

## Should axillary lymph nodes be monitored with ultrasound following breast cancer surgery?

"Moon's article definitely opens up a dialog for discussion for further imaging studies using ultrasound to evaluate for regional LNR."

Over the past decade, there have been significant advances in breast cancer screening with digital mammography, MRI and ultrasound. These imaging technologies have helped detect breast cancer at an early stage. Current surgical recommendations of early-stage invasive breast carcinoma include removal of the primary breast tumor and evaluation of the ipsilateral axillary lymph nodes [1]. The presence of axillary lymph node metastases is an important indicator in assessing prognosis and determines management of additional therapy for these patients [2]. Axillary staging is traditionally performed by means of axillary lymph node dissection (ALND).

Breast cancer mortality rates continue to decrease and overall survival rates increase with the use of surgery, radiation therapy, chemotherapy or a combination of one or more of the above [3]. Unfortunately, distant and local regional metastases occur and remain a significant problem in breast cancer management. Although regional lymph node recurrence (LNR) is not common, it can be difficult to manage [4]. The axillary and supraclavicular lymph nodes are the most common sites of regional LNR and both are associated with a poor prognosis [5,6].

A recent article published in *Radiology* by Moon *et al.* from Seoul, South Korea, addresses the issue of evaluation of LNR after breast cancer surgery using ultrasound. The purpose of their retrospective study was to determine the diagnostic indexes of lymph node ultrasound of the axillary and supraclavicular regions for detecting LNR after surgery and to assess the effect of lymph node evaluation on prognosis during bilateral breast ultrasound after breast cancer surgery [4].

Between January 2003 and December 2004, the researchers evaluated 3982 lymph node ultrasound examinations, including bilateral axillary and supraclavicular areas, on 1817 women (mean age: 49.9 years) after breast cancer surgery. Nine (0.5%) of the patients had a palpable mass. The majority of their patients underwent a mastectomy (1322 [72.8%]) and ALND (1759 [96.8%]). Diagnosis of LNR was based on cytopathology, clinical follow-up and imaging studies for at least 12 months after ultrasound according to the article.

Of their 1817 patients, 54 (3.0%) had suspicious ultrasound findings of LNR (28 at first, 20 at second, five at third and one at fourth follow-up ultrasound). A total of 39 (2.1%) had LNR, including nine (0.5%) patients with a palpable mass. The researchers determined that the sensitivity, specificity, accuracy, positive predictive and negative predictive value for lymph node ultrasound for detecting LNR per woman was 76.9, 98.7, 98.2, 55.6 and 99.5%, respectively. The mean diameter of an abnormal lymph node was 1.28 cm with a median recurrence time after breast surgery of 42 months. The most common sites of LNR in this study were ipsilateral axilla (23%) and ipsilateral supraclavicular (31%).

Moon's study also showed that distant metastases were detected more often in patients with ipsilateral LNR (62%) than in those without LNR (2.3%), and that the overall 3-year mortality rate of patients with ipsilateral LNR only was significantly lower than that in patients with distant metastases [4]. The 3-year mortality rate in this study among patients with ipsilateral LNR was 43.8% and for those patients who had ipsilateral or contralateral LNR with concurrent distant metastases it was 77.3% [4]. The authors conclude that ipsilateral LNR was a predictor of distant metastasis and lymph node evaluation during breast ultrasound and was useful for early detection of LNR in asymptomatic patients.

It is clear from their article that Moon and his researchers were able to achieve the aims of their retrospective evaluation of LNR after



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breast cancer surgery using ultrasound. In addition, they were able to share some valuable data from a single cohort of patients with the worldwide medical community in regards to regional LNR rates, locations of LNR, diagnostic indexes of ultrasound for detecting LNR and prognostic outcomes in these patients.

I agree with Moon that physical examination of the axilla can lead to an unacceptably high false-negative rate (up to 40%) and that mammography does not adequately image the entire axilla [4,7]. Nevertheless, ultrasound is a fast and easy imaging tool to evaluate the entire axilla and other sites of likely LNR. I believe Moon's diagnostic indexes of ultrasound for detecting LNR are acceptable and most likely reproducible from institution to institution, depending on the training and experience of the radiologist/sonographer performing the examination. Furthermore, with the continued improvement in ultrasound technology, I believe that higher sensitivities and positive predictive values could be achieved.

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As with every study, there are limitations. This was a retrospective study at a single institution that was composed of Asian women only in which the initial T and N stage or neoadjuvant/adjuvant status were not considered. In addition, the majority of these patients in this study underwent a mastectomy and ALND. Axillary staging has traditionally been performed by means of ALND. However, this type of surgery has significant and common side effects [8]. Therefore, sentinel lymph node (SLN) dissection, a minimally invasive test for axillary staging, has been developed to decrease side effects and it has achieved the same goals as ALND [8].

The current trend in the USA and other parts of the world is breast conservation surgery with SLN (Moon's study included less than 1% of these patients). The primary assumption for SLN is that the cancerous cells migrate from the primary breast cancer and metastasize to one or more SLNs before spreading to secondary lymph nodes [2]. A positive SLN is highly predictive of metastatic involvement in the axilla [2,9]. SLN biopsy has become routine practice in surgical therapy for breast cancer patients for clinically node negative axilla since it has acceptable rates of recurrence comparable to ALND [9,10].

The concern with SLN is the occurrence of a possible false-negative result. If that is the case, then effective adjuvant therapy may not be offered and axillary metastases would be left untreated; thus, increasing the potential for axillary LNR. Current literature demonstrates the recurrence rate of SLN to be less than 8% [11-13]. The current SLN recurrence rate at my institution is 1%.

Another limitation of Moon's study is that with the low incidence of LNR at this time it is not cost effective for many radiologists worldwide to routinely evaluate the axilla/supraclavicular regions with ultrasound for recurrence in asymptomatic postsurgical patients. However, we may be able to further decrease regional LNR with presurgical axillary ultrasound [14–16]. If radiologists are able to find an abnormal axillary or supraclavicular lymph node(s) prior to surgery, the lymph node(s) can be sampled using ultrasound guidance with a fine needle or core biopsy to upstage the patient prior to surgery, and further management and staging can therefore be established.

Moon's article definitely opens up a dialog for discussion for further imaging studies using ultrasound to evaluate for regional LNR. It would be very interesting to conduct a large, prospective, multicentric study with a varied ethnic patient population with known presurgical/neoadjuvant staging and clinical-pathological information to evaluate for regional LNR. The data could then be further evaluated in a reader study and the cost-effectiveness of ultrasound could be studied. This may allow us to perform targeted screening for regional LNR or develop other imaging tests such as with molecular imaging to increase patient survival.

## Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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