The Egyptian Journal of Hospital Medicine (October 2017) Vol. 69 (7), Page 2798-2803

# Breast Cancer Staging and The Role of Radiology

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## ABSTRACT

**Purpose:** To Compare tomosynthesis to mammography, ultrasound, MRI, and histology for the detection and staging of BI-RADS 4–5 anomalies, as a function of breast composition, histology, size, and lesion location.

**Materials and methods:** 25 patients underwent tomosynthesis, MRI, mammography, and ultrasound. The diagnostic accuracy of the different examinations was compared.

**Results:** The sensitivities for detection were as follows: 92.7% for MRI, 80.5% for ultrasound, 75.6% for tomosynthesis, and 61% for mammography. Tomosynthesis improves the sensitivity of mammography (P = 0.0001), but not the specificity. The detection of multifocality and multicentricity was improved, but not significantly. Tomosynthesis identified more lesions than mammography in 10% of cases and improved lesion staging irrespective of the density, but was still inferior to MRI. The detection of ductal neoplasia was superior with tomosynthesis Compared to mammography (P = 0.016), but this was not the case with lobular cancer. The visualization of masses was improved with tomosynthesis (P = 0.00012), but not with microcalcifications. Tomosynthesis was capable of differentiating lesions of all sizes, but the smaller lesions were easier to see. Lesion sizes measured with tomosynthesis, excluding the spicules, concurred with histological dimensions. Spicules lead to an overestimation of the size.

**Conclusion:** In our series, tomosynthesis found more lesions than mammography in 10% of patients, resulting in an adaption of the surgical plan.

**Keywords:** Breast, Tomosynthesis, Multifocality, Staging.

## INTRODUCTION

Worldwide, breast cancer is the most frequently diagnosed life-threatening cancer in women and the leading cause of cancer death among women [1]. Because of early detection, intervention, and postoperative treatment, breast cancer mortality has been decreasing. Mammography is the preferred screening examination for breast cancer. It is widely available, well-tolerated and inexpensive. Randomized controlled trials have demonstrated a mortality benefit for women from 40 to 74 years old. Some studies have shown that mammography might be mainly helpful for women who are 80 years of age and older [2, 3]. The earliest sign of breast cancer can be an abnormality depicted on a mammogram, before it can be felt by the woman or by her physician. When breast cancer has grown to the point where physical signs and symptoms appear, the patient feels a breast lump (regularly painless). The improved prognosis for breast cancers is partly linked to advances in treatment [4].

Ideal staging, to define the size of the tumor and the presence of extra lesions, is indispensable for suitable surgery with healthy margins. Multicentricity (two or more lesions in different quadrants), multifocality (more than two lesions in the same quadrant), or contralateral disease may require more extensive breast surgery[5,6]. Ignorance of additional lesions affects relapse and survival rates, but the literature is not consensual [7]. To detect these multiple lesions, mammography has a sensitivity of less than 50% [8-11], and mammary MRI of 94–99% [12-15]. Tomosynthesis, a new procedure in 3D breast imaging, obtains reconstructed volume data, the data is reconstructed secondarily in mammary slices from many radiographs achieved from different angles of view (−25° to +25° for Siemens®). It theoretically improves the sensitivity of detection by permitting enhanced delimitation of the lesion margins, and the specificity by avoiding the problem of glandular superimposition [16].



Received: 21/09/2017
Accepted: 30/09/2017
DOI: 10.12816/0042568

The key purpose of the current study was to compare tomosynthesis with 2D mammography, ultrasound, and MRI in cases with suspected BI-RADS 4 or 5 anomalies, to determine its potential benefit for staging, and in exact for multifocality and multicentricity. The secondary objectives were the detection of contralateral tumors;to grade the various imaging techniques using a qualitative "TOMOS" score for clinical performance;to calculate the sensitivity, specificity, and positive and negative predictive values (PPV and NPV) of tomosynthesis in comparison with mammography for all of the lesions; the comparative analysis of tomosynthesis and mammography for lesion detection according to breast density, histology, signal (mass, microcalcification), breast topography, and volume;the comparison of lesion sizes with tomosynthesis versus histology.

## MATERIALS AND METHODS

The study was prospective and monocentric, with 25 patients incorporated between 2016 and 2017; the patients were addressed to senology for the staging of a BI-RADS 4 or 5 lesion. The priority for inclusion was for patients with a sign for MRI, in compliance with suggestions (neoadjuvant treatment, young women, invasive lobular carcinomas, high family risk).

The criteria for non-inclusion were contraindications for MRI, pregnancy, and cognitive disorders preventing informed consent. Each patient experienced, for every breast, clinical examination, 2D mammography (anterior-posterior, lateral oblique, and additional views if needed), tomosynthesis (anterior-posterior, lateral), MRI, biopsies of suspicious lesions, ultrasound, and if necessary a second look ultrasound and biopsies of additional lesions. We utilized mammography with tomosynthesis, ultrasound, and MRI. These studies were re-read by two senologists (15 and 20 years of experience), in double blind, who were aware of the clinical presentation. The first reading was prospective, the second retrospective.

The data collected for every patient were as follows: age, gender, genetic mutations, menopausal status, previous history of breast cancer, the palpable nature of the main lesion, and the size of the breast (small, medium, or large).

We recorded the parameters for the main and satellite lesions such as breast density; the type of lesion (mass, microcalcification, architectural distortion); a qualitative "TOMOS" score representing the performance of each technique (mammography, ultrasound, tomosynthesis, and MRI) for staging. This score is the sum of the points attributed to each imaging technique (from 1 for the worst examination for staging to 4 for the best) for each of the following 3 criteria:

- Number of suspicious lesions (≥ BI-RADS 3). The reference was histological, taking into account both principal and satellite lesions in patients who were operated on from the outset, or residual lesions, or scarring in the event of neoadjuvant chemotherapy,
- Concordance of the BI-RADS classification (from 3 to 5) for each suspect lesion and each imaging technique,
- Variation of the lesion volume (as a percentage) for each imaging technique; the reference was the histology if the patient was operated on at the outset, and the initial MRI if neoadjuvant chemotherapy had made the lesion regress;the location of the tumor within the mammary quadrants and the depth (anterior-middle-posterior) of the tumor seen on the mammographies and tomosyntheses. The depth was determined by measuring the distance between the nipple and the pectoral muscle, and separating it into three equal parts. The third that is closest to the nipple was designated as "anterior", the third closest to the pectoral as "posterior", and the last third as the "middle";the tumor histology: type (ductal, lobular, in situ, other), SBR grade, hormone receptors (estrogens, progesterone), HER2, Ki67;the sensitivities, specificities, NPV, and PPV of the imaging techniques as a function of the histology.

The descriptive statistical analysis determined the frequencies for the qualitative variables and the distribution parameters for the quantitative variables. For the comparative analysis, the calculations for sensitivity, specificity, NPV, and PPV, were performed using the SEM software program [17].

Chi2 tests were used to compare the rates acquired for each group of patients according to the imaging techniques.The scores and volumes were compared using the Student t-test and Mann and Whitney U test.

The imaging techniques were compared for the same groups of patients using the t-test for unpaired series. The Pearson test was used to compare the lesion volumes.

**The study was done following the ethical board of Umm alQura university**.

**RESULTS**

The present study included 50 patients for breasts examination ,41 malignant lesions were found.

There were 25 patients; the mean age was 56 years. 52% of the patients had passed the menopause, 12% had a previous history of breast cancer, and 4% had a genetic mutation.

Out of the 25 affected patients, there were 25 homolateral principal lesions and 1 contralateral principal lesion. Out of these 26 principal lesions, 22 were palpable (76.9%), 4 subclinical (15.4%), 7 multifocal (26.9%), and 4 multicentric (15.4%). Bilateral disease was found in 1 of the 25 patients (4%).

On histology, 41 malignant lesions were diagnosed (principal and satellite); 39homolateral and 2 contralateral. Twenty-seven tumors were operated on immediately and 14undertook neoadjuvant chemotherapy. The mammographic appearance for 29 tumors (71%) corresponded to a mass, for 7 lesions (17%) to microcalcifications, and for 5 cases (13%) to an architectural distortion or various associations. Spicules were present in 18 of the 41 lesions (43.9%). The tumors were predominant in the superolateral quadrants (29%).

We counted 29 lesions with an anterior and middle topography (71%), and 12 posterior (29%).We found 49% invasive ductal carcinomas (IDC), 34.5% invasive lobular (ILC), 15% in situ, and 1.5% other lesions.

The overall detection sensitivity was 92.7% with MRI, 80.5% with ultrasound, 61% with mammography, and 75.6% with tomosynthesis (Tables 1 and 2).

Overall lesion detection was significantly improved by tomosynthesis (P = 0.0001) in comparison with mammography, with a slight reduction in specificity (P = 0.23) (Table 3).

**Table 1:** Number of malignant lesions detected on histology and for each breast imaging technique

| **Lesions seen (number)** | **Localization** | | |
|---|---|---|---|
| | All of the breasts | Contralateral breast | Homolateral breast |
| Histopathology | 41 | 2 | 39 |
| MRI | 38 | 2 | 36 |
| Tomosynthesis | 31 | 2 | 29 |
| Mammography | 25 | 1 | 24 |
| First look ultrasound | 33 | 2 | 31 |

**Table 2:** Sensitivity (%) of tumor detection for each breast imaging technique

| **Sensitivity (%)** | **Localization** | | |
|---|---|---|---|
| | All of the breasts | Contralateral breast | Homolateral breast |
| Histopathology | 100 | 100 | 100 |
| MRI | 92.7 | 100 | 92.3 |
| Tomosynthesis | 75.6 | 100 | 74.4 |
| Mammography | 61 | 50 | 62 |
| Firstlook ultrasound | 80.5 | 100 | 79.5 |

**Table 3:** Comparison of the diagnostic performance of mammography and of Tomosynthesis

| | **Mammography** | **Tomosynthesis** |
|---|---|---|
| Sensitivity (%) | 61 | 75.6 |
| Specificity (%) | 80 | 74 |
| NPV (%) | 52,5 | 66 |
| PPV (%) | 81 | 81 |

Tomosynthesis detected further lesions to mammography in 3 patients out of 25 (12%) and MRI in 4 patients out of 25 (16%). Tomosynthesis did not reveal any lesions that were not obvious on MRI.The increase in sensitivity of tomosynthesis for multifocality and multicentricity was 25% and 15% in comparison with mammography, but this was not statistically significant (P = 0.13 and P = 0.69), as a result of the small sample size.

## DISCUSSION

The patients incorporated into this study exhibited particular attributes. The patients all had breast neoplasia: multifocal, multicentric, and bilateral structures were in this manner more various than in the general population. Also, invasive lobular sorts were over-represented by a factor of three (33% in the investigation, 10% in the overall public) [18].The detection sensitivities were 92.7%, 80.5%, 75.6%, and 61% with MRI, ultrasound, tomosynthesis, and mammography respectively. This 15% increase in detection rate with tomosynthesis in comparison with mammography (P = 0.0001) agrees with different studies, where it has been indicated to be between 10 and 15% [19,20]. Recent series have shown enhanced affectability sensitivity with tomosynthesis, either alone with two occurrences, or with one occurrencesrelated with two views of mammography [21].Though, we did not record any dissimilarity in specificity between tomosynthesis and mammography (P = 0.23).

Recent studies have stated enhanced specificity with tomosynthesisover a reduction in incorrect positives. For **Skaane *et al*. [22],** Combining tomosynthesis and mammography reduced incorrect positives by 15% (P < 0.001) in comparison with mammography alone .(22). For **Gur *et al*. [21],** a combination of tomosynthesis and mammography improved the specificity by 8% in comparison with tomosynthesis alone, and by 12% in comparison with mammography alone (21) .

Tomosynthesisdecreased recall screenings by 40% for Rafferty [19]. In the present study, the specificity of tomosynthesis (74%) is lower than that of mammography (80%). This result, at the boundary of the literature, can be explained by the fact that our study included staging rather than screening, with the finding of a higher proportion of theoretically benign BI-RADS 3 anomalies. As the patients involved had at least one breast cancer, the readers might have over-classified borderline BI-RADS 2 or 3 lesions into the category above, decreasing the specificity of tomosynthesis at the expense of the sensitivity. Studies showing an better specificity only comprised BI-RADS 4 and 5 lesions [21,24, 25].We counted around twice as many contralateral lesions in our series (5%) than in the general population (1 to 3%) [26].

Tomosynthesis identified extra lesions that altered the therapeutic approach in 10% of cases (conversion from lumpectomy to quadrantectomy or mastectomy). MRI, the reference for identifying multicentricity and multifocality[27] resulted in a modified treatment plan in 16% of cases, which concurs with the 20% reported by **Houssami *et al***. [28].

Performing tomosynthesis after a BI-RADS 4 or 5mammography would outcome in the detection of extra lesions in 10% of cases, causing in a potentially wider surgery. Tomosynthesiscan be useful in "1-day senology workups", preferred by patients, where the biopsies are taken on the same day and the first diagnosis given by the surgeon in the evening. Further suspicious lesions in tomosynthesis would allow the surgeon to arrange the patient for a more radical surgery than initially planned, though the reference for further lesions is still MRI, performed in second intention. Only definitive histology allows pronouncement of the final management [30].

Biopsies guided by tomosynthesis are under improvement [31] for lesions that are only seen with this method. Anterior or middle mammary lesions were detected better than posterior lesions. Though, tomosynthesis proved to be superior to mammography, regardless of the location of the tumor (P = 0.00038). We expected better visualization of posterior lesions in mammography than with tomosynthesis, given that the depth of exploration is restricted in tomosynthesis by a small range of mammary compression, but this was not the case in practice. Mammography detected large lesions (> 1 cm3) much better than smaller ones (P = 0.01) [30]. Tissue superimposition hindered the visualization of small tumors buried in the mammary parenchyma [31]. Tumor volumes in ultrasound, mammography, and MRI were concordant with the histology. Tumor size in tomosynthesis, without comprising the spicules, was concordant with histology (overestimation of 2% of the mean volume) through an improved delimitation of the margins.

For screening, the further radiation linked with tomosynthesis (equivalent to 1.4 mammography films) [32] must correspondingly be considered. A dosimetric study carried out on our machine presented that the dose of one tomosynthesis occurrence was similar to one standard mammography film. One tomosynthesis film is often suggested as well as the standard two 2D mammography films per breast, increasing detection without significantly increasing irradiation,(33) .

**Svahn *et al*. [33]. Skaane *et al.* [22]** in their study of 18,000 patients demonstrated a 30%

increase in detection by adding one incidence of tomosynthesis per breast to the standard two mammography films (anteroposterior and oblique) [22].

## CONCLUSION

In this prospective monocentric series of 25 patients, all of whom had one BI-RADS 4 or 5 lesion, tomosynthesis (two views) significantly increased the sensitivity of the detection of masses, invasive ductal carcinomas, and small lesions (through enhanced visualization of the margins), and in breasts with an intermediate density for BI-RADS type 2 and 3.It did not provide any advantages for the detection of microcalcifications or invasive lobular carcinomas.In the present study, there was better visibility of additional lesions in 10% of patients. The detection sensitivity for multifocality and multicentricity was improved by tomosynthesis, but this was not statistically significant. MRI was still the most effective method. In this series, tomosynthesis proved superior to 2D mammography. It also enhanced the interpretation of other imaging techniques (ultrasound and MRI), without replacing them.

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