjust for the above ratios as well as the activity accumulation in the left groin are represented in Figure 1A. The data for the activity in the groin region occur primarily from tracer accumulation in the lymph nodes.

The flow *through* the lymph system is rapid relative to the time scale of the measurements: in a normal leg the activity in leg segments is maximum at the first measurement, there is no discernible lag between upper leg and lower leg measurements, and the first measurement shows accumulation in the groin. This means that flow of radioactivity from the injection site *into* the lymph channels occurs throughout the duration of the examination and that this step in the process is rate controlling (see Appendix).

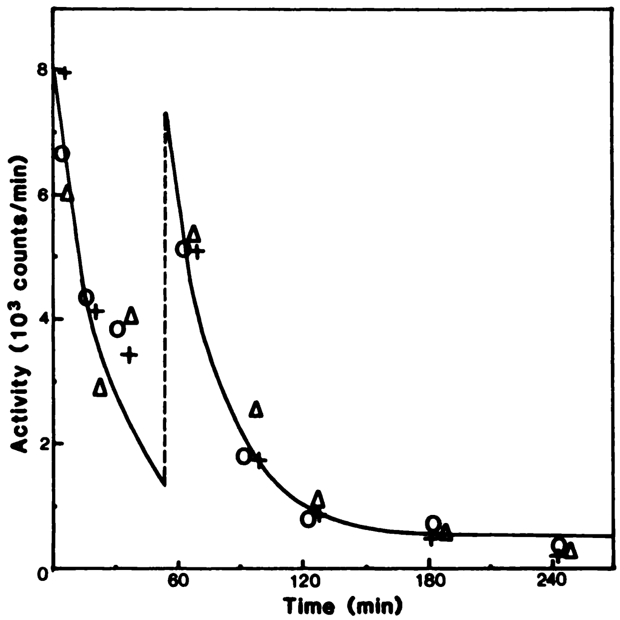

FIGURE 2
Effect of patient movement shortly before the 60-min reading. Time-activity curve of right extremity. Patient 26. Activity scales of knee and upper leg adjusted to the scale of lower leg by factor 4 and 8/5, respectively. 0 = lower leg; + = knee; and Δ = upper leg.

The normal functional state of the lymph system in the legs can be summarized as follows:

1. Fast flow through the legs relative to the time scale of the examination.
2. The activity measurements controlled by the rate at which tracer enters the lymph system, with the legs showing exponential decrease and the groin showing the integral of an exponential decrease.
3. The time constant for the exponential decrease consistent with the time scale of the examination.
4. The lower leg, knee, and upper leg showing the same activity pattern as a function of time.
5. A slowly varying accumulation of tracer in the soft tissue of the leg and of the groin.

In item 4, the ratios will vary from patient to patient and with the placement of markers on the patients' legs by the technologist, but they should remain constant for a particular patient throughout a given examination. The accumulation mentioned in item 5 represents background caused by an accumulation of tracer in lymph channel pockets and soft tissue (*12*), while in the groin most accumulation arises from an initial transient during massage and walking around.

Values for C_i, equivalent to the lymph capacity of the lower leg, range for the 20 normal legs from 2,700 to 5,400 cpm with a mean of 4,200 ± 600 cpm. If we define hyperplasia for cases with C_i values larger than 5,400 cpm that is larger than two standard deviations (s.d.s), and, correspondingly, hypoplasia for C_i values <3,000 cpm, ~99% of normals should fall in this normal range. However, since C_i is proportional to both the amount of activity that entered the lymph system and the volume of lymph in the lower leg, values for C_i will not only vary with changes in microcolloid particle size distribution and exercise protocol, but also with size of the normal lower leg among patients. This patient-to-patient variability suggests that comparison with the normal contralateral leg of the patient is a more sensitive — and, therefore, preferred — method of detecting abnormalities in lymph capacity. However, if the contralateral leg is suspected to be also involved in the edematous disease, the above range for normal C_i values should be used for comparison. A similar reasoning applies to the interpretation of biologic tracer half-life, τ, and D_i values. The normal range for τ was found to be 19–50 min, with a mean of 30 ± 10 min. Only three normal patients showed D_i values larger than zero with 750 cpm being the highest reading.

Clincial Series

The scintigraphic diagnoses, read from the films at 3 hr after injection and reassessed in the presence of the whole series of scintigrams, have been compared with the data for C_i, τ and D_i, gleaned from the TA curves and the diagnoses derived from there.

In four patients, no valid comparison between scintigraphic presentation and TA curves could be made for a variety of reasons. Of the 35 patients whose studies permit comparison, 20 patients (29 legs) were found to have normal lymphatics by either the 3-hr scan or the whole series of scintigrams, or both. Of these, 12 patients (18 legs) were so diagnosed by TA curve analysis. There were no scintigraphically unconfirmed patients with normal lymphatics by TA curve analysis, but the two methods of scintigraphic evaluation showed conflicting results in six patients (six legs). In five of these six patients, the results of the whole series evaluation agreed with the diagnosis from the TA curve analysis.

As shown in Table 1, 13 patients (19 legs) were diagnosed as suffering from hypoplasia or aplasia by TA curve analysis. Comparison with scintigraphic results was not possible for one patient and only the 3-hr reading was available for another three patients. Hypoplasia by TA curve analysis was confirmed in two patients (three legs) and read as normal in four patients (five legs) by one or both methods of scintigraphic evaluation. Similarly, aplasia by TA curve analysis was confirmed by scintigraphy for three patients (three legs) and was read as hypoplasia in six patients (eight legs). In none of these patients did the two scintigraphic methods of evaluation show conflicting results.

In Table 2, the scintigraphic results of five patients with a history of venous disease of the lower extremity and one patient with longstanding diabetes mellitus are compared.

TABLE 1
Lymphedema in Hypoplasia and Aplasia of the Lower Extremity in 13 Patients*
(Activity: 111 MBq lymphoscint Solco®)

	Patient (legs)	$C_i \cdot 10^3$	τ (min)	$D_i \cdot 10^3$
Hypoplasia $1{,}500 < C_i < 3{,}000$ cpm	6 (8)	2.5 ± 0.3	33 ± 8	0.0–0.2
Aplasia $0 < C_i < 1{,}500$ cpm	8 (11)	0.7 ± 0.6	34 − ∞	0.0–0.5

Patient 4 shows varicosity by venography, but no lymphatic involvement by scintigraphy. Time-activity curve analysis indicates normal lymphatics and no soft-tissue uptake but increased resistance to lymph flow, particularly of the right leg. In another patient (No. 6), the varicosity of the right leg was treated by stripping which caused lymph to leak into the soft tissues as indicated by an elevated D_i value, but the lymphatic system was otherwise normal.

Longstanding venous thrombosis was the underlying cause of lymphedema in two patients. The left leg of Patient 7 shows increased lymphatic capacity probably as a result of dilatation secondary to obstruction to flow as indicated by a τ value of 88 min. There also is increased soft-tissue uptake, possibly as a result of increased lymphatic permeability. The right leg is much less seriously affected. Our final diagnosis was left lymphedema secondary to chronic venous insufficiency. Similar findings, but much less advanced, were observed in Patient 12.

A venographically proved aneurysm of the popliteal vein in Hunter's canal was the cause of the swollen left lower leg of Patient 21 as indicated by a markedly increased resistance to lymph flow in an otherwise normal lymphatic system.

Patient 23 had a long history of diabetes mellitus but no proof of her vascular status. Curve analysis shows an increase lymph capacity of the right leg with mild soft-tissue uptake and resistance to lymph flow on the left, but correlation with her venous disease remained unconfirmed.

In Table 3, the results are shown for two patients with a history of groin node resection for disseminated neoplasma (Patients 10 and 30) and one patient suspect for malignancy with left groin node enlargement (No. 17). Patients 10 and 30 demonstrated activity patterns characteristic of dermal backflow (*8*) on transparent film (Fig. 3), which are essentially indistinguishable from a patient (No. 39) with a history of leg trauma. Their TA curves, on the other hand, showed very large values for C_i, τ, and D_i (Patient 30), or continuous, nonspecific accumulation of activity in all segments of the involved legs over the entire period of examination (Patient 10), which are not much different from a patient (No. 38) with nontraumatic lymphatic hyperplasia or megalymphatics (*7*) (Fig. 4). A similar accu-

TABLE 2
Lymphedema in Venous Disease: Comparison of Scintigraphy with TA Curve Analysis
(Activity: 111 MBq Lymphoscint Solco®)

Patient no.	Physical exam and HX	Venogram	Scintigraphy		TA curve analysis					
					$C_i \cdot 10^3$		τ (min)		$D_i \cdot 10^3$	
			R	L	R	L	R	L	R	L
4	L swollen leg Hx of filariasis	V	N	N	4.1	4.4	53	50	0.0	0.0
6	R swollen leg for 10 yr Stripped for varicosity	V	Ho	N	3.5	2.7	29	27	4.4	0.0
7	L swollen leg. Long hx of L thrombosis	T	N	Ho	5.2	5.8	28	88	0.7	2.5
12	Painful swollen leg Hx of DVT	DVT	S	S	5.4	5.5	53	53	0.0	0.5
21	Swollen L lower leg since 2.5 wk. Hydrops of L knee	AN	N	N	3.6	3.2	25	57	0.0	0.0
23	L swollen leg for several mo. Long hx of diabetes mellitus	—	N	N	6.4	4.4	37	53	0.5	0.0

Legend: AN = Aneurysm; DVT = deep venous thrombosis; Ho = hypoplasia; Hx = history; L = left; N = normal; R = right; S = slow flow; T = thrombosis; and V = varicose veins.

TABLE 3
Primary and Secondary Megalymphatics: Comparison of Patients with C_1 Larger Than 5,400 cpm. (Activity: 111 MBq Lymphoscint Solco®)

	Scintigraphy		TA-Curve Analysis					
			$C_i \cdot 10^3$		τ (min)		$D_i \cdot 10^3$	
	R	L	R	L	R	L	R	L
Primary megalymphatics								
Patient 22	N	N	6.4	5.6	47	42	1.4	0.5
Patient 25	N	N	5.8	5.2	22	33	0.4	0.0
Patient 38	N	Hr	4.2	AC	46	UM	2.4	AC
Secondary megalymphatics								
Malignancy								
Patient 10, S/P disseminated melonoma bilat. groin node resection	DB	N	AC	4.5	AC	62	AC	0.0
Patient 17, probably malignancy L groin node enlargement	S	S	6.4	5.3	71	68	0.7	1.3
Patient 30, disseminated neoplasm S/P bilat. groin node resection	DB	N	19.7	4.1	71	21	26.0	0.9
Trauma								
Patient 11, trauma to R leg	C	N	AC	5.4	AC	50	UM	0.7
Patient 39, trauma to L leg	N	DB	3.9	AC	19	UM	0.0	AC
Venous disease								
See Table 2								

Legend: AC = accumulation of lymph; C = lymphocele; DB = Dermal backflow; Hr = hyperplasia. Also see Table 2 for other abbreviations.

mulation, but restricted to one segment, was observed in one Patient (No. 11) who showed a well-defined area of uptake on film as a manifestation of a traumatic lymphocele (Fig. 1B).

Patient 15 who had a long history of a left swollen leg and was diagnosed as lymphedema praecox, was later reexamined for new complaints, this time, of right leg swelling. Time-activity curve analysis revealed an unchanged hypoplasia of the right leg with a C_i value of 2,200 cpm and a τ value within 5% of the previously observed value, demonstrating the reproducibility of the quantitative method.

In eight patients, the data sets of the 3-hr scintigram or the whole series were incomplete. Seven of 31 patients showed diagnostic disagreement between the 3-hr scintigram and the whole series. In two of these, the 3-hr reading agreed with the TA curve analysis, and in four patients, the whole series did. In one patient, the 3-hr film and the whole series were both at variance with the diagnosis from the TA curves.

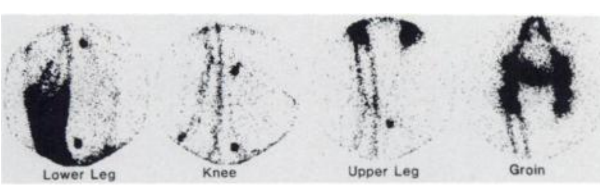

FIGURE 3
Film scintigrams of lower legs, knees, and upper legs, and groin at 120 min showing dermal back flow in right leg of Patient 30, status postbilateral groin node resection for disseminated malignancy. Left leg shows normal pattern. Anterior view.

DISCUSSION

Confidence should be placed in the TA curve results rather than the scintigraphic results because of the difficulty of assessing slow flow and decreased activity on a scintigram. Diagnostic differences between the scintigraphic and TA curve method of evaluation were found in 17 patients (49%). Of these, eight cases involved hypoplasia or aplasia. Since C_i is proportional to the amount of activity that enters the lymph system and to the volume of lymph in segment i, values for C_i provide a quantitative assessment of the lymph capacity and, therefore, of the relative hypoplasia and aplasia of segment i when injection and exercise protocol remain fixed. Comparison with the contralateral leg can then reveal small differences in lymph capacity between the two lower extremities that cannot be read or can only be read from conventional scintigrams with difficulty. The determination of the extent of hypoplasia is less accurate for patients who suffer from involvement of both lower extremities. This is also true when comparing different patients due to the normal variation in the size of the patients' anatomy and in the placement of markers on the legs by the technologist. This latter is exemplified by the relatively wide range (2,700–5,400 cpm) of C_i values found for the 16 patients with at least one normal lower extremity.

Values for τ range between 19 and 50 min (30 ± 10

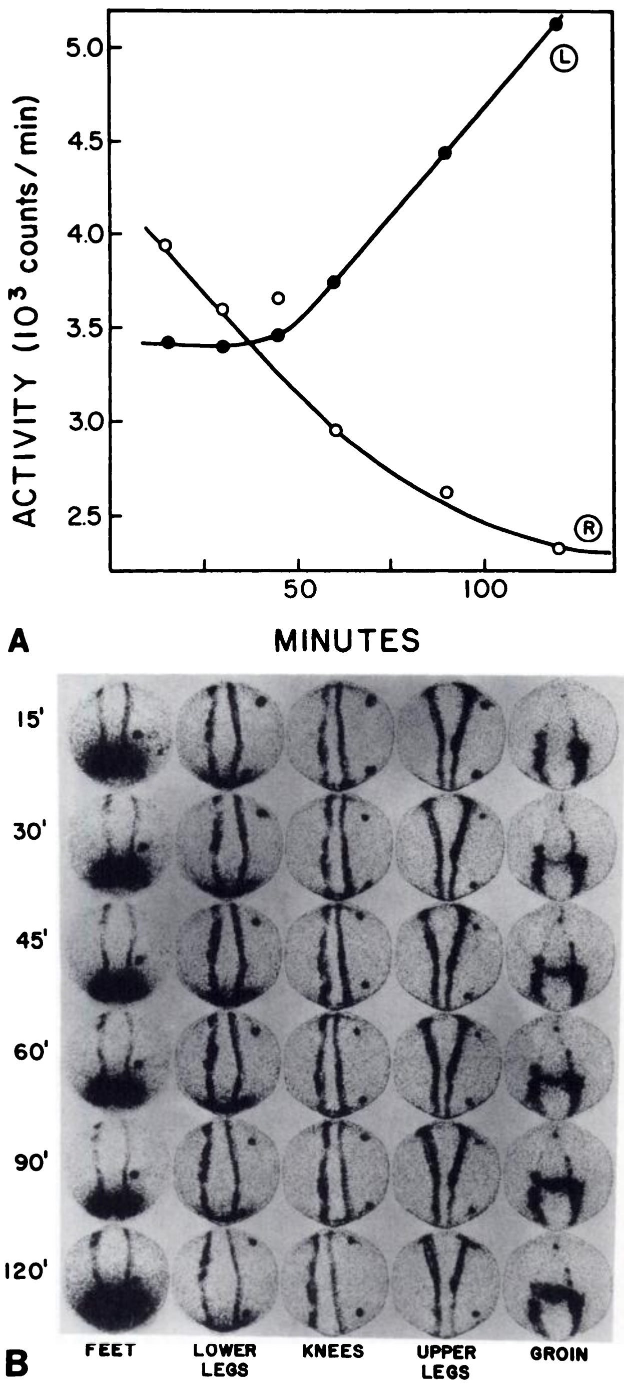

FIGURE 4
(A) Time-activity curves of the knee segment in Patient 38 with megalymphatics of the left leg. The right leg shows an abnormally large soft-tissue uptake but is otherwise normal. (B) Film scintigrams of Patient 38. Anterior view.

min) and provide an estimate of the rate of lymph flow through the segment for this series of normal legs under the standard protocol conditions. Large values are associated with restriction to flow (RTF) seen in the more severe varieties of hypoplasia and in virtually all cases of aplasia, as well as in some types of venous disease and in cases of primary and secondary lymphatic malformations. As such, τ values provide an important clue to the presence or absence of restriction to lymph transport.

Soft-tissue uptake (STU) of tracer, as expressed by D_i, is negligible or small for normal lymphatic status and hypoplasia and aplasia, but it is probably significant in lymphatic involvement of chronic venous insufficiency (2,500 cpm) and in recently stripped varicose veins (4,400 cpm), which may represent leakage of lymph into the soft tissues. Large values for D_i as well as increasing values for D_i during the course of the examination were observed for all cases that were diagnosed as dermal backflow on film and probably represent engorgement of the superficial and insufficient lymph vessels. Similar, aspecific accumulations were seen in cases of traumatic lymphocele and congenital megalymphatics, which can be diagnosed by specific patterns on film scintigrams.

The above findings have indicated that the values for C_i, τ, and D_i allow a quantitative evaluation of hyperplasia, hypoplasia and aplasia, of impaired lymph transport and flow, and of the extent of the STU. In addition, the contribution of each of these factors to the patient's lymphatic status can be separately assessed, a feature not provided by film scintigraphy. Thus, a quantitative gradation can be established of mild, moderate, and severe hypoplasia, as well as aplasia (here arbitrarily defined at <1,500 cpm) for comparison with clinical staging.

Restriction of lymph flow is (not unexpectedly) a consistent feature of severe hypoplasia and aplasia, but not of venous disease where its presence or absence has important therapeutic consequences (*13*). It is in this category that the advantages of separate assessment of lymph capacity, flow and STU by the TA curve analysis are most significant. Interestingly, in none of the six cases of venous disease in this series was there diagnostic agreement between the scintigraphic and TA curve method of evaluation.

In all cases of dermal back flow, traumatic lymphocele and megalymphatics, large or increasing values for C_i, τ, and D_i are found without, however, permitting further diagnostic differentiation. The film scintigrams, on the other hand, show the detailed patterns of activity distribution characteristic of each of these afflictions.

While it is evident from the above that these methods of evaluation are complementary, it appears that the TA curve analysis provides superior diagnostic information in patients with hypoplasia and aplasia of the lymph system and, particularly, in patients with venous disease with or without lymphatic involvement. Film scintigraphy, showing patterns of activity distribution, is preferable in cases of dermal back flow, lymphocele, and megalymphatics.

The results of our quantitative assessment of lymph capacity, lymph flow, and STU appear to agree, at least in part, with the findings of others (*7*). Using appearance time and uptake after 120 min of standardized passive and active muscular exercise for quantification, these authors found quantitative clearance data superior to qualitative image interpretation in detecting mild or incipient cases of lymphedema. However, their method of data collection does not permit separate quantitative assessment of lymph capacity, lymph flow, and transport and, consequently, does not provide all the available information. The latter is probably most significant in the evaluation of lymph involvement in venous disease.

In the absence of a gold standard or other rigorous correlation with lymphatic status, the present study displays the shortcomings of other studies (*7,14*) in that no absolute value of each method can be determined by ROC or multivariate analysis (*15*). X-ray contrast lymphangiography and interstitial lymphangiography (*16*), showing only part of the lymphatic system, cannot be correlated with lymph capacity, RTF or STU, but may be of value in detecting dermal back flow, lymphocele, or megalymphatics. However, in view of the limited information derived thereof and the justified reluctance to make incisions into the edematous tissues, we question the role of cannulation lymphangiography in the work-up of the edematous leg (*7*).

In summary, serial data collected by the technique described above is superior in diagnostic yield to a single 3-hr scintigram. Time-activity curve analysis has the advantages of quantitating hypoplasia and aplasia and, particularly, of assessing the involvement of the lymphatic system in chronic venous disease, which has important therapeutic consequences. Dermal back flow, lymphoceles, and congenital megalymphatics show as abnormal tracer accumulation patterns, which can be diagnosed on film scintigrams and quantitated by curve analysis. An inherent weakness of both methods remains the inability to rigorously correlate the findings with proof of venous and lymphatic status.

We have applied these methods of analysis to a small series of postmastectomy patients with upper extremity edema. Preliminary results have shown promise in correlating lymphatic involvement with clinical staging.

APPENDIX

Assuming that a certain quantity, Q, of tracer will enter the lymph channels in the time period of the examination and that the rate at which the tracer enters the lymph channels is proportional to the fraction f of Q which has not yet entered the channels, then:

$$\frac{df}{dt} = -\frac{f}{\tau}$$

for which the solution is

$$f = Q\,e^{-t/\tau}$$

with τ a time constant. It is then assumed that the flow in the legs is sufficiently rapid so that the lymphoscintigraphic data provide a measure of this rate, i.e., a measurement of activity, A_i, as a function of time, t, for leg segment, i, is given by:

$$A_i(t) = C_i e^{-t/\tau} + D_i,\ \ i = l, k, u.$$

The subscripts l, k, and u denote lower leg, knee and upper leg, respectively, and the constant Ci is proportional to Q, inversely proportional to τ, and also proportional to the volume of lymph in segment i. The parameter Q cannot be determined from the data and thus the data cannot be normalized. The additional factor D_i is caused by activity in the segment not directly associated with the flow of lymph, i.e., D_i represents soft-tissue accumulation (*12*).

Assuming that passage of tracer through the lymph nodes in the groin is very slow relative to the time scale of the lymphoscintigraphic examination (*10*), the data for the activity of the groin A_g yields a measure of the integrated flow:

$$A_g(t) = C_g\,(1 - e^{-t/\tau}) + D_g.$$

The procedure for obtaining numerical values for the leg parameters involved subtracting D_i to obtain a straight line from a plot of $(A_i - D_i)$ versus time on semilog paper. The t = 0 intercept and the slopes of these straight lines then yield values for C_i and τ_i, respectively. Values for D_i were determined by observing the remaining activity in the asymptotic part of the e-curve resulting from plotting measured activity versus time on regular graph paper. A similar procedure was followed to determine the groin parameters. To a good approximation, the values for τ_i are all equal and the ratio C_i/D_i is constant for each of the three leg segments. For example, the parameters for Patient 11 (Fig. 1) are $\tau = 50$ min, C_i = 5,463 cpm, D_i = 750 cpm, $C_k = 1/2\ C_i$, $C_u = 2/5\ C_i$, and C_g = 58,000 cpm, and D_g = 2,800 cpm.

Here C_i represents the activity uptake by the lower leg, but with the injection and exercise protocol strictly adhered to, provides a quantitative assessment of the lymph capacity when compared with the opposite leg. Similarly, τ is the average biologic half-life of the microcolloid in each segment but serves as a measure of rate of lymph flow under the standardized conditions. The absolute values of C, τ, and D will vary with microcolloid particle size distribution and with changes in injection, massaging, and exercise protocol, but their values relative to the opposite leg will not.

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