Comparative study between tomosynthesis, contrast enhanced spectral mammography and breast ultrasound as complementary techniques in mammography of dense breasts

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Purpose

Full Field Digital Mammography developments have been rapid, enabling high-quality breast images with higher contrast resolution, an improved dynamic range, and rapid processing of data and images when compared with Screen Film Mammography. However, some limitations still persist. \( \{2\} \)

Women with dense breast are doubly disadvantaged as they are both at higher risk of developing breast cancer and at greater risk that cancer will not be detected because of masking of the radiological signs of cancer by increased density. \( \{4\} \)

Mammography has low sensitivity and specificity in women with radiographically dense breast due to decrease contrast between a possible tumour and surrounding breast tissue and summation of tissues may obscure lesions. \( \{3\} \)

Therefore, the purpose of this study is to compare between breast Tomosynthesis, Contrast Enhanced Spectral Mammography(CESM) and breast Ultrasound as complementary techniques to mammography in dense breast parenchyma.
Methods and materials

The study included 37 patients with 63 inconclusive mammography breast lesions during the period from January 2014 to June 2014. Their ages ranged from 27 - 69 years (mean age (46.8 ± 9.88 SD). They all had mammography dense breast classified as 'C' or 'D' according to the American Cancer Society breast density classification [1]. They all performed single MLO view Tomosynthesis, Contrast Enhanced Spectral Mammography and breast Ultrasound.

**Technique of Contrast Enhanced Spectral Mammography:**

A wide bore canula was inserted into the antecubital vein of the arm contra lateral to the breast of concern. One shot intravenous injection of non-ionic contrast agent was then performed with a dose of 1.5 ml/Kg at a rate of 3 ml/s. Two minutes after the initiation of the contrast agent administration the breast was compressed in a CC position and a pair of low and high-energy images were obtained. The breast was then compressed in the MLO position and a new pair of low- and high-energy exposures were performed about 4 min after the initiation of contrast agent administration. A combination of low-energy and high energy images through a specific image processing unit is performed in order to generate two subtracted images with contrast agent uptake information (one in the MLO and one CC view).

**Technique of 3D Tomosynthesis:**

For 3D Digital Tomosynthesis single view (MLO) was obtained.3D DBT involved the acquisition of twelve to fifteen 2D projection exposures. The 3D volume of compressed breast was reconstructed from the 2D projections in the form of series of images (slices) through the entire breast. Images were assessed on the workstation.

**Technique of Breast Ultrasound:**

Radial scanning of the entire breast and axillary tail of both sides was performed while, the patient’s arm relaxed and flexed behind the head. Medial lesions were scanned in the supine position, and lateral lesions, including the axilla, were scanned with the patient in the contralateral oblique position. Longitudinal and transverse images of breast lesions were obtained.

**Image analysis and interpretation of Mammography:**

- Mammography findings were assessed in the low energy images of CESM.
- Breast density was assessed for each patient.
- Each lesion was evaluated regarding site, type (mass, architectural distortion, focal asymmetry ± calcifications).
• We determined the BIRADS category of each lesion according to the BIRADS atlas 2013, guided by the results of Clinical data and mammographic findings but blind to final pathologic diagnosis.

**Image analysis and interpretation of Contrast Enhanced Spectral Mammography:**

• CESM (MLO and CC views) were assessed for the presence or absence of enhancing lesions.
• Enhancing lesions were then classified as mass or non mass
• When an enhancing mass lesion was detected, it was further assessed for its margins (circumscribed, not circumscribed irregular or not circumscribed speculated), intensity of enhancement (mild, moderate and severe) and pattern of internal enhancement (homogenous, heterogeneous or ring enhancement).
• When non enhancing mass lesion was detected, it was further assessed for distribution (focal, ductal, segmental, regional or parenchymal), and pattern of internal enhancement (homogenous or heterogeneous) and intensity of enhancement (mild, moderate and severe).
• We determined the BIRADS category of each lesion in reference to BIRADS atlas 2013 as there is no standardized BIRADS Lexicon to CESM, guided by the results of clinical data and CESM findings but blinded to the final pathological diagnosis.

**Image analysis and interpretation of Tomosynthesis:**

• Each lesion was evaluated regarding site, type (mass, architectural distortion, focal asymmetry ± calcifications).
• We determined the BIRADS category of each lesion in reference to BIRADS Atlas of 2013, guided by the results of Clinical data and Tomosynthesis findings but blinded to the final pathological diagnosis.

**Image analysis and interpretation of breast Ultrasound:**

• Each lesion was evaluated regarding shape, boundary, margin, echo pattern, and posterior acoustic features, calcifications and axillary lymph nodes.
• We determined the BIRADS category of each lesion according to BIRADS atlas of Ultrasound 2013, guided by the results of Clinical data and breast Ultrasound findings but blinded to the final pathological diagnosis.
Results

In the current study, 34/37(92%) cases were assigned an ACR score of C and 3/37(8%) cases were assigned an ACR score of D according to the ACR breast density classification \{1\}.

Upon correlation with final diagnosis either by histopathological analysis of biopsy samples, fine-needle aspiration cytology or close follow up, there were 27/63(43%) benign lesions and 36/63(57%) malignant lesions Fig. 1 on page 29. The distribution of benign lesions according to final pathology is shown in Table 1 on page 29.

Mammographic findings among studied lesions are demonstrated in Fig. 2 on page 30. Mammography BIRADS category was given for each lesion according to the BIRADS mammography morphology descriptors; 19/63(30%) lesions were considered benign (BIRADS 1,2and3) while, 44/63(70%) lesions were considered malignant Fig. 3 on page 31. After revising results of pathology and/or regular follow up 30 lesions were true positives, 14 lesions were false positive, 6 lesions were false negatives and 13 lesions were true negatives. Diagnostic indices of mammography were: sensitivity of 83% specificity of 48%, positive predictive value of 68%, a negative predictive value of 68% and diagnostic accuracy 68% Table 2 on page 32.

Regarding CESM findings, 44/63(70%) lesions showed contrast uptake and 19/63(30%) lesions did not show contrast uptake. Enhancing lesions were classified into enhancing mass lesions 30/44(68%) lesions and enhancing non mass lesions 14/44(32%) lesions. Upon correlation with results of pathology and/or regular follow up 3/30(10%) enhancing mass lesions and 11/14(78.6%) enhancing non mass lesions were benign while 27/30(90%) enhancing mass lesions and 3/14(21.4%) enhancing non mass lesions were malignant while 13/19 (68%) non enhancing lesions were benign and 6/19(32%) non enhancing lesions were malignant Fig. 4 on page 32.

Enhancing mass lesions were assessed for their margins, intensity of enhancement and pattern of internal enhancement and enhancing non mass lesions were assessed for their pattern of distribution, and pattern of internal enhancement and intensity of enhancement. Accordingly a BIRADS category was given for each lesion; 28/63(44%) lesions were benign (BIRADS 1,2and3) and 35/ 63(56%) lesions were malignant (BIRADS 4 and 5) Fig. 5 on page 32. After revising the pathology results 31 lesions were true positives, 3 were false positives, 5 lesions were false negatives and 24 were true negatives. So, Contrast Enhanced Spectral Mammography had a sensitivity of 89%, a specificity of 89%, a positive predictive value of 91%, a negative predictive value of 86% and diagnostic accuracy 89% Table 3 on page 33.
Tomosynthesis findings among studied lesions are demonstrated in Table 4 on page 33. BIRADS category was given for each lesion according to morphology descriptor; 27/63 (43%) lesions were benign (BIRADS 1,2,and3) and 36/63 (57%) lesions were malignant (BIRADS 4 and 5) Fig. 6 on page 34. After revising results of pathology and/or regular follow up 31 lesions were true positives, 5 lesions were false positives, 5 lesions were false negatives and 22 lesions were true negatives. Tomosynthesis had a sensitivity of 86%, a specificity of 81%, a positive predictive value of 86%, a negative predictive value of 81% and diagnostic accuracy 84% Table 5 on page 35.

Regarding Ultrasound findings; 50/63 (79%) lesions presented by mass lesions while, 13/63 (31%) presented by non mass lesions. Mass lesions were further assessed regarding shape, margins, echogenicity and posterior acoustic enhancement and/or shadowing.

BIRADS category was given for each lesion according to Ultrasound morphology descriptors; 24/63 (38%) lesions were considered benign (BIRADS 1,2, and 3) and 39/63 (62%) lesions were considered malignant Fig. 7 on page 35. After revising the results of pathology and/or follow up; 35 were true positive, 4 were false positive, 1 lesion results was false negative and 23 were true negative. So, breast Ultrasound had a sensitivity of 97%, a specificity of 85%, a positive predictive value of 90%, a negative predictive value of 96% and diagnostic accuracy 92% Table 6 on page 35.

**Comparison of Diagnostic indices of Mammography, CESM, Tomosynthesis and breast ultrasound**

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammography</td>
<td>83%</td>
<td>48%</td>
<td>68%</td>
<td>68%</td>
<td>68%</td>
</tr>
<tr>
<td>CESM</td>
<td>89%</td>
<td>89%</td>
<td>91%</td>
<td>86%</td>
<td>89%</td>
</tr>
<tr>
<td>Tomosynthesis</td>
<td>86%</td>
<td>81%</td>
<td>86%</td>
<td>81%</td>
<td>84%</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>97%</td>
<td>85%</td>
<td>90%</td>
<td>96%</td>
<td>92%</td>
</tr>
</tbody>
</table>

References: M. M. H. Hanafy, R. M. Kamal, D. Salem, H. A. M. Azzam, A. Youssef; Cairo/EG
Case presentation

Case (1)

Clinical Background:

32 year-old patient with previous history of left breast ductectomy. She presented by mastalgia and palpable mass in the left breast.

Mammography revealed:

- Breast density: ACR C.
- Clusters of pleomorphic microcalcifications are seen in the left upper outer quadrant (BIRADS 4C)

Contrast Enhanced Spectral Mammography revealed:

Faint heterogeneous segmental non mass enhancement in the left upper outer quadrant (BIRADS 4C)
Fig. 9: Case 1: CESM MLO and CC views.

References: Cairo University (Women’s Imaging Program)

Tomosynthesis revealed:
- Clusters of microcalcifications are seen in left breast (BIRADS 4C)
Breast Ultrasound revealed microcalcifications (BIRADS 4C) with no associated mass lesions.
Fig. 11: Case 1: Ultrasound findings.

References: Cairo University (Women’s Imaging Unit) - Egyptian National Screening Program

Final diagnosis:

Invasive duct carcinoma and ductal carcinoma in situ (DCIS).

Case (2)

Clinical Background:

48 year-old patient (screening mammography).

Mammography revealed:

• Breast density: ACR C.
• Speculated mass is seen in the right upper outer quadrant (BIRAD 4b).
Contrast Enhanced Spectral Mammography:

An enhancing mass is seen in the right upper outer quadrant showing intense heterogeneous enhancement with not circumscribed speculated margins. (BIRADS 5)

Tomosynthesis revealed:
A speculated mass is seen in the right breast (BIRADS 5)

Fig. 14: Case 2: Tomosynthesis MLO view.

Breast Ultrasound revealed:

Irregular ill-defined speculated hypoechoic mass with posterior shadowing is seen associated with pathological lymph nodes. (BIRADS 5)
Fig. 15: Ultrasound findings

References: Cairo University (Women’s Imaging Unit) - Egyptian National Screening Program

Final diagnosis:

Invasive duct carcinoma.

Case (3)

Clinical background:

60 year-old patient with previous history of abscess excision in the right breast.

She presented by hard lump in the right breast.

- Breast density: ACR C.
- Speculated mass in the right upper outer quadrant with overlying skin thickening and retraction and pathological right axillary lymph nodes (BIRADS 4c).
• Left breast showed focal asymmetry (arrowed) (BIRADS 4a).

**Fig. 16:** Case 3: Mammography MLO and CC views.

**References:** Cairo University (Women’s Imaging Unit) - Egyptian National Screening Program

**Contrast Enhanced Spectral Mammography revealed:**

An intensely and heterogeneous enhancing speculated mass is seen in the right upper outer quadrant (BIRADS 5). The left breast showed faint homogenous non mass enhancement (BIRADS 2).

**Fig. 17:** Case 3: CESM MLO and CC views.
Tomosynthesis revealed:

A speculated mass in the right breast (BIRADS 5) with normal left breast (BIRADS 1)

Breast ultrasound revealed:

- Irregular illdefined hypoechoic mass in the right breast with posterior shadowing and pathological lymph nodes (BIRADS 4).
- The left breast showed adenosis (BIRADS 2).
Fig. 19: Ultrasound findings.
Kafayed El Cairo University (Women’s Imaging Unit) - Egyptian National Screening Program

Final diagnosis:
Invasive duct carcinoma in right breast and adenosis in left breast.

Case (4)
Clinical background:
36 year-old patient presenting by lump in the right breast.

Mammography revealed:
Breast density: ACR C.
• Two ill-defined masses are seen in the right upper outer quadrant (BIRADS 4b).

Fig. 20: Case 4: Mammography MLO and CC views.
References: Cairo University - Women's Imaging Unit - Egyptian National Screening Program.

Contrast Enhanced Spectral Mammography:
Two adjacent heterogeneous enhancing mass lesions with not circumscribed irregular margins are seen in the right upper outer quadrant (BIRADS 5).
Fig. 21: Case 4: CESM MLO and CC views.

References: Cairo University (Women's Imaging Unit) - Egyptian National Screening Program

**Tomosynthesis revealed:**

2 ill defined masses are seen in the right breast (BIRADS 4c).
Breast Ultrasound revealed:

2 hypoechoic irregular masses with ill-defined margins (BIRADS 4c).

Mammography revealed:

- Breast density: ACR C.
- Focal asymmetry and amorphous microcalcifications in left lower inner quadrant (blue arrow) (BIRADS 4c).
- Another well defined mass lesion is seen in left upper outer quadrant (red arrow) (BIRADS3).

Case (5)

35 year-old patient presented by pain in the left breast.
Case 5: Mammography MLO and CC views.

References: Cairo University (Women's Imaging Unit) - Egyptian National Screening Program

Contrast Enhanced Spectral Mammography revealed:

- Heterogeneous segmental non mass contrast enhancement in the left lower inner quadrant (BIRADS 4c).
- Circumscribed faintly enhancing mass lesion in the left UQQ (arrowed) (BIRADS 3).
Tomosynthesis revealed:

Focal asymmetry and amorphous microcalcifications in the left lower inner quadrant. Also, well defined oval mass is seen in the left upper outer quadrant (BIRADS 2).

Breast Ultrasound revealed:

Irregular ill-defined hypoechoic mass is seen with no posterior enhancement (BIRADS 4b). Another well defined oval isoechoic mass is seen in the upper outer quadrant (BIRADS 2).
Case 5

Ultrasound findings:

References: Cairo University (Women's Imaging Unit) - Egyptian National Screening Program

Final diagnosis:

- Invasive duct carcinoma (lesion in left lower inner quadrant).
- Fibroadenoma (lesion in left upper outer quadrant).

Case 6

Clinical background:

60 year-old patient presented by lump in the left breast.

Mammography revealed:

- Breast density: ACR C.
- Focal asymmetry in the left upper inner quadrant with microcalcifications (BIRADS 4b).
Contrast Enhanced Spectral Mammography revealed:

- Left breast showed a heterogeneously, moderately enhancing upper inner quadrant mass lesion with spiculated margins that is surrounded by satellite lesions (BIRADS 5).
- The right breast shows a tiny right retroareolar homogenously enhancing mass with not circumscribed irregular margins (BIRADS 4b).

Tomosynthesis revealed:

- Left breast shows a speculated mass with microcalcifications (BIRADS 4) in upper inner quadrant (BIRADS 4c).
• Right breast shows retroareolar ill defined mass with microcalcifications (BIRADS 4c).

Breast Ultrasound:

• Irregular ill-defined mass is seen in left upper inner quadrant. Left axillary infiltrated lymph nodes are seen (BIRADS 4c).
• Right retroareolar small irregular ill defined mass. Right axillary lymph nodes with preserved fat hilae (BIRADS4c).
Fig. 31: Case 6: Ultrasound findings.

References: Cairo University (Women’s Imaging Unit) - Egyptian National Screening Program

Final Diagnosis:

Bilateral invasive duct carcinoma.

Case 7

Clinical background:

32 year-old patient presented by palpable lump in her left breast.

Mammography:

- Breast density: ACR D.
- No specific abnormality detected.
Fig. 33: CESM MLO and CC views.

Cairo University (Women’s Imaging Unit) - Egyptian National Breast Screening Program

Assessment:

No specific abnormality detected.
Fig. 34: Case 7: Tomosynthesis MLO view.

References: Cairo University (Women’s Imaging Unit) - Egyptian National Screening Program

Breast Ultrasound:

An irregular ill defined hypoechoic mass within left breast seen at axillary tail region lesion deeply seated over pectralis muscle together with adjacent another hypoechoic irregular illdefined mass. Pathological left axillary lymph nodes of thick cortex and lost fatty hilum (BIRADS 4c)
Fig. 35: Case 7: Ultrasound findings.

References: Cairo University (Women's Imaging Unit) - Egyptian National Screening Program

Final diagnosis:

Multifocal invasive duct carcinoma.
Images for this section:

![Distribution of benign and malignant groups](image_url)

**Fig. 1:** Distribution of benign and malignant groups within the studied lesions

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<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of lesions</th>
</tr>
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<tbody>
<tr>
<td>Fat necrosis</td>
<td>2/27(7.4%)</td>
</tr>
<tr>
<td>Duct ectasia</td>
<td>2/27(7.4%)</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>11/27(40.7%)</td>
</tr>
<tr>
<td>Calcified cyst</td>
<td>1/27(3.8%)</td>
</tr>
<tr>
<td>Fibrocystic changes</td>
<td>3/27(11.1%)</td>
</tr>
<tr>
<td>Adenosis</td>
<td>6/27(22.2%)</td>
</tr>
<tr>
<td>Benign postoperative sequel</td>
<td>2/27(7.4%)</td>
</tr>
</tbody>
</table>

**Table 1:** The distribution of the different pathological entities within the "benign lesions" group.

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**Fig. 2:** Mammographic findings among studied lesions.

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**Fig. 3:** Benign and malignant mammography results for the studied lesions

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Table 2: Diagnostic indices of Mammography among studied lesions

<table>
<thead>
<tr>
<th>Mammography</th>
<th>Final Diagnosis</th>
<th>Final Diagnosis</th>
<th>Total</th>
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<tr>
<td></td>
<td>Malignant</td>
<td>Benign</td>
<td></td>
</tr>
<tr>
<td>Malignant</td>
<td>30 TP (a)</td>
<td>14 FP (b)</td>
<td>44/63</td>
</tr>
<tr>
<td>Benign</td>
<td>6 FN (c)</td>
<td>13 TN (d)</td>
<td>19/63</td>
</tr>
<tr>
<td>Total</td>
<td>36 (a+c)</td>
<td>27 (b+d)</td>
<td>63 (a+b+c+d)</td>
</tr>
</tbody>
</table>

Fig. 4: Distribution of benign and malignant diagnosis among enhancing and non enhancing lesions.

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Fig. 5: CESM results among studied lesions

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Table 3: Diagnostic indices of CESM among studied lesions

© M. M. H. Hanafy, R. M. Kamal, D. Salem, H. A. M. Azzam, A. Youssef; Cairo/EG
<table>
<thead>
<tr>
<th>Tomosynthesis</th>
<th>No of lesions</th>
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<tr>
<td>Normal</td>
<td>17/63</td>
</tr>
<tr>
<td>Masses</td>
<td>31/63</td>
</tr>
<tr>
<td>Focal asymmetry</td>
<td>7/63</td>
</tr>
<tr>
<td>Calcifications</td>
<td>5/63</td>
</tr>
<tr>
<td>Mass and calcification</td>
<td>2/63</td>
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<tr>
<td>Focal asymmetry and calcification</td>
<td>1/63</td>
</tr>
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</table>

Table 4: Tomosynthesis findings among studied lesions

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Fig. 6: Benign and malignant Tomosynthesis results for the studied lesions
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<table>
<thead>
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<th>Tomosynthesis</th>
<th>Final Diagnosis</th>
<th>Final Diagnosis</th>
<th>Total</th>
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<tr>
<td></td>
<td>Malignant</td>
<td>Benign</td>
<td></td>
</tr>
<tr>
<td>Malignant</td>
<td>31TP (a)</td>
<td>5FP(b)</td>
<td>36/63</td>
</tr>
<tr>
<td>Benign</td>
<td>5 FN (c)</td>
<td>22 TN (d)</td>
<td>27/63</td>
</tr>
<tr>
<td>Total</td>
<td>36 (a+c)</td>
<td>27 (b+d)</td>
<td>63 (a+b+c+d)</td>
</tr>
</tbody>
</table>

Table 5: Diagnostic indices of Tomosynthesis among studied lesions
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Fig. 7: Benign and malignant Ultrasound results for studied lesions.
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<table>
<thead>
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<th>Ultrasound</th>
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<th>Final Diagnosis</th>
<th>Total</th>
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<tbody>
<tr>
<td></td>
<td>Malignant</td>
<td>Benign</td>
<td></td>
</tr>
<tr>
<td>Malignant</td>
<td>TP (a) 35</td>
<td>FP(b) 4</td>
<td>39</td>
</tr>
<tr>
<td>Benign</td>
<td>1 FN (c)</td>
<td>23 TN (d)</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>36 (a+c)</td>
<td>27 (b+d)</td>
<td>63 (a+b+c+d)</td>
</tr>
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</table>

Table 6: Diagnostic indices of Ultrasound among studied lesions
Conclusion

3D Digital tomosynthesis resolves the problem of tissue overlap and reduces recall rates as well as number of biopsies from questionable sonomammographic findings.

Breast Ultrasound should be coupled with Mammography in screening of women with dense breast parenchyma as it reduces false negative results, detects solid and cystic lesion, allows assessment of solid lesions whether they are benign or malignant and allows assessment of axillary and supraclavicular lymph nodes.

CESM reduces false positive results therefore it can be used to detect occult lesions in mammography and assessment of locoregional extent.

Breast Ultrasound, Tomosynthesis and Contrast Enhanced Spectral Mammography showed better performance compared to mammography in dense breasts. However, Ultrasound being safe with no radiation hazards should be the second step modality of choice after mammography in assessment of mammography dense breast. Adding Tomosynthesis to mammography in screening increases its sensitivity. Contrast Enhanced Spectral Mammography should be reserved for cases with inconclusive sonomammographic results.
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