Feasibility of qualitative low dose multidetector row computed tomography in the diagnosis of breast cancer

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Abstract: Objective: To evaluate the role of low dose multidetector row computed tomography (MDCT) in detection and diagnosis of breast lumps and axillary lymph node (ALNS). **Patients and methods:** Twenty patients with 15 breast lumps pathologically proven malignant underwent low-dose MDCT in supine position. Morphological analysis of MDCT images (multiplanar reformation, maximal intensity projection and 3-dimensional reconstruction) to assess shape, size and attenuation and quantitative analysis was done by measurement of time-density curves of both breast lumps and abnormal ALNS. The results are confirmed by postoperative histopathological reports. **Results:** 10 (50%) showed a washout pattern, 6 (30%) showed a plateau pattern, and 4 (20%) showed a persistent pattern. Fifteen out of 20 patients underwent surgery, where 3 patients underwent modified radical mastectomy and 12 patients performed breast conservative surgery, and the pathologic findings revealed 10 invasive ductal carcinoma, 4 invasive lobular carcinoma and 1 metaplastic. Significant mean difference was found between the MDCT measurement of the mass and measurement of pathological specimen as well as ALNS measurement ($p < 0.001$). Regarding detection of positive ALNS, MDCT has accuracy 80.4%, sensitivity 80.4% and specificity 80%, positive predictive value 76.7% and negative predictive value 83.3%. **Conclusion:** MDCT may represent a useful investigative tool for the diagnosis of breast cancer and accompanying ALNS.
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1. Introduction

Breast cancer is by far the most common cancer among women of both developed and developing countries accounting for 22.9% of all female cancers[1]. Spiral CT is useful for elucidating problems in the diagnosis of breast lesions. Its advantages consist in the speed of the method, comfort for the patient, and absence of movement artifacts, easy standardization and wide applicability. Dynamic contrast-enhanced CT of the breast has been found to be effective for the detection of intraductal extension of breast carcinoma and is thought to be useful in the preoperative assessment of indications of breast-conserving surgery. Three-dimensional (3D) helical CT can provide good information about the spread of breast cancer and could be an alternative to 3D MRI for preoperative examination of breast cancer [2].

The purpose of this study was to evaluate the diagnostic role of low-dose multidetector computed tomography (MDCT) in the evaluation of breast lumps and the evaluation of the axillary lymph nodes (ALNS) as well.

2. Patients and Methods

1. Patients

A prospective study was conducted in Assiut University Hospitals (Main Hospital) and South Egypt Cancer Institute from March 2013 to December 2014. The study was approved by our institutional review board with oral and written informed consents were obtained from the patients. The study comprised 20 female patients with their age ranged between 27 and 70 years (mean age, 53years ±13) who have suspicious lumps on mammography and ultrasound. Exclusion criteria involved pregnant patients, patients planned for neoadjuvnt chemotherapy as well as patients with renal impairment and patients had previous breast surgery.

2. MDCT Protocol

MDCT examinations were performed with 64-rows MDCT (Aquilion Toshiba Medical Systems Co., Tokyo, Japan). Patients were examined in the supine position to simulate surgical positioning.

Bilateral whole breasts canning was performed as following: pre-enhanced scanning of the whole thoracic area. This was followed by contrast-enhanced scans were obtained from the level of the axilla to the lower edge of the breast. Nonionic contrast material (100 ml; 300 mg I/g) was injected IV at a rate of 3.0 mL/s [3]. All patients underwent three phases of scanning that started 1, 3 and 8 minutes after the injection of the contrast material.

Low-dose examinations were done with tube current modulation: tube voltage, 120 kV; and tube

current, 40 mAs gives a CTDI volume of 18 mGy .Other scan parameters were as follows: acquisition time, 0.8s/rotation; image matrix, 512 × 512; field of view, 32–42 cm; data were reconstructed at 0.6-mm increments.

***3.*Image Analysis:**

The images were transferred to a workstation. Multiplanar reformation (axial, oblique coronal, and sagittal) and maximum-intensity projection (MIP) images were used for evaluation of the breast lumps and ALNS. The breast CT findings were judged by two expert radiologists blinded to the patient's clinical data.

***3.1.*Qualitative (Morphological) analysis**

***3.1. 1.* Regarding the breast lumps:** They were divided into three groups based on the contrast pattern and shape:

Group1: nodules suspected to be malignant, including those with early enhancement and an unclear tumor boundary with a margin that was fluffy or serrate.

Group II: nodules suspected to be benign, including those with weak enhancement and a clear boundary and rough and large calcified nodules.

Group III: non-specific nodules that were not classifiable as malignant or benign, including nodular shadows that were very small or weakly enhanced and were difficult to evaluate[4]. The longest dimension of the main breast lump were measured in centimeters.

***3.1.2.* Regarding axillary lymph nodes:** multiple abnormal ALNs, only the longest dimension of the largest lymph node were measured in centimeters. The abnormal lymph nodes were nonfatty: They did not contain any fat and had no fatty hilus, denser, rounder, or larger than usually seen. Normal lymph nodes are typically less than 15 mm in size.[5]

***3.2.* Quantitative analysis by evaluation of time-density curve patterns:** lesion interpretation was performed using the region-of-interest (ROI) method for measurement of the attenuation value in Hounsfield units (HU) of all breast lesions and the largest ALNs at non-contrast and post-contrast CT images at 1, 3 and 8 minutes after the injection of the contrast material. Types of time-density curve patterns were categorized as washout (an abrupt decline in density 3-8 min after contrast material injection), plateau (stabilized enhancement without a change in density 3-8 min after the injection), or persistent (an increasing density throughout the 8-mm period) [6]. The muscle density was chosen as reference.

***4.* Histopathology examination of Tumors:**

Formalin fixed paraffin-embedded tissue sections were prepared from each specimen, and then sections were stained with H & E staining. Slides were examined by a pathologist without previous knowledge of The CT data. Histologic type, grade, and number of axillary lymph nodes involved were determined for each case. Tumour size and the size of the largest axillary lymph node were evaluated. Breast cancer stage were conducted according to the American Joint Committee on Cancer TNM staging of breast cancer [7]. The Pathological measurement of tumor size and the largest ALNS in cm was used as the gold standard.

***5.* Statistical Analysis**

Data were evaluated using SPSS Ver.16 software (IBM SPSS, Chicago, IL). Student's t-test was used to assess differences. Spearman rho correlation was used to assess the relation between the size of the mass and size of the pathological specimen. Sensitivity, specificity, positive predictive value and negative predictive value and accuracy of detection positive ALNS. We examined mean HU and range of the primary breast mass and ALNS on both non- contrast and post-contrast MDCT images at 1, 3, & 8 minutes. A $P<0.05$ was considered significant.

3. Results

3.1 MDCT morphological findings of breast lumps

Of 20 lumps, group I include 10 lesions have speculated margin. Group II include 4 lesions have round smooth outline and another 2 have lobulated oval shape. Group III include 4 lesions shows in determinant non mass distribution nodules. Three out of group II lumps show dense calcification. Seven of 20 lumps show peripheral rim enhancement, 4 show solid homogenous enhancement and 9 show heterogeneous enhancement. (Fig. 1 & Fig. 3). The mean widest diameter of the breast lumps is 2.9cm (range; 0.5-6.3cm).

3.2. MDCT morphological findings of ALNS:

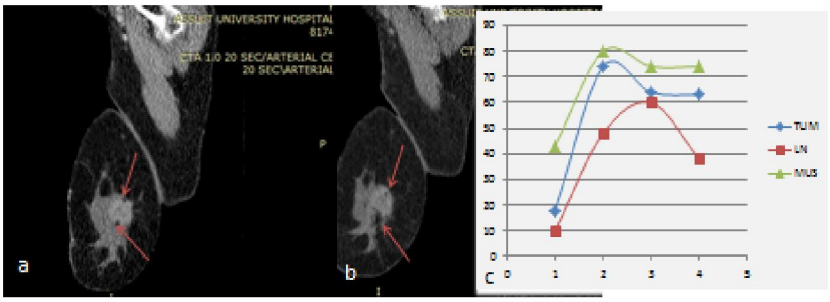
Ninety two ALNS are detected .The median widest diameter of the lymph node is 2.6cm (range; 0.8-2.9cm) .Thirty three of them are round in configuration and have no fatty hilus. (table1)(Fig. 2)

3.3. Assessment of Time-Density Curve Patterns:

Regarding breast lumps: 10 (50%) showed a washout pattern, 6 (30%) showed a plateau pattern, and 4 (20%) showed a persistent pattern. Mean CT density 48.18±107.5HU (range: 5.35-371.91 HU) on non-contrast image and the value increased to 83.67±75.45 HU (range: 17.03-280.95 HU) at 1 minute after contrast administration. Three minutes after contrast administration, the mean value was 80.94±51.03HU (range: 25.32-183.22) and on the delayed phase (eighth minute), mean attenuation was 68.03 ±35.53HU (range: 26.67=130.53 HU). (Fig. 1 & Fig. 3).

Regarding ALNS: 22 /33(66.7%) showed a washout pattern and 11/33 (33.3%) showed plateau pattern and none showed a persistent pattern. Mean CT density was 25.33±28.04HU (range: 2.99-88.22 HU) on non-

contrast image and the value increased to 53.18 ±30.29 HU (range: 1.47-117.72 HU) at 1 minute after contrast administration. Three minutes after contrast administration, the mean value was 68.05±24.44HU (range: 40.06-124.29) and on the delayed phase (eighth minute), mean attenuation was 59.59 ± 24.09HU (range: 32.6-114.11 HU). (Fig1& Fig.3).



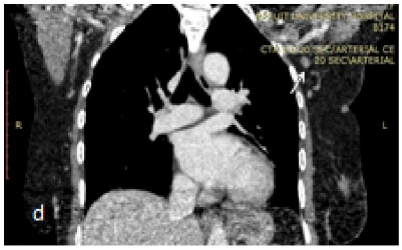


Fig1.55year female patients with irregular spiculated margin left breast lumpon arterial and delayed images (a ,b) (red arrowed) respectively, proved to be IDC, showing washout type 3 pattern(c) on dynamic CE-MDCT. Coronal reformate image(d) revealed enlarged left axillary lymph nodes(white arrowed) round and lacking fatty hilus.

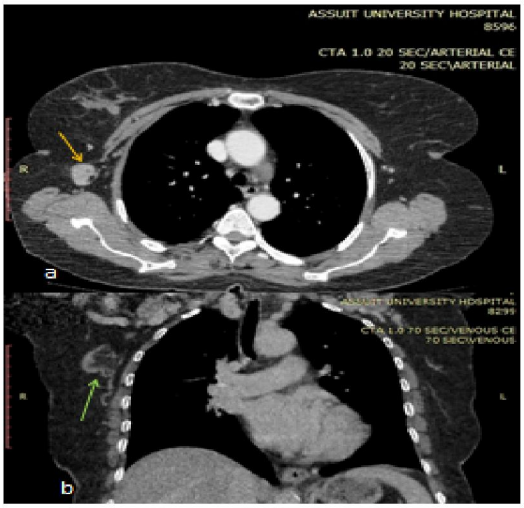


Fig2. axial(a) and coronal reformate (b)of different patients shows abnormal pattern of axillary lymph nodes. Round with no fatty hilum(orange arrowed) and thick cortex with eccentric fatty hilum (green arrowed)

Table (1) MDCT findings

Characteristic	Value
Number of lumps detected by MDCT Unilateral Bilateral Calcification	20 10 3 3
Number of ALNS by MDCT Round in configuration Median of the longest diameter of largest ALNS Range	92 33/92 26mm 8-29mm
Radiation Dose effective dose in mSv	6.986

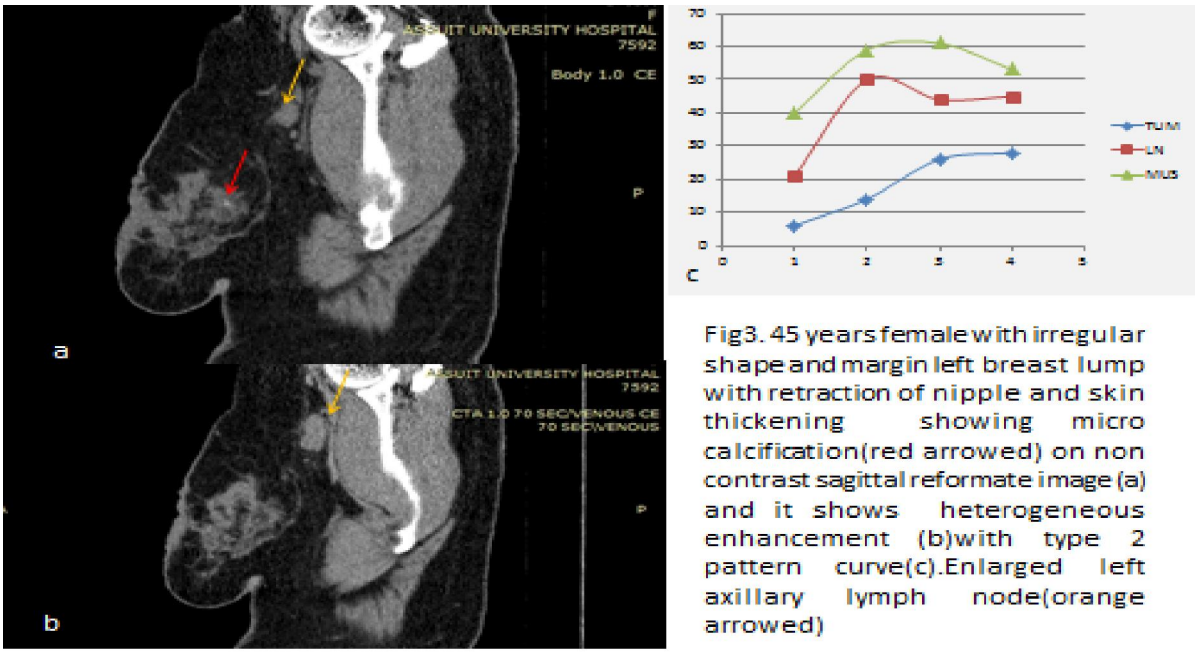


Fig3. 45 years female with irregular shape and margin left breast lump with retraction of nipple and skin thickening showing micro calcification(red arrowed) on non contrast sagittal reformate image (a) and it shows heterogeneous enhancement (b)with type 2 pattern curve(c).Enlarged left axillary lymph node(orange arrowed)

Table (2)Type of surgery and pathological data of patients

Characteristic	Value
Type of surgery BCS MRM	 12 3
Pathologic findings (No. of malignant tumors)	15
IDC	10
Grade 1	3
Grade 2	7
ILC	4
Metaplastic	1
No of positive ALNS Median of the longest diameter of largest ALNS Range	41/166 2cm 1.5-4cm
Tumor size (cm)determined by surgical histology T1 (≤2.0cm) T2 (>2–5.0cm) T3 (>5.0 cm)	 4 10 1
Pathologic (PN) pN0 pN1 pN2 pN3	 125 5 15 21
Stage Stage I A (T1N0M0) Stage IB (T1N1M0) Stage IIA (T2N0M0) Stage IIB (T2N1M0) Stage IIIA (T3N0M0)	 2 1 4 5 3

3.4. Correlation between MDCT and Histopathology Findings:

Fifteen out of 20 patients underwent surgery, where 3 cases underwent modified radical mastectomy and 12 patients performed breast conservative surgery, and the pathologic findings revealed 10 invasive ductal carcinmoma, 4 invasive lobular carcinoma and 1 metaplastic (table 2). The mean size of the pathological specimen was 8.95±8.99 cm and the largest dimension of ALNS was 3.6±1.9cm. Significant mean difference was found between the MDCT measurement of the mass and measurement of pathological specimen as well as ALNS measurement ($p < 0.001$) and good linear relation was found between them ($r = 0.857$; $P < 0.001$). Regarding detection of positive ALNS, MDCT has accuracy 80.4%, sensitivity 80.4% and specificity 80%, positive predictive value 76.7% and negative predictive value 83.3%.

4. Discussion

Carcinoma of the breast is the most prevalent cancer among Egyptian women and constitutes 37% of the total reported malignancies among Egyptian women. [8]. In the current study, we evaluated 20 patients using 64- rows MDCT in the differentiation of breast lesions suspected on mammography and sonography as **Inoue et al.** [3] who reported that high-spatial-resolution CT would enable acquisition of an accurate three-dimensional image of the entire breast and could improve detection of minor diseases in dense breasts or detection of lesions hidden by superimposed structures. The volumetric breast

imaging technique would also eliminate the need for painful compression of breasts, as in mammograph.

In the current study, Low dose MDCT was used with tube current modulation using tube voltage, 120 kV; and tube current, 40 mAs that gave a CTDI volume of 18 mGy instead of using tube current 60MAs that gave a CTDI volume of 32mGy and thus the estimated effective dose was 7.0 mSv for whole study that it is comparable less than that reported in previous studies [9-10], the radiation dose required for breast CT was reported to be 28 mSv, which is approximately 10 times greater than that used for standard mammographic examinations (2.8 mSv), and seven times higher than that required for a chest CT examination. Furthermore, both **Perrone et al.** [6] and **Ann Yi et al.**[11] reported that, at tube current value of 30–70 mAs it is possible to obtain good image quality with reduced total radiation dose.

For the morphologic features of the 20 lesions detected on MDCT in the current study, 15 lesions were proved to be malignant, 10 of them showed speculated margin and peripheral rim or heterogeneous enhancement on arterial phase with rapid wash out time-density curve on dynamic contrast enhanced study, the remaining 5 malignant lumps show round shape in 3 1 with homogenous enhancement and indeterminate non- mass distribution in 2 showing plateau time-density curve on dynamic contrast enhanced study, the latter two cases pathologically proved to be invasive lobular carcinoma. This in agreement with **Perrone et al.** [6] who reported that 25 malignant lesions detected on CT had a washout pattern (16 cases) or a plateau pattern (nine cases). While the rest 5 breast lumps were benign detected on MDCT in the current study. They had lobular and oval shape in 3, diagnosed as fibroadenoma and indeterminate mass lesion diagosed as fibrocystic disease in 2 cases. This is Similar to **Perrone et al** [6], **Nakahara et al**. [12], and **Tamaki et al**. [13] studies.

A statistically significant correlation was found between the MDCT measurement of the mass and measurement of pathological specimen($P<0.001$) and this in agreement with **Su Joa Ahn et al**. [14] who concluded that tumor size by MDCT is well correlated with pathology determined tumor size in breast cancer patients.

In our study, 33 out of 92 LNS were detected on dynamic MDCT depending on round configuration and loss of fatty hilus had accuracy 80.4%, sensitivity 80.4% and specificity 80%, positive predictive value 76.7% and negative predictive value 83.3%. in contrast to **Ogawa et al.** [15] who reported accuracy of 85.7%, sensitivity of 96.6%, specificity of 70%, positive predictive value of 82.4%, and negative predictive value of 93.3% and **Cheung et al.**[16] who also reported the sensitivity, specificity, positive predictive valve, negative predictive valve and accuracy of MCT in diagnosing the axillary lymph node metastases 72%, 40%, 85.7%, 22.2% and 66.7% respectively. The mean density of largest ALNS on non- contrast images was 25.33±28.04HU that comparable to that measured by **Urata et al**.[17] 29.17 ± 16.37 for positive nodes. The widest diameter of lymph node was 2.6cm detected on MDCT had significant mean difference to that of pathological diameter 3.6 cm ($p<0.100$).

Limitation: The limitations of this study are firstly, the low number of cases, secondly, the included patients had palpable symptomatic breast masses rather than screen cases and lastly, the measurement of CT attenuation value may subject to bias due to the partial volume effect or presence of dense calcification.

Conclusion: Low-dose MDCT of breast cancer is a useful investigative tool for preoperative assessment and staging of breast cancer and diagnosing ALNs metastases.

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