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Combined Analysis of Breast Morphometry, Compression and Volumetric Breast Density: Valuable Input to Improve Mammography Screening Using International Bench Marking

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ABSTRACT

Introduction: The aim of this study was to select parameters from a combined analysis of breast compression, breast morphometry and volumetric breast density, telling about the overall quality of breast positioning, and to apply these investigations on a Moroccan population at the start of new breast cancer screening activities. The study found that compression force in mammography varies greatly and has no specific limit. The researchers attempted to find correlations between compression force and mammographic factors to establish a range of values for standardized compression in mammography.

Material and Methods: The study was carried out in a university hospital, a candidate screening center, provided with new technology equipment, qualified staff and doctors of different specialties. Image acquisition was procured on a FFDM Siemens Inspiration system for 250 patients in diagnostic mammography and all patients' information was collected. The data about dose, the compression force and the thickness of the compressed breast were obtained directly from the DICOM header information, applying Volpara Density software.

Results: The results show a correlation between compression force and breast density. The volume of breast tissue compared to the total volume of the breast (VBD) decreased with increasing compressed breast thickness (CBT) and age. The mean VBD was 9.3% ± 6%, the compression force was 71±15 N and the CBT was 53±11 mm.

Conclusion: The global analysis and comparison of mammographic parameters showed good similarity between Moroccan and the previous studies population. The mammographic techniques can therefore be used to Moroccan screening programs.

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Introduction

Mammography is an effective exam for the early detection of breast cancer. As the glandular tissue in the female breast is considered a radiosensitive organ, the mammographic exam should be associated with the lowest achievable dose to the patient, usually expressed in terms of mean glandular dose (MGD) which is considered to be the most important quantity to estimate the risk of radiation-induced carcinogenesis [1, 2].

The distribution of adipose and fibroglandular breast tissue is variable and strongly correlated with age: in older women, breast density generally tends to decrease [3].

Breast density is a radiological entity representing the amount of radiopaque or dense mammary structures known as fibroglandular tissue, relative to radiolucent tissue such as fatty tissue [4]. This has an impact on the description of mammography's ability to detect lesions: the denser the breast, the lower the sensitivity of the mammogram. In addition, the high density is responsible for a higher rate of interval cancers and false positives [5].

Multiple studies that have investigated the connection between breast density and breast cancer have demonstrated that women with dense breasts have a significantly higher risk of developing cancer. In fact, mammography is less efficient for detecting cancers in dense breasts. Dense breast shots are more difficult to read and can also lead to additional exams [6, 7]. High density is an appreciable predictor of the

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risk of missing cancer detection at mammography. Density varies especially with age, but is also influenced by hormonal treatment and is seen only on mammograms. Quantitatively, volume breast density (VBD) can be measured from digital images with a proper algorithm.

The breast parenchyma structure depends strongly on the proportion of its different tissue components. It can be quite dense and can consequently mask the presence of a tumor [8]. The breast density, representing an important expression of the amount of fibroglandular tissue, is related to breast cancer risk [9]. Many studies have focused on this topic, especially regarding the relationship between density and breast cancer risk, which clearly seem to be correlated. Already in 1976, Wolfe investigated a relationship between mammographic parenchyma (functional tissue of a glandular organ) and the risk of breast cancer. The results showed four classifications: N1, P1, P2 and DY with a gradual progression of risk. N1 corresponds to a radiologically transparent mammary parenchyma, very low density, with the lowest risk and DY indicates a breast where the parenchyma is represented by diffuse or nodular densities and where the risk of cancer is the highest. P1 and P2 refer to densities associated with intermediate degrees of risk [10].

Later, N.F Boyd et al shown that mammographic densities are an important indicator of breast cancer risk [11]. They determined a quantitative classification of densities indicating higher risk gradients in general than other risk factors for breast cancer, using radiological and computer-assisted methods.

Giske Ursin et al [9] investigated the percent and absolute mammographic density of patients aged 35–64 years, from three different ethnic groups, using a computer-assisted method. The breast cancer risk increased with increasing percent mammographic density, for the three ethnic groups without noting a significant difference depending on the ethnicity. The impact of percent density on risk was stronger for older than for younger women.

Cancer risk prediction approaches, taking density into account, improve the predictive risk level. This is of great benefit for high-risk women as well as in screening strategies and diagnostic procedures [12].

Proper radiographic technique, applied on excellent technical performance of the x-ray device are crucial to minimize the dose and optimally visualize all the glandular tissue. Especially important in this regard is breast compression [13].

In mammography, it is important to exert a compression force on the breast in order to spread the gland, reduce breast thickness and thus obtain a better image of the inner breast inside [14]. This compression permits to separate the superimposed structures increasing the precision of the details [15].

However, the compression force cannot be fixed to a constant value. It is largely determined by the large variability in the pain threshold of the patient and the experience and training of the mammography practitioners [16, 17].

Ioannis et al [13] mentioned that there are no quantitative guidelines for the compressive force that should be applied for an adequate mammogram. Indeed, previous studies have concluded that there is great variability in the compressive force depending on screening centers and radiographers, and countries [14]. Other studies have shown [15] that several women complain of pain which may discourage them from participating in screening. Whelehan P et al even suggested reducing the compressive force in order to encourage them to undergo mammographic exams during screening companions [16].

An effective mammographic screening program is the most effective way to detect breast cancer in its early stages and has the potential to reduce the risk of death from breast cancer [17].

Breast screening is well established thanks to numerous measurement campaigns and global investigations across the countries of the European Union. Thus, in order to reduce the mortality rate due to this disease, systematic early detection by screening, effective diagnostic methods and optimal treatment were necessary [18]. National standards help to optimize the quality of screening programs and develop coordination between national, regional and European programs [18].

Special attention should therefore be devoted to a complete investigation and a combined analysis of all mammographic parameters to correctly apply the results to the local population at the beginning of a new screening program. Focused on this direction, this study will contribute to developing the screening methodology and will therefore increase its effectiveness in our country.

Previous studies concluded that a program to promote early detection of breast cancer needs to be tailored to the particular circumstances of each country, because of important differences between and within different populations. For instance, Shivaani Mariapun et al have pointed out a lower precision on mammographic results [19] due to the difficulty of visualizing mammographic details in the Chinese small breasts. A study carried out on the Lebanese population [20] showed that the distribution of breast density is similar to that of Western society and that a high breast density was statistically linked to breast cancer, especially in elderly and menopausal women.

This is why the first step of the study was to check whether there is a resemblance between the compression parameters evolution with the results of previous work based on European standards to be able to apply the same guidelines.

In the second part, an analysis of the combined compression parameters was proposed in order to extract possible suggestions relative to the compression range to adopt to guide practitioners when taking a mammographic image. For this; an attempt to identify possible relationships between compression parameters and mammographic density was suggested.

Materials and Methods

The present investigation was conducted in a mammography unit of a Moroccan university hospital where a full-field digital mammography system is used. In Table 1 the main technical characteristics of the system are summarized. The system was used in Automatic Exposure Control mode (AEC).

The study considered DICOM data from 250 patients recorded during mammographic exposures. In this study, the images were taken by several radiologists (non-technicians). The main technical and compression parameters were collected for each mammogram. For each breast, the CC and the MLO images were analyzed.

The Relationship's direction among the breast parameters was expressed by the Spearman correlation coefficient (Rs or ρ). All bivariate correlation analysis expresses the strength of association between two variables in a single value, which varies between -1 and +1. The sign of the correlation coefficient (Rs) indicates the direction of the correlation. A negative value of Rs means that the variables have an inverse relationship. The strength of the correlation increases as the value of Rs moves closer to 1 or -1. A value of 0 indicates that there is no correlation [21].

Table 1. Technical characteristics of the equipment

System	Detector type pixel and matrix size	Characteristics	X-ray system target/filter
Siemens Mammomat Inspiration (2013)	24 x 30 cm Direct Ray A-Se 85μm 2816*3584	SID =65 cm	Mo/Mo Mo/Rh W/Rh

Results

In the first part of this study we focused on the different mammographic factors, as thickness, glandularity and density related to patient's age.

Table 2. Overall statistics on patients of all age groups, breast characteristics and compression parameters.

Parameters	Mean ± SD	Median	Range
Age (y)	52±10	51	29-88
CBT(mm)	53.1±11.5	53	22-103
Breast volume (cm^3)	851.3±406.7	804.4	103-2342
Absolute dense	66.6±38.7	55.7	12-286
Volumetric breast	9.3±6	7.3	2.2-38.6
Glandularity (%)	17.8±11.4	14.5	4.3-73.6
Compression force	70.7±14.8	73	28-128
Compression	7.9±3.5	7.1	2-25.8

The average and median values of breast glandularity were 17.8% and 21.8% respectively (Table 2). It was also pointed out that the sample was composed of women in the 29-88 years age range (Figure1) candidate for diagnosis examinations.

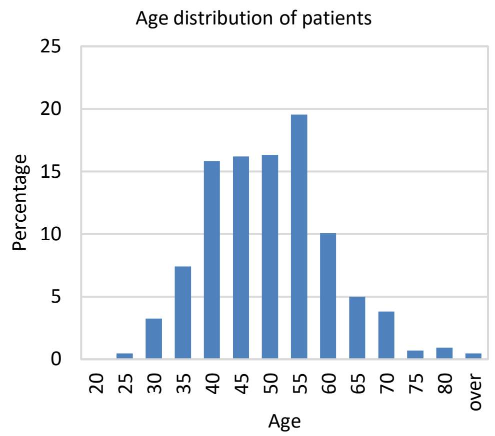

Figure 1. Age distribution of the patients' database

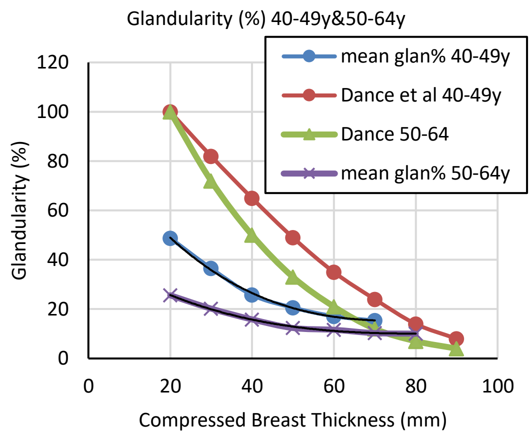

Figure 2. Comparison of glandularity's evolution with Dance results concerning two age groups

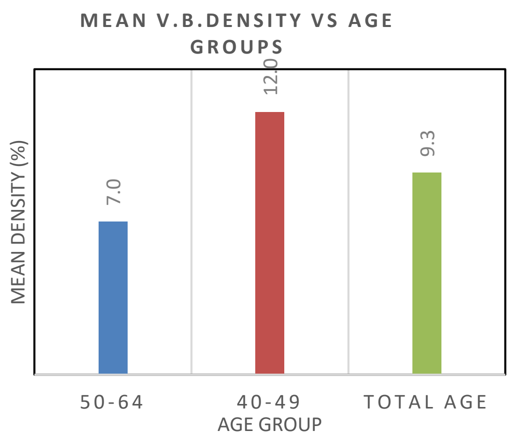

Figure 3. Variation of Volumetric Breast Density with age

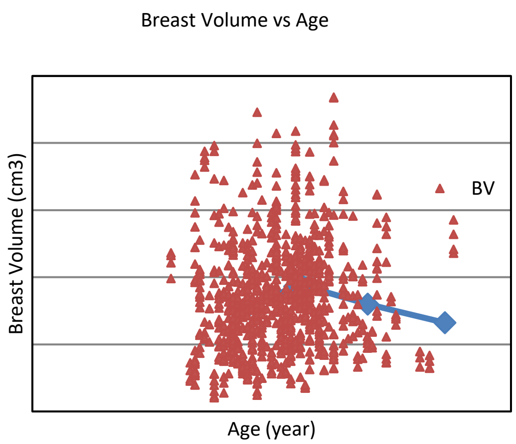

Figure 4. Variation of Breast volume versus age

The variation of mean glandularity depending on breast thickness for two groups of age (40-49y and 50-64y) is shown in figure 2. Results were compared to those reported by Dance et al [22]. The general trend is similar to that of Dance, but with much smaller amplitudes.

Figure 3 displays the variation of the mean volumetric breast density in two age groups. As expected, the density is generally higher for the younger people: the VBD for the 40-49y age range and the 50-64y age range varies up to 12% and about 7% respectively.

Figure 4 shows that the values vary around an average of 850 cm^3 and that they decrease from about 60 years. A previous study [23] indicated that the average breast volume increases with age and then decreases from a certain age.

The sample taken into consideration in the present part of study was 235 patients, of which the age was greater than or equal to 50 years. The analysis of the latter data was compared with those 250 patients from Leuven University Hospital, taken during a screening campaign. Figure 5 giving the average of the volumetric breast density in Morocco and Belgium, shows that the tendency of the two curves is exactly the same with a slight increase in for Belgian patients for small breast sizes. In addition, figure 6 shows that the values range of the compressive force is higher for the Belgian data relatively to the breast density and the breast volume respectively. It varies from 40 to about 100N for Moroccan patients while began from about 100N for Belgian population and can reach 160N.

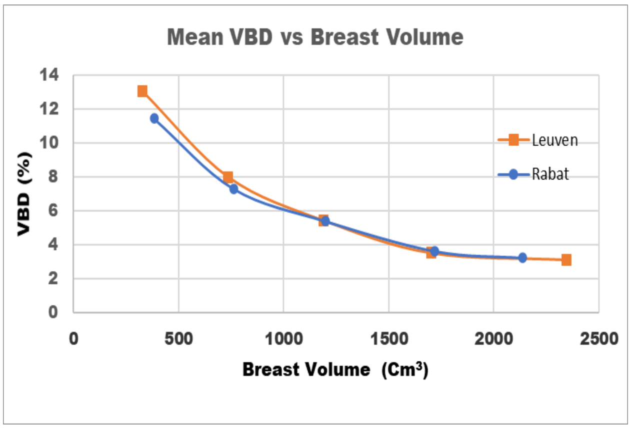

Figure 5. Variation of volumetric breast density versus breast volume for Moroccan and Belgian populations.

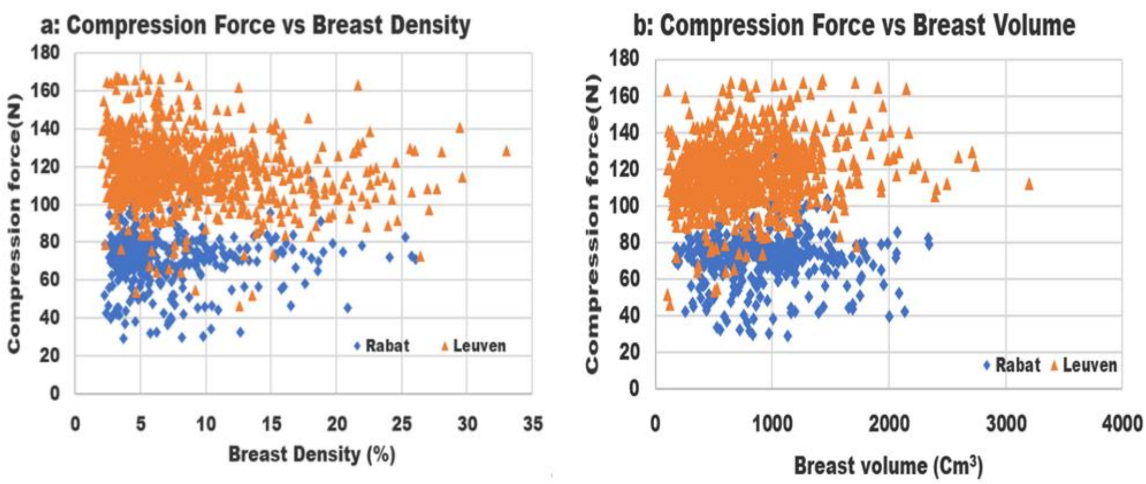

Figure 6. a) Variation of compression force with breast density for Moroccan and Belgian populations. b) Variation of compression force with breast volume for Moroccan and Belgian populations

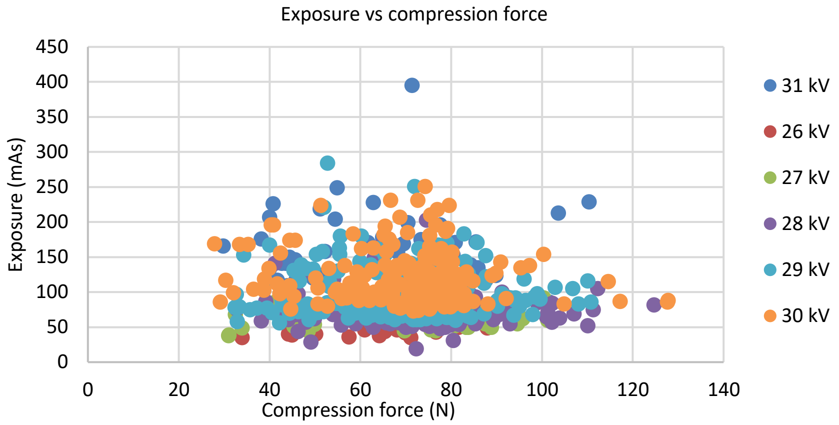

Figure 7. Variation of exposure versus compression force for different tube tension

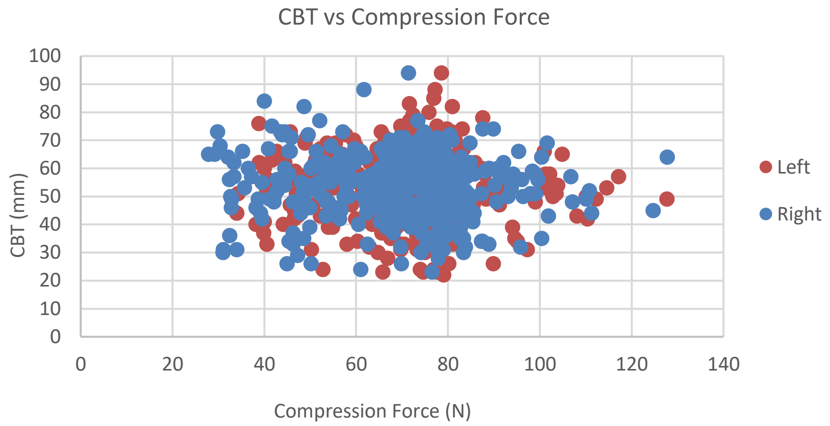

Figure 8. CBT vs compression force for left and right breast side.

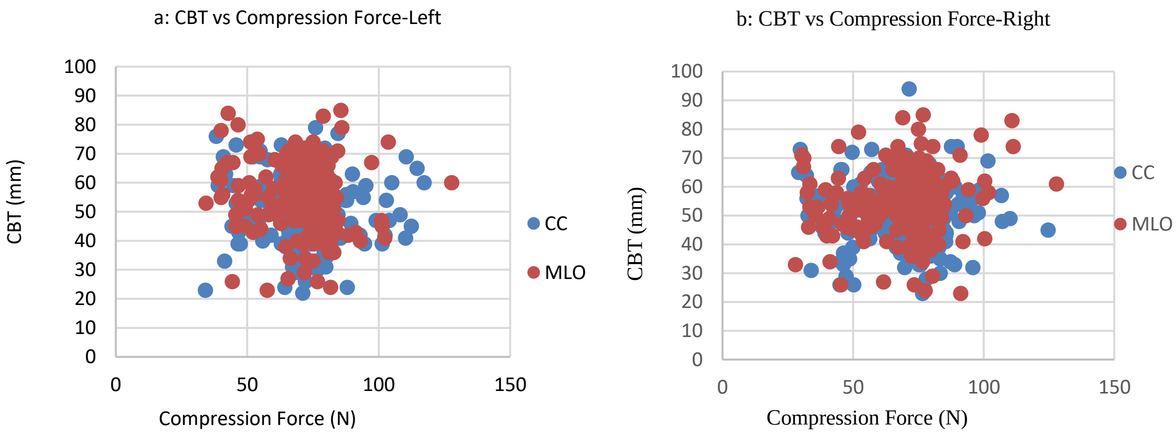

Figure 9. CBT vs compression force CC and MLO; a) left and b) right

It is noted that the results are conform to those established by Dance regarding the evolution of glandularity versus the women age groups. In addition, comparison with Belgian results where guidelines in the domain are used, gives similar conclusion. These directives can also be applied for our results, as in our country there are no guidelines yet to assess the results of this study.

For all the kV values used, the compressive force is generally between 25 and 80 N (figure 7). It is noted that for 26, 27, and 28 kV, the exposure is relatively low and less than 100 mAs permitting thus administered dose reduction.

Several previous studies showed that breast density is related to breast cancer incidence [10, 11], mainly because of the possible difficulty to visualize the fine details in mammogram. Precisely, when the breast is dense, it is more difficult to visualize the small details if the compressive force applied is not adequate in order to properly flatten the breast and consequently visualize the small details.

Compression in mammography represents the force exerted on the breast to flatten it by reducing its thickness. Although it has no explicit limitations and this practice can have a significant impact on the quality and visibility of the image. The same compression force may have different pain effects felt by the patient, depending on the size of the breast.

The CBT variation vs compression force (figure 8), for left and right breast sides are similar and the Rs factor calculation indicates that relationship is poor between these two parameters (Rs=-0,11 left value and Rs= 0,10 right value). CC and MLO left and right.

Figure 9 shows that the point cloud is concentrated between 20 and 80 N for the CC and the MLO projections and for left and right breasts.

In this part, combined analysis of breast compression, breast morphometry, and VBD were investigated to search the relationship between these imaging parameters.

Figure 10 shows that compression force values used for imaging are included between about 30 and 80N (81%) varying around an average of 75 N (rarely exceeding 100 N). Compression force did not exceed 80 N for volumes larger than 1500cm^2.

Figure 10 points out that a broad range of compression values is used for the same breast volume ranging from 30 up to 120N, but the large volumes are visualized with compression forces less than 80 N.

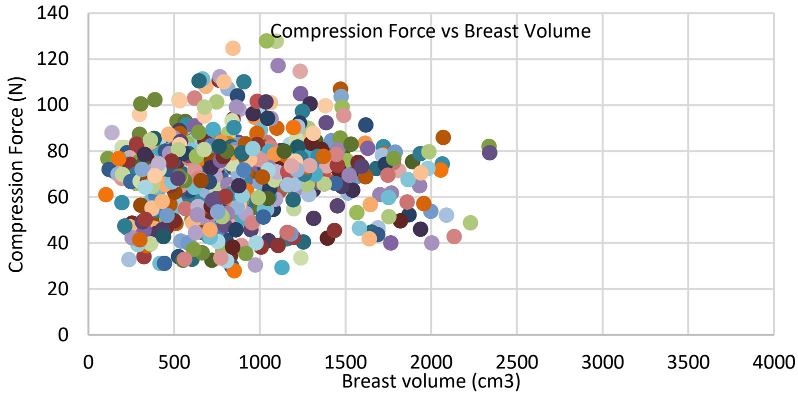

Figure 10. Variation of compression force versus breast volume

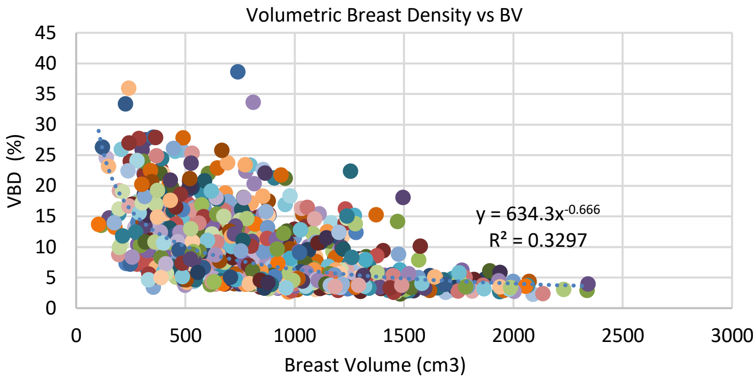

Figure 11. Variation of VBD versus breast volume

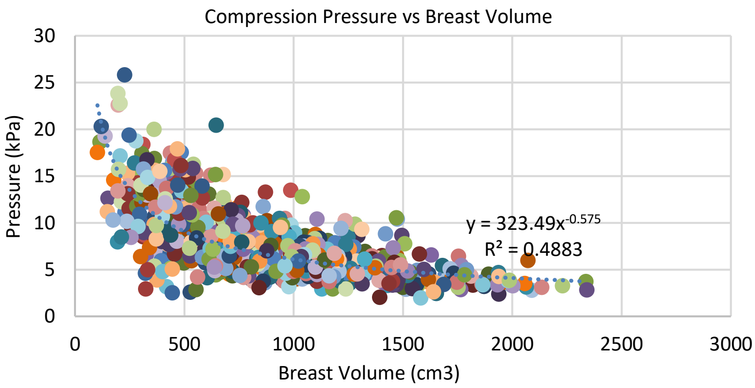

Figure 12. Variation of compression pressure versus breast volume

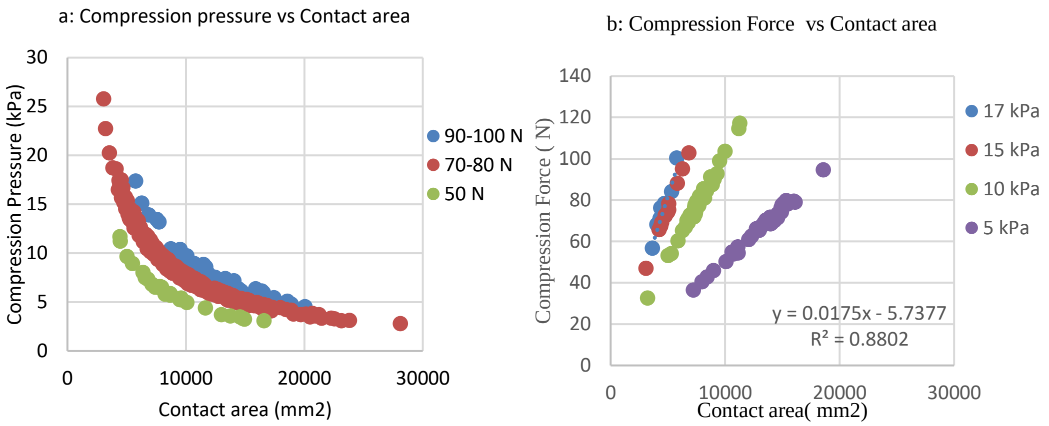

Figure 13. Variation of –a) compression pressure –b) compression force versus contact area

Figures 11 and 12 show that the density decreases with increasing volume and the lowest compression pressures correspond to large volumes.

It is observed that larger breasts are imaged using lower pressure (fig 12) and the small volumes correspond to higher pressures. A negative moderate correlation was observed between these parameters (Rs=-0,689). This trend was also emphasized by Holland et al [13]. These authors also suggest that additional research is needed to confirm the potential effects of pressure on mammographic performance and that greater attention should be considered to achieve a significant standardization of compression levels that could improve mammography in the future. The statistical results did not permit to clearly distinguish the relations between the pressure and the density but the calculation showed that there is a fair tolerable relationship between breast volume density and compressive pressure (Rs = 0.46).

Our results pointed that the lower pressures correspond to higher breast volumes and consequently to the higher contact areas. Figure 13a represents the variation of compression pressure versus the contact area, evince that effectively higher pressures are needed to display small breasts (small contact area). Figures 13a and 13b show that the pressure is all the higher as the contact surface is small and that for a given value of the contact surface several values of this one are used. This once again confirms the great variability of this parameter during mammographic examinations. Figure 13 gives interesting indications since it shows the implication of two compression parameters at the same time, according to the volume of the breast.

Discussion

The variation of glandularity according to age and breast size shows that it is higher for young patients and for compressed breast thickness (CBT) less than about 45 mm. This agrees well with the results of the dance (fig.2).

The direct comparison of the evolution of the compression parameters between the Moroccan and Belgian populations (fig.6), leads to a good similarity. It was also noted that the two populations had the same range of breast size. Moreover, for the same volume of breast, the density is lower in Moroccan patients probably due to the greater proportion of adipose tissue relative to fibrous one. This suggests that the guidelines already established in European countries can be used to carry out a mammography screening examination in our country, while waiting to develop our own.

Among the objectives of this investigation was to try to find correlations between compression parameters and mammographic and technical parameters, as there is not yet quantified limit for compression force.

Results analysis considered hypothesis testing ie: paired samples t-test to determine if compression vs left and right was different. A poor negative correlation was noted between CC and MLO (Rs=-0.11, Rs=-0,1) left, and right respectively.

The study pointed also out that there is no correlation between age and compression force (Rs=0.006). It was noted that coefficient Rs= -0.208 indicated that there is a negative poor correlation between age and compression pressure.

It was recorded that breasts with the same volume are imaged using a wide range of compressions (from about 30 up to 120 N), while for the large volumes forces less than 80N were applied. This can be explained by the fact that exerting a compressive force on a breast means flattening it; this does not mean changing its volume.

A strong negative correlation was found between the compression pressure and breast volume (Rs = -0.689), and a moderate negative correlation was found between the volumetric breast density (BVD) and breast volume (Rs = -0.57).

This trend was also observed by Moshina et al [24], except for the large breasts that were visualized using higher compression forces than used in this study. Indeed, an earlier study demonstrated a significant difference in the average compression used by different practitioners. This factor was categorized into three groups: low, medium, or high compression, and there was no significant difference in the average compression applied in each group. The compression applied varied significantly for a given volume and in general, higher compression was applied to larger breast volumes by the three groups of practitioners [25]. This study highlighted the variation in compression application by practitioners and emphasized the need for further research to provide a new perspective on the analysis of compression variables in mammography.

A wide spectrum of compression forces is generally used, depending on radiological practices in the mammography centers. This was noted in different previous works pointing out the absence of indications to follow for this parameter. According to European recommendations [26] it's denoted that, to have good image quality, the breast must be sufficiently compressed but no more than necessary, without giving a quantitative indication. Figure 10 showing the variation of compression force with breast volume indicates a similar trend between our results and those of recent work [13].

The similarity of the mammary characteristic's evolution according to the age, the breast thickness, and the compression parameters of the Moroccan population and the Western population was clearly exhibited. This was also exposed by a direct comparison of Moroccan and Belgian patient data. The European guidelines can then be extrapolated to the Moroccan population.

Furthermore, previous studies have shown that there is still no quantified limitation of the application of the compression force in mammography and that there is great variability in the values used depending on the collection centers of data [13, 14].

It was then necessary to study this parameter through the data collected in our population and to try to find out whether correlations are possible between the force used and the mammographic parameters. This is the subject of the second part of this work.

The compression forces applied in present investigation's hospital are generally weak compared to those described in previous works [24, 13]. It seems that the range depends on strategies adopted by the mammography service. Indeed, a comparative study between Netherland and in the USA, employing the same strategy, investigating the variation of compression force versus contact surface [14] concluded that the evolution trend of the two studies was similar but the compression forces range used clinically by each study was different; the values were lower for the US population. They were concentrated between 50 and 150 N for the US and between 100 and 200 for the Netherlands. Thus, the authors called for a need of mechanical standardization for breast compression.

The results of our work lead to the same conclusions but using the lowest compression forces, than those of these studies, rarely exceeding 80 N.

Compression parameters are important factors in breast examinations. Indeed, an adequate compression makes it possible to visualize the small details on the image and to help the radiologists to make a more accurate diagnosis. Dense breasts generally require the application of a greater compressive force than adipose breasts in order to facilitate image analysis and avoid making false negatives.

A recent study [27] investigated the relationship between volumetric density grade (VDG) and risk of breast cancer in premenopausal and postmenopausal age groups for Indian women. The authors suggested a positive association between high VDG and cancer risk in premenopausal and postmenopausal women. The standardization of compression parameters is then necessary. In a study conducted by Tien-Yu Chang et al [28], the creation of specific breast models led to the conclusion that a personalized and evidence-based compression force recommendation can be given to radiographers that takes into consideration the image quality, patient comfort, and radiation dose.

A literature review was conducted by Elizabeth Serwan et al [29] to explore existing breast compression force and pressure standardization protocols in clinical application. The authors propose that combining the results of previous studies in the field may lead to the adoption of a standardized compression pressure in mammography as a personalized approach in clinical practice. They also concluded that a compression pressure of around 10 kPa is suggested as a mammography guideline, as it leads to more consistent image acquisition, reduces pain levels, and minimizes variations in breast thickness, mean glandular dose, and image quality.

Conclusion

The patients considered in this investigation were a sample of Moroccan women, characterizing the population presented to a diagnostic mammography examination at a hospital that receives a large number of women.

The similarity of the mammary characteristic's evolution according to the age, the breast thickness, and the compression parameters was clearly exhibited. The comparison of Moroccan and Belgian patient data and Dance's investigation was satisfying. The European guidelines can then be extrapolated to the Moroccan population.

In previous studies there is a significant variability in the compression force use, noting an absence of range limit values. In this work, we tried to figure out whether there are correlations between the compression and the technical and mammographic parameters. This was the subject of the second part of the investigation.

A strong negative correlation was found between the compression pressure and breast volume, and a moderate negative correlation was found between the volumetric breast density (BVD) and breast volume. However, the study did not provide a specific range of values that should be used during radiological exams.

After this preliminary study, it would be interesting to include a larger number of establishments and equipment, to have a more complete idea of the exposure parameters used in Moroccan hospitals.

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