

## LYMPHSCINTIGRAPHY PREDICTS RESPONSE TO COMPLEX PHYSICAL THERAPY IN PATIENTS WITH EARLY STAGE EXTREMITY LYMPHEDEMA

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### ABSTRACT

*We investigated whether baseline lymphoscintigraphic findings can predict long-term response to complex physical therapy (CPT) in patients with early stage extremity lymphedema. Twenty patients with unilateral extremity lymphedema of clinical stage I or II underwent CPT after baseline lymphoscintigraphy. Therapeutic responses (good vs. poor) were evaluated at 1 year post-CPT based on changes in skin status and subjective symptoms, and percent volume reductions and compared with clinical factors and lymphoscintigraphic findings. Eleven patients showed good response to CPT with significant volume reduction of edematous extremities, and no significant volume reduction was observed in the remaining 9. Patients with good or poor responses to CPT showed no significant differences in terms of clinical variables. However, significant differences were observed between the lymphoscintigraphic findings of these patients. More specifically, a lymphoscintigraphic finding of main lymphatic vessels without collateral lymphatic vessels was the best predictor for a good response to CPT; the sensitivity, specificity and accuracy of this lymphoscintigraphic finding is 91% (10/11), 100% (9/9) and 95% (19/20), respectively. In patients with unilateral extremity lymphedema*

*of early stage, baseline lymphoscintigraphy may usefully predict long-term response to CPT.*

**Keywords:** lymphoscintigraphy, lymphedema, complex decongestive therapy, therapeutic response

Complex physical therapy (CPT), which consists of manual lymphatic drainage, bandage-wrapping compression, remedial exercise, and use of low-stretch elastic stockings, is the most effective conservative treatment known for extremity lymphedema (1). However, this therapy requires more than 2 weeks, is of relatively high cost, and requires high therapeutic compliance by the patients. Although clinical stage is frequently used to assess lymphedema severity, it has not been shown to predict response to CPT. Therefore, prediction of response before CPT is clinically important in patients with extremity lymphedema.

Lymphoscintigraphy is a non-invasive, useful modality for diagnosing lymphedema and for assessing post-therapeutic results (2,3). However, no previous study has addressed the use of lymphoscintigraphy to predict the results of physical therapy. In this study, we investigated whether baseline lymphoscintigraphic findings predict long-term response to CPT in patients with early clinical stage extremity lymphedema.

**TABLE 1**  
**Comparisons of the Clinical Factors and Baseline Lymphoscintigraphy**  
**Findings of Good and Poor Responders to CPT at Year 1 Post-Treatment**

Factors	Good response (n=11)	Poor response (n=9)	P value
Age (year)	40±16	46±20	NS
Sex (M : F)	0 : 11	2 : 7	NS
Location of edema (UE : LE)	4 : 7	3 : 6	NS
Etiology of lymphedema (primary : secondary)	4 : 7	5 : 4	NS
Occurrence of lymphangitis during follow-up (Y : N)	1 : 10	2 : 7	NS
<b>Lymphoscintigraphy</b>			
Axillary or ilioinguinal lymph node uptake (normal : decreased)	1 : 10	1 : 8	NS
Main lymphatic vessel (observed : not observed)	11 : 0	3 : 6	<0.005
Collateral lymphatic vessel (observed : not observed)	1 : 10	6 : 3	<0.05
Dermal backflow (observed : not observed)	6 : 5	7 : 2	<0.05

NS - not significant; UE - upper extremity; LE - lower extremity

## MATERIALS AND METHODS

### Subjects

The inclusion criteria for this study were as follows: 1) A diagnosis of unilateral extremity lymphedema of clinical stage I (reversible pitting edema) or II (spontaneously irreversible non-pitting edema) based on clinical history, a physical exam, magnetic resonance imaging, and lymphoscintigraphic findings; 2) The absence of vascular disease of the extremities; 3) A clinical follow-up of more than 1 year after CPT; and 4) The absence of cancer recurrence during follow-up in patients with lymphedema secondary to cancer treatment. Twenty patients with unilateral extremity lymphedema (2 males, 18 females; mean age 43 ± 18 yrs; upper extremity in 7, lower extremity in 13) met the study criteria, and were included. Among these, 9 patients had primary lymphedema and 11 secondary lymphedema.

### Lymphoscintigraphy

Lymphoscintigraphy was performed using a dual-headed gamma camera (Biad, Trionix Research Laboratory, OH, USA). Anterior and posterior images of both extremities were acquired 2 hours after injecting 148 MBq <sup>99m</sup>Tc-antimony sulfur colloid subcutaneously into the interdigital spaces of both hands or both feet. To improve the transport of radiopharmaceutical, a hand-grip exercise (using a rubber ball) or a walking exercise for 45 min was performed after radiopharmaceutical injection and imaging.

One nuclear medicine physician (unaware of the results of clinical follow-ups) interpreted lymphoscintigraphy findings. The uptake patterns of regional lymph nodes and main lymphatic vessels, and presence of dermal backflow and collateral lymphatic vessels were evaluated and compared with non-edematous normal extremities.

### CPT and clinical follow-up

A standard CPT protocol was for all patients as previously described (4) and all

patients completed a full course. Therapeutic response (good vs. poor) was evaluated at 1 year post-CPT by a physical medicine and rehabilitation physician (unaware of lymphoscintigraphy results) based on changes in skin status and subjective symptoms, and on percent volume reduction (cut-off = 15%) (4).

### Statistics

Mann-Whitney U-test and Fisher's exact t test were used to compare clinical variables and lymphoscintigraphic findings between poor and good responders to CPT. Numeric data are expressed as means  $\pm$  SD, and *p* values of  $< 0.05$  were considered statistically significant.

### RESULTS

At 1 year post-CPT, 11 patients showed good response with significant volume reductions of edematous extremities. No significant volume reduction was observed in the remaining 9 patients.

*Table 1* shows differences between the clinical factors and lymphoscintigraphic findings of good and poor responders. No significant differences in clinical variables, i.e., age, sex, location of edema, etiology of lymphedema, or occurrence of lymphangitis during follow-up was observed between poor and good responders. However, significant differences in lymphoscintigraphic findings were evident. In particular, main lymphatic vessels were visualized by lymphoscintigraphy in all good responders, and no collateral lymphatic vessel was observed in 10 of 11 good responders. Moreover, dermal backflow was more frequently observed in poor responders.

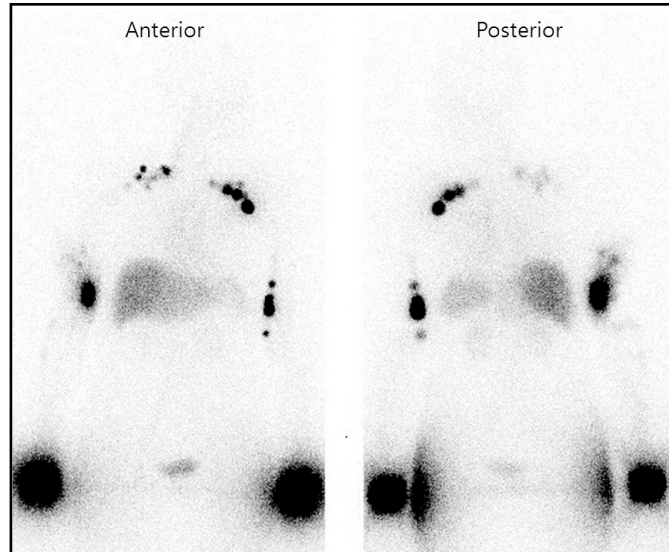
When a lymphoscintigraphic finding of a visualized main lymphatic vessel was taken as a diagnostic criterion for predicting a good response to CPT, the sensitivity, specificity, and accuracy of lymphoscintigraphy were 100% (11/11), 66.7% (6/9) and 85% (17/20), respectively. When a lymphoscintigraphic

finding of a non-visualized collateral lymphatic vessel was considered a diagnostic criterion for predicting a good response to CPT, the sensitivity, specificity and accuracy of lymphoscintigraphy were 91% (10/11), 66.7% (6/9) and 80% (16/20), respectively. When a lymphoscintigraphic finding of a visualized main lymphatic vessel but without collateral lymphatic vessels was considered a diagnostic criterion for predicting good response for CPT, the sensitivity, specificity and accuracy of lymphoscintigraphy were 91% (10/11), 100% (9/9) and 95% (19/20), respectively. *Figs. 1 and 2* depict representative lymphoscintigraphic images of good and poor responders to CPT.

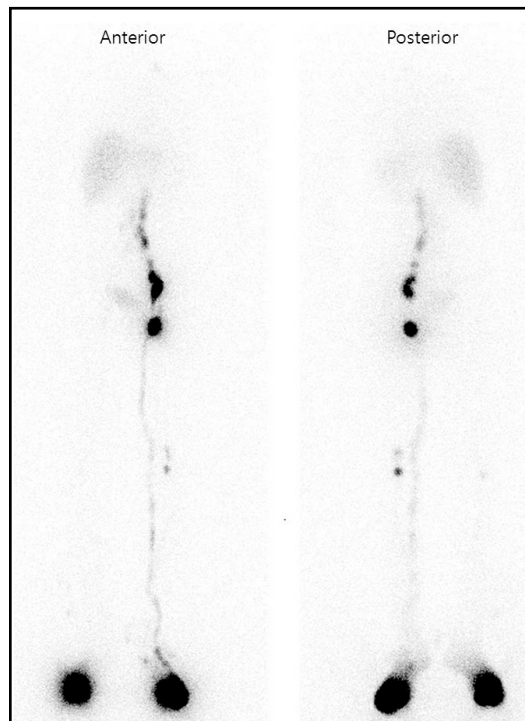
### DISCUSSION

Our results suggested that baseline lymphoscintigraphy is potentially useful for predicting the response of patients with unilateral extremity lymphedema of early clinical stage to CPT. The clinical factors examined failed to differentiate good and poor responders. On the other hand, a lymphoscintigraphic finding of a visualized main lymphatic vessel but without collateral lymphatic vessels was found to have a sensitivity of 91%, a specificity of 100% and an accuracy of 95%. These results have important clinical implications for the treatment of lymphedema. Lymphedema is a chronic disease which is difficult to cure. Currently, conservative physical therapy including CPT is the major treatment modality. However, this type of therapy requires a long treatment period and relatively high patient compliance. Moreover, poor compliance with physical therapy is an important cause of treatment failure. Thus, if the therapeutic effect for CPT can be predicted, patients expected to respond to treatment well can be encouraged to actively participate in physical therapy.

In the present study, the presence of main lymphatic vessels by lymphoscintigraphy without collateral vessels was found to be



*Fig. 1. Anterior (left) and posterior (right) lymphoscintigraphic images of a 53-year-old female patient with right upper extremity post-mastectomy lymphedema. Main lymphatic vessel of the right upper arm and dermal backflows of the right elbow and collateral lymphatic vessel of the right forearm are demonstrated. This patient responded well to CPT.*



*Fig. 2. Anterior and posterior lymphoscintigraphic images of a 43-year-old female patient with right lower extremity primary lymphedema. No main lymphatic vessel uptake, collateral lymphatic vessel uptake or ilioinguinal lymph node uptake were observed in the right lower extremity. She responded poorly to CPT.*

the best lymphoscintigraphic finding for predicting a good response to CPT. The main mechanism underlying the effect of CPT in lymphedema is thought to be the opening of lymphatic drainage pathways and stimulating smooth muscle contraction of lymphatic vessels, which demands the presence of functioning lymphatic vessels (5,6). If main lymphatic vessels are observed by lymphoscintigraphy, those can be said to be functional considering the principle of lymphoscintigraphy. This might result in a good response to CPT. Collateral lymphatic vessels are usually activated when main lymphatic vessels are either hypo- or non-functioning. In the present study, 4 patients showed collateral lymphatic vessels without main lymphatic vessels, and 3 of these responded poorly to CPT, which suggests that the presence of functioning collateral lymphatic vessels without a functioning main lymphatic vessel indicates a poor response to CPT.

In conclusion, the present study indicates that baseline lymphoscintigraphy can be useful to predict long-term response to CPT of patients with early stage unilateral extremity lymphedema. Further studies in patients with advanced clinical stage lymphedema are necessary.

#### ACKNOWLEDGMENT

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