

# Long-term changes on lymphoscintigraphy and their association with clinical parameters in secondary lymphedema after breast cancer surgery

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## Introduction

- Clinical diagnosis of Breast cancer related lymphedema (BCRL) is based on physical examination and imaging studies.
- Lymphoscintigraphy** is a first-line diagnostic imaging tool for BCRL, but the usage this modality has primarily **limited for the diagnostic purpose at initial work-up**
- Little has been reported for the **longitudinal changes** in lymphatic circulation visualized in lymphoscintigraphy
- The purpose of this study is to **investigate the relationship between long-term changes in pattern of lymphoscintigraphy and clinical features** in patients with BCRL

## Methods

### Design

- Single-center retrospective study
- Patients with BCRL who underwent lymphoscintigraphy between March 2008 and May 2022

### Inclusion criteria

- Secondary lymphedema after breast cancer surgery
- Patients who underwent baseline and follow-up lymphoscintigraphy

### Exclusion criteria

- Intervening axillary node dissection
- Surgical lymphovenous anastomosis and/or lymph node transplantation were performed
- Bilateral lymphedema

### Arm evaluation with circumference

- The circumference of the upper limb was measured at multiple locations selected from 5, 10 cm above or 5, 10, 15 cm below elbow from the lateral epicondyle level
- The percentage of excess circumference (PEC) was calculated as follows
- PEC = [(Circumference of the affected side – circumference of the unaffected side)/circumference of the unaffected side] × 100%.

### Lymphoscintigraphy acquisition

- images were obtained at 1 and 2 hours after subcutaneous injection of **99mTc-pyphate**
- According to the Taiwan lymphoscintigraphy stage proposed by Cheng et al, each image was categorized into 0–6 stages.

Category	Normal Lymphatic Drainage	Partial Obstruction				Total Obstruction			
Stage	L-0	P-1	P-2	P-3	T-4	T-4	T-4	T-4	
Proximal Lymph Nodes	++	+	-	-	-	-	-	-	
Intermediate Lymph Nodes	++	+	-	-	-	-	-	-	
Lymphatic Drain	++	<Distal	Distal	Distal	Distal	Distal	Distal	Distal	
Dorsal Backflow	++	(Proximal) (Distal)	(Distal) (Distal)	(Distal) (Distal)	(Distal) (Distal)	(Distal) (Distal)	(Distal) (Distal)	(Distal) (Distal)	
Upper Extremity	++	++	++	++	++	++	++	++	

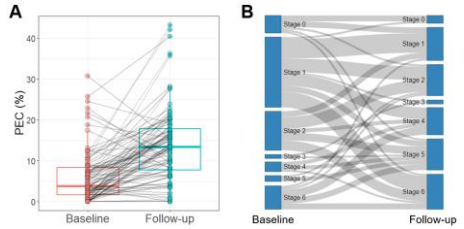
## Results

- 87 patients** were included in our analysis

**Table 1.** Patient characteristics

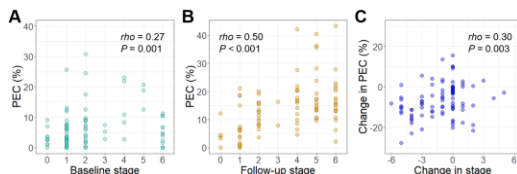
Variables	Median (IQR) or n (%)
Age at baseline	48 (43, 55)
Female sex	87 (100%)
BMI at baseline LSG (kg/m <sup>2</sup> )	23.2 (21.7, 26.2)
BMI at follow-up LSG (kg/m <sup>2</sup> )	23.5 (21.3, 26.2)
T stage (Tis/1/2/3/4)	2/18/44/14/4 (2/21/51/16/5%)
N stage (N0/1/2/3)	13/32/26/11 (15/37/30/13%)
Surgery	
Breast-conserving operation	40 (46%)
Mastectomy	47 (54%)
Axillary lymph node dissection	75 (86%)
Number of dissected lymph node <sup>†</sup>	16 (11, 19)
Nodal radiation	60 (69%)
Chemotherapy	82 (94%)
Cellulitis	23 (26%)
Poor compliance	19 (22%)
Interval between surgery and LSG (mo.)	7 (2, 14)
Interval between surgery and follow-up LSG (mo.)	78 (49, 116)

- Both lymphoscintigraphy stage and PEC showed variable change during the study period, with overall increases in their severity (median PEC: 3.8–13.4%; median lymphoscintigraphy stage: 1 to 4).



**Fig. 1** Boxplot showing changes in PEC (A) and a Sankey plot illustrating changes in lymphoscintigraphic stage (B) between baseline and follow-up.

- PEC and lymphoscintigraphy stage showed **positive correlations** at baseline ( $\rho = 0.27, P = 0.001$ ) and follow-up ( $\rho = 0.50, P < 0.001$ ).



**Fig. 2** Scatter plots comparing PEC and lymphoscintigraphic stage at baseline (A), follow-up (B), and change in PEC and change in stage between baseline and follow-up (C).

- Stepwise multivariable analysis revealed **cellulitis** (adjusted  $\beta$ : 4.34; 95% confidence interval [CI]: 0.77–7.91) and **lymphoscintigraphy stage at follow-up** (adjusted  $\beta$ : 1.47; 95% CI: 0.67–2.28) to be **independent variables for PEC at follow-up**.

**Table 2.** Results of univariable and multivariable linear regression analyses for prediction of PEC at follow-up lymphoscintigraphy

Variables	Univariable		Multivariable	
	Crude $\beta$ (95% CI)	P	Adjusted $\beta$ (95% CI)	P
Interval between surgery and lymphoscintigraphy (mo.)	0.04 (0.01, 0.07)	0.024	Not included	
BMI (kg/m <sup>2</sup> )	0.11 (-0.41, 0.64)	0.673	Not included	
ALND (vs SNB)	4.88 (-0.44, 10.19)	0.072	Not included	
Nodal radiation (vs none/non-nodal)	5.19 (1.4, 8.97)	0.008	Not included	
Chemotherapy (vs none)	7.11 (-1.35, 15.57)	0.098	Not included	
Bandage compression n at follow-up (vs not)	4.28 (0.7, 7.86)	0.020	Not included	
Cellulitis (vs none)	4.97 (1.04, 8.89)	0.014	4.34 (0.77, 7.91)	0.018
Poor compliance (vs not)	5.68 (1.5, 9.86)	0.008	2.96 (-0.57, 6.49)	0.099
Lymphoscintigraphy stage at baseline	0.98 (0.05, 1.9)	0.039	0.63 (-0.17, 1.43)	0.121
Lymphoscintigraphy stage at follow-up	1.98 (1.19, 2.78)	<0.001	1.47 (0.67, 2.28)	0.001
Change in lymphoscintigraphy stage	-0.84 (-1.61, -0.07)	0.033	Not included	

## Conclusion

- Clinical courses and patterns of lymphoscintigraphy and clinical features varied over time in patients with BCRL.
- In addition to initial lymphoscintigraphy for the diagnostic purpose, follow-up lymphoscintigraphy can objectively and visualize diverse changes in functional lymphatic system, which may help categorize the clinical severity and guide the optimal management plan in patients with BCRL.

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