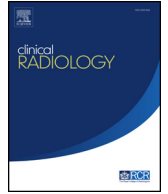


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Review

# Evolving imaging techniques for staging axillary lymph nodes in breast cancer

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## ARTICLE INFORMATION

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The presence and extent of axillary nodal metastases at the time of breast cancer diagnosis is a critical factor in disease prognosis and plays a central role in deciding the best treatment for patients. Accurate assessment of the axilla is therefore an essential component in staging breast cancer. Over the years, axillary staging has evolved from surgical axillary lymph node dissection (ALND), with its numerous associated long-term complications, to the much less-radical surgical sentinel lymph node excision biopsy (SLNB), the current reference standard. In parallel, radiological staging of the axilla has become increasingly more useful as our knowledge and techniques have improved. Preoperative axillary ultrasound is used widely to stage patients with breast cancer, providing an evaluation of node morphology and allowing targeted biopsy of abnormal nodes. This is important in helping stratify which patients should proceed directly to ALND and which should undergo SLNB first. Grey-scale ultrasound on its own is not perfect and can over- and underestimate axillary disease. Newer ultrasound techniques such as elastography may help to improve diagnostic confidence when visually assessing axillary nodes; for example, in more accurately assessing the extent of axillary disease burden or in differentiating benign reactive nodes from malignant nodes in equivocal cases. The use of intradermal “microbubbles” has shown great promise in being able to locate and biopsy the sentinel lymph node under ultrasound guidance, and raises the possibility that in the future such techniques may obviate the need for surgical SLNB in select patient populations.

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## Introduction

The presence and extent of axillary nodal metastases at the time of breast cancer diagnosis is a critical factor in

disease prognosis and plays a central role in deciding the best treatment for the patient.<sup>1</sup> Accurate assessment of the axilla is therefore an essential component in staging breast cancer. Historically, the axilla was staged surgically by axillary lymph node dissection (ALND), a radical procedure whereby all axillary nodes are excised, allowing each node to be individually assessed by the pathologist for evidence of metastases. Although effective at assessing axillary

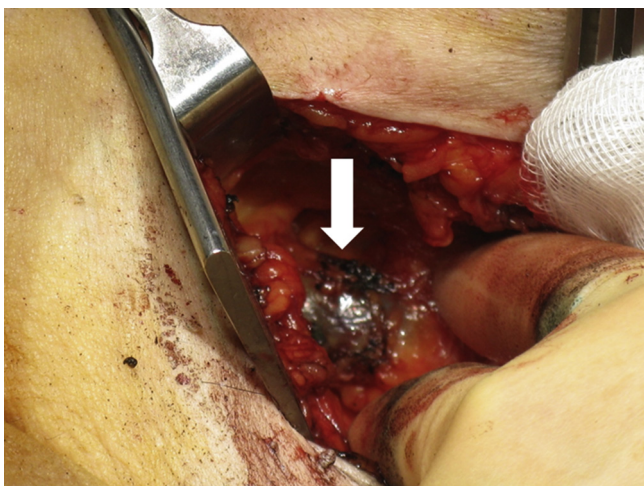
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disease burden, it can be associated with significant long-term morbidity, including ipsilateral arm lymphoedema and paraesthesia, in addition to shorter-term post-operative complications such as wound infections and seromas.<sup>2</sup> As well as living with these complications, for the many women that are subsequently found not to have metastatic nodes, this procedure would arguably have been unnecessary.

Routine staging by ALND has since been superseded by surgical sentinel lymph node (SLN) excision biopsy (SLNB), which is a much smaller operation and aims to excise only the sentinel axillary node. Because the SLN is, by definition, the first node in the lymphatic chain draining the breast, it is the first node in which breast cancer metastases should be detectable. Prior to the surgical procedure, a radiotracer (technetium-99m sulphur colloid) and blue dye are injected subdermally into the periareolar upper outer quadrant region,<sup>3</sup> whereupon they enter the lymphatics and drain into the SLN. The surgeon identifies the position of the SLN first using a handheld gamma camera to detect radioactivity prior to making an incision, and then using a combination of the gamma camera and visual inspection of the stained blue node(s) once the incision is made (Fig 1).

SLNB has been shown to accurately reflect the status of the axillary basin draining the primary breast cancer<sup>4</sup> and has become the widely accepted standard for initial surgical staging of the axilla; if the SLN does not contain metastases it implies the remainder of the axilla is also deemed disease-free and there is no benefit from undergoing subsequent ALND.<sup>5</sup> After 10 years of follow-up, the risk of local recurrence in patients with a negative SLNB is low (1.6 %).<sup>6</sup>

The accepted complications of wound infection, seroma, arm lymphoedema, and paraesthesia<sup>2</sup> are much less for SLNB than ALND. For example, 6% of patients undergoing SLNB had lymphoedema >12 months post-surgery, compared to 19% following both SLNB and ALND, 9% of those undergoing SLNB had paraesthesia at 12 months



**Figure 1** Intraoperative identification of the axillary SLN stained with blue dye (white arrow).

compared to 39% undergoing both SLNB and ALND.<sup>2</sup> There are also intra-operative complications, such as the small, but serious, risk of anaphylaxis following injection of the blue dye,<sup>7</sup> as well as a small risk of breast tattooing, which can last for at least a year.<sup>8</sup> Technetium-99m lymphoscintigraphy is also not without its problems. Although it may indicate the position of the SLN, by the time of surgery the small size of the radioactive colloid means that the isotope may have passed through the SLN and entered other regional lymph nodes.<sup>9</sup> There are also important considerations related to obtaining, handling and disposing of radioactive material. Finally, a meta-analysis of 69 studies found surgical SLNB to have a median false-negative rate of 7%.<sup>10</sup> Until recently, conventional surgical treatment of the axilla dictated that all patients with SLN metastases required a completion ALND to excise the remainder of potentially malignant lymph nodes. The publication of the ACOSOG Z0011 trial in which patients with SLN metastases were randomised to either ALND or no further surgery changed practice and ushered in the concept of axillary conservation.<sup>11</sup> Despite the fact that 27.3% of patients in the ALND arm had further lymph node metastases, there were no statistical differences in local and regional recurrences between the groups.<sup>12</sup> These results emphasise the key role that modern adjuvant therapy plays in achieving loco-regional disease control.

As current medical and surgical approaches to managing the axilla strive to become less invasive, state of the art imaging techniques now play an increasingly important role in staging the axilla, providing as much preoperative information as possible. By developing approaches that optimise the sensitivity and negative predictive value (NPV) of imaging tests, radiologists are beginning to guide the operative management of the patient, minimising the number and extent of surgical procedures the patient undergoes. Identifying high-volume metastatic axillary nodes preoperatively would enable the patient to proceed directly to ALND obviating a two-stage surgical procedure. Alternatively, if axillary metastases can be excluded, this would spare the patient axillary surgery and the potential complications and associated morbidity. Accurate diagnosis and quantification of axillary disease in an outpatient setting could lead to individualised patient-appropriate treatment plans where only affected nodes are excised or monitored, or non-surgical treatment regimens are informed by accurate outpatient staging and review.

Surgical management of the axilla is highly controversial, with both clinicians and patients concerned about “over-treatment” resulting from diagnosis of axillary disease, or conversely, “under-treatment” where high-volume axillary metastases are missed and not excised. Furthermore, some studies have suggested that preoperative diagnosis of axillary disease is not as critical as initially thought in the management of the axilla. The purpose of this review is to discuss the current status of radiological assessment of the axilla, and, in the light of recent clinical trials on management of the axilla, the directions we may be headed over the coming years.

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