REVIEW ARTICLE
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BREAST TOMOSYNTHESIS: A BETTER MAMMOGRAPHY

Tomossíntese mamária: uma mamografia melhor

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ABSTRACT

Digital mammography is an excellent method for detecting breast cancer at an early stage, but overlap of breast structures may lead to both false-positive and false-negative results. The digital breast tomosynthesis (DBT) is addressed to overcome this limitation of conventional 2D mammography. The purpose of this study was to discuss the multiple aspects related to this new tool, including its role in breast cancer screening, through a literature review. DBT, or 3D mammography, provides a three-dimensional representation of the breast, with the ability to scroll through breast tissue in the reconstructed images, thereby reducing the effect of tissue superimposition. This leads to improved sensitivity and specificity in breast cancer screening. In diagnostic cases, tomosynthesis increases the accuracy with better characterization and localization of the lesions. Prospective and retrospective studies confirm that DBT is superior to digital mammography in breast cancer screening, with 27 to 53% increase in cancer detection and 17 to 37% reduction in false-positive recalls. A total of 40 to 49% of the cancers detected by DBT were invasive: 40 to 48% of histological grade 2 or 3 and more than 75% were node negative. DBT is the most promising new modality for breast cancer screening. Further studies are needed to evaluate the reduction of interval cancers with this modality.

KEYWORDS: mammography; mass screening; breast neoplasms.

RESUMO

Mamografia digital é um método excelente para detecção precoce do câncer de mama. Porém, a sobreposição das estruturas mamárias pode levar a resultados falso-positivos e falso-negativos. A tomossíntese mamária é dirigida para superar essa limitação da mamografia 2D convencional. O objetivo deste estudo é discutir os múltiplos aspectos relacionados a essa nova ferramenta, incluindo, através de uma revisão da literatura, seu papel no rastreamento do câncer de mama. A tomossíntese mamária, ou mamografia 3D, proporciona uma representação tridimensional da mama, com a habilidade de podermos visualizar as imagens reconstruídas em diversos planos, reduzindo o efeito da sobreposição. Isso conduz a uma melhora da sensibilidade e da especificidade no rastreamento mamográfico. Nos casos diagnósticos, aumenta a acurácia com melhor caracterização e localização das lesões. Estudos prospectivos e retrospectivos confirmam que, no rastreamento do câncer de mama, a tomossíntese mamária é superior à mamografia digital, com aumento da detecção de 27 a 53%, e na redução das reconvocações falso-positivas entre 17 e 30%. De 40 a 49% dos cânceres detectados pela tomossíntese foram invasivos: de 40 a 48% de grau histológico 2 ou 3 e mais de 75% foram linfonodo negativos. Tomossíntese mamária é a nova modalidade mais promissora para o rastreamento do câncer de mama. São necessários estudos adicionais com essa nova modalidade para a avaliação da redução dos cânceres de intervalo.

PALAVRAS-CHAVE: mamografia; programas de rastreamento; neoplasias da mama.

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INTRODUCTION

Breast tomosynthesis or 3D mammography is a technological advancement in digital mammography, which allows three-dimensional representation of breast tissue from two-dimentional projections. It was developed to overcome an important limitation of conventional digital mammography (2D), which is normal overlapping tissue during the acquisition of the radiographic image. This limitation of 2D mammography may lead to low sensitivity in detecting some cancers and high false-positive recall rates (due to summation images). Tomosynthesis reduces the impact of overlapping breast tissue by depicting tissue on a dynamic sequence of thin cross-sectional images which results in a considerable increase in diagnostic accuracy (Figure 1A)[1-4].

HOW IS TOMOSYNTHESIS OBTAINED?

Tomosynthesis uses a digital mammograph, in which the X-ray source moves in an arc above the compressed breast and a series of low-dose x-ray projections are acquired at different angles (Figure 1B). From these two-dimensional projections, 3D images (tomosynthesis slices) are reconstructed, with 1 mm thickness, parallel to the detector. The number of slices depends on breast thickness : thus, in a 5-cm breast, 50 slices per mammographic incidence are obtained. All images are analyzed in high resolution monitors, either individually or in cine mode (Figure 2)[4-6].

The are different commercially systems available with variations in scan angle, number of projections and scan time.

Exam technique

Patient positioning and breast compression at tomosynthesis are similar to that at DM, typically using standard craniocaudal and mediolateral oblique projections. The approval of tomosynthesis by the Food and Drug Administration (FDA), in the United States, in 2011, was based on the "combo mode": 3D images are obtained along with 2D DM images during the same compression. Although tomosynthesis is superior to detect non-calcified lesions (nodules and architectural distortions), the 2D images gives us a panoramic view of the breasts, which allows better analysis of asymmetries and comparison with previous examinations[3,4].

Similar to conventional mammography, two views of each breast are recommended with tomosynthesis, since some lesions may be seen only in one projection. Clinical studies have shown that about 9% of the tumors may be missed if only one incidence of tomosynthesis is used.

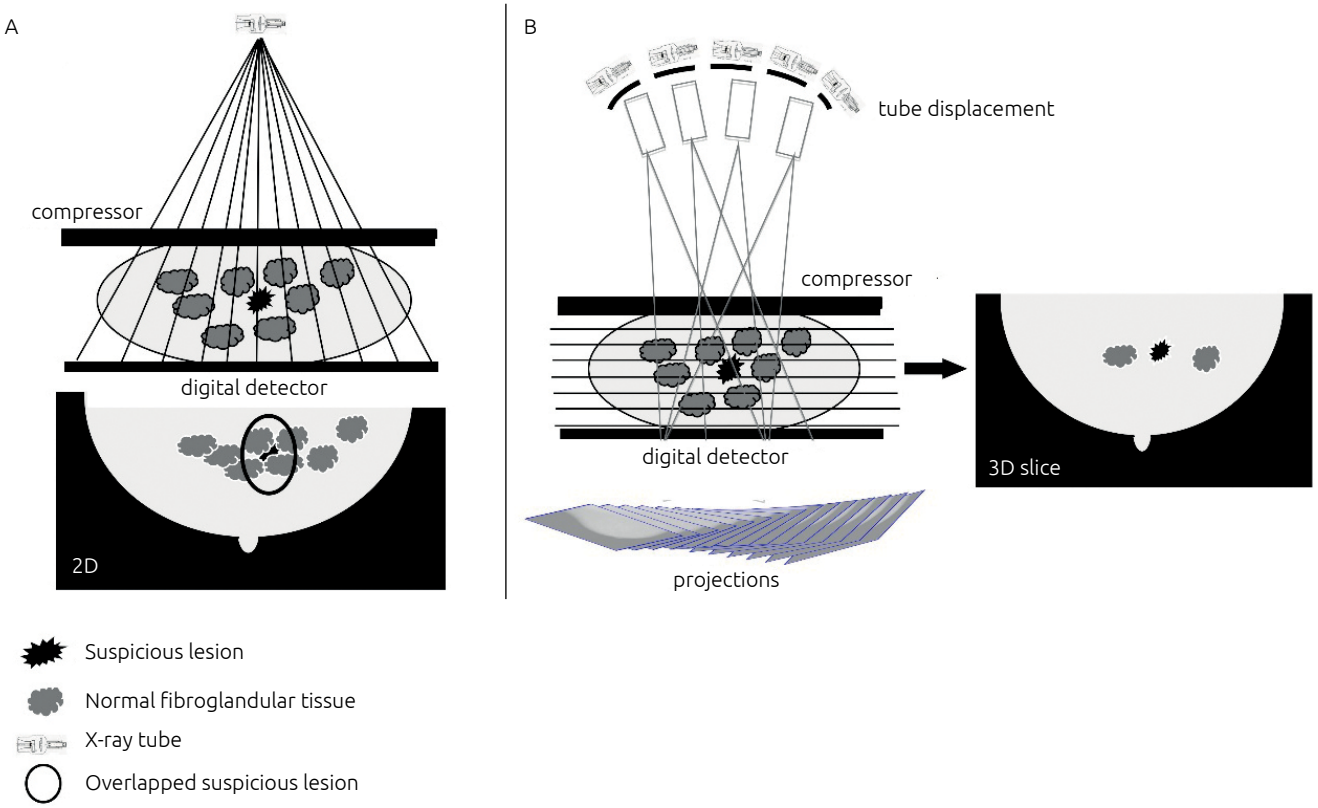


Figure 1. Schematic acquisition of mammographic images during breast compression: (A) conventional digital mammography (2D) shows overlap of normal structures and suspicious lesion; (B) tomosynthesis (3D) reduces tissue overlap by detecting the suspicious lesion in one of the slices.

Radiation dose

The disadvantage of combination of DM and tomosynthesis is an approximate twofold increase in radiation dose, although the total dose still falls within the safety limits determined by American and European regulatory agencies[7]. Concerns regarding increased radiation dose has led to other alternatives, such as:

1. Replace 2D mammography by SM (synthesized mammography), in combination with tomosynthesis. In this case, the performance of the combined test is similar, without increasing the total radiation dose[8-10];
2. Tomosynthesis with only one view, combined to 2D mammography [4,11]. However, this option can reduce sensitivity and especificity of the exam, when compared to tomosynthesis performed in two projections[11-13].

2D SYNTHESIZED MAMMOGRAPHY

Synthesized mammography (SM) is a technique that generates two-dimensional images from the DBT dataset, eliminating the need for a separately acquired FFDM examination and thereby decreasing the radiation dose to the patient. [8,10]. Although SM's initial version was not well accepted due to its limited technical quality, recent studies found that its updated version presented the same performance of the conventional 2D image. Although the mathematical algorithms to obtain synthesized images are different among the manufacturers, the objective is similar and consists in obtaining the information provided by 2D images – panoramic view of the breasts, comparison with previous mammograms and evaluation of microcalcifications - without extra dose of radiation. It is important to emphasize that the SM must be analyzed along with the tomosynthesis slices, never as an isolated study[10].

Breast anatomy in tomosynthesis

Although normal anatomy is similar in 2 D and 3Ds images, the reduction of overlapping tissue in the tomosynthesis slices allows better individualization of breast structures. In slices closest to the detector and the compressor, the dermis and cutaneous pores (round radiolucent images) and eventual cutaneous lesions, such as *nevi*, or calcifications are better seen. Cooper ligaments and linear structures in pre-parenchymal fat are seen brighter in tomosynthesis slices than in conventional mammography. The fibroglandular tissue is gray, with a lower density in relation to the 2D image, due to the smaller amount of breast tissue evidenced in each slice. High density objects, such as markers and metal clips and larger calcifications, may produce artifacts that, however, do not interfere with image interpretation. Tomosynthesis increase lesion conspicuity with better definition of margins and spicules, due to reduction in tissue overlapping.[3,4].

The characteristics of the parenchyma texture in the tomosynthesis correlate better with breast density than digital mammography, and may become a method of measuring breast density, resulting in a quantitative biomarker to estimate the risk of cancer.

SM presents its own characteristics, different from the conventional image: brighter mammary parenchyma, blurring of skin and subcutaneous tissue, loss of resolution of axillary area, pseudocalcifications and artifacts generated by clips or other high-density images. SM enhances linear structures - such as Cooper's ligaments or spicules associated with masses or architectural distortions - and increases brightness and contrast of calcifications. The extreme dense breasts (ACR D) appear brighter in the SM due to the summation of the tomosynthesis slices (Figure 3).

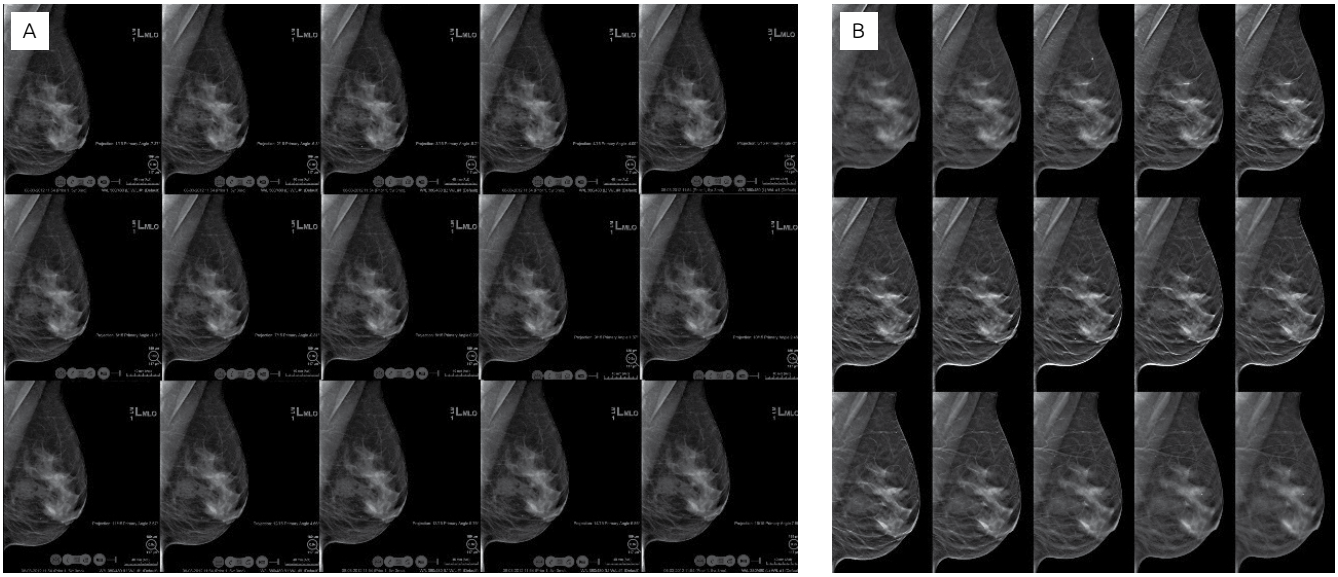


Figure 2. (A) Low-dose radiation projections; (B) from which 1 mm thick tomosynthesis slices are reconstructed.

Exam interpretation

Due to the large number of images obtained with tomosynthesis, the analysis of the exam must be performed in a systematic way, with implementation of a hanging protocol in the high-resolution monitor, to optimize reading time. Interpretation of the exam starts with the analysis of the 2D images (conventional or synthesized) for detection of calcifications, asymmetries, masses or architectural distortions. Next, a comparative analysis is performed with previous mammograms to characterize developing asymmetries or other new lesions. Tomosynthesis images are interpreted with two-dimensional mammography, using the latter as a "road map" for each mammographic incidence[1,4,14].

It is necessary to obtain conventional (2D) digital mammography along with tomosynthesis, since each method provides different types of information in the analysis of mammographic findings (Chart 1).

Tomosynthesis slices must be seen sequentially (cine mode), breast by breast and incidence by incidence. It is important to mentally divide the breast into 2 or 3 segments and look at each of them separately, during at least one cine mode cycle, to increase detection of small lesions[1,14].

Exam interpretation time

Tomosynthesis is an easy-to-implement technology because the examination is performed in the same way as conventional or digital mammography. However, interpretation time is longer due to a large number of images to be analyzed, which requires more concentration and focus from the radiologist, resulting in greater mental and visual fatigue[15,16]. One of the alternatives proposed to reduce interpretation time is to abolish the double reading of tomosynthesis examination, which, according to Houssami et al.[17], does not change the benefits of tomosynthesis (increase in detection of invasive cancer and reduction of false-positive recalls), compared to DM alone.

The learning curve and the optimization of reading time with the implementation of a flowchart in the monitor (report flow) are fundamental to reduce the time of interpretation in tracing[14]. The availability of computer-aided detection (CAD) systems for synthesized image and tomosynthesis slices and the use of thicker tomosynthesis images (slabs), instead of 1 mm slices, are alternatives for the reduction of interpretation time.

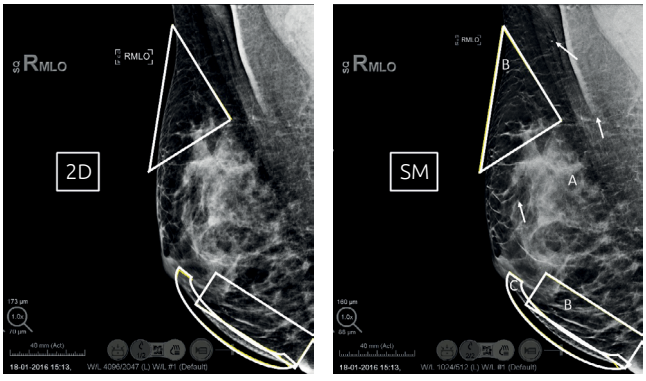


Figure 3. Comparison of 2D with synthesized mammography: in synthesized mammography (SM), there was an increase of the contrast with the parenchyma (A) with greater intensity (whiter), greater enhancement of the ligaments (B) and of the linear structures in pre-parenchymatous fat, greater prominence of calcifications (arrows). The increased intensity in the peripheral area of the image (C) dos not represent greater skin thickness and is associated to the reconstruction program, noticing lesser prominence in more recent versions.

IMPACT OF TOMOSYNTHESIS IN COMPUTER DEPARTMENTS

In tomosynthesis examination, the images of each slice generate the same volume of data as a 2D. The number of slices is proportional to breast thickness and usually 30 to 70 slices are obtained, with the total volume of data generated by the tomosynthesis, by incidence, significantly higher than in 2D. This fact has several implications for the storage of images.

The size of the tomosynthesis file also implies the time and speed of transmission and retrieval of the examination. Compaction softwares are used for better storage and transmission performance of tomosynthesis.

Chart 1. Degree of information provided by tomosynthesis and conventional digital mammography on different aspects in the analysis of the images.

	2D	Tomosynthesis
Visibility of lesions	++	+++
Margin analysis	+	+++
Location of the lesions		+++
Extent of the lesions		+++
Multifocality	+	+++
Density associated with calcifications		+++
Reduction of summation	+	+++
Recall reduction	+	+++
Asymmetries	+++	+
Interval changes	+++	+
Comparison with previous ones	+++	+
Calcifications (detection)	+++	++
Calcifications (distribution)	+++	+

+: low grade; ++: medium grade; +++: high grade.
Source: Rafferty and Belfer[15].

INDICATIONS OF TOMOSYNTHESIS

The indications for tomosynthesis are the same as for conventional digital mammography: it can be used as a diagnostic or screening test for early cancer detection. Due to the reduction of tissue overlap, tomosynthesis presents several advantages over the 2D, such as:

1. Increase in cancer detection rate (Figures 4, 5 and 6);
2. Reduction of false-positive recalls and additional mammographic projections, especially spot compression, which means reduction of the total dose of radiation (Figure 7);
3. Increase in the conspicuity of noncalcified lesions (masses, asymmetries and architectural distortions) (Figures 8, 9 and 10);
4. Reduction in the percentage of category 3 lesions (ACR BI-RADS), especially asymmetries;
5. Detection and location of lesions seen in only one incidence (Figures 11 and 12);
6. Confirm cutaneous lesions (Figure 13);

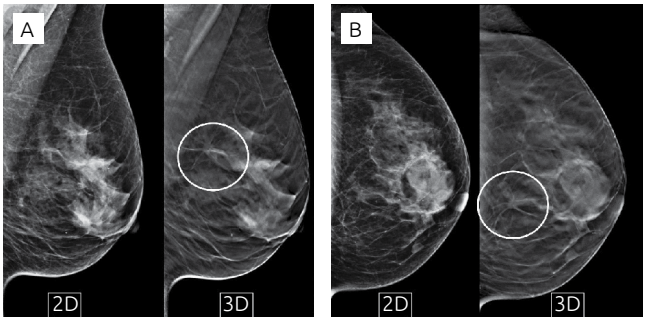


Figure 4. Conventional digital mammography (2D) and tomosynthesis representative slice (3D), 1 mm thick, evidenced spiculated nodule (circle): (A) mediolateral incidence; (B) craniocaudal incidence. Histology: invasive carcinoma.

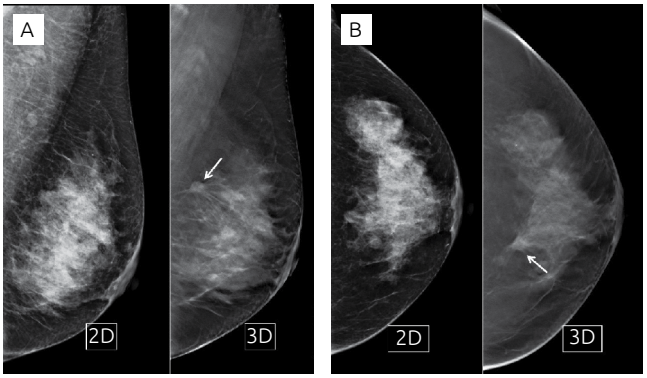


Figure 5. Conventional digital mammography (2D) and representative tomosynthesis slice (3D), 1 mm thick, evidenced spiculated nodule (arrows) identified only in tomosynthesis: (A) mediolateral incidence; (B) craniocaudal incidence. Histology: invasive carcinoma.

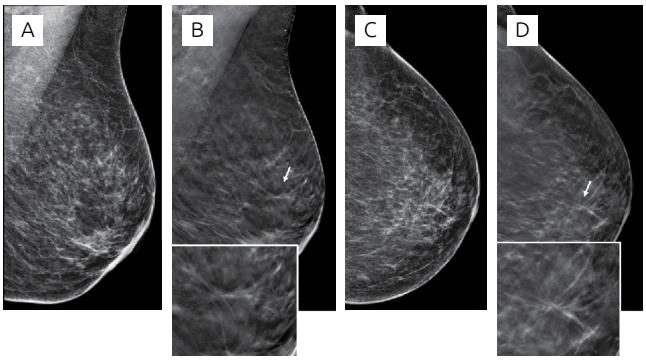


Figure 6. Architectural distortion (arrows and details) evidenced in tomosynthesis slices (B and D) and not expressed in 2D (A and C). Histology: invasive lobular carcinoma.

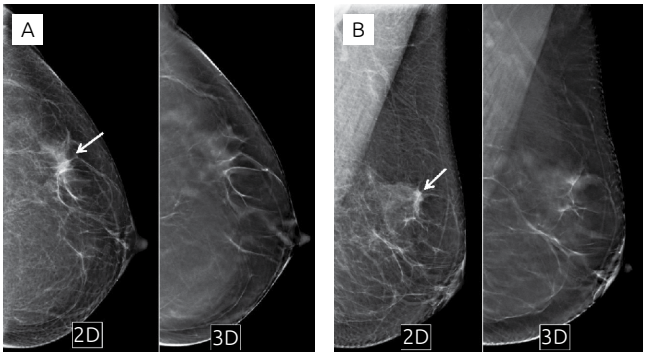


Figure 7. The density (arrows) observed in conventional digital mammography (2D) does not correspond to tomosynthesis slices (3D), representing overlap of normal tissues (pseudolesion): (A) craniocaudal incidence; (B) mediolateral incidence.

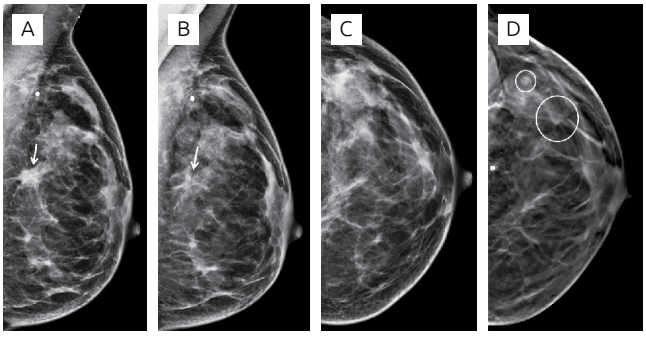


Figure 8. Patient was recalled for evaluation of irregular asymmetry in the upper/posterior third of her left breast (arrow), in the oblique mediolateral incidence in 2D (A). Tomosynthesis slice (B) was shown to be tissue overlap. In tomosynthesis slice, in craniocaudal incidence (D), an architectural distortion area (larger circle) was observed, not evidenced in 2D in craniocaudal incidence (C) and an irregular nodule (smaller circle) was better characterized in the same slice (D).

TOMOSYNTHESIS IN SCREENING

Performance of tomosynthesis in screening was investigated in a series of prospective, retrospective, single-institution or multi-center studies, all using 2D mammography along with tomosynthesis *versus* the 2D one alone. The first publications on tomosynthesis emphasized the reduction of the recall rate (15 to 37%) as its primary advantage[18,19]. The multicenter study, published by Rafferty et al. in 2013, was crucial in demonstrating that tomosynthesis, in addition to reducing the number of recalls, significantly increased the diagnostic accuracy in relation to 2D mammography[20].

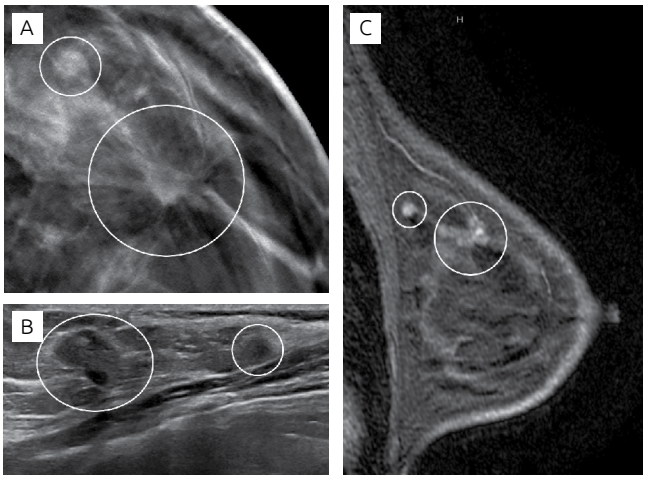


Figure 9. Correlation between tomosynthesis (A), ultrasonography (B) and magnetic resonance imaging (B) showing the nodule (smaller circle) and area of architectural distortion (larger circle).

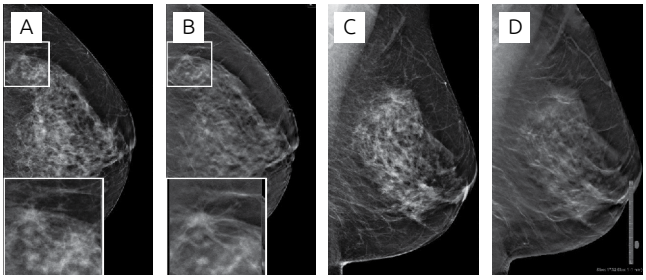


Figure 10. Nodule evidenced in craniocaudal incidence, in 2D (A) shows radiolucent center in tomosynthesis slice (B) and represents intramammary lymph node.

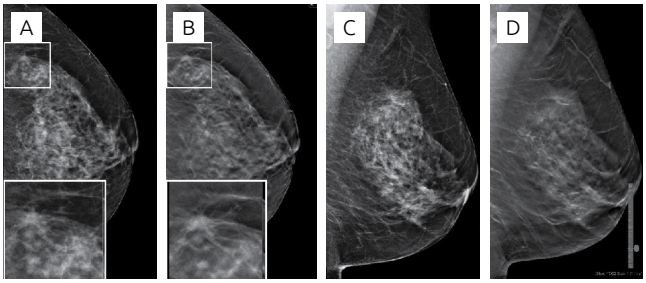


Figure 11. Finding observed only in craniocaudal incidence in 2D (A). Lesion's infiltrative margins are characterized in tomosynthesis slices in craniocaudal incidence (B). The lesion is not observed in 2D nor in tomosynthesis in mediolateral incidence (C and D). Histology: Invasive Lobular carcinoma grade I.

Prospective studies

Prospective clinical studies are all European, although they have different study designs. The largest one, carried out in Oslo (Oslo Tomosynthesis Screening Trial – OTST), used independent double reading and analyzed the first results in 12,631 women in the screening program at the University of Oslo, aged between 50 and 69, who performed 2D together with tomosynthesis, two views per breast and per modality. The combination of tomosynthesis and 2D increased the cancer detection rate by 27% compared

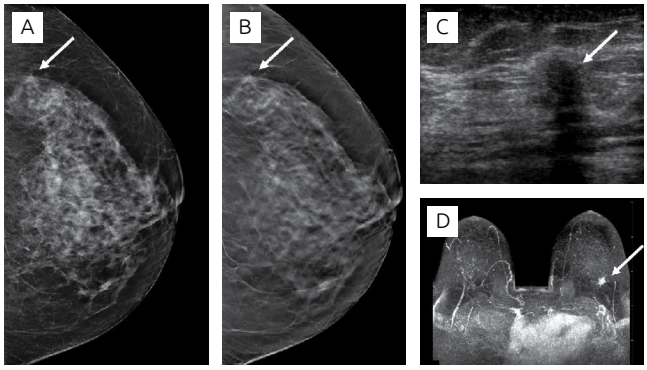
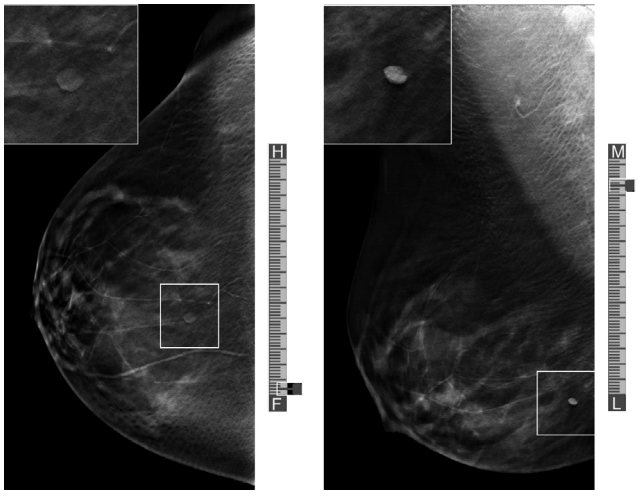


Figure 12. Correlation of the finding observed only in craniocaudal incidence in (A) and in tomosynthesis (B) with ultrasound (C) and with magnetic resonance imaging (D). Histology: Invasive Lobular carcinoma grade I.



H: head; F: feet; M: medial; L: lateral.

Figure 13. Location of the lesion in tomosynthesis. The lateral bar demonstrates the lesions are in the lower (F) and medial (M) quadrant, at the extremity of the bar, demonstrating the quadrant and its cutaneous location.

to 2D alone (absolute increase of 1.9 cancers/thousand women screened by tomosynthesis) and, at the same time, reduced the recall rate[17].

The Italian study (Screening with Tomosynthesis OR standard Mammography – STORM1), carried out in two cities Trento and Verona, included 7,292 women who did both - 2D and tomosynthesis – in two views per breast per modality, with double sequential reading. Their final results were promising: a relative increase of 53% in cancer detection with tomosynthesis (an increase of 2.8 cancers/thousand) and 17% fewer recalls[21].

STORM 2 is another population-based prospective study, based on STORM 1, which included 9,672 women. In this study, all patients were screened with 2D and tomosynthesis, and SM was also used: the combined examination, either with a 2D (COMBO mode) or with SM (TOMOHD mode), detected more cancers than the digital mammography alone. There was an increase of 35 and 40% (COMBO and TOMOHD, respectively) in cancer detection rate, with an increase of 2.2 and 2.5 cancers/thousand). However, there was a slight increase in false-positive recall with the combined examination, compared to 2D alone, especially with the use of SM[22].

The study performed in Malmö, Sweden (Malmö Breast Tomosynthesis Screening Trial – MBTST), differs from the previous ones because it was designed to evaluate the efficacy of only one view of tomosynthesis (mediolateral oblique) *versus* two views of 2D mammography (craniocaudal and MLO). The first results included 7,500 women, aged 40 to 74 years old, invited to perform both modalities. Tomosynthesis (in just one view-MLO) increased cancer detection rate by 43% (2.6 more cancers/1000 women). Although radiation dose was lower, there was an increase in the recall rate, probably due to the use of only one view of tomosynthesis[23].

In summary, prospective studies showed a 26 to 43% increase in cancer detection rate with the addition of tomosynthesis to 2D mammography, basically at the expense of invasive carcinomas. It is important to remember that these results reflect prevalent exams, that is, the first tomosynthesis examinations in these populations (Table 1)[24].

Retrospective studies

American studies on tomosynthesis are retrospective, comparing isolated 2D *versus* digital mammography associated with tomosynthesis. Some of them should be highlighted as pioneers: Rose et al.[19], with a 25% increase in cancer detection, in a private clinic; Haas et al.[18], with an increase of 10% in an academic center and reduction of recall rate from 37 to 30%. The work of McCarthy et al.[25] has, in fact, demonstrated the impact of tomosynthesis on screening after its implementation in a population in a single academic center in the United States. The screening was performed in all women, from October 2011 to February 2013 (n = 15,571 women) with a significant reduction in the number of recalls in the group with tomosynthesis. Overall, the increase in cancer detection was small (0.9 additional cancers/thousand women), but analysis of subgroup showed a significant increase in cancer detection among women younger than 50 years[25]. In 2014 , a large US retrospective multicenter study was published (13 academic or private institutions), including 281.187 women undergoing FFDM only and 173.663 women having 2D+ 3D . The results showed a 29% increase in cancer detection rate and 15% decrease of recalls, after implementation of tomosnthesis,.

In 2015, data from the TOMMY TRIAL (Comparison of TOMosynthesis with digital Mammography in the UK NHS Breast Screening Programme), a retrospective, multicenter study with the participation of several radiologists was published, comparing the performance of tomosynthesis and 2D *versus* isolated 2D in the mammography screening program of the United Kingdom. Women aged between 29 and 85 years (mean 56 years) were recruited from July 2011 to February 2013 and the final analysis consisted of 7,060 cases. All participants performed 2D (on two incidences) and tomosynthesis (on two

Table 1. Resultas obtained with prospective and retrospective studies in the screening of breast cancer.

Design of the study	Type of Reading	Population (n)	Age range (years)	Recall rate	Detection rate /1000 (2D)	Detection rate/1000 (tomosynthesis)	Relative carcinoma increase
Prospective paired	Sequential pair	7,292	48 to 71	-17%	5.3	8.1	53%
Prospective paired	Independent pair	12,631	50 to 69	-13%	6.1	8.0	27%
Prospective paired	Sequential pair	7,500	40 to 74	43%	6.3	8.9	43%
Prospective	Sequential pair	9,672	53 to 63	16%	6.3	8.8	35%
4 arms				30%	6.3	8.8	40%
Retrospective unpaired	Single reading	2D: 281,187		-16%	4.2	5.4	29%
		3D: 173,663					

incidences), with SM replacing 2D, as of 2011. The results showed increased specificity with tomosynthesis in all subgroups: age range, breast density and mammographic findings. Regarding sensitivity, tomosynthesis, compared with isolated 2D, was superior in dense breasts, invasive carcinomas of 11 to 20 mm and lesions presented as nodules, with no significant difference between 2D and SM[27].

In Brazil, we have few published data regarding the performance of tomosynthesis. In the private clinic data obtained by one of the authors (Bauab SP) from July 2, 2012 to August 31, 2012, which included 1,220 women aged 40-83 years, submitted to tomosynthesis (COMBO mode or 2D complementary tomosynthesis), 12 cases of invasive cancer were found in asymptomatic patients. Tomosynthesis showed the lesion better in 9 cases, and in 3 cases the lesion was detected only by tomosynthesis, resulting in a 33% increase in the diagnosis of cancer in asymptomatic women.

Data from another private clinic (Aguillar VLN), included 4,314 women - 82% between 40 and 69 years and 58% with dense breasts (ACR C or D) - from September 2011 to August 2014, who were submitted to COMBO mode tomosynthesis, two views for each modality. Twenty-one carcinomas (10 *in situ* and 11 invasive) were detected by 2D and 27 carcinomas (10 *in situ* and 17 invasive) were detected by 3D. The six invasive carcinomas detected by tomosynthesis-only, were all seen as architectural distortions and stage I, positive hormone receptors and only one SL positive, with micrometastases. The cancer detection rate with 2D was 4.87 carcinomas/thousand exams; and with 3D, 6.26 carcinomas/thousand exams, representing an absolute increase of 1.4 carcinomas/thousand exams and a relative increase of 28.6%. Invasive detection rate with 2D was 2.54 invasive carcinomas/thousand exams, whereas with 3D it was 3.94 invasive carcinomas/thousand exams, representing a relative increase of 54%.

Regarding the characteristics of the carcinomas detected only by tomosynthesis, similar results were demonstrated in the prospective and retrospective studies. There was a significant increase in the detection of invasive carcinomas with tomosynthesis: 40% in the study by Oslo[13], 49% in STORM 1[21], 41% in Malmö[23] and 45% in the American multicenter retrospective study[26]. Forty to forty-eigth had histological grade 2 or 3 and 76 to 90% presented with negative sentinel lymph node[14,23]. There was no significant increase in carcinoma *in situ*.

Another important finding were the preliminary results from Malmo Trial (MBTST), presented at the European Congress of Radiology (Vienna, 2017), including all participants of the study (15.000 twomen). Among the additional invasive carcinomas detected only by tomosynthesis, 58% were ductal and 26% were lobular, whereas in the group detected by 2D, only 17% were lobular. The authors suggest that tomosynthesis may have a higher sensitivity for detection of lobular carcinomas compared to 2D mammography (Table 2, Figures 14 and 15)[28].

Diagnostic tomosynthesis:

In diagnostic cases, tomosynthesis increases accuracy, reduces the number of additional mammographic incidences[29,30] and reduces the probability of category 3 lesions of ACR BI-RADS, mainly focal asymmetries[31-33]. Tomosynthesis plays an important role in the confirmation of cutaneous lesions, in the evaluation of findings in a single incidence (mainly asymmetries) and in palpable lesions. It reduces need for additional mammographic incidences, with a faster and cheaper workflow and lower radiation dose[34,35].

Cutaneous lesions such as warts, sebaceous cysts or calcifications are observed in the more superficial slices of tomosynthesis, in which dermis and cutaneous pores are also visualized, confirming the superficial location of these lesions. Tomosynthesis does not require tangential incidences[34].

For asymmetries, tomosynthesis proves that most of the findings observed in only one incidence represent normal breast overlapping with no need for additional projections[33].

For palpable lesions, tomosynthesis, together with ultrasonography, in general, are diagnostic, with no need for extra views, such as spot compression or roll angle incidences (Figure 16)[34,35].

In the presence of a nodule of circumscribed margins evidenced in the tomosynthesis, an ultrasonography should be used to characterize its cystic or solid nature (Figures 17 and 18).

Table 2. Carcinomas detected only by tomosynthesis.

Study	Detection rate/thousand (2D)	Detection rate/thousand (tomosynthesis)	Relative carcinoma increase	Relative invasive carcinoma increase	Histological grade 2 or 3	Negative sentinela lymph node
STORM1[21]	5.3	8.1	53%	49%		60%
OTST[17]	6.1	8.0	27%	45%	40%	76%
MBTST[23]	6.3	8.9	43%	42%	48%	90%
STORM2[22]	6.3	8.8	35%		69%	86%
	6.3	8.8	40%			
Multicenter United State[26]	4.2	5.4	29%	41%		

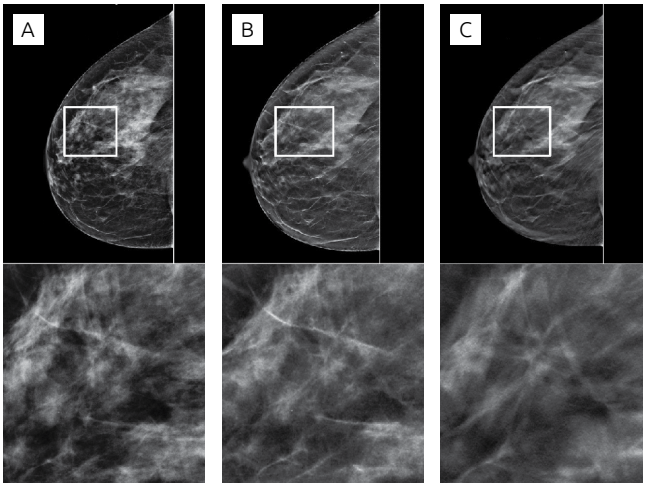


Figure 14. Focal architecture distortion is not evidenced in 2D (A) nor in synthesized 2D mammography (B). It is characterized in tomosynthesis (C).

Breast density and tomosynthesis

A multicentric study specifically developed to correlate the efficiency of tomosynthesis in different mammographic patterns of ACR BI-RADS found that tomosynthesis is better than 2D DM alone in dense or non-dense breasts, justifying its use in any mammographic pattern. However, the subgroup analysis showed that the sensitivity of tomosynthesis is lower in extremely dense breasts (ACR D) than in the other groups due to lack of adipose tissue in the breast, necessary for lesions detection. (Table 3)[36].

Preliminary results with 15,000 participants from the Swedish prospective study by Malmö[23] show that tomosynthesis increases cancer detection in all mammographic patterns. Of the tumors detected only by tomosynthesis, 46% were in women with non-dense breasts (ACR A and B) and 54% in dense breasts (ACR C and D).

In daily use, the greatest gain in tomosynthesis screening is observed in women with scattered fibroglandular densities (ACR B)

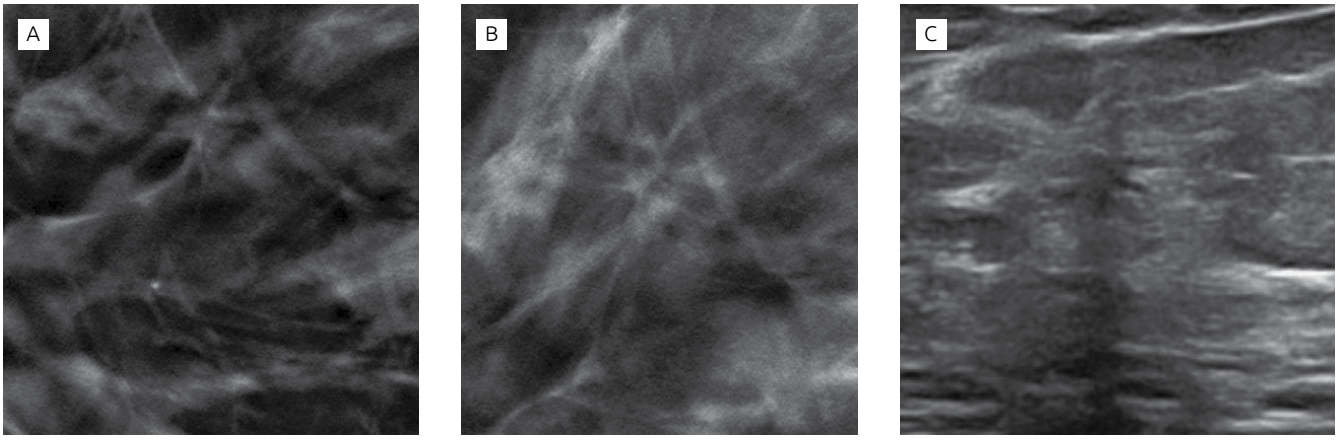


Figure 15. Focal architecture distortion only in oblique mediolateral (A) and craniocaudal (B) incidences in tomosynthesis (B). It is characterized in ultrasound (C). Histology: invasive lobular carcinoma grade I.

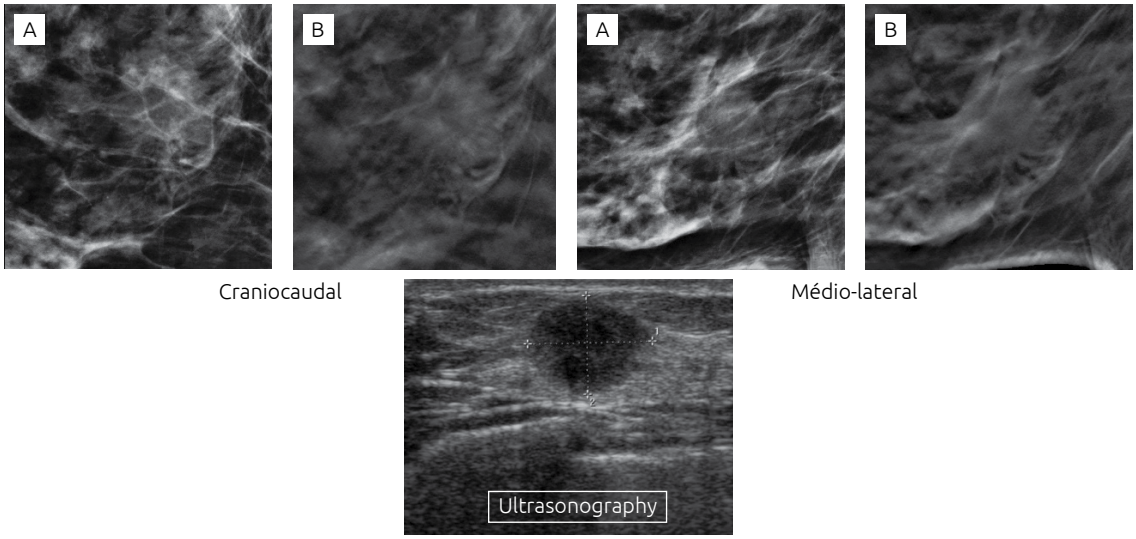
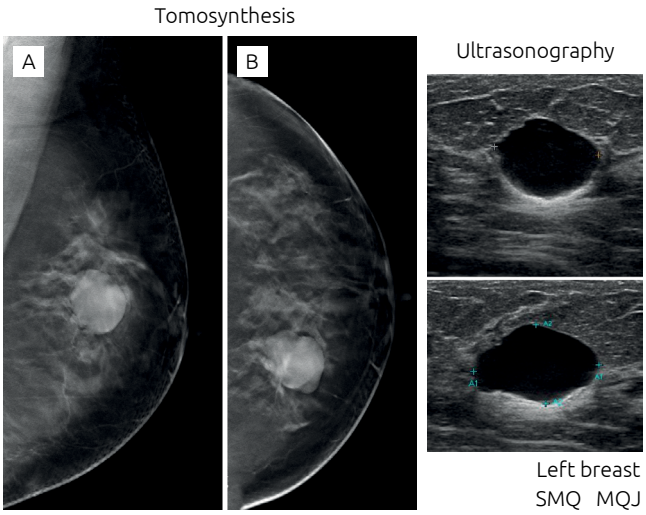
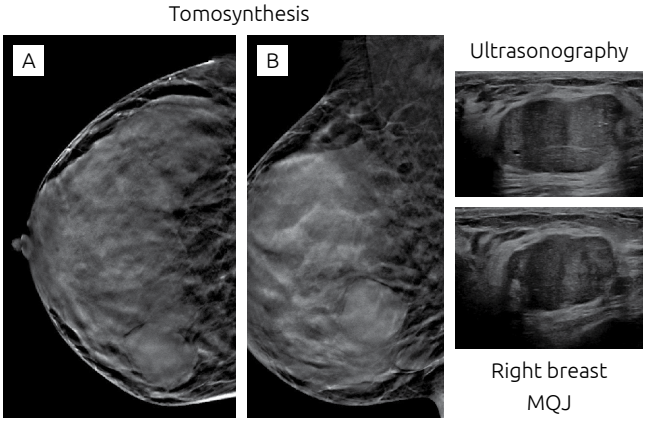


Figure 16. Palpable nodule to the right in heterogeneous dense breast, not observed in 2D (A) is presented in tomosynthesis (B) with spiculated margins. Ultrasonography shows a 1.4 cm nodule . Histopathology: invasive carcinoma g2.



SMQ: superomedial quadrant; MQJ: medial quadrant junction.

Figure 17. Heterogeneously dense breast. Tomosynthesis shows circumscribed margins of the lesion: (A) mediolateral incidence; (B) craniocaudal incidence. Ultrasonography shows cyst.



MQJ: medial quadrante junction.

Figure 18. Heterogeneously dense breast. Tomosynthesis shows circumscribed margins of the lesion: (A) mediolateral incidence; (B) craniocaudal incidence. Ultrasonography characterizes the solid nature of the lesion. Histology: fibroadenoma.

and heterogeneously dense breasts (ACR C), which represent the majority of breast density patterns. In women with extremely dense breasts (ACR D), complementary ultrasonography will continue to play an important role due to the lower sensitivity of tomosynthesis in this group (Figure 19)[33].

Detection of calcifications in tomosynthesis

Although there is no doubt that tomosynthesis is superior to 2D in the detection and characterization of noncalcified lesions (nodules, asymmetries and distortions), there are still questions related to grouped calcifications. Some studies showed that tomosynthesis is at least equal to 2D in detecting microcalcifications[37,38]. However, the detection of clusters of small and faint calcifications can be a challenge to be perceived in tomosynthesis for several reasons:

1. The low radiation dose in the raw images can reduce reconstructed images' spatial resolution;
2. Movement of the patient during the acquisition of the tomosynthesis or the 2D image;
3. Tomosynthesis slices have parallel reconstruction to the detector, while suspicious microcalcifications have radial distribution in the breast. Therefore, grouped calcifications with linear or segmental distribution will be visualized in more than one slice of tomosynthesis, which makes it difficult to analyze its morphology and distribution. The addition of several 1-mm slices in a single image (slab) facilitates the visualization of the whole group although with loss of spatial resolution and bigger impact in small particles.

SM increases the brightness and contrast of calcifications and can improve their perception and characterization when combined with tomosynthesis. However, the detection of clustered calcifications in tomosynthesis or SM does not exclude the need for extra views with magnification spot compression amplified in both incidences (craniocaudal and 90 degrees mediolateral), essential for the characterization of their morphology and distribution and recommendation of management (Figure 20).

Table 3. Breast density and tomosynthesis.

	Adipose		Sparse densities		Heterogeneous density		Extremely dense		Not dense		Dense	
	2D	3D	2D	3D	2D	3D	2D	3D	2D	3D	2D	3D
Recall/thousand screenings	57	55	97	84	128	110	114	98	90	79	127	109
Cancer/thousand screenings	3.2	4.2	4.4	5.3	4.5	6.1	3.8	3.9	4.2	5.1	4.5	5.8
Invasive câncer/ thousand screenings	2.3	3.5	3.2	4.1	3.0	4.5	1.9	2.6	3.0	4.0	2.9	4.2
Positive predictive value by recall	6.2	8.4	4.9	6.9	3.8	5.9	3.7	4.3	5.1	7.1	6.2	8.4

Source: adapted[36].

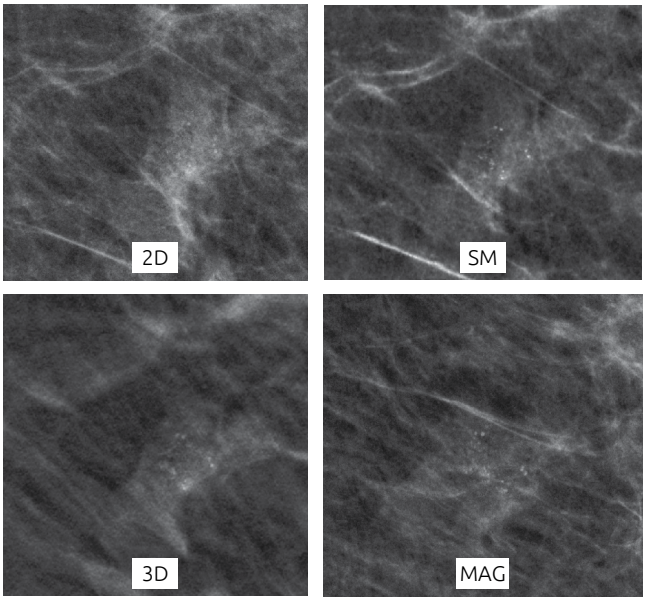
In some cases, tomosynthesis may add to the final mammographic diagnosis by detecting radiographic changes associated with clustered calcifications, such as focal architectural distortion, asymmetries or nodules (Figure 21).

Management of lesions detected only in tomosynthesis

Some lesions are detected only in tomosynthesis (hidden in the 2D), mainly spiculated nodes and architectural distortions, due to better resolution of spicules in tomosynthesis. In cases where the change is only suspected, selective compression can be performed to confirm the finding[33].

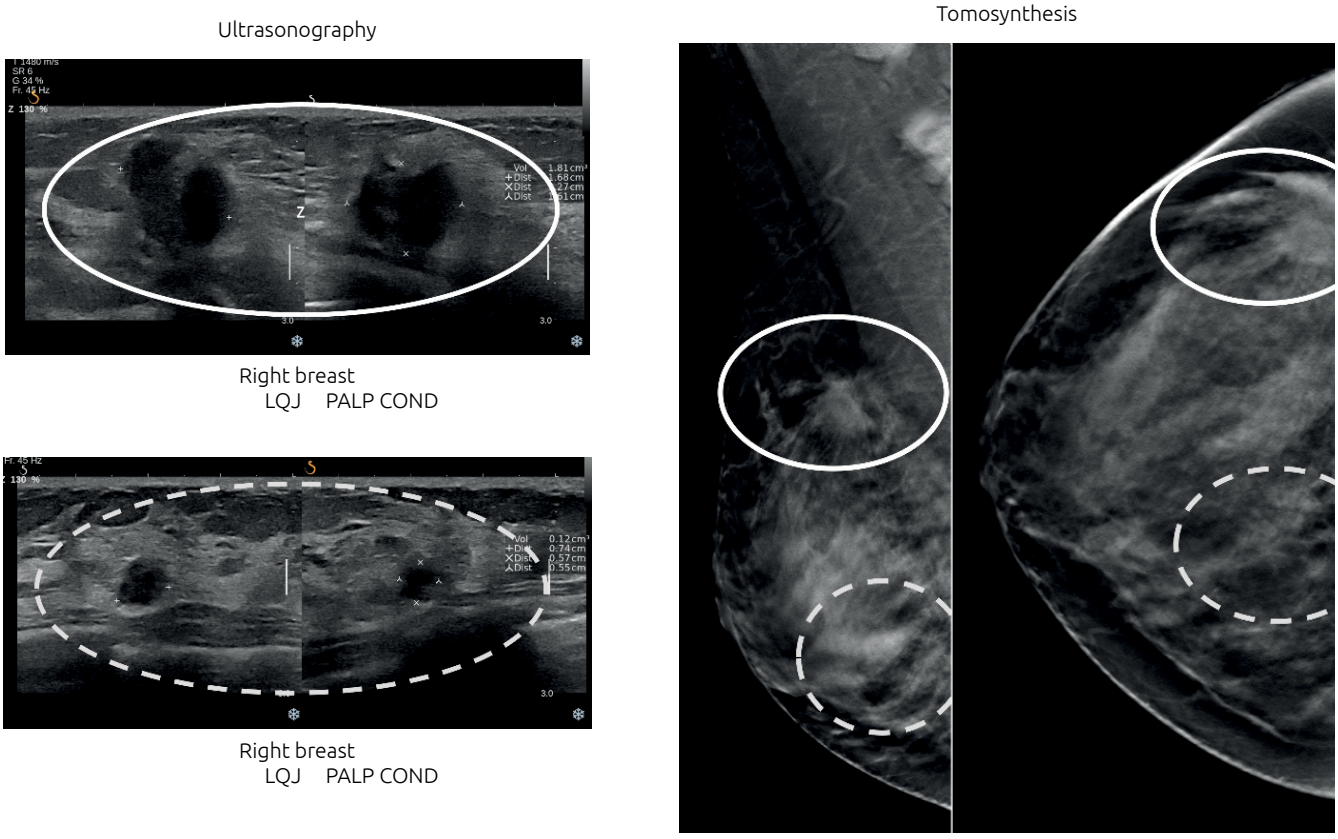
Tomosynthesis facilitates the localization of a lesion in the breast, through the lateral bar shown in its slices: for example, in the craniocaudal incidence, the bar demonstrates whether the lesion is in the lower or upper quadrant and, in the mediolateral incidence, it demonstrates whether the lesion is lateral or medial. The sidebar also guides the location of the lesion on the second look examination and helps when the image is only seen in one incidence[39].

Most of the changes observed only in tomosynthesis are also characterized by second look ultrasound which allows for



MAG: magnified radiography.

Figure 20. Calcifications in 2D synthesized mammography (SM) presents better conspicuity than in 2D. Although calcifications can be detected in tomosynthesis (3D), the magnified spot compression (MAG) better characterizes their shape and distribution. Histopathology: ductal carcinoma *in situ*.



SMQ: superomedial quadrant; PALP COND: palpable density; LQJ: lower quadrant junction.

Figure 19. In breasts with extremely dense pattern (D pattern), even in tomosynthesis the lesion may be obscured by dense tissue (dashed line). Ultrasonography is able to detect these lesions. The largest and most peripheral lesion (continuous line) was detected in both methods. Histopathology: multicentric invasive ductal carcinoma.

a percutaneous biopsy by this method. In cases where the lesion is not evident on ultrasonography, magnetic resonance imaging (MRI) is an option, if it enhances. Percutaneous vacuum biopsy may be guided by this modality. In cases where the lesion is not characterized on ultrasonography or does not show MRI enhancement or MRI is not available, a tomosynthesis-guided percutaneous biopsy may be performed, when available, on the biopsy prone table or in the biopsy equipment coupled to the tomosynthesis equipment. If the tomosynthesis biopsy equipment is not available, the tomosynthesis-guided preoperative location can be performed through tomosynthesis equipment : the procedure is performed similarly to the biplanar preoperative location (Figures 22 and 23)[40].

Among the findings seen only in tomosynthesis, architectural focal distortion is the most frequent finding and may be associated to several pathologies (Figure 24). However, it has a high positive predictive value (PPV) for malignancy. Recent studies, with retrospective analysis of findings detected only by tomosynthesis, show PPV from 21 to 53%. The work of Partyka et al.[41], a retrospective analysis of 9,982 tomosynthesis

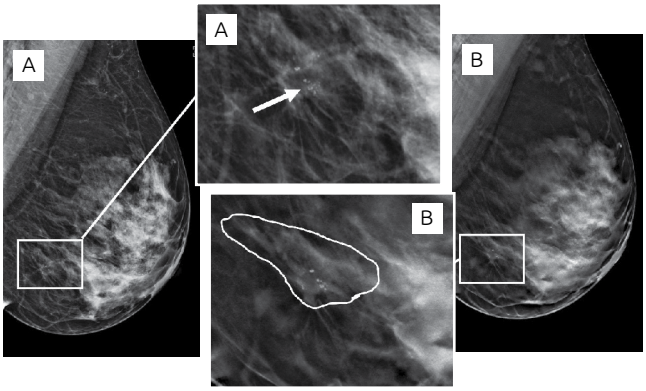


Figure 21. Conventional digital mammography (A) shows suspicious calcifications (arrows) and tomosynthesis (B) shows architectural distortion as an additional finding to microcalcifications, which may represent an invasive component of the lesion.

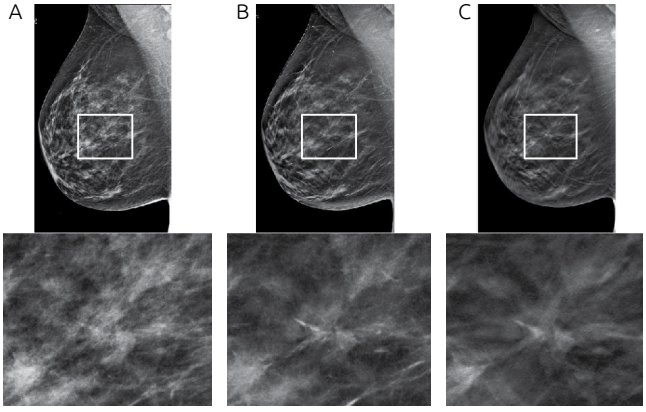


Figure 22. Focal architecture distortion is not evidenced in 2D (A). In mediolateral incidence, it is characterized in SM (B) and in tomosynthesis (C). Ultrasound and MRI not showing this finding.

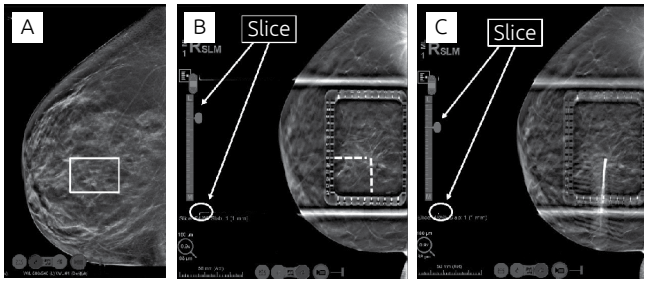


Figure 23. Preoperative location in mediolateral incidence, assisted by tomosynthesis, of the focal architecture distortion not seen in ultrasound and MRI (Figure 23). The positioning of the needle on axes x and y (dashed line) is provided by synthesized mammography (A) and depth (Z axis) by tomosynthesis (B). Positioning of the needle confirmed by tomosynthesis slice (C).

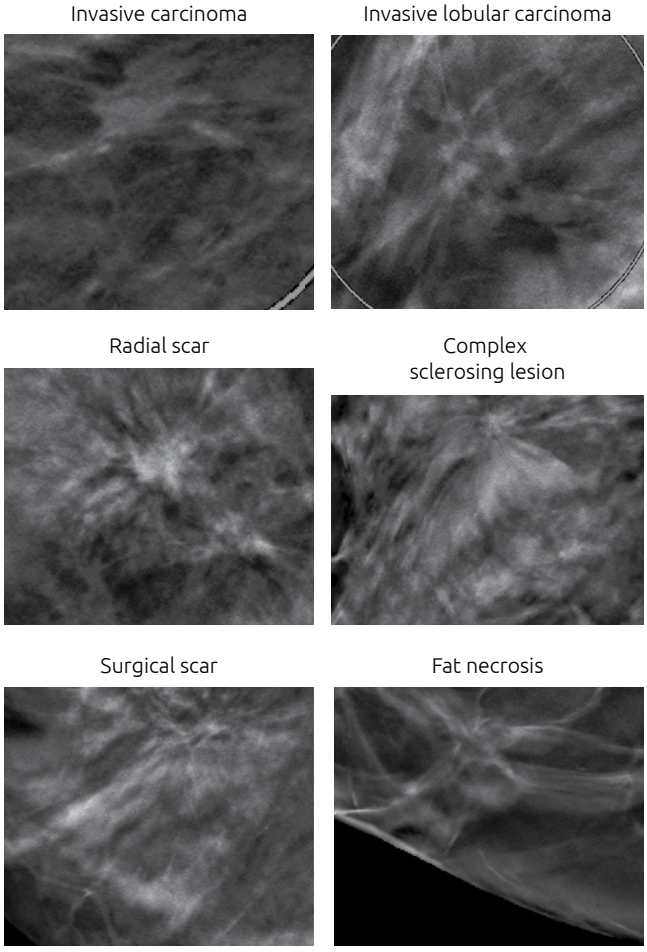


Figure 24. Architectural distortion may be associated with several diseases, requiring a histological study

examinations, found 26 cases of architectural distortion, of which 19 (73%) were detected only in tomosynthesis, with a PPV of 21% (4/19). Ray et al.[42] retrospectively analyzed 19 lesions detected by tomosynthesis only (14 cases of architectural distortion and 5 of spiculated masses), of which 10 were malignant (5 invasive ductal carcinomas and 3 invasive lobular carcinomas), with PPV of 53%.

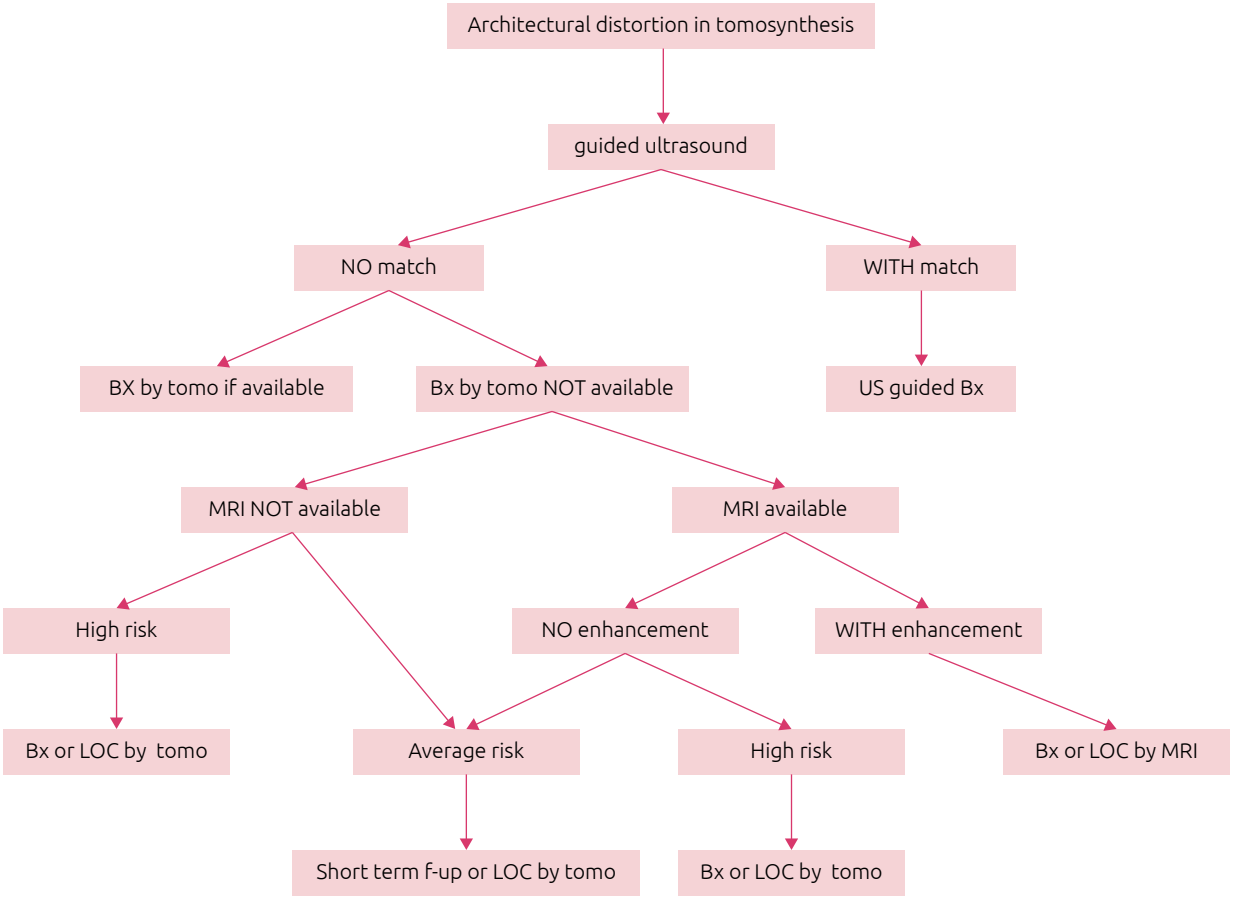
Risk factors for breast cancer should be taken into account, and biopsy may be indicated instead of follow-up for high-risk patients. A modified algorithm by Durand et al.[39] is proposed, considering the risk of breast cancer and the availability or not of MRI (Figure 25).

Future studies are needed to determine the likelihood of malignancy in architectural distortions detected only in tomosynthesis, without characterization in ultrasound or in MRI, to establish new protocols related to these lesions.

Could tomosynthesis replace ultrasound?

Dense breasts reduce mammography's sensitivity, being recommended, in those cases, complementary tracing with other methods. Numerous studies have found that ultrasonography, as well as tomosynthesis, detect small invasive cancers, not seen on mammography, even retrospectively, in women with dense breasts. Tomosynthesis has the advantage of being only one exam (an improved mammography), with high PPV, but with a higher implementation and maintenance cost. Ultrasonography is an additional exam, with low cost and widely available, without radiation addition, though it has low predictive value and needs an experienced radiologist to be performed. There is little information on which exam to choose, as a complement to 2D, in women with dense breasts: only ultrasonography, only tomosynthesis or both?

Tagliafico et al.[43] published a multicenter study with 3,231 women, mean age of 51 years, in which tomosynthesis and ultrasonography were performed, with independent interpretation, in women with dense breasts and negative mammography. The study observed the detection of 24 additional cancers in relation to digital mammography, with 23 invasive ones. The detection rate was 4/1000 with tomosynthesis and 7.1/1000 with ultrasonography, with a similar recall rate in both methods. The study concludes that ultrasound detects more cancers than tomosynthesis in women with dense breasts.



Bx: biopsy; tomo: tomosynthesis; US: ultrasonography; MRI: magnetic resonance imaging; LOC: preoperative location; F-up: follow-up.

Figure 25. Algorithm for management in architectural distortion evidenced in tomosynthesis.

Therefore, tomosynthesis does not exempt complementary ultrasonography in dense breast breasts.

An important finding was the detection, through tomosynthesis, of more than 50% of the additional cancers found, showing that potentially, tomosynthesis could replace 2D as the primary cancer screening method in dense breasts. Unlike ultrasonography, tomosynthesis increases cancer detection without increasing the rate of false positives, which is the most critical point in relation to ultrasound screening.

We must remember that the results published are preliminary and that this study needs to be reproduced in other centers. In addition, it was the first shift with tomosynthesis in this group (little experience of the authors with tomosynthesis), while most of the ultrasound examinations were incident and performed with professionals experienced in the method (Table 4)[43].

In clinical practice, it can be observed that tomosynthesis does not completely replace ultrasound. In very dense and heterogeneously dense breasts, complementary ultrasonography should still be recommended, since it is possible to detect small lesions on ultrasound, not characterized in tomosynthesis, especially in breasts with extremely dense pattern, in which there is insufficient adipose tissue to make contrast in tomosynthesis slices (Figure 19).

Table 4. Carcinomas detected only by tomosynthesis.

	Positive ultrasound	Negative ultrasound	Total n (%)
Positive tomography	12	1	13 (54.2)
Negative tomography	11	0	11 (45.8)
Total n (%)	23 (95.8)	8.9 (4.2)	

Source: adapted[43].

Interval carcinomas and tomosynthesis screening

The rate of interval cancers (ICR) after introduction of tomosynthesis into screening still needs to be investigated. Evidence that tomosynthesis (combined with 2D) reduces the rate of interval carcinoma is still limited .Skaane et al.[44] didn't show reduction in the ICR after the first year of introduction of tomosynthesis: 2,0 IC/1000 with 2D and 2,1 IC/1000 with 2D+3D. On the other hand, a study from Pensylvannia [45] which analyzed the results of three years follow-up with tomosynthesis, demonstrated a small reduction in ICR with tomosynthesis (0,7/1000 with 2D versus 0,5/1000 with tomo). However, these are individual studies with small number of patients and more data is needed.

CONCLUSION

Tomosynthesis (3D mammography) is a new mammographic technique that increases sensitivity and specificity when combined to 2D mammography (conventional or synthesized)

In screening, tomosynthesis has a positive impact because increases detection of small , low grade, RH positive and LN negative invasive cancers and reduces unnecessary recalls or need for additional mammographic incidences.

In diagnostic cases, the technique increases diagnostic accuracy by allowing for a better characterization and location of the lesions, making the conventional diagnostic approach unnecessary, with reduction of patients' anxiety and lower financial cost.

With the development of SM, reconstructed from tomosynthesis to replace conventional 2D imaging, the problem of increased total radiation dose — considered an obstacle to this method in screening — has been solved.

Future studies of interval cancer incidence and cost-benefit analysis of this technology should provide new data for implementation of tomosynthesis in large-scale breast cancer screening.

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