Diagnostic Approach Of Non-Mass Forming Breast Calcifications

(Analysis Of 85 Cases)

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Abstract

\textbf{Purposes}: To evaluate diagnostic approach of non-mass forming breast calcifications, to find out correlation between Age of the patients and Morphology of calcifications. (Benign or malignant) and how to avoid unnecessary interventions.

\textbf{Background}: Micro calcification diagnosis is challenged by presence of dense parenchyma resulting in low specificity values and unnecessary biopsies.

\textbf{Patients and methods}: The study included 85 female patients; between 23-52 years age range divided into; Group A: 30 (35%) \leq 35 years old and Group B: 55 (65%) >35 years old. All patients undergoing Mammography, Guided biopsy (US. Guided FNAC was done for 12 cases where trucut biopsy was contraindicated) or Trucut wide bore biopsy using automated gun-shot and Surgical biopsy (by Hook-wire needle localization).

\textbf{Results}: There were satisfactory results obtained by mammography in detection of benign calcifications; 38 (45%) cases (13% in group A & 32% in group B) and its sensitivity increased with age; (P-Value =0.03). Guided biopsy diagnosed 36 (76.6%) cases out of 47 as benign while 33 (70.2%) out of 47 were diagnosed benign after surgical biopsy i.e. Total benign calcifications were 71(84%) cases out of 85.

\textbf{Conclusions}: Mammography is essential document for detection of benign calcifications. Use of FNAC is not recommended. Core biopsy plays important role to diagnose majority of calcifications; despite its disadvantages in certain cases. But
surgical biopsy is the most accurate to diagnose all calcifications; despite its disadvantages are cost and lengthened procedure. Most of breast calcifications are benign but malignant calcifications are diagnosed by biopsy.

Key words: Breast, Benign or malignant calcifications, No mass, Diagnostic approach.

Introduction:

The basic functional unit in the breast is the lobule, also called the terminal ductal lobular unit (TDLU). The TDLU consists of 10-100 acini, that drain into the terminal duct.\(^{(1,2)}\)

The terminal ductal lobular unit is an important structure because most invasive cancers arise from the TDLU. It also is the site of origin of ductal carcinoma in situ (DCIS), lobular carcinoma in situ, fibroadenoma and fibrocystic disease, like cysts, apocrine metaplasia, adenosis and epitheliosis.\(^{(3)}\)

Most calcifications in the breast form either within the terminal ducts (intraductal calcifications) or within the acini (lobular calcifications).\(^{(1,2)}\)

Intraductal calcifications are calcified cellular debris or secretions within the intraductal lumen. These calcifications are extremely variable in size, density and form (i.e. pleomorphic from the Greek \textit{pleion 'more'} and \textit{morphe 'form'}). Sometimes they form a complete cast of the ductal lumen. This explains why they often have a fine linear or branching form and distribution. Intraductal calcifications are suspicious of malignancy.\(^{(3,4)}\)

But; Lobular calcifications fill the acini, which are often dilated. These calcifications usually have a diffuse or scattered distribution, since most of the breast is involved in the process that forms the calcifications. Lobular calcifications are almost always benign.\(^{(5,6,7)}\)

Diagnosis of microcalcifications (MCs) is challenged by the presence of dense parenchyma, resulting in low specificity values and so in unnecessary biopsies.\(^{(4,8,9)}\)

The mainstay of a detection of microcalcifications is mammography. Typical size of microcalcifications ranges from 50-500 microns in size, mammography is well
suited to the task of demonstrating the presence of microcalcification. The morphology of microcalcification can be further characterized using magnification views.\(^{(10)}\)

Magnification views enable the microcalcifications to be further analyzed according to the degree of clustering, density, morphology and distribution. The indeterminate and suspicious clusters of microcalcification can be localized and biopsied under US. Guidance in order to achieve histological diagnosis.\(^{(11)}\)

High frequency US Can be used to detect mammographic microcalcifications. The ability to reliably detect benign microcalcifications remains low.\(^{(10,12)}\)

Nevertheless; clustered suspicious microcalcifications demonstrated on mammography can be visualized using US. Malignant clustered microcalcifications of suspicious appearance, particularly if extensive, can be detected as either masses or focally dilated ducts. The use of power Doppler may also improve the detection of invasive foci of disease.\(^{(12)}\)

Most mammograms are acquired on X-ray film, with radiation dose is about 0.1cGy; however in recent years, a digital X-ray acquisition systems have been developed in which the information in the image are a matrix of numbers (Pixels). The digital image may be printed on film or displayed and viewed in the screen. The use of digital mammogram offers a number of significances by performing mathematical operations on matrix of numbers, facilitating viewing by adjusting the contrast or brightness. Quantitative information can be extracted from monitoring the response to treatment. A further advantage of using digital images is that they can be rapidly transmitted to other sites and multiple copies may be made available without loss of image quality. Microcalcification detection by digital imaging is more easier and can detected 98% of microcalcifications.\(^{(13)}\)

Breast calcifications seen on mammography often represent difficult and complex diagnostic challenges, especially a non mass forming calcifications.\(^{(5)}\)
Sakka et al., 2006; (14) described diagnostic mammographic algorism for breast calcifications according to distribution, size, shape, and polarity as follow: (Fig. 1)
**Patients & methods:**

After local ethical committee of Benha university approval and obtaining written fully informed patients consent, the current study was conducted at Mammography unit and General surgery Department, Benha University Hospital and a private radiology center from September 2010 till July 2014. This prospective randomized controlled study was conducted on 85 female patients selected from the Mammography unit diagnosed with non-mass forming breast calcifications; between 23-52 years age range divided into; Group A: 30 (35%) \(\leq 35\) years old and Group B: 55 (65%) \(>35\) years old.

All patients presenting were subjected to detailed clinical evaluation; history for past breast surgery or implants, pregnancy, lactation, and history of malignancy. Examination generally for fitness and locally to detect severe breast tenderness and to exclude breast scarring. Also laboratory assessment for fitness for surgical biopsy and coagulation profile is done for all patients submitted for trucut biopsy.

Inclusion criteria in this study included; patients fit for general anesthesia; but exclusion criteria in this study included: Morbid obese patients, pregnancy, lactation, history of malignancy (radiology effect), past history of breast surgery (scarring) or implants and severe agonizing breast pain.

**Interventional procedures:**

The used techniques in this study was Mammography, The guided biopsy (US. Guidance for FNAC), Trucut wide bore biopsy using automated gun-shot and Surgical biopsy (by Hook-wire needle localization).

The mammographic data were obtained by using mammographic unit, Trophy Alpha III and supplemented by digital unit Agfa CR30-X. Sonographic data were obtained by high frequency probes and color duplex examination using GE unit Logiq 5 & Siemens –Acuson X300).\(^{(14)}\) (**Fig. 2**).

Guided biopsy was done by US Guidance for cases of indeterminate signs 47 cases. FNAC was done for 12 cases. Trucut wide bore biopsy using automated gun-shot (Manan short and long through gun with short and long through trucut needles
10-13 cm length with 14-16 Gauge) was done for 35 cases. (Fig. 3).

The FNAC is done for 12 cases where the trucut biopsy is contraindicated i.e. retroarealar location (4 cases), deeply seated calcifications (6 cases) and anxiety of the patient (2 cases).\(^{(15,16)}\)

The technique of guided biopsy is explained to the patient. Skin sterilization with alcohol and local anesthesia (Xylocaine 4%) for the skin is applied.

The all indeterminate cases (47 cases) are sent for surgical biopsy; which taken by **Hook-wire needle localization**: It is necessary to place a localization wire to enable removal of the lesion without an excessive amount of surroundings. A wire can be placed using mammographic or sonographic guidance. Mammographic units with digital capability can reduce by half both radiation dose and time for procedure.

The wire should lie through the lesion at least within 5 mm of it, with the hook of 1 cm beyond the lesion then the surgical biopsy is taken (Fig. 4).

Localization can be done by **Cryoprobes**: which freezes the lesion together with 5 to 10 mm of surrounding breast tissue, creating a palpable ice ball and obviating needle localization.\(^{(17)}\)

All obtained specimens were sent for pathological assessment and The data obtained from mammography, sonomammography, guided biopsy and surgical biopsy were correlated and tabulated.

**Statistical analysis:**

Analysis of data was done by using SPSS version 16 (Bristol university; in United Kingdom). Quantitative data were presented as mean and standard deviation and were analyzed by using one way ANOVA test. Qualitative data was presented as numbers and percentages and were analyzed by using Chi-square and Fisher exact tests. (P-value <0.05) was considered significant while (P-value <0.01) was considered highly significant. But (P-value >0.05) was considered insignificant.
These all data were shown in the following images:-

Tram-line sign of vascular calcification      Pleomorphic calcification of high-grade DCIS.

Mammographic images of breast calcification (Fig. 2).

(Fig. 3): Automated gun-shot                 (Fig. 4A): Hook-wire needle.

(Fig. 4B): Hook-wire needle with trocar.     (Fig. 4C): Hook-wire needle alone.

(Fig. 4D): Surgical biopsy by "Hook-wire" needle localization
Results:

In the present study, 85 female patients with non-mass forming breast calcifications were selected from mammographic unit in Benha University Hospital and a private radiology centre: 23 -52 years age range, 38 patient had sure benign criteria of calcifications in mammography and sonomammography; in the form of coarse microcalcifications, arc and rings, bilateral calcifications, skin and vascular calcifications(Fig.4). This group of patients is not amenable for any type of biopsy and recall.

Forty seven patients presented by indeterminate criteria of breast calcifications in mammography in the form of radial scar, non-polarized microcalcifications, clustered pleomorphic calcifications, ductal distribution of calcifications, rod and branching shaped. as well as changes in morphology of calcifications over time.

The age of the patients were 23 to 52 years old (mean age 35).In this study; 85 female patients with non-mass breast calcifications were divided into 2 groups: according age (group A: 30 cases) & (group B: 55 cases); This indicates breast calcifications increases with age. (Tab.1,Graph.1).

(Tab. 1): Age distribution of the studied cases:

<table>
<thead>
<tr>
<th>Age of the patients</th>
<th>Number of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A: ≤ 35 years old</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td>Group B: &gt;35 years old</td>
<td>55</td>
<td>65</td>
</tr>
<tr>
<td>Total</td>
<td>85</td>
<td>100%</td>
</tr>
</tbody>
</table>

(Graph. 1): Age distribution of the studied cases:
But; according morphology by mammography into (Benign group: 38 cases) & (Indeterminate group: 47 cases). The morphology by mammography revealed benign group included 11 (13%) cases in group A: ≤ 35 years old and 27 (32%) cases in group B: > 35 years old. But, the indeterminate group included 19 cases in group A: ≤ 35 years old and 28 cases in group B: > 35 years old (P-Value = 0.03). This indicates sensitivity of mammography increased with age. (Tab. 2A Graph. 2A & B).

(Tab. 2A): Correlation between Calcification morphology by mammography & age of the patients:

<table>
<thead>
<tr>
<th>Mammography</th>
<th>Group A</th>
<th>Group B</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO</td>
<td>%</td>
<td>NO</td>
<td>%</td>
</tr>
<tr>
<td>Benign group</td>
<td>11</td>
<td>13</td>
<td>27</td>
<td>32</td>
</tr>
<tr>
<td>Indeterminate group</td>
<td>19</td>
<td>22</td>
<td>28</td>
<td>33</td>
</tr>
</tbody>
</table>

(Graph. 2): Correlation between Calcification morphology by mammography & age of the patients:

(Tab. 2B): Distribution of 38 cases with sure benign criteria of calcifications (mammographic and sonomammographic criteria):

<table>
<thead>
<tr>
<th>Shape</th>
<th>No. of lesions</th>
<th>Location</th>
<th>US diagnosis</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial calcifications</td>
<td>single</td>
<td>Parenchymal</td>
<td>Confirmed by color Doppler</td>
<td>7</td>
</tr>
<tr>
<td>Small rings with lucent center</td>
<td>numerous</td>
<td>Dermal</td>
<td>Calcified sebaceous glands</td>
<td>8</td>
</tr>
</tbody>
</table>
Small rings with lucent center | numerous | Parenchymal | Ductectasia | 9
Large egg-shell calcifications | Few | Parenchymal | Fibroadenosis | 12
Lobulated coarse dense | Two | Retroareolar | Duct papilloma | 1
Coarse irregular 'lava-shaped' calcifications. larger than 0.5 mm and have a lucent center. | numerous | Parenchymal | Fat necrosis | 1
Total | | | | 38

The U/S guided FNAC done for 12 cases where the trucut biopsy is contraindicated revealed benign 4/5 cases in group A: ≤ 35 years old and 5/7 cases in group B: >35 years old. But, revealed malignant 1/5 cases in group A: ≤ 35 years old and 2/7 cases in group B: >35 years old (P-Value =0.5). (Tab. 3, Graph. 3).

(Tab. 3): Correlation between U/S guided FNAC for 12 cases of indeterminate group & age of the patients:

<table>
<thead>
<tr>
<th>U/S guided FNAC</th>
<th>Group A</th>
<th>Group B</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO</td>
<td>%</td>
<td>NO</td>
<td>%</td>
</tr>
<tr>
<td>Benign</td>
<td>4/5</td>
<td>33</td>
<td>5/7</td>
<td>42</td>
</tr>
<tr>
<td>Malignant</td>
<td>1/5</td>
<td>8</td>
<td>2/7</td>
<td>17</td>
</tr>
</tbody>
</table>

(Graph. 3): Correlation between U/S guided FNAC for 12 cases of indeterminate group & age of the patients:
But, the Trucut wide bore biopsy for 35 cases of indeterminate group revealed benign 11/14 cases in group A: \( \leq 35 \) years old and 16/21 cases in group B: \( >35 \) years old. But, revealed malignant 3/14 cases (1/3 ductal carcinoma in situ DCIS & 2/3 Invasive carcinoma) in group A: \( \leq 35 \) years old and 5/21 cases (2/5 DCIS & 3/5 Invasive carcinoma) in group B: \( >35 \) years old. (P-Value = 0.9). (Tab. 4 Graph 4).

(Tab. 4): Correlation between Trucut wide bore biopsy for 35 cases of indeterminate group & age of the patients:

<table>
<thead>
<tr>
<th>Trucut biopsy</th>
<th>Group A</th>
<th>Group B</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO</td>
<td>%</td>
<td>NO</td>
<td>%</td>
</tr>
<tr>
<td>Benign</td>
<td>11/14</td>
<td>31</td>
<td>16/21</td>
<td>46</td>
</tr>
<tr>
<td>Malignant</td>
<td>3/14</td>
<td>9</td>
<td>5/21</td>
<td>14</td>
</tr>
</tbody>
</table>

(Graph. 4): Correlation between Trucut wide bore biopsy & age of the patients:

Finally, the surgical biopsy done for 47 cases of indeterminate group revealed benign 14/19 cases in group A: \( \leq 35 \) years old and 19/28 cases in group B: \( >35 \) years old. But, revealed malignant 5/19 cases (2/5 DCIS & 3/5 Invasive carcinoma) in group A: \( \leq 35 \) years old and 9/28 cases (4/9 DCIS & 5/9 Invasive carcinoma) in group B: \( >35 \) years old. So, 36 cases out of 47 were diagnosed by guided biopsy as benign while 33 out of 47 were diagnosed benign after excision biopsy i.e. so the total benign
calcifications in this study were 71(84%) cases out of 85. So, 36 cases out of 47 were diagnosed by guided biopsy as benign while 33 out of 47 were diagnosed benign after excision biopsy i.e. so the total benign calcifications in this study were 71(84%) cases out of 85. (P-Value =0.7). (Tab. 5 Graph.5).

(Tab. 5): Correlation between Surgical biopsy for 47 cases of indeterminate group & age of the patients:

<table>
<thead>
<tr>
<th>Surgical biopsy</th>
<th>Group A</th>
<th>Group B</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO</td>
<td>%</td>
<td>NO</td>
<td>%</td>
</tr>
<tr>
<td>Benign</td>
<td>14/19</td>
<td>30</td>
<td>19/28</td>
<td>40</td>
</tr>
<tr>
<td>Malignant</td>
<td>5/19</td>
<td>11</td>
<td>9/28</td>
<td>19</td>
</tr>
</tbody>
</table>

(Graph.5): Correlation between Surgical biopsy for 47 cases of indeterminate group & age of the patients:

Discussion:

Non mass breast calcifications are impalpable clinically and detected incidentally. Because of their significance, they represent a diagnostic challenge. (18)

The mainstay of a detection of microcalcifications is mammography. Typical size of microcalcifications ranges from 50-500 microns in size, mammography is well suited to the task of demonstrating the presence of microcalcification. The morphology of microcalcification can be further characterized using magnification views. (10)
Mammography is essential document for detection of benign calcifications and its sensitivity increases with age because, the breast become less dense. Use of the mammography is very important, being save, noninvasive & easy to apply and to repeat, not only to avoid invasive biopsy. But also, mammographic imaging represent a target for biopsy either guided biopsy or surgical biopsy. But; its disadvantages are 5-15% false results and patient discomfort. \(^{8,9}\)

Mammographic magnification technique not more than 1.5 magnification factor with digital imaging is helpful for confirming the morphologic criteria and distribution of calcifications. The rapid technical progress in digital mammography supplemented by high resolution US. facilitate the assessment of benignity and malignancy of this type of calcifications. But; The US. guided biopsy and surgical biopsy add more information in this respect.\(^{19}\)

Each technique of guided biopsy and surgical biopsy has its advantages and disadvantages. The use of FNAC is not recommended as it is not possible to confirm representative sample & permits cytologic evaluation. \(^{19,20}\)

The main advantages of Core-Biopsy are low cost, low complication rate, no scarring & speed to accurately diagnose majority of calcification clusters; But its disadvantages are the lower calcification yield than surgical biopsy and difficult in sampling calcifications behind the nipple. Repeated biopsy is more common in core biopsy than surgical biopsy. The advantages of surgical biopsy are the increased calcification retrieval and more accurate to diagnose small clusters, diffuse calcifications and retroareal calcifications. The disadvantages of surgical biopsy are cost and lengthened procedure as compared to core biopsy.\(^{20}\)

Both; Core biopsy & the surgical biopsy permit the analysis of breast tissue and allow the pathologist to determine whether invasive cancer is present. This permit the surgeon & patient to discuss the specific management. \(^{19,20}\)

The current study, mentioned that, The morphology by mammography revealed benign group included 11(13%) cases in group A:≤ 35 years old and 27(32%) cases in group B:>35 years old. But, the indeterminate group included 19 cases in group A:≤ 35 years old and 28 cases in group B:>35 years old.(P-value; 0.03).

So, there is a significant correlation between breast calcifications that increased with age & sensitivity of mammography that also increased with age.
In the present study, It was found that 36 cases out of 47 were diagnosed by guided biopsy as benign while 33 out of 47 were diagnosed benign after excision biopsy i.e. Total benign calcifications in this study were 71(84%) cases out of 85.

This results with Evans et al 2002 who demonstrated that 87% of breast calcifications are benign, most of them are diagnosed only by its sure mammographic criteria of benignity, while few cases are diagnosed only as benign calcifications after biopsy i.e. most of non-mass breast calcifications are benign.

Conclusions: Mammography is essential document for detection of benign calcifications. The use of FNAC is not recommended. Core biopsy plays important role with no scarring & more speed to diagnose majority of calcification clusters; despite it has many disadvantages in certain cases. But surgical biopsy is the most accurate to diagnose all calcifications; despite its disadvantages are cost and lengthened procedure. Most of breast calcifications are benign. But malignant calcifications are diagnosed only by biopsy.

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