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Purpose

Screen-Film Mammography had a great impact in breast cancer detection, thanks to its possibility of early diagnosis, that leads to mortality reduction [1]. Moreover mammography represents the only imaging tool, which permits to reduce mortality [2].

Digital Mammography (DM) represents an evolution of Screen-Film Mammography, that demonstrates to have similar overall diagnostic accuracy of film mammography, but digital mammography is more accurate in women under the age of 50 years, women with radiographically dense breasts, and premenopausal or perimenopausal women [3].

However, the overlap of fibro-glandular tissue in dense breasts may affect sensitivity and specificity of DM by masking, creating a False Negative (FN) case, or mimicking a cancer, creating a False Positive (FP) one [4].

Digital Breast Tomosynthesis (DBT) is a new imaging technique aimed to overcome tissue overlap. It is based on a moving x-ray source and a digital detector used to obtain a quasi-three-dimensional (quasi-3D) volume of thin section data. Images are then reconstructed with proper algorithms to obtain a set of thin image sections parallel to the breast platform [5].

This technique is expected to improve lesions detectability, characterization of masses and architectural distortions, especially in dense breasts [6-7]. DBT has the potential of being superior to DM, in particular with two-views, and for readers with least experience [8]. DBT can also reduce the recall rate [9] thanks to its ability of reducing FP [10-11]. But DBT is still under investigation.

Regarding surgical specimen, thank to the widespread of Breast Conservative Surgery (BCS), various strategies have been developed through the years in order to obtain adequate surgical margins, reducing the need of a second operation after BCS [12]. DM represents a tool used to correctly evaluate surgical margins. In literature there are different results about the use of specimen-mammography for margins evaluation; some authors suggest that there is a correlation between specimen mammography and histological results [13] and others demonstrate that specimen-mammography does not provide a satisfactory evaluation of the histological margins [14].

The purpose of our study was to compare DBT and DM in breast cancer detection in breast surgical specimens. For this reason we compared the Diagnostic Yield (DY) of both images techniques. As the second endpoint we evaluated the subjective impression
of the readers in the detectability of lesions. Moreover we analysed if lesions margins were fully visible or not.
Methods and Materials

Population

During a 7 months period (from November 2011 to May 2012) we retrospectively obtained 51 surgical specimens (44 mastectomies and 7 quadrants) from 51 patients with an age range 40-86 (mean age 60.5 years). We chose only specimens with thickness of at least 2 cm, that was the less thickness required to perform DBT. For this reason the number of mastectomy in our study population was higher than the one of quadrantectomy. All patients referred to surgery for a histological proved breast cancer obtained from preoperative US core needle biopsy or stereotactic vacuum assisted biopsy performed in our Institution. Approval of the institutional review board was obtained before the collection of the data. A total of 67 breast cancer were at the pathologic examination of the specimen, used as the standard of reference.

Surgical procedures were performed in our Hospital and consist in BCS (breast conservative surgery) or mastectomy, concomitantly with sentinel lymph node mapping in all patients. The pectoral fascia was included in all patients with lesions close to the chest wall. An ellipse of overlying skin was included when lesions were very close to the skin.

The surgeon marked the margins of the specimen with a short suture for the superior margin, a long suture for the lateral margin and a middle suture for the medial ones. In this way it was possible to orient each specimen (Fig. 1 on page 7).

Imaging protocol

After orienting the specimen we sequentially performed DM and DBT by using the same digital system (Giotto TOMO, IMS, Bologna, Italy), which implements: (i) a W-target x-ray source, combined with Rh-filter or Ag-filter depending on breast thickness; (ii) an a-Se digital detector (ANRAD LMAM), with a sensitive area of 24×30 cm² and a squared pixel pitch of 0.085 mm.

Surgical specimens were positioned in the system and anteroposterior view were performed DM and after 90° rotation of the specimen another perpendicular view were performed. The DM position corresponding to the largest thickness of the specimen was used to perform one single DBT view. For DBT, the movable x-ray source spanned an overall angular range of ±20°, acquiring 13 projections at the requested position. Exposure parameters were determined by Automatic Exposure Control (AEC). AEC for DBT in one view was defined so as to deliver a radiation dose approximately 1.4 times that for digital mammography in one view.
Image reconstruction was based on an iterative method that used Total Variation (TV) regularisation, and by default reconstructed voxel size of 0.085 mm×0.085 mm×1.0 mm.

**Image analysis**

Images were reviewed in separate sessions on a dedicated workstation (Raffaello, IMS, Bologna, Italy) by two radiologists with more than 10 years of experience in breast imaging. Both readers were blinded to lesions dimension and pre- and post-surgical histopathological results.

DM and DBT images of the same patients were presented in independent reading sessions separated by a 4 week interval in order to avoid recall bias. In each reading session, DM and DBT cases were showed randomly. All discordant results were resolved by consensus.

For each specimen, readers recorded - both on DM or DBT images - the number of malignant lesions they detected, together with the lesion type according to the following categories:

- mass;
- microcalcifications cluster;
- mixed lesions (in the case of a combination of the two former types).

They also recorded their subjective impression of lesion detectability, defined as lesions visibility against the background of fibro-glandular tissue (detectability score). For this analysis a 1-5 score was used as follows: 1=very low; 2=low; 3=mild; 4=good; 5=very good.

Moreover, for the lesions seen with both imaging techniques (excluding lesions classified as microcalcifications), the readers give a subjective impression of the visibility of lesions. Margins visibility was expressed as a dichotomic value as follows: 1 when ≥50% of lesion margins were visible (fully visible) and 0 when <50% of margins were visible.

**Data Analysis**

Analysis was performed on a per-lesion basis.

We estimated the diagnostic yield (DY) of DM and DBT as the ratio between the number of correctly detected lesions over the total number of lesions found at histopathological examination (Fig. 2 on page 7). Binomial exact 95% C.I. were calculated.
For the lesions seen with both technique we compared the image detectability scores of the two techniques by using the Wilcoxon signed-rank. Statistical significance was assumed for an alfa value less than 0.5.

The concordance in the visualization of margins between DBT and DM was evaluated with weighted-Kappa.
Fig. 1: The figure shows the orientation of specimens. To correctly orient the specimens, their margins were marked by the surgeon with a short suture for the superior margin (green), a long suture for the lateral margin (red) and a middle suture for the medial ones (blue).

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Fig. 2: The figure showed the estimation of the diagnostic yield (DY) for the data analysis.

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Results

A total of 67 malignant lesions were found at the histopathological analysis of the specimens. Of these lesions 32 were Invasive Ductal Carcinomas (IDCs), 5 Ductal Carcinomas In Situ (DCISs), 15 Ductal Carcinomas In Situ + Invasive Ductal Carcinomas (DCISs+IDCs), 9 Invasive Lobular Carcinomas (ILCs), 2 Lobular Carcinomas In Situ + Invasive Lobular Carcinomas (LCISs+LDCs) and 4 rare histotypes (TAB 1). Regarding rare histotypes 2 were Mucinous Carcinomas, one was a Papillary Invasive Carcinoma and one was a Apocrine Breast Carcinoma (Table 1 on page ).

Table 1: Lesions found at the histopathological analysis of the specimens. All the lesions found at the analysis of all 7 quadrantectomy were unifocal. Multifocal disease were found at histology in the 44 mastectomies analysed, for a total of 60 lesions (*).

References: Azienda ospedaliero-universitaria Santa Maria della Misericordia Udine, Institute of Radiology - Udine/IT
Concerning multifocality, 16 additional lesions were found at histology. In particular 5 patients showed 1 IDC + 1 IDC+DCIS, 1 patient showed 3 IDCs, 4 patients showed 2 IDCs, 1 patient showed 1 papillary ca. + 1 DCIS, 1 patient showed 3 ILC and 2 patient showed 2 ILC.
DBT and DM correctly recognized 47 suspicious lesions. Concerning their appearance, both of them recognized 21 lesions as masses, 8 as microcalcifications and 18 as mixed ones. (Table 2 on page 13 Table 3 on page 14).

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<thead>
<tr>
<th>Final diagnosis</th>
<th>Number of lesions</th>
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<tr>
<td></td>
<td>Mass</td>
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<tr>
<td>IDC</td>
<td>11</td>
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<tr>
<td>IDC + DCIS</td>
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<tr>
<td>DCIS</td>
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<td>ILC</td>
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<td>Rare histotypes</td>
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<td>Total</td>
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Table 2: Lesions correctly found with both DBT and DM. DBT and DM recognized 47 suspicious lesions. Twenty-one appeared as masses, 8 as microcalcifications and 18 as mixed lesions.

References: Azienda ospedaliero-universitaria Santa Maria della Misericordia Udine, Institute of Radiology - Udine/IT
Table 3: Malignant lesions correctly recognized with DBT and DM. As you can see DBT and DM correctly found 47 lesions. DM detected 5 lesions not seen with DBT and DBT correctly recognized 11 lesions missed by DM. Both DM and DBT missed 4 lesions.

References: Azienda ospedaliero-universitaria Santa Maria della Misericordia Udine, Istitute of Radiology - Udine/IT

DBT showed 11 lesions, not seen with DM. They were 11 masses that at the histological analysis corresponded to 7 IDCs, 1 DCISs, 2 ILCs and 1 ILC+LCIS. The range largest diameter of these lesion was 7-32 mm, with a mean of 16.8 mm (Fig. 3 on page 15).

DM correctly showed 5 malignant lesion, not seen with DBT. They were 1 mass, corresponding to 1 IDC at histology and 4 mixed lesions, corresponding to 3 DCISs and 1 DIC+DCIS at histology. The range of the largest diameter of these lesion was 12-40 mm, with a mean of 21.5 mm.

Lesions missed by DBT were a total of 9; 5 of them were those correctly recognized by DM and 4 were missed by both techniques. DM did not recognized a total of 15 lesions; 11 of them were those showed only by DBT and 4 were those recognized only by histopathological analysis.
Concerning the 4 lesions recognized only by histology, they were 2 IDCs, 1 DCIS and 1 IDC+DCIS. The range of the largest diameter of these lesions was 8-40 mm, with a mean of 16.2 mm.

DBT correctly recognized a total of 58 malignant lesions with a DY of 86.6% (95% C.I. 76.4-92.8). DM showed 52 with a DY of 77.6% (95% C.I. 66.3-85.9) smaller than the one of DBT. The lesions recognized only with DBT were 5 masses and 1 mixed lesion.

For the 47 cancer seen with both technique, scores for lesion detectability were significantly higher (p=0.011) for DBT compared to DM. In particular the mean detectability score for DBT and DM was 4.55±0.68 and 4.25±0.90, respectively (Fig. 4 on page 16 Fig. 5 on page 17).

Concerning the visibility of lesion margins, the margins of lesions were fully visible in 38/39 (97.4%) cases with DBT, while in 24/39 (61.5%) with DM. The agreement in margin definition was low (k=0.08), with DBT the margins were judged as fully visible in a greater number of cases (Fig. 5 on page 17).
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Fig. 3: Surgical specimen (mastectomy) of a 60 years-old woman treated for a IDC confirmed at histopathological analysis. Readers missed the lesion with DM (A), but with DBT (B) they found the lesion as a spiculated mass (C).

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Fig. 4: Plot of the detectability scores of DBT and DM. DBT showed significantly higher scores in confront of DM, with a mean score of 4.55±0.68. The mean detectability score of DM was 4.25±0.90.

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**Fig. 5:** Surgical specimen (quadrantectomy) of a 53 years-old woman with a IDC confirmed at histology. The readers gave a score of 4 to DM (A) and 5 to DBT (B). With DBT the margins were better seen and judge as fully visible (arrow).

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Conclusion

This study done on surgical specimens demonstrates as DBT showed a higher DY than DM in malignant lesion detection. DBT recognized a greater number of cancers compared to DM. DBT recognized 11 lesions not seen with DM. DM, on the contrary, recognized 5 lesions not showed by DBT. Both techniques missed 4 lesions, that were 2 small (< 10 mm) IDC, a DCIS and a IDC + DCIS with a mean diameter of 16.2 mm.

DBT showed also a statistically significant higher detectability score, that is the reader's subjective impression of visibility of the lesion. In fact for the 47 lesions recognized by both techniques, the detection score of DBT given by the readers, were higher. This means that with DBT the readers were more confident in seeing the lesions against the fibro-glandular tissue, than DM.

With DBT the margins of lesions were better seen and judge as fully visible in a greater number of cases compared to DM.

DBT can become a new tool in evaluating breast surgical specimens, thanks to better lesions detection. Moreover DBT can help the reader to became more confident in lesion recognition and definition of margins. For this clinical application other study were required in order to evaluate the ability of DBT in recognized lesions margins, in comparison to DM.

The main limitation of our study is the small sample size. Moreover we evaluated not only surgical specimens obtained by BCS, but also mastectomy-specimens. For these reasons we are collecting new cases and in particular BCS-specimens.


