





# IMAGING OF CUPax

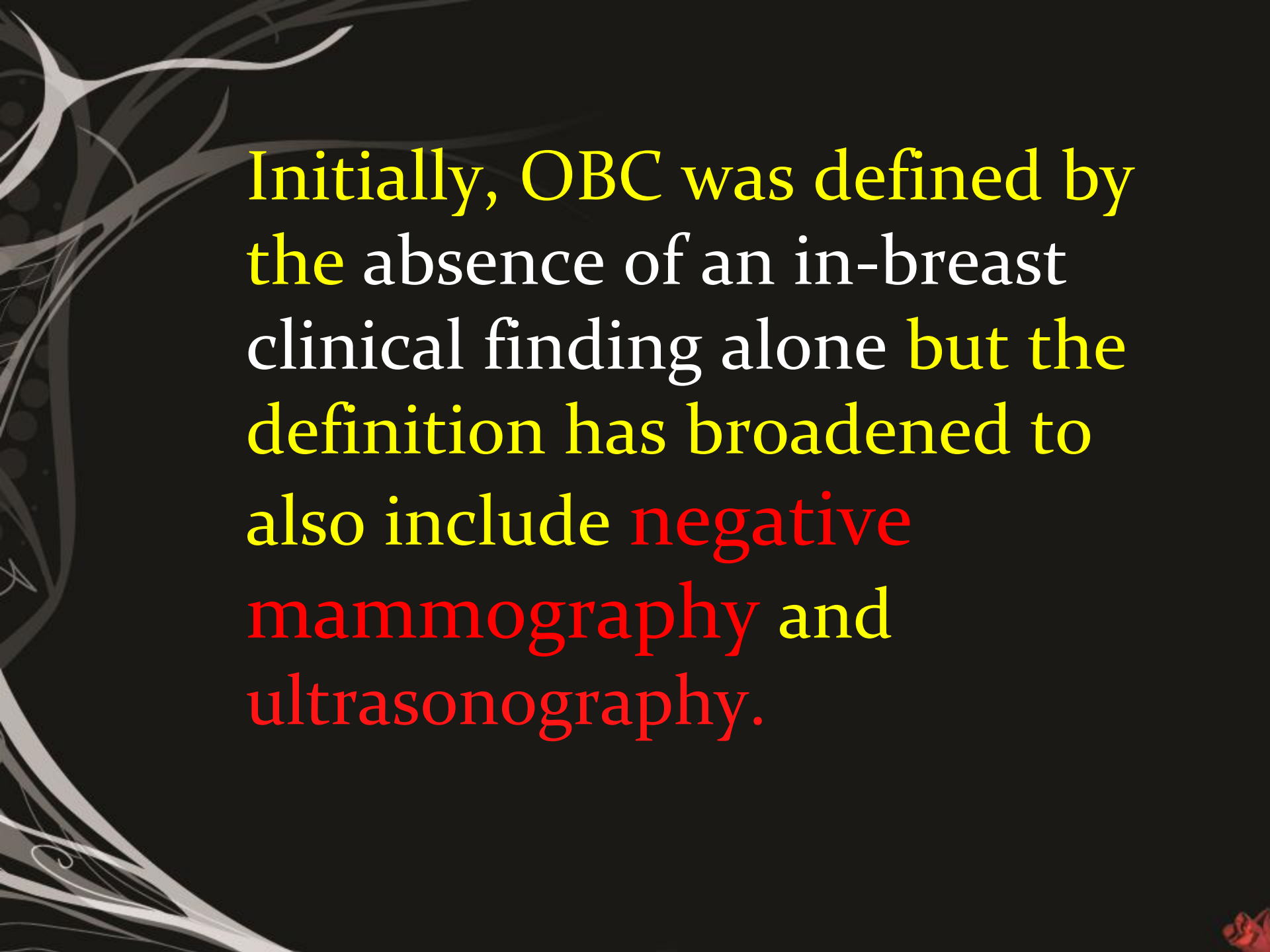


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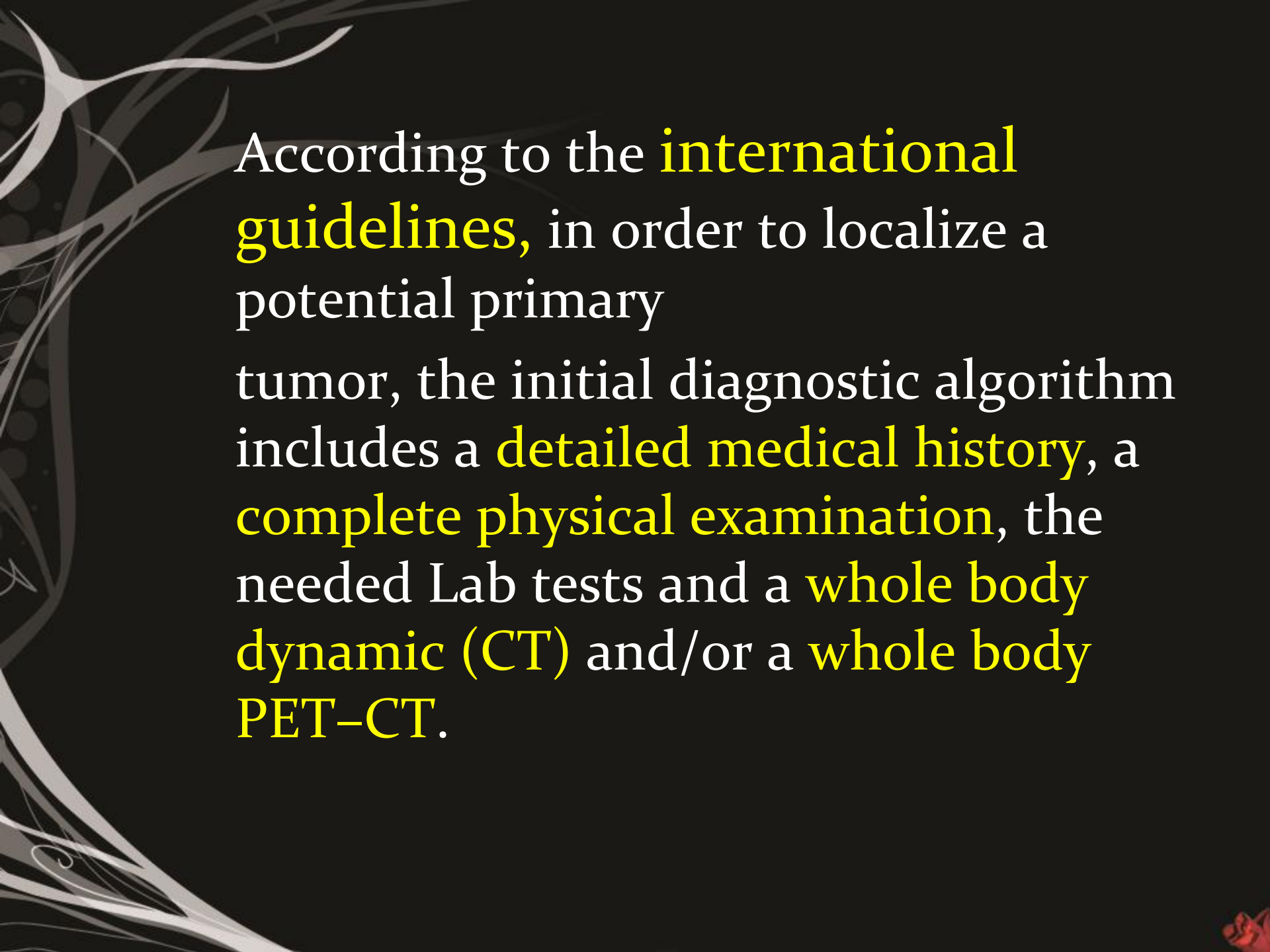


# CUPax

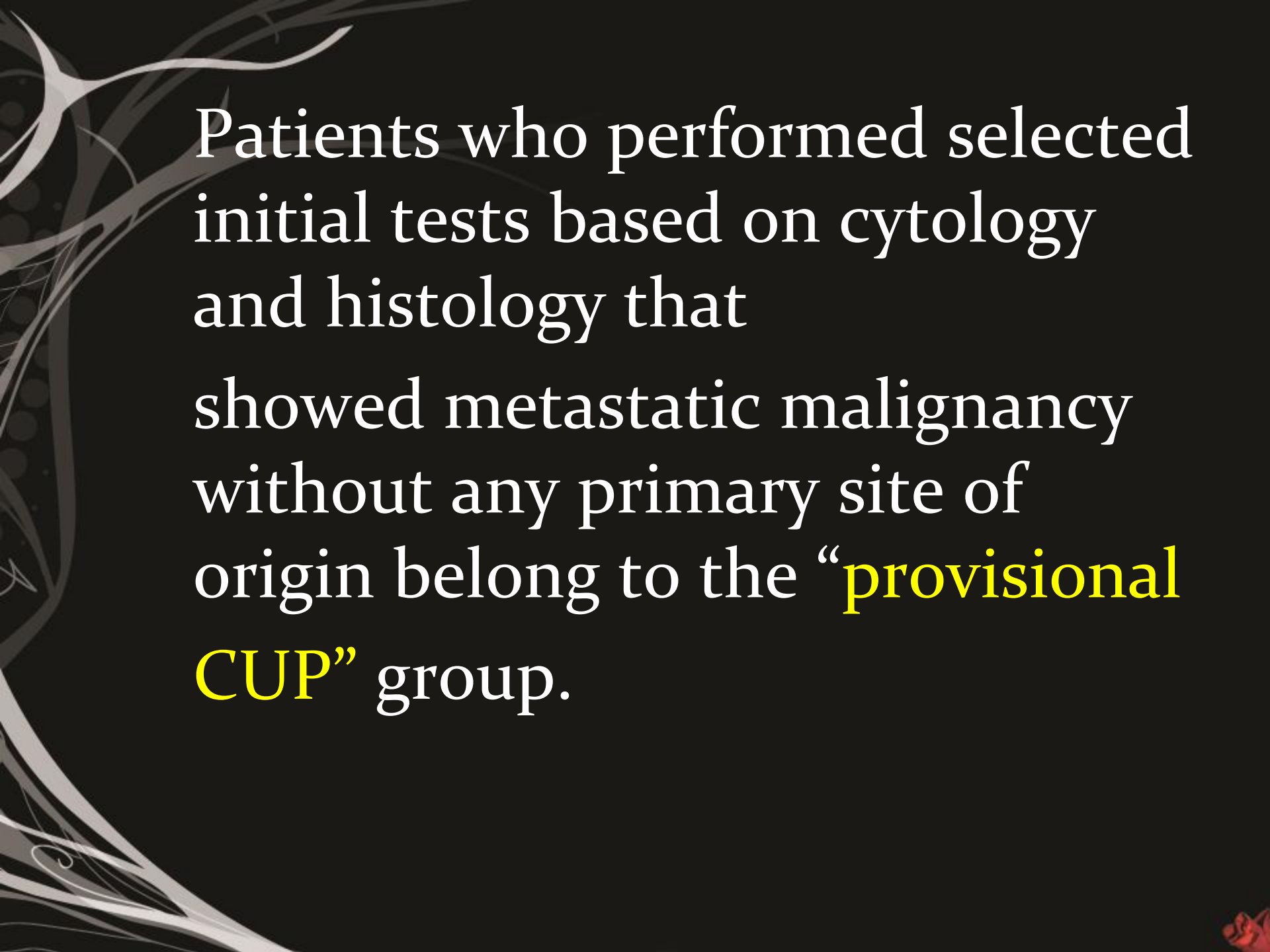
Axillary lymph node metastases of occult primary cancer (CUPax) is an unusual condition that represents both a diagnostic and therapeutic challenge.



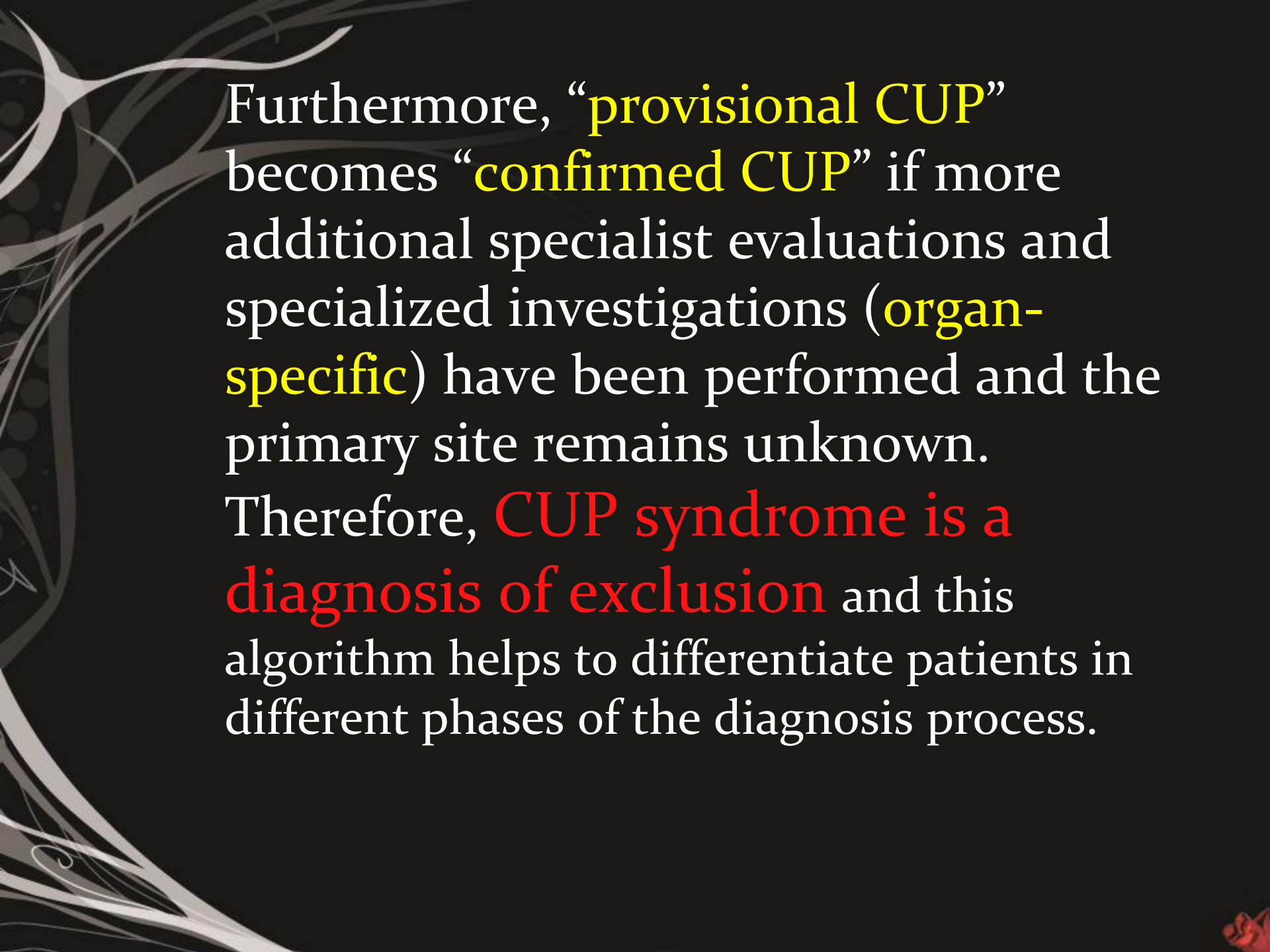
Initially, OBC was defined by the absence of an in-breast clinical finding alone but the definition has broadened to also include negative mammography and ultrasonography.



According to the **international guidelines**, in order to localize a potential primary tumor, the initial diagnostic algorithm includes a **detailed medical history**, a **complete physical examination**, the needed Lab tests and a **whole body dynamic (CT)** and/or a **whole body PET-CT**.

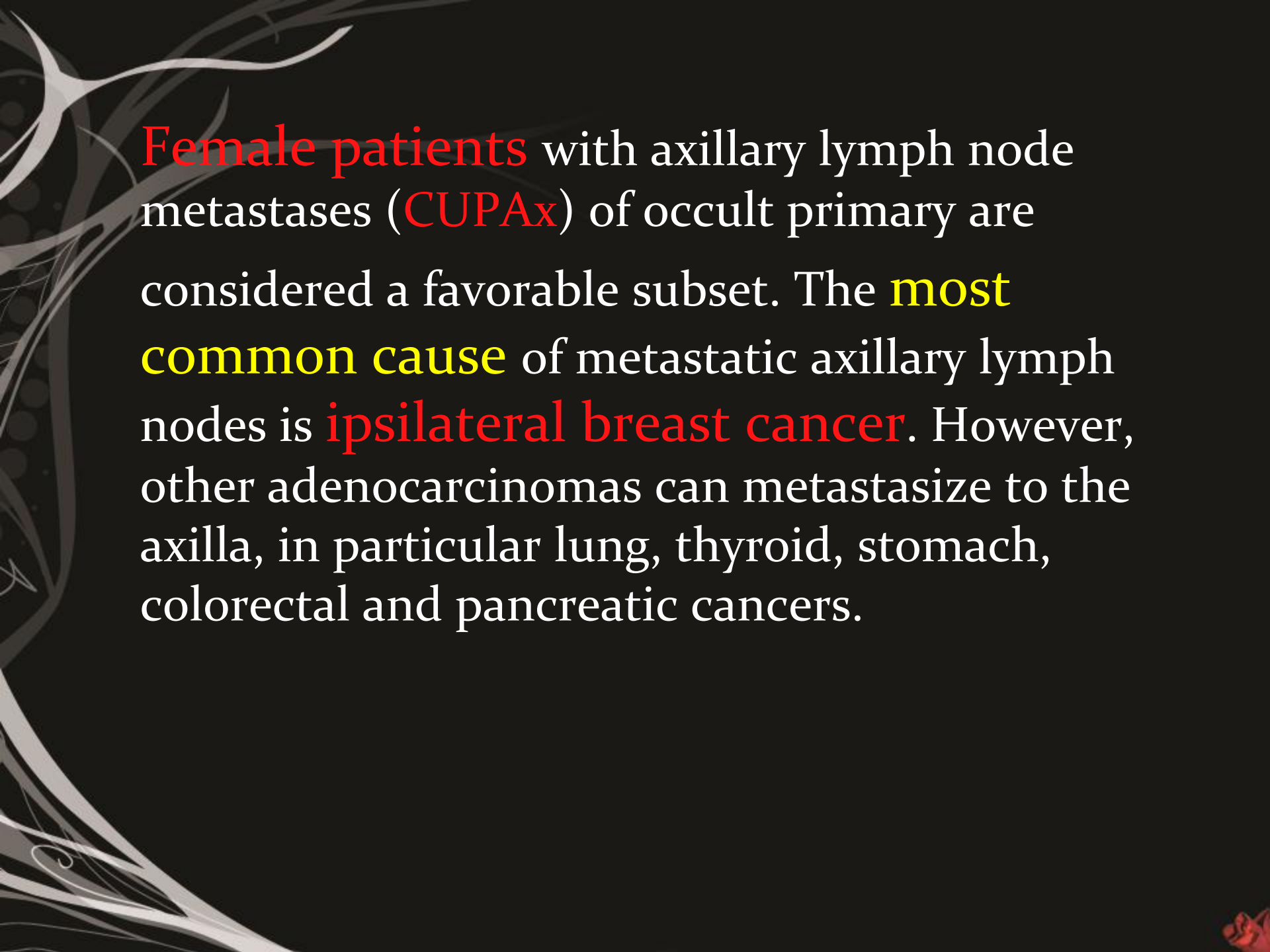


Patients who performed selected initial tests based on cytology and histology that showed metastatic malignancy without any primary site of origin belong to the “provisional CUP” group.



Furthermore, “**provisional CUP**” becomes “**confirmed CUP**” if more additional specialist evaluations and specialized investigations (**organ-specific**) have been performed and the primary site remains unknown.

Therefore, **CUP syndrome is a diagnosis of exclusion** and this algorithm helps to differentiate patients in different phases of the diagnosis process.



**Female patients** with axillary lymph node metastases (**CUPAx**) of occult primary are considered a favorable subset. The **most common cause** of metastatic axillary lymph nodes is **ipsilateral breast cancer**. However, other adenocarcinomas can metastasize to the axilla, in particular lung, thyroid, stomach, colorectal and pancreatic cancers.

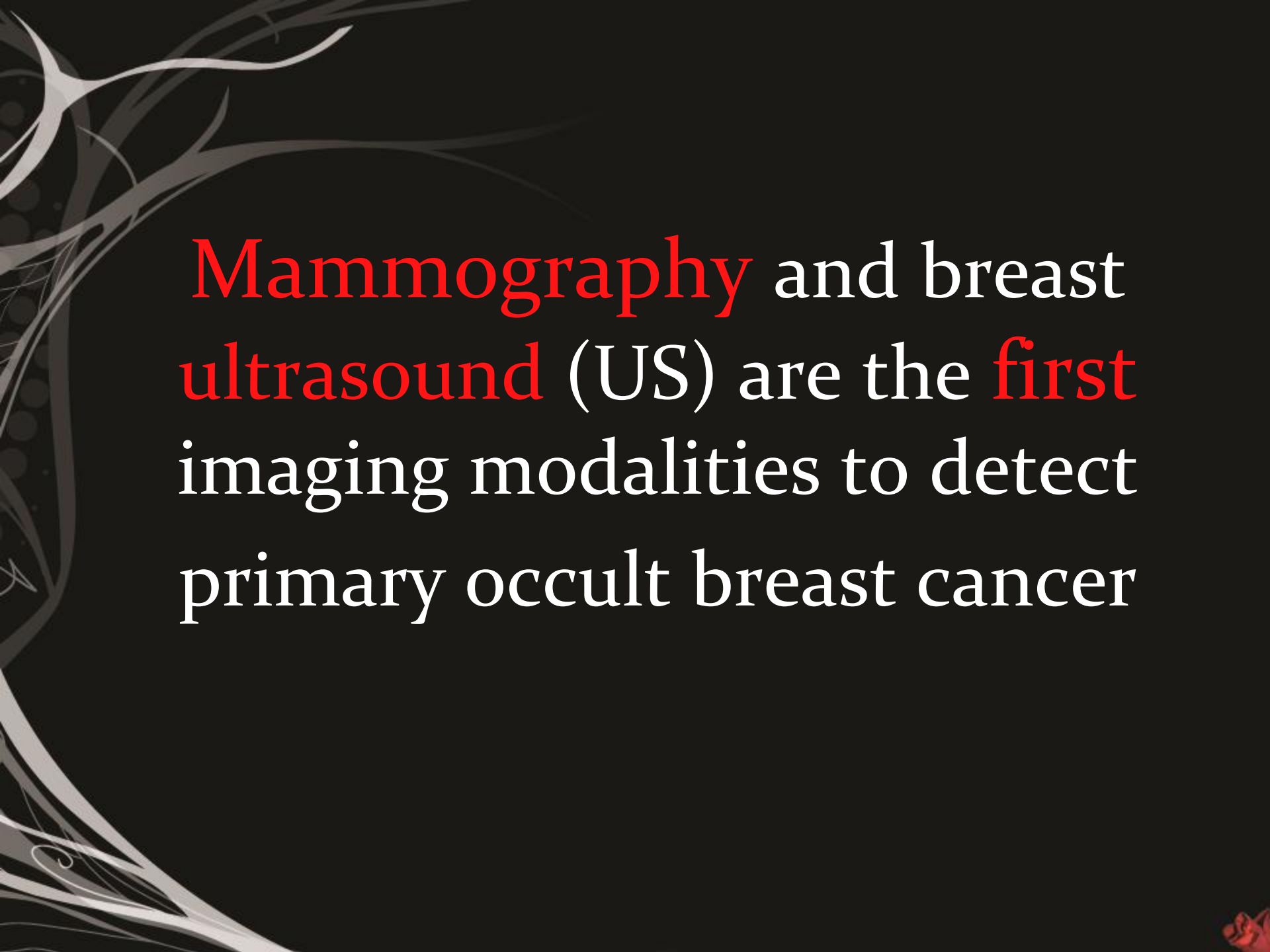


In 0.3–1% of all women with •  
breast cancer, metastatic  
adenopathy of the axilla is  
the first symptom of the •  
disease and it occurs mainly in  
the post-menopausal age.

The fulcrum of the diagnostic strategy  
... is the **biopsy of the pathological lymph node**

and the **IHC** and molecular analyses of the sample.

When the histology confirms an **adenocarcinoma** or a **poorly differentiated carcinoma**, the presence of occult ipsilateral breast cancer is the most likely.



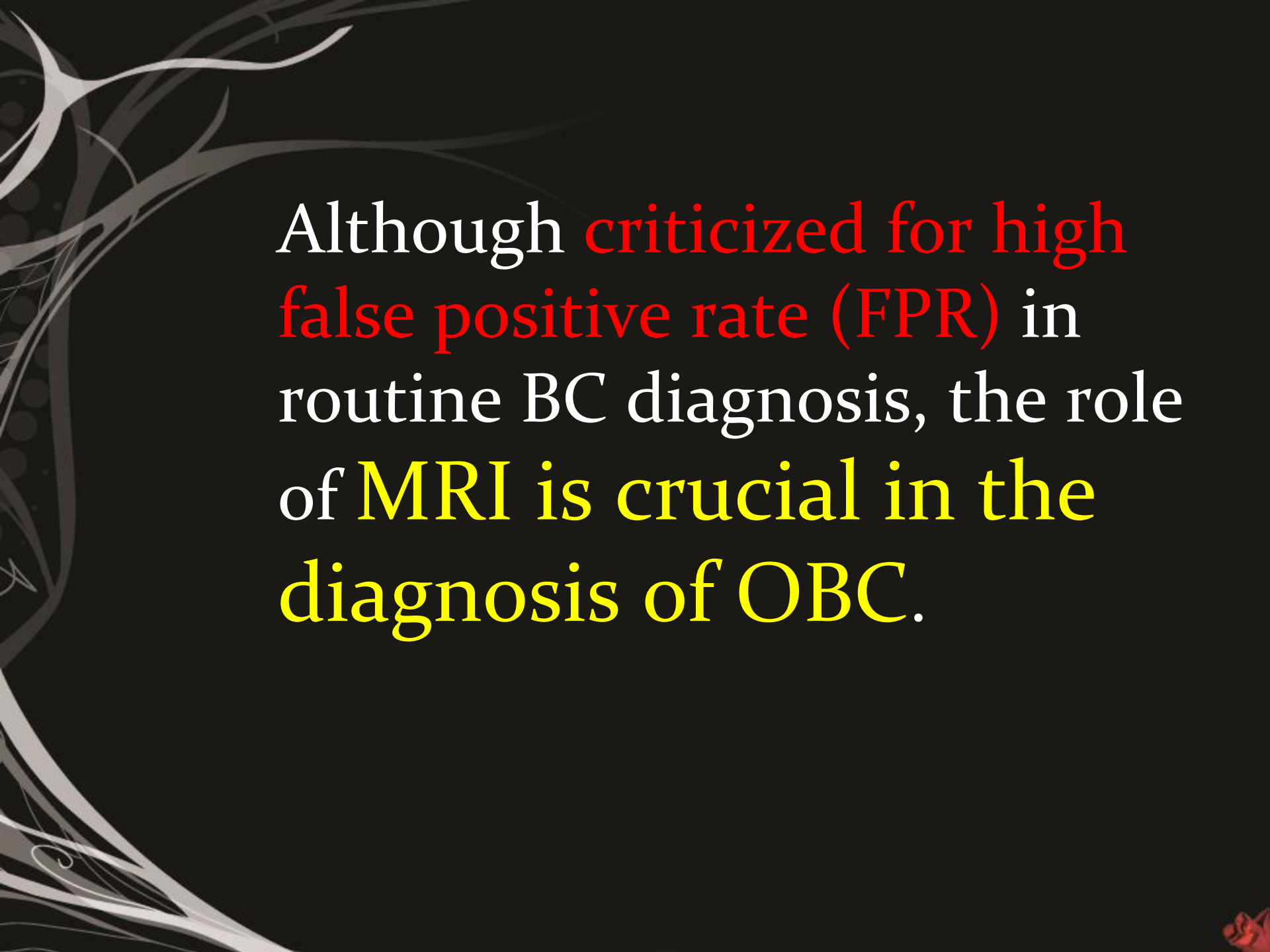
**Mammography** and breast **ultrasound** (US) are the **first** imaging modalities to detect **primary occult breast cancer**



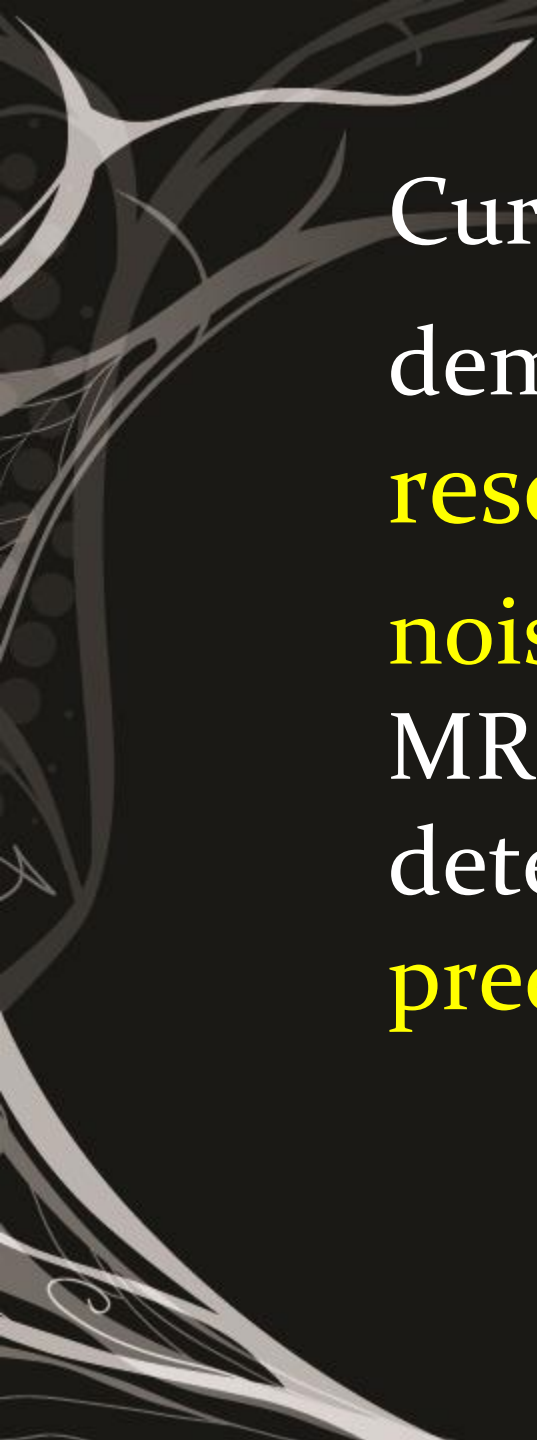
The **ACR** recommends:

the use of **MRI** for OBC patients that do **not** have evidence of a breast **primary** on traditional radiological examination (mammogram and ultrasound) and clinical exam.

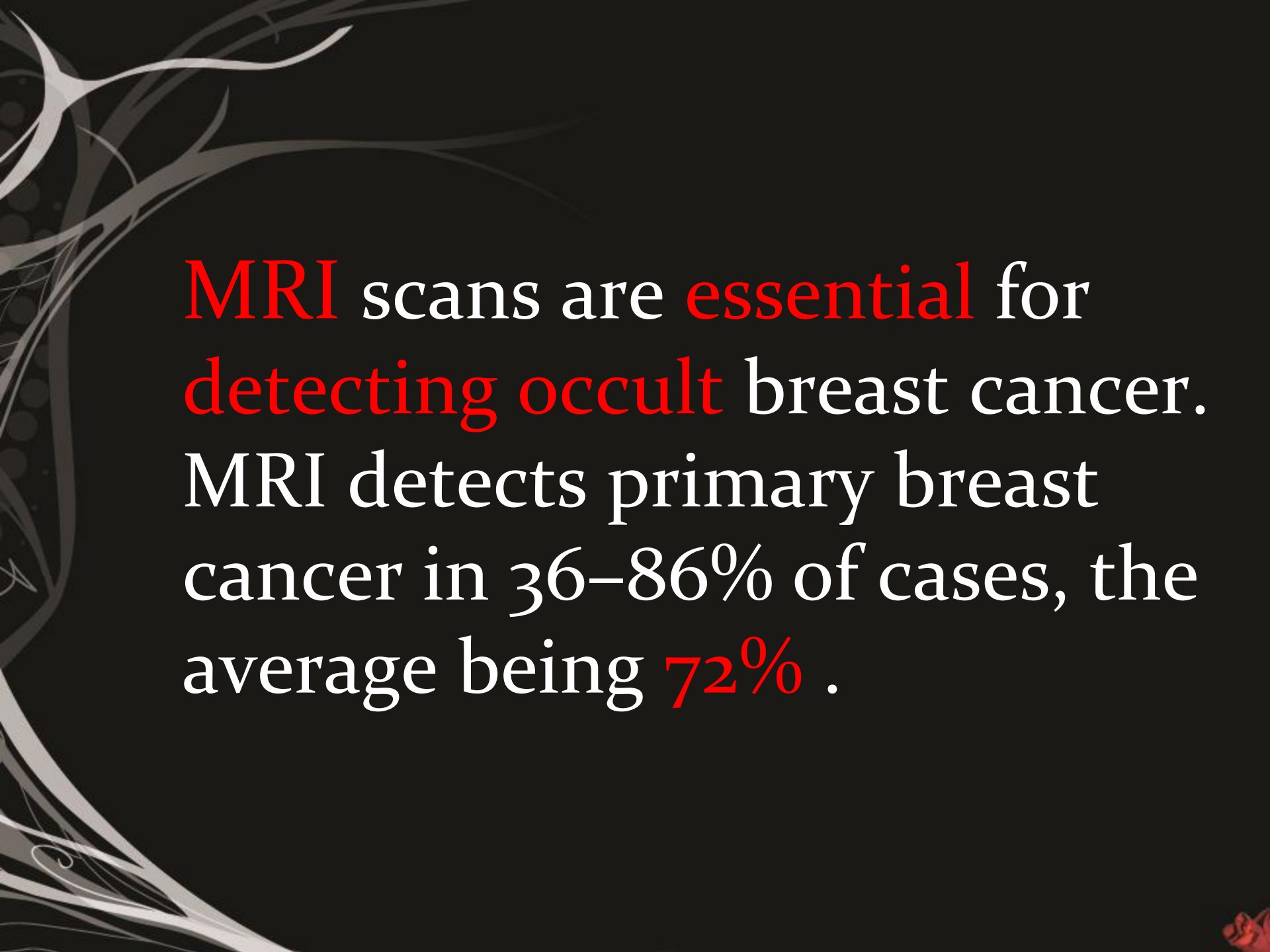
Level I evidence has shown MRI is significantly more sensitive in detecting a primary lesion than mammography or ultrasound; identifying a primary in 72% of cases that were deemed occult.



Although criticized for high false positive rate (FPR) in routine BC diagnosis, the role of MRI is crucial in the diagnosis of OBC.

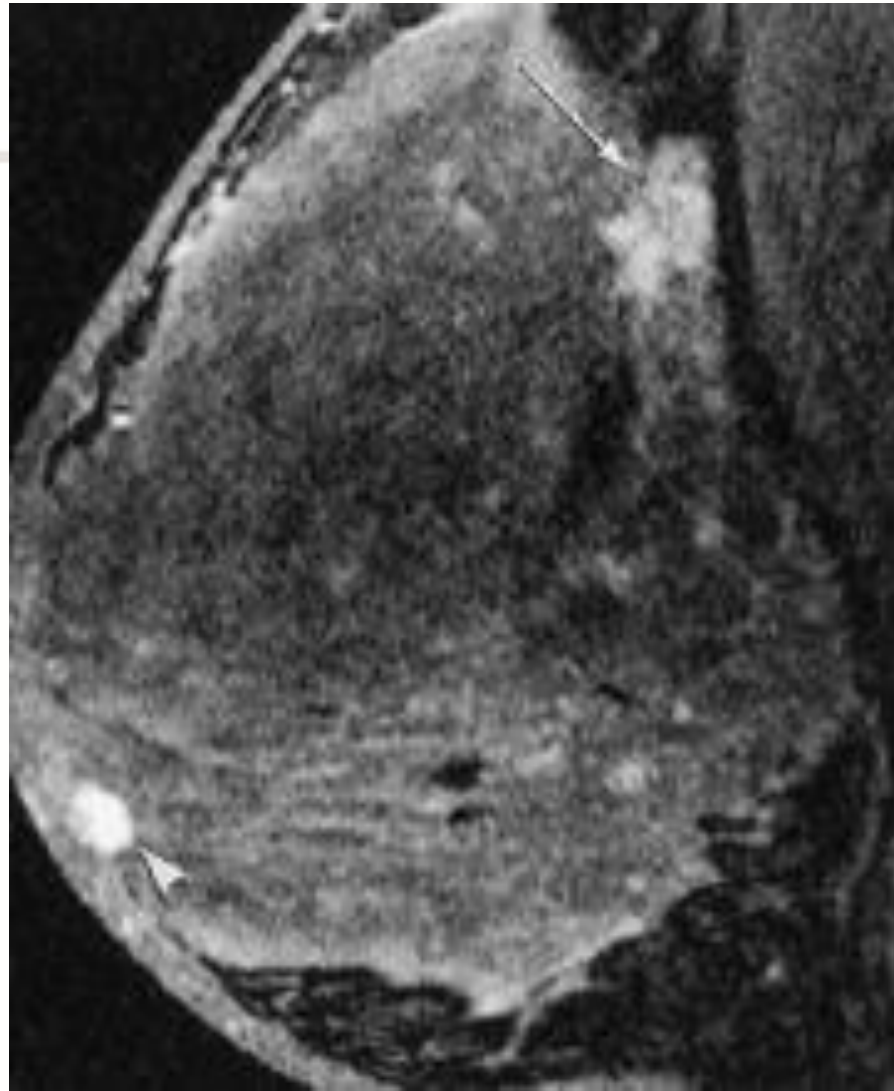


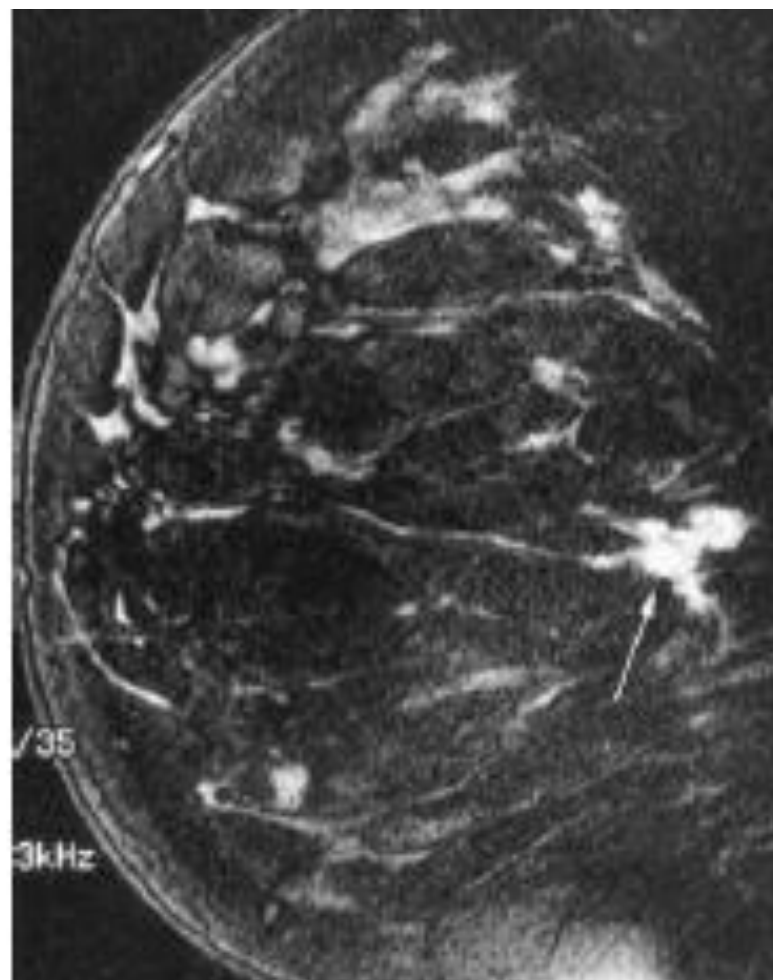
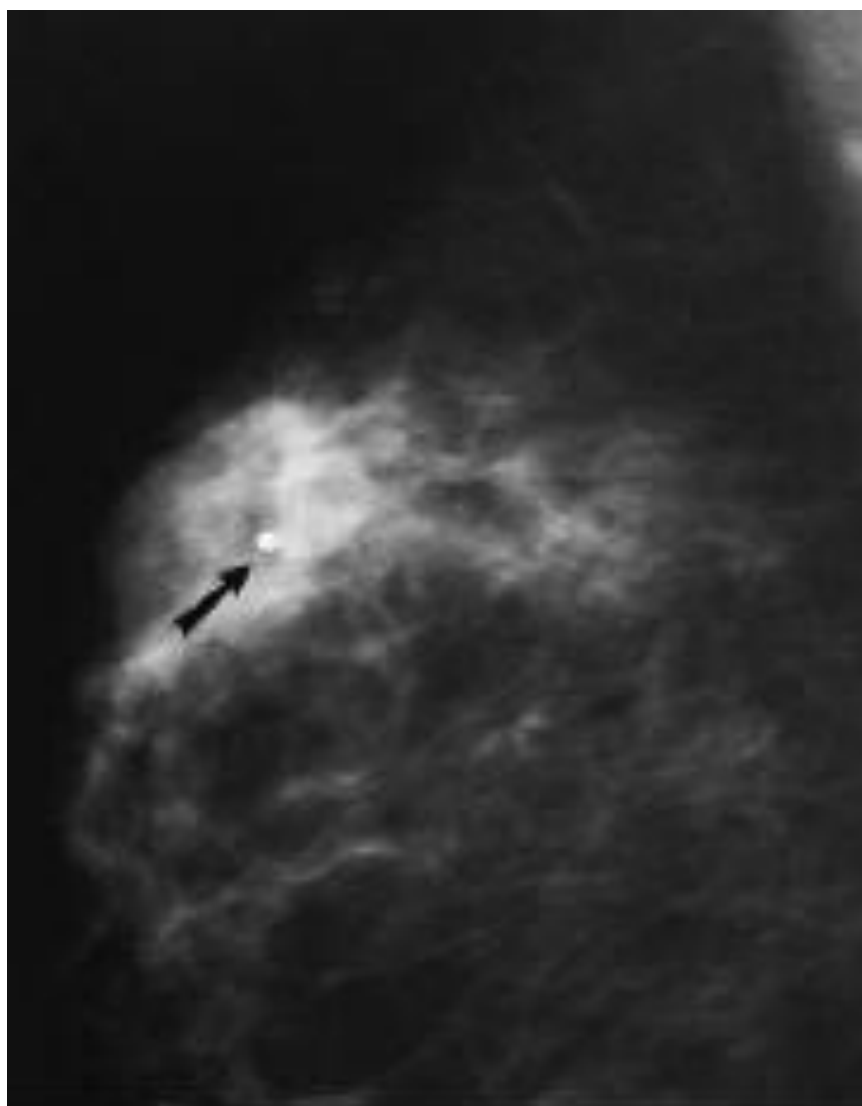
Currently, **3T** breast **MRIs** have demonstrated greater **spatial resolution** and improved **signal to noise ratio**, compared to earlier **1.5T** MRIs .This has resulted in improved detection and a better **positive predictive value**.

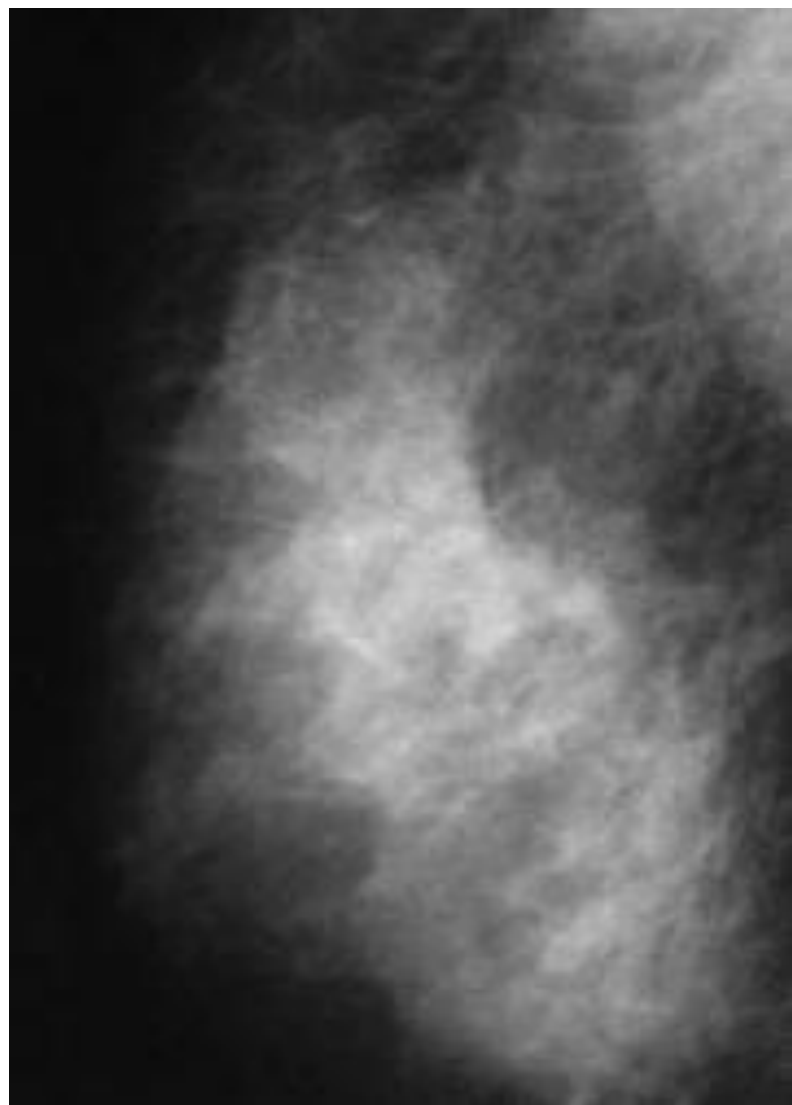


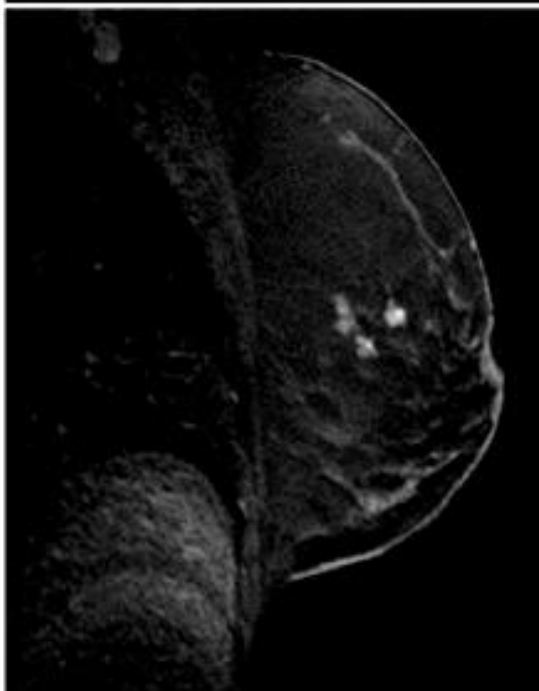
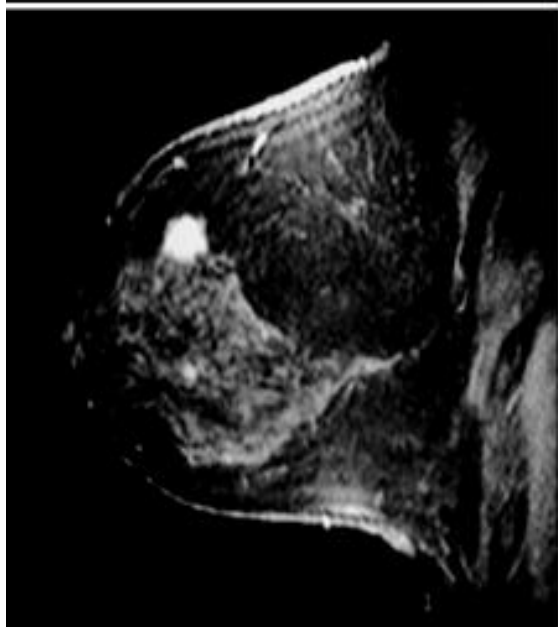
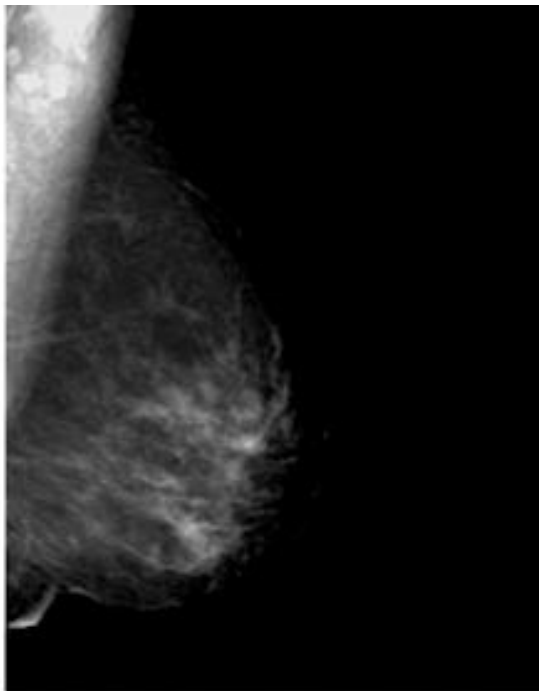
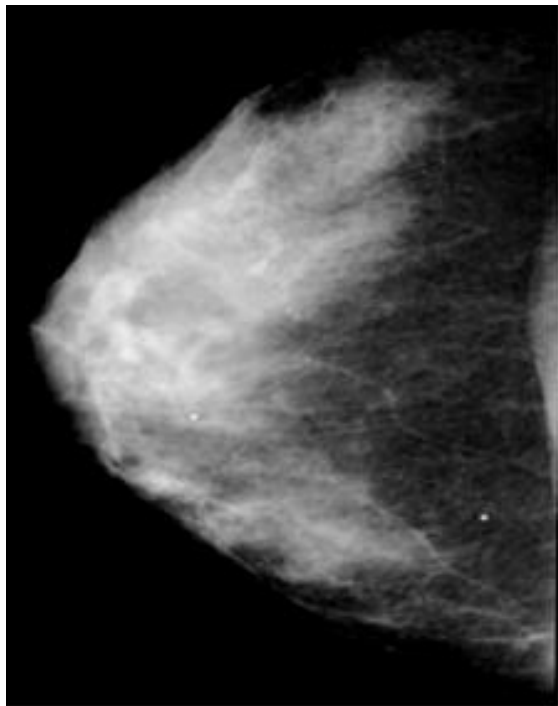
**MRI** scans are **essential** for **detecting occult** breast cancer. MRI detects primary breast cancer in 36–86% of cases, the average being **72%** .



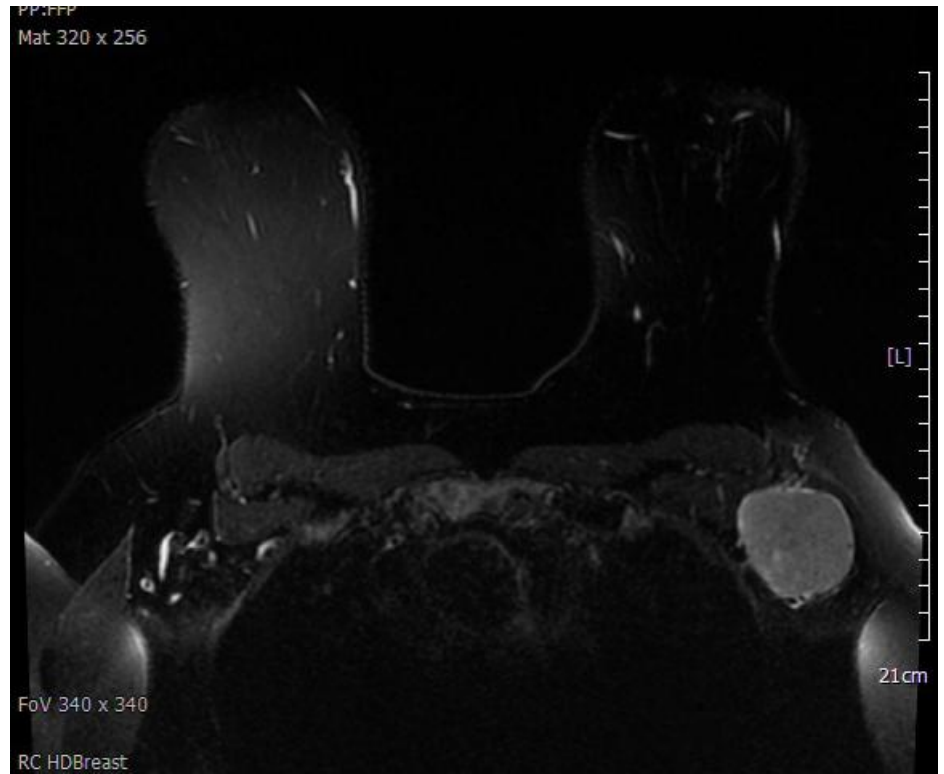


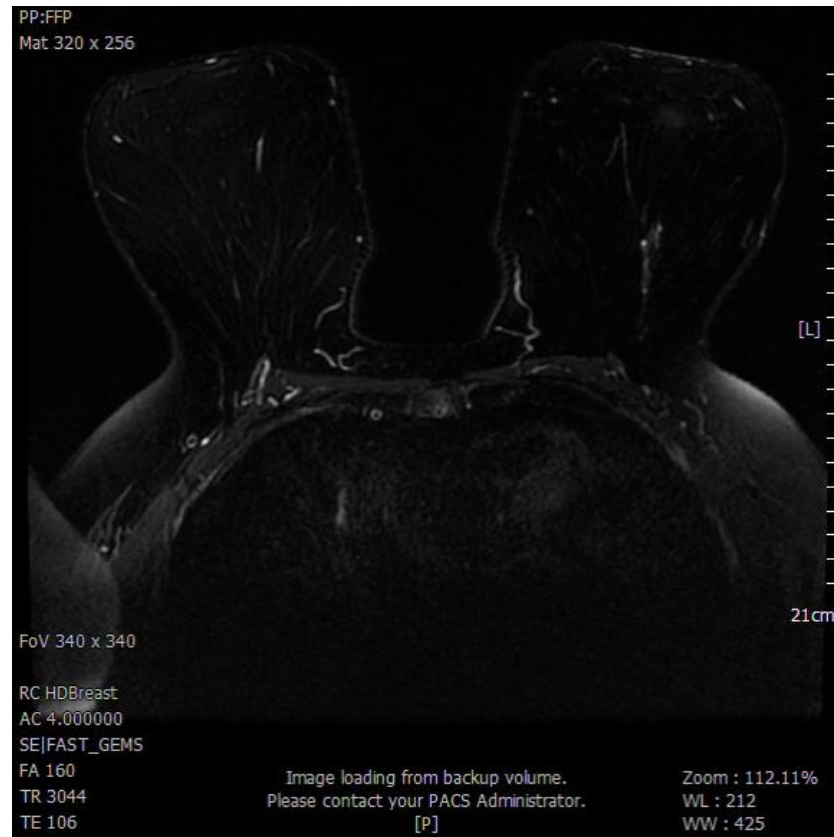
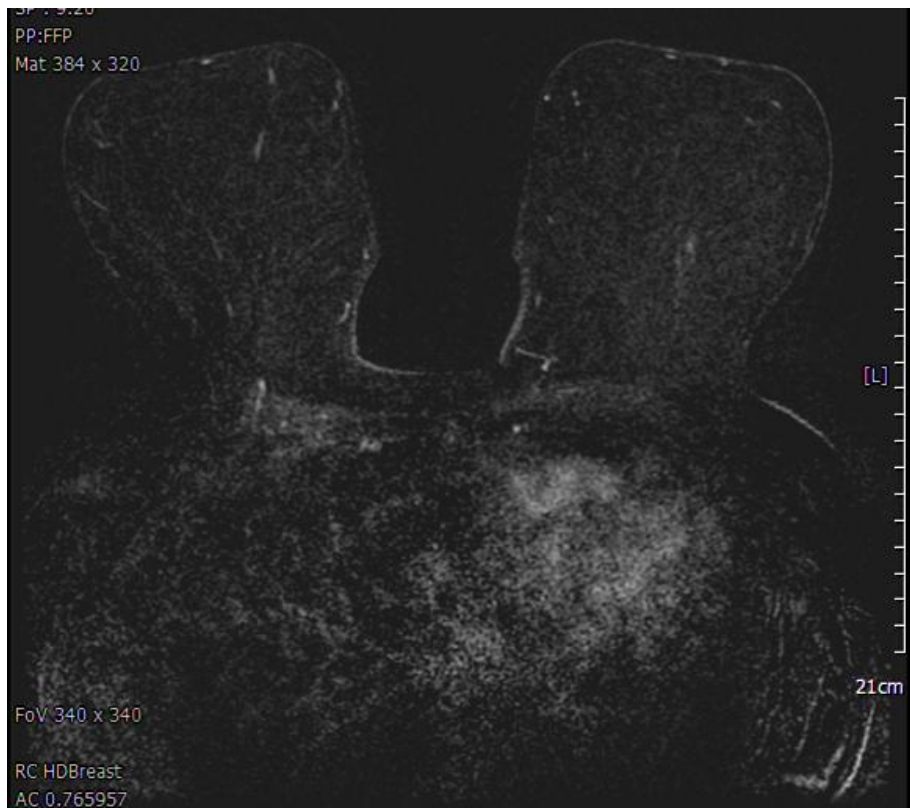


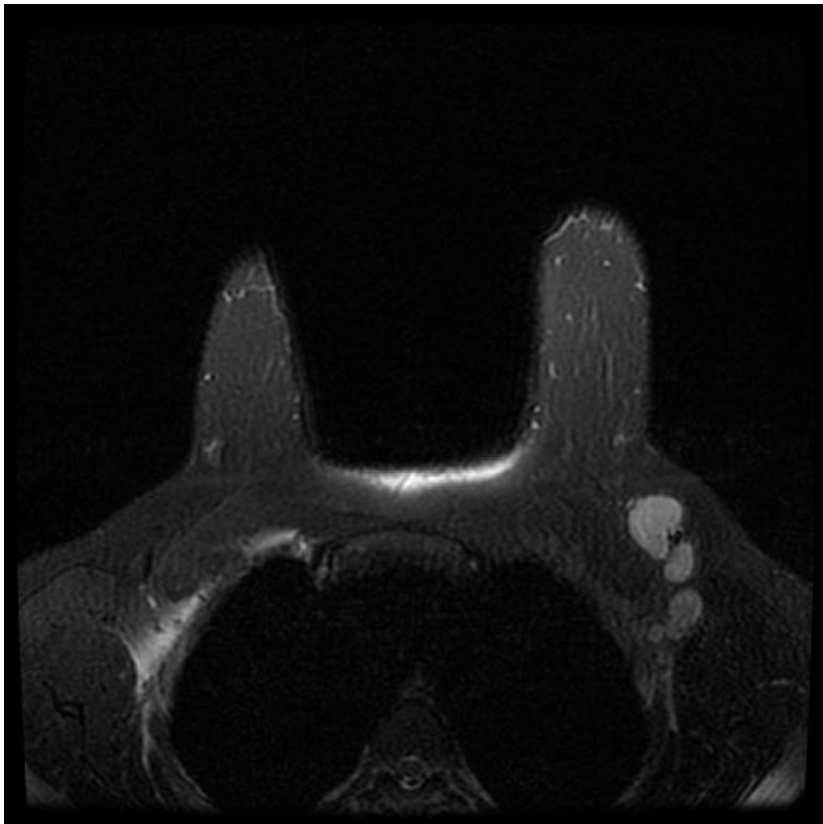




G. 6. Mammographically occult breast carcinoma visualized by



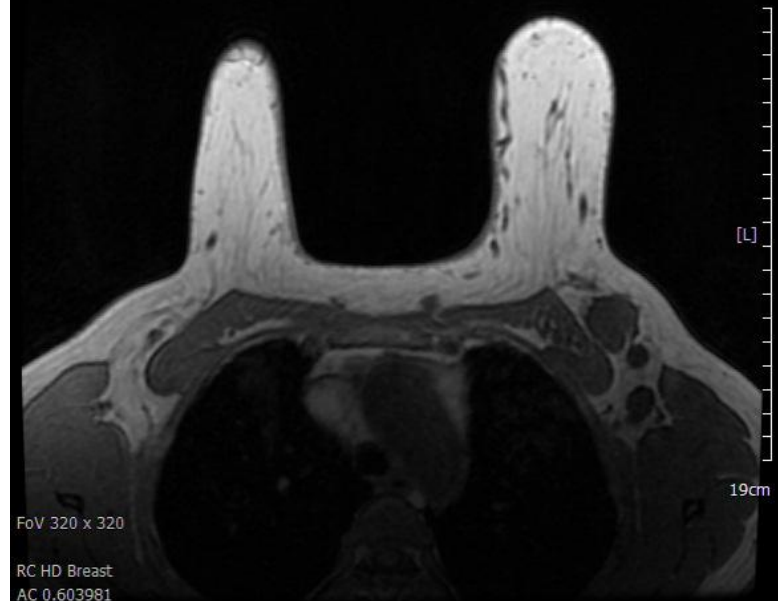




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EMAM KHOMEINI TEHRAN  
DISCOVERY MR750w  
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Srs:4  
Img:39

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SP : 78.49  
PP:FFP  
Mat 320 x 256



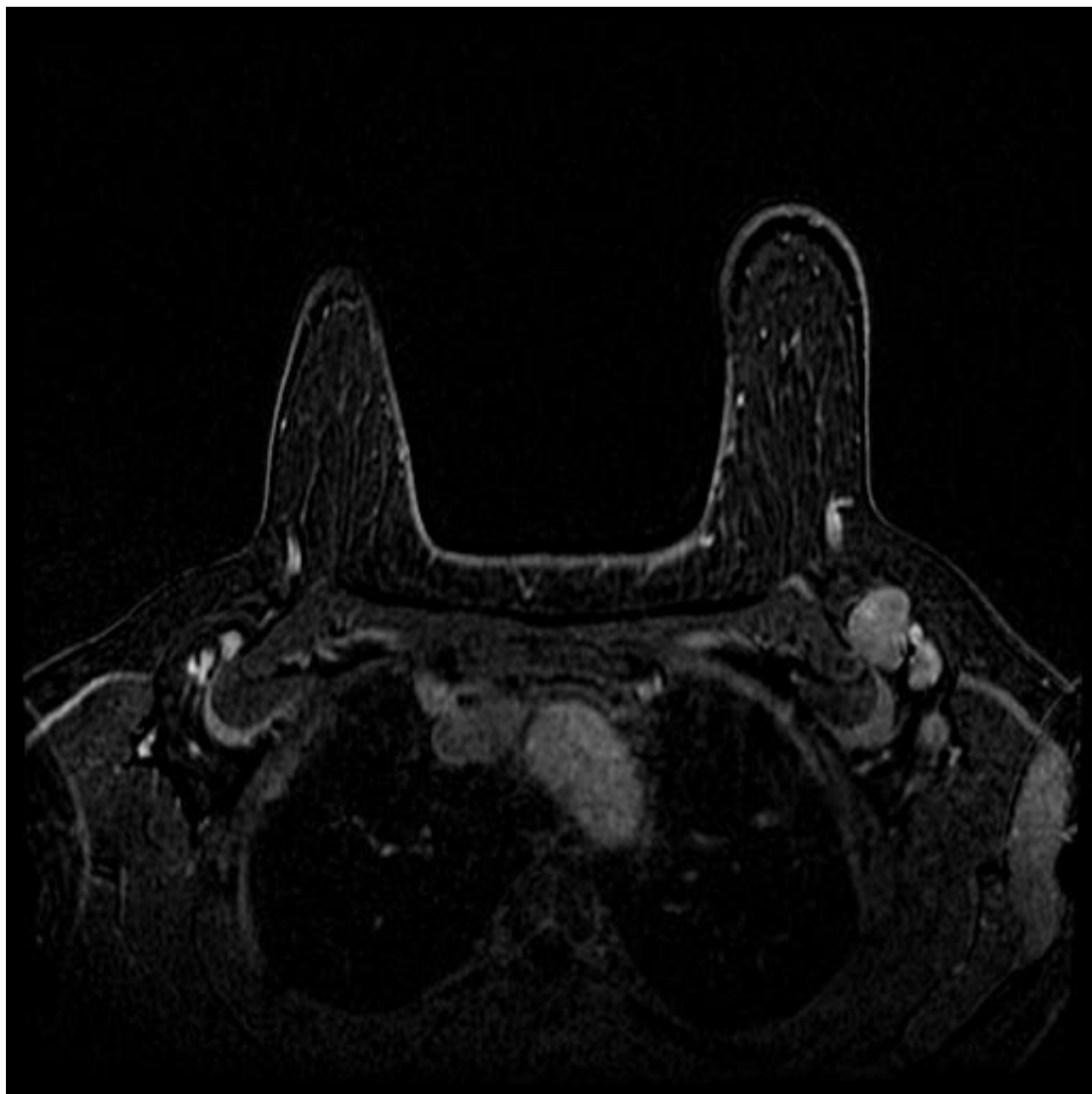
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RC HD Breast  
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GR|FAST\_GEMS

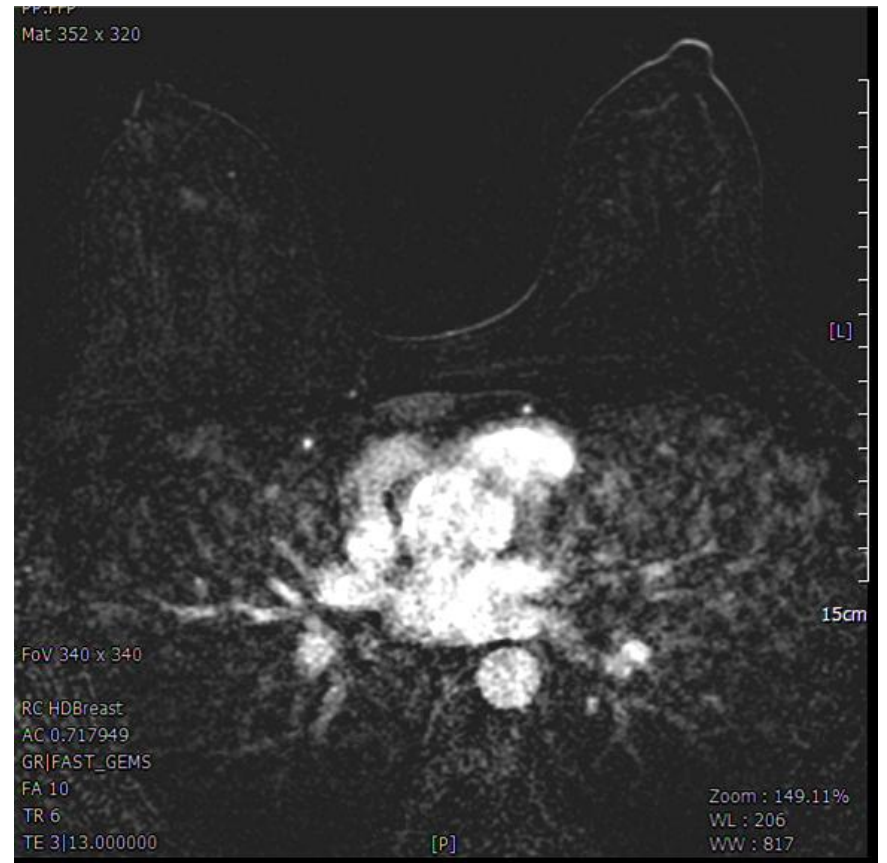
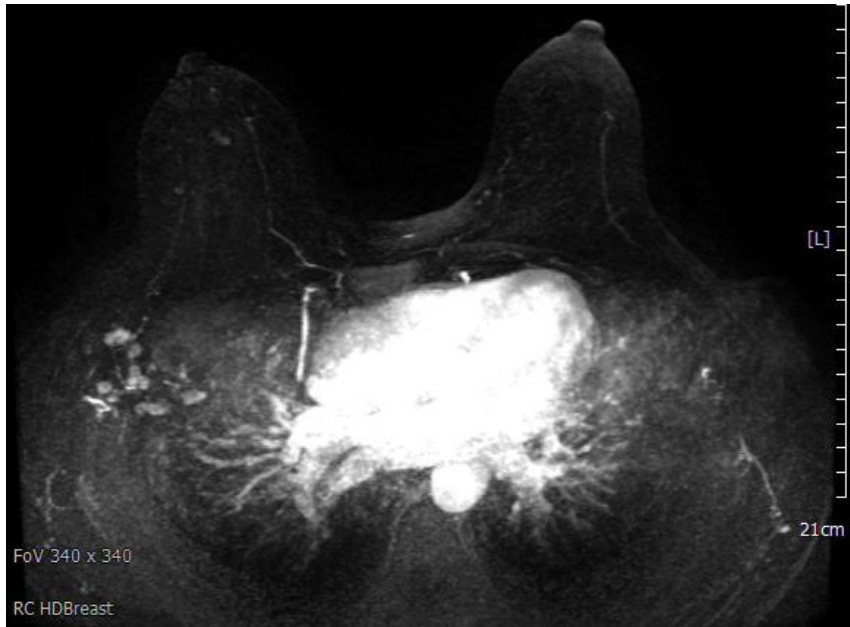
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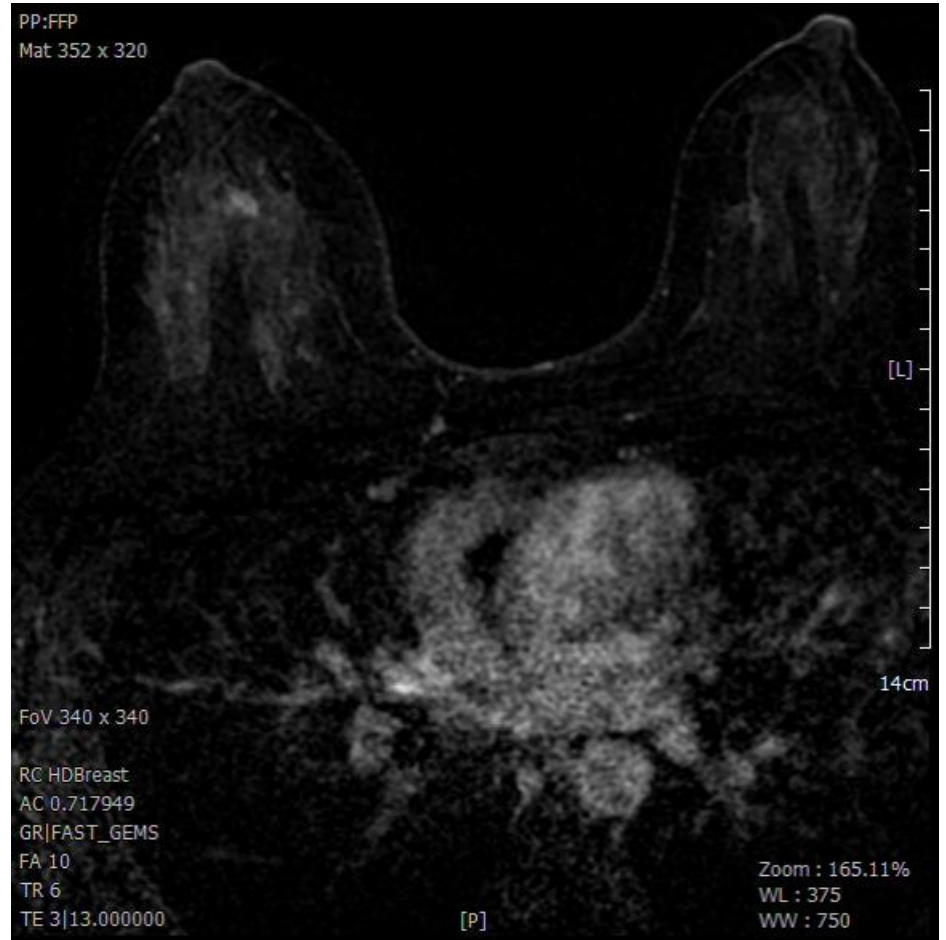
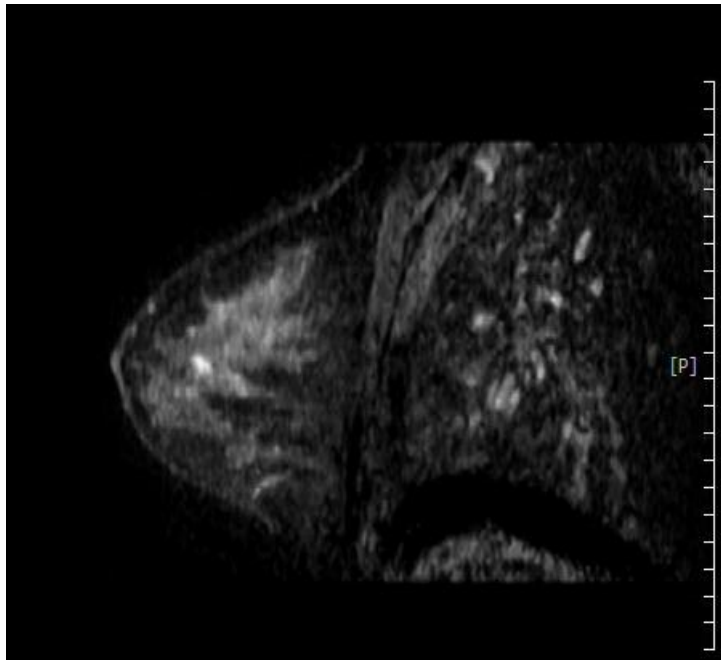
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EMAM KHOMEINI TEHRAN  
DISCOVERY MR750w  
Acc:97.11.24\*MF  
Srs:3  
Img:53

SL : 2.60|sp1.30  
SP : 28.07  
PP:FFP  
Mat 320 x 320



GHOLI OO ZARISH|061Y|F  
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EMAM KHOMEINI TEHRAN  
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In one study :

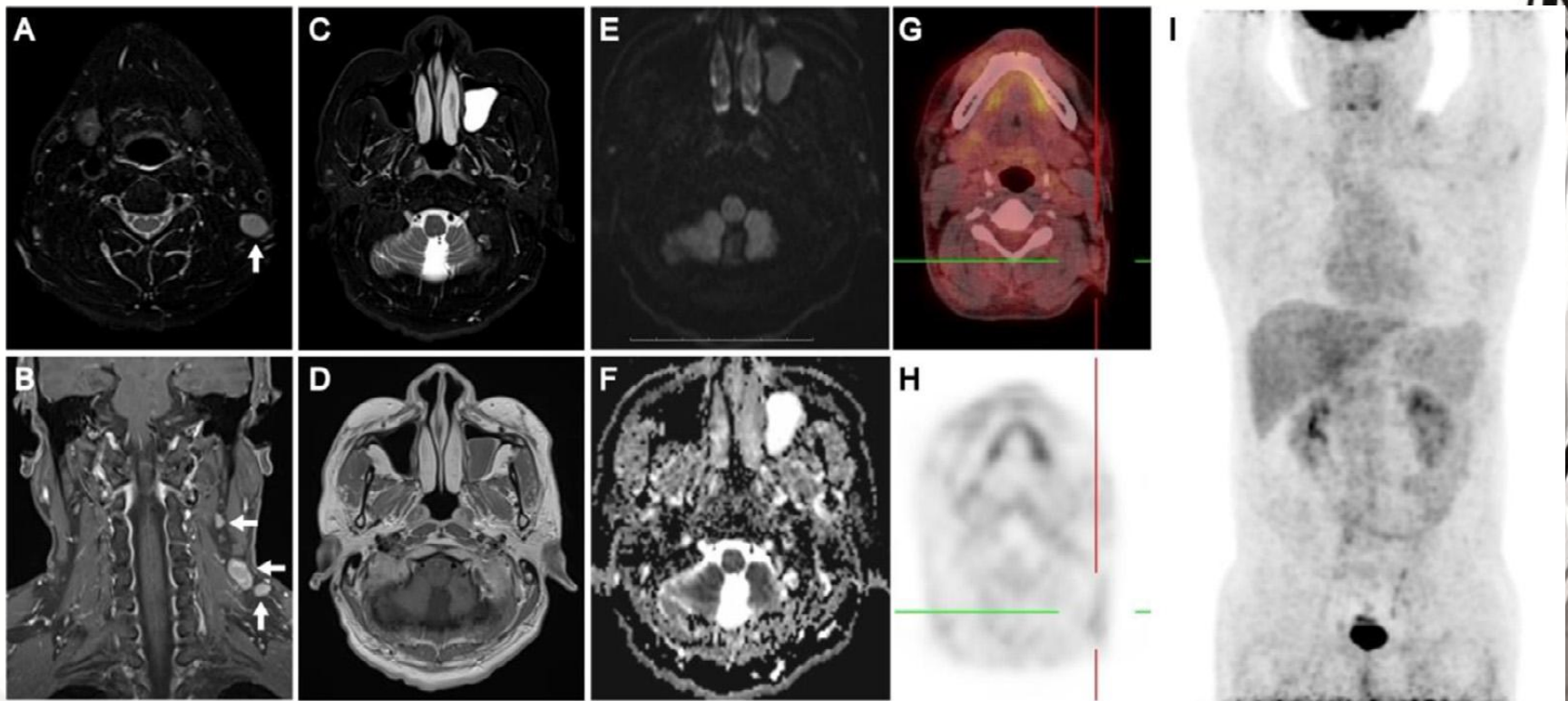
Of the 55 patients; **13 had a negative-MRI** (23.6%), of these **8 underwent mastectomy** with a **primary breast lesion** found in **2 cases**. Only 20% did not have a primary found after MRI and pathology were performed.

# Diffusion-weighted (DW) MRI

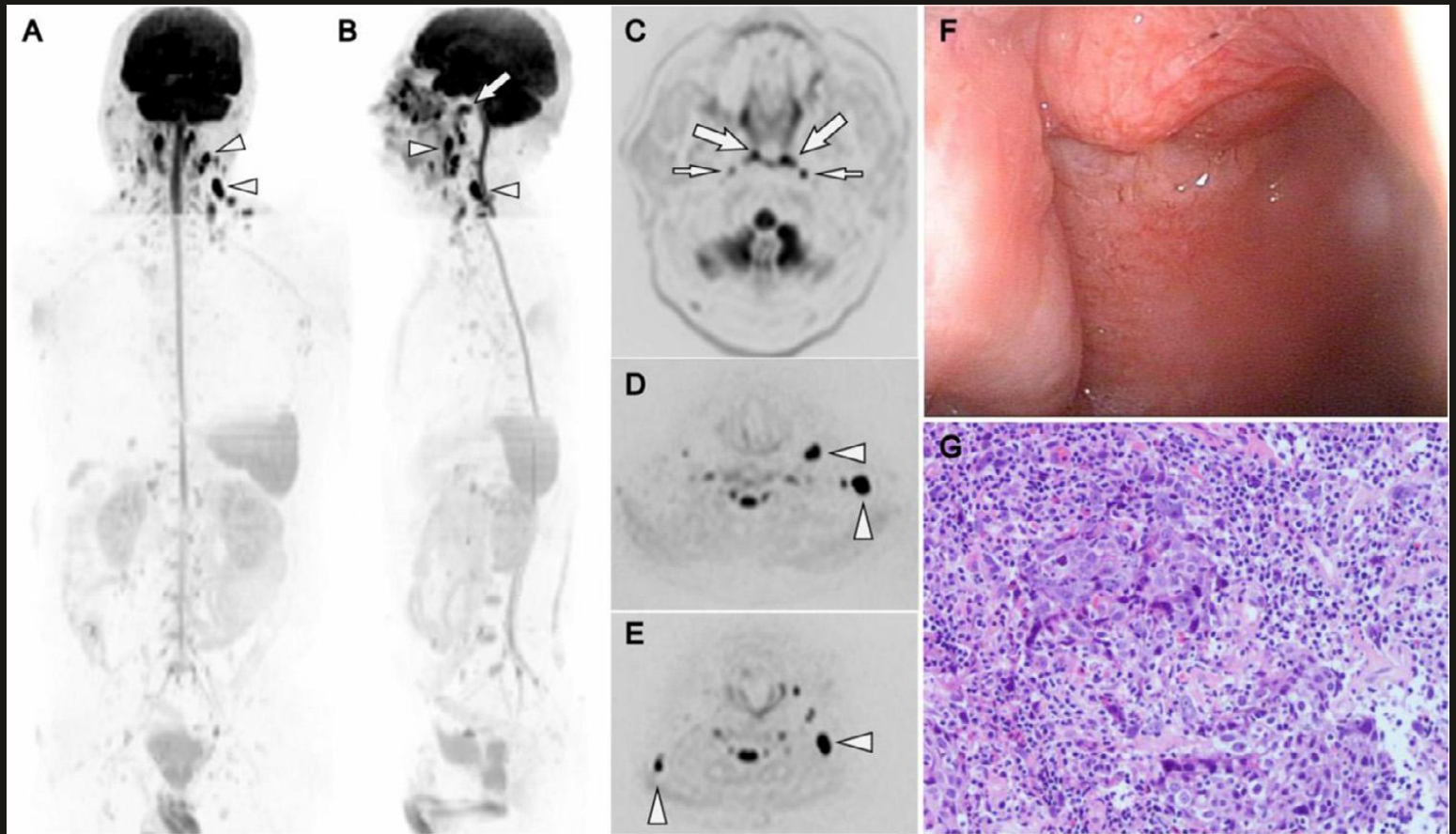
...(where water molecule mobility is decreased in the cancer microenvironment and contrast is not required) may be **an adjunct to existing MRI techniques** .

DWMRI may be useful in the future in **increasing detection rates**, however it still requires further standardization to ascertain its true sensitivity and specificity .

A 43-year-old man presented to our hospital with a 3-year history of painless nodules on the left side of neck. He observed a peanut-sized mass on the left side of his neck in 2015, and 3 years later, another walnut-sized mass was found beneath the first mass,



# whole-body diffusion-weighted imaging



# Contrast-Enhanced Spectral Mammography (CESM)

CESM is a new breast imaging technique that is proving to have **good performance in breast cancer detection** and that is showing **potential** in the identification of occult breast cancer in a **CUPAx** setting.

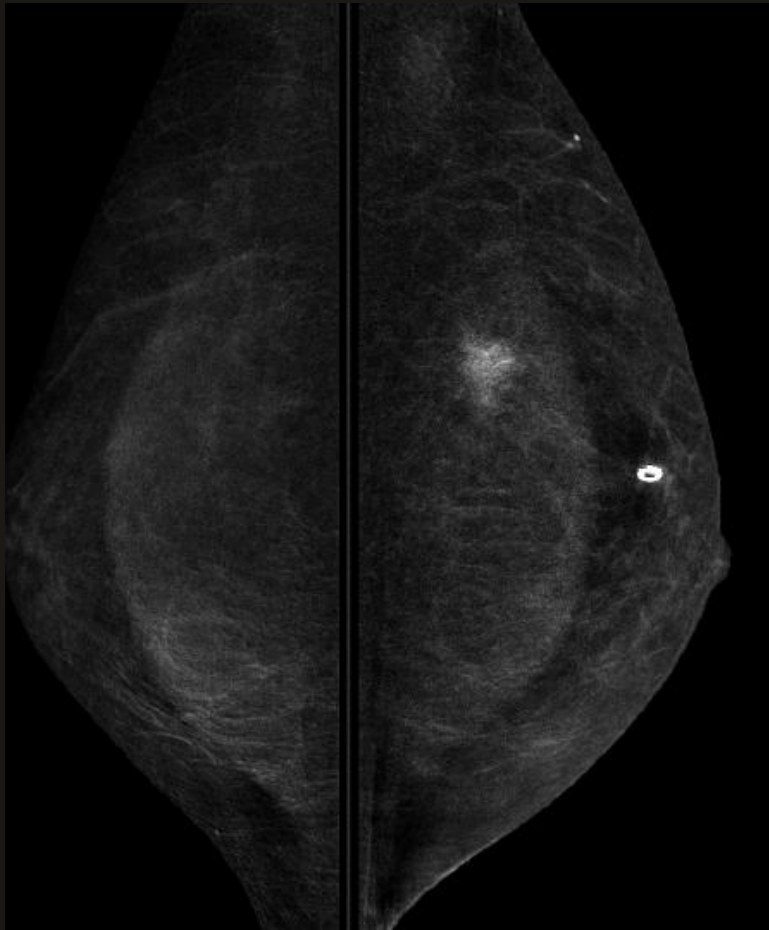
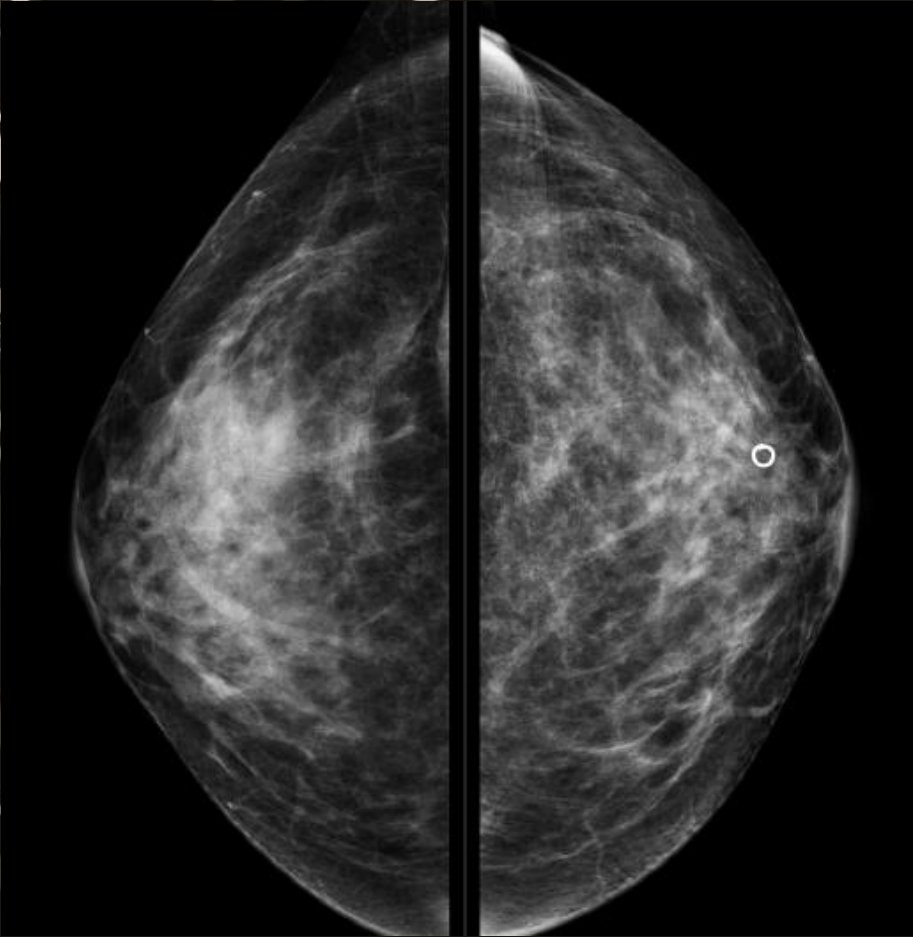


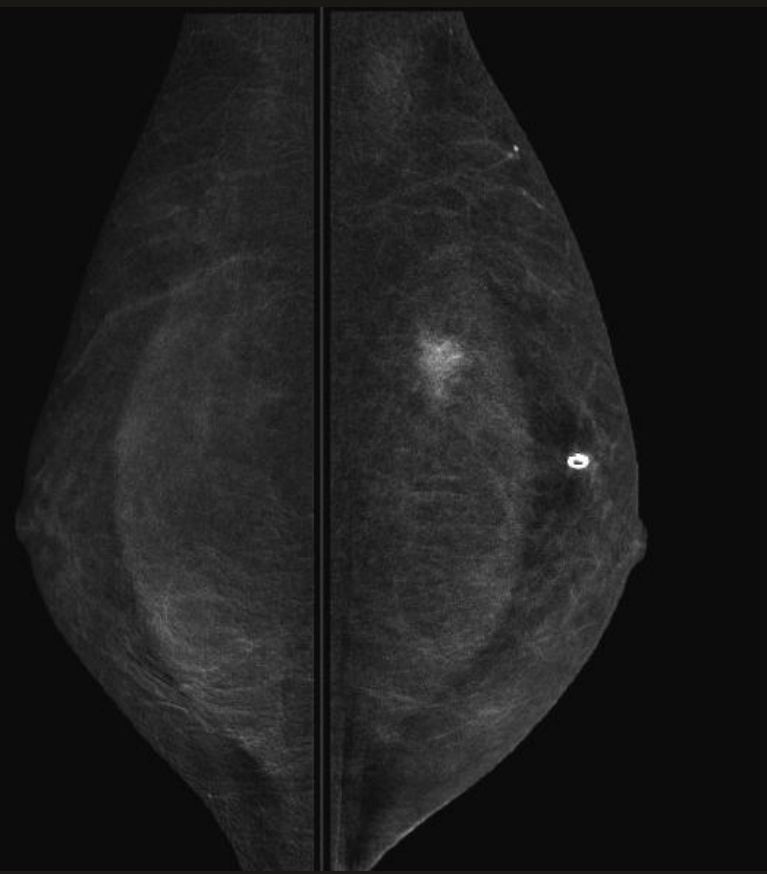
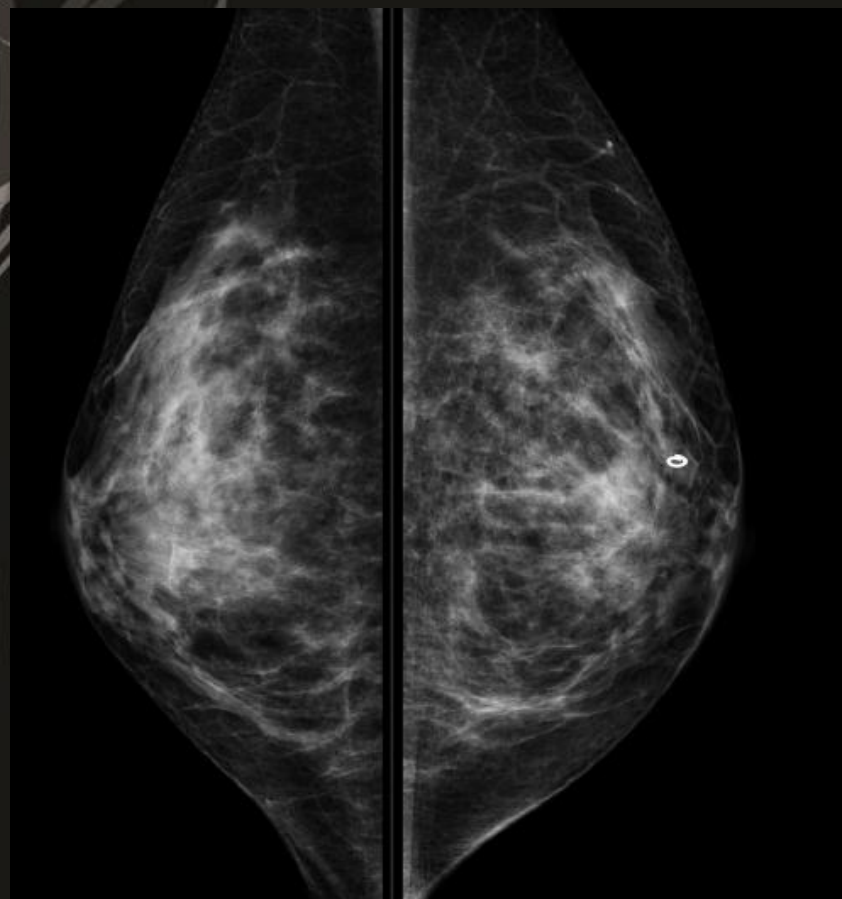
# CESM

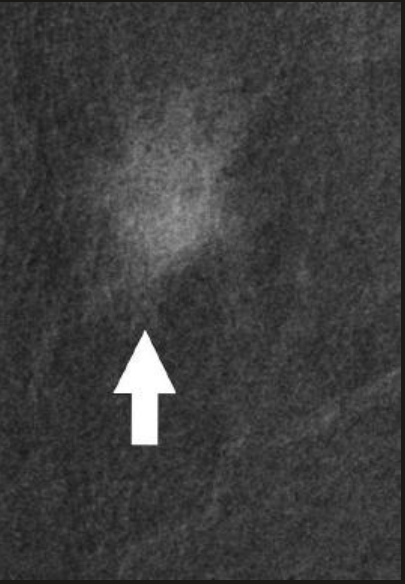
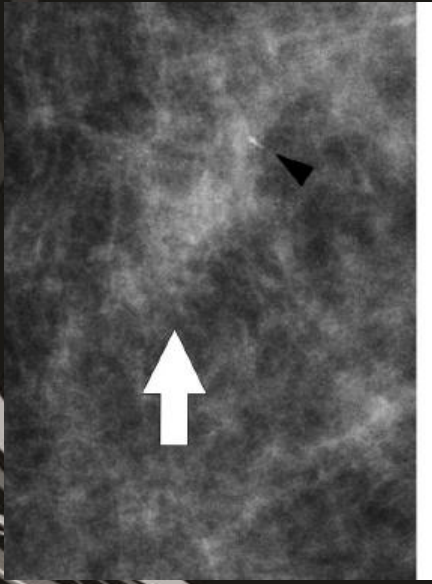
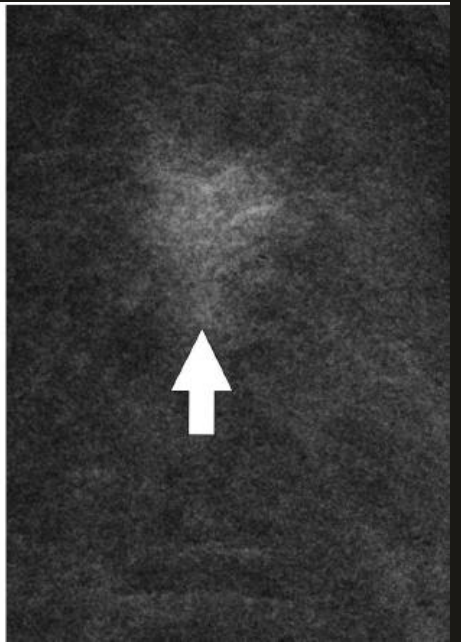
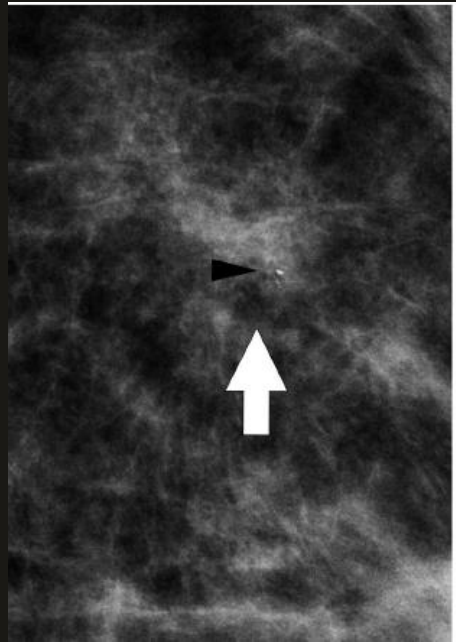
...is a special type of mammogram that uses a **dual energy exposure** in combination with **intravenous contrast medium administration**.

For each mammogram projection, a pair of low- and high-energy images are acquired and the relative **subtracted** images are obtained

Therefore, **CESM** offers both a **regular mammogram** image and a **subtracted image** that contains **dynamic information**. **CESM highlights** areas of **abnormal blood flow supply** in the breast, helping the detection of **tumor neovascularity** similar to breast MR imaging.



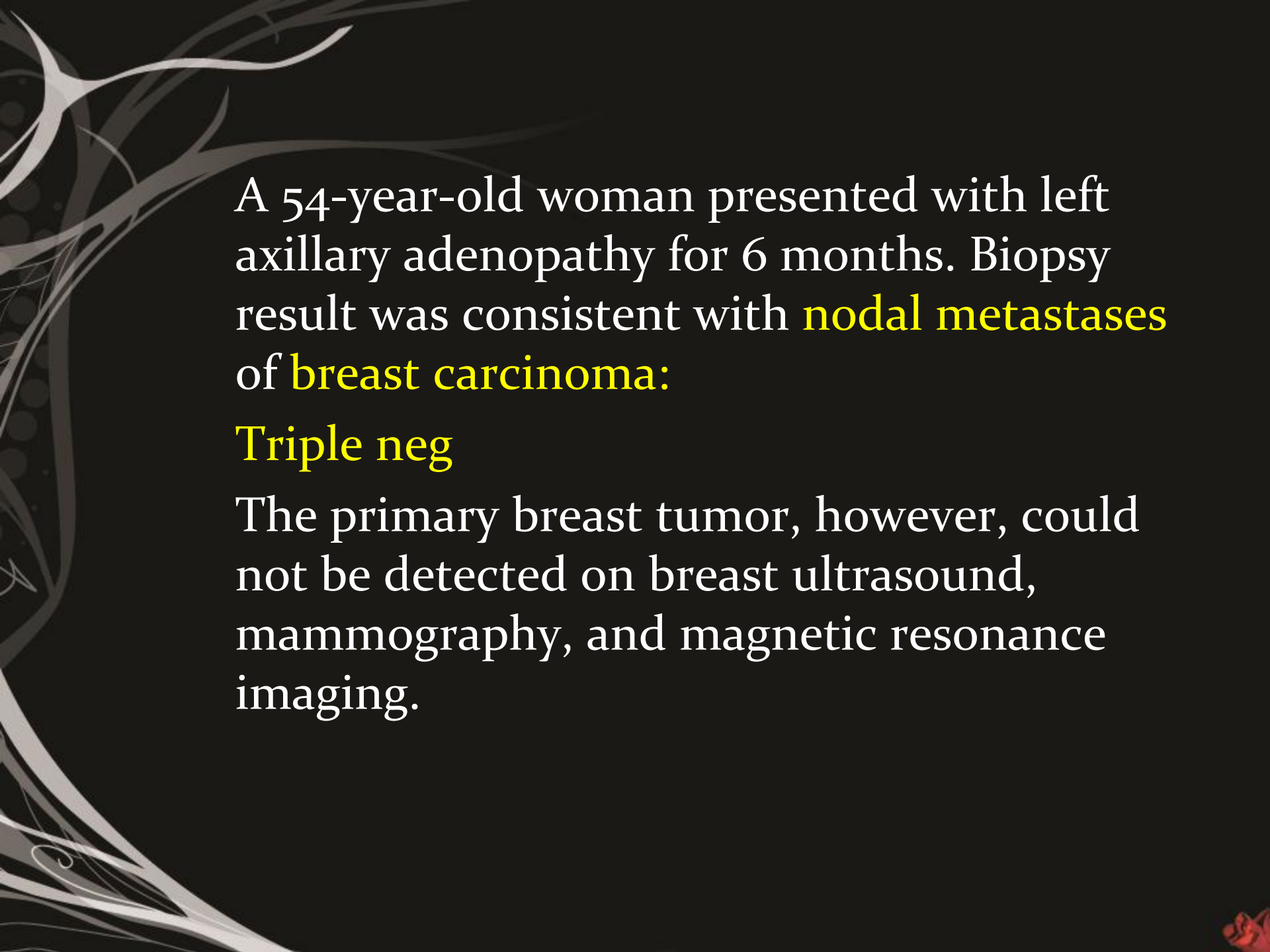




# Fluorodeoxyglucose (FDG)- positron emission tomography (FDG PET/CT)

...has been used in occult breast cancer, however there is only one case report in the literature to date, in which FDG PET/CT has detected a primary breast tumor over MRI.

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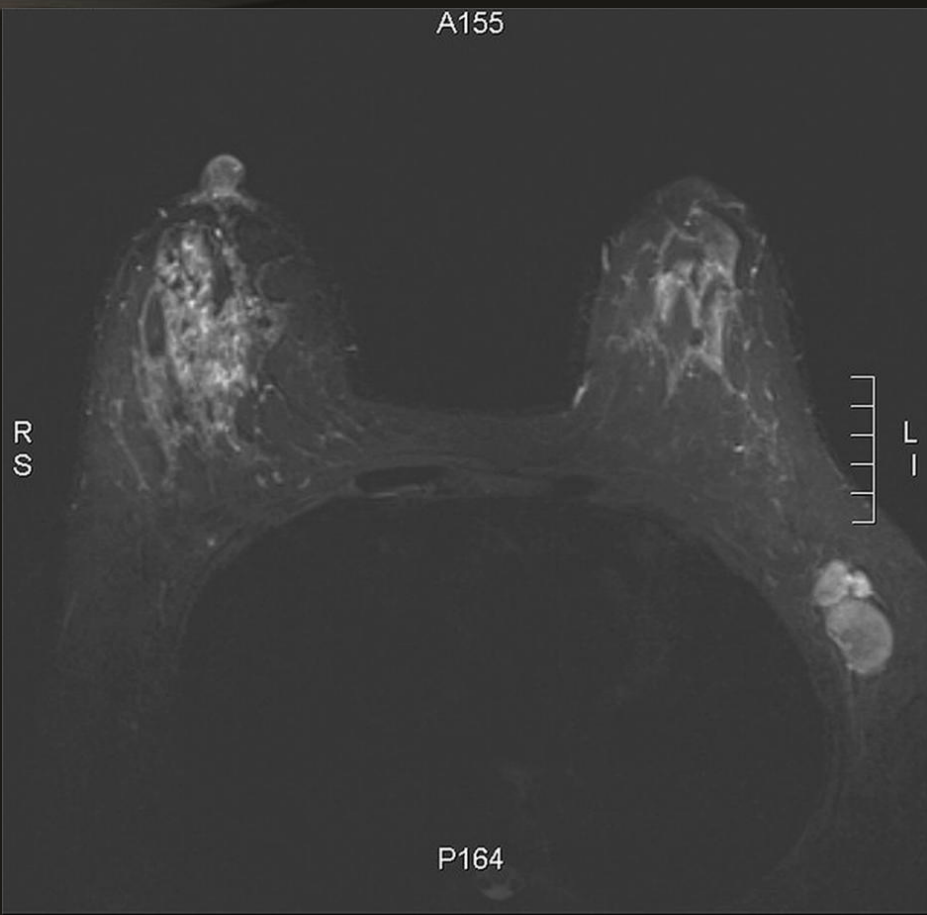


A 54-year-old woman presented with left axillary adenopathy for 6 months. Biopsy result was consistent with **nodal metastases of breast carcinoma:**

**Triple neg**

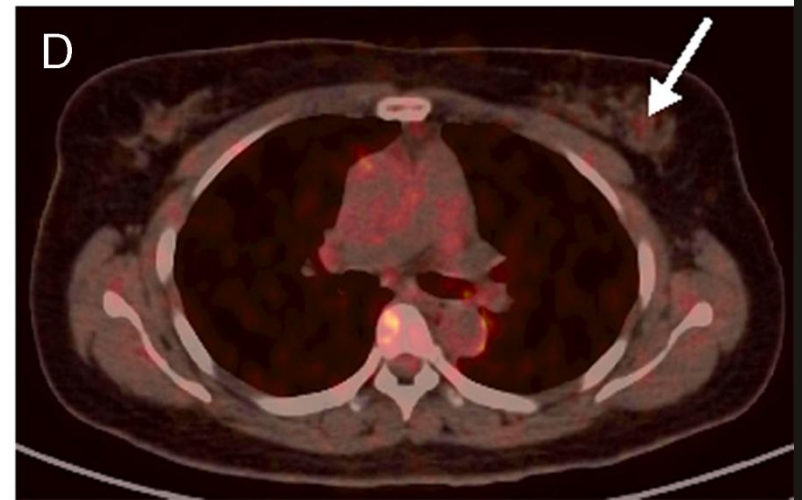
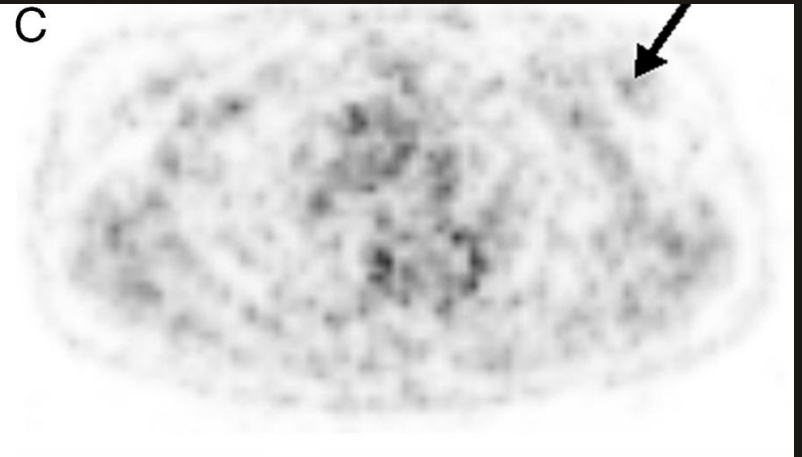
The primary breast tumor, however, could not be detected on breast ultrasound, mammography, and magnetic resonance imaging.

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# MOLECULAR IMAGING

-**FDG-PET** imaging,

-**FLT PET**  $^{18}\text{F}$ -fluoro-L-thymidine

(FLT) has been developed to image increased cellular **DNA synthesis**.

-imaging, **hormone receptor PET** imaging,  
and

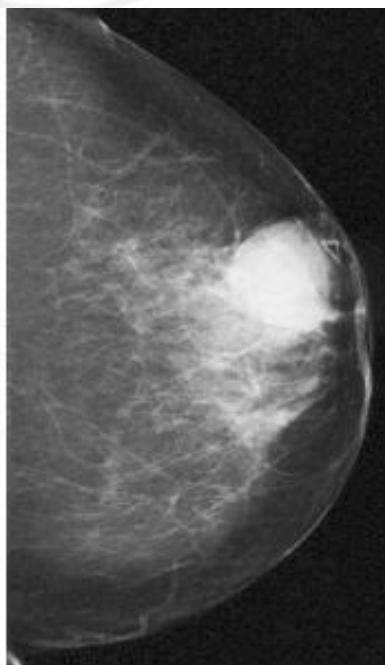
-**HER<sub>2</sub> PET** imaging.

# Positron emission mammography

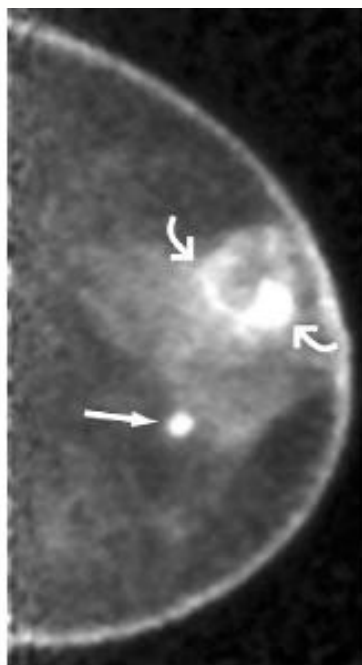
(PEM) is a newly emerging investigatory tool, which uses FDG to localize smaller tumors especially those **less than 1 cm** and has a **greater sensitivity than PET/CT** in this subset of patients with small tumors .

# PEM

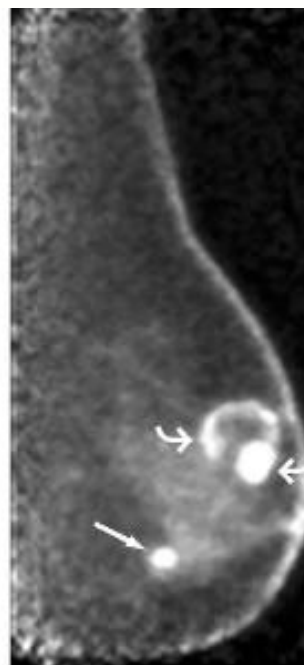
...is an alternative for women who cannot tolerate MR imaging. PEM has **improved specificity** compared with MR imaging and is therefore less likely to prompt unnecessary biopsies.



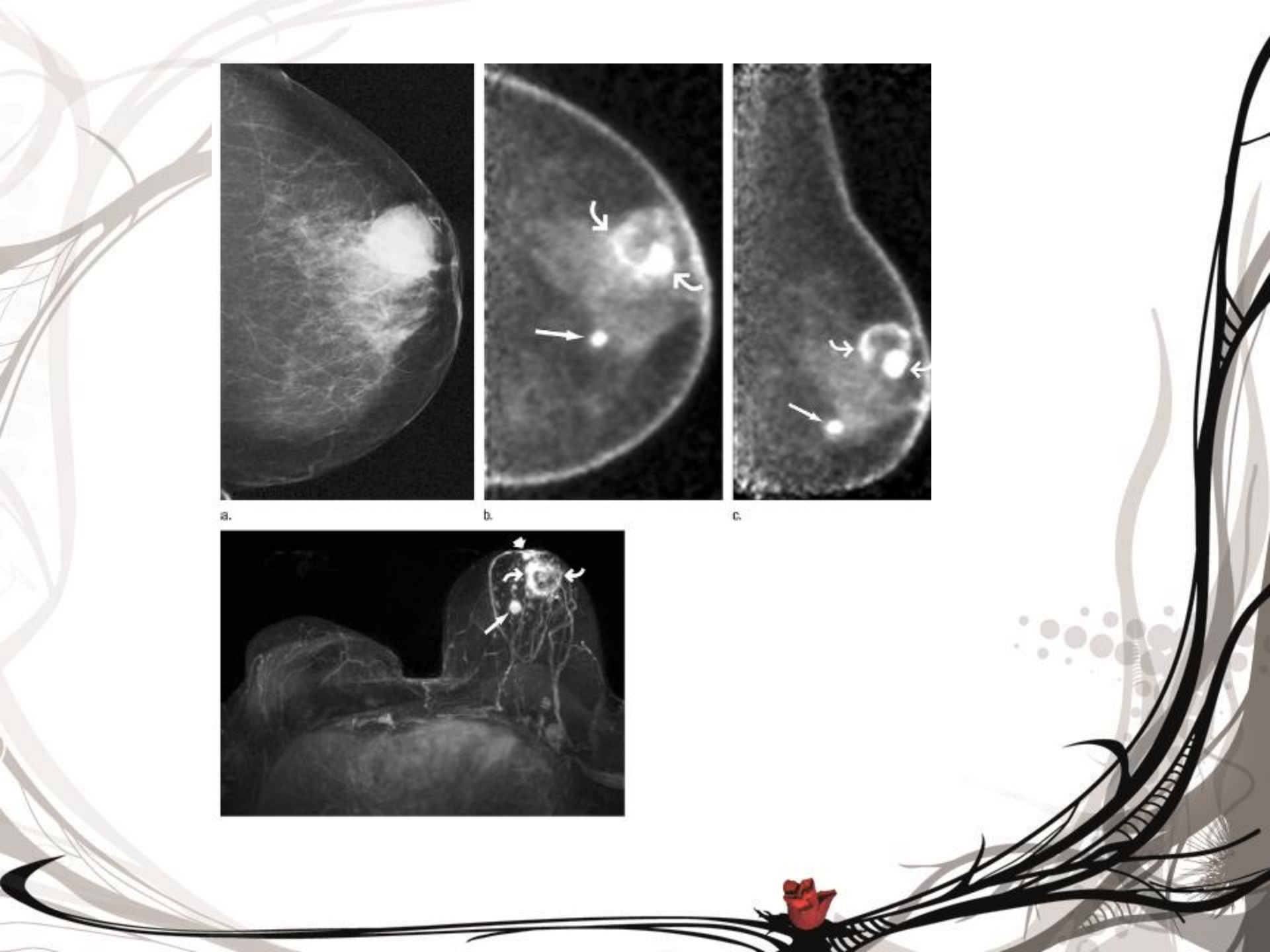
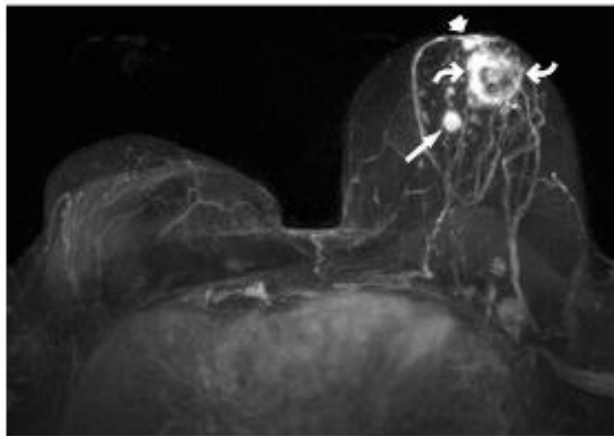
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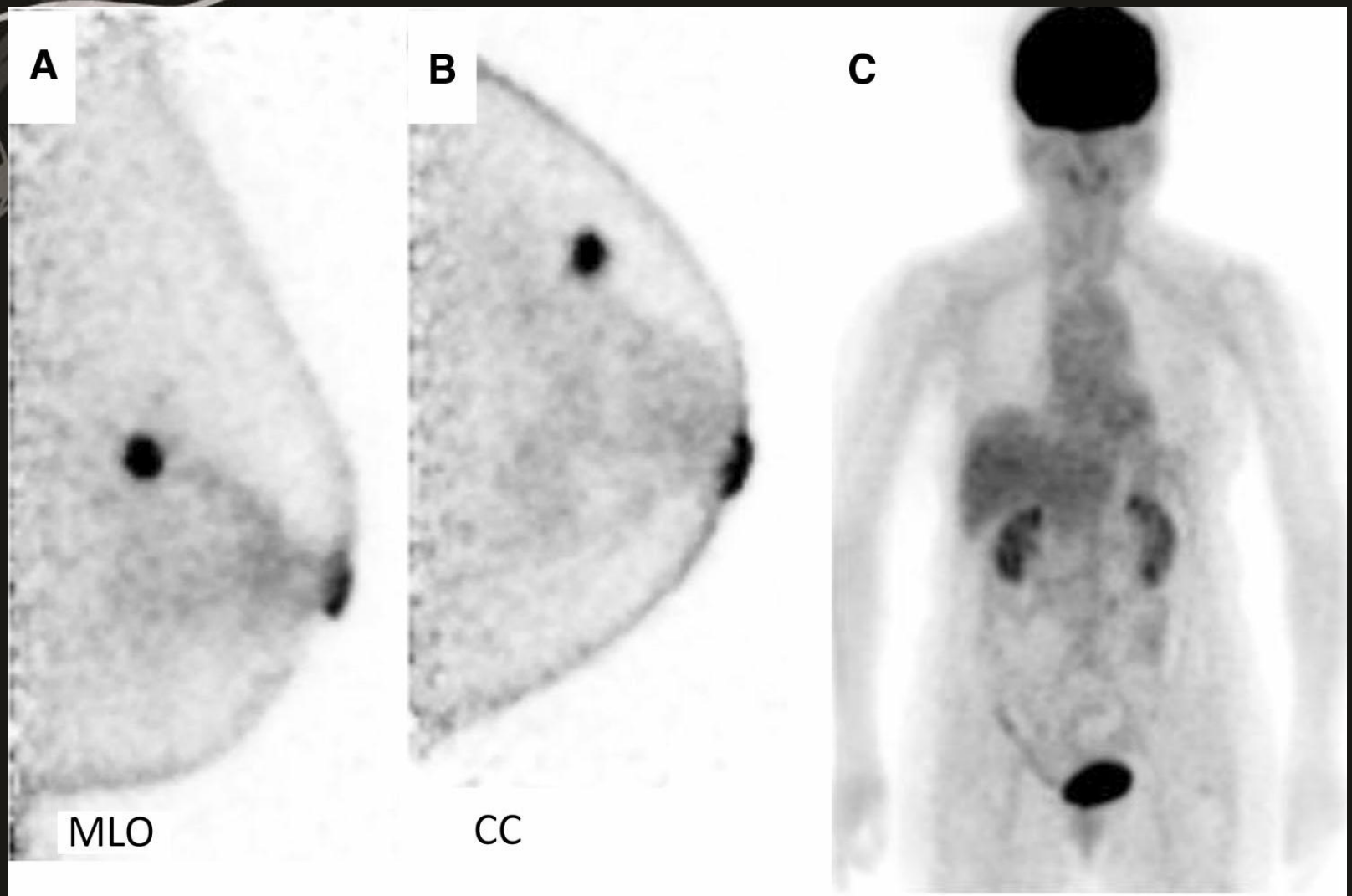


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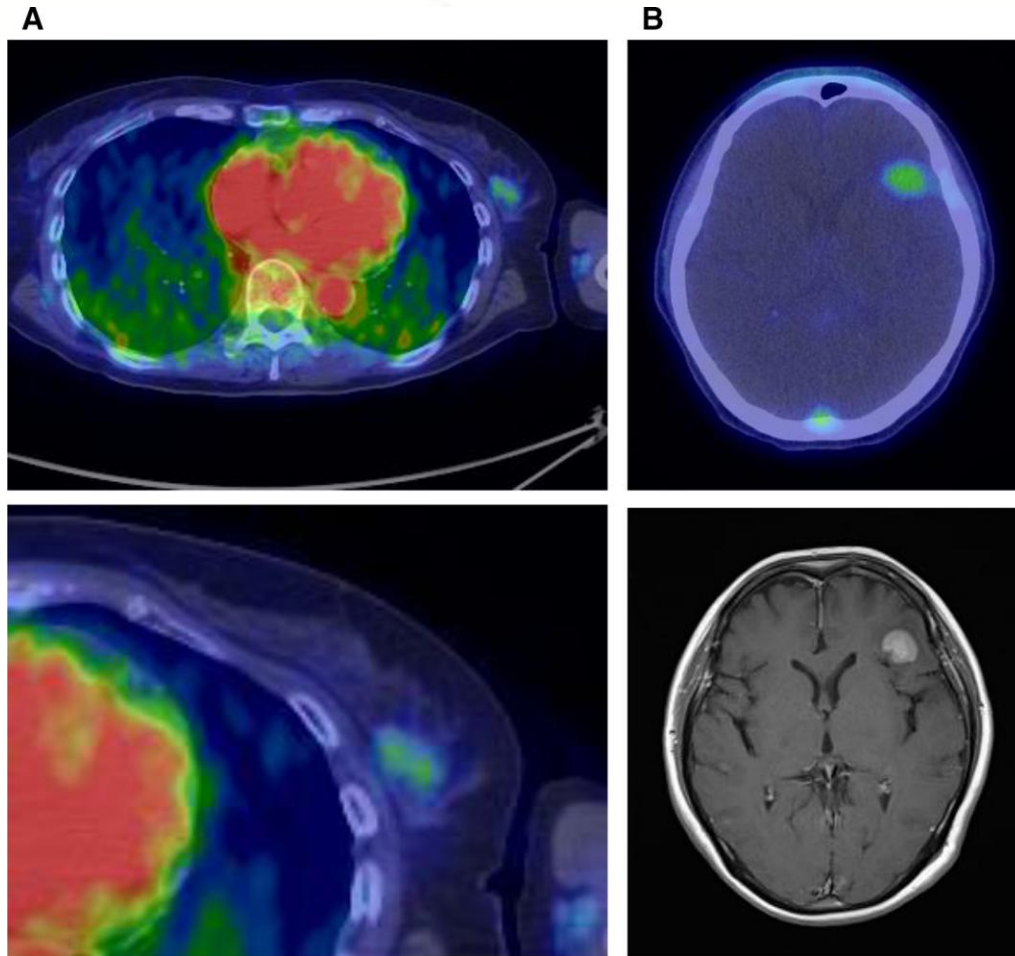


c.





# 64Cu-DOTAtrastuzumab PET images of HER2-positive breast cancer and metastatic brain lesion.



A randomized multicentre study by Berg et al. (2011) compared **PEM** to **MRI** in 388 newly diagnosed breast cancer patients. Though **PEM** had **higher specificity** (91.2% vs 86.3%), **MRI** showed **greater sensitivity** in detecting additional cancers (53% vs 41%). **PEM is therefore not recommended over MRI at this time.**



## FLT-PET/CT.



An MIP image of whole body FLT-PET/CT in a 64-year-old woman. FLT has been developed to visualize the activity of DNA synthesis that is increased in tumor cells compared to normal cells

Overall, 61 (16%) of the 388 participants had an appropriate change in surgical management based on MR findings; this was more than the 41 (11%) women with an appropriate change based on PEM findings ( $P = .003$ ) and fewer than the 71 (18%) women with an appropriate change based on combined PEM and MR findings ( $P = .004$  for comparison with MR imaging alone).

سیاس از توجه شما

