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Comparison of Calcification Specificity in Digital Mammography Using Soft-Copy Display versus Screen-Film Mammography

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Abstract: ***Breast cancer represents the most frequent cancer within women. The damage that cancerous tumors cause to various important organs in the body can lead to serious illness, so an early detection is important for a better treatment and recovery. The most common range of age attacked by breast cancer is between 40-50 years old and until the menopause, the breast cancer rate incidence increase decreases dramatically. Two kinds of breast imaging tests are currently used. Screening , which is performed in patients with no symptoms to detect cancer when it is still too small to be felt by a woman or her physician; and diagnostic, which is performed in women who either have a breast complaint or have had an abnormality found during screening. Screening film mammography, which is also known as conventional mammography produces view of the women breast in the shape of hard copy or film that can be examined by one radiologist at a time and may suffer a number of disadvantages. Digital mammography, on the other hand, gives the radiologist a chance for enhancement of resolution, contrast, and overcome most of the disadvantages of the screen film mammography such as micro calcifications in the breast. The aim of the thesis is " Comparison of Calcification Specificity in Digital Mammography Using Soft-Copy Display Versus Screen-Film Mammography".***

Keywords: Breast cancer-Medical Imaging-SPSS Photoshop 7

1. Introduction

Cancer is a condition that affects people all over the world. Research in this area beginning since 1900 and cancer was a disease without cure. As other cancers, breast cancer arises when cells growth and multiply uncontrollably, which produces a tumor or a neoplasm. The tumors can be benign when the cancerous cells do not invade other body tissues or malignant if cells attack nearby tissues and travel through the bloodstream or lymphatic system to other parts of the body, spreading a cancer by a process known as metastasis. [3,4] .The most common range of age attacked by breast cancer is between 40-50 years old and until the menopause, the breast cancer rate incidence increase decreases dramatically. There are other risk factors that lead to develop a breast cancer as like age at menarche and menopause, age at first pregnancy, family history, previous benign breast disease and radiation.[5]

Micro calcifications are small deposits of calcium of size from 0.33 to 0.7 mm and are slightly brighter than surrounding tissues. These lesions are difficult to detect in mammography because they appear with low contrast due to their small size, although have high inherent attenuation properties. Associated with extra cell activity in breast tissue micro calcifications may show up in clusters or in patterns.[6,7].Masses are lesions more difficult to detect in monographs than micro calcifications because the features of a mass bear semblance to those of the normal breast parenchyma. In general, mass shape can be round, oval, lobulated or irregular, and margins can be from circumscribed to speculated.[10].When a mass is detected it is difficult to distinguish if is benignant or malignant but there are differences in the features of shape and texture between them. Benign masses are typically smooth and distinct, and their shapes are similar to the round. On the other hand, malignant masses are irregular and their boundaries are usually blurry. A mass with regular shape has a higher probability of being benign whereas a mass with an irregular shape has a high probability of being malignant.[11-13]

Techniques are also used for breast imaging ,i.e., ultrasonography, and magnetic resonance imaging. However, mammography is the most widespread test for the early detection of breast cancer and the chosen method for screening.[19-22].Digital mammography generally detects to varying degrees the following signals/signs of breast cancer: clustered micro calcifications, speculated lesions, circumscribed masses, ill-defined masses, and architectural distortions. Many methods of analyzing digital mammograms have been recently examined and yielded varied success.[23]

Although radiographic breast imaging and screening has allowed for more accurate diagnosis of breast disease at earlier stages of development, 10-30% of malignant cases (biopsy proven cancerous) are not detected for various reasons such as technical problems in the imaging procedure, abnormalities that are not observable, and abnormalities that are misinterpreted.[24].Several classifications have been used for classify the breast lesions and, although all of them are similar, the more accepted is the classification proposed by American College of Radiology (Breast Imaging Reporting and Data System – BI-RADS).[25,26].Histogram based techniques are widely used in digital mammography to separate the breast region from the background under the assumption that the background has a homogeneous gray level. This can be problematic

because a homogeneous background is not always the case, so the threshold should be carefully selected. This technique has been used based on simple threshold by Hoyer and Spiesberg (1979)[27]; Lau and Bischoff (1991)[28] and; Byng and Boyd (1996).[29] Bick and Geiger (1995)[30], used a combination of threshold, region growing and morphological filtering. Masek and Attikiouzel (2000)[31], proposed a local threshold method. The aim of this work is the Comparison of Calcification Specificity in Digital Mammography Using Soft-Copy Display Versus Screen-Film Mammography.

2. Materials and Methods

2.1 Patients

A total of 60 female breast cancer patients were enrolled in this study. The patients were divided into two main groups, each group includes 30 female cancer patient. One group was submitted to Screen Film Mammography using Philips mammography. The other group was submitted to Digital Mammography using General Electric Mammography. However, each group was divided into three sub-groups according to age. Patients were treated at the (Hospital El-Sheekh Zaeed), 6 October, El-Giza, Egypt. A written informed consent was obtained from each female's patient for performing either the screen film mammography or the soft-copy digital mammography. Excluded subjects excluded included incubated pregnant or breast feeding mothers. Female's patient presents with signs and symptoms of breast cancer or assessment of breast symptoms such as breast pain or nipple discharge. The Ethics Committee of the Medical Research Institute, Alexandria University; approved the study protocol and all experimental procedures are in accordance with the Helsinki Declaration of 1975, as revised in 1983.

2.2 Study Design

Each blood sample was centrifuged for 15 min. at 200 xg and plasma was collected for measuring tumor markers namely; CA 125 and CA15.3. Tumor markers were measured before the diagnosis procedure. These tumor markers (CA 125 and CA15.3)[172-176] were measured using ALCYON 3000 i analyzer, Abbott laboratories, USA/Canada. Spinreact kits (Ctra, Santa Coloma, Espana) were used in the measurement according to the method described by (Bergmeyer et al., 1978)[177].

Breast Imaging Questionnaire

Name……. Patient ID #…….. Birth Date…….
Please answer ALL the questions.

1. Mammograms and physical exams are both important in finding breast cancer. 10% of breast cancers are only by physical exam; 40% are found only by mammograms and; 50% are found by both exams.
2. Did you have a physical exam by your health practitioner ? When……..
3. Have you had a previous mammogram ? No……..Yes…….When?……..Where……

1. Do you have any significant breast problems ? Yes…….No…… If yes, mass…….lump……..pain……..nipple
2. discharge……. Which side ? Right……Left……..
4. Have you had breast surgery ? Yes……..Right…….Left……. No…….
5. What type of surgery was performed ? Mastectomy…….Biopsy……..
6. Did you have breast cancer ? Yes…….Side……When……. No……..
7. Have you had radiation therapy for breast cancer ? Yes……No……
8. Have you had non-breast cancer surgery ? Yes……..Where……When…….. What kind: needle biopsy, aspiration, surgical biopsy, breast augmentation by implant, breast reduction, Other……
9. Are you nursing a baby at present ? Yes…….No…….
10. Are you pregnant ? Yes……No……
11. Have you stopped having menstrual periods ? No…….If yes, when……..
12. Have you taken female hormone pills (like Premarin or birth control pills) in the last 10 years ? If yes, date started…….Still taking…….Stopped…….
13. Do you have relatives who have had breast cancer ? No…….. Yes……Who……Age at onset……

Today's date…….. Signature…….

2.3 Mammography Unit

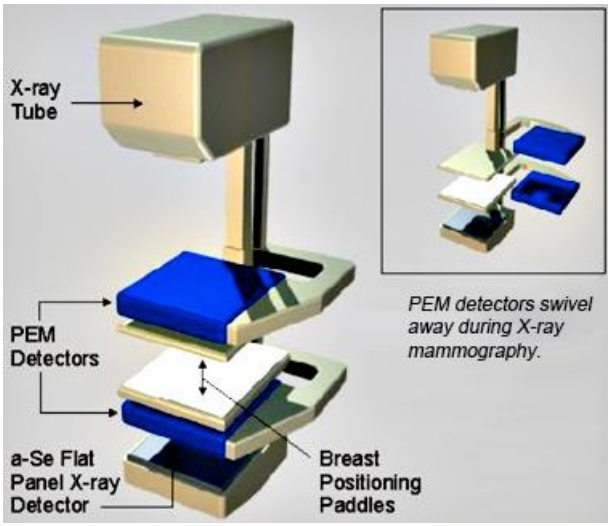


Figure (4-1): Schematic diagram for the mammography unit

Figure (4-2): Digital Mammography

A mammography unit, Fig.4 -1, is a rectangular box that houses the tube in which x-rays are produced. The unit is used exclusively for x-ray exams of the breast, with special accessories that allow only the breast to be exposed to the x-rays. Attached to the unit is a device that holds and compresses the breast and positions it so images can be obtained at different angles. Digital mammography, Fig. 4-2, is developmental stages consists of the following: X- Ray Tube * Mo & Re*, compression device, digital detector, plate reader, control room, computer unit and printer

The screen-film images were all acquired with one of Mammomat 300 systems (Siemens Medical Systems, Erlangen, Germany) with Min-R 2000 film and Min-R 2190 screens (Eastman Kodak, Rochester, NY) in standard and large formats. Molybdenum and 24 kV were always used. Full-field digital images were acquired with a Seno graphe 2000D system (GE Medical Systems, Milwaukee, Wis).The unit is equipped with an automatic mode (automatic optimization of parameters),in which anode-filter combination and kilovolts are selected automatically after analysis of a short pre exposure image .The automatic optimization of parameters was used according to the manufacturer's recommendations. The area of the image detector was 19 -23 cm. Mammograms of both imaging modalities included two standard views (craniocaudal and mediolateral oblique) of each breast.

2.4 Procedure of Digital Mammography

During the procedure, the breast is compressed by a dedicated digital mammography machine to even out the tissue, to increase image quality, and to hold the breast still (preventing motion blur). Both front and side images of the breast are taken. Until some years ago, digital mammography was typically performed with screen-film cassettes. Now, digital mammography is undergoing transition to digital detectors, known as Full Field Digital Mammography (FFDM). This progress is some years later than in general radiology. A digital mammography unit is a rectangular box that houses the tube in which x-rays are produced. The unit is used exclusively for x-ray exams of the breast, with special accessories that allow only the breast to be exposed to the x-rays. Attached to the unit is a device that holds and compresses the breast and positions it so images can be obtained at different angles. During digital mammography, a specially qualified radiological technologist will position your breast in the mammography unit. The breast will be placed on a special plat form and compressed with a paddle (often made of clear Plexiglas or other plastic). The technologist will gradually compress the breast. The patient will be asked to change positions between images. The routine views are a top-to-bottom view and an oblique side view. The process will be repeated for the other breast. The Screening digital Mammograms are two x-ray views for each breast, typically cranial-caudal view, (CC) and mediolateral-oblique (MLO) as shown below, Figs.3 -3 to3- 5.Accordingly a total of 240 mammogram was obtained throughout the work.

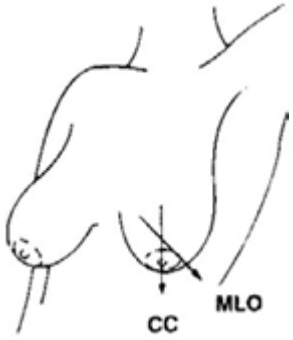


Figure (4-3): Schematic diagram describing the craniocuadal (CC) and mediolateral blique (MLO) views

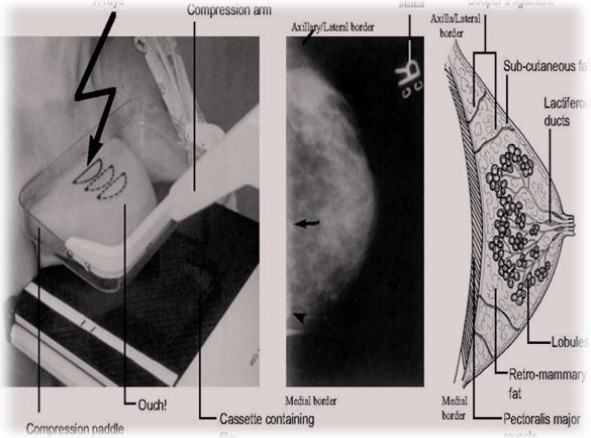


Figure (4-4): Crania-caudal (CC) view.

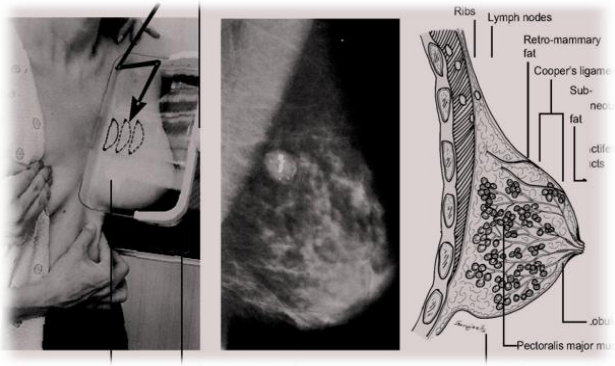


Figure (4- 5): Mediolateral oblique (MLO) view.

2.5 Mammography Processing

It is worth to mention that, the methods used to obtain mammograms, are either FSM or DFM. In screen film mammography, after completing mammography image recording, the film enclosed in the cassette is processed by chemical developers to obtain the hard copy. This method is known as the Conventional Method, Fig. 4- 6. The second method, which is also illustrated in Fig4-6, the image can be seen as a Digital Image by a digital camera, which is known as a Digital image, or the Direct Method. However, there is a method which is known as the Indirect Method. In this method, the image can be converted to visual image which can be printed as a copy, Fig. 4-6.This process was used to obtain both hard copy and soft copy mammograms using Philips instrumentation

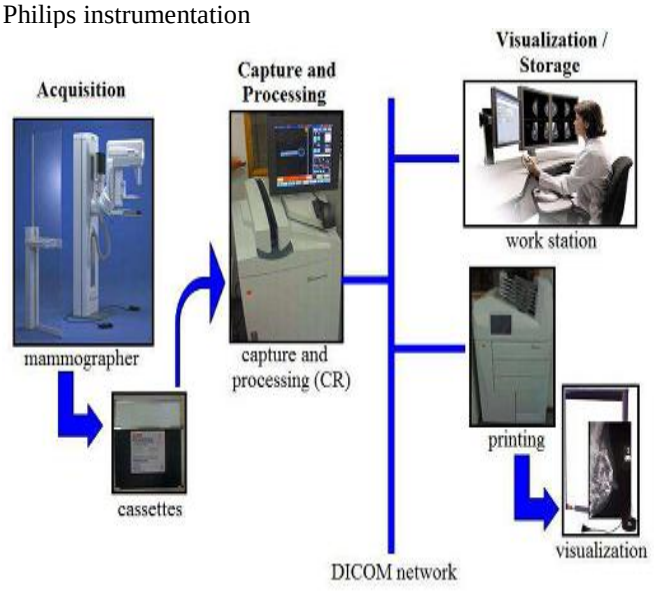
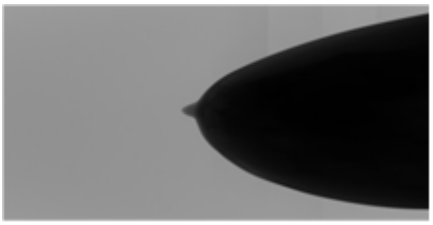


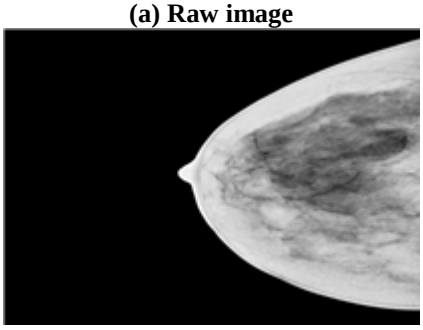
Figure (4-6): Mammography processing

2.6 Breast Calcifications on a Digital Mammogram

Evaluation of the calcification was done by site in the breast, shape (regular or irregular). The description was based on the different categories given by the BI-RADS.[179, 180] This abnormal mammogram is not necessarily cancerous. Also seen are calcifications through ductal patterns. The patient would have a follow-up mammogram in three months for a comparison. Micro calcifications are tiny bits of calcium that may show up in clusters or in patterns (like circles) and are associated with extra cell activity in breast tissue. Usually the extra cell growth is not cancerous, but sometimes tight clusters of micro calcifications can indicate early breast cancer. Scattered micro calcifications are usually a sign of benign breast tissue.



(a) Raw image



(b) Processed image

Figure (4-7): Images produced in digital mammography

2.7 Program Photo Shop 7

Program Photo shop 7 is a program that will be used to describe the obtained data. The method for the analysis of breast composition will be accomplished using transforms pixel values. Pixel uniformity is another important consideration that impacts the accuracy and integrity of the image, which can also influence the presence of noise. Each image will be divided into 512 x 512 pixels. Each pixel is roughly a square of side 0.5 mm with resolution (1 mm = 2 pixel). The binary number representing the image brightness or gray level of each pixel will be stored in a frame of 512 x 512 pixel memory location.

2.8 Validation Measures

Sensitivity and specificity are statistical measures of the performance of a binary classification test. Sensitivity (also called the true positive rate), measures the proportion of actual positives which are correctly identified as such (e.g. the percentage of sick people who are correctly identified as having the condition). Specificity measures the proportion of negatives which are correctly identified as such (e.g. the percentage of healthy people who are correctly identified as not having the condition, sometimes called the true negative rate).The test results for each subject may or may not match the subject's actual status. In that setting: True positive: Sick people correctly diagnosed as sick. False positive: Healthy people incorrectly identified as sick. True negative: Healthy people correctly identified as healthy. False negative: Sick people incorrectly identified as healthy. Sensitivity relates to the test's ability to identify positive results.
Sensitivity of a test is the proportion of people that are known to have the disease who test positive for it. This can also be written as:

$$\text{Sensitivity (\%)} = \frac{\text{No. of true positives}}{\text{No. of true positives} + \text{No. of false negatives}} \times 100$$

Specificity relates to the test's ability to identify negative results. This can also be written as:

$$\text{Specificity (\%)} = \frac{\text{No. of true negative}}{\text{true negatives} + \text{No. of false positives}} \times 100$$

$$\text{Positive predictive value (PPV, \%)} = \frac{\text{No. of true positives}}{\text{No. of true positives} + \text{No. of false positives}} \times 100$$

$$\text{Negative predictive value (NPV, \%)} = \frac{\text{No. of true negatives}}{\text{No. of true negatives} + \text{No. of false negatives}} \times 100$$

A sensitivity of 100% means that the test recognizes all actual positives – i.e. all sick people are recognized as being ill. Thus, in contrast to a high specificity test, negative results in a high sensitivity test are used to rule out the disease. [178]

2.9 Statistical Analysis

Continuous variables were recorded as mean ± SD; ANOVA-f test, followed by Tukey's test, was used to evaluate the significance of difference ($P < 0.05$) among group. The local ethic committee approved this study .Informed consent was obtained from each patient included in this study .Data were expressed as mean ± standard error (S.E). Data analysis was made by Fisher's exact and Pearson's correlation tests. Using SPSS for Widows (Chicago, II, USA) when appropriate $p < 0.05$ was considered statistically significant.. Histogram analysis combines techniques that compute statistics and measurements based on the gray-level intensities of the image pixel. The Student's t – test, and other statistical analysis were performed using statistical SPSS -12 program. The t-test assesses whether the means of two groups are statistically different from each other

3. Results

A total of 60 female breast cancer patients were enrolled in this study. The patients were divided into two main groups; each group includes 30 female cancer patient. One group was submitted to Screen Film Mammography using Philips mammography. The other group was submitted to Digital Mammography using General Electric Mammography. However, each group was divided into three sub-groups according to age. Table 5-1, describes the frequency and age range of each sub-group, and mean age ± SD, for both (SFM) And (DM). It is clear from these two tables the close of ages of the two patient groups enrolled in this work.

Table (5-1): Patients Age Ranges Enrolled in this Work

Digital Film Mammography		*Screen Film Mammography*		*Age range*
S.E.	Mean	S.E.	Mean	
0.8	39.2	0.7	38.1	(30-40) years
1.19	48.6	1.1	47.2	(41-51) years
1.08	59.3	1.6	56.9	(52-62) years

Tumor Markers Results:

Tumor markers namely; CA 125, and CA 15-3 were analyzed using the blood serum of each patient. Table 5-2 and Table 5-3, illustrate the levels of the two cancer bio-markers for the different sub-groups for patients.

Table (5-2): The Mean CA 125 And CA 15.3 Levels ± S.D. (IU/L) of Females Breast Cancer Patients Submitted To DM.

Cancer bio-markers activity		FEMALES BREAST CANCER GROUP (Age Range)
CA 125 Normal Range Up to 37 IU/L (mean± S.D)	CA 15-3 Normal Range Up to 39 IU/L (mean± S.D)	
62 ± 2.8	50 ± 1.8	(30-40) years
69 ± 1.77	49 ± 1.6	(41-51) years
61.5 ± 1.70	54 ± 1.77	(52-62) years

Fig.5 -1, and Fig. 5-2, illustrate hard copy (FSM) images recorded by Philips mammography. While Fig. 5-3, illustrates digital mammogram images recorded by General Electric mammography.

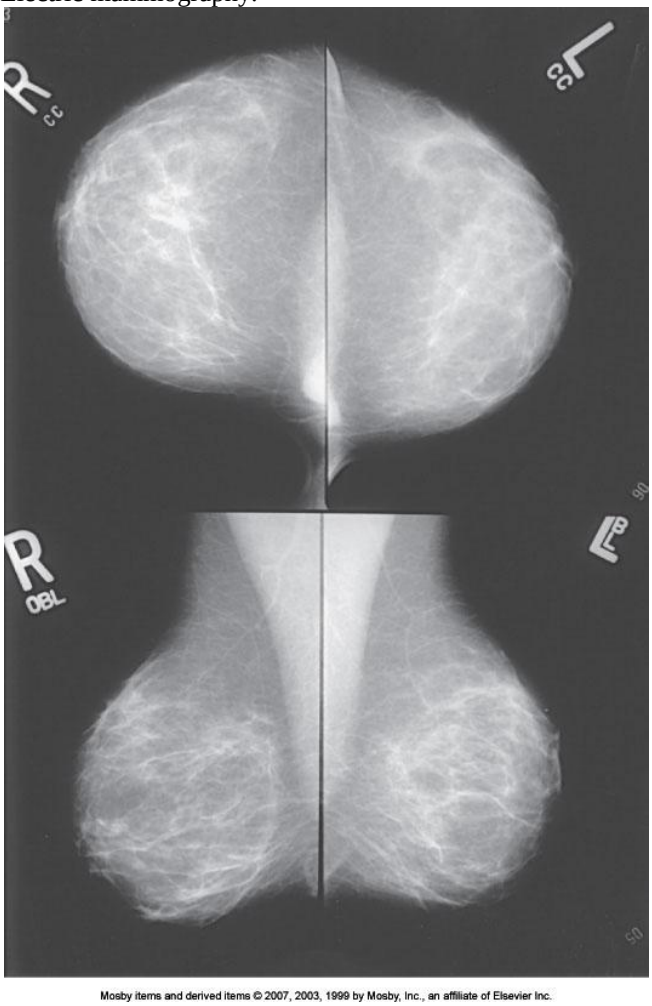


Figure (5-1): Hard copy images

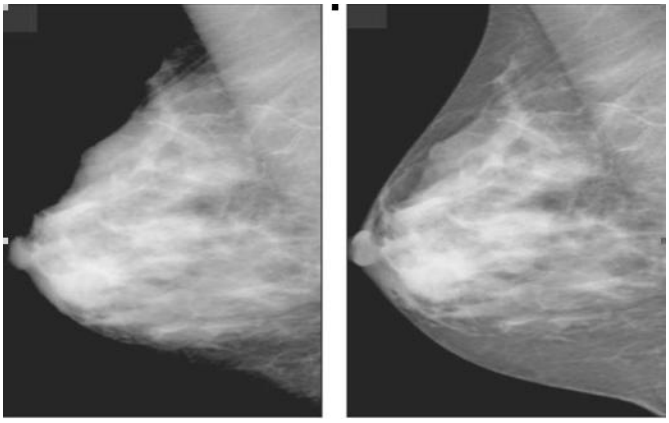


Figure (5-2): Hard copy images (Philips mammography system) (A)Crania-caudal (CC) and (B) Mediolateral oblique (MLO) Fig. (5-3), Represents mammographic images using digital mammography.

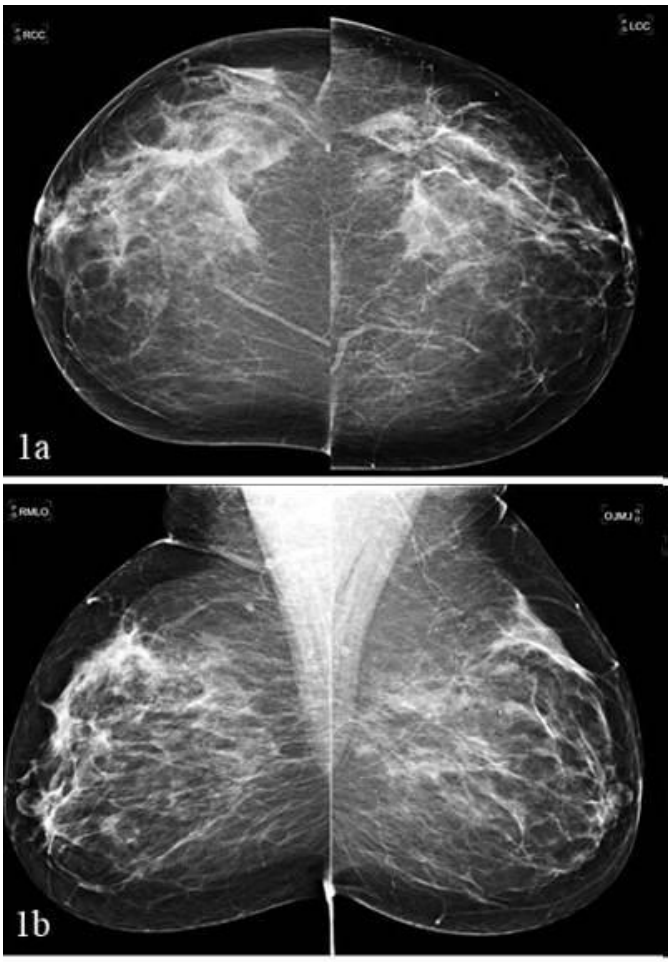


Fig. (5-3): Digital film images. (A):Cranio-caudal (CC) and (B): Mediolateral oblique (MLO)

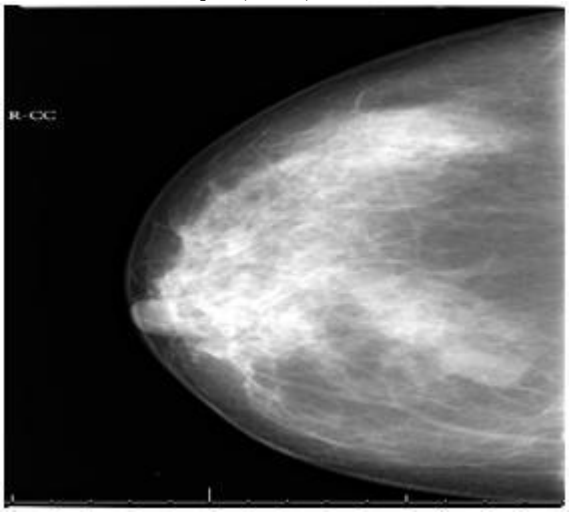


Figure (5-4): Normal breast mammograms by Philips

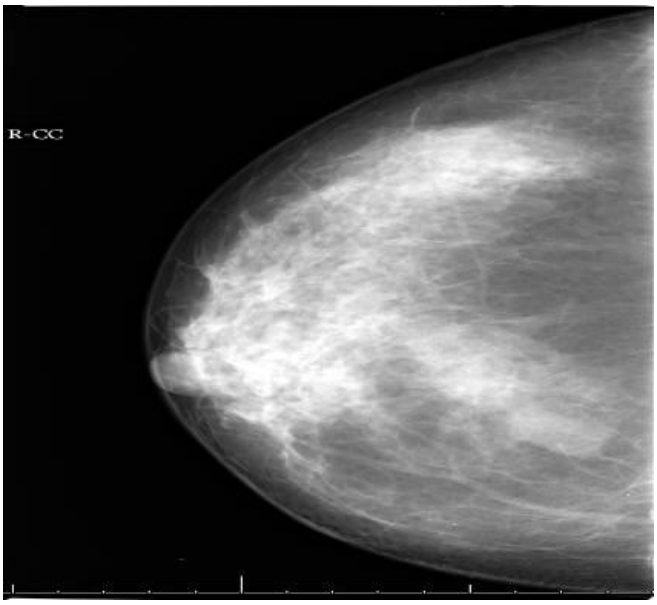
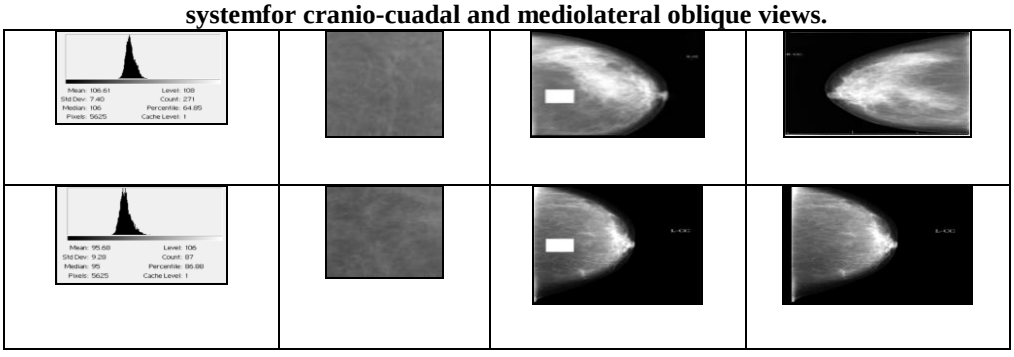


Figure (5-5): Abnormal breast mammograms by Philips

Figs. 5-6 to 5-9, represent mammograms for normal and abnormal breast tissues, recorded by Philips mammography systemfor cranio-cuadal and mediolateral oblique views.



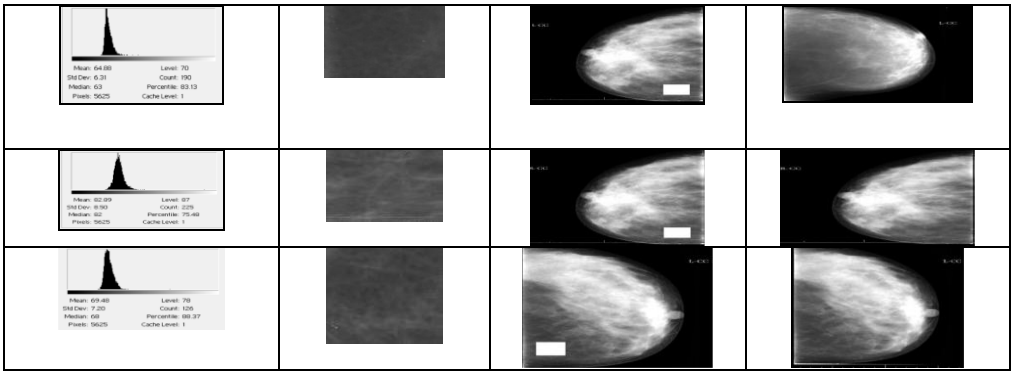


Figure (5-6): Five mammograms for normal breast tissues, recorded by Philips for the cranio-cuadal view.

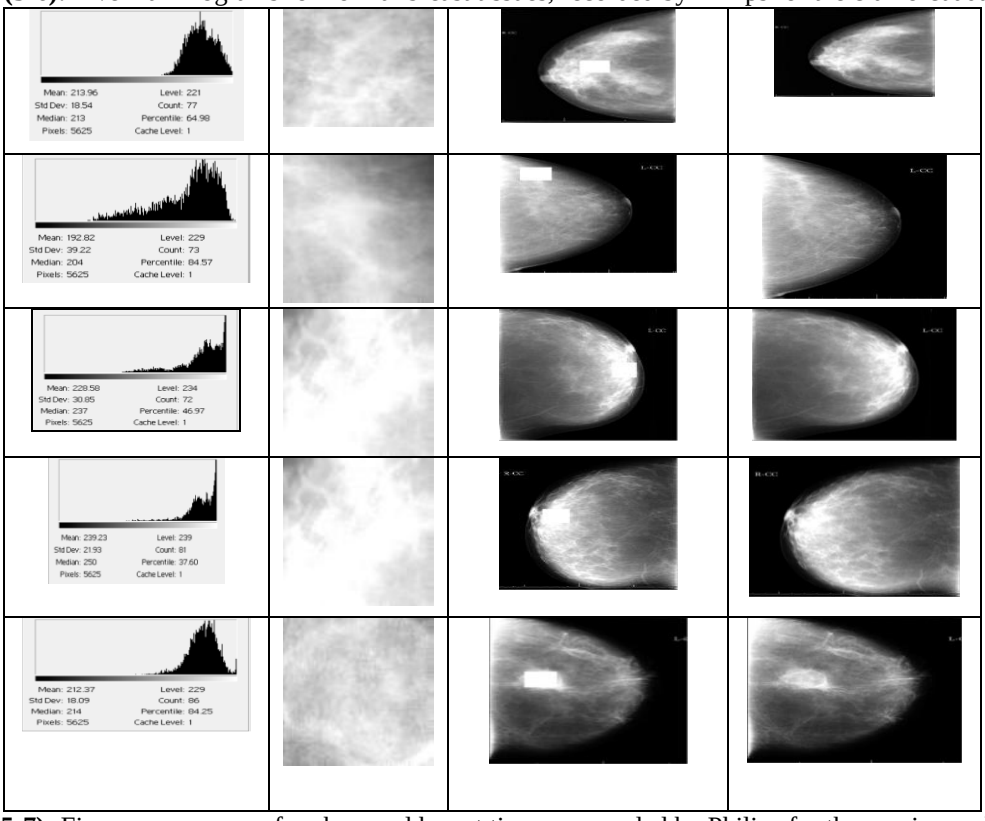


Figure (5-7): Five mammograms for abnormal breast tissues, recorded by Philips for the cranio-cuadal view.

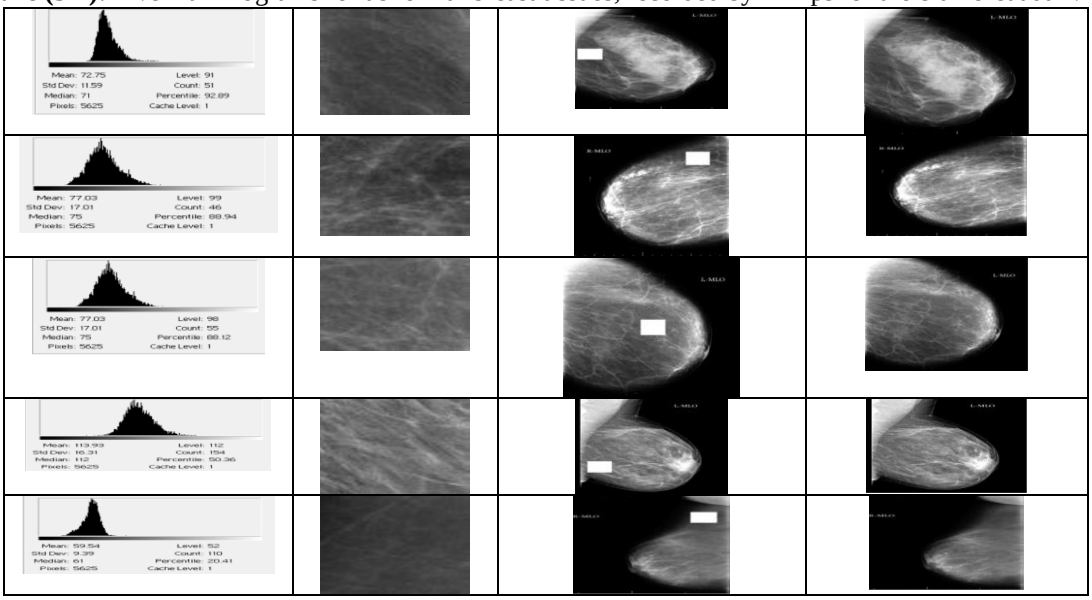


Figure (5-8): Five mammograms for normal breast tissues, recorded by Philips for the mediolateral oblique view.

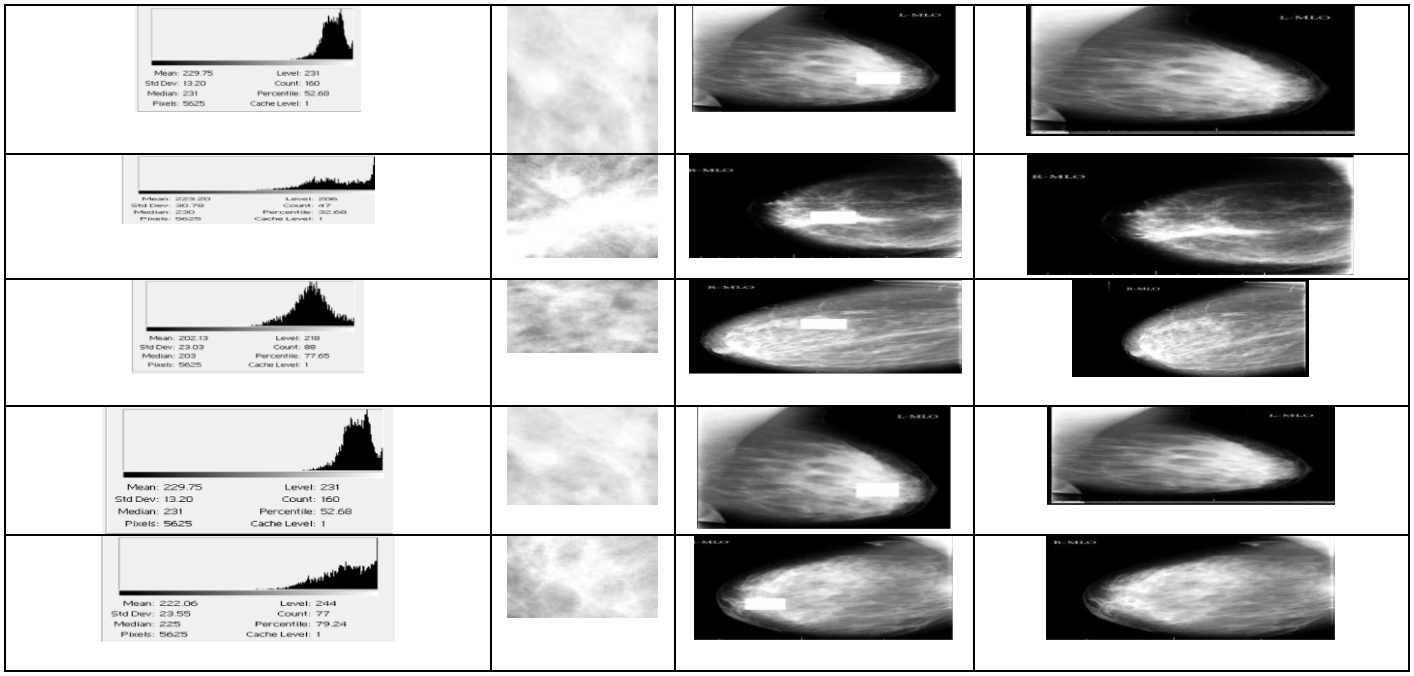


Figure (5-9): Five mammograms for abnormal breast tissues, recorded by Philips for the mediolateral oblique view

Figure (5-10 to 5-13): Represent mammograms for normal and abnormal breast tissues, recorded by General Electric system for cranio-cuadal and mediolateral oblique views.

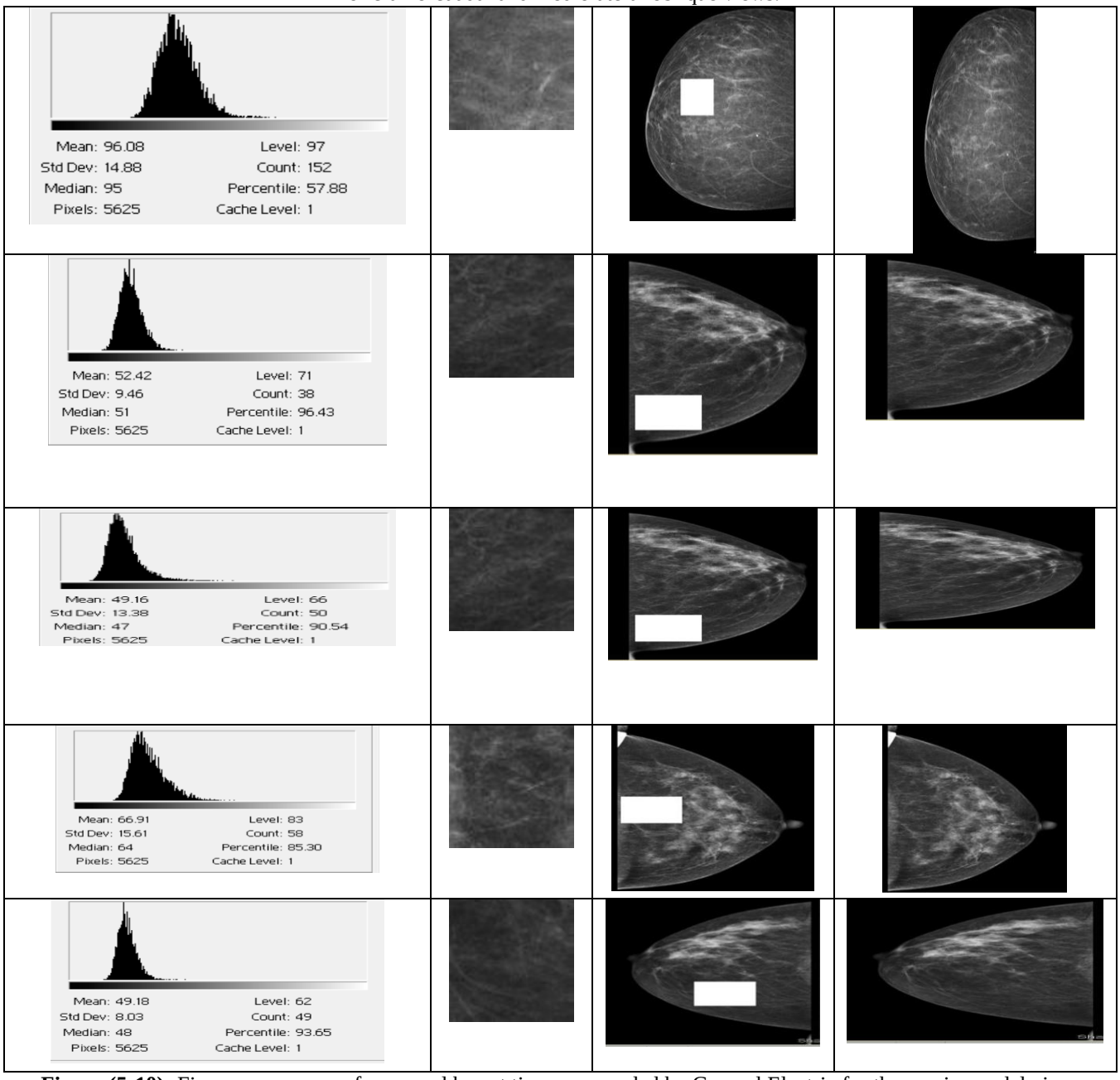
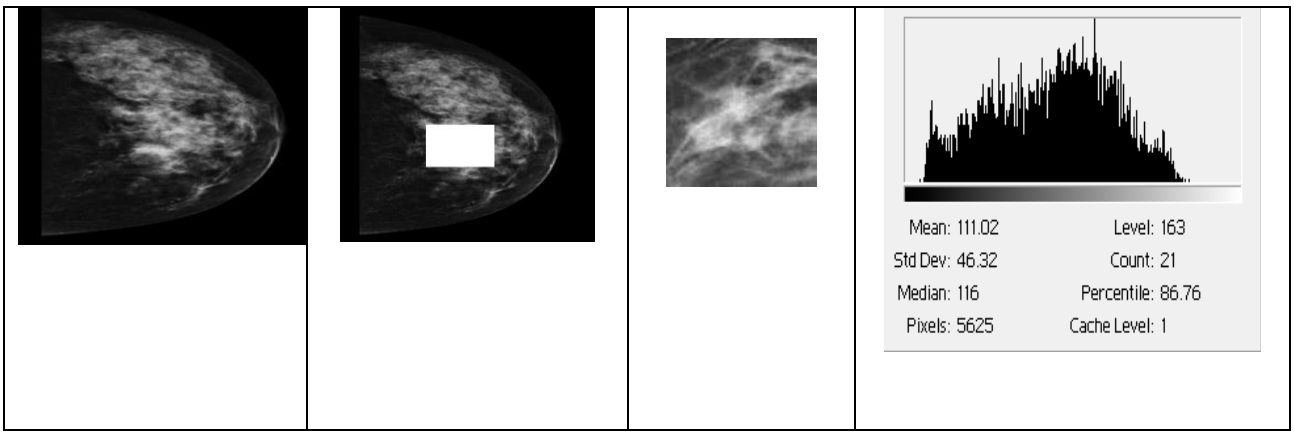


Figure (5-10): Five mammograms for normal breast tissues, recorded by General Electric for the cranio-cuadal view.



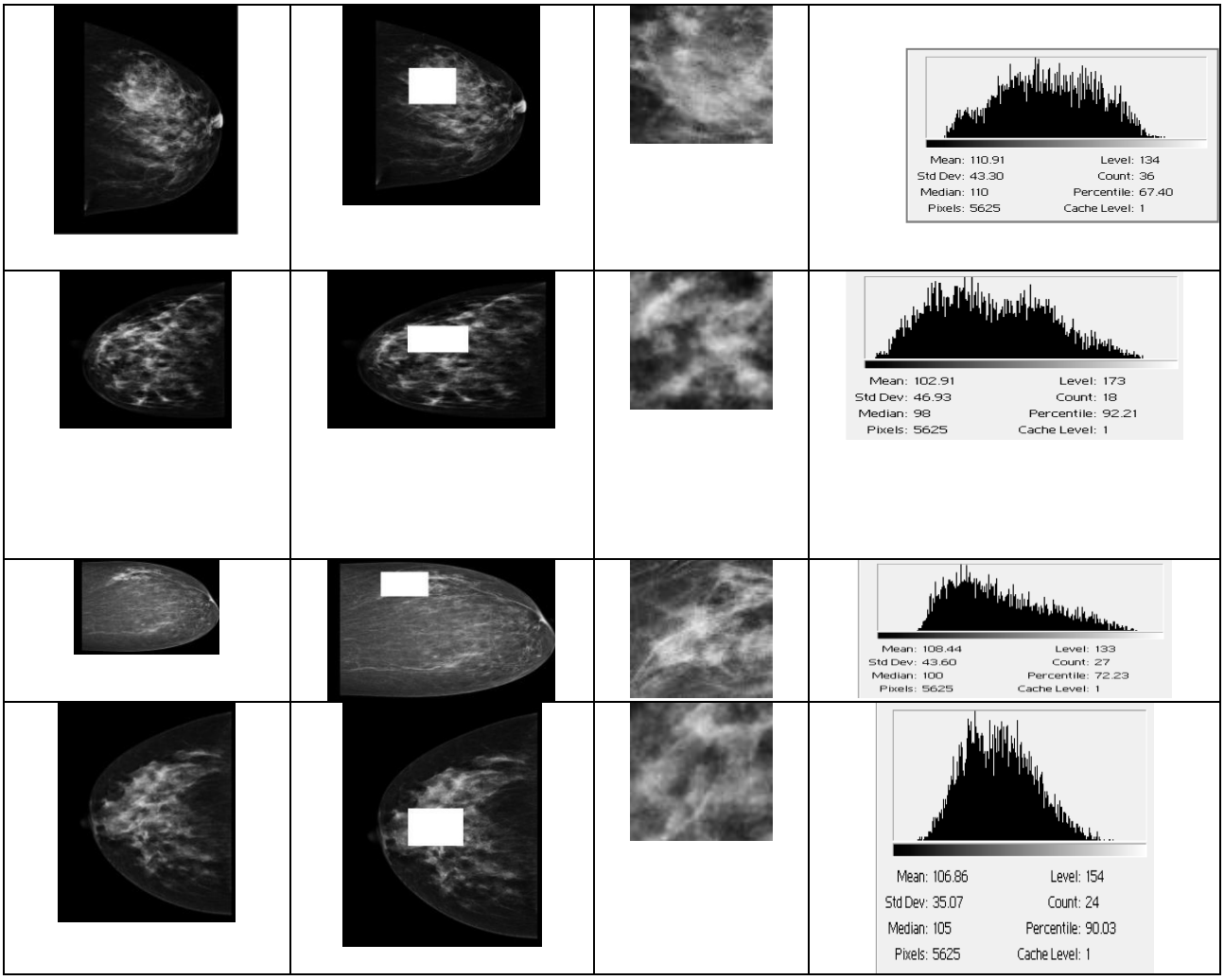
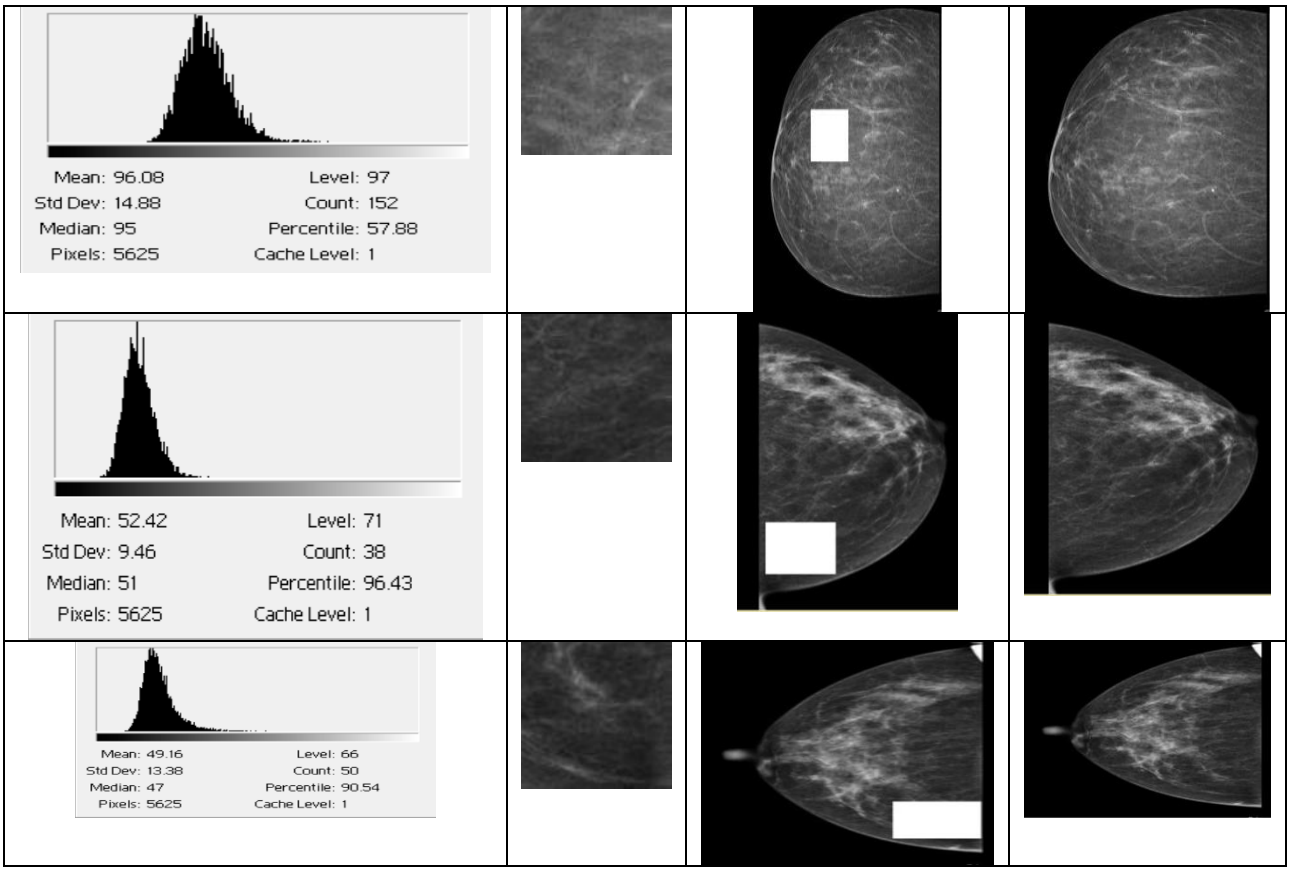


Figure (5-11): Five mammograms for abnormal breast tissues, recorded by General Electric for the cranio-cuadal view.



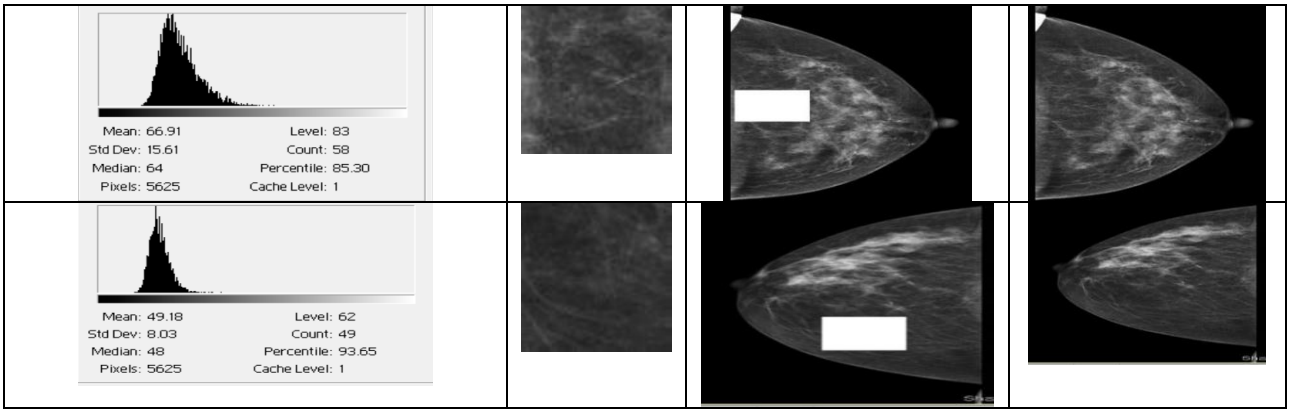


Figure (5-12): Five mammograms for normal breast tissues, recorded by General Electricfor the mediolateral oblique view.

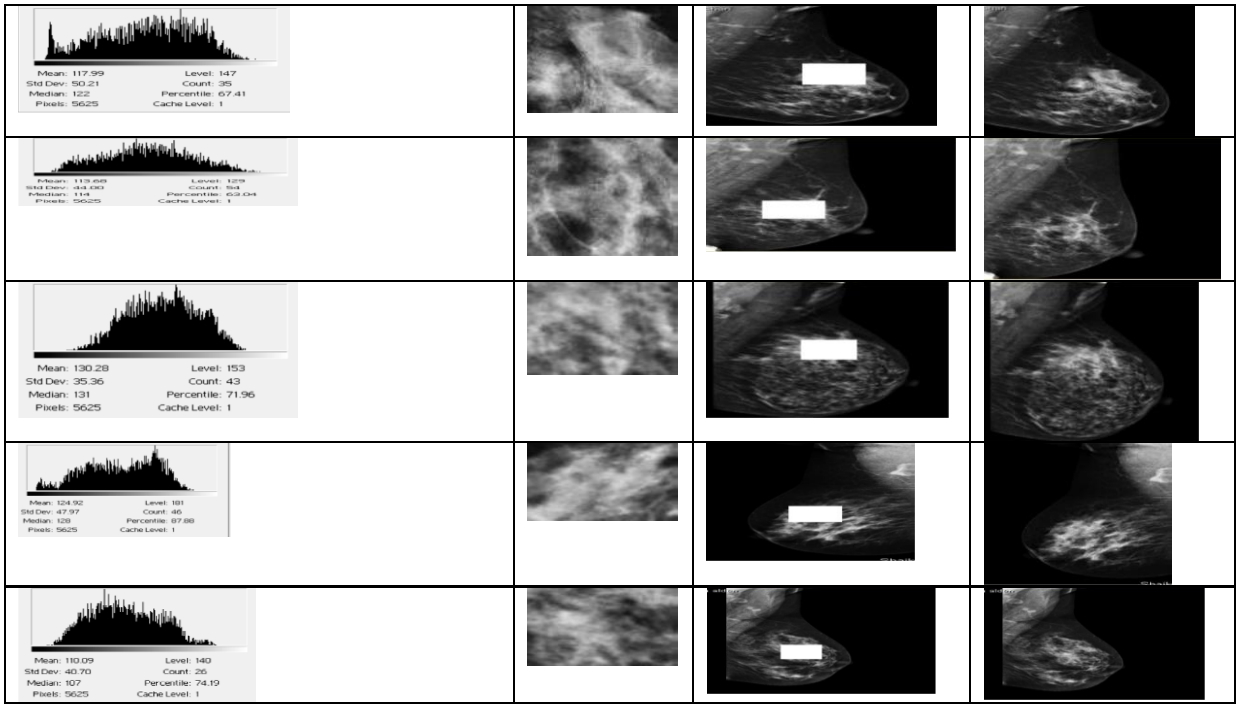


Figure (5-13): Five mammograms for abnormal breast tissues, recorded by General Electricfor the mediolateral oblique view.

Tables 5-8 to 5-11, illustrate the statistical data obtained for the Philips and General Electric mammography systems performed on the histograms data .

Table (5-8): Comparison between the normal and abnormal recorded histograms grey levels for cranio-caudal (CC) views using Philips (Ph) mammography.

P (Value)	*Abnormal*	*Normal*	*CC -[Philips]*
			Mean
<0.001*	118.05 – 247.89	27.54 – 114.70	Min. – Max.
	218.45 ± 25.52	74.12+ ± 24.80	Mean ± SD
	226.91	76.44	Median
			SD
0.001*	8.44 – 47.95	6.31 – 39.18	Min. – Max.
	23.09 ± 8.91	14.77 ± 9.12	Mean ± SD
	22.04	10.37	Median
			Median
<0.001*	120.0 – 252.0	11.0 – 114.0	Min. – Max.
	221.90 ± 26.38	72.43 ± 27.31	Mean ± SD
	228.50	75.50	Median
			COV
0.003*	0.04 – 0.26	0.07 – 0.87	Min. – Max.
	0.11 ± 0.05	0.26 ± 0.24	Mean ± SD
	0.10	0.13	Median

p: p value for Student t-test for comparing between the two studied group
*: Statistically significant at $p \leq 0.05$.

Table (5-9): Comparison between the normal and abnormal recorded histograms grey levels for medio-lateral (MLO) oblique views using Philips (Ph) mammography.

P-(Value)	*Abnormal*	*Normal*	*MLO [Philips]*
			Mean
<0.001*	128.35 – 235.89	20.36 – 113.93	Min. – Max.
	178.76 ± 30.63	65.56 ± 24.03	Mean ± SD
	175.88	63.20	Median
			SD
<0.001*	13.20 – 44.44	7.09 – 29.19	Min. – Max.
	24.43 ± 6.89	15.68 ± 5.39	Mean ± SD
	25.03	16.09	Median
			Median
<0.001*	126.0 – 251.0	20.0 – 112.0	Min. – Max.
	184.50 ± 34.73	64.70 ± 24.24	Mean ± SD
	184.50	63.0	Median
<0.001*			**COV**

	0.06 – 0.22	0.13 – 0.57	Min. – Max.
	0.14 ± 0.04	0.27 ± 0.12	Mean ± SD
	0.14	0.23	Median

p: p value for Student t-test for comparing between the two studied group
*: Statistically significant at $p \leq 0.05$

Table (5-10): Comparison Between the Normal and Abnormal Recorded Histograms Grey Levels for Cranio-Caudal (CC) Views Using General Electric(GE) Mammography

P-(Value)	*Abnormal*	*Normal*	*CC-GE*
			Mean
<0.001*	84.03 – 154.84	13.51 – 96.76	Min. – Max.
	103.69 ± 12.44	50.33 ± 26.71	Mean ± SD
	103.42	49.17	Median
			SD
<0.001*	24.09 – 54.73	6.0 – 18.95	Min. – Max.
	37.10 ± 7.06	12.06 ± 3.47	Mean ± SD
	37.10	11.85	Median
			Median
<0.001*	78.0 – 160.0	11.0 – 95.0	Min. – Max.
	100.63 ± 14.64	47.67 ± 26.87	Mean ± SD
	100.0	47.0	Median
			COV
0.064	0.23- 0.52	0.12 – 0.66	Min. – Max.
	0.36 ± 0.07	0.30 ± 0.15	Mean ± SD
	0.36	0.27	Median

p: p value for Student t-test for comparing between the two studied group
*: Statistically significant at $p \leq 0.05$

Table (5-11): Comparison between the normal and abnormal recorded histograms grey levels for medio-lateral (MLO) views using General Electric (GE) mammography.

P-(Value)	*Abnormal*	*Normal*	*MLO-GE*
			Mean
<0.001*	75.25 – 236.37	11.91 – 84.39	Min. – Max.
	113.38 ± 36.51	36.48 ± 17.98	Mean ± SD
	99.29	32.22	Median
			SD
<0.001*	17.06 – 71.71	4.57 – 23.08	Min. – Max.
	44.45 ± 10.52	10.95 ± 4.27	Mean ± SD
	44.66	10.93	Median
			Median
<0.001*	66.0 – 240.0	11.0 – 83.0	Min. – Max.
	113.20 ± 44.85	34.53 ± 18.19	Mean ± SD
	96.50	30.0	Median
			COV
0.001*	0.07 – 0.60	0.15 – 0.57	Min. – Max.
	0.42 ± 0.10	0.33 ± 0.10	Mean ± SD
	0.42	0.32	Median

p: p value for Student t-test for comparing between the two studied group
*: Statistically significant at $p \leq 0.05$

Figures 5-14 to 5-17, illustrate graphical representations of Philips and General Electric histograms statistical data.

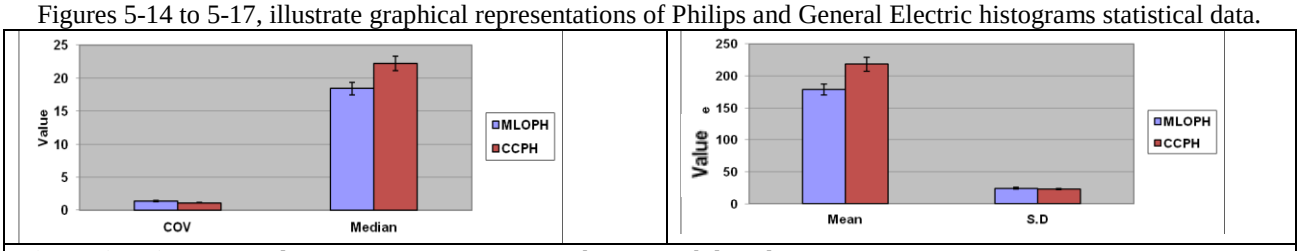


Figure (5-14): Statistical comparison representation between Philips data.

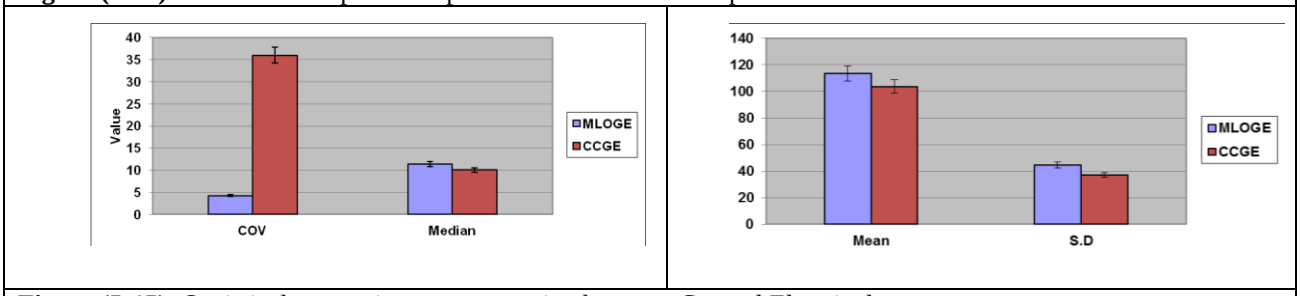


Figure (5-15): Statistical comparison representation between General Electric data.

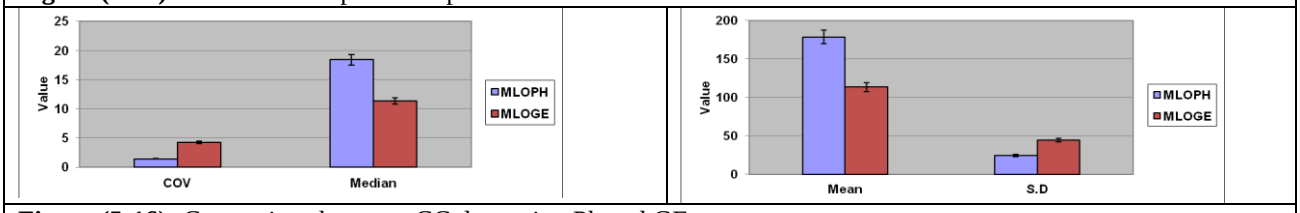


Figure (5-16): Comparison between CC data using Ph and GE.

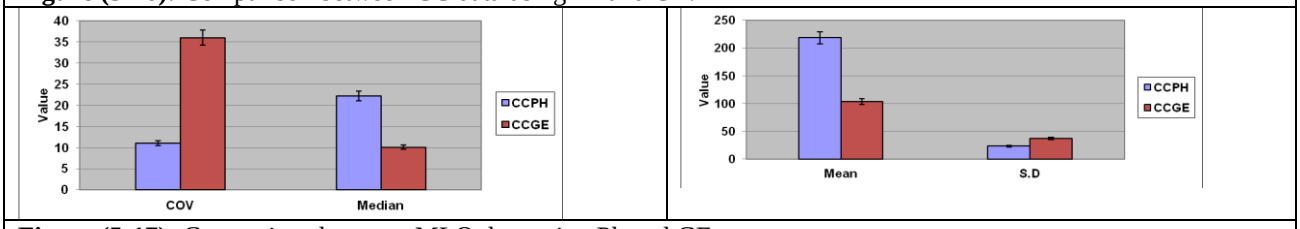


Figure (5-17): Comparison between MLO data using Ph and GE.

Sensitivity and Specificity:
A total of 240 image views were considered to calculate the sensitivity and specificity of the two mammographic systems used. These views were divided equally between the two systems, i.e., 120 view each. The following relations were used to calculate the *sensitivity* and *specificity* :

Table (5-12): Presents a summary of these studies, along with their sensitivities and specificities for General Electric and Philips Mammography

Negative predictive value (NPV, %)	Positive predictive value (PPV, %)	Specificity (%)	Sensitivity (%)	Non Responders		Responders		
				True negative	True positive	True negative	True positive	
44.1%	90%	65%	80%	19	8	15	78	PH
44.4%	93.3%	80%	73%	25	5	20	70	GE

4. Discussion

Mammography is the process of using low-energy-X-rays (usually around 30 kVp) to examine the human *breast* and is used as a diagnostic and a screening tool. The goal of mammography is the early detection of *breast cancer*, typically through detection of characteristic masses and/or *micro calcifications.* Mammography plays a major role in early detection of breast cancers, detecting about 75% of cancers at least a year before they can be felt. So, most doctors believe that mammography reduces deaths from *breast cancer*, although a minority do not.In many countries routine mammography of older women is encouraged as a screening method to diagnose early breast cancer. In 2009, the U.S. Preventive Services Task Force (USPSTF) recommended that women with no risk factors have screening mammography's every 2 years between age 50 and 74. They found that the information was insufficient to recommend for or against screening between age 40 and 49 or above age 74.[(181)] Altogether clinical trials have found a relative reduction in breast cancer mortality of 20%.[(182)] Some doctors believe that mammography do not reduce deaths from breast cancer, or at least that the evidence does not demonstrate it.[(183)].In the present work, a total of 60 female breast cancer patients were enrolled in the study. The patients were divided into two main groups, each group contains 30 female cancer patient. One group was submitted to Screen Film Mammography (SFM) using Philips mammography. The other group was submitted to Digital Mammography using General Electric Mammography (DFM). However, each group was divided into three sub-groups according to age.

According to Table (5- 1), no significant differences are exist between the ages of the two main groups or between their sub-groups. Before the diagnosis procedure, two important biomarkers , namely; CA 125 , and CA 15-3 were clinically estimated in the fresh blood serum of each patient.CA-125 is a cancer antigen 125 or carbohydrate antigen 125[(184)] that has found application as a tumor marker or biomarker that may be elevated in the blood of some patients with specific types of cancers, or other benign conditions.[(185)] CA 15-3 is a tumor marker that is elevated in the serum/plasma of approximately 75% of women with metastasized breast cancer. CA 15-3 levels can also be raised due to the presence of other conditions or cancers (for example, colorectal cancer, hepatitis, and benign breast disease) [(186,187)].Physicians use the CA 125 and/or CA 15-3 test results in conjunction with other diagnostic test results and full medical history to make decisions about the management of their patients. A physician typically requests a CA 125 or CA 15-3 or both tests prior to the patient receiving treatments. This result serves as a baseline to compare with future measurements. During therapy, serial CA 125 and CA 15-3 results may be used to monitor response to therapy. Increasing results may be indicative of progressive disease, decreasing results may be indicative of response to therapy and constant results may be associated with stable disease status.

The clinical normal activity of these biomarkers are : 39 IU/L for CA 125 , and 37 IU/L for CA 15-3. It is clear from Table (5-2) that all patients enrolled in the work exhibit significant higher activity levels of the two markers with respect to the normal clinical level. Also, no significant differences exist between the levels of the two tumor biomarkers in the different sub-groups. These results indicate the presence of breast cancer, but can't be used as a single confidence indication of the breast cancer because these biomarkers can't define the site of the tumor or its volume or other features of the tumor. Cancer marker tests are immunological methods, that are produced as cancer grows and are detectable even before it reaches a size big enough for detection by other methods. This early detection system is vital for early medical intervention that significantly improves the chances of recovery. It must be mentioned that, CA 125 and CA 15-3 have become widely tumor markers which are measured most often in women with cancers of the reproductive system including the uterus, fallopian tubes and ovaries. Other cancers that may cause abnormal CA 125 and CA 15-3 levels include cancer of the pancreas, lungs, breast and colon. Also, these biomarkers can be elevated during menstruation, pregnancy or in individuals with ovarian cysts, hepatitis, cirrhosis of the liver and even in 1-2% of healthy individuals. In comparing digital mammography to screen-film mammography two modality of mammography were employed in this work. The Philips (Ph) and General Electric (GE) mammography. The Philips mammography was used to obtain hard copy mammograms for 30 patient, and General Electric was used to obtain Digital Mammograms for 30 female patients. The conventional mammography as described and illustrated in Figs 5-1, 5-2, and 5-5 either for CC or MLO uses film ,i.e., hard copy. It is clear, as an example, that hard copy mammograms can't give clear views of the breast, i.e., the skin border of the breast which is not the case of digital mammography, as illustrated in Fig.5-3. Also, conventional mammography faces the problem of bad processing, pressure during storage, and archiving. Moreover, during

each examination, only four images are obtained, i.e., CC and MLO for each breast and they cannot be evaluated by more than one specialist at the same time in different places. In addition, image quality in copies is rather poor. Frequently, the images are scanned and digitized. However, the digitized images do not provide any new information and images wrongly taken cannot be enhanced.[188] On the other hand, full-field digital mammography, briefly digital mammography, uses an electronic detector and overcomes all the disadvantages of the conventional systems. Moreover, digital images do not need to be developed as film, they are directly available and can be seen on a monitor seconds after the take. This allows not only being able to examine more women during the day, but also reduces the stress that the patient experiences while waiting for the results.[188] .In general, conventional mammography has limited contrast, while digital mammography has a high contrast. Though the human eye perception capabilities for contrast may not profit from this, computer-aided diagnosis does. Computer-aided diagnosis is possible since the existence of digital images. Different programs can access the images and perform semi or full-automated evaluations. Image parts can be depicted where suspicious tissue is highlighted, that the physician may have not discovered from just looking to the image.

Digital mammography allows having multiple copies of an image without loose of quality. Moreover, many specialists may evaluate the image at the same time in different places. Contrast and brightness of digital mammograms can be modified on a computer.[188] .In conventional mammography, some difficulties face the radiologist to give good decision about the existence of tumors or not, calcifications or micro calcifications in the mammogram image. Film development and fixation, i.e., film processing,[189] play important factors that may affect the film quality. These difficulties result in either repeating mammography to obtain more clear mammograms or performing other tests, e.g., ultrasonography, magnetic resonance imaging or taking sample biopsy. In addition, the presence of artifacts and the method of film storage , also, affect the film quality. So, the final decision of the radiologist depends, in many cases, on its practice and experience. The use of other tests such as ultrasonography, MRI may reveal the existence of masses in the breast not more. Also, the need for sample biopsy carries the possibility of spreading the cancer or tumor cells to other healthy cells during this process.

Like all x-rays, mammograms use doses of ionizing radiation to create images. However, mammography uses low dose x-rays, achieved by using targets made of low atomic weight alloys (eg, molybdenum and rhodium). Filters made of aluminum, molybdenum, beryllium, rhodium, or palladium are used. It uses high-contrast, high-resolution (with single-sided emulsion) film to demonstrate micro calcifications smaller than 100 µm. Radiologists then analyze the image for any abnormal findings. It is normal to use lower energy X-rays (typically Mo-K) than those used for radiography of bones.
In this work, and using the instructions given by the Philips and General Electric manufactures, the average mean glandular dose were 1.84 ± 01.11 mGy and 1.67 ± 01.21 mGy for the two instruments, respectively. The difference is statistically highly significant ($p < 0.05$). This means that, the x-ray radiation dose received by the patient using General Electric is much lower than that of the Philips. However, both the mean doses are well below the acceptable glandular dose limit of 3.0 mGy. It must be mentioned that, in screen-film imaging, reducing dose can result in lower image quality scores depending on the sensitometer properties of the film, which is the reason of lowering radiation dose in digital mammography than that in screen-film mammography.

Also, in case of repeating the mammogram, which actually occurs with screen-film mammography, the patient may be exposed to unnecessary x- ray radiation dose. Although x-radiation doses in mammography is much less than radiation dose received by a passenger in a local plan journey, some opinions predict developing breast cancer even with small radiation doses. So, it can be said that, although mammograms require very small doses of radiation, and the risk of harm from this radiation exposure is extremely low, but repeated x-rays have the potential to cause cancer.[189] This is true because there is a direct proportionality between cancer development and the radiation dose. This is the case of conventional mammography, but with the digital mammography the radiation dose used is lower than that of the screen-film mammography, the risk factor of developing cancer is much more less. This is also adds to the advantages of the digital mammography. Digital mammography, in general, has an advantage over screen-film mammography because higher contrast resolution is available with the ability to adjust the contrast of the mammograms through use of image processing.[184] However, Screen-Film Mammography has higher spatial resolution than digital mammography, and more detailed image features may be obvious. Several studies show that despite the limiting lower spatial resolution, visibility of calcifications on digital mammography is not significantly different from that on screen-film mammography.[185] A previous study reported that although screen-film mammography did recall a larger number of cases containing calcifications, the number of cancers manifesting as micro calcifications was the same with both techniques.[186] A higher percentage of digital mammography-only calcification findings were positive at biopsy suggesting that the soft-copy capabilities of digital mammography might allow image manipulations that provide improved visibility of lesion features and give the radiologist more information due to image quality, detail visibility, image exposure, and reduced or elimination of artifacts.[188]

In spite of the advantages of the digital mammography over the conventional mammography, digital mammography image analysis usually requires a network environment involving multiple computers that communicate with each other. Typically, the images are transferred to a medical archive. In a modern hospital, a so-called “Picture Archiving and Communication System” connects all the digital imaging modalities via a communication network. The images are stored in the standard format DICOM in a central archive from where they can be retrieved for display and analysis on any suitable workstation. DICOM stands for

"Digital Imaging and Communications in Medicine" and it was developed by the American College of Radiology (ACR) and companies that manufacture medical equipment, members of the National Electrical Manufacturers Association.[190,191] DICOM appeared as response to the need of a standard method for transferring images and related information between devices from different companies. be exchanged using these protocols;- As a matter of fact, the main purposes of using the DICOM are: To support communication of digital image information, independently from device manufacturer; To ease the expansion and development of PACS (Picture Archiving and Communication Systems) being able of interfacing with other hospital information systems; To allow the creation of diagnostic information databases that could be accessed by a variety of geographically distributed devices.

By this way, the DICOM standard indicates: A set of protocols for network communications; The syntax and semantics of commands and related information that can set of media storage services for media communication; A file format and a medical directory structure to ease access to the images and associated information stored on interchange media; Information that must be provided with an implementation for which conformance to the standard is stated. So, it can be said that, the digital mammography and its possible facilities, either in hand or in the near future, represent a solid step towards improving the methods that help the radiologist singly or with co-operation with other radiologists to minimize greatly the error of giving wrong decision about a critical and life shorting disease like breast cancer. It is of value to mention that, quantitative analysis on the obtained mammograms may allow improvement of the overall diagnostic performances compared with visual analysis to characterize breast cancer and normal breast. Accordingly, the present study develops a method for assessing quantitative analysis of the micro calcifications appear in the mammograms through the statistical analysis of the ROC . The analysis employs quantitative analysis of the grey levels of the histogram. Intensity using photo shop program. Also, the hard copy mammograms recorded by Philips were converted into digital mammography to be able to compare between the histograms of the two groups of mammograms recorded by Philips and general electric techniques.

All the data obtained by either Philips or general electric, e.g., the mean gray level, the standard deviation of the mean, the median and the coefficient of variation were significantly different from the control group. This means that the sensitivity of the histogram method used is very indicative and can be used to differentiate between the presence of normal and abnormal tissues in the breast of the examined cases. The distribution in the grey levels in the histograms of the control regions of interest takes , in general, the shape of sharp and narrow peaks. This is a good indication that the control tissue is homogeneous. In addition, the location of the peaks is nearly in the middle of the histogram image, for either the CC or MLO views recorded by Philips. The histograms of the regions of interest of the suspected tumor tissues take the form of wide peak or more than one peak which indicate that the non-homogeneity of the tumor tissue. In addition, the peaks in this case are margined toward the right of the histogram image. These two differences in the shape and location of the peaks can be used as a method of differentiation between the tumor and control breast tissues.

The case of General Electric recording, the situation is nearly similar, i.e., the peaks of the control breast tissue are sharp and locate in the middle of the histogram images. In addition, the peaks of the tumor breast tissues are margined toward the left of the histogram images. These two differences, i.e., these two differences in the shape and location of the peaks can be used as a method of differentiation between the tumor and control breast tissues using the General Electric technique.

In comparing between the Philips and General Electric techniques, it is clear from either the descriptive statistics or the raw data obtained for the histogram grey levels of either the control or the tumor tissues of the regions of interest that, the mean grey levels values are much higher in case of the Philips than that with the General Electric technique. In our opinion, this is mainly due to conversion process of the hard copy images, of Philips, to digital mammography which results in less or reduction in the grey level in addition to some other factors that may affect the quality of the hard-copy images, as mentioned before, such as less contrast and the film quality. For more benefits of the present method, ANOVA one way statistics were applied on the obtained data using SPSS –version 11.5. The results enabled us to obtain good correlation between the normal and abnormal tissue data, and could be represented by linear correlation equations. The correlations revealed that the value of the independent variable, i.e., the normal/abnormal, affects the dependent value which refuses the null hypothesis and accept the hypothesis that the independent variable affects the dependent variable and the regression line fits the data. From these equations, of the General Electric and the Philips data, a computer program was developed for these group of data. Once we introduce the data of the independent value, i.e., the normal and the abnormal mean of the histogram grey level, the end result gives the case of the tissue, whether it is normal or abnormal. The program is not confined to the mean grey levels of the normal and abnormal tissue data but also for the standard deviation, the median and the coefficient of variation. The application of this computer program to all of these variables gave satisfied results. In case of any discrepancies in the histogram grey levels shape or location , we can directly return to the developed computer program to give more confident result as described before.

False-positive results may arise when benign micro calcifications are regarded as malignant. Tissue summation shadows may appear as local parenchyma distortion; this may be erroneously called malignant tissue. A benign circumscribed lesion may show signs suggestive of malignancy, along with other findings, such as an irregular border and no halo sign. According to data from the present work, the false-negative rate of mammography is approximately 16% and 21% for Philips and General Electric respectively. This means that women with a clinically suspicious abnormality, a negative mammogram, and a negative sonogram may still have breast cancer.False-

positive rates are approximately 7% and 4% for Philips and General Electric respectively. The rate of false-positive rate is lower in case of General Electric mammography system. However, the sensitivity and specificity are nearly the same in case of the two systems. So, using the histogram method, the tumor detection in breast is a promising method which raises the sensitivity and specificity of breast cancer detection.

5. Conclusion

Together with the increasing importance of medical imaging in clinical practice, the need for medical image analysis to extract objective, quantitative information from medical images has grown considerably. Mammography , on the other hand, represent a critical point of view because it concerns with a fatal disease, breast cancer, that is increasing worldwide. However, with the advent in modern technology, and the existence of well qualified personnel, the early diagnoses of the disease may be improved. Nowadays two main mammographic techniques are widely used, i.e. Screen Film Mammography (SFM) and Digital Film Mammography (DFM). The results of this work show that both (SFM) and (DM) have its own advantages and disadvantages. Simply, the advantages of Screen Film Mammography can be summarized in the as follows:(Easy in manipulation. Faster in obtaining a diagnostic decision. Does not need complicated systems, e.g. computers and/or network).In some cases, its sensitivity and specificity are comparable to Digital Mammography.

However, its disadvantages are numerous. These can be summarized as follows :(The limitations of human perception, because the diagnoses depends on the experience of the radiologist manual visual. The film suffers from variation in sensitivity during storage before and after use. Following film processing, variation in the ambient temperature, humidity, shelving, and compression during storage may affect the film and the image quality which may develop fogging and image artifacts. The probability of obtaining the recalled image mammograms after prolonged time may be low with the high probability of lost. The possibility of repeating mammography is relatively high, which results in over radiation dose to the patient. Radiation exposure dose, is relatively higher).

The Digital Film Mammography, with its probability of wide spread during the near future, represents the hope to increase the sensitivity and specificity of breast cancer diagnoses. In fact, this modality enjoy more manipulation facilities to improve the image quality including high contrast and resolution using computer program's facility. Also, the probability of repeating mammograms, as the case of Screen Film Mammography, is absent. However, this system needs highly qualified personnel, relatively higher costs, and DICOM network. But, the benefits in using the Digital Film Mammography is an invaluable. It reduces the probability of obtaining false positive values and vice versa, i.e., increasing the probability of the true positive values. On the other hand, using this diagnoses modality, the radiologist has the possibility to investigate any arbitrary or suspicious location of the image. In spite of all the previous advantages, the Digital Mammography system enables the distribution of the mammograms to other clinics or medical centers for co-operation to obtain more accurate diagnoses decision, which is forbidden in case of Screen Film Mammography. Finally, the histogram grey level distribution provides a simple way to differentiate between normal and abnormal breast tissues. This increases the recommendation to use this method and the Digital Mammography system in breast cancer diagnoses.

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