Magnetic Resonance Imaging, Vol. 10, pp. 549–558, 1992

0730-725X/92 $5.00 + .00

● *Original Contribution*

MAGNETIC RESONANCE IMAGING IN HUMAN LYMPHEDEMA: COMPARISON WITH LYMPHANGIOSCINTIGRAPHY

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Magnetic resonance (MR) imaging and isotope lymphography (lymphangioscintigraphy, LAS) was done in 32 patients with peripheral lymphedema (19 primary and 13 secondary). MRI characteristically showed diffuse dermal and subcutaneous edema, a nonedematous, occasionally hypertrophied skeletal muscle compartment, variability in regional lymph node size and appearance depending on the underlying clinical disorder, serpiginous "channels" or "lakes" consistent with dermal collateral lymphangiectasis and sequestered lymph, and increased subcutaneous fat. In contrast, LAS showed dermal diffusion ("backflow"), cross-over with retrograde tracer backflow (reflux), delayed tracer transport, and depending on the cause of lymphedema (i.e., primary or secondary), discrete or poorly defined lymph trunks (tracer "bands") and delayed or nonvisualization of regional lymph nodes. Although not a first-line clinical test, MR particularly in conjunction with LAS noninvasively provides accurate anatomical definition of the peripheral lymphatic system. In contradistinction to LAS, MR can visualize lymph trunks, nodes, and soft tissues proximal to sites of lymphatic obstruction. Together these imaging modalities may substitute for conventional oil contrast lymphography in the evaluation of the pathogenesis and evolution of most lymphologic disorders.

Keywords: **Magnetic resonance; Lymphoscintigraphy; Lymphedema.**

A major impediment to understanding the pathophysiology of lymphedema syndromes and formulating new treatments with accurate anatomical follow-up has been the inability to easily and repeatedly visualize the peripheral lymphatic system. Conventional lymphography using oil contrast has long been the gold standard for depicting lymphatics and lymph nodes, but this technique requires dissection with direct lymphatic cannulation and, therefore, is cumbersome, time-consuming, and at times unsuccessful in patients with severe lymphatic dysplasia. Moreover, despite recent refinements in lymphangioscintigraphy (LAS or isotope lymphography) using "sweeping" whole-body lymphatic images[1] and semi-quantitative estimates of tracer transport,[2] a continued need persists for improving simultaneous lymphatic, nodal, and soft tissue imaging particularly in anatomic areas not readily depicted by LAS.

Magnetic resonance (MR), a noninvasive imaging modality, provides excellent detail of soft tissues. Although MR has proved useful for delineating blood vascular abnormalities,[3] its value for visualizing and depicting the lymphatic system has scarcely been investigated[4] except in assessing lymphadenopathy associated with malignancies.[5,6]

In this report, we summarize MR images of 32 patients with either primary (i.e., congenital) or secondary (i.e., acquired) lymphatic dysfunction and compared the findings with lymphangioscintigraphic images in these same patients.

METHODS

Thirty-two patients (24 females and 8 males) (ages 8–77 yrs; mean 41 yrs) with lymphatic abnormalities involving one or more extremities underwent a total of 33 MR studies. From the clinical history and after imaging studies, 19 patients were classified as primary

RECEIVED 1/27/92; ACCEPTED 3/16/92.
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Table 1. Clinical summary of patients with primary lymphedema

Patient #	Age (yr)	Gender (M/F)	Diagnosis	Limb edema	Genital edema	LAS	MRI
1	16	M	Congenital, chylous reflux	LLE	+	Slow transport, cross-over with reflux, dermal diffusion	Sub-Q edema, dermal and retroperitoneal lymphatic collaterals
2	20	F	Congenital, Prader-Willi syndrome	LLE, RLE, RUL, LUL	–	Lymphatic dysplasia	Sub-Q edema
3	49	F	Tarda	RLE	–	Dermal diffusion	Sub-Q edema, dermal collaterals
4	15	F	Precox	RLE	–	Intact trunks, dermal diffusion	Sub-Q edema, L-ectasia
5	42	F	Tarda	LLE	–	Dermal diffusion, nonvisualized groin nodes	Sub-Q edema, pelvis and dermal L-ectasia
6	59	F	Tarda	LLE	–	Dermal diffusion, faint groin nodes	Varicose veins, sub-Q and fascial edema
7	13	M	Precox; reflux	LLE	+	Dermal diffusion, nonvisualized groin nodes, scrotal reflux	Hydrocele, lymphadenopathy R groin
8	62	F	Precox	RLE, LLE	–	Severe hypoplasia	Dermal L-ectasia
9	37	F	Congenital	RLE	±	Dermal diffusion, nonvisualized groin nodes	Sub-Q edema, muscle hypertrophy, dermal L-ectasia
10	15	M	Precox	RLE, LLE	±	Intact trunks, dermal diffusion	Dermal L-ectasia
11	15	F	Precox	RLE	–	Severe hypoplasia	Dermal L-ectasia, muscle hypertrophy, ↑ sub-Q fat
12	40	M	Precox	RLE	–	Dermal diffusion, nonvisualized groin nodes	Sub-Q edema, atretic groin nodes, mild L-ectasia
13	27	F	Precox	LLE	–	Dermal diffusion, nonvisualized groin nodes	Dermal L-ectasia
14	8	F	Congenital, intra-abdominal lymphangioma	LUE, RLE	–	Severa hypoplasia	Minimal dermal collaterals, lymphangioma mesentery
15	10	F	Congenital, chylous reflux	LLE	–	Dermal diffusion, cross-over with reflux	↑ Sub-Q fat and edema, dermal and retroperitoneal L-ectasia
16	32	F	Tarda	LLE	–	Dermal diffusion, faint groin nodes	Sub-Q edema, dermal L-ectasia
17	43	F	Precox	LLE	–	Dermal diffusion	Sub-Q edema, dermal L-ectasia, mild muscle hypertrophy, knee effusion
18	19	F	Precox	LLE	–	Severa hypoplasia	Sub-Q edema, mild dermal L-ectasia, normal groin nodes
19	8	F	Congenital	LLE	–	Dermal diffusion	Sub-Q edema, dermal L-ectasia

LAS = lymphangioscintigraphy; RLE = right lower extremity; LLE = left lower extremity; RUE = right upper extremity; LUE = left upper extremity; Sub-Q = subcutaneous; L-ectasia = lymphangiectasia; R = right; L = left; M = male; F = female; yr = years.

and 13 as secondary lymphedema (Tables 1 and 2). The patients chosen to undergo these diagnostic studies were selected both to clarify the pathophysiology of peripheral lymphedema and to define more accurately, the anatomical derangement(s) for the purpose of facilitating optimal therapy and follow-up (e.g., nonoperative treatment with pneumatic compression, elastic stockinettes vs. operative management using either microsurgical lymphatic-venous shunting or staged "debulking" of lymphedematous subcutaneous tissue in the affected limb).

In the primary lymphedema group, nine were diagnosed as lymphedema precox, four lymphedema tarda, and six congenital lymphedema (early in childhood). Three had a reflux syndrome including two with chylous reflux. Of these patients, 15 had unilateral limb edema, 3 had involvement of two or more extremities, and 4 also had genital involvement (scro-

Table 2. Clinical summary of patients with secondary lymphedema

Patient #	Age (yr)	Gender (M/F)	Diagnosis	Limb edema	Genital edema	LAS	MRI
1	67	F	Radical mastectomy	LUE	–	Discrete trunks, dermal collaterals, nonvisualized L axillary nodes, dermal diffusion	Sub-Q edema, dermal L-ectasia, no L axillary adenopathy
2	55	M	Filariasis	LLE	–	Dermal diffusion, nonvisualized L groin iliac nodes	Sub-Q edema, dermal L-ectasia
3	53	F	Superficial venous varicosities	LLE	–	Dermal diffusion	↑ Sub-Q fat, mild muscle hypertrophy, dermal L-ectasia
4	41	M	Radical groin dissection (melanoma)	LLE	–	Dermal diffusion, nonvisualized L groin nodes	↑ Sub-Q fat, mild muscle atrophy, dermal L-ectasia
5	30	F	Radical hysterectomy	RLE	–	Discrete trunks, dermal diffusion	Sub-Q edema
6	71	F	Radical mastectomy	RUE	–	Discrete trunks, dermal diffusion	Sub-Q edema and ↑ fat
7	40	M	Radical orchiectomy (embryonal ca)	RLE, LLE	+	Discrete trunks, dermal diffusion	Scrotal, thigh, pelvic Sub-Q edema, nonvisualized groin nodes, dermal L-ectasia
8	64	F	Radical hysterectomy	LLE	–	Dermal diffusion, nonvisualized L groin nodes	Sub-Q edema and ↑ fat, dermal L-ectasia, muscle hypertrophy
9	58	F	Radical groin dissection	RLE	–	Dermal diffusion	↑ Sub-Q fat, dermal L-ectasia
10	44	M	Radical groin dissection	LLE	–	Discrete trunks, dermal diffusion, absent L groin nodes	↑ Sub-Q fat, dermal L-ectasia
11	65	F	Radical hysterectomy, pelvic irradiation	RLE	–	Dermal diffusion, nonvisualized R groin nodes	Dermal and pelvic L-ectasia, ↑ Sub-Q fat
12	77	F	Radical mastectomy	LUE	–	Discrete trunks, dermal diffusion	Dermal L-ectasia, no axillary adenopathy L
13	50	F	Multiple vein stripping and ligation with groin dissection	RLE	–	Lower leg dermal diffusion, intact upper trunks	Sub-Q edema, dermal L-ectasia (lower leg); thigh normal

For abbreviations—see Table 1 footnote.

tal-penile or labial-vulval). Among the 13 patients with secondary lymphedema, all had undergone either limited or radical regional node dissection (axillary, groin, or retroperitoneal), and one also had had filariasis. Twelve had unilateral limb edema, one had edema of two or more extremities, and one also had scrotal edema.

Each patient underwent LAS as previously described[2] either before or on the same day as MRI. Technetium radiolabeled human serum albumin (Tc99m-HSA) was injected intradermally (0.05 ml) into a digital webspace (500 μCi or 1.85×10^7Bq) and using a GCA-90B digital camera (Toshiba Medical System), whole body images were obtained serially from 20 min up to 4–6 hr after injection. In patients with one swollen extremity, the image of the contralateral limb was used for comparison. T_1-, T_2-, and proton density weighted axial and/or coronal magnetic resonance images with 5–10 mm slice thickness were obtained on each patient using a 0.5-T Toshiba MRT-50A magnet operating at a resonant frequency of 21.5 mHz for protons and a quadrature transmit-receive body coil with a 25 cm field of view. T_1-weighted images: TR 200–500 msec, TE 15–20 msec; T_2-weighted images: TR2000–2500 msec, TE 30–40 msec to 90–120 msec.

RESULTS

In swollen limbs with primary lymphedema, MRI characteristically showed diffuse dermal and subcutaneous edema with an intact (nonedematous) subfascial compartment, variability in regional lymph node size and appearance depending on the underlying clinical disorder, seripiginous "channels" or "lakes" consistent with dermal collateral lymphatics and sequestered "lymph," increased subcutaneous fat (two patients), and occasionally skeletal muscle hypertrophy (two patients). Lymphangioscintigraphy, in contrast, showed in the abnormal limb poorly defined or absent lymph trunks, delayed or nonvisualization of regional nodes, dermal diffusion, little or no tracer transport (i.e., severe hypoplasia), and cross-over with retrograde tracer backflow (reflux) (Figs. 1–4).

In swollen limbs with secondary lymphedema, MRI showed both small and large serpiginous "channels," absent, normal, or enlarged regional lymph nodes (depending on the clinical syndrome), dermal collateral lymphangiectasis, and subcutaneous edema. In all patients, the subcutaneous edema demonstrated a decreased signal intensity on T_1-weighted images either isointense or hypointense to muscle. On T_2-weighted images, the edema fluid was seen as a homogeneous high signal intensity. Despite extensive subcutaneous edema and increased subcutaneous fat (seven patients), the subfascial compartment was unremarkable except for occasional muscle hypertrophy (three patients) and, moreover, its signal intensity was normal. Lymphangioscintigraphy, in contrast, characteristically showed discrete lymphatic trunks, delayed or nonvisualization of regional nodes, delayed tracer transport, and progressive dispersion of the radiopharmaceutical into the soft tissues (dermal "backflow") (Figs. 5–8).

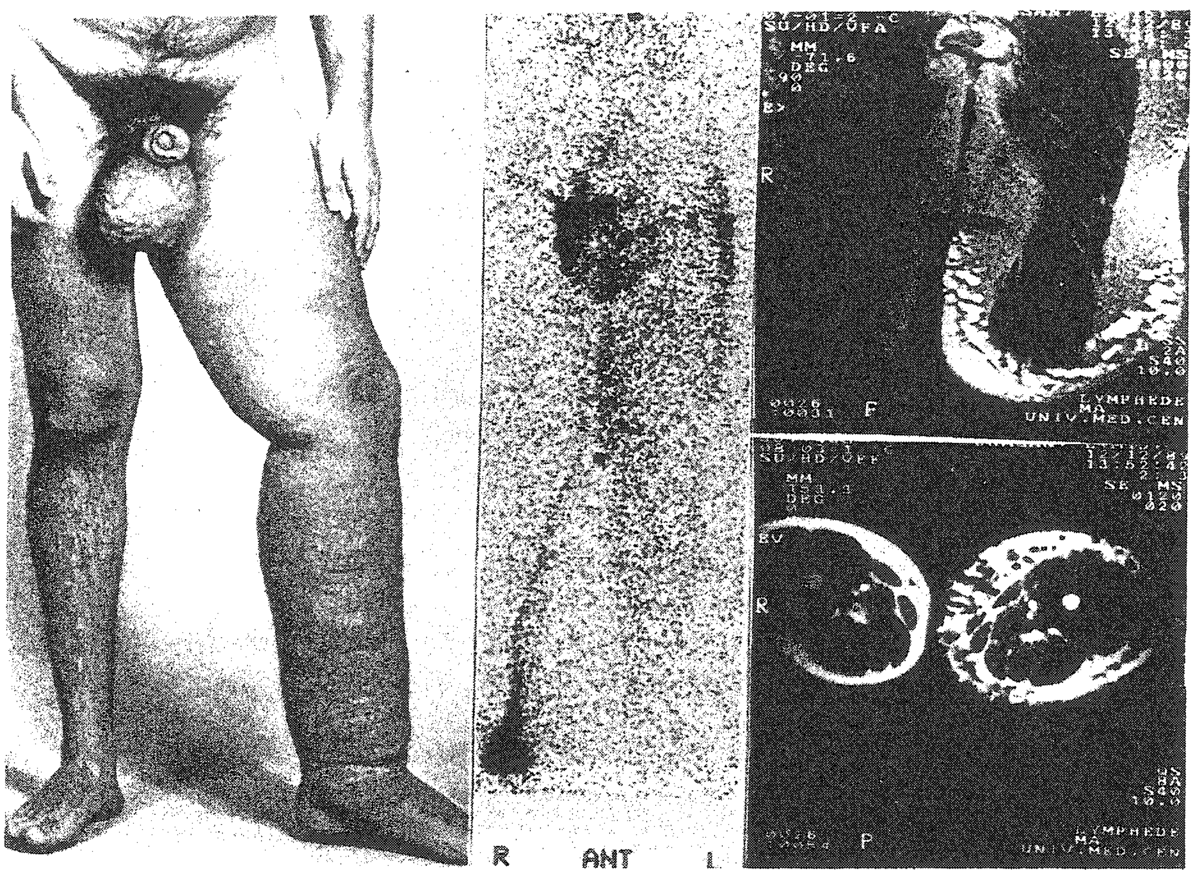

Fig. 1. A 16-year-old man (Table 1, #1) with massive edema of the left leg and scrotum with chylous vesicles (left). Lymphangioscintigraphy (middle) via the right leg shows tracer transport to the right groin with crossover and retrograde dermal diffusion into the left leg consistent with chylous reflux. MRI (right) show massive lymph "lakes" in the left thigh and scrotum (coronal section T_2-weighted; axial section T_1-weighted). Note the skeletal muscle compartment is unremarkable.

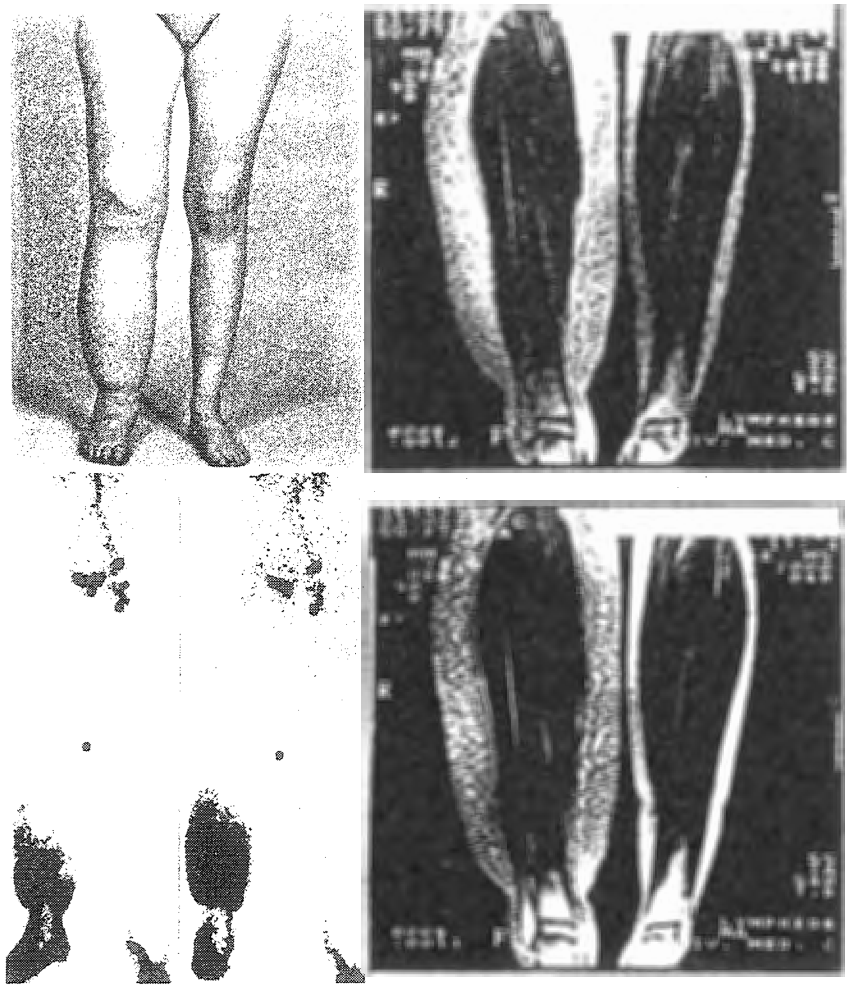

Fig. 2. A 37-year-old woman (Table 1, #9) with right leg edema (upper left) since 3 years of age. MRI (upper and lower right) show massive calf-angle soft tissue edema with prominent dermal lymphatics (T_2-weighted). Note that the skeletal muscle is slightly hypertrophied compared with the left (normal) side. Lymphangioscintigraphy (lower left) shows tracer dermal diffusion with nonvisualization of both the right groin nodes and retroperitoneal trunks (compare with the normal left leg).

A comparison of the findings on MRI with lymphangioscintigraphy is summarized in Table 3.

DISCUSSION

In patients with lymphedema syndromes, MR is a promising noninvasive imaging technique for depicting in any plane peripheral and more central lymph trunks as well as other soft tissue abnormalities particularly when used in conjunction with LAS. T_2-weighted images more vividly depict soft tissue changes including dermal thickening and serpiginous "channels" or "lakes" consistent with dilated dermal lymphatic collaterals. Whereas these "channels" may alternatively be nonendothelial-lined fluid-filled tissue clefts, they seem to conform with lymphatic anatomy as depicted by LAS and conventional oil contrast lymphography. The role of MR at this stage is only complementary to that of LAS, but MRI can visualize more central lymph trunks, nodes, and "tumors" especially in lymphatic obstruction (i.e., secondary lymphedema) and in chylous reflux syndromes. For example, in patients with chylous reflux, MR displayed extensive retroperitoneal lymphatic dysplasia best seen on T_2-weighted images (see Fig. 4). Moreover, with severe lymphatic hypoplasia regional nodes were non-visualized on LAS yet MRI depicted these nodes to be normal (Fig. 3). Despite its imaging advantage, MR is costly, but once practical

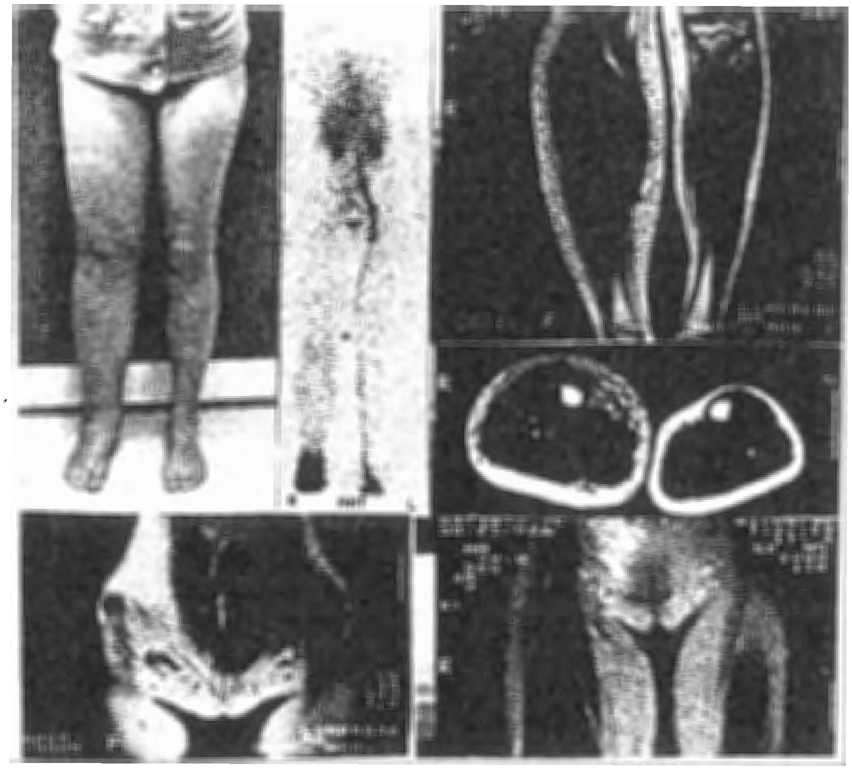

Fig. 3. A 13-year-old girl (Table 1, #11) with right left lymphedema precox (upper left). Lymphangioscintigraphy (upper middle) shows normal tracer transport on left but little or no ascent of the radiopharmaceutical on the right with nonvisualization of regional lymph nodes. MRI (upper right and bottom) show extensive dermal lymphatic collaterals and normal appearing inguinal lymph nodes. Note also skeletal muscle hypertrophy of the right leg.

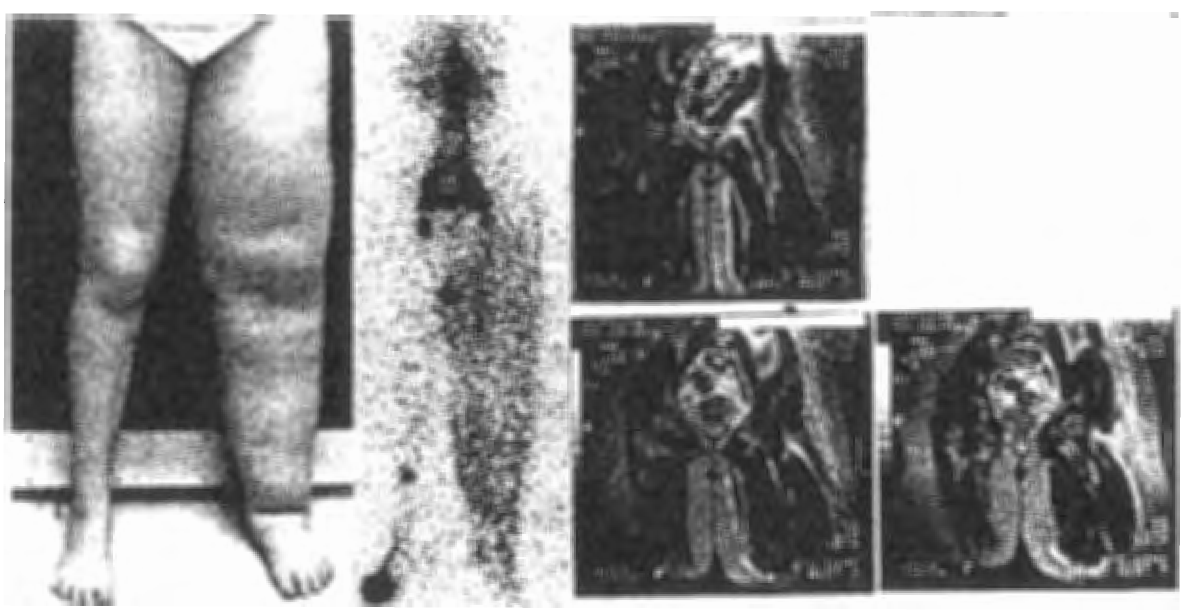

Fig. 4. A 10-year-old girl (Table 1, #15) with congenital lymphedema (extreme left). Lymphangioscintigraphy (LAS) (right leg injection) shows dense retroperitoneal radioactivity with tracer crossover and regurgitation into the left leg (middle). Coronal MR imaging (T_2-weighted) shows lymphangiectasis and edema of the retroperitoneum, upper thigh and left lateral abdominal wall (right). These MRI and LAS findings are consistent with the clinical picture of "milky" thigh vesicles containing chylomicrons (chylous reflux).

Table 3. Magnetic resonance imaging (MRI) compared with lymphangioscintigraphy (LAS) in patients with peripheral lymphedema

MRI	LAS
Soft tissue (dermal and subcutis) edema and increased fat	Discrete or poorly defined trunks
Deep (extremity) compartment unremarkable; occasional muscle ("work") hypertrophy	Dermal diffusion ("backflow")
Regional nodes—atrophic, absent, enlarged, or unremarkable	Delayed or nonvisualized regional nodes
Dermal lymphatic collaterals, "lakes" or "cisterns"	Delayed tracer transport
Retroperitoneal or other visceral soft tissue abnormality	Cross-over with retrograde tracer flow ("reflux")

contrast agents become available for human use, lymphatic images should be further sharpened and prove still more valuable. For example, in experimental animals, iron oxide compounds administered intravenously highlight regional lymph nodal imaging with reduced signal intensity,[7,8] and in early films after intradermal injection even lymph truncal anatomy has been depicted.[9]

It is also noteworthy that MR images of the subfascial compartment of the lymphedematous extremity generally fail to show edema or other major abnormality. On occasion, the skeletal muscle mass is enlarged, a finding consistent with increased work effort required for locomotion with an unwieldy limb. These images support the clinical observation that limb muscle function usually is preserved even with extreme

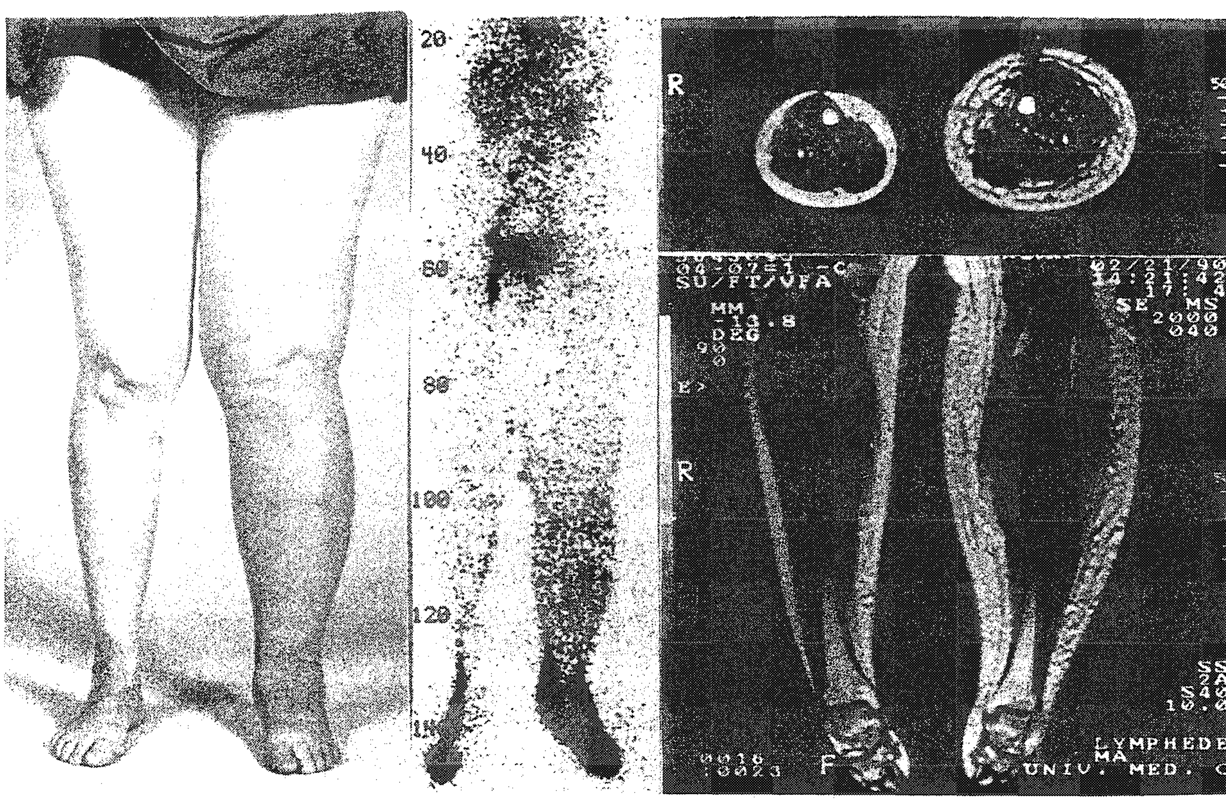

Fig. 5. A 53-year-old woman (Table 2, #3) with marked edema of the left leg (left) following repeated groin dissection for removal of venous varicosities. Lymphangioscintigraphy (middle) shows delayed tracer transport on the left with nonvisualization of groin nodes and dermal diffusion. These findings are confirmed by MRI of the lower legs showing left leg dermal lymphatic collaterals on both transaxial and coronal views (upper and lower right, respectively). Slight muscle hypertrophy is also seen in the left leg.

Fig. 6. A 41-year-old man (Table 2, #4) with marked left leg edema ten years after radical groin dissection for malignant melanoma (upper left). MR imaging (coronal sections) of upper and midthigh (right) shows massive soft tissue edema with dermal lymphatic collaterals. Lymphangioscintigraphy (lower left) shows extensive dermal diffusion of tracer and nonvisualization of groin nodes on the left.

lymphedema. Moreover, the lack of subfascial edema illustrates how tightly fascial compartments normally surround the musculature and act to restrict edema, and furthermore, the relatively limited importance of lymphatic drainage as an edema protective mechanism at this site. The finding also explains the necessity of fasciectomy to relieve skeletal compartment pressure from severe intramuscular edema as in reperfusion injury after prolonged ischemia.[10]

In conclusion, MR is a potentially useful diagnostic test particularly in conjunction with LAS to anatomically define and delineate deranged patterns in lymphedema. In the future, it may also be possible using these imaging modalities to assess objectively changes, if any, in the status of the lymphatic system after therapy (e.g., physiomanual decongestion,[11] external pneumatic pump compression,[12] and operative lymphatic-venous decompressive shunts).[13] In contrast to LAS, MR can visualize lymph trunks, nodes, and soft tissues proximal to sites of lymphatic obstruction. Superparamagnetic agents (e.g., iron oxide) to intensify lymphatic truncal-nodal images, although not yet clinically perfected, should notably sharpen images obtained with MR[7-9] and alone or together with LAS effectively substitute for conventional oil contrast lymphography in the evaluation of the pathomechanisms, evolution, and management of most lymphological disorders.

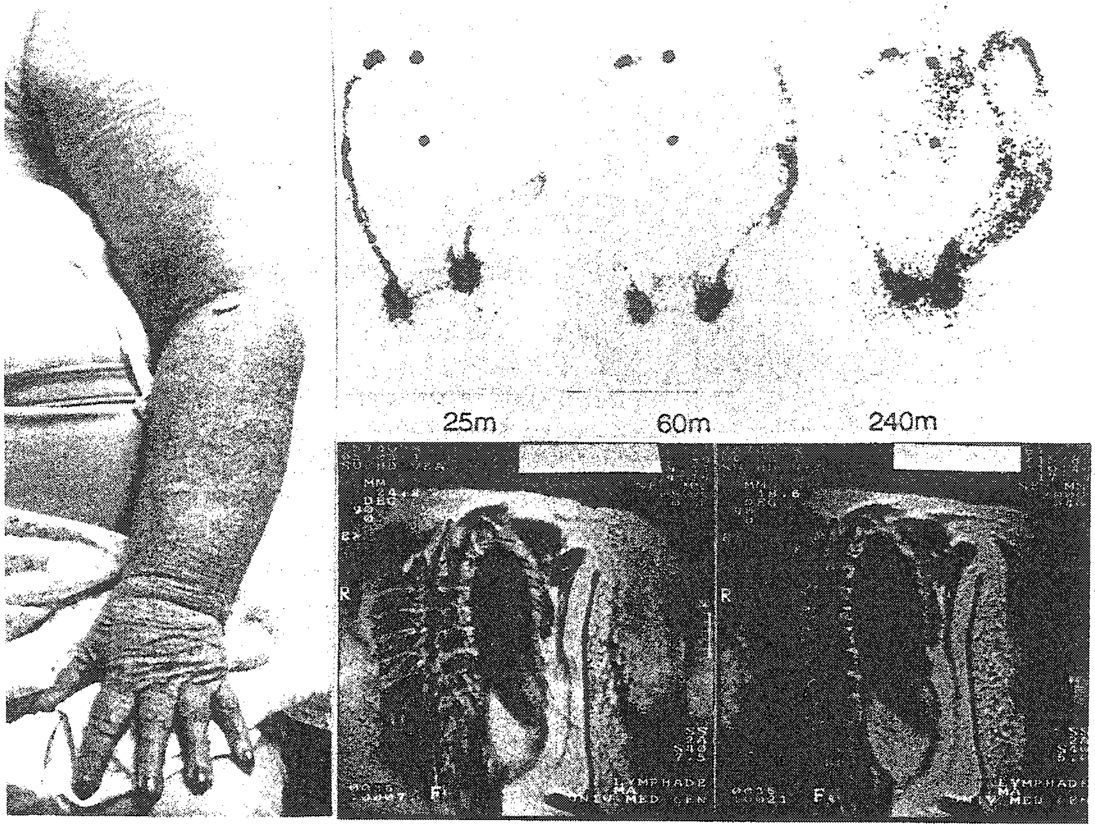

Fig. 7. A 77-year-old woman (Table 2, #12) with left arm edema following modified radical mastectomy (left). Lymphangioscintigraphy (upper right) demonstrates delayed left-sided truncal transport, later dermal diffusion of tracer, and non-visualization of periaxillary nodes. MR imaging shows dermal lymphatic collateralization (lower right) with no axillary adenopathy (T_1- and T_2-weighted images).

Acknowledgments—This investigation was supported in part by a grant from the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (ID No. 870051).

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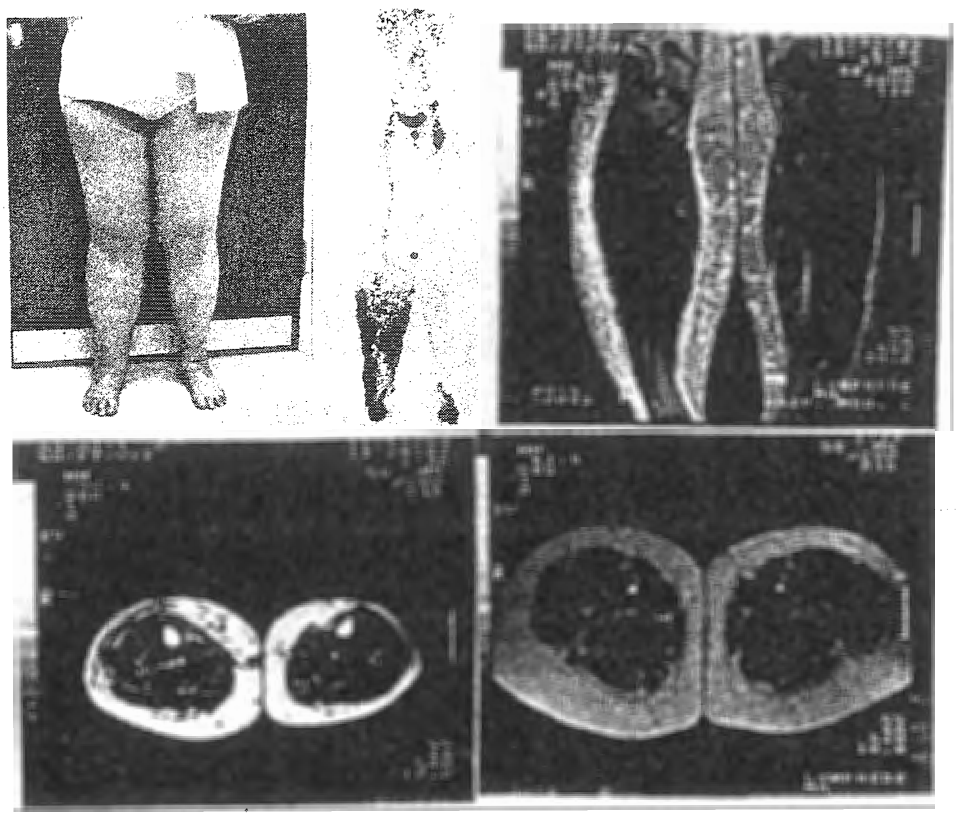

Fig. 8. A 50-year-old woman (Table 2, #13) with right lower leg edema (upper left) following multiple stripping and ligation operations for venous varicosities. Lymphangioscintigraphy (upper middle) shows on the right diffuse dermal diffusion of tracer in the lower leg with intact thigh and retroperitoneal lymphatic trunks. Right groin nodes are not visualized and probably have been excised. These findings are confirmed by coronal (upper right) and transaxial (lower left and right) MR imaging which shows diffuse dermal lymphatic collaterals and edema of the right lower leg (T_2-weighted, upper right; T_1-weighted, lower left) with normal transaxial sections in the mid-thigh (lower right).

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