의학 석사 학위논문

자기공명 림프관조영술을 이용한 상지에서의 림프부종 평가: 림프관 신티그래피와의 비교

Evaluation of lymphedema in upper extremities by MR lymphangiography: comparison with lymphoscintigraphy

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서울대학교 대학원

의학과 영상의학 전공

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이 논문을 의학석사 학위논문으로 제출함

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2017년 1월

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Abstract

Evaluation of lymphedema in upper extremities by MR lymphangiography: comparison with lymphoscintigraphy

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Purpose: To validate usefulness of magnetic resonance (MR) lymphangiography for evaluation of peripheral lymphedema in upper extremities by comparison with lymphoscintigraphy.

Materials and Methods: This prospective study had institutional review board approval and written informed consent was obtained from all patients. Initially, protocol of MR lymphangiography for upper extremity was established in seven healthy volunteers with 3.0T fat-saturated three-dimensional gradient-echo MR after gadobutrol injection. Then six patients with unilateral lymphedema of the upper extremities were examined with MR lymphangiography and lymphoscintigraphy, and the results were correlated with each other.

Results of both techniques were separately evaluated by two radiologists and a nuclear physician in terms of delay and pattern of lymphatic drainage, conspicuity of the visualization of lymph vessels and axillary lymph nodes, and enhancing levels of lymphatic system. We calculated sensitivity and specificity of both techniques by using a combined consensus of clinical presentations and imaging findings of the patients determined by the radiologist, nuclear physician, and referring physician as the reference standard. We also evaluated correlation of both techniques.

Results: MR lymphangiography and lymphoscintigraphy showed delayed drainage and partially diffuse drainage in all patients. Axillary lymph node was not visualized on both techniques. MR lymphangiography demonstrated lymphangiectasia with moderate conspicuity in all six patients while lymphoscintigraphy showed lymph vessels with moderate conspicuity in one patient, poor conspicuity in four patients, and no visualization in the other patient. Both MR lymphangiography and lymphoscintigraphy showed lymph vessels up to upper arm in one patient, forearm in four patients, and only hand in the other patient. MR lymphangiography showed sensitivities of 100% for all four categories, while lymphoscintigraphy yielded a sensitivity of 83.3% for delineation of lymph vessels and 100% for the other three categories. Specificity of MR lymphangiography was 85.7% for delay of drainage and 100% for other three categories, while lymphoscintigraphy showed specificity of 100% for delay of lymphatic drainage, depiction of lymph vessels and enhancement of axillary lymph nodes, and 66.7% for pattern of lymphatic drainage. Delay and pattern of drainage was same in 83.3% and non-visualization of axillary LNs was indistinguishably noted in all patients on both techniques. Anatomic level of enhanced lymph vessel

was identical in 66.7% of the patients.

Conclusion: MR lymphangiography showed better performance for depiction of lymph vessels. MR lymphangiography and lymphoscintigraphy yielded same results in all or most patients for evaluation of axillary lymph nodes enhancement and lymphatic drainage in upper extremity.

Keywords: MR lymphangiography, Lymphedema, Upper extremity, Lymphoscintigraphy

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INTRODUCTION

Peripheral lymphedema is a chronic and progressive swelling of extremity caused by failure of the lymphatic drainage system. In upper extremity, it is a common complication after breast cancer surgery that up to 42 percent of patient who had underwent breast cancer surgery including axillary lymph node dissection suffers from it (1). Although conservative management such as complete decongestive therapy has been the primary treatment of choice for peripheral lymphedema, many patients with long-standing symptoms are unresponsive to conservative therapy and may benefit from emerging operative intervention including lymph node transplantation or lymphaticovenous anastomosis (2, 3). These promising microsurgical methods, however, require precise anatomic information of lymph vessels or nodes for excision of non-functioning lymphatic segment and reconstruction of lymphatic drainage (4).

Magnetic resonance (MR) lymphangiography with gadolinium chelates yields isotropic images with high spatial resolution that enable multiplanar reconstruction and facilitate identification of delicate lymphatic vessels and lymph nodes feasible for transplantation (5, 6). In addition to diagnostic value, safety of the MR lymphangiography has been proved as well (7). Currently, lymphoscintigraphy is widely used in patients with peripheral lymphedema. Despite limited temporal and spatial resolution, and risk of exposure to ionizing radiation, lymphoscintigraphy has high

specificity for lymphatic system by virtue of the colloid-binding tracer (8). In contrast, gadolinium chelates used in MR lymphangiography are so small and water soluble that contamination of images by venous drainage might be possible (4). As these two modalities differ in strengths and weaknesses, it is warranted to compare these two methods to achieve a better comprehension of lymphatic system. However, evaluation of MR lymphangiography for lymphedema in comparison with lymphoscintigraphy has only performed in lower extremity (5). Therefore, the purpose of this study was to validate usefulness of MR lymphangiography for evaluation of peripheral lymphedema in upper extremities by comparison with lymphoscintigraphy.

MATERIALS AND METHODS

The institutional review board of Seoul National University Hospital approved this prospective study. Written informed consent was obtained from all patients.

Patients

Six patients with upper extremity lymphedema were enrolled in this prospective study by the surgeon (H.J. with 26 years of experience in plastic surgery) of department of plastic surgery between November 2015 and April 2016 and referred for MR lymphangiography and lymphoscintigraphy. The inclusion criteria were as follows: the patient (a) had undergone surgery for breast cancer (Table 1); (b) had developed lymphedema at the ipsilateral upper extremity with a diagnosis of lymphedema clinically established according to the criteria proposed by International Society of Lymphology classification from 2013 (9) (Table 2). Exclusion criteria were (a) contraindications to gadolinium based contrast medium, such as decreased renal function with a glomerular filtration rate < 30 mL/min, allergy, pregnancy as well as (b) contraindications for MR imaging such as claustrophobia or MR-incompatible devices such as cardiac pacemaker, and there was no patient excluded in this study based on the criteria. As a result, a total of six patients with upper extremity lymphedema (all female patients; mean age, 61 ± 9 [standard deviation] years; age range, 48-71 years) were included in this study.

Control participants

Seven healthy volunteers with no known underlying disease (one male and six female volunteers; mean age, 28 ± 5 years; age range, 21 – 37 years) were enrolled in this study. MR lymphangiography was performed in bilateral upper extremities in one male volunteer and in unilateral upper extremity in the other six female volunteers. Therefore, a total of eight upper extremities were enrolled.

Lymphoscintigraphy

For LS, 110 MBq of 99mTc-labeled nanocolloid (human serum albumin) (Nanocoll; GE Healthcare, Munich, Germany) was injected into the subcutaneous tissue of the first interdigital space of each hand. The patients then stimulated lymphatic drainage by following a semistandarized protocol of active muscular exercise involving contraction of the forearm for approximately 10 minutes after the radiopharmaceutical was injected. The sites of injection were covered with lead plates.

Sequential images with a scan speed of 5 cm/min from hand to shoulder were acquired 10 minutes after injection by using a large – field-of-view gamma camera (e.cam Dual-Head; Siemens Healthcare, Erlangen, Germany) fitted with a low-energy, all-purpose collimator with a 256 × 1024 matrix. Acquisition was stopped after 2 hours or when the axillary lymph nodes were detected (approximately 60 – 120 minutes after injection).

MR Imaging

MR Protocol

To establish adequate parameters and delay times after contrast injection, MR lymphangiography was performed in the seven healthy volunteers prior to application in patients. All MR lymphangiography imaging was performed at a 3T scanner (Magnetom Trio; Siemens Healthcare Erlangen, Germany) using two body 16-element coils from the same manufacturer (Siemens Healthcare, Erlangen, Germany).

Prior to the contrast injection, a T2-weighted coronal rapid acquisition with spectral fat saturation and sampling perfection with application optimized contrasts using different flip angle evolution (SPACE) (repetition time msec/echo time msec, 4000/221; flip angle, 120°; section thickness, 1.5 mm; in-plane resolution, 1.0 × 1.4 mm^2; field of view, 350 mm; intergrated parallel acqusition technique with acceleration factor of three) was performed at the upper arm and forearm level for the evaluation of the extent of lymphedema.

Subsequently, MR lymphangiography was performed before and after injection of contrast agent by using a coronal T1-weighted three-dimensional gradient-echo sequence (three-dimensional fast low-angle shot) with spectral fat saturation. The sequence parameters were as follows: 3.5/1.3; flip angle, 14.9°; number of sections, 112; number of signals acquired, one; section thickness, 1.2 mm; intersection gap, 0 mm; bandwidth, 511 Hz/pixel; field of view, 279 mm; matrix, 288 × 202; in-plane resolution, 1.0 × 1.4 mm^2; and

acquisition time, 70 seconds. Parallel imaging by using the intergrated parallel acqusition technique was applied at an acceleration factor of two, with 24 reference lines and auto - matrix coil mode. We examined upper extremity at two subsequent anatomic levels: first, hand with forearm, and second, upper arm with axilla. The total acquisition time of two levels at each phase was approximately 5 minutes and the acquisition time for whole dynamic study was 70 minutes.

MR Imaging in Patients

After establishment of the protocols, MR lymphangiography was performed in six patients. Patients underwent lymphoscintigraphy prior to MR lymphangiography on a separate day because of organizational reasons. Time interval between lymphoscintigraphy and MR lymphangiography ranged from 3 days to 613 days (mean value, 116 days ± 244 [standard deviation]).

Contrast Agent Administration

A solution of 4.5 mL of gadobutrol (Bayer Schering, Leverkusen, Germany) was mixed with 0.5 mL lidocaine (Daihan Pharma, Seoul, Korea) for local anesthesia. One milliliter of this mixture was injected intracutaneously in the four interdigital spaces of the hand of the affected extremity by using 24-gauge cannulas inserted at an angle of about 10 - 15° to form a wheal. The injection site was massaged for 2 minutes and then MR lymphangiography was started

immediately. The patient was encouraged to inspect the injection site and to visit emergency department if he or she feels any significant discomfort at the injection site.

Image Analysis

Assessment of the results of MR lymphangiography and lymphoscintigraphy was performed separately. Two radiologists (R.E.Y., J.S.B., with 2 years of MR lymphangiography experience, respectively), blinded to the findings on lymphoscintigraphy, evaluated MR lymphangiography images in consensus and a nuclear medicine physician (G.J.C., with 19 years of lymphoscintigraphy experience), blinded to the findings on MR lymphangiography, assessed lymphoscintigraphy images. For comprehensive assessment of the lymph vessels, we reconstructed maximum intensity projections from MR lymphangiography data sets with thin-section (section thickness, 5 mm) at a workstation (MBBW VB17; Siemens Healthcare, Erlangen, Germany). Two sets of images of forearm including hand and upper arm including axilla were composed to generate a long-arm display by using software (Syngo Composing Task Card; Siemens Healthcare, Erlangen, Germany). The lymphoscintigraphy images were evaluated by using a dedicated workstation (Phoenix-PACS; Phoenix, Freiburg, Germany).

Given that there is no established standard reporting guidelines for upper extremity lymphedema, we adopted those for

lower extremity lymphedema to perform visual assessment of all MR lymphangiography and lymphoscintigraphy images (5). A four-point scale was used to assess the pattern of drainage (score 0, no drainage; score 1, diffuse enhancement, interstitial; score 2, partially diffuse enhancement, interstitial and vascular enhancement; score 3, directed, vascular enhancement), the delay of drainage (score 0, no drainage; score 1, substantial delay [axillary level > 60 minutes for MR lymphangiography and > 120 minutes for lymphoscintigraphy]; score 2, slight delay [axillary level > 20 minutes for MR lymphangiography and > 60 minutes for lymphoscintigraphy]; score 3, no delay [lymph vessel enhancement in the first series of images, reaches axillary level < 20 minutes for MR lymphangiography and < 60 minutes for lymphoscintigraphy]) and the depiction of lymph vessels (score 0, no lymph vessels; score 1, poor conspicuity; score 2, moderate conspicuity; score 3, good conspicuity). We used a four-point scale instead of the three-point scale (5) to evaluate the depiction of lymph vessels because 'moderate conspicuity' was so broad that it also included barely visible lymph vessels. A three-point scale was used for enhancement of axillary lymph nodes (score 0, no lymph nodes; score 1, moderate conspicuity; score 2, good conspicuity). Anatomic levels up to which lymph vessel enhancement was visible were also evaluated based on a four-point scale (level 0, hand; level 1, forearm; level 2, upper arm; level 3, axilla). In addition, the diameter of lymph vessels was measured in both healthy volunteers and patients on MR lymphangiography.

Statistical Analysis

Sensitivities and specificities of MR lymphangiography and lymphoscintigraphy for abnormalities: 1) delay of drainage, 2) abnormal pattern of drainage, and 3) abnormal lymph nodes, and 4) abnormal lymph vessels were calculated. Fisher's exact test was performed to compare sensitivities of both imaging modalities. The reference standard was established by the three readers (R.E.Y., J.S.B., and G.J.C.) and the referring physician (H.C.) based on combined data of both clinical presentation and imaging findings on MR lymphangiography and lymphoscintigraphy. Comparison of diameter of lymph vessels in healthy volunteers and patients was performed using Mann - Whitney test. Analysis of data was performed with MedCalc version 14.8.1 (MedCalc Software, Mariakerke, Belgium).

RESULTS

Examinations were well tolerated in all volunteers and all patients. There was no complication at the injection site and no side effects related to the injected gadobutrol mixture.

Normal Drainage

Failure of injection of contrast agent was occurred in one of the normal volunteers in whom no lymphatic drainage was demonstrated. Thus, normal drainage was evaluated in seven normal upper extremities in six volunteers for MR lymphangiography and six unaffected upper extremities in six patients for lymphoscintigraphy. One patient had scintigraphic images of forearm only and therefore delay of lymphatic drainage, enhancement of axillary lymph nodes, and anatomic level of lymphatic drainage were not assessed in the patient on lymphoscintigraphy.

Enhancement of lymph vessels was observed in early phases of MR lymphangiography images in all seven normal upper extremities. Normal lymph vessels demonstrated moderate enhancement and beaded appearance, whereas veins showed smooth contour (Fig 1). On lymphoscintigraphy, normal lymph vessels were visualized in all unaffected extremities of six patients. Regarding the delay of drainage, no delay or slight delay was observed in six and one normal extremities on MR lymphangiography, respectively. Five unaffected extremities showed no delay on lymphoscintigraphy. For

the pattern of drainage, all seven extremities with visible lymph vessels demonstrated directed, vascular enhancement on MR lymphangiography, while four and two patients had directed and partially diffuse enhancement on lymphoscintigraphy, respectively. Axillary lymph nodes were visualized in all seven healthy extremities on MR lymphangiography and all unaffected extremities on lymphoscintigraphy. As for the depiction of lymph vessels, MR lymphangiography demonstrated good conspicuity in all seven visible instances, while lymphoscintigraphy yielded moderate conspicuity or poor conspicuity for three unaffected extremities each. Anatomic level of visible lymph vessels was also higher on MR lymphangiography with axillary level in all seven traceable cases, compared with one of axillary level and four of forearm level in five unaffected extremities on lymphoscintigraphy.

Imaging Findings in Patients

Imaging features of MR lymphangiography and lymphoscintigraphy in the affected upper extremities of six patients are summarized in Table 3.

Delay of Drainage

From medical photographs of the patients which suggested severe lymphedema, delay of lymphatic drainage was expected in all patients. On MR lymphangiography, all six patients showed delayed drainage. Meanwhile, five patients showed delayed drainage and one patient

showed no drainage on lymphoscintigraphy.

Drainage Pattern

Clinically, all patients were diagnosed as having advanced lymphedema (stage II). All patients showed abnormal pattern of lymphatic drainage which consisted of interstitial and vascular enhancement (partially diffuse, score 2) on MR lymphangiography, while five patients showed partially diffuse drainage and the other patient demonstrated no drainage on lymphoscintigraphy (Fig 2). Diffuse interstitial enhancement is reflective of leakage of the gadobutrol or radiotracer into the subcutaneous tissue which is caused by failure of lymphatic drainage system. This phenomenon was observed within 15 minutes after gadobutrol injection on MR lymphangiography and approximately 30 minutes after the radiotracer injection on lymphoscintigraphy in all patients. Insufficient fat saturation was present in all MR lymphangiography examinations; however, it did not impede interpretation of the results (Fig 3).

Lymph Nodes

There was no definite enhancement of axillary lymph nodes in all patients at MR lymphangiography. This result was consistent with the finding of lymphoscintigraphy which showed no uptake of radiotracer by lymph nodes at the affected side.

Depiction of Lymph Vessels

With MR lymphangiography, lymph vessels were delineated in all six patients with moderate conspicuity. Compared with those of healthy volunteers, typical beaded appearance of lymph vessels and multifocal dilatation of some lymph vessels (lymphangiectasia) were more prominently demonstrated in patients. On lymphoscintigraphy, lymph vessels were depicted in 5 of 6 patients (moderate conspicuity in 1 and poor conspicuity in 4) (Fig 5).

Levels with Lymph Vessel Enhancement

Lymph vessels were demonstrated up to the upper arm level in one patient, forearm level in four patients, and only hand level in the other patient on MR lymphangiography. On lymphoscintigraphy, lymph vessels were visible up to the upper arm level in one patient, forearm level in three patients, and hand level in one patient. Axillary lymph vessels were not detected on both MR lymphangiography and lymphoscintigraphy.

Diagnostic Performances of MR Lymphangiography and Lymphoscintigraphy

We established standard of reference based on the clinical finding and combined results of MR lymphangiography and lymphoscintigraphy. We evaluated sensitivity of both imaging studies for the affected extremity, whereas we assessed specificity of MR lymphangiography for healthy volunteers and that of lymphoscintigraphy for unaffected extremity. MR lymphangiography showed sensitivities of 100% (6 of

6) for all four categories, while lymphoscintigraphy yielded a sensitivity of 83.3% (5 of 6) for delineation of lymph vessels, and sensitivities of 100% for the other three categories (for drainage pattern, 6 of 6; for delay of drainage and enhancement of axillary lymph nodes, 5 of 5). Specificity of MR lymphangiography was 85.7% (6 of 7) for delay of drainage and 100% (7 of 7) for the other three categories. On the contrary, lymphoscintigraphy showed specificity of 100% (for depiction of lymph vessels, 6 of 6; for delay of drainage and enhancement of axillary lymph nodes, 5 of 5) for delay of lymphatic drainage, enhancement of axillary lymph nodes and depiction of abnormal lymph vessels, and 66.7% (4 of 6) for pattern of lymphatic drainage. Findings are summarized in Table 4. On Fisher's exact test, MR lymphangiography showed higher sensitivity than lymphoscintigraphy in depiction of abnormal lymph vessels without statistical significance ($P > .050$).

Correlation between MR lymphangiography and lymphoscintigraphy

MR lymphangiography and lymphoscintigraphy yielded same results in 80% (4 of 5) of the patients for delay of drainage. The concordance rate between the two imaging modalities was 83.3% (5 of 6) of the patients for pattern of drainage. Both techniques identically demonstrated no enhancement of axillary lymph nodes in all patients. Depiction of lymph vessels in both imaging modalities was relatively discordant among patients: only one of six patients

(16.7%) had same result on MR lymphangiography and on lymphoscintigraphy. Anatomic level of lymph vessels showed 66.7% of concordance rate between both techniques.

Diameter of lymph vessels

The mean diameter of lymph vessels in healthy volunteers was 1.98 ± 0.30 mm (range, 1.58-2.48 mm), whereas those measured in patients was 3.06 ± 0.78 mm (range, 2.22-4.20 mm). Mann - Whitney test revealed that the diameter of lymph vessels was greater in patients than those in volunteers with statistical significance (p = 0.0047).

DISCUSSION

Lymphedema in upper extremity is a chronic, debilitating condition and in many cases, is a devastating complication in patients who underwent axillary lymph node dissection for breast cancer. Although not life-threatening, it is a cosmetically distressing condition and poses a significantly negative effect on patients in psychosocial aspect (10). Traditionally, lymphoscintigraphy has been performed as a primary imaging modality for evaluation of peripheral lymphedema in spite of limited spatial resolution and radiation hazard. Recently, MR lymphangiography is gaining popularity in assessment of lymphedema owing to excellent spatial resolution and clear concordance with lymphoscintigraphy has been reported only in lower extremities (5). Therefore, comparison of MR lymphangiography and lymphoscintigraphy for lymphedema in upper extremity is warranted.

One might argue that lymphoscintigraphy has advantage in selective uptake of colloid particles by lymphatic system, whereas gadolinium chelates used in MR lymphangiography are small enough to penetrate into microcapillary and cause venous contamination (4). Although venous enhancement was noted with MR lymphangiography in the present study, it did not substantially impede interpretation of the result. Morphologically, the margins of veins were straight and smooth, while those of lymph vessels were irregularly dilated and tortuous. Regard to dynamics, venous flow was faster than lymphatic flow and therefore venous enhancement disappeared earlier in the

dynamic study images. Because of these differences between MRL and LS, there was no significant difficulty in assessing lymph vessels in the background of venous enhancement.

To date, most studies on MR lymphangiography reported that the advantage of MR lymphangiography lies in acquisition of images with high spatial resolution (5, 6, 11). Our study also demonstrated better depiction of lymph vessels with MR lymphangiography than with lymphoscintigraphy. This benefit could be exploited especially when planning microsurgery for lymphedema including transplantation of lymph vessels or lymph nodes. In addition, isotropic images of MR lymphangiography enables reconstruction of images with arbitrary planes and thereby facilitate microsurgery for lymphedema, which could not be expected from lymphoscintigraphy (12). Furthermore, MR lymphangiography provides additional information of the arm such as the severity of lymphedema, degree of fat accumulation, and volume of muscle of the affected extremity, thereby giving aid for planning of surgery (13). Lastly, MR lymphangiography is free from the issue of ionizing radiation.

The sensitivities of MR lymphangiography were 100% for all four categories in our study. This high performance could be resulted from small number of patients and selection of patients with long-standing, severe peripheral lymphedema. It is in concordance with near-perfect sensitivity in evaluation of lymphedema in lower extremity (5). According to the previous studies, lymphoscintigraphy

was expected to demonstrate reasonable sensitivity because it was a primary imaging method in evaluation of peripheral lymphedema (14). As expectedly, lymphoscintigraphy yielded sensitivities of 100% in all four categories but depiction of lymph vessels; 83.3% of sensitivity for delineation of lymph vessels was noted in the present study. This discrepancy is probably caused by the lower spatial resolution of lymphoscintigraphy compared with MR lymphangiography. For example, delay and pattern of drainage are less dependent on spatial resolution than depiction of lymphatic vasculature and show the same results.

In the present study, axillary lymph nodes at the affected side were not visualized on both techniques, which is in concordance with previous studies: axillary lymph node in lymphedema is weakly demonstrated or not detectable with both MR lymphangiography and lymphoscintigraphy (14). This result is not surprising as all six patients in our study had undergone axillary lymph node dissection and therefore the number of their axillary lymph node would have been markedly reduced. In addition, there could have been injuries to lymph vessels that led to blockage to drainage to axillary lymph nodes.

Among the five categories of the result of the MR lymphangiography and lymphoscintigraphy, delay and pattern of drainage showed same results in 80% and 83.3%, respectively, and non-visualization of axillary LNs was also equivalently noted in both

modalities. Anatomic level of enhanced lymph vessel was same in 67% of the patients, which is in concordance with the result performed in the lower extremity that showed good correlation (κ = 0.77) (5). In addition, the results of the remaining patients differed by only one point in four-point scale. Therefore, better agreement would have been achieved if there were a larger number of patients.

Although there had been studies on size of lymph vessels in lower extremity in healthy population or patients with lymphedema, there had been no report on upper extremity (15, 16). In our study, the diameter of lymph vessels in upper extremity of patients (mean 3.06 ± 0.78 mm) was greater than those of volunteers (mean 1.98 ± 0.30 mm). This quantitative result is in accordance with the qualitative depiction of dilated lymph vessels in patients with progressed lymphedema on MR lymphangiography. On lymphoscintigraphy, lymph vessels of affected extremity were visualized as only faint dots and were not adequate for measurement of diameter.

There are some limitations in our study. First, the number of patients was small and thus the statistical significance of the results was limited. Further investigation with large number of patients is warranted. Second, MR lymphangiography was only performed at upper arm in volunteer group, thereby excluding hand and forearm level. Therefore, the result of MR lymphangiography at the level of below elbow could not be compared with those in control group.

Third, there were a few issues related to intracutaneous gadobutrol injection. Although there have been studies that reported the safety of the intracutaneous injection of gadobutrol (5, 7), it has not been approved yet. This issue of off-label use of gadobutrol should be settled down. In addition, gadobutrol might not have been injected strictly intracutaneously because of severe edematous thickening of interdigital soft tissue of the patients. This could have led to discrepancy in the amount of injected gadobutrol among patients and venous contamination. Lastly, insufficient fat saturation was present around the margin of the coil on all MR lymphangiography examinations in our study. Although interpretation of the results was not impeded by virtue of comparison with precontrast images, those artifact should be avoided for easier assessment of the result of MR lymphangiography.

In conclusion, MR lymphangiography showed better performance for depiction of abnormal lymph vessels. MR lymphangiography and lymphoscintigraphy yielded same results in all or most patients for evaluation of axillary lymph nodes enhancement and lymphatic drainage in upper extremity. MR lymphangiography may play a complementary role in the imaging of peripheral lymphedema in upper extremity.

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Table 1. Patient Information

Patient index	Age	Sex	Underlying disease	Treatment for underlying disease	Laterality of lymph-edema to affected side of breast cancer	Stage of lymph-edema
1	66	female	breast cancer	modified radical mastectomy with axillary lymph node dissection (2003)	ipsilateral	II
2	48	female	breast cancer	left quadrantectomy with axillary lymph node dissection (2007)	ipsilateral	II
3	56	female	breast cancer	modified radical mastectomy with axillary lymph node dissection (2011)	ipsilateral	II
4	71	female	breast cancer	modified radical mastectomy with axillary lymph node dissection (1999)	ipsilateral	II
5	55	female	breast cancer	modified radical mastectomy with axillary lymph node dissection (1998)	ipsilateral	II
6	71	female	breast cancer	modified radical mastectomy with axillary lymph node dissection (2004)	ipsilateral	II

Table 2. 2013 Classification of the International Society of Lymphology

Stage	Clinical Presentation	Pitting
I	early accumulation of fluid relatively high in protein content which subsides with limb elevation	Pitting may occur
II	limb elevation alone rarely reduces tissue swelling and pitting is manifest	The limb may or may not pit
III	lymphostatic elephantiasis; trophic skin changes such as acanthosis, further deposition of fat and fibrosis, and warty overgrowths have developed	Pitting can be absent

Table 3. Results of MR lymphangiography and lymphoscintigraphy

Category and Examination	Score 0	Score 1	Score 2	Score 3
Delay of drainage				
MR lymphangiography		6		
Lymphoscintigraphy	1	4		
Drainage pattern				
MR lymphangiography			6	
Lymphoscintigraphy	1		5	
Enhancement of lymph nodes				
MR lymphangiography	6			
Lymphoscintigraphy	5			
Depiction of lymph vessels				
MR lymphangiography			6	
Lymphoscintigraphy	1	4	1	
Anatomic levels				
MR lymphangiography	1	4	1	
Lymphoscintigraphy	1	3	1	

Note.—MR: magnetic resonance. Data are numbers of patients. Findings were assigned scores as follows: For delay of drainage: score 0, no drainage; score 1, substantial delay; score 2, slight delay; and score 3, no delay. For drainage pattern: score 0, no drainage; score 1, diffuse; score 2, partially diffuse; and score 3, directed. For enhancement of lymph nodes: score 0, no enhancement; score 1, moderate conspicuity; and score 2, strong conspicuity. For depiction

of lymph vessels: score 0, no depicted vessels; score 1, poor conspicuity; score 2, moderate conspicuity; and score 3, good conspicuity. For anatomic levels: score 0, hand; score 1, forearm; score 2, upper arm; and score 3, axillary level.

Table 4. Diagnostic performance of MR lymphangiography and lymphoscintigraphy

Category	Sensitivity		Specificity	
	MR lymphangiography	Lymphoscintigraphy	MR lymphangiography	Lymphoscintigraphy
Delay	100% (6/6)	100% (5/5)	85.7% (6/7)	100% (5/5)
Pattern	100% (6/6)	100% (6/6)	100% (7/7)	66.7% (4/6)
Enhancement of lymph node	100% (6/6)	100% (5/5)	100% (7/7)	100% (5/5)
Depiction of lymph vessels	100% (6/6)	83.3% (5/6)	100% (7/7)	100% (6/6)

Note.－MR: Magnetic resonance. Data are percentages that was calculated with the numbers in parentheses.

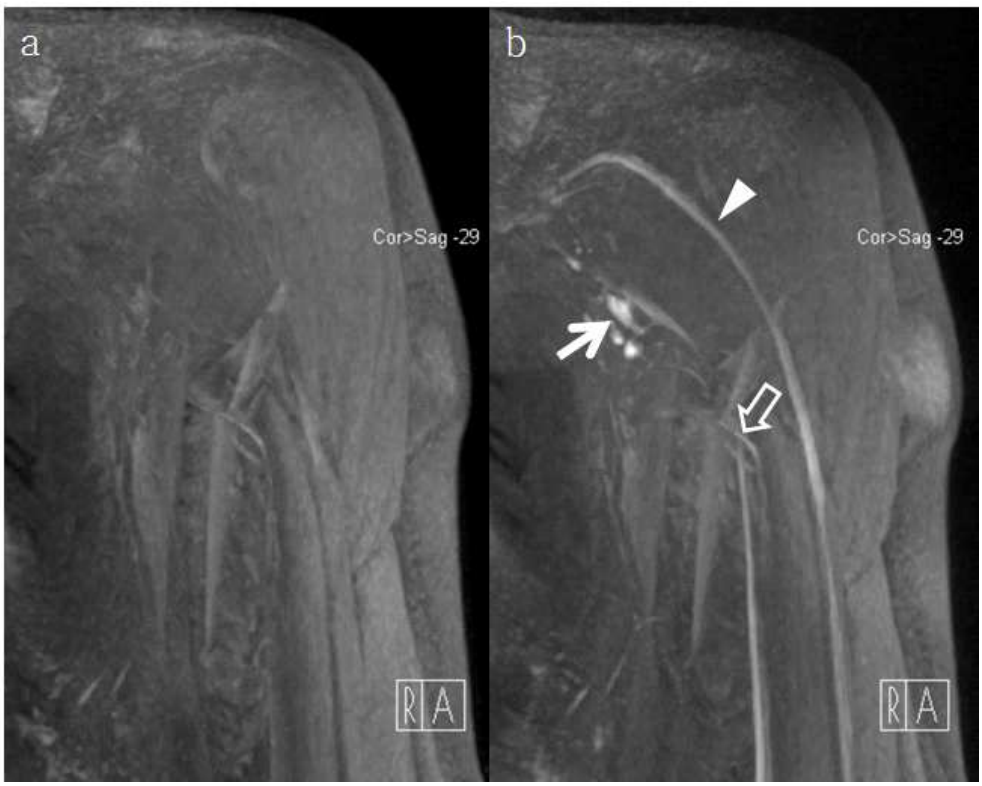

Figure 1. Visualization of a lymph vessel and node in the left upper extremity of 20-year-old female volunteer. The MR lymphangiography images acquired before (a) and 5 minutes after gadobutrol injection (b) depict brightly enhancing axillary lymph nodes (arrow). The lymph vessels (empty arrow) showed a normal appearance. Physiologic venous enhancement (arrowhead) was seen as a relatively broad line with lesser degree of enhancement as compared with axillary lymph nodes.

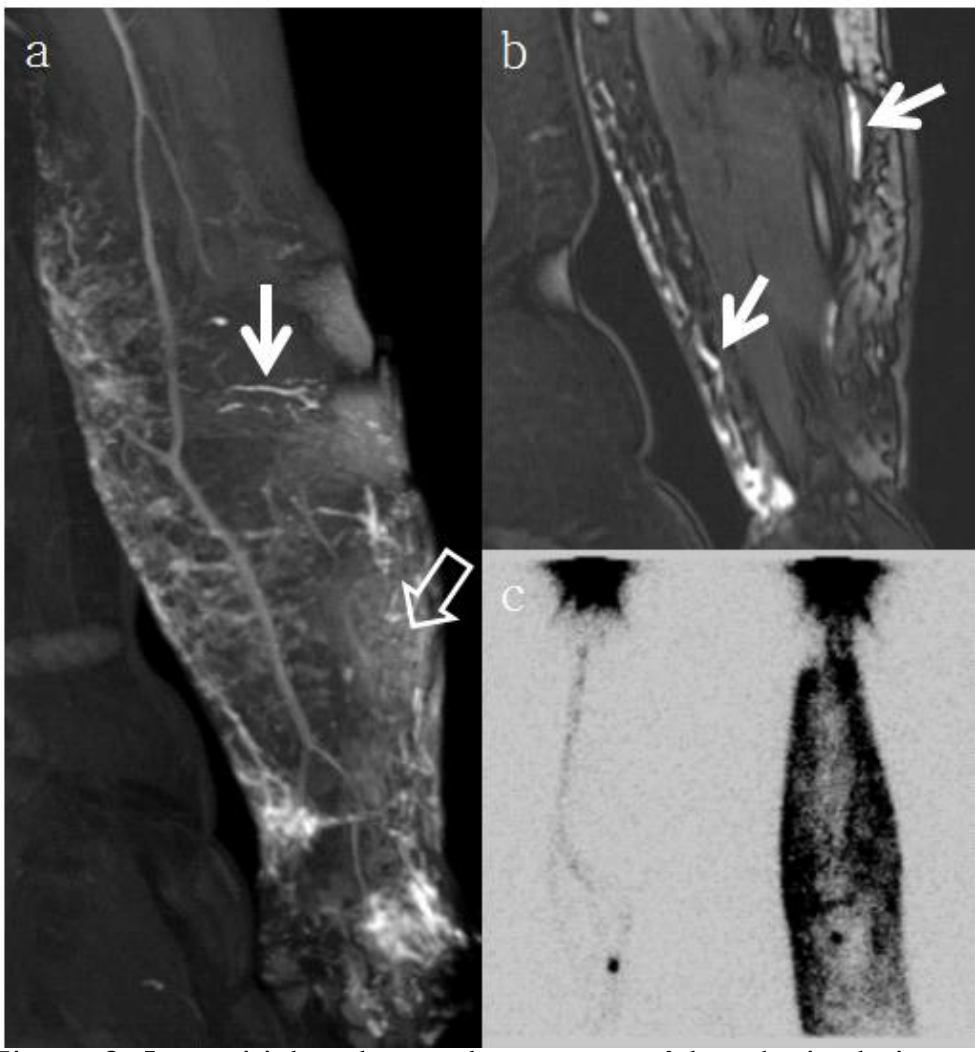

Figure 2. Interstitial and vascular pattern of lymphatic drainage in a 48-year-old female with stage II lymphedema of the left arm. (a, b) Beaded, dilated appearance of lymph vessels (lymphangioectasia) (solid arrow) and diffuse, interstitial enhancement (open arrow) around lymph vessels are visualized on maximum intensity projection imagges of MR lymphangiography 15 minutes after gadobutrol injection (a). The anatomical depth of lymph vessels (solid arrow) is demonstrated on coronal images (b).

Lymphoscintigraphy image acquired 2 hours after radiotracer injection shows diffuse lymphatic drainage at the left forearm (c).

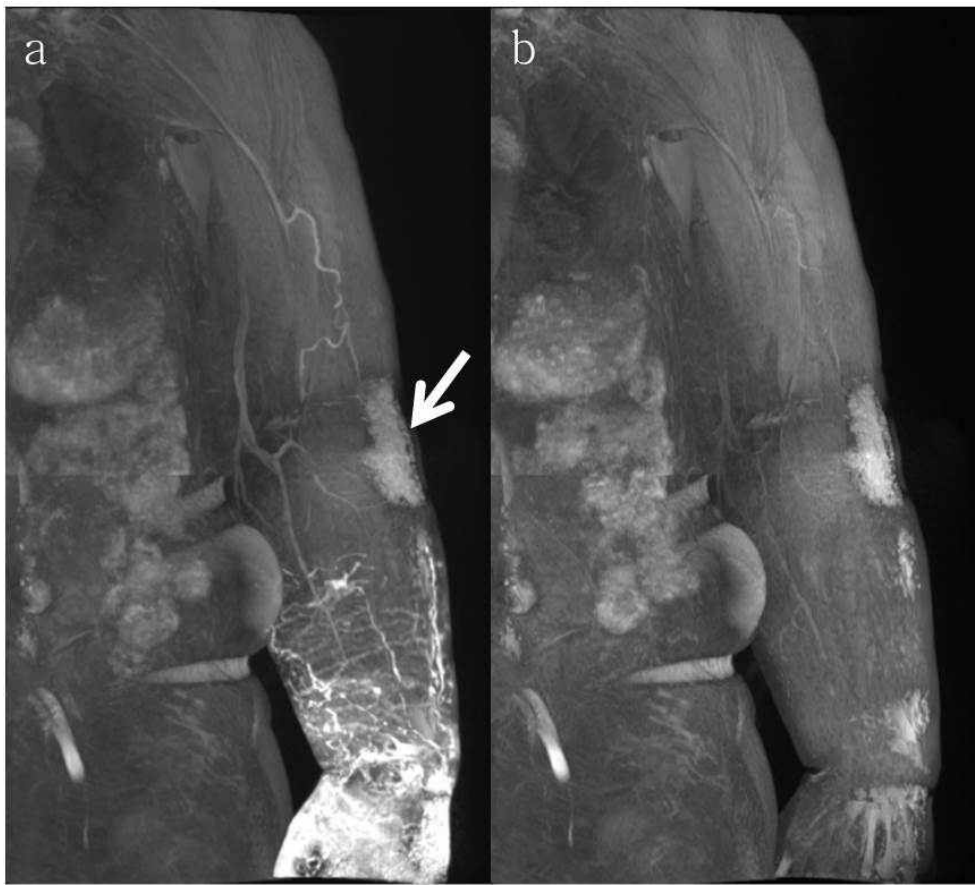

Figure 3. Insufficient fat saturation detected in a 71-year-old female. The MR lymphangiography image at 5 minutes (a) shows patchy area of high signal intensity (white arrow) in the left forearm that could be appreciated as diffuse lymphatic drainage. By comparison with the precontrast image (b), these patchy areas could be concluded as pseudolesions caused by insufficient fat saturation.

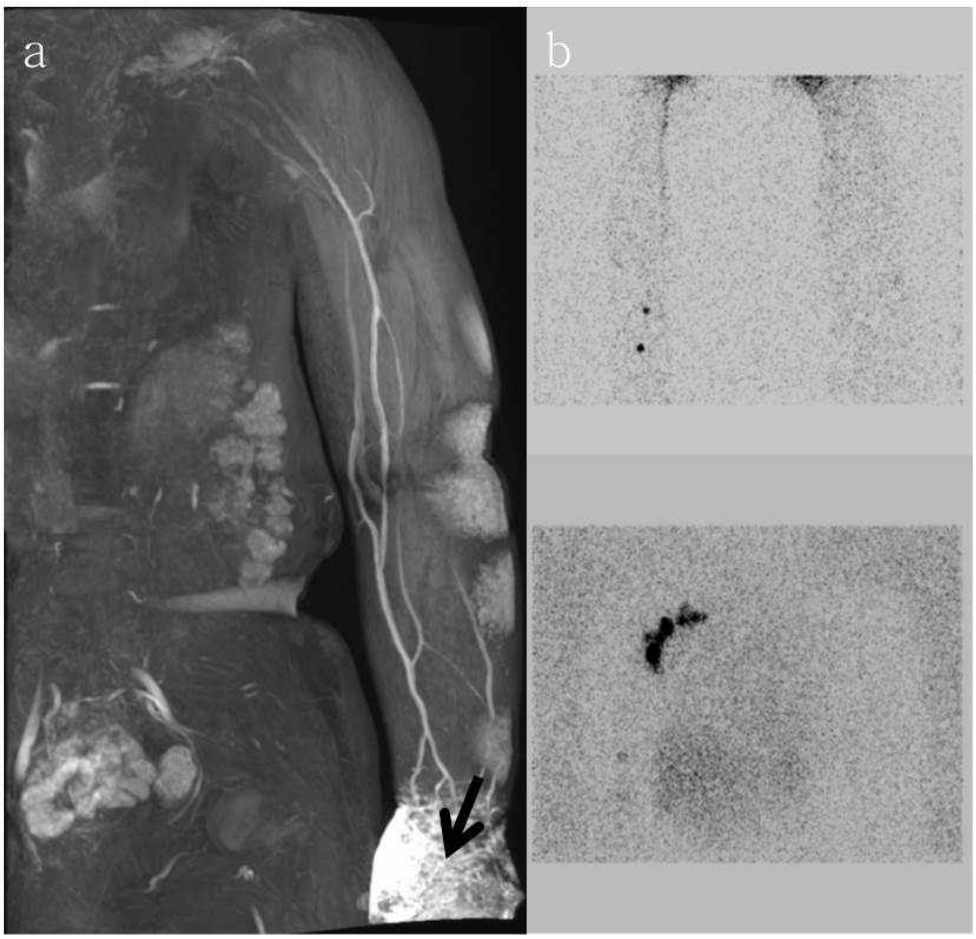

Figure 4. Comparison of demonstration of lymph nodes in a 71-year-old patient with stage II lymphedema on the left side. (a) MR lymphangiography image shows no depiction of axillary lymph nodes after 10 minutes of gadobutrol injection. Dermal backflow with beaded appearance of lymph vessels (black arrow) are prominent at left hand. (b) Lymphoscintigraphy image also demonstrates no lymph node at the ipsilateral axilla after 90 minutes of radioactive tracer injection. Note the lymph nodes at axilla and elbow of the unaffected side.

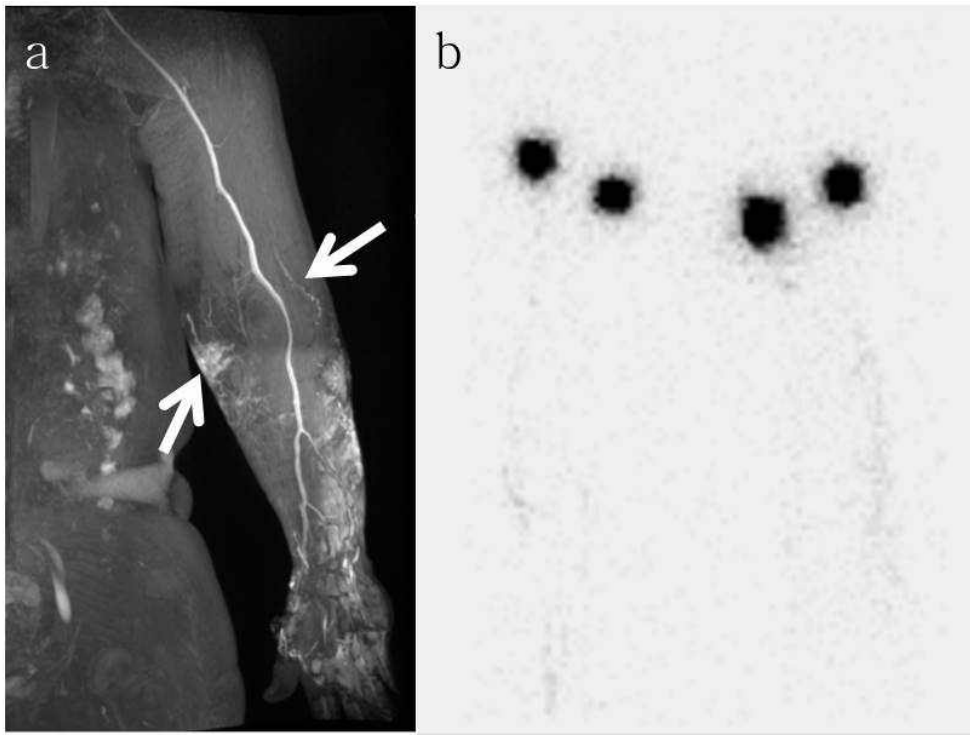

Figure 5. Comparison of depiction of lymph vessels by MR lymphangiography and lymphoscintigraphy in a 55-year-old female with stage II lymphedema. (a) MR lymphangiography clearly demonstrates beaded appearance of lymph vessels (white arrows) at the left elbow at both ulnar and radial side. (b) Lymphoscintigraphy revealed only faint dotted line at the corresponding area.

국문초록

목적: 상지 림프부종을 평가함에 있어서 자기공명 림프관조영술의 유용성을 림프관 신티그래피와 비교하여 평가한다.

대상 및 방법: 본 연구는 본원의 의학연구윤리심의위원회 승인을 받았으며 모든 자원자 및 환자에서 서면 동의를 받은 후 진행하였다. 우선 7명의 자원자에서 가도부트롤 피내주사를 한 뒤 3.0T 장비에서 지방포화 3차원 경사에코 자기공명 기법으로 영상을 획득하여 자기공명 림프관조영술의 프로토콜을 확립하였다. 그리고 일측성 림프부종 환자 6명에서 자기공명 림프관조영술과 림프관 신티그래피를 시행하여 그 결과를 서로 비교하였다. 두 영상 기법의 실험 결과는 각각 2명의 영상의학과 의사와 1명의 핵의학과 의사가 분석하였으며, 림프 배액의 양상 및 지연 정도, 림프관과 림프절의 선예도, 그리고 림프관이 시각화되는 해부학적 높이의 다섯 가지 항목에 대해서 평가하였다. 환자의 임상 소견과 영상 검사 결과를 토대로 각 환자에서의 진단 기준을 설정한 후에 이를 바탕으로 자기공명 림프관조영술과 림프관 신티그래피의 민감도와 특이도를 계산하였다.

결과: 자기공명 림프관조영술은 모든 환자에서 지연된 림프 배액을 보여준 반면 림프관 신티그래피는 6명 중 5명의 환자에서 지연된 림프 배액을 나타내었다. 림프 배액 양상에 관해서는 자기공명 림프관조영술과 림프관 신티그래피 각각에서 모든 환자에서 부분적으로 퍼져있는 림프 배액이 보였다. 액와부 림프절은 두 영상 기법 모두에서 시각화되지 않았다. 자기공명 림프관조영술 상에서는 모든 환자에서 늘어나있는 림프관이 중등도의 선예도로 나타났으나, 림프관 신티그래피 상에서는 1명에서 중등도의 선예도로, 4명에서 불량한 정도의 선예도로

나타났으며 1명에서는 림프관이 보이지 않았다. 림프관이 영상화된 높이는 두 검사 모두에서 상완 1명, 전완 4명, 그리고 수부 1명이었다. 자기공명 림프관조영술은 4개의 항목 모두에서 100퍼센트의 민감도를 보인 반면, 림프관 신티그래피의 민감도는 림프관 묘사 항목에서는 83.3퍼센트였고, 나머지 3개 항목에서는 100퍼센트였다. 자기공명 림프관조영술의 특이도는 림프 배액의 지연 항목에서 85.7퍼센트였고 나머지 항목에서는 100퍼센트였으며, 림프관 신티그래피의 특이도는 림프 배액의 양상 항목에서 66.7퍼센트였고 나머지 항목에서는 100퍼센트였다. 두 검사의 각 항목 결과값에서는 림프 배액의 지연 정도와 양상이 83.3퍼센트에서 일치하였고 두 검사 모두에서 모든 환자의 액와부 림프절이 보이지 않았다. 관찰된 림프관의 해부학적 높이는 66.7퍼센트의 환자에서 일치하였다.

결론: 자기공명 림프관조영술은 림프관의 형태를 평가함에 있어서 림프관 신티그래피보다 우월한 결과를 보였다. 그밖에 액와부 림프절의 조영증강 여부와 림프관 배액 평가에 있어서는 두 영상 기법이 모든 환자 또는 거의 모든 환자에서 동일한 결과를 보였다.

주요어: 자기공명영상 림프관조영술, 림프부종, 림프관 신티그래피

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