AXILLARY STAGING OF BREAST CANCER

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- Identifying the presence of axillary node and internal mammary node metastases in patients with invasive breast cancer is critical for determining prognosis and for deciding on appropriate treatment. Sentinel lymph node biopsy (SLNB) is the definitive method to exclude axillary metastases

- Patients with positive SLNB results generally undergo axillary lymph node dissection (ALND). The benefit of preoperative identification of axillary metastases is that it allows the surgeon to proceed directly to ALND and to avoid an unnecessary SLNB and the need for a second surgical procedure involving the axillary nodes.

AXILLARY ANATOMY

- Knowledge of the important anatomic landmarks of the axilla is important in finding and accurately reporting suspicious lymph nodes.

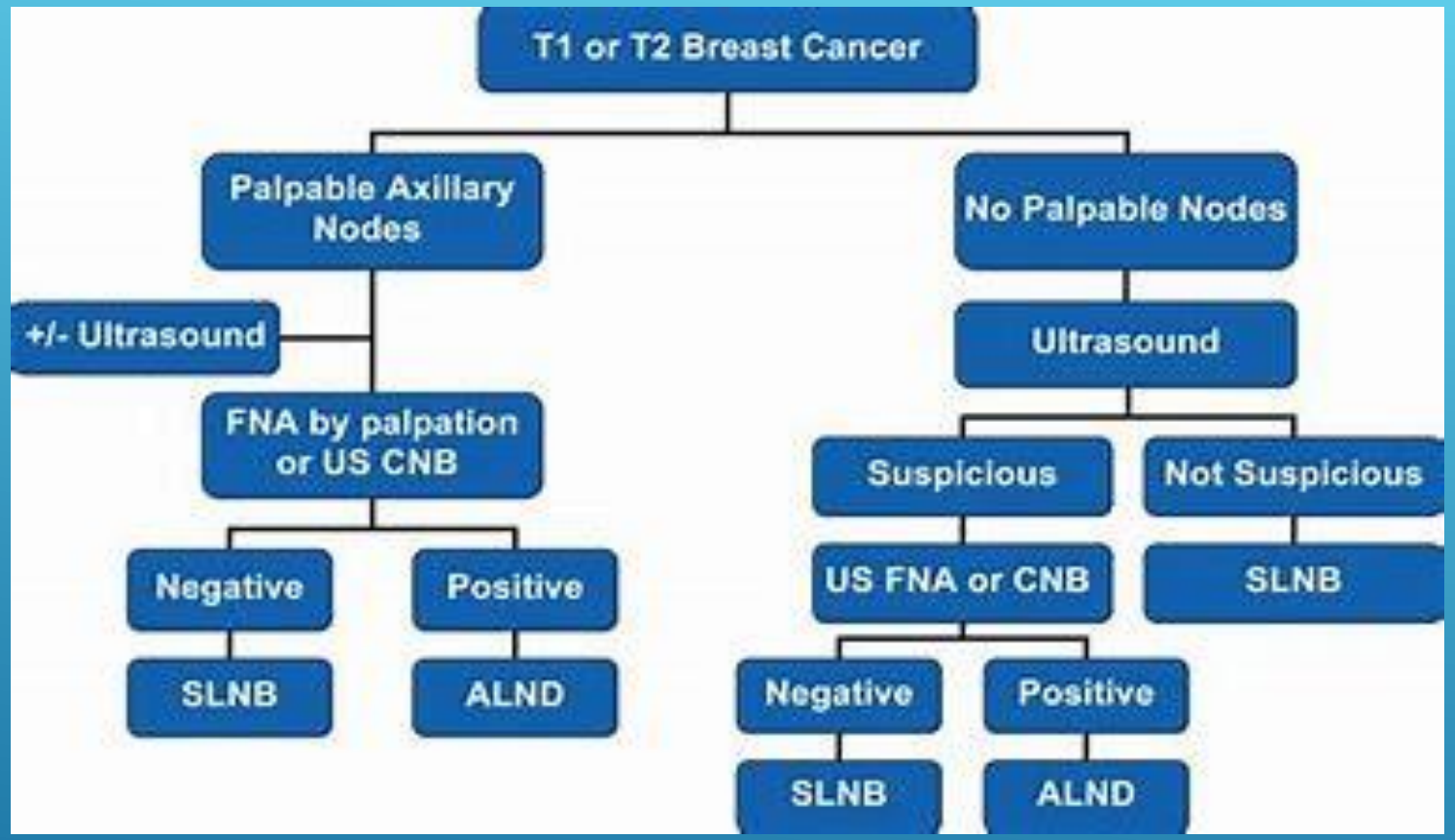
- The presence of axillary node metastasis and the size of the primary tumor are the two main prognostic factors used clinically for evaluation of breast cancer patients .Diagnosis of axillary metastasis is also important for determining the need for systemic chemotherapy as well as radiation therapy.

- Axillary lymph node dissection (ALND) is the definitive method to diagnose axillary metastasis, but sentinel lymph node biopsy (SLNB) has supplanted this procedure as the primary method of evaluating the axilla in most cases of early stage breast cancer because SLNB has a significantly lower rate of morbidity than does ALND and a low false-negative rate.

- In current clinical practice, most patients with invasive breast cancer and palpable axillary nodes or nodal metastases that are identified before surgery by means of imaging (also known as “clinically node-positive” patients) will undergo ALND without undergoing SLNB. “Clinically node-negative” patients with T1 or T2 tumors currently undergo SLNB.

- Patients with positive SLNB results traditionally underwent “completion” ALND ,however, the role of ALND in these patients is being reassessed. The recently published results of the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial suggest that there may be no survival benefit for performing ALND in some patients with limited disease (as diagnosed with SLNB) .Although the results of this trial are currently being debated, the implication is that in the future, ALND may not be necessary in some patients with limited axillary metastases

- The strategy for identifying axillary metastases before surgery varies among institutions, ranging from imaging only patients with suspicious but inconclusive findings from physical examination of the axilla, to axillary imaging being performed in all patients with invasive breast cancer (Fig 1)


T1 or T2 Breast Cancer
Palpable Axillary Nodes
No Palpable Nodes
+/- Ultrasound
Ultrasound
FNA by palpation or US CNB
Suspicious
Not Suspicious
Negative
Positive
US FNA or CNB
SLNB
SLNB
ALND
Negative
Positive
SLNB
ALND

- Some institutions follow more specific protocols, such as imaging those patients with invasive tumors larger than 1 cm or those with tumors that demonstrate angiolymphatic invasion,

- Lymph nodes with a suspicious appearance at imaging are usually sampled by means of either ultrasonography-guided fine needle aspiration (US-FNA) or ultrasonography-guided core needle biopsy (US-CNB) to confirm the presence of a metastasis before ALND

- The benefit of preoperative identification of axillary metastases is that it allows the surgeon to proceed directly to ALND, thereby avoiding an unnecessary SLNB and the need for a second axillary surgical procedure. With SLNB, the frozen section specimens have traditionally been sent to the pathologist, who determines whether completion ALND is necessary. This process adds considerable operative and anesthesia time and expense to the procedure, and frequently, a second trip to the operating room is required. Avoiding this situation by using imaging is therefore appealing.

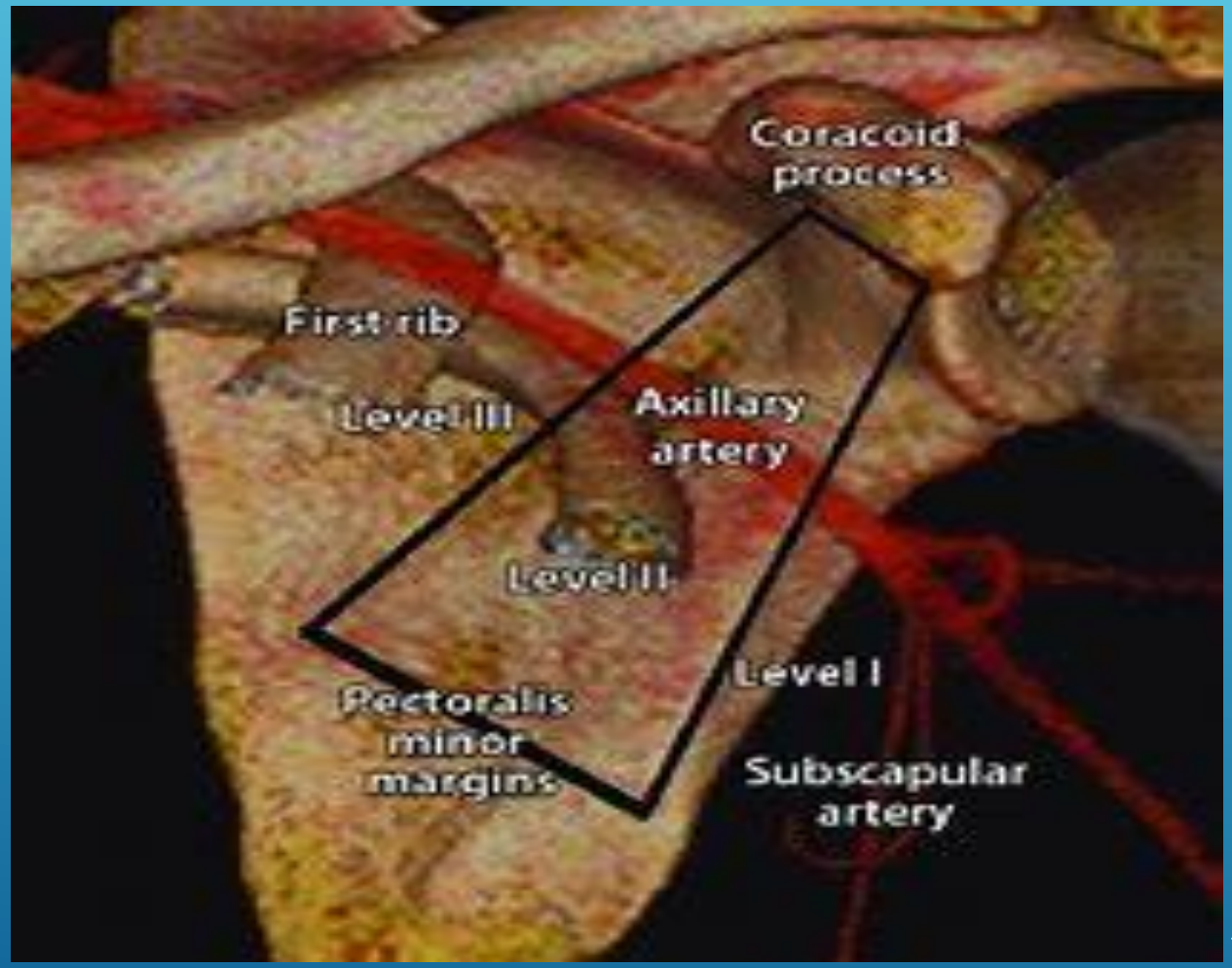
- They suggested that the routine use of preoperative imaging with possible US-FNA may decrease the overall cost of care for patients with invasive breast cancer. Additional benefits of preoperative diagnosis of metastatic lymph nodes mentioned by Boughey et al include the improved ability to plan for postmastectomy radiation therapy and possible neoadjuvant chemotherapy, as well as the ability to better prepare the patient for surgery and counsel the patient about immediate breast reconstruction.

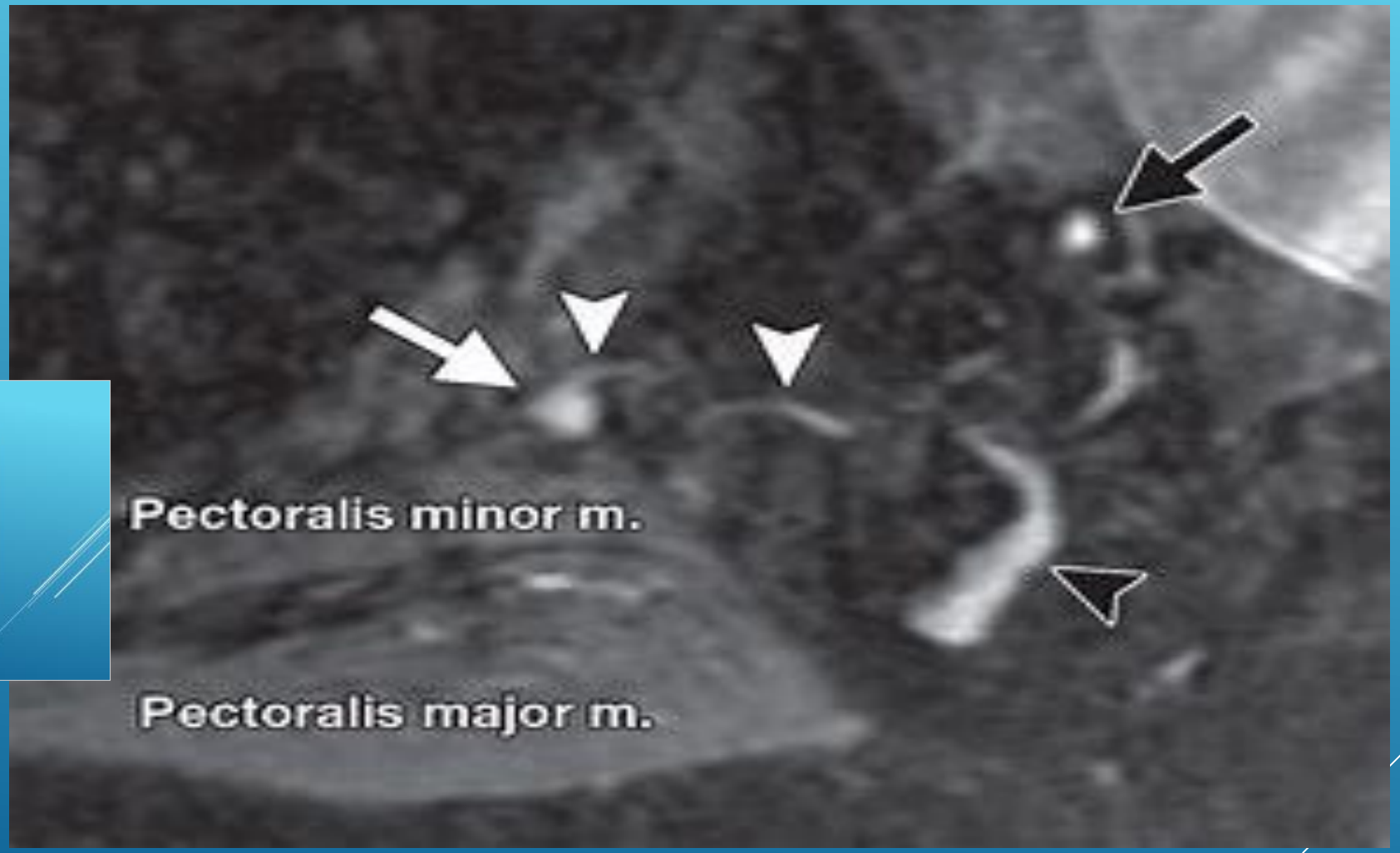
- The important thing for the radiologist to keep in mind is that in current clinical practice, axillary surgery is the definitive test for determining the absence of disease in the axilla. The main goal for preoperative imaging is to identify the presence of axillary metastases with a positive predictive value that is high enough to be useful to the surgeon in deciding when to proceed directly to ALND

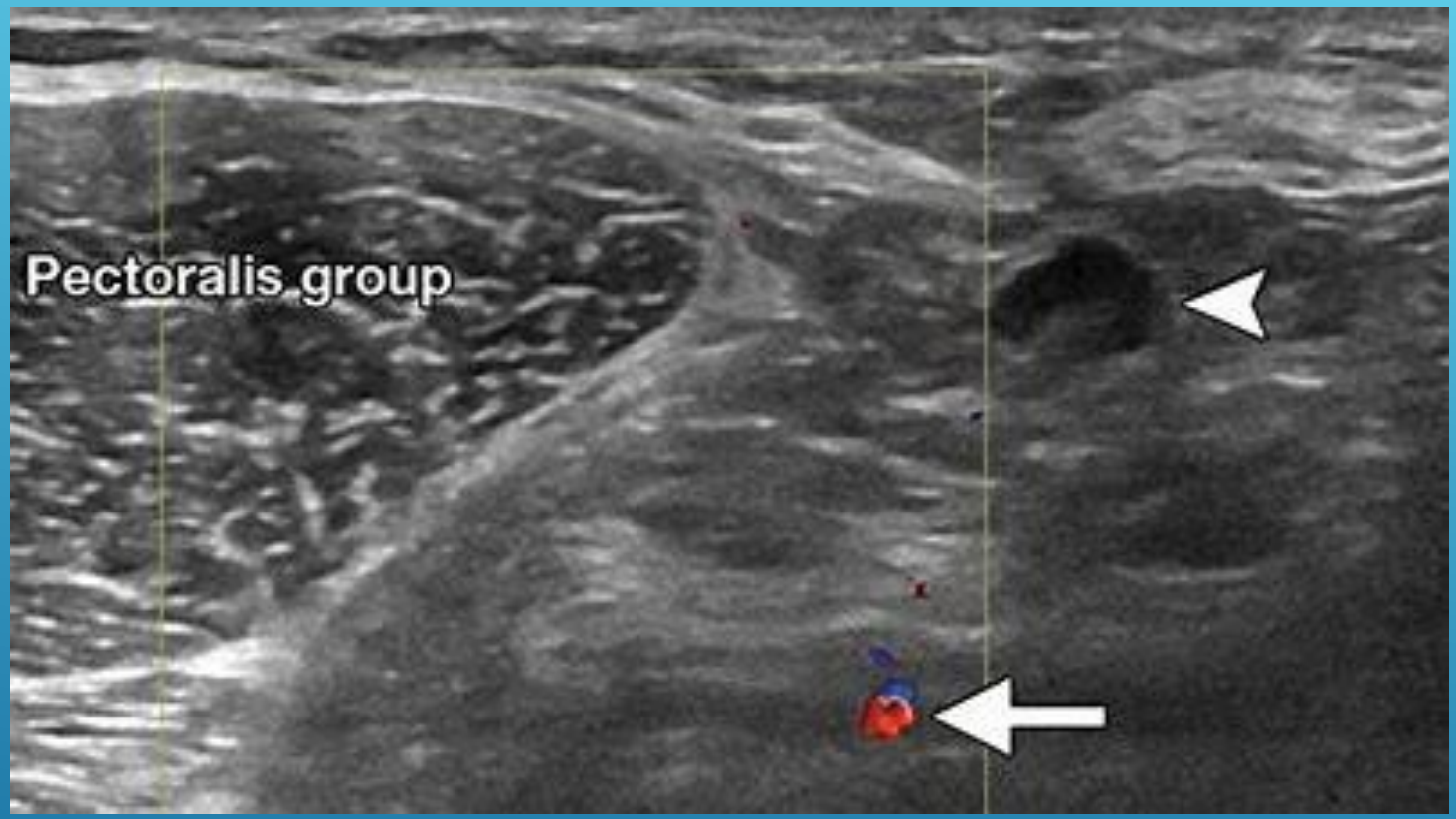
- If false-positive findings from axillary imaging lead the surgeon to perform an unnecessary ALND, or if ambiguous axillary imaging findings result in too many negative percutaneous biopsies, then axillary imaging will become clinically irrelevant or, even worse, detrimental. These scenarios can be avoided by understanding the appearances of normal and metastatic nodes with all imaging modalities and through accurate preoperative sampling of suspicious lymph nodes

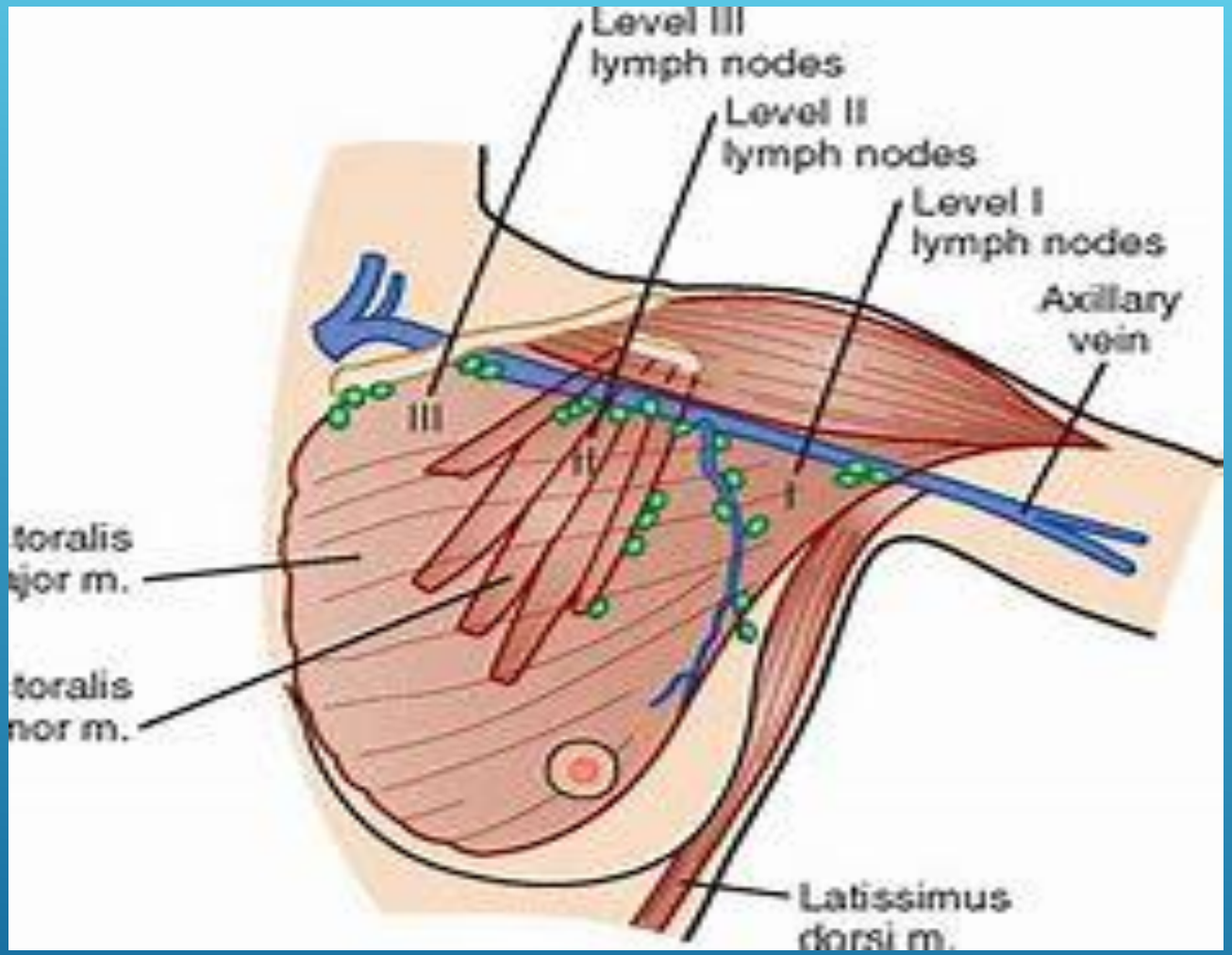
ANATOMY OF THE AXILLA

- Getting oriented in the axilla can be confusing, especially with US, and being familiar with the few existing landmarks is helpful. The axilla is divided into three levels by the pectoralis minor muscle, just as the axillary artery is divided into three segments ,There are five groups of lymph nodes in the axilla: three in level I, which is inferolateral to the pectoralis minor; one group in level II behind the pectoralis minor; and one group superomedial to the pectoralis minor in level III. Drainage generally proceeds in a stepwise fashion from level I to level II, to level III, and finally into the thorax


Coracoid process
First rib
Level III
Axillary artery
Level II
Level I
Pectoralis minor margins
Subscapular artery


Pectoralis minor m.
Pectoralis major m.


Pectoralis group


Level III
lymph nodes
Level II
lymph nodes
Level I
lymph nodes
Axillary
vein
III
II
I
toralis
jor m.
toralis
nor m.
Latissimus
dorsi m.

- The three groups of level I nodes are divided into the lateral group (deep), the subscapular group (posterolateral), and the pectoral group (anteromedial). A systematic approach to evaluating level I nodes begins with the third segment of the axillary artery and the accompanying axillary vein, which run through the deep portion of level I, serving as the first important landmark. Lymph nodes of the lateral group can often be seen near the axillary vein. These nodes predominantly drain the upper extremity. The second useful landmark at cross-sectional and US imaging of

- the axilla is the subscapular artery, which is the largest branch of the axillary artery and the only branch that is seen arising from the inferior surface of the axillary artery in level I of the axilla .After the trunk of this vessel, with its characteristic hook shape is identified, the main terminal branches, the thoracodorsal artery, and the circumflex scapular arteries can often be identified .Short segments of the circumflex scapular artery and its branches are seen as they dive into the muscles that form the posterior wall of the axilla: the latissimus dorsi, the subscapularis, and the teres major The thoracodorsal artery is found along the margin of these posterolateral muscles as it continues through the axillary fat along the chest wall .Lymph nodes of the subscapular group are located along the course of this vessel and the axillary portion of its terminal branches

- These nodes are also frequently seen in isolation in the axillary fat. This group of nodes predominantly drains the scapular region and the posterior chest wall. The third important landmark, the lateral thoracic artery, is found along the anteromedial margin of level I and is seen running parallel and posterior to the lateral margin of the pectoralis minor muscle, with branches into the muscle The lateral thoracic artery is one of the two primary arteries that supply the breast, and it arises from the terminal portion of the second segment of the axillary artery. Lymph nodes of the pectoral group can be found along its course, as well as centrally in the axillary fat

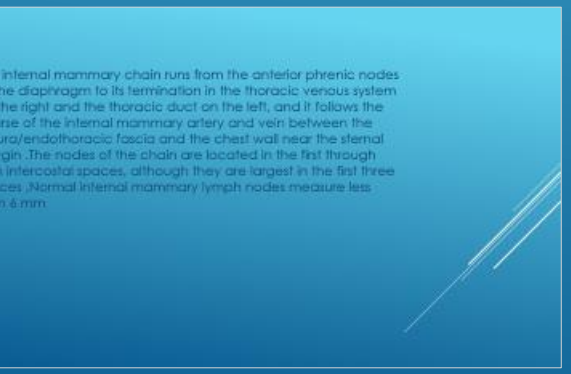
- from the breast is predominantly to the pectoral group of nodes, although any axillary node group can contain the “sentinel” nodes that receive lymph directly from the breast .Most level I nodes are found in the axillary fat without any adjacent structures. Frequently, however, they are seen next to a vessel or close to a particular muscle, and occasionally the hilar vessels to a particular node can be traced back to their artery of origin

PRIMARY AXILLARY LYMPHATIC DRAINAGE

- The central or level II group of axillary lymph nodes is located in the fat behind the pectoralis minor muscle .These nodes receive lymph from level I nodes. Nodes are also located between the pectoralis minor and pectoralis major muscles in an area called the Rotter space .The presence of nodal metastases in level II has the same implication for cancer staging as do those in level I. According to the seventh edition of the AJCC TNM classification, metastases to less than four nonmatted, moveable level I or level II nodes is considered N1 disease

- The apical or level III group of lymph nodes is the final step in lymph drainage through the axilla .The from level II nodes and drain into the subclavian lymphatic trunk and supraclavicular nodes, a path that ultimately leads to the thoracic duct on the left side of the thorax and the right lymphatic duct on the right side. Metastasis to this level automatically indicates N3 nodal staging and therefore stage IIIC disease level III nodes receive lymph.

- **cNX**: regional nodes cannot be assessed (e.g., previously removed)
- **cN0**: no evidence of nodal metastasis (by imaging or clinical examination)
- **cN1**: metastasis to mobile ipsilateral level I/II axillary lymph nodes
  - **cN1mi**: micrometastases (larger than 0.2 mm but none larger than 2.0 mm)
- **cN2**: metastasis to fixed/matted ipsilateral level I/II axillary lymph nodes or to ipsilateral internal mammary artery lymph nodes alone
  - **cN2a**: metastasis to fixed/matted ipsilateral level I/II axillary lymph nodes
  - **cN2b**: metastasis to ipsilateral internal mammary lymph nodes alone without axillary lymph node metastases
- **cN3**: metastasis to ipsilateral infraclavicular (level III axillary) lymph nodes or to ipsilateral internal mammary lymph nodes and level I/II axillary lymph nodes or to ipsilateral supraclavicular lymph nodes
  - **cN3a**: metastasis to ipsilateral infraclavicular (level III axillary) lymph nodes
  - **cN3b**: metastasis to ipsilateral internal mammary lymph nodes and level I/II axillary lymph nodes
  - **cN3c**: metastasis to ipsilateral supraclavicular lymph nodes



- The internal mammary chain runs from the anterior phrenic nodes at the diaphragm to its termination in the thoracic venous system on the right and the thoracic duct on the left, and it follows the course of the internal mammary artery and vein between the pleura/endothoracic fascia and the chest wall near the sternal margin .The nodes of the chain are located in the first through sixth intercostal spaces, although they are largest in the first three spaces ,Normal internal mammary lymph nodes measure less than 6 mm

- Metastases to the internal mammary nodes usually occur after a tumor has metastasized to the axilla, in which case the nodal staging is considered N3b and therefore indicates stage IIIC disease .Isolated metastases to the internal mammary nodes occur in 1%–5% of breast cancers and usually come from deep or medial lesions ,In the absence of axillary metastases, involvement of the internal mammary nodes constitutes N2 disease .

- There is nosurvival benefit to surgical treatment of internal mammary node metastases, and because of the morbidity, dissection of the nodes is not usually performed .However, the presence of internal mammary node metastases, either in isolation or with concomitant axillary disease, does have prognostic significance and also carries a small but definite risk of local recurrence .Long-term survival is reduced in patients with isolated internal mammary node metastases and is reduced even further in patients with both internal mammary and axillary metastases . In addition, standard tangential beam radiation therapy of the breast does not necessarily include the internal mammary nodes. Radiation treatment planning may therefore be altered if metastases of the internal mammary nodes are identified

- Breast metastases generally enter the node through an afferent lymphatic and then deposit in the subcapsular sinusoids Metastatic deposits measuring less than 0.2 mm are called "isolated tumor cells," and deposits between 0.2 and 2.0 mm are called "micrometastases" This level of disease is not identifiable at imaging.

- Growth at this location can result in a focal cortical bulge or eccentric cortical thickening detectable at imaging ,Tumor neovascularity associated with a subcapsular metastasis may be one cause of nonhilar cortical blood flow (NHBF) seen in metastatic nodes at color Doppler imaging . Isolated tumor cells can be found in different microanatomic sites in the node (parenchyma, sinuses, and vascular space) other than the subcapsular sinusoids, and the significance of these deposits in relation to metastatic potential, disease prognosis, and appropriate staging is being investigated One model suggests that tumor cells spread in an orderly fashion from the cortex into the deeper nodal parenchyma, proliferating along the medullary sinuses and then into the efferent lymphatics These deposits spread in the nodal parenchyma in a heterogeneous fashion, replacing the normal architecture as they proliferate This type of destruction can lead to distortion of the

- intranodal “angioarchitecture,” resulting in engorgement of peripheral vascularity that may be another cause of the NHBF seen at color Doppler US .This process may also explain the heterogeneous enhancement of metastatic nodes sometimes seen at DCE MR imaging.

- After continued growth, metastases can obliterate the histologic features of large portions of the node and eventually replace the entire node. Nodal replacement by tumor may prevent a positive sentinel node from taking up radiocolloid or blue dye in the SLNB procedure because the radiopharmaceutical or dye cannot penetrate the “packed” sentinel node

- The imaging finding that reflects this process is the appearance of a uniform hypoechoic node with obliteration of the fatty nodal hilum Extranodal spread of tumor into the adjacent axillary fat can occur and is associated with primary tumors in which lymphatic invasion is seen, tumors that are larger than 2 cm, and the involvement of four or more lymph nodes

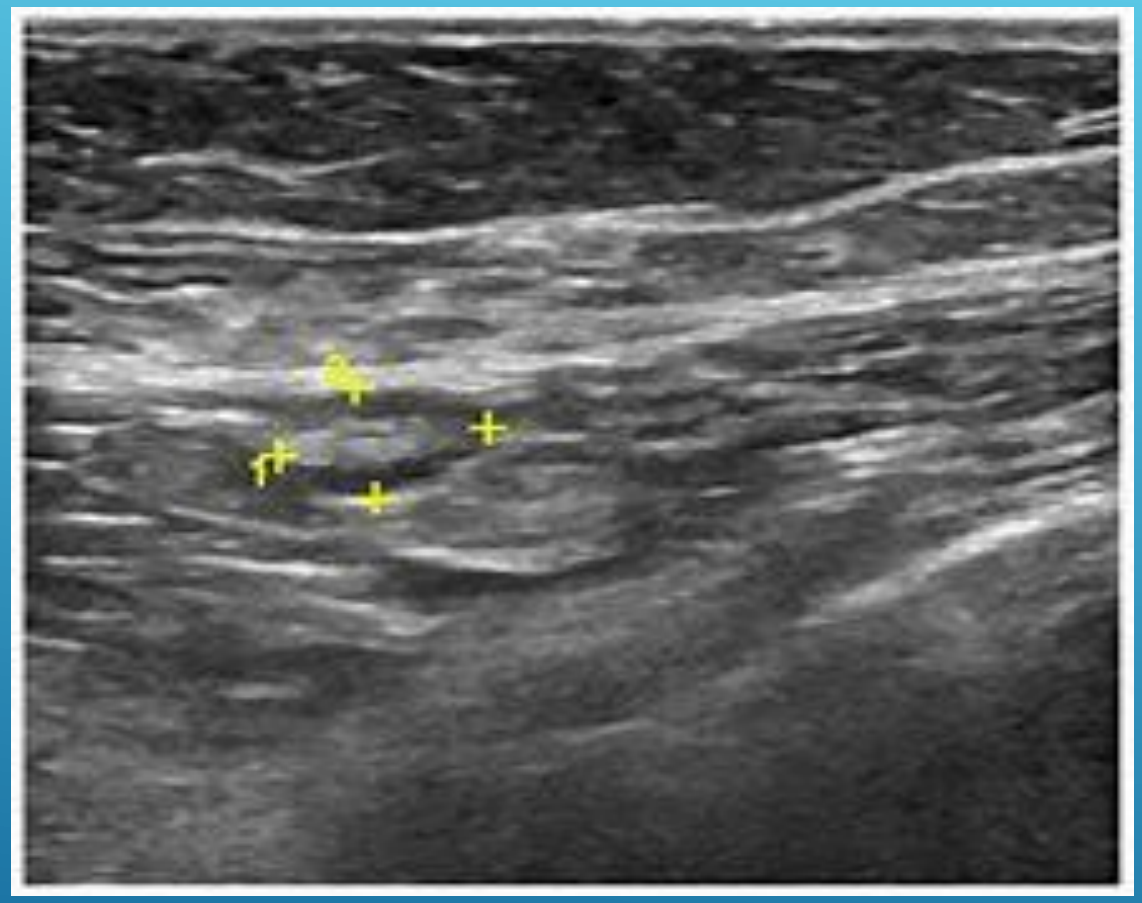
- At imaging, microscopic extranodal deposits can cause loss of definition of the cortical margin or the appearance of spiculation Microscopic extranodal deposits can also stimulate growth of perinodal neovascularity which is perhaps another source of abnormal NHBF detected at US. Ultimately, the node may be replaced by an irregular mass, which is readily recognizable at imaging.

- US is the primary nonsurgical method for evaluating axillary nodes
  It is moderately sensitive and can be highly specific, especially when morphologic criteria are used as the primary diagnostic criteria,

- Overall size of the node has very poor diagnostic accuracy for predicting metastasis, however, and in the absence of other associated findings, overall size should not be used as a criterion (.The normal axillary lymph node should be oval and should have a smooth, well-defined margin ,The cortex should be slightly hypoechoic and uniformly thin, measuring 3 mm or less. Nodes that meet this description have a very high negative predictive value for excluding metastases .The echogenic hilum should constitute the majority of the node. Arterial flow in the hilum can be demonstrated with color Doppler imaging

- . A focal cortical bulge or thickening is considered the earliest detectable morphologic change in the presence of metastasis, but this criterion is difficult to apply and has a low positive predictive value because it is nonspecific

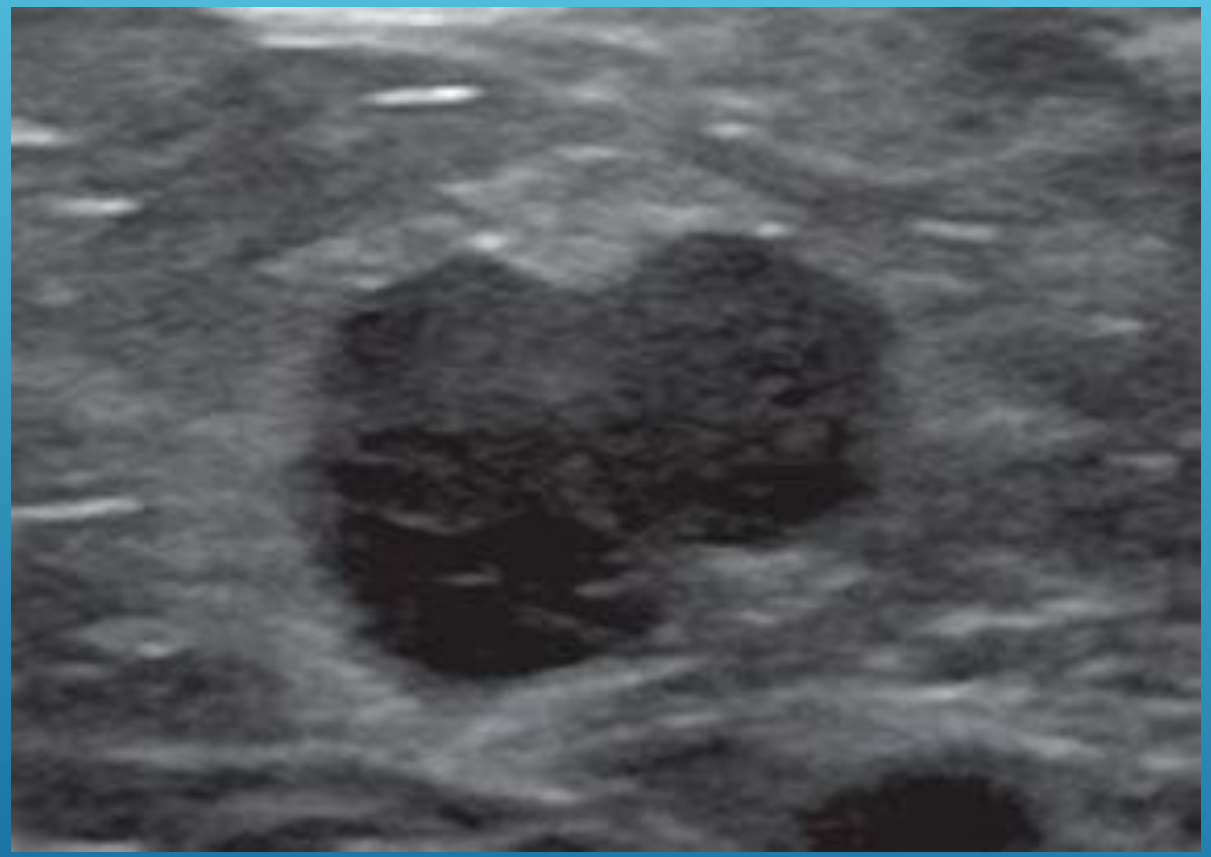
- . This finding is therefore considered indeterminate. Normal lymph nodes often have a lobulated shape because of concurrent constrictions and bulges of both the cortex and fatty hilum. A true abnormal cortical bulge is seen as focal thickening of the cortex that does not follow the margin of the echogenic hilum and should be distinctly hypoechoic.

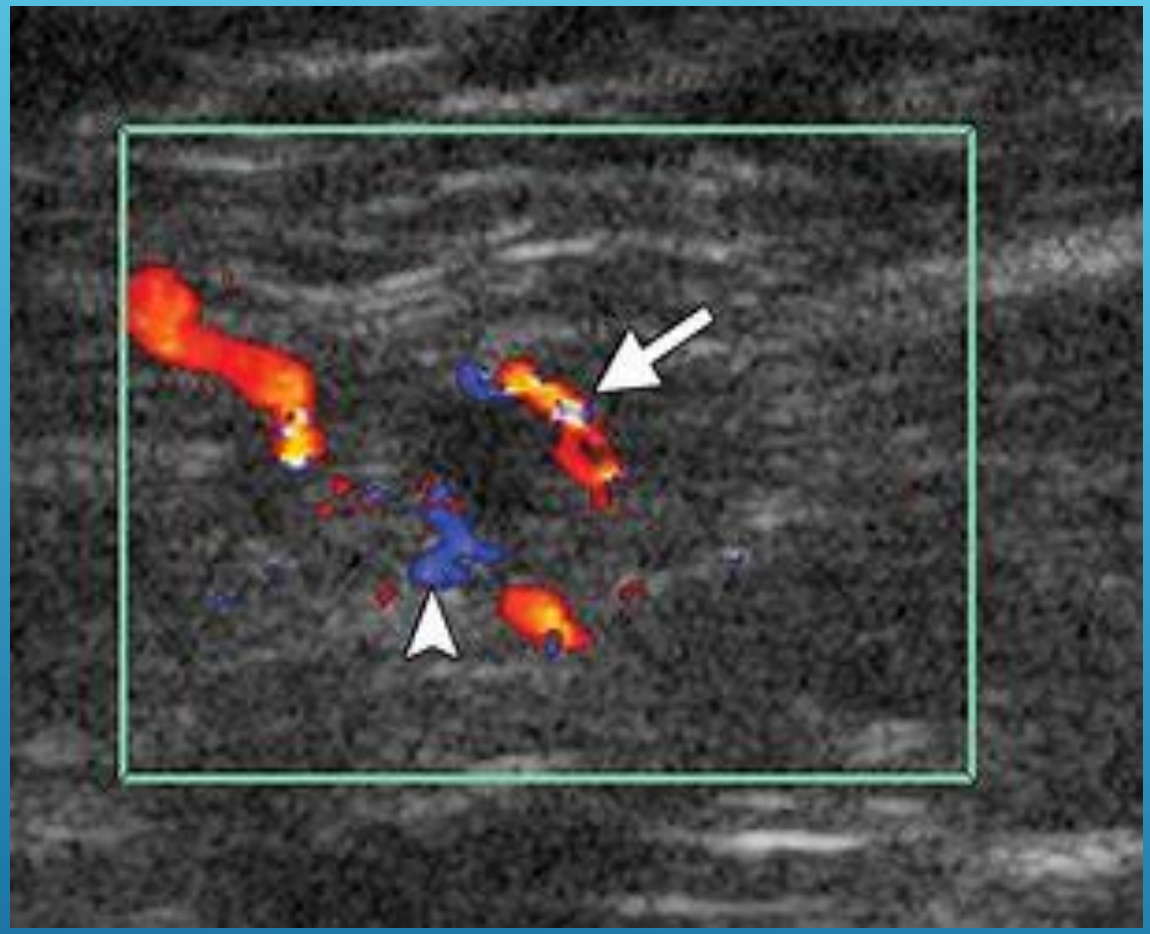


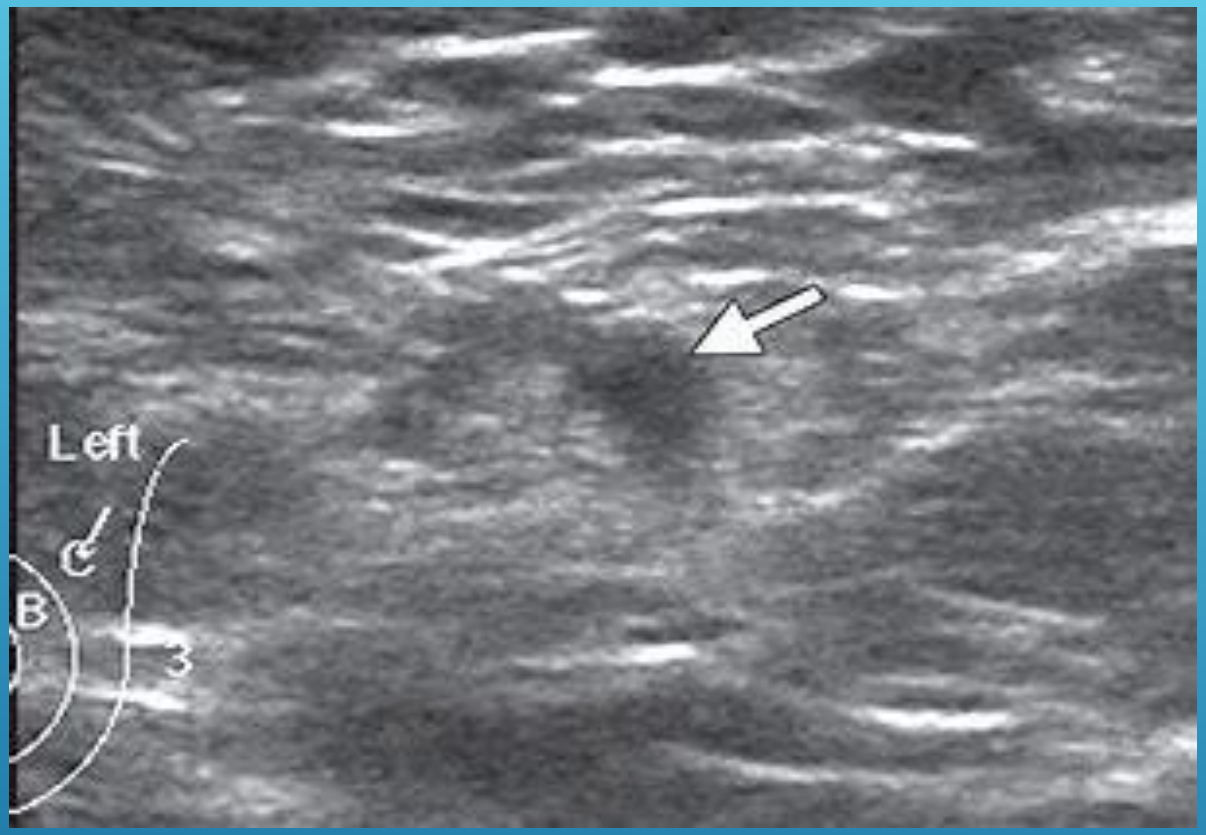
- When used as a diagnostic sign, the focal bulge should be conspicuous, and the sign is more accurate if it is associated with another finding such as NHBF .Diffuse cortical thickening can also be seen with metastasis, but this finding is even more nonspecific, often being associated with a reactive node. Thickness can be evaluated subjectively or by measurement ,Measurements to determine the upper limit of normal cortical thickness that have been reported in the literature range from 2 to 3 mm

US Findings	Comments	Figure
Diffuse cortical thickening	Cortical thickness > 3 mm, relatively nonspecific, can be seen in reactive nodes	...
Focal cortical bulge	Should be distinct, otherwise less specific; more specific if associated with another finding such as NHBF	Fig 17
Eccentric cortical thickening	Should be distinctly eccentric, otherwise less specific	Fig 18
Rounded hypoechoic node	High specificity in the setting of invasive cancer	Fig 19
Complete or partial effacement of the fatty hilum	High specificity in the setting of invasive cancer	Fig 19
NHBF on color Doppler images	Nonspecific unless combined with another finding, such as effacement of the fatty hilum	Figs 17–19,
Complete or partial replacement of the node with an ill-defined or irregular mass	High specificity	Fig 20
Microcalcifications in the node	Should correlate with microcalcifications in the primary tumor	Fig 21

- The ratio of the cortical thickness to the short axis diameter cutoff of 50%, is also used . Eccentric cortical thickening is slightly more suspicious than diffuse thickening, which can be seen in reactive nodes, but is still nonspecific. Findings seen in cases with more advanced nodal involvement, such as effacement of the fatty hilum or a rounded hypoechoic node, have a higher positive predictive value in patients with invasive breast cancer, and performance of US-FNA or USCNB has been recommended for these nodes by some authors



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B
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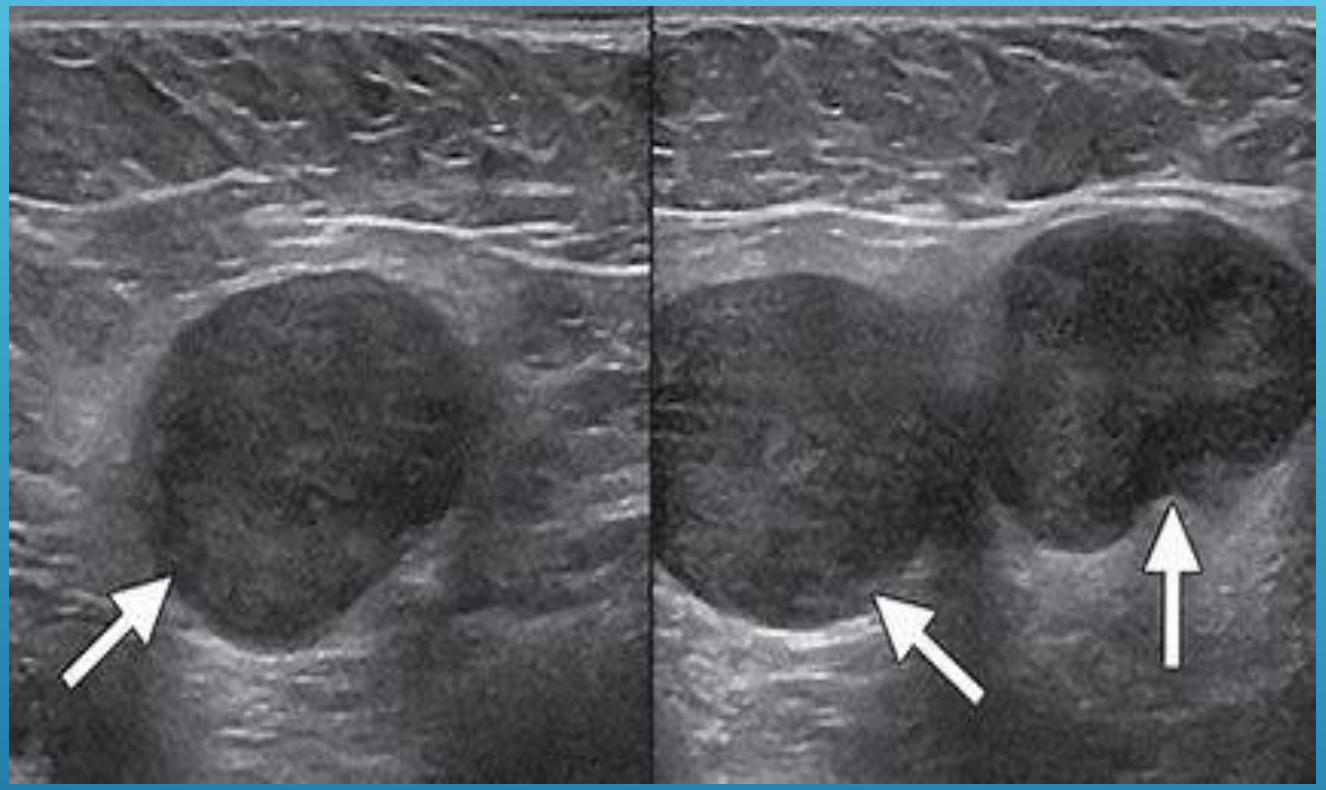
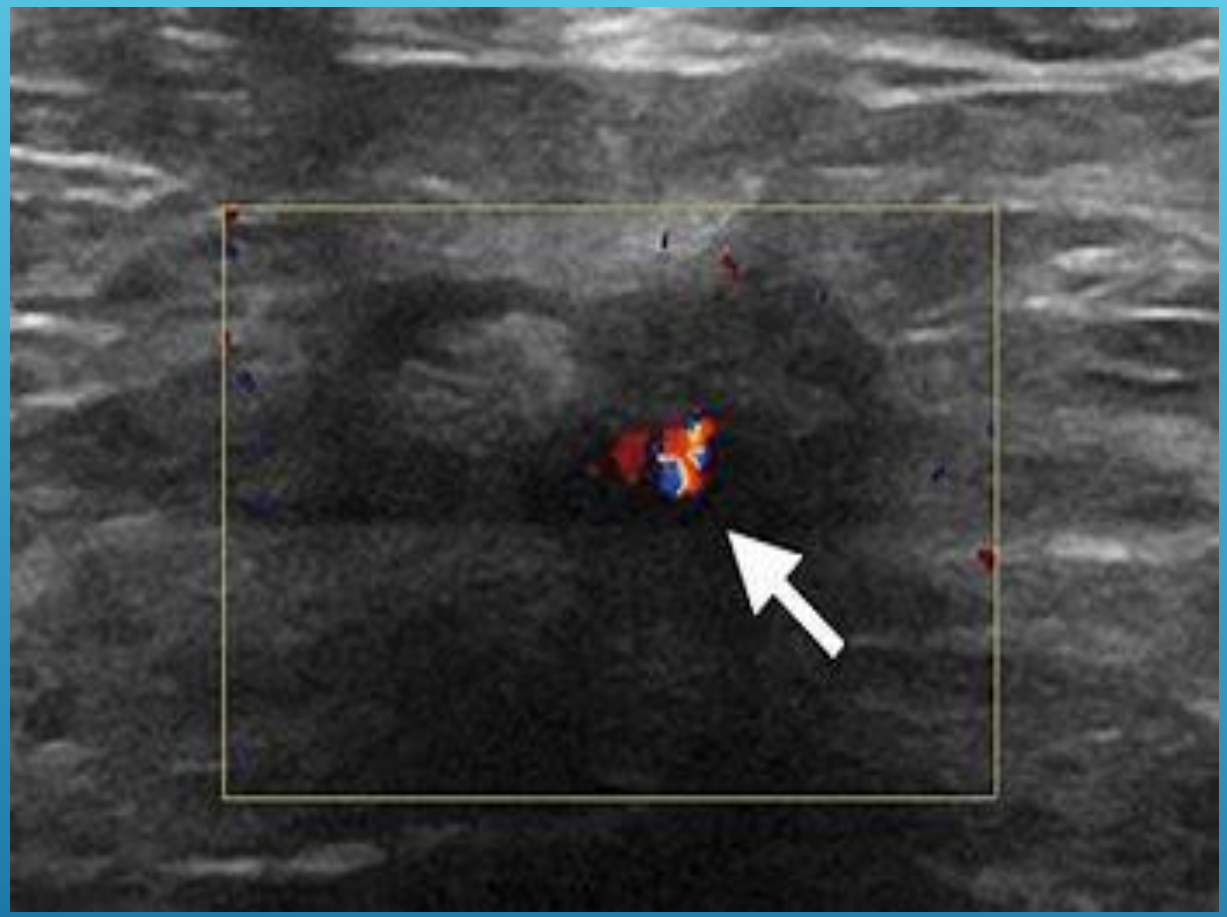
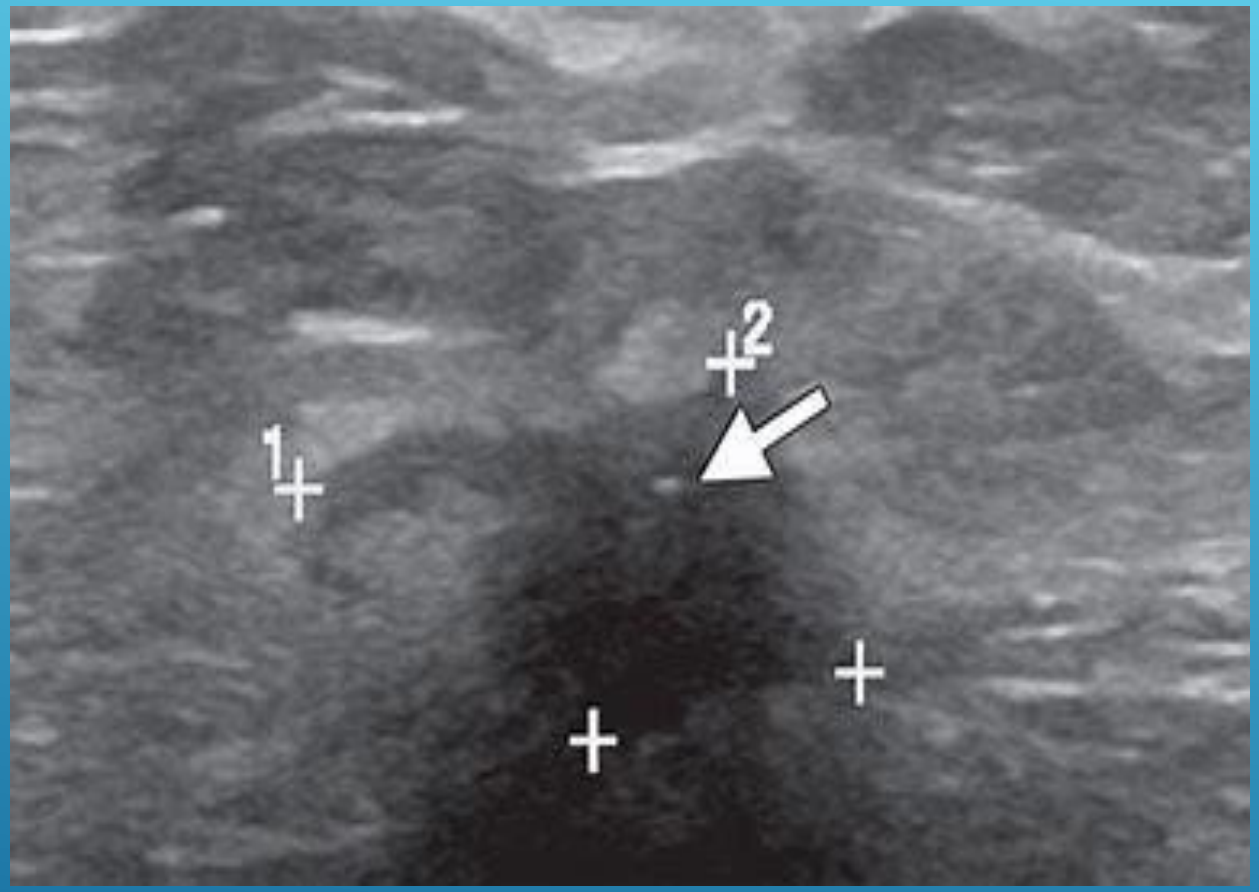


- Replacement of theentire node or a portion of the node by an illdefined mass is a highly suspicious finding ,Occasionally, microcalcifications can be seen in the node at US,

- Color Doppler US is useful for identifying NHBF, which is the appearance of peripheral vascular flow at the cortex of the node with no detectable connection to the hilum .This finding has been shown to have a high positive predictive value for metastasis in the setting of an ipsilateral invasive breast cancer Diffuse hyperemia arising from the hilum can also be seen in metastatic nodes but this finding is not specific and can be seen in reactive lymph node

- Because SLNB has a very high sensitivity, the choice of sonographic criteria used to diagnose metastatic nodes should be made with the goal of achieving as high a specificity as possible, even at the expense of some sensitivity. As with axillary imaging in general, US is less useful if its results lead to unnecessary ALND or too many US-FNA or US-CNB procedures with negative findings.

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- Confirming Imaging Findings with US-FNA and US-CNB When axillary imaging is employed for preoperative evaluation of patients with invasive breast cancer, percutaneous procedures, either US-FNA or US-CNB, are indispensable to confirm that a suspicious node harbors a metastasis before the patient undergoes full ALND (Both forms of sampling have a high positive predictive value because the basis of a positive result is cytologic or histologic. The shortfall comes in the sensitivity of these tests, partly because of thelimitations of imaging and partially because of limitations inherent in the small samples obtained (a problem that is more pronounced in FNA than CNB). The results for axillary US-FNA have varied, with reported sensitivities ranging from 25% to 87.2%

- Authors have described various methods for increasing the positive yield of US-FNA, including (a) limiting the selection criteria for patients undergoing the procedure to those with large primary tumors, (b) selecting patients with primary tumors that have lymphovascular invasion, or (c) measuring tumor markers in the FNA aspirate in conjunction with a cytology examination .Limitations to US-FNA include the fact that it is operator dependent, it requires the cooperation of an experienced cytopathologist, and it has a high false-negative rate

- . US-FNA and US-CNB have a low rate of morbidity, with multiple studies reporting no significant complications .An “open trough” technique has been described for US-CNB to reduce the risk of hematoma that results from the “throw” of the core biopsy needle .Because US-FNA has a significantly higher false-negative rate compared with that of US-CNB and because US-CNB has been shown to be safe, many institutions have abandoned US-FNA entirely. It should be noted that these procedures do add expense to patient management, especially if they return a negative result

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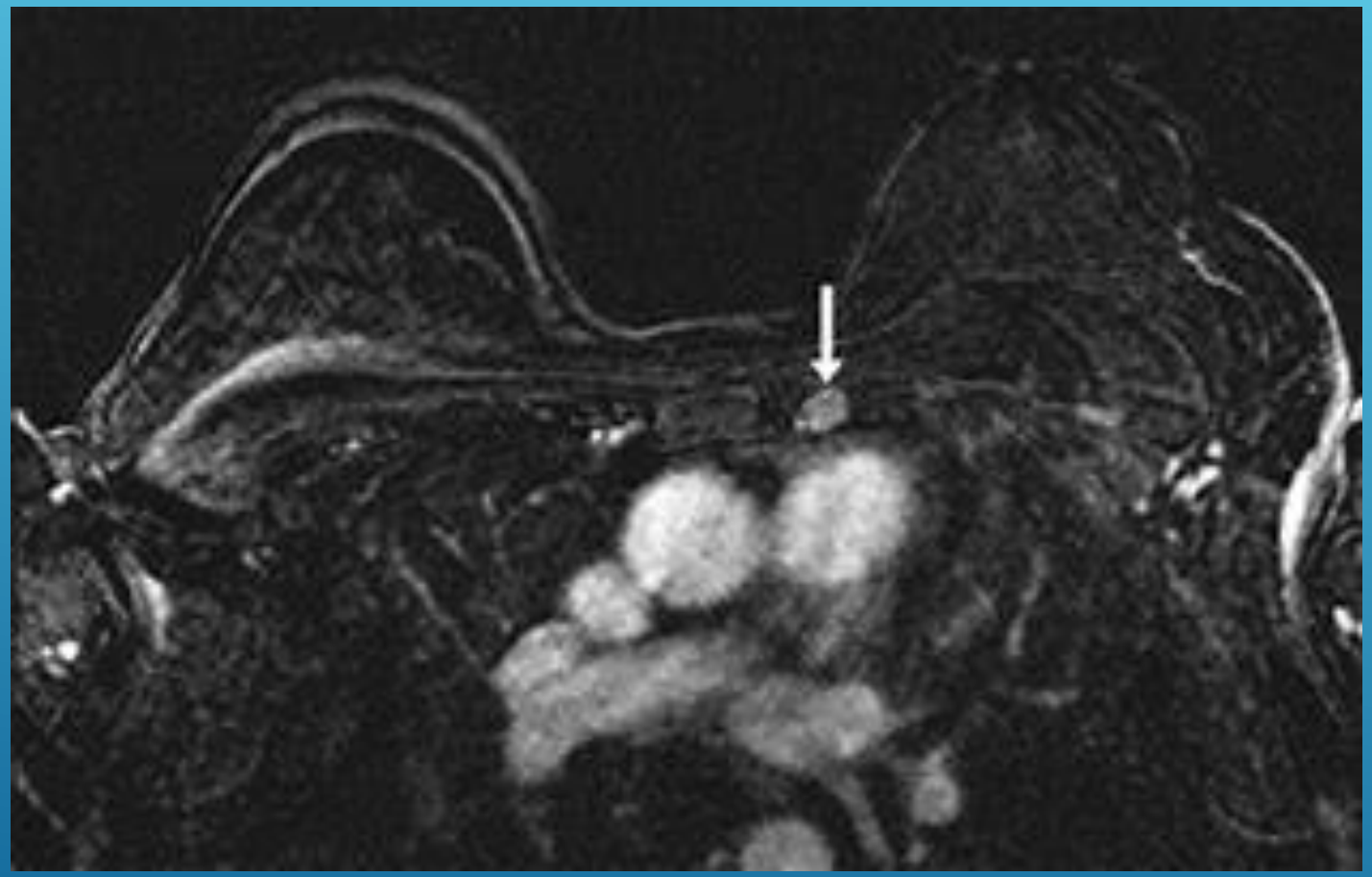
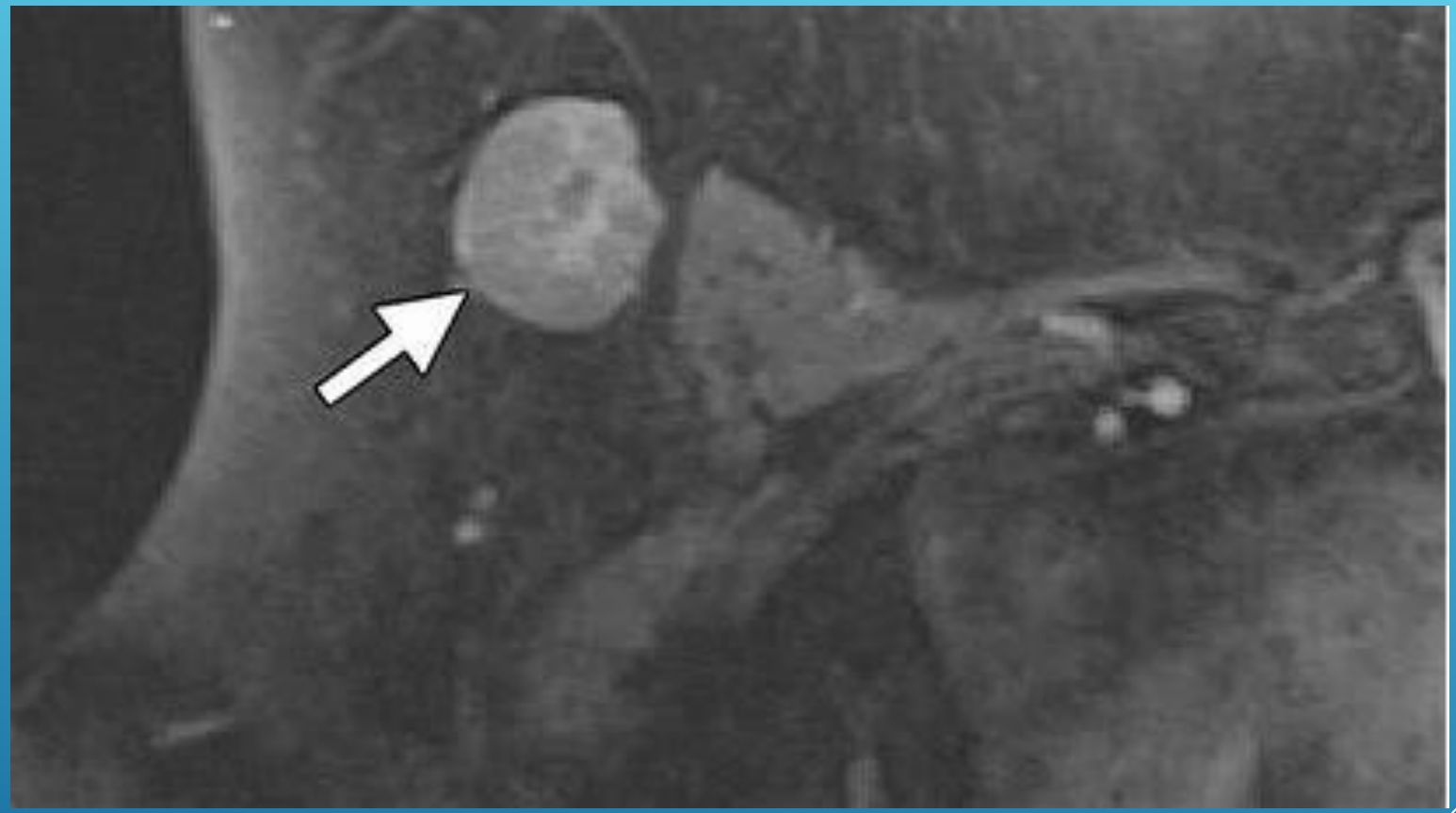
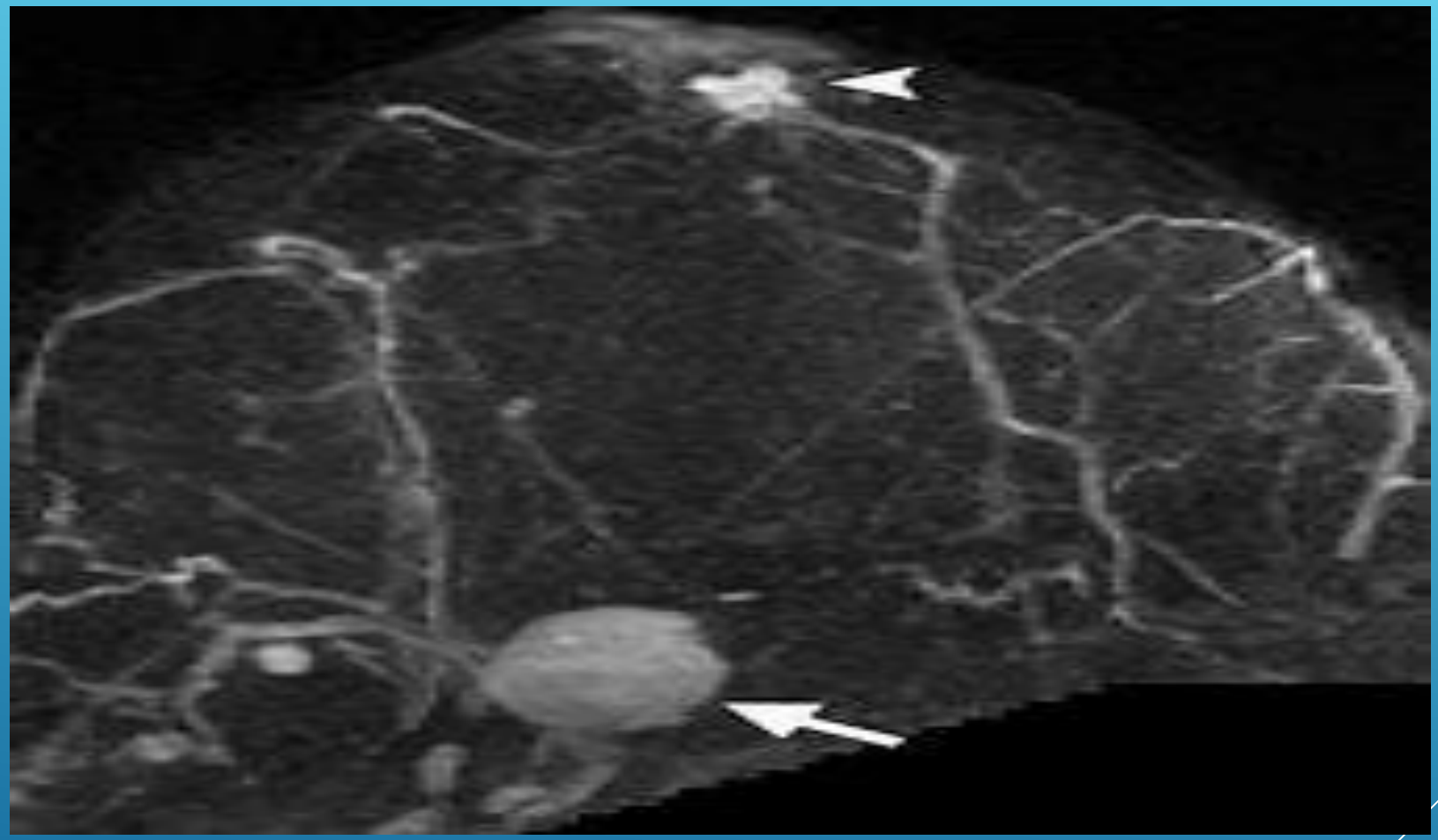
- . Although this additional cost can be balanced by the reduction in expenses from avoiding SLNB and a second trip to the operating room, use of US-FNA or US-CNB should be reserved for patients with lymph nodes that demonstrate abnormal sonographic features that have a relatively high likelihood of yielding a positive result .

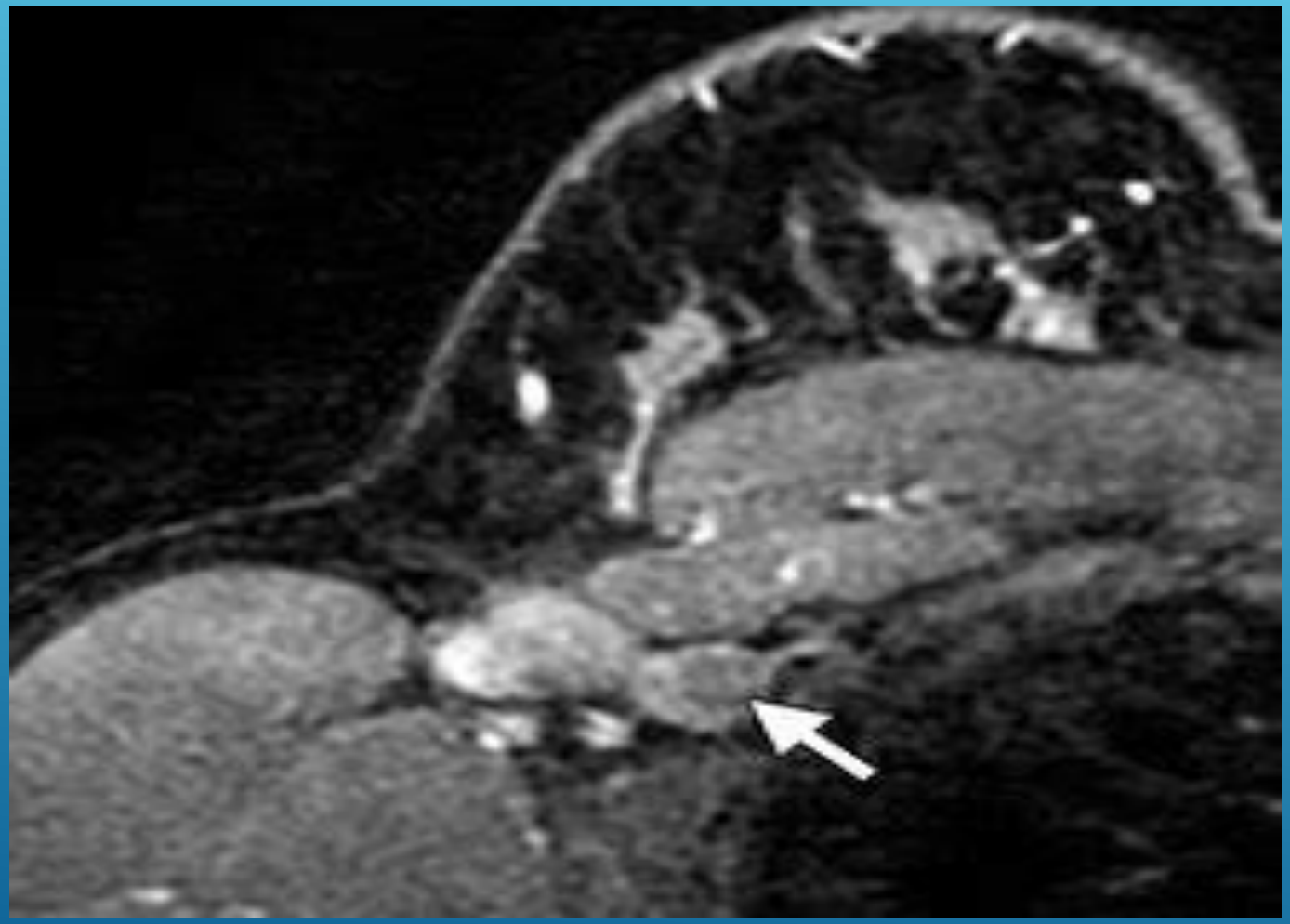
- MR Imaging Evaluation of Axillary Lymph Nodes The axilla is usually included in the field of view in clinical breast MR imaging examinations. However, visualization of the axilla can be limited , Although the familiar gross reniform morphology of normal lymph nodes is better demonstrated at US, it can be appreciated at MR imaging



- Morphologic features that can be seen with metastasis include cortical thickening, loss of fatty hilum, heterogeneous enhancement, and round shape or a long axis to short axis ratio of less than 2Two MR imaging features that have potential diagnostic utility when present are “perifocal edema,” which is defined as the presence of areas with marked T2 prolongation in the fat surrounding a node, and “rim enhancement,” which is defined as signal intensity that is higher at the periphery of a node than at its center on DCE MR images obtained 11 minutes after infusion .Both of these findings had a 100% positive predictive value for the detection of metastases in the study by Baltzer et al








Pectorialis major m.
Pectoralis minor m.
Chest wall
RT BREAST 12:00 9CM RAD

- As with other modalities, MR imaging depiction of nodal size is not useful for identifying metastatic nodes In one study, however, small lymph nodes (as measured by nodal area with a threshold of with a threshold of had a high negative predictive value for excluding metastasis ,Similar to the results of other modalities, the MR imaging findings that are highly suggestive of metastatic disease in patients with invasive breast cancer are markedly enlarged and morphologically grossly abnormal lymph nodes, especially when they are distinctly different from other visible axillary nodes

- Conventional PET has insufficient sensitivity for detecting metastases, ranging from 25% to 84% across multiple studies, and is not recommended for axillary staging .A more recent systematic review of 26 PET and PET/CT studies included in a cost-effectiveness analysis also showed that these modalities had poor sensitivity but high specificity in the diagnosis of axillary metastases .The mean sensitivity for the seven PET/CT studies in that review was 56%. Positron emission mammography is being studied as an alternative to DCE MR imaging for local staging of early breast cancer, but data relating to axillary staging are limited.

- 1. Ipsilateral level I and II axillary nodes that are fixed to each other or to adjacent structures (ie, matted) indicate N2 disease. N2 disease raises the stage to at least IIIA .Metastases in ipsilateral internal mammary nodes in the absence of axillary node metastases indicate N2 disease. 3. Ipsilateral level III node metastases with or without level I or II involvement indicate N3 disease. N3 disease raises the stage to at least IIIC , Ipsilateral internal mammary node involvement with level I or II axillary involvement represents N3 disease 5. Ipsilateral supraclavicular nodes regardless of axillary involvement represent N3 disease

NODAL PORTION OF THE AJCC TNM STAGING SYSTEM

- In the long run, imaging may play a more important role in the staging of axillary disease. The ACOSOG Z0011 trial is part of a trend toward performing less axillary surgery