Diagnostic accuracy of Tomosynthesis (DBT) vs Magnetic resonance imaging (MRI) and Mammography (DM) in assessing breast tumor size; a preliminary evaluation on 60 female patients.

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Aims and objectives

Breast cancer size is one of the main prognostic factors and a determining indicators in the choice of surgical treatment planning. The accuracy of the assessment of the tumor size through the use of diagnostic imaging, is essential for a correct therapeutic planning. Preoperative measurements of the breast lesions are commonly obtained with DM and/or US and, in accordance with the European guidelines, only in selected cases with MRI. Recent imaging technique introduced as a complementary and/or additional to DM, DBT seems to be able to overcome one of the major limits of 2D technique, by reducing the obscuring effect of overlying tissues and allowing a better view of lesion margins. Our hypothesis is that DBT can be more precise than DM in evaluating measurements of the lesion size for its peculiar method, approaching the accuracy of the MRI. Thus the aim of the study was to compare the accuracy of DM, DBT, and MRI in the preoperative assessment of tumor size taking into account histological examination (used as a gold standard) in 60 patients with breast cancer.
Methods and materials

The institutional review board approved this retrospective study in which we reviewed 71 breast cancers in 60 patients waiving the requirement to obtain any informed consent. All patients underwent DM, DBT, and MRI between January 2015 and March 2017, before definitive surgery. The patients had a mean age of 52.5 years (range, 34-71 years). Patients undergone to neoadjuvant chemotherapy were excluded from the study. All patients meeting the following inclusion criteria (approved by the local ethics committee) in accordance with the literature and the European Society of Breast Cancer Specialists (EUSOMA) guidelines. The 60 patients included in our study underwent preoperative MRI staging for: (1) newly diagnosed invasive lobular carcinoma; (2) high risk of breast cancer; (3) being eligible candidates for partial breast irradiation (PBI) on the basis on conventional imaging. Others EUSOMA recommendations, considered in our study, included patients: (1) with dense breasts; (2) with multifocal, multicentric or bilateral cancer (invasive and/or ductal carcinoma in situ, DCIS) demonstrated on conventional imaging and confirmed by pathology; (3) with unilateral unifocal pure DCIS at conventional imaging (to exclude synchronous ipsilateral or contralateral invasive carcinoma); (4) candidate for total skin-sparing mastectomy (evaluation of nipple-areola complex). Furthermore all patients underwent combined DM and DBT (combo mode): (1) women proposed for needle biopsy; (2) asymptomatic women between 30 and 80 years. Before to be undergoing the mammographic examination, all patients were informed about the technical aspects, benefits and risks of the DBT, and they subsequently gave their informed consent. Combo mode is performed through the acquisition of standard bilateral two-view mammograms (cranio-caudal and medio-lateral oblique) once in DBT and then within a single compression for each projection in DM. The mammography machine was Senographe Pristina 3D. Nine low-dose DBT projection images are acquired during movement of the x-ray tube through a 25° arc (±23.4°). Overall scanning time is about 5 seconds and reconstruction time about 10 seconds. All patients were subsequently underwent preoperative MRI (Area 1.5 T, Siemens) using a dedicated 4-channel phased-array coil. The DBT, DM (evaluated individually or in combination) and MR images were reviewed for retrospective independent interpretation by two experienced radiologists in breast imaging (with more than 2 years of experience in DBT); the radiologists were aware of the study purpose, but were blinded to the histological lesion size. Images of each modality were presented randomly to each reader in separate sessions and any discrepancy in opinion was resolved by consensus. For each lesion visible on DM, DBT and MRI, the the major axis of the tumour size using dedicated software on the workstation. All patients underwent surgical excision of the primary tumour and sentinel lymph node biopsy and/or axillary dissection. The breast sample were sent to the Pathology Department laboratories of the of our hospital, after verification of current presence of the lesion in the surgical specimen by radiographic evaluation. Each sample, after macroscopic measurement, was cut into multiple 4-mm-thick sections from the deep margin to the superficial edge towards the skin. Each slice of
breast tissue was placed on sheet of blotting paper, taking care to maintain the orientation established by the surgeons. If the lesion was visible, it was macroscopically measured along the two main axes, and its distance from each surgical resection margin was recorded. When the tumour was not macroscopically identified, sampling was performed following the indications of the radiologist and showing the exact position of the lesion on the radiograph of the piece, received at the Pathology Department. Moreover, in each individual case the opportunity to perform macrosements was evaluated, which were set up especially in cases where the tumor was (i) particularly extended, (ii) not delimitable with certainty for the presence of spicule or thickening around to the neoplasm, (iii) not visible macroscopically, as in the case of in situ tumors with intra-adipose growth and diffusion and identifiable only for the presence of microcalcifications. The sampling phase was carried out using a photographic equipment, installed under the extraction hood, which allows images of each level to be acquired, as well as marking on them the exact location of the single sampling. The samples were placed in special plastic biocassettes and then in the automatic processor where they underwent passages in alcohols, xylene and paraffin. After processing, the tissue in the biocassettes was included in paraffin and were cut from this section 4 micron thickness, which were placed on slides and stained with hematoxylin and eosin. The microscopic histological dimensions of the lesions were made on the slides using a metric eyepiece. Moreover, in cases that are more difficult to delimit, given the presence of multiple foci in different areas, the overall extension has also been obtained through 3D reconstructions. In fact, if the visualization of the neoplasia occurred on sections at different levels, being aware of the thickness of the single level, it was possible to obtain a three-dimensional measurement of the lesion.

Statistical Analysis: for each lesion the difference in millimeters was calculated between the measurement detected by each imaging method and the histological examination, in order to evaluate the concordance and to reproduce the dispersion of the sample. Measurements were considered consistent with histology if included within ± 5 mm, underestimated and overestimated respectively if <5 mm and > 5 mm compared to histological examination. In the assessment of concordance, the lesions were also stratified according to the dimensions 2 cm and > 2 cm. The statistically significant differences between the values observed in the study were calculated using the Student’s t test, using a value of p <0.01 as significance threshold.
Results

The agreement between the measurements performed with the individual imaging methods and the definitive histological examination is shown in Table 1. DM was the least consistent method with histological examination: 38 cases (53.5%) were concordant, 10 underestimated (14%) and 10 overestimated (14%); 13 lesions were not visible to DM (18.3%). For lesions measuring 2 cm the concordance between DM and histological examination was 65.9%, for tumors > 2 cm was instead of 39.1%. The DBT had a concordance with the histological examination of 66.1% (47 cases); 8 cases were underestimated (11.2%) and 8 overestimated (11.2%); 8 lesions were not visible (11.2%). By dividing the concordance according to the dimensions found in the histological examination, for lesions measuring 2 cm the concordance was 77.6%; for lesions > 2 cm it was 51.6%. The MRI was the absolute method with the greatest concordance with respect to histology: in fact, 50 lesions, equal to 70.4%, were concordant, 6 (8.4%) underestimated and 12 (16.9%) overestimated. 3 lesions (4.2%) were not diagnosed with MRI. For cases of lesions of 2 cm we had a concordance of 83.5% with histology; in > 2 cm instead it was 53.1%. Overall, among the three imaging modalities, the differences between the concordances that were statistically significant (p < 0.01) were between MRI and DM and between MRI and DBT. The differences in concordance between DBT and DM were not statistically significant (p > 0.01). As can be seen in Table 2 the correlation coefficient we obtained (R: 0.89) is comparable to the R: 0.86 value described in the study by Förnvik et al. The MRI in our work has proved to be the best method for the evaluation of the extent of infiltrating carcinomas, although the DBT has obtained a value only slightly lower (R: 0.89). In particular, MRI confirmed, in agreement with the literature [1-11], the method with the highest correlation with the histological examination (R: 0.92), but the DBT obtained similar values (R: 0.89) thus allowing a similar preoperative staging. The DM instead obtained lower values (R: 0.83) (Figure 1).
Fig. 1: Figure 1. DM, DBT and MRI examinations of an asymptomatic 44-year-old patient with dense breasts (BI-RADS 3). (a,b) The right and left medio-lateral oblique (MLO) mammograms projections show architectural distortion of the mammarian glands bilaterally and respectively between outer quadrants and inner quadrants (c,d) On the 3D images respectively in the outer and inner quadrants of the right and left breasts the margins of these lesions are more defined in particular it is possible to notice a well defined retroareolar spiculated mass in left medio-lateral oblique (MLO). (e,f,g,h) The axial MRI dynamic acquisitions confirmed the masslike lesions between the outer quadrants of the right breast and inner quadrants of the left breast characterized by
heterogeneous contrast enhancement and irregular shapes. (i) The MIP axial image show extensions of the lesions bilateraly on the breasts on unique plane.

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<table>
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<tr>
<th>CONCORDANCE</th>
<th>DM</th>
<th>DBT</th>
<th>RM</th>
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<tr>
<td>UNDERESTIMATE</td>
<td>10</td>
<td>8</td>
<td>6</td>
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<tr>
<td>ACCORDANT</td>
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<td>47</td>
<td>50</td>
</tr>
<tr>
<td>OVERESTIMATED</td>
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<td>8</td>
<td>12</td>
</tr>
<tr>
<td>NOT VISIBLE/ NOT MEASURABLE</td>
<td>13</td>
<td>8</td>
<td>3</td>
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<tr>
<td>TOTAL</td>
<td>71</td>
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Table 1

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Table 2

<table>
<thead>
<tr>
<th>Years</th>
<th>Authors</th>
<th>Cases, n</th>
<th>Mean lesion diameter (mm)</th>
<th>Statistical test</th>
<th>DM</th>
<th>DBT</th>
<th>MRI</th>
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<tr>
<td>1996</td>
<td>Davis et al.</td>
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<td>22</td>
<td>R</td>
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<td>33</td>
<td>R</td>
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<td>=</td>
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<tr>
<td>2001</td>
<td>Hieken et al.</td>
<td>146</td>
<td>15</td>
<td>R</td>
<td>0.40</td>
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<td>=</td>
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<tr>
<td>2003</td>
<td>Bosch et al.</td>
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<td>17</td>
<td>R²</td>
<td>0.44</td>
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<tr>
<td>2006</td>
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<td>400</td>
<td>14</td>
<td>R²</td>
<td>0.74</td>
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<td>Onesti et al.</td>
<td>91</td>
<td>=</td>
<td>R</td>
<td>=</td>
<td>=</td>
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<td>2008</td>
<td>Mann et al.</td>
<td>67</td>
<td>=</td>
<td>R</td>
<td>0.27</td>
<td>=</td>
<td>0.85</td>
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<td>2009</td>
<td>Wasif et al.</td>
<td>61</td>
<td>=</td>
<td>R</td>
<td>0.26</td>
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<tr>
<td>2010</td>
<td>Vrtelova et al.</td>
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<td>R</td>
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<td>R</td>
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<td>2012</td>
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<td>25</td>
<td>R</td>
<td>0.83</td>
<td>0.89</td>
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Conclusion

Accurate measurement of tumour size is essential for the preoperative staging of breast carcinoma, in order to establish correct surgical treatment planning, especially when breast-conserving surgery is being contemplated\(^5\). Although the final histological examination is considered as the gold standard, surgical and therapeutic decisions must be made on the basis of imaging, mainly with conventional modalities (DM and US), and supported by MRI in selected cases. The US technique often underestimates tumour size, even though it is especially useful in patients with dense breasts, in which mammographic lesions are difficult to assess due to overlying tissues or the summation of different structures \(^2,5\). However, while US is capable of measuring in multiple planes, it should be noted that often the largest dimension of the lesion cannot be measured, especially if we consider that many cancers are vertical lesions with prevalence of height on the width. These lesions are characterized by the presence of a rear shadow cone that obscures the deep margin, thus making the measurement on the major axis more difficult\(^2\). According to the literature data\(^1,9,10,11\), MRI is the most accurate and sensitive preoperative imaging modality for the evaluation of tumour extent (although it has a substantial risk of overestimation) and for the detection of multifocal, multicentric breast cancer\(^3,6\). In addition, MRI is currently considered the most reliable method for preoperative staging of invasive lobular carcinomas; in fact, as reported in a recent literature review\(^12\), MRI has a sensitivity of 93% in detecting this special type of tumour and a high level of agreement with histology; MRI also allows the detection of contralateral occult lesions in 7% of cases, changing the surgical approach in about 25% of patients\(^4\). The MRI, according to the literature, is the most accurate and sensitive exam among all the pre-operative imaging modalities for the evaluation of the real tumor extension (although it tends to overestimate it) and for the diagnosis of multifocality and multicentricity. As outlined above, DM lesion measurements are often difficult due to the effect of masking and to the tissues superposition. Moreover, DM tumour measurement can be influenced by variations in the distance between the tumour and the detector, by poorly delineated tumour outlines and by compression of the breast during examination. In addition, standard mammographic projections do not always capture the maximum tumour size. The use of additional mammographic views (magnification or compression) can improve visualisation of lesion margins\(^2\). Actually, there is only one published study\(^5\) that analysed the accuracy of DBT in the evaluation of tumour size, and no studies comparing DBT and MRI in the preoperative assessment of breast cancer size. In our study, MRI and DBT measurements had the highest correlation with pathological tumour size and thus provided better results than DM. DBT and DM (the latter had the lowest agreement with pathology compared to the other imaging modalities) had an equal number of over- and underestimated cases. Most literature reports, however, state that DM underestimates the true size of lesions, especially spiculated lesions, due to difficulties in assessing their margins\(^5\). MRI, consistent with other studies\(^1,4,6\) tends
to overestimate true tumour size (in 16.9% of cases in our series), but it proved to be the most accurate modality, as it had the least standard deviation from the size at pathology and therefore showed the least dispersion in the sample\textsuperscript{9}. MRI and DBT can provide different types of information about suspicious breast lesions, thanks to the use of contrast medium; MRI is able to provide information about vascularized lesion which DBT cannot provide. The first clinical experiences, however, seem to indicate a favourable impact of DBT in the detection of breast lesions. Tomographic reconstruction allows to isolate breast lesions which are more affected by tissue overlap and thus by overlying structures on conventional mammography. Therefore, DBT seems to be able to play a major role in breast imaging and, according to our data, even in the preoperative staging of breast cancer\textsuperscript{13,14}. Despite the good results in terms of dimensional accuracy and breast lesion detection demonstrated by DBT, compared to DM and US, we have to consider some limitations of our study. The retrospective review of the DM, DBT, US and MRI images and the lesion measurements were performed by the same two radiologists who, although unaware of pathological size, were not blinded to the individual methods, so it cannot be excluded that one type of imaging may have partly influenced the other ones. In conclusion, although DBT is superior to DM in the evaluation of tumour size and our results confirm that MRI still remains the most accurate imaging technique in preoperative staging of breast cancer.
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