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Estudo da localização da densidade mamária pontual em diferentes espessuras da mama comprimida

Study on the location of punctual breast density in different thicknesses of the compressed breast

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Resumo

A densidade da mama, definida como a porcentagem de tecido fibroglandular na mama, tem o potencial de ser usada como um preditor de risco de câncer de mama. Estudos recentes indicam que a densidade mamária pontual máxima, que é uma medida pouco explorada, é um fator que tem maior ligação com o câncer de mama em comparação com a densidade mamária global, esta última é a mais utilizada para medir a densidade mamária. Este estudo tem como objetivo identificar se o ponto de maior densidade da mama (1cm2) está localizada em diferentes regiões da mama, correlacionando com a espessura da mama comprimida (EMC). Neste estudo retrospectivo, foram analisadas imagens mamográficas nas projeções medial-lateral oblíqua (MLO) e crânio caudal (CC) de 1192 mulheres com idade entre 25 e 89 anos e EMC entre 30 e 89 mm. As informações utilizadas foram: EMC (mm), as distâncias das bordas posterior, superior e medial da mama, (DBPM) (mm), (DBSM) (mm) e (DBMM) (mm), respectivamente, até a localização do 1 cm2 da densidade pontual máxima da mama (DPMM), a densidade volumétrica da mama global (DVMG) (%), a DPMM (1 cm2) e o volume da mama (cm3). Os resultados deste estudo mostram que a DPMM segue o mesmo comportamento do DVMG, em relação à influência da EMC. A respeito das distâncias do DPMM até as bordas da mama, somente entre os intervalos de EMC de 40 - 49 mm e 50 - 59 mm e entre os intervalos de 60 - 69 mm e 70 - 79 mm foi encontrada uma diferença estatística significativamente para as bordas posterior e medial, respectivamente. Portanto a EMC não demonstrou ser um fator de forte influência na localização da DPMM.

Palavras chaves: densidade mamária global, densidade mamária pontual, mamografia de rastreamento.

Abstract

Breast density, defined as the percentage of fibroglandular tissue in the breast, has the potential to be used as a predictor of breast cancer risk. Recent studies indicate that the maximum punctual breast density, which is an underexplored measure and is a factor that has a greater link with breast cancer compared to the global breast density, the latter is the most used to measure breast density. This study aims to identify whether the point of greatest breast density (1cm2) is located in different regions of the breast, correlating with the compressed breast thickness (CBT). In this retrospective study, mammographic images were analyzed in the medial-lateral oblique (MLO) and craniocaudal (CC) projections of 1192 women aged between 25 and 89 years and CBT between 30 and 89 mm. The information used was: CBT (mm), the distances from the posterior, superior, and medial edges of the breast, (DPEB) (mm), (DSEB) (mm), and (DMEB) (mm), respectively, up to the location of the 1 cm2 of the maximum breast density punctual (MBDP), the volumetric density of the global breast (VDGB) (%), the MBDP (1 cm2) and the volume of the breast (cm3). The results of this study show that MBDP follows the same behavior as VDGB in relation to the influence of CBT. Regarding the location of the MBDP, there is little evidence that CBT is a factor of strong influence. Regarding the distances from the MBDP to the edges of the breast, only between the CBT intervals of 40 - 49 mm and 50 - 59 mm and between the intervals of 60 - 69 mm and 70 - 79 mm was a statistically significant difference found for the posterior and medial edges, respectively. Therefore, CBT did not prove to be a factor with a strong influence on the location of MBDP.

***Keywords**: global breast density, punctual breast density, screening mammogram.*

1. Introduction

Breast cancer is the oncological pathology that causes the death of women worldwide (1,2). When detected in the initial phase, this pathology has a good prognosis and this occurs thanks to breast cancer screening programs (3,4).

Breast density, defined as the percentage of fibroglandular tissue present in the breast, has the potential to be used as a predictor of breast cancer risk. This is because breasts with high density have a masking effect in screening mammography exams, making diagnosis difficult (5). Although high breast density is associated with a higher subsequent risk of breast cancer, it is not known whether breast density is directly related to risk, in tumors arising within the radiodense tissue itself, or a simple marker of susceptibility. However, higher density breasts have been shown to correspond to higher rates of breast cancer development (6,7).

Numerous methods have been developed to measure breast density, among them are visual methods such as BIRADS and automated methods. The automated ones are mostly volumetric or area methods (8) However, all of these methods measure global breast density. Recent research results (9,10) indicate that punctual breast density, which is an underexplored measure currently, is a factor that has a greater link with breast cancer than global breast density. This stronger connection can be explained by the fact that it is in these places of higher density than the nodules end up being masked. Therefore, it is relevant that a greater number of studies be carried out to identify which factors influence punctual breast density in different populations of women. Regarding global breast density, studies are more advanced, researchers have already established numerous factors that influence it, for example, patient age (11) and compressed breast thickness [CBT], number of pregnancies, among others (12).

Although mammography is the widely used test for breast cancer screening worldwide, the benefit of this test is not isonomic for different groups of women, as the sensibility of mammography is dependent on breast density. In breasts with high density, the sensitivity of the mammographic examination decreases. Because of this, many studies indicate other types of exams for breasts with high density, such as ultrasound and tomosynthesis (13). So that in the future screening programs for breast cancer in Brazil will be more unique to each patient, taking into account the breast density of women, studies on breast density in groups of women in Brazil are extremely important, therefore, will contribute to this subject being discussed more broadly.

This study aims to identify whether the punctual breast density of 1cm^2 in the area is located in different points of the breast in breasts with different CBT and to analyze the correlation of punctual breast density with CBT.

2. Materials and Methods

In this retrospective study, mammographic images were analyzed in the medial-lateral oblique (MLO) and craniocaudal (CC) projections of 1192 women residents of the Southeast region of Brazil aged between 25 and 89 years and CBT between 30 and 89 mm. The study was approved by the Ethics Committee of the Faculty of Medical Sciences of Minas Gerais according to the CAAE protocol: 18934019.2.0000.

The VolparaDensity software (VolparaSolutions, Version 1.1, Wellington, New Zealand), is an artificial intelligence (AI) developed by Volpara Health Technologies Ltd (https://www.volparahealth.com/) and certified by the Food and Drug Administration (FDA) (8). This IA was used to perform the analysis of the mammographic images, and as a result, presents an electronic spreadsheet with numerous information regarding the composition of the breast. In this study, the information used was: CBT (mm), the distances from the posterior, superior and medial edges of the breast, (DPEB) (mm), (DSEB) (mm), and (DMEB) (mm), respectively, up to the location of the 1 cm2 of the maximum breast density punctual (MBDP), the volumetric density of the global breast (VDGB) (%), the MBDP (1 cm^2) and the volume of the breast (cm^3). Figure 1 demonstrates a map of breast density in the MLO and CC projection. In the MLO projection, the posterior and medial edges of the breast are identified and in the CC projection, the posterior and superior edges of the breast. In both projections, it is possible to visualize the location of the MBDP, represented by the square box.

For DPEB calculation, VolparaDensity uses images from both CC and MLO projections. As for the DMEB calculation, it uses only images in the CC projection and for the DSEB calculation, the software uses only images in the MLO projection. Therefore, to have only one information per patient, for each of the distances from the MBDP to the three breast edges included in this study, it was performed the average of the values of the right and left breast for both projections, MLO and CC for the DPEB and for DMEB and DSEB, only the average of the values of the right and left breasts was performed.

The information on the three distances from the edges of the breasts to the MBDP with an area of 1 cm2 was separated into six CBT intervals, 30 – 39 mm; 40 - 49 mm; 50 - 59 mm; 60 - 69 mm; 70 – 79 mm and 80 – 89 mm, forming six samples for each of the distances from the edges of the breasts to the MBDP. Using tests of statistical significance for the mean difference, it was verified whether there was a statistically significant difference between the six samples at each of the distances from the edges of the breasts to the MBDP. For DPEB samples, the parametric test ANOVA with post hoc Tukey was used, as there was homogeneity between the samples of the different CBT, according to Levene's test, and all had an n > 50. For the DSEB and DMEB samples, the non-parametric Man Whitney test, because, although the samples for all CBT's had an n > 50, there was no homogeneity between the samples of the different CBT's.

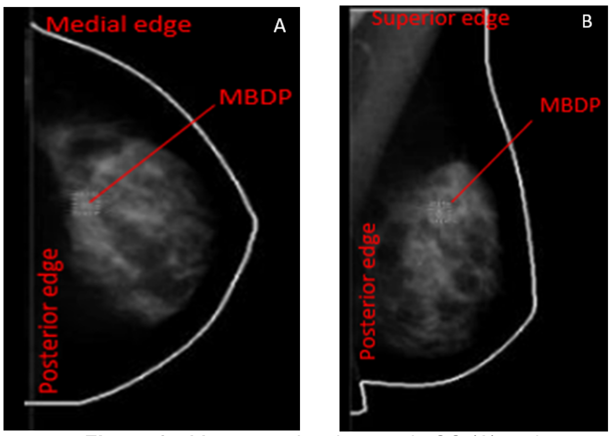

Figure 1 : *Mammary density map in CC (A) and MLO (B) projections.*
Source : VolparaDensity software.

3. Results and Discussion

The sample of this study consisted of 4768 images of 1192 patients who underwent the exam for mammography screening for breast cancer, these had a mean CBT of 60.7 ± 11.9 mm, mean age of 53.4 ± 11.1 years, mean breast volume of 769.2 ± 386 .4 mm3, mean VDGB of 9.4 ± 5.9%, and mean MBDP of 31.9 ± 14.6 cm3.

Table 1 shows the average valours breast volume and two breast density metrics, VDGb and MBDP, at different CBT intervals.

Table I: Information on breast volume, volumetric density of the global breast (VDGB) and maximum breast density punctual (MBDP) of patients at different compressed breast thicknesses (CBT) intervals.

Intervals CBT (mm)	Breast volume (mm^3)	VDGB (%)	MBDP (cm^3)
30 - 39	270.5	13.6	39.7
40 - 49	407.7	13.4	39.4
50 - 59	629.5	10.1	34.1
60 - 69	857.3	8.0	29.6
70 - 79	1128.0	6.9	25.9
80 - 89	1380.4	6.0	25.5

Source: The Author (2023).

The breast compression force (N), which results in CBT, reduces the radiation dose needed to make a mammographic image and increases image quality by reducing the amount of scattered radiation. In addition, it spreads the overlapping tissue, allowing a reduction of false negative findings resulting from the masking caused by the glandular tissue to the nodules (14). Analyzing the data in Table 1, it is noted that the breast volume increases gradually, as the CBT intervals increase, demonstrating that the breast volume is positively related to the CBT. Regarding breast density metrics, both VDGM and MBDP have a negative relationship with CBT and breast volume. About the positive correlation between CBT with breast volume and the negative correlation between the global breast density metric, the VDGM, with CBT and breast volume, are expected results, and well established by science, as demonstrated in the studies (14,15). This can be explained by the fact that breasts with greater volume and, consequently, greater CBT, have a greater proportion of adipose tissue and a smaller proportion of glandular tissue (14,15).

In the work of (14), it was found that women with larger breasts received greater compression force at the time of the examination when compared to women with small breasts. These findings may also be related to the amount of glandular and adipose tissue present in the breast, as the high percentage of glandular tissue is associated with greater discomfort and pain at the time of the examination, due to its greater sensitivity (15). Therefore, in breasts with high global density, in addition to the masking caused by the high proportion of glandular tissue, the image quality can be affected due to the difficulty for the professional radiologist to apply the necessary compression force due to the higher level of pain and discomfort felt by these patients.

In relation to the negative correlation between MBDP, which is currently a little utilized breast density metric, with breast volume and CBT, no other studies were found in the literature that corroborate with the results obtained, that MBDP behaves in the same way as VDGB, decreasing with increasing breast volume and CBT.

The averages of the DPEB, DSEB, and DMEB values up to the MBDP for each of the samples corresponding to the different CBT intervals are shown in Table 2.

Table 2: Distances from the posterior, superior and medial edges of the breast, (DPEB) (mm), (DSEB) (mm), and (DMEB) (mm), respectively, up to the location of the 1 cm2 of the maximum breast density punctual (MBDP) at different compressed breast thicknesses (CBT) intervals.

Intervals CBT (mm)	DPEB (mm)	DSEB (mm)	DMEB (mm)
30 - 39	41.9	131.9	137.3
40 - 49	39.9	136.9	139.3
50 - 59	47.4	132.2	141.7
60 - 69	48.7	135.8	141.8
70 - 79	48.7	140.6	149.8
80 - 89	37.5	138.4	153.5

Source: The Author (2023).

As shown in Table 2, for DPEB and DSEB, no pattern was found that corresponds to the increase in CBT's. As for DMEB, the distances gradually increased along with the CBT.

In the tests of statistical significance for the difference in mean, in relation to the DPEB, the ANOVA test resulted in a $p < 0.05$, only between samples from the CBT intervals of 40 - 49 mm and 50 - 59 mm. For DMEB, the Man Whitney test resulted in a $p < 0.05$ in the samples from the CBT ranges of 60 – 69 mm and 70 – 79 mm. As for DSEB, the Man Whitney test did not obtain any p-value < 0.05. These results demonstrate that, for this sample of images, the point of greatest breast density had a significant difference in the distance from the posterior edge of the breast between samples from the CBT ranges of 40 - 49 mm and 50 - 59 mm and a significant difference in the distance from the medial edge of the breast between the samples in the 60 - 69 mm and 70 - 79 mm intervals. Therefore, CBT proved to be an influencing factor of the difference in the location of the point of greatest breast density only in these two situations.

Currently, in clinical practice, breast density is estimated by visual and qualitative assessment, using the ACR BI-RADS (Breast Imaging Reporting Data System) categories (8). However, this measurement has limited reproducibility, as it can result in significant differences when performed by different radiologists (14). Therefore, works on methods that measure breast density quantitatively and reflect the distribution of glandular tissue, such as VolparaDensity, contribute to in the future use of these methods in clinical practice more widely, ensuring the supply of a more accurate representation of dense breast tissue.

Even though breast density is a well-established factor regarding the risk of developing breast cancer, the relationship between masking and breast density is more complex than a simple dependence on the amount of glandular tissue. One of the factors is the way in which the glandular tissue is distributed in the breast, and when distributed in localized points of maximum density, the risk of masking is even greater (8,9). Thus, the relevance of this work is to demonstrate how the point of greatest breast density is located in different CBT intervals and what is the influence of CBT on the points of greater breast density.

5. Conclusions

With the analyzes carried out in this study, it is concluded that the MBDP follows the same behavior as the VDGB regarding the correlation with the CBT, decreasing as the CBT increases. Regarding the location of the MBDP, little evidence was found that the CBT is an influencing factor, since in a few CBT intervals a statistically significant difference was found in the location at the point of greatest breast density.

These findings are recent and may provide new measurements of breast density that better perform the function of predicting the masking of breast nodules. The future prospects for this field of study are that these metrics contribute to an improvement in breast cancer screening programs in the future, taking into account the individual characteristics of punctual breast density.

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