



● *Original Contribution*

## ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION OF NON-PALPABLE AND SUSPICIOUS AXILLARY LYMPH NODES WITH SUBSEQUENT REMOVAL AFTER TATTOOING: FALSE-NEGATIVE RESULTS AND CONCORDANCE WITH SENTINEL LYMPH NODES

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**Abstract**—Ultrasonography-guided fine-needle aspiration (US-guided FNA) for axillary lymph nodes (ALNs) is currently used with various techniques for the initial staging of breast cancer and tagging of ALNs. With the implementation of the tattooing of biopsied ALNs, the rate of false-negative results of US-guided FNA for non-palpable and suspicious ALNs and concordance with sentinel lymph nodes were determined by node-to-node analyses. A total of 61 patients with breast cancer had negative results for metastasis on US-guided FNA of their non-palpable and suspicious ALNs. The biopsied ALNs were tattooed with an injection of 1–3 mL Charco-trace (Phebra, Lane Cove West, Australia) ink and removed during sentinel lymph node biopsy or axillary dissection. We determined the rate of false-negative results and concordance with the sentinel lymph nodes by a retrospective review of surgical and pathologic findings. The association of false-negative results with clinical and imaging factors was evaluated using logistic regression. Of the 61 ALNs with negative results for US-guided FNA, 13 (21%) had metastases on final pathology. In 56 of 61 ALNs (92%), tattooed ALNs corresponded to the sentinel lymph nodes. Among the 5 patients (8%) without correspondence, 1 patient (2%) had 2 metastatic ALNs of 1 tattooed node and 1 sentinel lymph node. In multivariate analysis, atypical cells on FNA results (odds ratio = 20.7,  $p = 0.040$ ) was independently associated with false-negative FNA results. False-negative ALNs after US-guided FNA occur at a rate of 21% and most of the tattooed ALNs showed concordance with sentinel lymph nodes. (E-mail: [mamrad@knu.ac.kr](mailto:mamrad@knu.ac.kr)) © 2017 World Federation for Ultrasound in Medicine & Biology.

**Key Words:** Fine-needle aspiration, Axillary lymph node, False-negative results, Breast carcinoma, Tattooing.

### INTRODUCTION

Surgical staging of the axilla is crucial in patients with breast cancer, because the presence of metastatic axillary lymph nodes (ALNs) is a key prognostic and decisive factor to tailor the treatment (Krag et al. 1998). Sentinel lymph node biopsy (SLNB) has become a standard method of axillary staging in patients with clinically node-negative breast cancer, because SLNB achieves similar clinical outcomes with a lower morbidity compared with axillary lymph node dissection (ALND)

(Lucci et al. 2007; Veronesi et al. 1997). For patients expected to have a high risk of advanced nodal disease, a two-stage surgical procedure of SLNB with subsequent ALND is associated with an increased cost of lymphoscintigraphy and surgery time. SLNB is also an invasive procedure with several complications, which have been documented through large prospective trials (Lucci et al. 2007; Wilke et al. 2006). Thus, the preliminary staging of the axilla before surgery to help decide whether to perform SLNB has been of interest to date (Hyun et al. 2016; Tucker et al. 2016).

For preliminary staging of the axilla, physical examination alone is neither sensitive nor specific, because metastatic ALNs are often non-palpable, and palpable ALNs can be reactive (de Freitas et al. 1991; Pamilo

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et al. 1989; Sacre 1986). Ultrasonography (US) of the axilla has been increasingly performed to overcome the limitation of physical examination. In a systematic review, US for the diagnosis of non-palpable axillary metastases is moderately sensitive (49%–87%) and fairly specific (56%–97%) (Alvarez et al. 2006). Nonetheless, because the signs of US for metastatic ALNs overlap with those of benign reactive change, US-guided fine-needle aspiration (FNA) is often added (Cho et al. 2009; Ciatto et al. 2007). However, although the addition of US-guided FNA increases the specificity, the sensitivity might be lowered by 10%–30% as a result of the false-negatives from the US-guided FNA (Baruah et al. 2010; Park et al. 2011). Furthermore, SLNB is not a perfect method to evaluate the status of the axilla, and the rates of false-negative SLNB have varied at a range of 0%–19% in previous studies (Kelley et al. 2004; Martin et al. 2005; Veronesi et al. 1997).

Therefore, to compensate for the false-negatives from US-guided FNA and SLNB, suspicious ALNs with negative results for metastasis on US-guided FNA were localized through pre-operative tattooing and consecutively removed along with SLNB. This procedure allowed node-to-node analysis in which the suspicious ALNs on US were exactly matched to the ALNs with final pathologic results, in contrast to previous studies that have demonstrated the diagnostic performance of US or US-guided FNA based on a patient-based analysis. In addition, the concordance of suspicious ALNs on US to the sentinel nodes has rarely been evaluated. In this study, we performed node-to-node analyses in the two aspects as follows: (i) correlation of the histologic results on US-guided FNA to the final pathologic results for a suspicious node identified at US, and (ii) correlation of the biopsied node with the sentinel node.

Therefore, the purpose of the present study was to determine the rate of false-negative results of US-guided FNA for suspicious ALNs and to evaluate the concordance of suspicious ALNs with sentinel lymph nodes by node-to-node analyses.

## MATERIALS AND METHODS

### *Patients*

The institutional review board of Kyungpook National University Medical Center approved this retrospective review of data, and the requirement of an informed consent was waived. A total of 67 patients with breast cancer had negative results for metastasis on US-guided FNA for their non-palpable and suspicious ALNs June 2013–October 2016. Nodes were defined as suspicious ALNs when 1 of the following characteristics was observed, on the basis of previous studies: cortical thickness >2 mm, eccentric cortical thickening, loss of fatty

hilum and round shape (Cho et al. 2009; Park et al. 2013; You et al. 2015). Of the 67 patients, we excluded those with excisional breast biopsy (n = 1) before US-guided FNA and those who underwent neoadjuvant chemotherapy (n = 5). A total of 61 patients with 61 ALNs were included in this study.

### *US-guided FNA and tattooing*

FNA and tattooing were performed by 1 of 3 attending radiologists who have 5, 10 and 18 y of experience in breast imaging and intervention using real-time visualization with US.

For FNA, a 23-gauge needle was inserted into the cortex of the ALN using a to-and-fro method with manual aspiration. Tattooing of the aspirated ALNs was performed through the injection of 1–3 mL of Charcotrace black ink (Phebra, Lane Cove West, Australia) into the cortex of ALNs and the adjacent soft tissue after local anesthesia (Fig. 1). Tattooing was generally performed on the same day or 1 d before surgery by the same radiologist who performed the FNA. The US-guided tattooing took approximately 5 min per patient. The radiologist marked the location of the ALNs on the skin with an oil-based pen to guide the surgical incision. All patients underwent FNA of the most suspicious-appearing ALN with subsequent tattooing.

### *SLNB and intra-operative evaluation*

To identify sentinel lymph nodes, a dual method of radioisotopes and blue dye was used (n = 56). However, in 5 patients, only a radioisotope (n = 4) or blue dye (n = 1) was used because of the unavailability of the agent or lymphoscintigraphy. The radioisotope (technetium-99 m phytate) or blue dye was injected before or at the time of surgery. ALNs identified by a gamma probe or ALNs containing blue dye were regarded as sentinel nodes and removed. All tattooed ALNs were identified and subsequently removed through inspection of the axilla during the SLNB. We reviewed the surgical records for the correspondence between the tattooed ALNs and the sentinel lymph nodes. All sentinel lymph nodes and tattooed ALNs were submitted for intra-operative frozen sections. If 3 or more ALNs were positive for metastasis on the frozen section, then axillary lymph node dissection was performed immediately after SLNB. Three attending breast surgeons and trainees performed all the operative procedures.

### *Pathologic evaluation*

Acquired cells obtained from FNA were stained according to the classic Papanicolaou method. The cytologic results were classified into inadequate sampling, benign, atypical, suspicious for malignancy or definitely malignant (Goyal et al. 2013). A negative result for

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