Noncontrast three-dimensional magnetic resonance imaging vs lymphoscintigraphy in the evaluation of lymph circulation disorders: A comparative study

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Background: **Visualization of the lymphatic vessels is a challenge in patients with disorders of the lymphatic circulation. In an effort to improve the diagnostic scope of lymphatic imaging, we compared traditional lymphoscintigraphy (LSG) with three-dimensional magnetic resonance imaging (3D MRI).**

Methods: **From October 1, 2002, to May 30, 2004, 39 patients (27 males and 12 females) with lower extremity lymphedema and/or skin lymphorrhea in the abdominal wall or the external genitalia underwent LSG and 3D MRI. Patients' ages ranged from 3 to 71 years. Assessment of the imaging studies included the degree and quality of visualization of the malformations of the lymphatic collectors, lymphatic trunks, lymph nodes, and tissue edema.**

Results: **In patients with lymphedema, chylous reflux syndrome, or both, LSG depicted the enlarged lymphatics and nodes as a fused band or mass. In 3D MRI, the dilated superficial lymphatic collectors and deep lymphatic trunks, as well as the accumulation of chyle and node enlargements, were clearly visualized. In patients with hypoplasia or aplasia of the lymphatics, LSG usually displayed the pattern of dermal backflow in the form of radiotracer filling of the dermal lymphatics or stagnation of the isotope at the injection point. The images obtained by 3D MRI were able to demonstrate the extent of tissue fluid accumulation and distinguish edema fluid from subcutaneous fat.**

Conclusions: **In patients with peripheral and central lymphatic malformations, LSG provided images representative of the function of the lymphatic vessels but failed to give detailed information regarding its anatomy. 3D MRI provided extensive information on the anatomy of the lymph stagnated vasculature as well as on the effects of lymphatic dysfunction on local structures and tissue composition. (J Vasc Surg 2005;41:69-75.)**

The development of lymphatic system imaging has lagged behind the rapid progress of blood vessel imaging. Because of their anatomic and structural character, visualization and access to the lymphatics are not easy. The Kinmonth method of direct lymphography (exposure of the lymphatic vessels and injection of oil contrast into a cannulated lymphatic), even though it provides very clear visualization of the lymphatic vessels, is no longer the method of choice because it is a one-time procedure with a risk of damage to the lymphatic endothelium and pulmonary oil embolization. The Kinmonth method has been largely replaced by isotope lymphography - lymphoscintigraphy (LSG), for which a small intradermal amount of a radiotagged macromolecule is injected between the fingers or toes and provides images representative of the function of the lymphatic system and its capability to transport the isotope to the groin, axilla, or intra-abdominal lymph nodes and vessels.[1] LSG also provides morphologic imaging, even though the results are not comparable to those of direct lymphangiography. In 1996, we adopted magnetic resonance imaging (MRI) for the diagnosis of lymphatic disorders.[2] The two-dimensional MRI was able to demonstrate diffuse subcutaneous edema, as well as dilated lymphatic collectors. However, the information provided by cross-section imaging was quite limited. In our efforts to improve imaging of the lymphatic vasculature, we evaluated three-dimensional MRI (3D MRI), which has the potential to provide comprehensive anatomic information about lymphatic malformation and dysfunction. In this report, we compared the results of 3D MRI with those of LSG in 39 patients with lymphatic disorders.

METHODS

From October 1, 2002, to May 30, 2004, 39 consecutive patients with lymphatic circulation disorders underwent LSG and 3D MRI. Most patients with suspected lymphatic disease are tested by LSG in our clinic. 3D MRI was performed mainly in patients with primary lymphedema or in cases of difficult diagnosis. We excluded patients with a definite etiology such as postmastectomy lymphedema due to breast cancer. There 27 were males and 12 females. Ages ranged from 3 to 71 years. Lymphedema of the lower extremities was present in 37 of 39 patients. Thirteen had involvement of the external genitals, and four had bilateral lymphedema. Twenty of the 39 patients were

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Competition of interest: none.

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Table I. Patient characteristics

Variable	*No. Patients*
Lower extremity lymphedema	37
Unilateral	33
Bilateral	4
Primary lymphedema	35
Aplasia/hypoplasia	10
Hyperplasia	20
No visible changes of superficial lymphatic and node	5
With chylous reflux	11
With external genital edema	13
In KTS	2
Secondary lymphedema	2
Trauma	1
Malignant tumor	1
Upper extremity lymphedema (unknown reason)	1
External genital lymphedema (primary)	1

KTS, Klippel-Trenaunay syndrome.

diagnosed as having hyperplastic lymphatics. Eleven of these had associated chylous reflux with milky vesicles on the thigh, calf, scrotum, and skin. Other patient characteristics are listed in Table I.

Imaging by 3D MRI was performed with a 1.5-T whole-body scanner (Magnetom Vision Plus; Siemens AG, Medizinische Technik, Erlangen, Germany). Patients were examined in a body array coil with a flip angle of 150°. An optimized protocol for imaging of stationary fluid with a high-signal intensity was used. The serial turbo sequences included fat saturation turbo spin-echo and half-Fourier acquisition single-shot turbo spin-echo (HASTE). The turbo spin-echo is a strong T2-weighted multiecho sequence with a repetition time of 2800 ms and an echo time of 1100 ms. The scan matrix was 256^2. Because of the long echo train, 60- to 100-mm-thick slabs were used to display fluid without a soft tissue signal. HASTE with a repetition time of 11.90 ms and an echo time of 95 ms can produce a shorter measurement time to reduce arterial pulse artifacts and increase the T2 contrast to enhance the display of lymphatic vessels. Seventeen interleaved slices of 3-mm thickness and a 176×256 scan matrix were selected in HASTE. The slice distance was 0 mm. Maximum-intensity projection and source images were used to reconstruct the images of the lymphatic system.

LSG was performed with technetium-radiolabeled dextran (Syncor International Corporation, Shanghai, China) injected intradermally into the first digital webspace (1-2 mCi or 37-74 MBq) of the feet. Gamma camera images (Hawkeye SPECT; GE, Milwaukee, Wis) were obtained 15 minutes and 2 hours after injection.

RESULTS

Unlike the arterial and venous circulation, where flow is continuous, the lymphatic flow is not a continuous column. In a healthy individual, LSG displays a single continuous or intermittent lymphatic collector, as well as the inguinal nodes of the extremity and the iliac and lumbar lymph nodes in the abdomen and trunk. In patients with aplasia or hypoplasia of the lymphatics, the numbers of lymphatic channels and/or lymph nodes were reduced or not visualized at all on LSG. Noncontrast 3D MRI cannot depict lymphatics in an intact lymphatic system, nor can it depict the single faint collector (with narrowed channel) detected by LSG in patients with lymphatic hypoplasia.

In five patients with lymphedema of the lower extremities, scintiscan displayed normal superficial lymphatic collectors and inguinal nodes. However, the deep lymphatic system, the popliteal nodes, and its afferent vessels that could not be visualized under normal conditions also appeared.

In patients with lymphangiectasia, the stagnated lymph in the dilated channels showed high signals on the T2-weighted image under the specific acquisition. Thus, the affected vessels (superficial and deep) could clearly be visualized on 3D MRI. In 9 of 27 patients with unilateral lymphedema of the lower extremities, 3D MRI displayed bilateral lymphatic varicosities in the pelvis and retroperitoneum (Fig 1). In all 11 cases of chylous leakage, 3D MRI clearly detected the significantly dilated superficial and deep lymphatic collectors (Fig 2). In two of the patients who had severe chyle leakage (100-200 mL/d), MRI displayed large lymphangiectatic lesions (Fig 3). These abnormal vessels, when examined on LSG imaging, were indistinguishable because the multiple lymphatics became a solitary band or mass (Fig 4). In four cases of lymphatic hyperplasia of the extremity, LSG could not depict the markedly dilated lymphatics in the thigh because the tracer dispersed in the distal part of the limb instead of being transported by the vessels (Fig 5). The imaging features of 3D MRI and LSG in the 39 cases of lymphatic disorders are compared in Table II.

Edema fluid in the form of water was not visualized by LSG. However, MRI clearly identified edema fluid by suppressing the fat, evaluating the severity of edema, and distinguishing lymphedema from lipoedema. In lymphedema patients examined by MRI, the subfascial compartment appears normal. This feature distinguishes lymphedema from venous edema. Among our patients, there were two Klippel-Trenaunay patients with an important lymphedema component in the affected limbs. No lymphatic channels or nodes were found. MRI detected lymphatic fluid collections in the subcutaneous tissue where obvious blood vascular anomalies were also present.

DISCUSSION

Patients with lymphedema and related problems should undergo proper imaging to understand the pathophysiology for optimal clinical management. However, the ideal method for lymphatic examination has been elusive. The invasiveness and associated morbidity of conventional lymphangiography and the unsatisfactory morphologic imaging of LSG have motivated the search for more advanced lymphatic imaging methods. MRI is a multiparameter imaging technique that can detect pathologic changes of different tissues and provide large-field scanning. On the basis of our previous work, we recently adopted noncon-

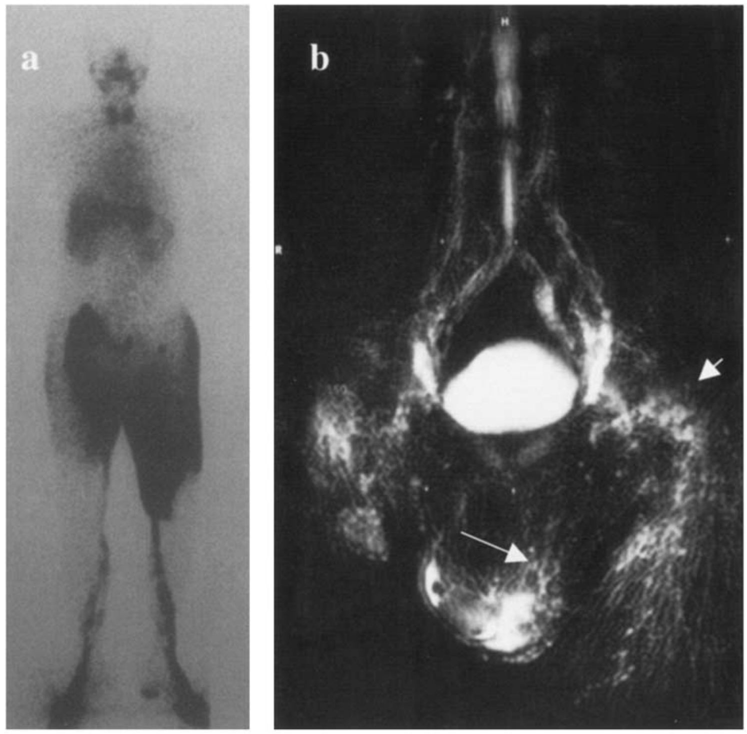

Fig 1. External genital chylorrhea in 45-year-old man. **a,** Lymphoscintigraphy shows extensive backflow in the inguinal region, the lower abdomen, and the scrotum, with intact lymphatic collectors of the lower extremities. **b,** The magnetic resonance imaging clearly displays massively enlarged inguinal *(arrowhead)*, iliac, and scrotum *(arrow)* lymphatics and inguinal nodes. The large lumbar trunks are clearly seen.

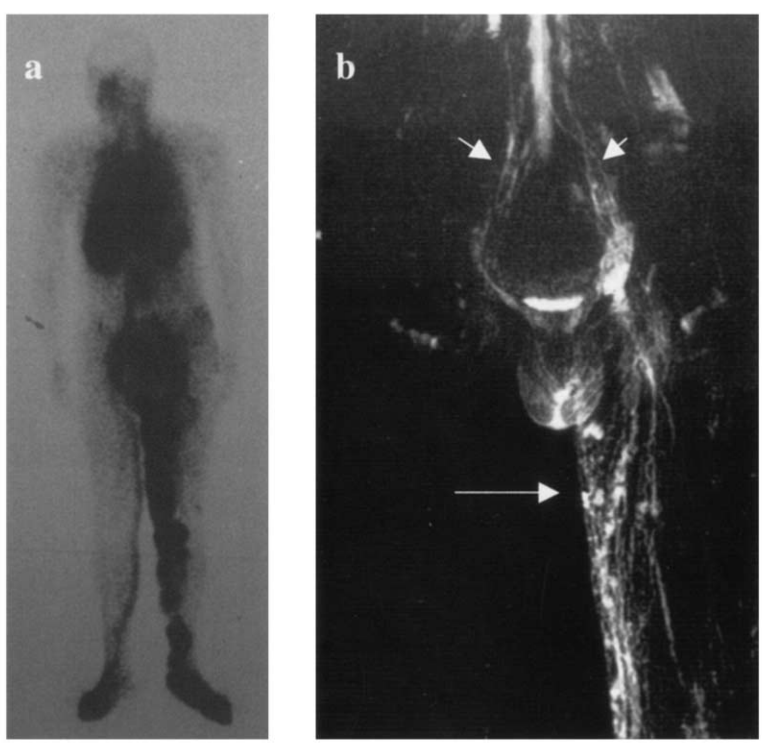

Fig 2. A 34-year-old man with lymphatic hyperplasia of the left leg. **a,** Lymphoscintigraphy shows an intensive radioactive signal along the medial part of the left lower extremity and in the pelvis, groin, and scrotum. **b,** Three-dimensional magnetic resonance imaging depicts enlarged lymphatics in the thigh *(arrow)*. The estimated diameter of the lymphatics is 2 to 5 mm. Clusters of dilated inguinal, iliac, scrotum, and lumbar trunks *(arrowhead)* are also visualized.

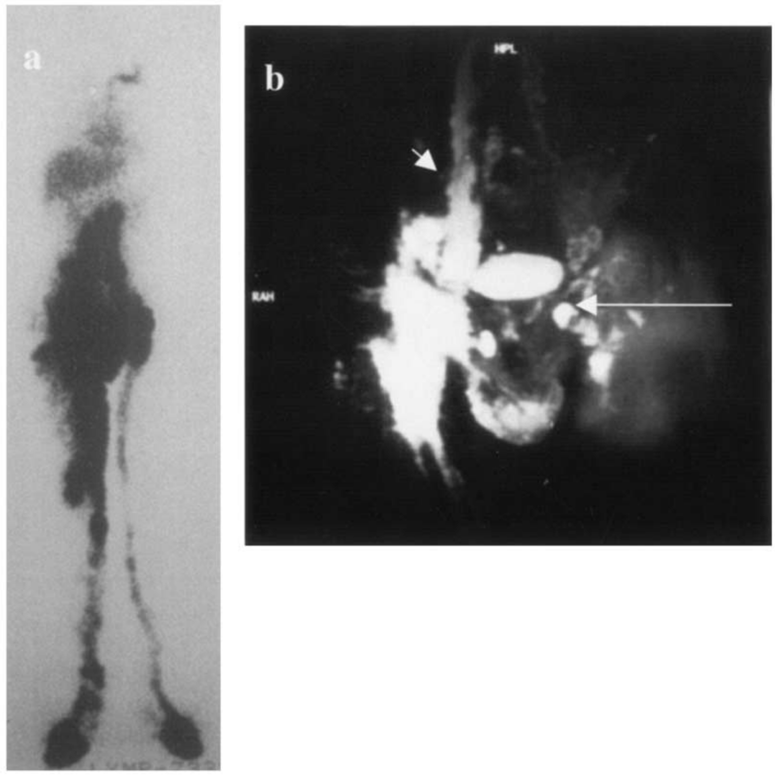

Fig 3. A 48-year-old man with right leg lymphedema and severe inguinal chylous reflux. **a,** Lymphoscintigraphy demonstrates that lymphatic transport in the limbs is intact, but there is prominent radiotracer filling in the thigh, inguinal, iliac, and retroperitoneal regions on the right. **b,** Three-dimensional magnetic resonance imaging displays extremely dilated chyliferous inguinal and iliac collectors with accumulated chyle, as well as lumbar trunks *(arrowhead)*. The inguinal nodes on the left are also enlarged.

trast 3D MRI in our clinical work and discovered its distinctive role in displaying abnormalities of the superficial and deep lymphatics. Under normal conditions, lymph circulation is not a continuous column of fluid. The slow lymphatic flow cannot be visualized on noncontrast MRI. However, when the lymph flow is impaired and the channel is dilated and filled with stagnated lymph, this can be detected with 3D MRI. Under heavy T2-weighted imaging, the static or motionless fluid (lymph in the vessels and edema fluid in the tissues) displays high signals. When the background is saturated, lymph flow itself may act as a contrast medium to highlight the path of the lymphatic channels. In lymphatic hyperplasia, eg, chylous reflux syndromes, LSG imaging could hardly identify individual vessels because of the false shadow caused by the gamma emissions of radiotracer in the vessels. The best imaging of lymphatic varices in the past was provided by conventional direct lymphography. Our results, however, show that noncontrast 3D MRI can provide imaging of a quality similar to that of direct lymphangiography. The enlarged lymphatic vessels with channels (approximately 1.0 mm or more) and local dilated lesions can be clearly depicted. A special advantage of 3D MRI over LSG is its ability to display deep lymphatic trunks, ie, abnormalities of the inguinal, iliac, and lumbar branches with increased channels. With the help of 3D MR imaging, we have diagnosed and treated patients with superficial and deep lymphatic malformations. In our study, 9 of 27 patients with unilateral limb lymphedema were found to have bilateral abnormalities of the pelvic and retroperitoneal trunks. The massive bilateral abnormal changes of the deep vessels prompted us to reflect that lymphovenous anastomosis of a few lymphatics into neighboring veins might not be sufficient to release the congested lymph in lymphedema patients. For those patients, a conservative method (heating therapy plus manual lymph drainage and diet control) was recommended instead of bypass operation. After two or three courses of treatment, edema was reduced and lymph leakage was stopped in all seven treated patients. In two patients with severe chylous reflux in whom the 3D MRI clearly showed the location and size of the lymphangiectatic "lakes," we selected sclerotherapy by injection of bleomycin directly into the lesion instead of ligation of the lumbar trunks. After several staged treatment sessions, chylous leakage stopped. In two patients with elephantiasis in whom MRI displayed numerous dilated lymph collectors (meaning that they still had some function), we chose to preserve those vessels during debulking operations. A complex decongestion compression

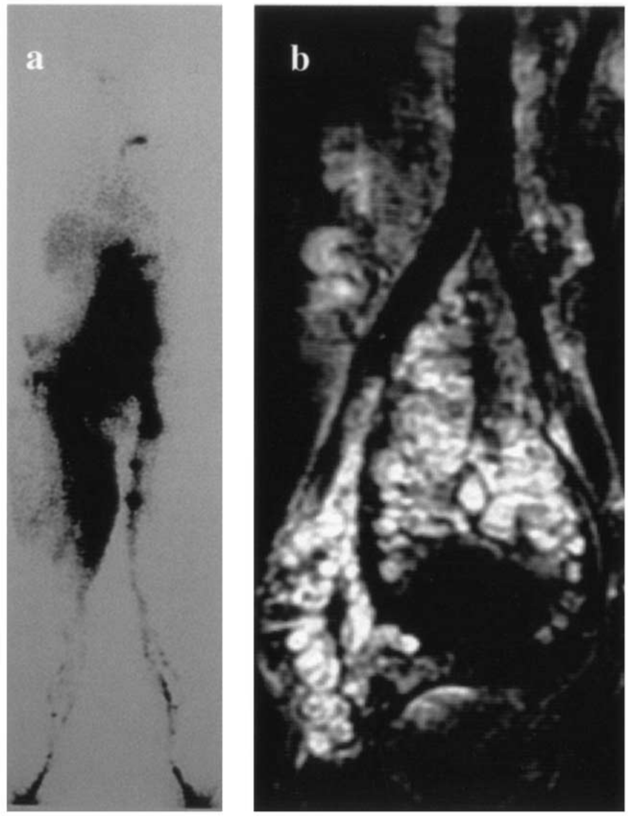

Fig 4. Chylorrhea in a 24-year-old man. **a,** Lymphoscintigraphy displays strong radioactivity in the abdomen, right groin, and thigh areas. **b,** Magnetic resonance imaging demonstrates massive lymphatic varices of the inguinal and iliac regions and extremely dilated periaortic and peri-iliac lymphangiectasia.

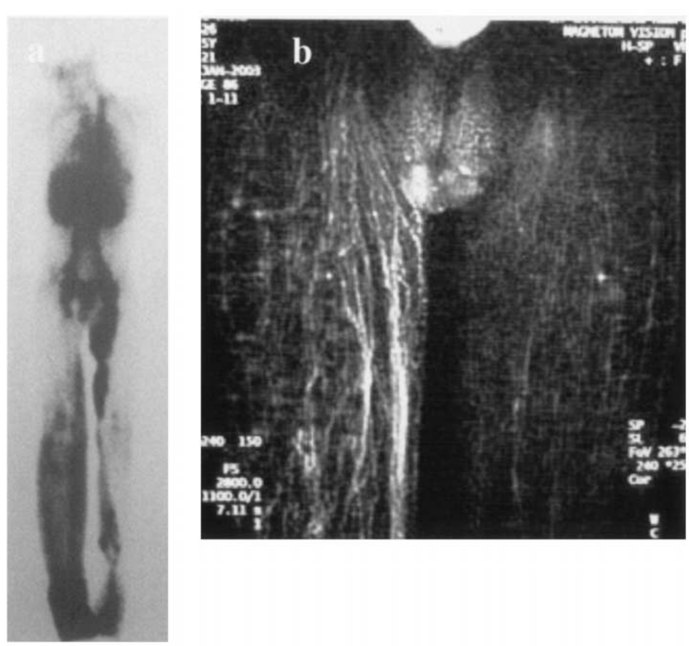

Fig 5. Lymphedema tarda in a 15-year-old boy. **a,** Lymphoscintigraphy demonstrates that the radiotracer accumulates in the right leg without identified lymphatic collectors in the thigh. **b,** Stereo magnetic resonance imaging provides clear picture of bundles of lymphatic collectors in the thigh with a significantly increased number and diameter.

Table II. Comparison of the imaging features of 39 lymphatic anomalies in 3D MRI and LSG

Variable	*3D MRI*	*LSG*
Normal limbs	No lymphatics visualized; regional nodes are visible	One or two lymphatics, but the trunks are not clear; regional and central nodes always appear
Primary lymphedema		
Hypoplasia/aplasia	No visible lymphatic collectors; small lymphatic channels or edema fluid in subcutis	No patent lymphatic vessel is visible, scanty or no lymph nodes; dermal back flow in distal part of the affected limb
Hyperplasia	Enlarged nodes with increased number; superficial lymphatic varices with increased number; very dense iliac and lumbar trunks in front of the lumbar vertebrae, often bilateral; extremely dilated segments of trunks with accumulated lymph in chylous reflux	Strong radioactivity in the region of node and trunks but hard to identify individual vessels and nodes; the isotope is dispersed in skin of distal part without vessel shown in thigh; in chylous reflux a dark mass is seen in pelvic and abdominal cavities
Secondary lymphedema		
Malignant tumor	Enlarged regional nodes, edema in the subcutis; no visible collectors; tumor was found in pelvic cavity	Dermal back flow in the limb, often proximally; reduced number or absence of regional nodes; blockage of lymph flow at the level of metastatic node
Trauma	No visible lymphatics; high signals on T2 weighted imaging represent numerous small lymphatics or accumulated edema fluid above the deep fascia	Reduced number of nodes; no or single collector; dermal back flow in the affected limb
Lymphedema in KTS	Subcutaneous thickness with high and lower signal structure at T2 weighted imaging represent abnormal blood vasculature and stagnated lymph; no visible lymphatic collectors	No lymphatic collector or nodes were displayed, or a decreased number of regional nodes; isotope deposited in the distal part of the affected limb; enlarged deep femoral vein and tortuous saphenous vein

3D MRI, Three-dimensional magnetic resonance imaging; *LSG,* lymphoscintigraphy; *KTS,* Klippel-Trenaunay syndrome.

treatment was used in the postoperative period to improve the function of the remaining lymphatic vessels.

Both LSG and 3D MRI are safe, noninvasive or minimally invasive, and easy to repeat. LSG imaging has the limitation of contrast injection (usually one point per limb; only the vessels and nodes draining contrast media from that point can be observed), whereas 3D MRI has the possibility for a wide-range visualization, no need for contrast material, and a lack of ionizing radiation. In the diagnosis of a swollen limb, it is very helpful to observe the location and amount of edema fluid. On 3D MRI, the motionless water, ie, diffuse dermal and cutaneous edema, and sequestered lymph are clearly displayed, and the location and severity of edema and other pathologic changes such as fat deposition in the tissues can be easily identified. Through fat suppression, MRI can easily differentiate lymphedema from lipoedema. LSG cannot directly display water in the tissue. The most common image of lymphedema on LSG studies is dermal backflow, which is tracer diffused in the skin vessels without lymphatic collectors or contrast stagnated in the injection site without transportation. Thus, LSG cannot provide information other than the lymphatic vessels.

Functional evaluation is also an important goal for lymphatic imaging. On LSG imaging, the display of regional nodes after uptaking of contrast is the functional proof of the system. In a subtype of primary lymphedema (Table II), LSG displays not only superficial lymphatics and nodes, but also the deep lymph-draining system, the popliteal node, and its afferent collectors. This phenomenon is due to the functional disability of the superficial lymphatics; therefore, the lymph flow is drained through the deep system. Edema happens because neither of the systems is efficient at transporting the lymph load. Noncontrast MRI can display lymph nodes but cannot make a functional assessment of the lymphatics and nodes to identify the source of lymph to the node (superficial or deep). Although LSG has proven to be effective in functional imaging without the drawbacks of conventional lymphography, exposure of the lymphatic vessels, pressure injection, contrast-induced lymphatic injury, low resolution, and requirements for handling radioactive isotopes have hampered its use. Contrast MRI might be the substitution of LSG for creating functional imaging concerning lymphatic transportation and nodal uptake. Experimental studies with the use of superparamagnetic contrast agents such as gadolinium-albumin compounds and ferrous oxide contrast MRI have shown an ability to diagnose diseases of the lymphatic system.[3,4] If this technique could be practiced clinically, the combination of contrast-enhanced and 3D MRI might generate an image of lymphatic function superimposed on detailed anatomy without the real or imagined risks imposed by radiation exposure with LSG and might further improve the diagnostic potential of lymphatic diseases. Until this can be realized, LSG and 3D MRI should still be practiced as complementary diagnostic procedures. As a dynamic measurement, LSG provides an image that reflects lymph flow, ie, the blockage of lymph flow or dysfunction of the lymphatic system. For a correct diagnosis, it may not be enough. If the patient has chylous reflux or if LSG imaging shows massive dermal backflow or strong radioactive accumulation in the body, noncontrast MRI should be used to demonstrate the anomalies of lymph stagnated vessels for the proper treatment.

Magnetic resonance angiography is a useful method for the assessment of peripheral vascular disease.[5] Noncontrast or contrast-enhanced magnetic resonance angiography is integrated into routing diagnostic modality. Lymphatic MRI may give us an opportunity to combine the inspection of the two circulation systems. Blood and lymph vascular systems can be scanned during the same procedure but under different sequences. The collected data may further be analyzed to reconstruct the 3D images. This might be helpful in the diagnosis of combined malformations of blood and lymphatic vessels, such as the Klippel-Trenaunay syndrome, and other congenital vascular malformations, such as the Proteus syndrome, in which the relationship of the lymphatic and blood vascular systems needs to be examined.

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