Original Investigation

# Positive Predictive Value of Mammographic Lymphography in the Evaluation of Patients with Breast Cancer: A Preliminary Study

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**Rationale and Objectives:** The study aimed to investigate the positive predictive value (PPV) of mammographic lymphography (MLG) for assessing malignant breast disease and lymphatic metastasis in patients in a typical clinical setting.

**Materials and Methods:** Patients who underwent mammography with Breast Imaging Reporting and Data System (BI-RADS) category 4 or 5 lesions and had abnormal mammographic findings in the upper-outer quadrant of the breast were enrolled. Next, MLG was performed. A water-soluble agent was subcutaneously injected into the upper-outer periareolar region of the bilateral breast, and mammography was then performed. Morphologic characteristics, including lymphatic vessel development, the presence of lymphatic vessel defects, and dilation, were recorded for evaluation.

**Results:** Fifty-one patients with BI-RADS category 4 lesions and 40 patients with BI-RADS category 5 lesions were included in the study. Sixty-one patients were found to have malignant disease, whereas 30 patients were found to have benign disease. Morphologic characteristics were recorded for evaluation. The interobserver agreement was evaluated and was classified as excellent according to kappa analysis. The PPV of MLG characteristics for malignant breast disease and lymphatic metastasis was analyzed by logistic regression, and the presentation of a lymphatic vessel defect was the most predictive characteristic of a malignancy (PPV: 0.89; *P* value: 0.02) in patients with BI-RADS category 4 lesions. Meanwhile, in patients with malignant breast disease, the PPVs for predicting lymphatic metastasis with lymphatic vessel defect and dilation were 0.50 (*P* value: 0.02) and 0.67 (*P* value: <0.01), respectively.

**Conclusion:** The assessment of morphologic characteristics by MLG has the potential to predict malignant breast disease and lymphatic metastasis.

**Key Words:** Positive predictive value; mammographic lymphography; breast cancer.



## INTRODUCTION

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer deaths among females, accounting for 23% of the total cancer cases and 14% of the cancer deaths worldwide (1). Malignant spread to axillary lymph nodes is one of the most important predictors of survival in patients with breast cancer, increasing the 10-year recurrence rate from 20%–30% to nearly 70% (2,3). Sentinel lymph node (SLN) mapping and biopsy are currently performed intraoperatively via a radiocolloid scintigraphic method combined with the use of a blue dye (4). Although this method has proven to be successful for SLN mapping, a technique is still required to determine the condition of the lymphatic system preoperatively. Imaging via the intradermal injection of a contrast agent in the breast under another modality is thought to be a safe method to evaluate the condition of the lymphatic system. A previous study demonstrated that computed tomographic (CT) lymphography using the non-ionic contrast medium iopamidol is useful in SLN evaluation, and patients with a positive result tend to have some typical features in lymphography that are absent in patients proven to be negative by SLN biopsy (4,5). However, the true value of these features in diagnosis has not yet been properly discussed. Theoretically, the lymphatic vessel may also be visible in mammography through the use of intradermal contrast injection under CT. Thus, the objective of this study was to retrospectively investigate the positive predictive value

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(PPV) of imaging characteristics in mammographic lymphography (MLG) to predict lymphatic metastasis in patients in a typical clinical setting. Meanwhile, the value of the imaging characteristics associated with MLG in predictive malignancy is also discussed. To the best of our knowledge, this report is the first attempt to study the value of lymphography under mammography.

## MATERIALS AND METHODS

The protocol in our study was approved by the institutional review board of our hospital, and informed consent was obtained from all patients. Patients who underwent mammography and were assigned Breast Imaging Reporting and Data System (BI-RADS) classifications of 4 or 5 from June 2009 through January 2011 were all enrolled in our study, whereas pregnant patients and patients with a history of axillary lymphadenectomy and renal insufficiency were excluded.

### Contrast Agent

A water-soluble agent (Iopamiron 370; Bracco, Milan, Italy) was mixed at a 10:1 ratio with 1% mepivacaine hydrochloride and 0.5 ml intermixture was used for all injections with a 1 ml. Mepivacaine hydrochloride was added to alleviate pain during intradermal injection. All injections were performed using a 1-mL tuberculin syringe and a 26-G needle.

### MLG

All mammograms were acquired using a General Electric (GE) Senographe 2000D FFDM unit (General Electric Medical Systems, Milwaukee, WI). MLG was performed in two steps. First, mammography was performed in the craniocaudal and mediolateral oblique views for each breast, and one of the two radiologists with more than 25 years of experience in mammography viewed the image and assigned BI-RADS classifications. Patients assigned to BI-RADS category 4 or 5 who had abnormal mammographic findings located in the upper-outer quadrant of the breast were included, whereas other patients were eliminated from the database. Patients with bilateral abnormal mammography findings were excluded. Next, the contrast agent described previously was subcutaneously injected into the upper-outer periareolar region of the bilateral breast. Finger massage was performed for approximately 90 seconds at the injection site to facilitate the penetration of contrast into the lymphatic system, and mammography was performed again. Finally, the patient's side effects, including systemic reaction and local reaction, were recorded by a nurse after MLG.

### Image Analysis

Two radiologists (one with more than 25 years of experience in mammography and the other with 5 years of experience in mammography) participated in the image analysis. The imaging data obtained in the first step were used to assign BI-RADS categories only by the radiologist with more than 25 years of experience in mammography. The morphologic characteristics found by MLG, including poor lymphatic vessel development and the presence of a lymphatic vessel defect and dilation, were recorded for evaluation. Lymphatic vessel development was defined as the development of a part of or the entire lymphatic vessel after the injection of contrast agent, whereas poor lymphatic development was defined when lymphatic vessels were completely undeveloped. A lymphatic vessel defect was defined as the presence of discontinuity of the developed lymphatic vessel, and a lymphatic vessel was defined as dilated if its diameter was at least 50% greater than the diameter of the lymphatic vessels in the contralateral normal breast. Typical examples of lymphatic vessel development (good and poor) and the presence of a lymphatic vessel defect and dilation are shown in Figures 1 and 2, respectively.

### Reference Standard

All patients included in our study underwent surgery or biopsy, and histopathologic information was obtained from pathology reports. The SLN was identified using a dye-guided method with methylene blue. Lymph nodes that were dyed blue or black or that were suspicious based on palpation were also excised. Intraoperative touch imprint cytology was routinely applied to every SLN acquired, and a level I and II axillary lymph node dissection was performed if the touch imprint cytology was positive. Patients in which SLN failed to be

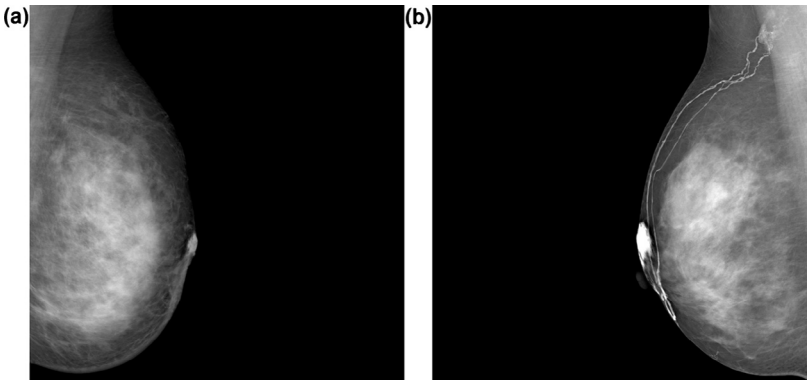


**Figure 1.** Patient with left breast invasive ductal carcinoma with no lymphatic metastasis. (**a**) Mediolateral oblique (MLO) view of the left breast with poor lymphatic vessel development. (**b**) MLO view of the right breast with good lymphatic vessel development.