US and US-guided fine-needle aspiration biopsy of internal mammary nodes in patients with breast cancer

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Learning objectives

- To describe the technique of ultrasonography (US) of the internal mammary (IM) lymph nodes and illustrate the normal US anatomy of the IM nodal basin.
- To illustrate the typical US appearances of IM nodal metastases and discuss some common pitfalls.
- To describe the technique of US-guided fine-needle aspiration (FNA) biopsy of IM nodes.
**Background**

Like the axillary lymph nodes, the IM lymph node chain is a first-echelon nodal drainage site in breast cancer. Although the status of the IM nodes is uncertain in the majority of breast cancer patients treated today, IM nodal metastases are known to be more frequent in patients with medial tumors, in patients with larger tumors, and in young patients. An estimated 10% of patients have IM nodal metastasis without nodal axillary involvement (1, 2). The consistent finding that patients with medial tumors have worse outcomes than patients with similarly stage lateral tumors suggests the underdiagnosis of IM nodal metastases and possibly the undertreatment of patients with IM nodal disease.

The sixth edition of the UICC's TNM staging system was altered to reflect the impact of a positive IM node on breast cancer stage (3):

- **N2b** Metastases only in clinically detected ipsilateral IM nodes and in the absence of clinically evident level I and II axillary lymph node metastases
- **N3b** Metastases in ipsilateral IM node(s) and axillary lymph node(s)

As a result, the detection of a metastatic IM node automatically categorizes a breast cancer as stage III.

<table>
<thead>
<tr>
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<th>N2</th>
<th>M0</th>
</tr>
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<td>N2</td>
<td>M0</td>
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<td>T4</td>
<td>N2</td>
<td>M0</td>
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| Stage IIIC   | Any T | N3   | M0  |

*Table 1: Impact of the diagnosis of an ipsilateral IM nodal metastasis on stage of breast cancer (3).*

A positive IM biopsy can lead to the addition of chemotherapy for those with negative axillary nodes, omission of axillary dissection for those with “failed” lymphoscintigraphy
that found no axillary sentinel nodes, and modification of radiation fields to encompass the IM chain. Therefore, accurate pre-operative diagnosis of IM node involvement potentially impacts surgical, chemotherapeutic, and radiation treatment decisions.

Surgical biopsy of IM sentinel nodes is more difficult than biopsy of axillary sentinel nodes, with success rates of 70% to 100% and complications occurring in approximately 5% of patients (4, 5). A less invasive means of detecting and confirming occult IM nodal metastases is therefore needed to refine staging and thereby facilitate treatment decisions.

In patients with newly diagnosed breast cancer, morphological criteria are used for the US diagnosis of regional lymph node metastases. However, significant overlap exists between benign reactive hyperplasia and metastatic disease, hence the need for the liberal use of US-guided FNA of any indeterminate node. At The University of Texas MD Anderson Cancer Center, we have used US and US-guided FNA of regional nodes for the regional nodal staging of newly diagnosed breast cancer for more than 2 decades (6).
**Technique of US examination of IM nodes**

The same high-frequency linear-array broadband transducer that is used for breast imaging can be used to scan the IM nodal chains, although in overweight patients it may be necessary to use a transducer of lower frequency. In some individuals with a small chest or narrow intercostal spaces, a high-frequency hockey-stick type transducer or a short-radius convex-array probe like those used for neurosonology in children may be beneficial owing to their small footprint.

Longitudinal sonograms of the IM nodal chains are obtained by scanning along the edge of the sternum (Fig 1) (7). Extended-field-of-view sonograms are particularly helpful to demonstrate the first 3 to 4 intercostal spaces and the cross-sections of the costal cartilages in a single frame, thus allowing simultaneous visualization of all spaces and documentation of the exact location of any abnormal node.

Transverse sonograms are obtained by placing the probe transversely in each intercostal space with its medial end covering the edge of the sternum (Fig. 2). The first 3 spaces are easily examined but the lower 3 usually cannot be fully assessed owing to their small size.

The internal thoracic (IT) artery (ITA) and vein(s) (ITV) can be seen on gray-scale sonograms. The pulsations of the ITA in real time help identify it. Vessel wall calcifications may be seen in the elderly. The identity of the IT vessels is readily confirmed with power Doppler US and spectral Doppler analysis.

The US examination takes only 2 to 3 minutes unless an abnormality is detected. If there is any doubt about an abnormality, examination of the contralateral IM nodal chain should be performed for comparison.

**Normal US anatomy of the IM region**

On sonograms, the sternum, the clavicle, and the ribs are easily identified by their strong cortical reflectivity and the associated marked shadowing. The costal cartilages are markedly hypoechoic but do not block the US beam’s propagation as the cortical bone does; therefore some visualization of the structures lying distal to the costal cartilages (e.g., the parietal pleura) is usually possible (Fig. 3). With advancing age, coarse internal calcifications often develop in the costal cartilages and produce focal acoustic shadowing. A tip to quickly enumerate the cartilages is to identify the sternal angle, at the level of which lies the second cartilage.

On longitudinal sonograms, the IT vessels are seen coursing over the pleura (Fig. 4). On transverse sonograms, these vessels are identified immediately anterior to the pleura and at the posterior aspect of a triangular fat-containing space that shows a low-to-moderate
echogenicity (Fig. 5). Located more anteriorly, are the thin internal intercostal muscle and the external intercostal membrane, beneath the pectoralis major muscle.

Although there is only 1 ITA on each side, there may be 1 or 2 ITVs (Table 2).

<table>
<thead>
<tr>
<th>Number of right ITVs</th>
<th>Number of left ITVs</th>
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<td>2</td>
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<td>56%</td>
</tr>
<tr>
<td>2</td>
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<td>20%</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>16%</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>8%</td>
</tr>
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</table>

Table 2: Number of ITVs per side in 100 cadavers (from ref 8)

When the ITV bifurcates into 2 veins, bifurcation can occur at any of several levels (Table 3).

<table>
<thead>
<tr>
<th>Level of bifurcation of ITV</th>
<th>Right side</th>
<th>Left side</th>
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<td>2&lt;sup&gt;nd&lt;/sup&gt; rib</td>
<td>36%</td>
<td>0%</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; rib</td>
<td>30%</td>
<td>52%</td>
</tr>
<tr>
<td>4&lt;sup&gt;th&lt;/sup&gt; rib</td>
<td>10%</td>
<td>20%</td>
</tr>
<tr>
<td>No bifurcation (single ITV)</td>
<td>24%</td>
<td>28%</td>
</tr>
</tbody>
</table>

Table 3: Level of bifurcation of the ITVs in 100 cadavers (from ref 8)

The ITA is generally lateral and the ITV medial, but variations occur. When there are 2 ITVs, they usually course on each side of the ITA.

The mean diameter of the ITVs at the level of the third rib is 2.5mm.

The IT vessels are commonly used for anastomosis of the flap pedicle vessels in free flap breast reconstruction. At M.D. Anderson Cancer Center we have used color Doppler US to assess the IT vessels prior to breast reconstruction using free flaps (9).

Access to the IT vessels for anastomosis requires the resection of a costal cartilage. After free flap breast reconstruction, the absence of this cartilage is well seen on the panoramic sagittal sonograms (Fig. 6).
Normal IM nodes are usually only 3 to 4 mm in diameter and thus are too small to be seen on US. However, they can be seen on MRI.

**US appearances of benign IM nodes**

Very rarely, benign, mildly enlarged, fat-containing benign nodes are demonstrated in an intercostal space in an asymptomatic individual (Fig 7). Benign conditions that can result in such benign-appearing nodes include sarcoidosis and infectious or inflammatory conditions of the breast.

Silicone-induced granulomas involving IM nodes have a pathognomonic appearance consisting of bright echogenicity and a "snowstorm" artifact (Fig. 8). This appearance signals a history of a ruptured silicone-gel implant.

**US appearances of IM nodal metastases**

The US diagnosis of lymph node metastases is based on nodal enlargement, nodal deformity, and markedly decreased echogenicity of the tumor deposits (10). Any hypoechoic node visualized along the IM chain in a patient with breast cancer should be viewed as a potential metastasis.

IM nodal metastases appear as spherical or ovoid hypoechoic masses that are adjacent to the IT vessels (Fig. 9). IM metastases are frequently found lateral to the vessels, but can also be found between them (Fig. 10) and medial to them (Fig. 11). The vast majority of IM nodal metastases develop between the cartilages in the intercostal spaces, but some may lie directly posterior to a costal cartilage.

Power Doppler US can demonstrate internal hypervascularity in IM nodal metastases, although this may be difficult to appreciate if the nodes are small.

**Potential pitfalls**

The site where branches of the ITA perforate the pectoralis major muscle may appear as a focal hypoechoic area, possibly mimicking a small mass (11). Color Doppler US confirms the vascular nature of the hypoechoic area and the absence of a lesion. Rarely, a prominent or focally distended vein can also mimic a small focal lesion. In this case, color Doppler US may be useless in confirming the varix if blood flow inside the lesion is too slow to be detected. However, swirling echoes may be seen on standard gray-scale real-time examination. Compression with the transducer, which should confirm the disappearance of the varix, may not be possible in patients with a thick chest wall.

The fat that surrounds the IT vessels is usually of medium echogenicity. On occasion, however, a small lobule of fat may appear hypoechoic, and in a breast cancer patient, the question may be raised whether this represents a small, early lymph node metastasis. Fat
lobules usually retain an elongated shape, and their hypoechogenicity remains moderate; in contrast, lymph node metastases tend to be more rounded and more hypoechoic.

Not every solid hypoechoic oval-shaped mass along the IT vessels is a suspicious node. Neurofibromas can be found in that location, mimicking malignant nodes (Fig. 12).

The presence of multiple markedly hypoechoic nodes in the IM chains, especially bilaterally, should raise the suspicion of lymphoma.

**US-guided needle biopsy of IM nodes**

Because of limited access to the IM nodes, the usual small size of the target-lesions, the proximity of vital structures, and the risk of serious complications, US-guided needle biopsy of IM nodes should be performed only by imagers with extensive experience in interventional US and only in patients in whom the result of the procedure is expected to affect staging and clinical management. Pre-biopsy discussion with the treating physician is therefore essential.

Discontinuation of anticoagulation therapy is recommended prior to the needle biopsy. Because there is no room to safely accommodate the throw of an automated large-core biopsy needle, core biopsy cannot be performed on the IM nodes. US-guided FNA is the tool of choice because of the precision with which the needle tip can be advanced under continuous real-time monitoring: this precision makes the procedure safe as long as the needle is seen on the monitor.

FNA is performed with a 20-ml syringe and a 3.5-inch-long 20-gauge or 2-inch-long 21-gauge needle using a lateral-to-medial approach through the pectoralis major muscle (Fig. 13). First the IT vessels are carefully identified using color or power Doppler US. Then, adequate local anesthetization is performed under full US monitoring. A 2-inch-long 21-gauge needle is used to inject 5 to 7 cc of lidocaine along the selected pathway for the FNA needle, i.e., following the same lateral-to-medial approach through the pectoralis major muscle. The FNA needle is then inserted with a very shallow angle in order to remain as “parallel” to the pleura as possible for increased safety. Any other approach (e.g., inferior-to-superior or medial-to-lateral) should be avoided because it would result in a steep angle relative to the pleura and heightened risk of complications.

Extreme care must be taken to clearly visualize the needle tip during its entire progression and to keep it at a safe distance from the IM vessels and from the pleura. This distance can be as short as a couple of millimeters as long as the needle tip is clearly identified (Fig. 14). Aspiration of cellular material from lymph nodes-benign or malignant-is easy because of their rich cellularity. As a rule, in experienced hands, a single needle pass of 20 to 30 seconds’ duration will provide a sufficient sample (Figs. 15, 16).
Deformities of the anterior chest wall (e.g., pectus excavatum) or the location of the abnormal node behind the sternal edge or behind a costal cartilage may render FNA very challenging or even impossible.

Potential complications of FNA of the IM nodes include bleeding from injury to the IM vessels and pneumothorax from pleural breaches. My colleagues and I have not encountered any such complication.
Fig. 1: Diagram shows the placement of the transducer to acquire longitudinal sonograms of the IM nodal chain.

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Fig. 2: Diagram shows the placement of the transducer along a single intercostal space to acquire transverse sonograms of the IM nodal chain.

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**Fig. 3:** Normal US anatomy of the IM nodal chain. Extended-field-of-view gray-scale sonogram shows the cross-sections of the first 5 costal cartilages (C).

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**Fig. 4:** Normal US anatomy. Longitudinal power Doppler sonogram of the first intercostal space. Note the artifactual mirror image of the ITA posterior to the parietal pleura.
Fig. 5: Normal US anatomy. Transverse power Doppler sonogram of the first intercostal space. Note the artifactual mirror images of the IT vessels posterior to the parietal pleura. The ITV lies medial to the ITA. S, Medial edge of the sternum; Pect, pectoralis major muscle.

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Fig. 6: Longitudinal extended-field-of-view sonogram after free TRAM flap reconstruction of the breast. The ipsilateral third costal cartilage has been resected to enable pedicle anastomosis.

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**Fig. 7:** Benign IM node. Longitudinal sonogram shows a benign IM node with echogenic fat replacement (arrows) in an asymptomatic woman.

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**Fig. 8:** Silicone-induced granulomas. Longitudinal sonogram of the first intercostal space shows 3 silicone-induced granulomas (arrows) replacing IM nodes. Note the marked distal "snowstorm" artifact. C, second costal cartilage.

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**Fig. 9:** Typical IM nodal metastases from breast cancer. Longitudinal sonogram of the third right intercostal space shows 2 oval markedly hypoechoic IM nodal metastases (arrows).

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**Fig. 10:** IM nodal metastasis from breast cancer. Transverse power Doppler sonogram of the second right intercostal space shows a small 5-mm-diameter nodal metastasis (arrows) located between the ITA (laterally) and the ITV (medially).

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**Fig. 11:** IM nodal metastasis from breast cancer. Transverse color Doppler sonogram of the second left intercostal space shows a nodal metastasis (arrows) located medial to the IT vessels. S: sternum.

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Fig. 12: Neurofibroma in a patient with neurofibromatosis. Longitudinal sonogram of the second right intercostal space shows an elongated hypoechoic solid mass resembling a malignant IM node. The tapering of the superior pole of the mass (arrow) suggests a connection with a nerve. C: costal cartilage.

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**Fig. 13**: US-guided FNA of IM node. Diagram shows the lateral-to-medial insertion of the needle along the intercostal space.

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Fig. 14: US-guided FNA of a small (6 x 4 mm) metastatic IM node in the first left intercostal space. Transverse sonogram shows the entire shaft of the needle. The needle tip is in the center of the node, a few millimeters from the ITA (arrow).

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**Fig. 15:** Videoclip shows US-guided FNA of a metastatic IM node in the second left intercostal space in a patient with breast cancer. Color Doppler US is used first to identify the IT vessels. Note that the right-handed operator is working from the patient's head to be able to use a lateral-to-medial approach to this left-sided node. The needle is then seen to traverse the pectoralis major muscle and reach the center of the node. A 20-second-long pass yields the cytologic material shown in Figure 16. The diagnosis was metastatic breast adenocarcinoma.

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Fig. 16: Cytologic smear obtained from US-guided FNA of the metastatic IM node shown in Figure 15 shows abundant metastatic adenocarcinoma that has completely replaced the node’s lymphoid tissue.

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Conclusion

US and US-guided FNA of IM nodes are useful for the detection and minimally invasive diagnosis of occult IM nodal metastases. Information on IM nodal status allows refinement of the clinical stage and potentially affects the treatment of breast cancer patients.
References


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