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Automatic Quantification and Classification of Breast Density in 2D Ultrasound Images

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Resumo

O cancro da mama é uma doença grave que afeta milhões de pessoas em todo o mundo, tendo a densidade mamária sido identificada por vários estudos como um fator de risco para o cancro da mama. Assim, a avaliação da densidade mamária é importante na prevenção do cancro da mama. Os ecógrafos disponíveis comercialmente não fornecem uma estimativa da densidade mamária, sendo a avaliação da densidade baseada na observação visual subjetiva de imagens ecográficas, pelos médicos, por esse motivo a exatidão dessa avaliação depende da capacidade e experiência do médico, a qual pode variar entre eles.

Têm sido propostos vários métodos para avaliar a densidade mamária em mamografia e ultrassonografia notando que existem vários métodos para a mamografia, mas poucos para ultrassonografia.

Neste estudo, foi analisado um conjunto de imagens de ecografias mamárias. A densidade mamária neste conjunto de imagens foi avaliada visualmente por dois médicos, incluindo duas avaliações distintas realizadas pelo primeiro médico em diferentes períodos de tempos.

Foi realizada uma avaliação quantitativa e qualitativa utilizando algoritmos semiautomáticos e automáticos com algoritmos de limiar do histograma e do método de Otsu, resultando num total de seis algoritmos. Foi definido um intervalo para a análise quantitativa em que o valor mínimo corresponde ao menor valor das três observações feitas pelos médicos para uma dada imagem e o valor máximo corresponde ao valor mais elevado das referidas observações.

Para o algoritmo BDthr128, 56% dos casos pertencem ao intervalo, enquanto que o correspondente valor foi de 73% para o algoritmo BDthrAuto; estes resultados mostram que o algoritmo BDthrAuto tem melhor desempenho que o do que o primeiro, de acordo com a avaliação da densidade mamária feita pelos médicos. É também descrita a aplicação de um algoritmo que isola a glândula mamária em BDthr128 e BDthrAuto resultando nos algoritmos automáticos BDCombo128 e BDComboAuto. O procedimento utilizado para a análise dos resultados de densidade mamária foi o mesmo que o definido para os algoritmos BDthr. Depois de considerar o intervalo com o máximo e o mínimo das observações da mesma imagem, 28% dos valores obtidos aplicando os algoritmos estavam dentro do intervalo para o algoritmo

BDCombo128 e 42% para o BDComboAuto,o que mostra que o algoritmo automático Tem melhor desempenho consideração as avaliações dos médicos.

Considerando os valores das três observações fornecidas pelos radiologistas e os valores obtidos para a densidade mamária através dos quatro algoritmos desenvolvidos, aos correspondentes valores e para cada imagem de ecografia mamária, foi atribuído consoante o valor, o correspondente tipo considerando a avaliação qualitativa BIRADS (1, 2, 3 ou 4). Com três coincidências com os valores dos radiologistas, foram obtidas 33% das 85 imagens utilizando o algoritmo de BDthr128 e 48% das 85 imagens, utilizando o algoritmo de BDthrAuto. Por outro lado, o algoritmo BDthr128 obteve coincidência, com pelo menos duas das observações dos radiologistas em 69% das 85 imagens enquanto o BDthrAuto obteve 86% na mesma situação. No que diz respeito aos algoritmos automáticos e com três coincidências, o algoritmo BDCombo128 obteve 25% das 85 imagens e o BDComboAuto 47%. Com pelo menos duas coincidências o algoritmo BDCombo128 obteve 58% e o algoritmo BDComboAuto 79% das 85 imagens de ecografia mamária.

Para a aplicação do método de Otsu, não foram consideradas imagens com nódulos mamários porque, com base nos resultados obtidos usando os algoritmos anteriores, foi concluído que este tipo de imagens necessita de especial atenção em investigação futura. Assim e para 82 imagens de ecografia mamária, quando foi aplicado o algoritmo semiautomático BDthrOtsu, obtiveram-se 65 % das imagens no intervalo considerado, enquanto para o BDthrAuto esse valor é de cerca de 70%. Quanto aos algoritmos automáticos, tem-se para o algoritmo BDComboAuto, 49% das imagens dentro do intervalo e para o BDComboOtsu o valor é de 61%. No caso da avaliação qualitativa, com total coincidência com as observações dos radiologistas, obtiveram-se 46% dos valores para o algoritmo BDthrOtsu e o mesmo valor para o BDthrAuto. Assim, apenas na avaliação quantitativa o algoritmo BDComboOtsu apresenta um melhor desempenho que o BDComboAuto.

Pode concluir-se que a densidade mamária pode ser calculada usando um método semiautomático baseado na seleção manual da área glandular nas imagens de ecografias e usando um limiar automático do intervalo de intensidade cinza ou utilizando um método automático baseado na extração automática de área glandular e o limiar de Otsu.

Palavras-chave

Densidade mamária; Imagem de ecografia; avaliação da densidade mamária; analise assistida por computador; algoritmo para avaliação da densidade mamária, Histograma; Limiar.

Resumo Alargado

Introdução

Numa primeira fase é descrito o enquadramento da Tese, definindo-se posteriormente o problema abordado, os objetivos do trabalho de investigação e o argumento da Tese. De seguida, são abordados os principais temas objeto de investigação nesta Tese: estimativa de um valor para a densidade mamária. As metodologias são brevemente discutidas bem como as contribuições resultantes do trabalho desenvolvido. Por último, apresentam-se as principais conclusões.

Enquadramento da Tese

O Cancro é um flagelo que atinge cada vez mais pessoas hoje em dia. O cancro da mama está associado a uma imagem de grande gravidade, uma vez que atinge um órgão cheio de simbolismo na maternidade e na feminilidade.

O cancro da mama é um tumor maligno que se desenvolve nas células do tecido mamário. É muito mais frequente nas mulheres no entanto, pode também atingir os homens.

Os dados mais recentes relativos à incidência do cancro em Portugal, revelam que o cancro da mama aparece em segundo lugar nos cancros registados. Em relação à Europa estimam-se milhares de novos casos de cancro da mama nos próximos anos e nos Estados Unidos, este tipo de cancro ocupa o segundo lugar nas causas de morte. No entanto e apesar da incidência da mortalidade do cancro da mama continuar a ser relevante a diminuição dessa mesma taxa está diretamente relacionada com o diagnóstico precoce.

Assim para além do autoexame, que a mulher pode efetuar, existe um conjunto de exames que permitem identificar a existência ou não da doença: A Mamografia, Exame clínico da Mama, Ecografia, entre outros, que devem ser realizados com alguma periodicidade especialmente a partir dos 40 anos e são usados essencialmente como forma de diagnóstico precoce.

Existem vários fatores de risco associados ao risco de cancro da mama, no entanto, um dos fatores de risco que tem vindo a tomar cada vez mais relevância é a densidade mamária. Inclusivamente em alguns estados dos Estados Unidos da América é obrigatório o envio da informação do valor qualitativo densidade mamária a mulheres com densidade mamária elevada, de modo a que estas decidam se devem submeter-se a exames mais detalhados. Neste sentido o objetivo da presente investigação é abordar a questão da densidade mamária e respetivo cálculo.

Considerando que o tecido mamário varia de mulher para mulher e depende da composição da glândula mamária que está dividia em tecido glandular e tecido adiposo, esta diferença é notória nas mamografias e nas ecografias mamárias, assim as zonas mais claras representam o tecido gandular e as zonas mais escuras o tecido adiposo ou gordura. A densidade mamária é avaliada em função do tecido glandular existente.

Sendo o exame realizado com mais frequência e há mais tempo, a mamografia, diversas abordagens, na maioria com uma avaliação qualitativa para o cálculo da densidade mamária foram desenvolvidas, o mesmo não acontece com a ecografia mamária, para a qual existem muito poucas abordagens.

Os métodos desenvolvidos para a avaliação da densidade mamária assentam na manipulação de imagens por computador, assim seguem as etapas definidas no processamento de imagem: Aquisição da imagem; Processamento da Imagem; Extração de Características; Classificação.

Descrição do problema e objetivos de investigação

O objetivo do trabalho descrito nesta tese é a melhoria da deteção precoce do cancro da mama através do desenvolvimento de uma classificação e quantificação da densidade da mamária em imagens de ecografias mamárias.

O trabalho encontra-se centrado num um objetivo principal:

A densidade da mama é fator de risco para o cancro de mama. Ter uma medida para a densidade da mama que permita aos radiologistas perceber se as mulheres têm um risco potencial, é importante, para prevenir a doença. Os ecógrafos existentes no mercado não fornece um valor de densidade da mama, assim, os seus valores são obtidos por meio da observação visual efetuada por radiologistas, podendo esta avaliação ser subjetiva e varia entre observações de diferentes radiologistas. Considerando estes fatos o principal objetivo é assim, estimar um valor para a densidade da mama em imagens de ecografia mamária.

De modo a cumprir o objetivo principal desta tese, os seguintes objetivos intermédios foram definidos de modo a dividir e organizar o trabalho de investigação.

- Identificar as principais etapas de avaliação e classificação de densidade da mama:

  - De modo a compreender a avaliação da densidade da mama, um dos objetivos deste trabalho é estudar as diferentes abordagens de avaliação e classificação existentes.
  - Análise dos métodos de classificação propostos na de forma a aprender sobre o processamento de imagem e conhecer o estado da arte nesta área de intervenção.

- Investigar a possível aplicação de abordagens desenvolvidas para mamografia em imagens de ecografia mamária.
- Obter um conjunto de imagens de ecografias mamárias e respetiva classificação visual fornecidas por radiologistas. É importante ter um conjunto de imagens para avaliar e ter a respetiva classificação considerando diferentes radiologistas para posterior validação das propostas desenvolvidas.
- As propostas desenvolvidas sob a forma de algoritmos poderem vir a integrar os equipamentos de ecografia mamária de modo a suportar a avaliação efetuada pelos radiologistas.

Argumento da Tese

Esta tese propõe uma nova abordagem para a quantificação e classificação da densidade mamária em imagens de ecografias.

Especialmente, o argumento de tese é o seguinte:

A densidade mamária é considerada um fator de risco no entanto os ecógrafos comercializados não fornecem uma estimativa para esse valor o que complica a obtenção de um valor correto para a densidade mamária. A avaliação da densidade mamária é efetuada por radiologistas por observação visual das imagens de ecografias mamárias, sendo que esta avaliação é subjetiva e com possibilidade de variar em diferentes observações efetuadas pelo mesmo radiologista ou efetuadas por radiologistas diferentes. A densidade mamária pode ser obtida usando um método semiautomático onde a área da glândula é selecionada manualmente e que usa um limiar automático definido no intervalo da escala de cinzentos do histograma da imagem e outro automático baseado num método de extração automática da glândula mamária e no limiar de Otsu.

Principais contribuições

A primeira contribuição desta tese é uma síntese da investigação sobre métodos usados no cálculo da densidade mamária em imagens de mamografias e ecografias mamárias, tendo presente a relevância da densidade mamária como um fator de risco no cancro da mama e o facto do diagnóstico e deteção precoce ser predominante na redução da mortalidade associada a esta doença.

Existindo diversas abordagens para mamografia e poucas para ecografia mamária, assim o ponto de partida passou por uma análise de alguns dos métodos desenvolvidos para mamografia, nomeadamente na extração de caraterísticas, não se verificando resultados satisfatórios.

A segunda contribuição desta tese é a descrição do desenvolvimento de quatro algoritmos baseados na análise do limiar aplicado ao histograma de escala de cinzentos. Sendo apresentados dois algoritmos semiautomáticos, em que a escolha da região da glândula mamária a analisar é feita por seleção manual de modo a selecionar a área mais representativa da glândula e evitar os ecos provocados pelo aparelho de ultrassom na imagem. Efetuando a seleção de três regiões na mesma imagem diminui-se a variabilidade existente no tecido mamário. O primeiro dos algoritmos usa um limiar predefinido, o segundo, usa um limiar automático com base no histograma cumulativo ambos aplicados à matriz normalizada da imagem.

O terceiro e quarto, algoritmos aplicam os limiares definidos para os algoritmos anteriores a um método de segmentação automática da glândula mamária.

Os resultados obtidos foram comparados com três observações efetuadas por radiologistas, duas delas, efetuadas pelo mesmo radiologista com vinte dias a separar as duas observações. Permitindo na análise destes valores constatar as diferenças significativas, em alguns casos, existentes nas avaliações dos dois radiologistas e mesmo nas avaliações efetuadas pelo mesmo radiologista, tendo estas uma variação menor que as anteriores. Conclui-se dessa comparação que os algoritmos que usam limiar automático têm melhor desempenho que os que usam o limiar predefinido.

Foi efetuado ainda, o enquadramento de cada um dos valores obtidos pelos algoritmos, bem como as classificações atribuídas pelos radiologistas para cada imagem, num sistema de classificação qualitativo e também neste caso os algoritmos que usam limiar automático revelaram-se ter melhor desempenho.

A Terceira contribuição desta tese foi o desenvolvimento de dois novos algoritmos que seguem os paradigmas de funcionamento dos algoritmos definidos na contribuição anterior, alterando apenas o limiar definido para o limiar de Otsu e sem utilizar a normalização da matriz. O procedimento de análise dos resultados passou por comparar os resultados obtidos dos novos algoritmos com os algoritmos definidos na segunda contribuição, bem como a comparação com os valores fornecidos pelos radiologistas. Nesta comparação o algoritmo semiautomático, que usa limiar automático com base no histograma cumulativo revelou-se com melhor desempenho do que o que usa o limiar do Otsu e este melhor que o algoritmo que usa o limiar predefinido. No entanto quando o limiar do Otsu se aplica ao algoritmo de extração automática da glândula mamária, este revela melhor desempenho.

Quando se trata da avaliação qualitativa dos algoritmos, os resultados obtidos são semelhantes, havendo no entanto uma aproximação dos valores nos algoritmos semiautomáticos, tendo o algoritmo de Otsu um desempenho ligeiramente melhor.

Abstract

Breast cancer is a disease that affects millions of people. Several studies have identified breast density as an important risk factor for breast cancer. Thus, the evaluation of breast density is important for preventing breast cancer. Current commercially available ultrasound systems do not provide an estimation of breast density, and the evaluation of breast density is based on subjective visual observation of breast ultrasound images by radiologists; therefore, the accuracy of this evaluation is dependent on the skills of the radiologist, which may vary among radiologists.

Several methods have been proposed to evaluate breast density in mammography and ultrasonography noting that there are several methods for mammographic evaluation but only a few for ultrasound evaluation.

In this study, a set of breast ultrasound images was analyzed. Breast density was manually evaluated by two radiologists using this image set, including two distinct evaluations by the first radiologist in different periods.

A quantitative and qualitative assessment was performed using semiautomatic and automatic algorithms with histogram thresholding algorithms and the Otsu method, resulting in six algorithms. An interval was defined for a quantitative analysis where the minimum value corresponds to the lowest value of the three radiologist observations, and the maximum value corresponds to the highest value of those observations.

For the BDthr128 algorithm, 56% of the cases fall within the interval, whereas the value was 73% for the BDthrAuto algorithm; these findings show that the BDthrAuto algorithm has better performance than the former according to the radiologist evaluation of breast density. The application of an algorithm that isolates the mammary gland in BDthr128 and BDthrAuto resulting in BDCombo128 and BDComboAuto automatic algorithms is also described. The procedure used for the analysis of the breast density results was the same as that defined for the BDthr algorithms. After considering the range with the maximum and minimum for the observations of the same image, 28% of the values obtained by applying the algorithms were within the range for the BDCombo128 algorithm and 42% for the BDComboAuto showing that the automatic algorithm performs better according to the radiologist evaluations.

Considering the three breast density observations for each image provided by radiologists and each breast density obtained with the four algorithms for each image, according to the qualitative BIRADS assessment, 3 hits were obtained for 33% of the 85 images using the BDthr128 algorithm and for 48% of the 85 images using the BDthrAuto algorithm. On the other hand, the BDthr128 algorithm achieved at least 2 hits with the radiologist observations in 69% of the images, whereas the BDthrAuto algorithm obtained 86% in the same situation. The BDCombo128 algorithm with 3 hits obtained 25% and the BDComboAuto algorithm obtained 47% in the same situation. With at least 2 hits, the BDCombo128 algorithm obtained 58%, and the BDComboAuto algorithm obtained 79%.

For the application of the Otsu method, images with mammary nodules were not considered because based on the results obtained when using the previous algorithms, it was concluded that this type of image deserves special attention in future research. Thus and for the set of 82 breast ultrasound images, applying the BDthrOtsu semiautomatic algorithm, 65% of the images fall within the considered range, while for BDthrAuto this value is about 70%. Regarding automatic algorithms, BDComboAuto algorithm leads to 49% of images within the range, while the BDComboOtsu leads to 61%. For qualitative evaluation, with full coincidence with the radiologist observations, we obtained 46% of the values for the BDthrOtsu algorithm and the same value for the BDthrAuto. Thus, only in the quantitative assessment, the BDComboOtsu algorithm performs better than the BDComboAuto.

In conclusion, breast density may be computed using a semiautomatic method based on manual selection in glandular areas of breast images and automatic thresholding of the interval of gray intensity or using an automatic method based on automatic extraction of the glandular area and Otsu thresholding.

Keywords

Breast density; Breast ultrasound image; Breast density evaluation; Computer-aided analysis; algorithm for breast density evaluation; Histogram based threshold methods.

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Acronyms

ABUS	Automated Whole Breast Ultrasound
ACR	American Cancer Society
BDCombo128	Automatic Breast Density estimation with the interval of the gray intensity split in half for thresholding algorithm
BDComboAuto	Automatic Breast Density estimation with automatic thresholding of the interval of the gray intensity values
BDComboOtsu	Automatic Breast Density estimation with Otsu method
BDthr128	Breast Density with the interval of the gray intensity split in half for thresholding algorithm
BDthrAuto	Breast Density with automatic thresholding of the interval of the gray intensity values algorithm
BDthrOtsu	Breast Density with Otsu method algorithm
BIRADS	Breast Imaging Reporting and Data System
CAD	Computer-aided design
ECO	European Cancer Organization
EEC	European Economic Community
EFTA	European Free Trade Association
EU	European Union
GD	Gland Segmentation
NASA	National Aeronautics and Space Administration
RE	Radiologist Evaluation
US	Ultrasound

Chapter 1

Introduction

This thesis addresses the problem of quantification and classification of breast density in 2D ultrasound images. Because breast density is a relevant risk factor and because the ultrasound equipment does not facilitate such evaluations, it is important to provide values to avoid the subjectivity of the radiologist's observations. The focus and scope of this thesis are further described in this chapter together with research objectives, thesis statement, main contributions and the organization of the thesis.

1.1 Thesis focus and scope

Breast cancer [1], [2] is a malignant tumor that develops in the cells of the breast tissue. It is much more common in women but can also affect men. Breast cancer often presents as a hard, irregular mass that when palpated, differs from the rest of the breast based on its consistency. Studies published in 2011 [1] state that 230,480 new cases of breast cancer were estimated in 2011 in the United States, and this cancer ranks second in cause of death from cancer. According to the American Cancer Society (ACR) [1] and the European Cancer Organization (ECO) [2], factors identified as risk factors are common. They include factors related to lifestyle (smoking, obesity, alcohol, poor diet, and sedentary life), hereditary factors, age (over 65 years old, above 30 years old at first pregnancy carried to term, early menstruation, and late menopause), infection, exposure to ultraviolet light, exposure to toxins, hormone treatments and more recently, breast density.

As the causes are still undetermined, early detection by medical examinations is of utmost importance. There are several clinical exams, as well as additional tests for the diagnosis of breast cancer in women: mammography, ultrasound, aspiration cytology and biopsy. Black and Welch described in [3] the importance of tests such as mammography and ultrasound, among others. In the case of breast cancer, the authors refer to the advantage of tests, using technology for detecting cancer and focusing on the tests used to detect it. The authors also indicate that women who have undergone a mammography have reduced mortality.

The use of breast ultrasound for the diagnosis of breast diseases has been evolving. Breast ultrasound was first used around 1960, initially with some rudimentary techniques. More recently, breast ultrasound technology has advanced to the use of computers, facilitating an improvement in image quality, both by increasing the resolution and through new possibilities for contrast, leading to an increase in the diagnostic possibilities [4, 5].

Breasts vary from woman to woman, depending on breast composition: glandular tissue and fat tissue. In exams such as mammography or breast ultrasound, the breast tissue presents itself differently: darker regions indicate fat and clearer regions indicate glandular tissue. Breast density depends on factors such as number of children, weight and age.

In 1976, Wolfe [6] established a relationship between the mammary gland density and the risk of breast cancer. Since then, several studies have confirmed this relationship [7-14]. Breast density is measured according to the presence of higher or lower amounts of fat in the breast tissue. Because the most common exam is mammography, almost all of the proposed methods were developed for mammograms [15-39], and only a few methods consider ultrasound [40-42]. These measurement methods are based on image processing and its steps: image acquisition, image processing, segmentation, feature extraction and image classification [43]. For mammography, there are several algorithms for the classification of the breast density, but in almost all cases, they provide only a qualitative assessment. However, such algorithms have been shown to be unsuitable for processing ultrasound images. Therefore, breast density in ultrasound images is evaluated by radiologists through direct visual observation of the images and may depend on the skills of the radiologist, which may lead to subjective evaluations. This thesis addresses the problem of computer-based estimation and classification of breast density in ultrasound images.

1.2 Research objectives

The main objective of this thesis is the proposal and validation of algorithms for the estimation and classification of breast density based on 2D ultrasound images to support the diagnosis made by radiologists. To fulfill the main objective, the following intermediate objectives were defined to divide and organize the required research work:

- Identification of the main steps for the evaluation and classification of breast density in ultrasound images. To understand the evaluation of breast density, one of the objectives of this thesis is to study the different approaches for the evaluation and classification of breast density in mammograms and ultrasound images. The evaluation and classification methods proposed in the literature and the related works are analyzed to learn about image processing and to assess the state of the art in this area. This intermediate objective also includes the understanding of the process of the breast density evaluation from a medical perspective.

- Investigation of the possible application of approaches to ultrasound images that have already been proposed for the successful evaluation and classification of breast density in mammograms.
- Proposal and validation of methods for the quantitative and qualitative evaluation of breast density in ultrasound images, starting from the methods that are already used for mammograms.
- Obtaining a suitable set of breast ultrasound images for the testing and validation of the methods to be proposed and performing an evaluation of the breast density in the set of images based on visual observation of the images by different radiologists to assess the consensus in their observations.
- Evaluation of the performance of the proposed methods regarding the manual evaluation of breast density performed by the radiologists.

1.3 Thesis statement

This thesis proposes new approaches for evaluating breast density on ultrasound images. Specifically, the thesis statement is as follows:

Breast density is a risk factor for breast cancer, but current commercially available ultrasound systems do not provide an estimation of breast density due to the complexity in obtaining reliable breast density values. Currently, the evaluation of breast density values is based on the subjective visual observation of breast ultrasound images by radiologists, which indicates that the breast density evaluation depends on their skills and may produce possible variations based on different observations of the same image by the same radiologist at different times or by different radiologists. Breast density may be computed using a semiautomatic method based on the manual selection of the glandular area of breast images and automatic thresholding of the interval of gray intensity or using an automatic method based on automatic extraction of the glandular area and Otsu thresholding.

To support this thesis statement, the following research approach was adopted.

The problem and research field were studied, and the literature on breast density evaluation and classification was reviewed. The methods for image processing were analyzed as well as the solutions proposed by other researchers. The medical perspective of the evaluation of breast density was also addressed.

A few methods for breast ultrasound image were found in the literature, but none was directly applied to images acquired by ultrasound systems; it was difficult to accurately evaluate the breast density on ultrasound images using original images. Moreover, some extracted features used in mammography were tested, and the obtained results were unsatisfactory.

Because the base of a digital image is the pixels, thresholding histograms present a possible solution to be explored in the thesis. Therefore, algorithms for estimating breast density with intervals of gray intensity split in half, with automatic thresholding of interval of gray intensity values or with Otsu Thresholding were specified. In these algorithms, the breast density was evaluated from a mean of three rectangular areas selected by the radiologist from the glandular area in the ultrasound images. This procedure allows the selection of a more relevant area for the breast density evaluation, avoiding areas where echo affects the image and reducing the variability of breast tissue.

For the same thresholding histogram paradigm used by those three previous algorithms, it is possible to replace the process of selection of three rectangular areas from the glandular area in ultrasound images by the process of automatic extraction of the glandular area in breast ultrasound images.

The performance of the proposed algorithms for the evaluation of breast density is analyzed and compared among them and with the values provided by the radiologists.

1.4 Main contributions

This section briefly describes the main scientific contributions resulting from the research work presented in this thesis.

The first contribution of this thesis is a description of the existing approaches for the evaluation and classification of breast density in mammograms and ultrasound images and a comprehensive analysis and review of the literature. This study is described in chapter 2, which consists of an article submitted for publication in an international journal [44].

The second contribution of this thesis is the development of four algorithms, two semiautomatic and two automatic based on gray level histogram thresholds. The two semiautomatic algorithms use the mean of three rectangular areas selected by the radiologist from the glandular tissue to evaluate breast density, whereas the two automatic algorithms use an algorithm for segmentation and extraction of the glandular areas. The breast density values obtained with the algorithms were compared with values provided by three visual classifications performed by two radiologists, where the first radiologist performed two observations at different time points. In this study, the classification, according to the BIRADS lexicon, of the values provided by the radiologists and the values obtained with the four algorithms is also considered. This study is described in chapter 3, which consists of an article submitted for publication in an international journal [45].

The third contribution of this thesis is the specification and validation of two algorithms based on Otsu thresholding, resulting in one semiautomatic and the other automatic. Considering the algorithms defined in the previous study [45], the thresholding based gray level histogram is replaced by Otsu thresholding. The results obtained with the six algorithms were analyzed and compared. This study is described in chapter 4, which consists of an article submitted for publication in an international journal [46].

1.5 Thesis organization

The thesis is organized as follows:

In **Chapter 1: Introduction,** a brief introduction to the thesis is presented, including the focus and scope, research objectives, thesis statement, major contributions of the work and the thesis organization.

The background concepts behind the research are presented and discussed both in **Chapter 2: A survey of the methods used to classify breast density in mammograms and ultrasound images** and **in** an overview of breast cancer density evaluation in mammography and ultrasound; in addition, the methods behind the algorithms are presented. Methods for feature extraction in ultrasound images were also investigated.

Four algorithms, two semiautomatic and two automatic, for the quantitative evaluation of breast density were specified, and the results of those algorithms were compared with the observations of the three radiologists. The values obtained with the four algorithms and the values provided by the radiologist observations were converted in a qualitative assessment and compared and described in **Chapter 3: Semiautomatic and Automatic Methods for Evaluating Breast Density in Ultrasound Images**.

Based on the algorithms developed in the preceding chapter, a new approach for two algorithms was proposed in **Chapter 4: New Methods for Evaluation and Classification of Breast Density in Ultrasound Images Using Otsu Threshold**. Following the paradigms defined for the four algorithms proposed and described in chapter three, two new algorithms using Otsu Thresholding are proposed, and the obtained results are compared quantitatively and qualitatively with the ones obtained by the other four algorithms and with radiologist observations.

In **Chapter 5: Conclusion and Future Work,** the most important conclusions and contributions of this thesis are presented as well as a discussion about directions for future work.

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Chapter 2

A survey of the Methods Used to Classify Breast Density in Mammograms and Ultrasound Images[1]

Abstract

Introduction: Breast cancer is a serious disease that affects millions of people, most of whom are women. Breast density has been shown to be an important risk factor and must be considered in breast cancer screening and prevention. This review article highlights the importance of breast density as a risk factor associated with breast cancer, both as a single factor and associated with other known risk factors.

Objective: The objective of this article is to analyze the methods used to evaluate breast density in the most common complementary diagnostic procedures used by radiologists: mammography and breast ultrasound.

Conclusion: Many methods are used to calculate breast density using mammography, but there are fewer methods for evaluating breast density using ultrasound. The set of computational methods used to evaluate breast density in ultrasounds is difficult to apply in practice. Given the importance of ultrasound in the diagnosis of breast cancer, the specification of breast density calculation methods for this type of supplementary means of diagnosis is relevant. Some of the most commonly used methods in mammography do not provide satisfactory results when they are applied in breast ultrasound. Nevertheless, this analysis provides a starting point to further research in breast density assessment in ultrasound.

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[1] This chapter consists of the version submitted for possible publication of the following article: Oliveira A, Pereira M., Moutinho J., Freire M.M. A survey of the methods used to classify breast density in mammograms and ultrasound images, submitted for publication in an international journal. Available at: http://www.di.ubi.pt/~mario/Angela1.pdf.

Keywords: breast cancer; breast density; breast density evaluation; breast density classification

2.1 Introduction

Cancer is a scourge that affects many people [1]. Breast cancer is associated with an image of severe gravity because it affects a body part full of symbolism in motherhood and femininity. Breast cancer is a malignant tumor that develops in the cells of the breast tissue. It is much more common in women, although it can also affect men [2].

In Europe, the incidence of breast cancer in 2008 within the 27 member states of the European Union (EU) [3] Belgium, Bulgaria, Czech Republic, Denmark, Germany, Estonia, Ireland, Greece, Spain, France, Italy, Cyprus, Latvia, Lithuania, Luxembourg, Hungary, Malta, Netherlands, Austria, Poland, Portugal, Romania, Slovenia, Slovakia, Finland, Sweden and the United Kingdom and three European Free Trade Association (EFTA) countries, i.e., Iceland, Norway and Switzerland, totaled 332,771 cases, which corresponds to approximately 7% of the population, and a mortality rate of 89,797, which corresponds to approximately 3% in 27 countries and a total of approximately 500 million people. The distribution of breast cancer in these 27 countries is illustrated in the chart of Figure 2.1.

The most recent data on the incidence of cancer in Portugal, which is included in the National Cancer Registry 2001 [4], shows that breast cancer ranks second and represents 14% of registered cancers. According to the Portuguese Institute of Oncology (IPO) in Porto [5] data, from the period of 1989 to 2009 in Northern Portugal, breast cancer has significant values of malignant tumors, which first appear in 30-40% of the cases.

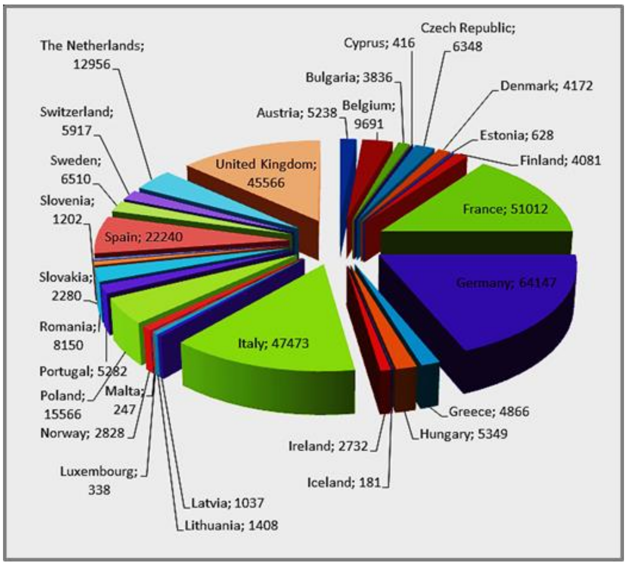


Figure 2.1 - Number of cases of breast cancer in EEC and EFTA - Statistical Data from EEC and EFTA [3].

In Figure 2.2, the percentage of breast cancer compared with other types of cancer is presented; breast cancer is in 2nd place in the list of the highest number of cases in 1990 and in 1st place in the remaining years.

The number of patients who received diagnoses during 1989-2009 increased. Society has shown a greater concern with the possibility of having any type of cancer. This interest is important because early detection and subsequent treatment indicates a lower mortality rate. Figures 2.2 and 2.3 illustrate not only the importance of breast cancer compared with other types of cancer but also a significant increase in the cases treated over the years and in the number of cases where a malignant tumor exists.

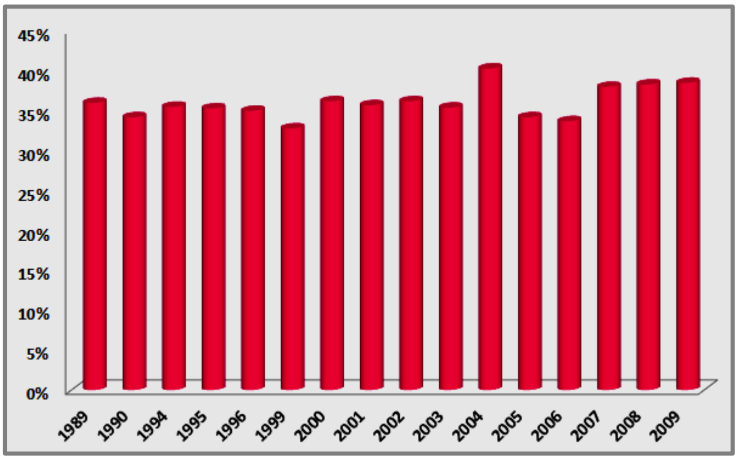
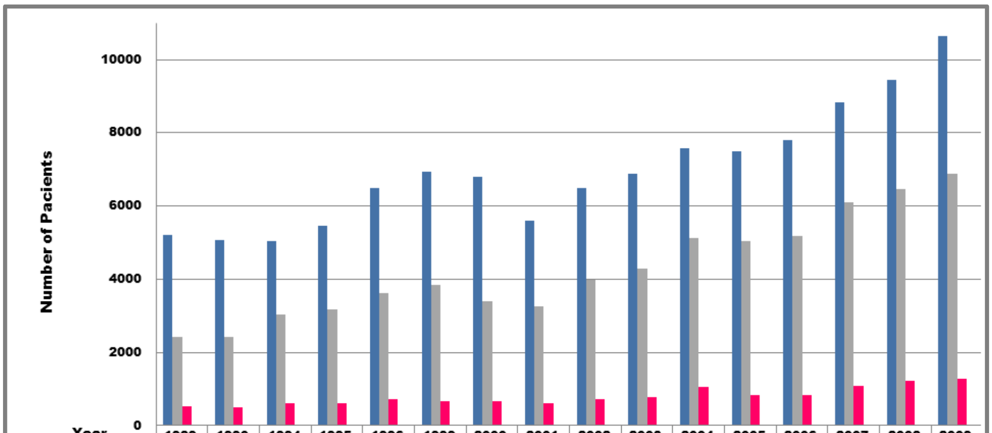


Figure 2.2 - Percentage of breast cancer in different years based on the Statistical Data from the Portuguese Institute of Oncology of Porto [5].



Year	1989	1990	1994	1995	1996	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Patients Received	5195	5075	5050	5453	6502	6931	6789	5584	6501	6878	7573	7500	7808	8823	9452	10650
Malignant Tumors	2410	2430	3036	3176	3614	3829	3408	3256	3975	4277	5125	5052	5171	6085	6460	6880
Breast Cancer	532	493	614	622	710	669	655	610	732	772	1048	842	820	1086	1223	1281
Breast Cancer (%)	35.9%	34.1%	35.4%	35.2%	34.9%	32.7%	36.1%	35.6%	36.1%	35.3%	40.2%	34.1%	33.6%	37.9%	38.2%	38.4%

Figure 2.3 - The number of patients receiving a diagnosis with malignant tumors, namely breast cancer, in women - Statistical Data from the Portuguese Institute of Oncology in Porto [5].

According to IPO, in 2000-2001, women who had been observed during the previous five-year period had a relative survival of 83% in 99% of the breast cancer cases detected in those years [5].

Considering the relationship between the demographics in European countries [6] and the number of breast cancer cases in each country in 2008, breast cancer generally occurred more often in more densely populated countries, where there is an increased number of breast cancer cases. Figure 2.4 illustrates the relationship between the number of breast cancer cases and the population of each of the 27 countries of the European Union plus the 3 countries of the European Free Trade Association.

The American Cancer Society - Breast Cancer Facts and Figures 2011 [7] shows that 230,480 new cases of breast cancer were estimated to occur in 2011 in the United States. This cancer ranks second in cause of death. However, the same study stated that although the incidence of mortality of breast cancer continues to be relevant, the decreasing rate is directly related to early diagnosis. In a similar study in 2007 by the European Cancer Organization [8], similar conclusions were obtained: it is essential to early detect and screen to prevent and cure disease. Ferlay [3] also found that breast cancer ranked second, with a percentage of 13%.

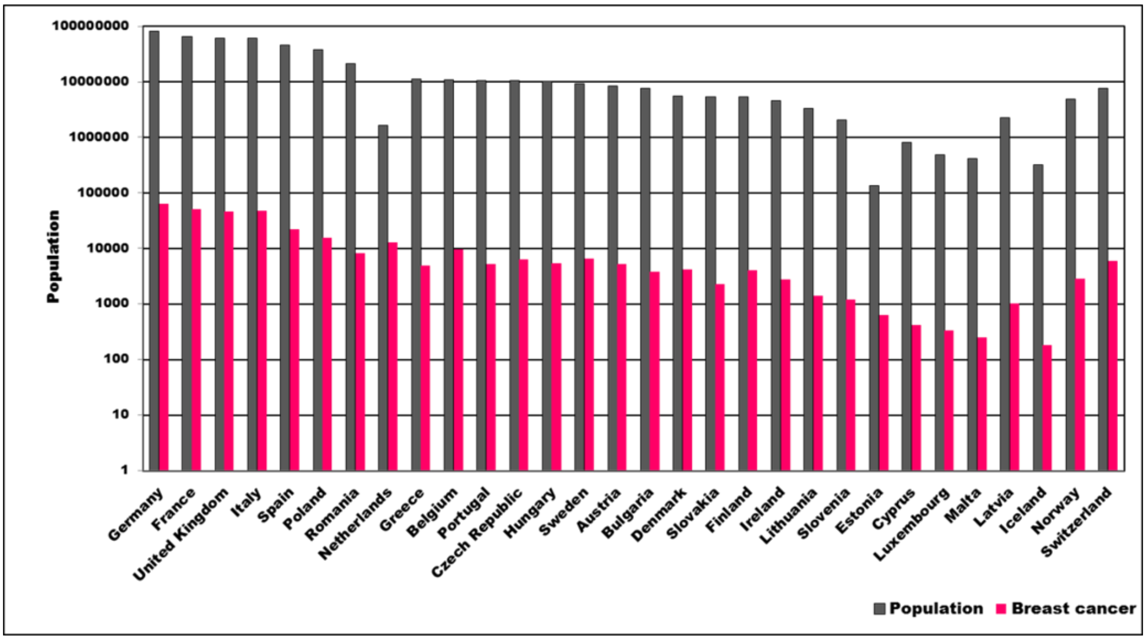


Figure 2. 4 - Relation between population from EU and the number of breast cancer cases [3].

The National Breast and Ovarian Cancer Center, in a 2009 publication [9], considered the following risk factors: moderate to strongly increased, slightly increased or decreased. The moderate to strongly increased group accounts for factors such as **sex** because women are naturally prone to breast cancer: they are 100 times more likely to have breast cancer than are men. A**ge** is another factor that influences the propensity to having breast cancer; older women are at a higher risk. Studies indicate that 75% of breast cancer occurs in women over the age of fifty. **Affluent** countries that are highly populated show a higher number of breast cancer cases, as shown in Figure 2.1. Genetics are another risk factor, as indicated by **family history.** Women who have had first-degree relatives, such as a mother or sister, with breast cancer show a higher propensity towards the disease. This risk increases proportionally with the number of first-degree relatives who have breast cancer. Breast condition is also a risk factor and includes **breast density**. Women with high breast density present a four to six times increased risk compared with women who have low breast density. Women presenting higher levels of estrogen have a two-fold increased risk.

For the slightly increased or decreased group, **hormonal factors,** such as reproductive history, menstrual history, menopausal status and exogenous hormone, and **personal lifestyle** are important factors to consider. However, they depend on women's habits, namely overweight and obesity, alcohol consumption, and physical activity.

Other factors that have been considered risk factors have no evidence of support in this study, including factors such as pregnancy termination or abortion, smoking or environmental pollutants. Because the causes of breast cancer are still undetermined, early detection using medical examinations is important. The earlier that signs of the disease are detected, the greater the likelihood of successful healing is. In addition to self-examination, there is a set of medical tests that can be used to identify the presence or absence of the disease: a clinical breast examination and imaging tests, which may include mammography or ultrasound and can be performed with some frequency, especially after the age of 40. These are primarmily used for early detection, whereas tests such as MRI (Magnetic Resonance Imaging) and biopsy are performed when there are signs of cancer.

William Black and Gilbert Welch [10] reported the importance of tests such as mammography and ultrasound. The article discusses the advantages of tests using technology of many types, focusing on the tests used to detect cancer. A reduction of mortality from breast cancer in women was found for those who had mammograms, which is one of the most commonly performed tests. The risk factor that has become increasingly important is breast density, which is therefore the focus of this paper.

2.2 Breast density as a risk factor

Presentation of the breast varies from woman to woman and depends on breast composition, including both glandular and fat tissue. Therefore, in exams such as mammography or breast ultrasound, breast tissue presents itself differently: darker regions indicate fat, and clearer regions indicate glandular tissue. Breast density is a way to describe the types of tissue that make up the breast. The breast is made up of glandular or ductal tissue, fibrous connective tissue and fatty tissue. The amount of each of these tissues varies in women. Women who have more fibrous connective and glandular tissue than fatty tissue have greater breast density. Breast density depends on factors such as the number of children, weight and age. Breast density is measured according to the presence of a higher or lower amount of fat in the breast tissue. Because the most common exam is mammography, almost every study was developed considering mammograms.

As a relevant risk factor, studies published have considered breast density to be important since 1976, when Wolfe [11] established a relationship between the mammary gland density and the risk of breast cancer.

Several studies have been developed in this area, thus giving relevance to breast density based on different approaches:

- "Mammographic Densities and Breast Cancer Risk" [12] analyzes the literature published during 1976-1997 under terms such as mammography and breast cancer risk. Qualitative and quantitative methods for classifying parenchymal patterns are presented and compared. In this study, mammographic densities and other risk factors for breast cancer are analyzed, and mammographic densities are identified as an independent risk factor.
- The literature review "Applications and literature review of the BI-RADS classification" [13] concerns the usefulness and limitations of the BI-RADS lexicon.
- "Breast Density and Parenchymal Patterns as Markers of Breast Cancer Risk: A Meta-analysis" [14] states that mammographic features are associated with the risk of breast cancer. This association varies considerably between studies, and it is uncertain whether this relevance is modified when associated with other risk factors. Reviews of other studies have been performed, and the findings revealed that breast density is one of the strongest risk factors. Therefore, more consideration should be given to the routine measurement of mammographic density because this marker has potential to be used for the research and prevention of breast cancer.
- In the study "A Comparison of Breast Tissue Classification Techniques" [15], different strategies for extracting features from tissue and their classification systems are reviewed, and the feasibility of estimating breast density by using automatic computer vision techniques and the benefits of segmentation of the breast based on internal tissue information are demonstrated.
- The study "Breast Image Registration Techniques: a survey" [16] gives an overview of the current state-of-the-art in the breast image registration techniques: Image registration; and reviews literature on intra-modality breast image registration on the design of co-registered multimodality breast imaging acquisition systems and validation of breast registration methods.
- The study "Comparison between Wolfe, Boyd, BI-RADS and Tabár Based Mammographic Risk Assessment" [17] provides a comparative study of the Wolfe, Boyd, BI-RADS and Tabár-based assessment approaches for mammographic image classification methods.

- In the study “Comparing Measurements of Breast Density” [18], the authors undertake a theoretical analysis of physical breast density definitions and area versus volumetric estimation techniques and analyze both the images and the results of applying the various techniques.
- In the study “Mammographic Density. Measurement of mammographic density” [19], Martin Yaffe reviews the techniques for measuring density and gives some consideration for strengths and limitations.
- The paper “Automated breast cancer detection and classification using ultrasound images: A survey” [20] reviews Computer-aided design (CAD) systems for breast cancer detection and classification using ultrasound images and summarizes the techniques developed. The advantages and disadvantages are discussed, different performance evaluation metrics are studied and future developments and trends are also investigated.
- The paper “Automatic Breast Density Segmentation: an integration of different approaches” [21] states that in most studies, breast density is assessed by using a user-assisted threshold method that is both time-consuming and subjective. In this study, the authors develop a breast density segmentation method that is fully automatic and is based on pixel classification, considering different approaches known in literature, such as breast density segmentation.
- The paper “A review of automatic mass detection and segmentation in mammographic images” [22] reviews the existing approaches for automatic detection and segmentation of masses in mammographic images. The advantages and disadvantages of the various approaches are demonstrated.

The above studies show the interest in breast density and its relevance for risk of breast cancer. The studies mention classification systems that involve breast density and image analysis techniques, thus revealing a great interest in image processing and breast density evaluation. Since Wolfe’s publication in 1976, several studies have considered the relationship between breast density and the risk of breast cancer.

Both Boyd [23] and Ursin [24] reported that women with a high mammary density have a greater probability of developing breast cancer. A new model based on the Gail Model [25] was built, and breast density was added as a risk factor, as presented by Chen [26]. The conclusions determined that with the newly developed model, women with a higher breast percentage density have a higher propensity for breast cancer.

In 2006, Titus-Ernstoff presented [27] a study that evaluates the risk factors of breast cancer that are associated with breast density. Although the density of the breast is a risk factor for breast cancer, the study suggested that with more efficient mammary density measurements, a higher amount of consistent studies can be produced.

In 2007, Boyd presented [28] a study using mammography that related breast density to the risk of cancer. In the conclusion of that study, breast density was reported to be strongly associated with an increased risk of breast cancer: the higher the density, the higher the risk of cancer; further, this risk persists for a considerable period of time. The calculation of assigned risk shows that breast density explains a significant proportion of cases of breast cancer in young women and demonstrates that a large percentage of women have more than 50% mammary density. In 2007, Vachon presented [29] a study where several models were evaluated and to which another risk factor is added, namely breast density. The conclusion was that breast density is important not only in women who are considered to be at risk and are receiving mammograms but also in women at younger ages. In 2008, Jeffrey presented [30] a breast density analysis in a group of women. The conclusions were that women with low breast density had a lower risk, unless they had a family history of breast cancer.

The impact of breast density associated with several risk factors has been widely analyzed to demonstrate that breast density is a risk factor of breast cancer. In 2011, Boyd stated [31] that in future studies, breast density should be improved by calculating the percentage of breast density, which should be included in the definition of individual risk.

In America, there are 19 states with breast density notification laws [32], which require physicians to notify women who present mammographic breast density. This information is sent to women with dense breasts. Working groups of experts in breast imaging and breast cancer risk conducted several studies related to breast density to provide women and radiologists with accurate information [33], [34].

Table 2.1 shows several studies that aim to address the combination of breast density and other risk factors of breast cancer and thus consider breast density to be a risk factor.

Table 2.1 - Summary of studies considering breast density associated with other risk factors.

Studies Risk Factors	Maskarinec G et al [35]	Maskarinec G et al [36]	Vachon C et al [37]	Barlow W et al [38]	Palomares M et al [39]	Mitchell G et al [40]	Boyd N et al [41]	. Boyd N et al [42]	Kerlikowske K et al [43]	Yaghjyan L et al [44]
Ethnicity	✓	✓		✓						
Age		✓	✓	✓	✓		✓	✓	✓	
Residence		✓	✓							
Exam Date			✓							
Menopause Status			✓	✓			✓	✓		
Age at Menopause				✓			✓			
Type of Menopause				✓						
Number of Mammograms			✓							
Postmenopausal										✓
Interval Between Mammograms			✓	✓						
Age at Menarche				✓	✓		✓	✓		
Age at the Birth of First Child				✓	✓		✓	✓		
Number of Live Births							✓			
Use of Hormone Therapy				✓			✓			
Not use of Hormone Therapy									✓	
Personal History of Breast Cancer				✓	✓					✓
Family History of Breast Cancer				✓	✓			✓		
First-degree Relatives with Breast Cancer					✓		✓			
Number of Breast Biopsies					✓					
Atypical Hyperplasia					✓					
BRCA1 Mutation Carriers or Not						✓				
BRCA2 Mutation Carriers or Not						✓				
Height (cm)							✓	✓		
Weight (kg)							✓	✓		
BMI (Body Mass Index)							✓			

2.3 Qualitative classification of breast density

Breast density is generally quantified by a technician or doctor who performs the exam, and there are several approaches to this classification [11]. However, this classification in most cases depends on the skills of the person who made the observation and therefore does not allow a uniform assessment.

D'Orsi [46] found that the evaluation of body part thickness shows a thicker density in larger areas. When calculating the size and thickness of the breast, the same standards are followed. According to the same author, the breast can be classified into three broader categories, depending on the relative amounts of glandular tissue versus adipose tissue [46]:

- Glandular breast: In general, a young breast is denser because it contains a relatively small amount of fat tissue. This usually occurs in women under 30 years; however, an older woman who has never carried a pregnancy to completion may also be included in this category. Nevertheless, pregnant and lactating women can still be included in this category.
- Fatty and glandular breast: With increasing age, the tendency is for the fat in the breast to increase. There is an approximation in the amount of fatty tissue and glandular tissue. Women between 30 and 50 years old are usually included in this category.
- Fatty breast: Women aged 50 and/or upon the occurrence of menopause are included in this category. With the end of reproductive life, the breast loses fibrous mass and turns into fat.

Although it may be based on the above categories, the process of quantifying breast density is not exact, and several approaches have been defined over time. In most situations, the quantification of breast density is performed by the technician who is performing the test. There are several ways of classifying it [28], the most common of which involves two radiologists analyzing breast density and distinguishing it as fitting into one of the following six categories: 0%, <10%, from 10% and <25%, from 25% and <50%, from 50% and <75%, and >75%.

In conclusion, breast density is an important risk factor, but a method for assessing breast density is also important. As shown in Tables 2.2 and 2.3, several algorithms have been developed to evaluate breast density by ultrasound.

Among the most widely used classifications, the Wolfe classification [11] is based on mammograms and is a visual classification method that can be defined as follows:

- N1 corresponds to fatty normal breast;
- P1 corresponds to prominent ducts occupying less than 25% of the breast;
- P2 corresponds to prominent ducts occupying between 25% and 75% of the breast;

- Dy corresponds to breast dysplasia and is extremely dense.

The classification of Breast Imaging Reporting and Data System - BI-RADS [17, 46], which is based on standard reports for viewing mammograms developed by the American College of Radiology (ACR) [47], is divided into the following categories:

- Category 1: Breast is mostly made up of fat <25% breast density.
- Category 2: Approximately 25% to 50% breast density.
- Category 3: Approximately 51% and 75% breast density.
- Category 4: Extremely dense > 75% breast density.

In Table 2.2 of [29], the classification of BI-RADS and Wolfe, are presented as qualitative classifications. Three methods of quantitative classification are also presented:

- First, acetate is placed in superposition on the mammography image, and a technician searches for areas of breast density. The total amount of breast density is measured using a delimitation tool. The percentage of breast density is assigned on a scale of 0% to 100% and is then fitted into five levels of 0%, 1% to 24%, 25% to 49%, 50% to 74% and larger or equal than 75%.
- Second, a computer-assisted method is used, in which mammograms are digitized, and two initial points are selected. The first separates the background image of the breast, and the second identifies the boundary of the dense tissue. In the calculated pixels, some represent the total breast area and others represent the dense area, thus providing a formula to calculate the breast density percentage.
- Third, breast density is classified by experts in radiology [28].

2.4 Breast density evaluation

Digital Image Processing, dating from the 1960s, was developed by research projects at NASA in the United States of America. Shortly thereafter, studies that require the knowledge provided by this method, such as medicine, microscopy, and meteorology, appeared.

Since the discovery of X-rays by Wilhelm Konrad Roentgen in 1895, medical images have become an important resource and are widely used in the practice of medicine. There are many methods, approaches and objectives for medical image processing. The methods allow doctors to noninvasively inspect the human body for abnormalities and allow for fast diagnostic decisions [48].

2.4.1 Computer-based image processing

Computer vision addresses theories and algorithms for automating the process of visual perception and involves tasks such as noise removal, smoothing, edge sharpening, image segmentation to isolate object regions, and interpretation. Therefore, image processing may be defined as applying a series of processes of acquisition, correction, improvement, or image compression and processing to improve image quality and information. To perform breast density evaluation, the following steps, as illustrated in Figure 2.5, were defined [49].

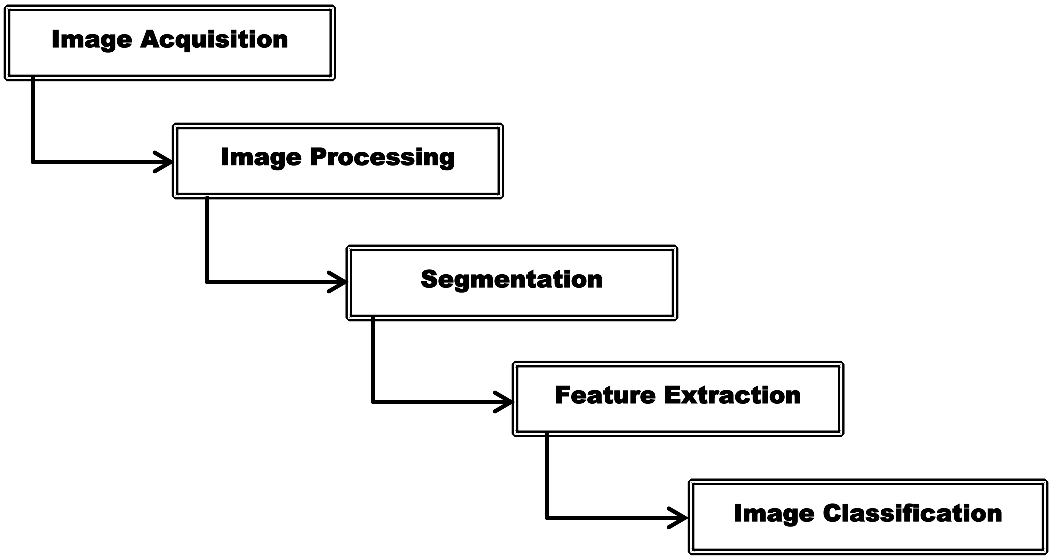


Figure 2.5 - Steps for processing medical images [49].

Image acquisition – Generally, scanning an image means making it computationally manageable. When transforming an image to a digital form, it is necessary to convert it into a signal. The definition of this signal, which represents the image, is a process where each pixel is represented by an integer value proportional to the brightness and color at the corresponding point in the image.

Image Preprocessing - Processing techniques are used to improve some aspects of the image such as mitigating noise and enhancing contours; edge detection; image registration; and improving the characteristics of intensity, color and texture.

Segmentation – Dividing an image into distinct regions where the pixels of each region have similar characteristics. The success of image analysis depends on an effective image segmentation process. There are different approaches and different ways of performing the segmentation process [50].

Some researchers have proposed the divisions of segmentation as follows:

- Texture segmentation
- Region segmentation

In texture segmentation, segmentation as a graph-cut problem is formulated. Other researchers have considered a partition of a color image based on different modes within the estimated empirical distribution by extracting regions of interest in the image [51-54].
In region segmentation, important information about the structure of the objects in the image is given. Several methods have been proposed to combine color and texture with the contours of the image [55-57].

Another approach considers the divisions to be as follows [58]:

- Non-contextual segmentation techniques
- Contextual segmentation techniques

In a non-contextual technique, the relationships among features of an image are not considered, and image segmentation is performed by considering the global attributes. In contextual segmentation, the features are relevant for the segmentation process. The simplest process for a non-contextual process is thresholding. The input to a thresholding operation is typically a grayscale or color image, and the output is a binary image that represents the segmentation. The binary map contains two values: if the pixel's intensity is higher than the threshold, then it is labelled with a value of one and the pixel is set to white. Conversely, if the pixel's intensity is lower than the threshold, then it is labelled with a value of zero and is set to black. The segmentation depends on both the image property being thresholded and the chosen threshold.

Adaptive thresholding or color thresholding can also be used. In adaptive thresholding, the thresholds change dynamically over the image [59]. In color thresholding, there is more information regarding the pixel levels; thus, it involves partitioning the color space [60]. Contextual segmentation includes a spatial analysis, i.e., each pixel is analyzed, as are its neighboring pixels. In general, context segmentation includes methods such as region growing and merging or splitting techniques [61].

Region growing is a region-based segmentation in which pixels that have similar properties are grouped into a large region. The pixels are grouped together and are marked by principals of similarity and spatial proximity. Region splitting and region merging are opposite methods. The splitting process starts with the whole image, which is recursively divided into sub-regions until a homogeneity condition is satisfied. The merging process starts with a small region and merges regions with similar characteristics.

Another approach separates traditional image segmentation methods into three categories [61]:

- Pixel-based segmentation
- Edge-based segmentation

- Region-based segmentation (described previously).

Pixel-based segmentation corresponds to the thresholding segmentation that were previously presented in non-context segmentation. Edge-based segmentation consists of detecting edges between regions. Some authors consider a fourth method: clustering-based segmentation, which clusters tokens with high similarity (small distance in the feature space).

Feature Extraction - This is the process by which parameters are obtained for use in the classification process, which are, in most situations, derived from segmentation. Image classification is the biggest task after extracting the image characteristics because it classifies the extracted object into a category.

Image Classification - This process depends on the feature that it aims to classify. Different ways of dealing with the variability lead to different ways of classifying images, but two basic image classification strategies are presented [62]:

- Supervised classification: the algorithms for supervised classification are conventional pixel-labelling algorithms. Examples include multidimensional thresholding; Minimum-distance classification; maximum likelihood classification; and support vector machine.
- Unsupervised classification – the algorithms for unsupervised classification examine a large number of unknown pixels and divide them into a number of classes based on natural groupings present in the image values. Examples include K-means, fuzzy K-means, hierarchical, and histogram-based clustering.

The process is illustrated in Figure 2.6.

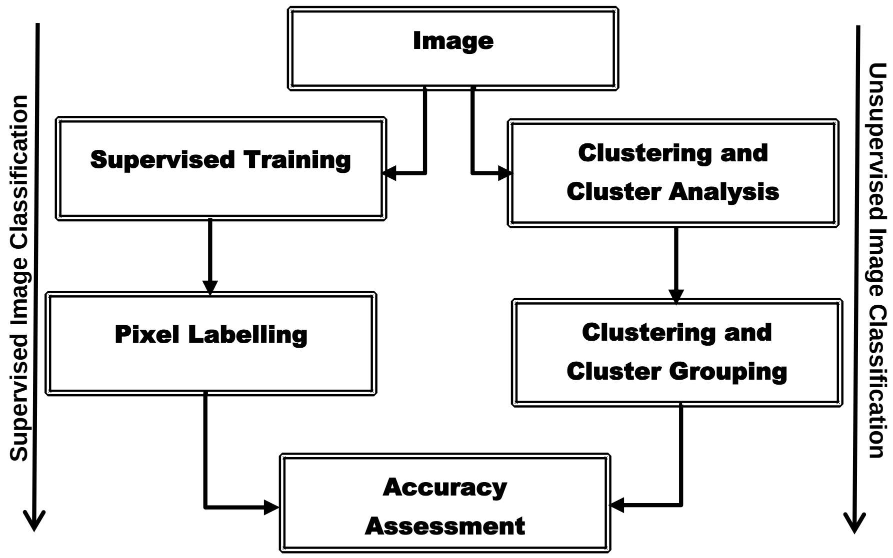


Figure 2.6- Supervised and unsupervised image classification processes.

2.4.2 Algorithms for breast density evaluation

Breast density was first evaluated according to a qualitative classification scheme, with its origin in the work developed by Wolfe [11]. Quantitative approaches using visual estimation, plan metrics, and computer-assisted methods were later developed. Several studies and different methods for classifying breast density based on mammograms have been proposed. Over time, several approaches to achieve an improvement in the final evaluation have been presented. These studies also use a comparison of the density value calculated by semi-automatic or automatic methods with a value assigned by an expert in accordance with a system of classification to fit the results into a category. In breast density evaluation, image classification often involves a classification scheme and a classification metric. The classification scheme fits one of the classifications of Wolfe [11] or BI-RADS [17], [46]. Metric classification uses statistical classification or a classifier such as KNN (K - Nearest Neighbors).

Table 2.2 shows different proposals for breast density classification in mammographic images, and Table 2.3 shows different proposals for breast density classification in ultrasound. As shown by these tables, only a few algorithms have been proposed to evaluate breast density in ultrasound images.

The methods proposed in [87] and [88] and those mentioned in Table 2.3 follow the same approach: data acquisition, preprocessing data for speckle reduction and density classification.

In both cases, image acquisition was performed using an SSD-5500 ultrasound machine with a linear 6 cm ASU-1004 transducer. In this ultrasound system, the probe was immersed in a water bath coupling, and three passes were performed to cover the entire breast. The acquired images were stored in a DICOM (Digital Imaging and Communications in Medicine) file, and a DICOM reader decomposed them into serial 2D images. The second step consists of preprocessing, which includes speckle noise reduction and an adaptive threshold, which detects the region of interest through an algorithm that distinguishes the pixels of the different regions, and roughly divides the regions into fibroglandular tissue and fat tissue. Finally, in the third step, two methods, threshold- and proportion-based, were applied to provide a measure of breast density and the corresponding classification according to BI-RADS.

Thus, by analyzing the procedure used in the methods described in [87] and [88], the specific form of image acquisition through breast submersion, the pre-processing of the obtained images in DICOM format and the respective qualitative classification are similar.

Table 2.2 - Different approaches for breast density classification in mammograms.

AUTHOR/YEAR	SEGMENTATION FEATURE AND/OR FEATURE EXTRACTION	CLASSIFICATION METRIC	CLASSIFICATION SCHEME
Taylor P et al 1994 [63]	Threshold	Statistical and texture measures	Wolfe categories
Byng J et al. 1994 [64]	Threshold	Threshold	Six categories
Suckling J et al 1995 [65]	Feature vector	Neural networks	Comparison between algorithm and radiologist
Byng J et al 1996 [66]	Fractal analysis	Threshold	Six categories
Byng J et al 1997 [67]	Threshold	Histogram and Fractal geometry Proportional hazards regression model	Six density categories
Karssemeijer N et al 1998 [68]	Threshold	K-Nearest Neighbors classifier	Four categories
Byng J et al 1998 [69]	Threshold	Percent density	Six categories
Zhou C et al 2001[70]	Histogram	. Rule-based classification	Four categories
Sivaramakrishna R. et al 2001 [71]	Threshold	Percent density	Comparison between algorithm and radiologist
Saha P et al 2001 [72]	Fuzzy methods	Sum of intensities of pixels	Comparison between algorithm and radiologist
Bovis K et al 2002 [73]	Threshold	Fourier transform; Laws' texture masks; Discrete Wavelet Transform	BI-RADS
Muhimmah I et al 2005 [74]	Histograms	Feature vectors and k-nearest- neighbor approach: an Euclidean distance, Bayesian Probability, major voting	Six categories and radiologist.
Torres-Mejía G et al 2005 [75]	Histograms	Percent density	Percentage of dense pixels compared with Wolfe categories
Oliver A et al 2005 [76]	Fuzzy methods	k-Nearest Neighbours algorithm and a Decision Tree classifier	Three categories
Martin k et al 2006 [77]	Threshold	Percent density	Histogram Classification
Oliver A et al 2006 [78]	Histograms	. Bayesian classifier :with k-Nearest Neighbours algorithm and the C4.5 decision tree	BI-RADS
Muhimmah I et al 2006 [79]	Histogram e	Feature vectors in combination with a multiclass Directed Acyclic Graph - Support Vector Machine	Three categories
Lu L et al 2007 [80]	Histogram	Percent density	BI-RADS
Heine J et al 2008 [81]	Threshold	Percent density	BI-RADS
Oliver A et al 2008 [82]	Fuzzy methods	Bayesian combination of a number of classifiers	BI-RADS
Oliver A et al 2010 [22]	Fuzzy methods	Karhunen-Loeve transform	Two categories
Subashini T et al 2010 [83]	Threshold	Vector machine	Three density categories
Liu L et al 2010 [84]	Histogram	Feature vectors	Three categories
Mustra M et al 2010 [85]	Covariance matrix	IB1 Classifier	Three categories
Bueno G et al 2011 [86]	Covariance matrix	k-NN, SVM and LBN	BI-RADS

Table 2.3 - Different approaches for breast density classification in ultrasound.

Author/Year	Segmentation Feature and/or Feature Extraction	Classification Metric	Classification Scheme
Chang R et al 2006 [87]	Adaptive Speckle Noise	Threshold	BIRADS
Chen J et al 2009 [88]	Adaptive Speckle Noise	Threshold	BIRADS
Chang R. et al 2010 [89]	Volumetric breast density	Fuzzy methods, Percent density	No Scheme

Chang et al. [89] used a three-dimensional ultrasound technique called automated whole breast ultrasound (ABUS) that is used to automatically scan a large area of breast with two to five passes such that the whole breast is scanned completely. After segmenting the breast region, the fuzzy c-mean classifier was used to differentiate the fibroglandular and fatty tissues in the ABUS images. The percent density and fibroglandular tissue volume were compared and correlated in both ABUS and MRI imaging modalities with the linear regression analysis.

2.5 Methods for feature extraction in ultrasound images

Based on the analyses discussed above, three methods have been used for feature extraction in mammography: basic histogram thresholding, fuzzy c-means and gray-level co-occurrence matrix. We performed a preliminary investigation on the applicability of these features for classifying breast density in ultrasound images.

2.5.1 Thresholding in ultrasound images

An ultrasound image is selected and converted into grayscale. To apply the thresholding to the image, the histogram is generated from a selected area that represents the glandular area of the breast ultrasound image, as illustrated in Figure 2.7.

As shown in Figure 2.7, the histogram from the selected breast area has a maximum value close to 0.6. All values are concentrated in the dark area of the histogram. A thresholding that divides the range of grayscale [1:256] into two ranges [1:128] and [129:256] is considered. The values of each range are counted; dark pixels are identified in [1:128] and white pixels are identified in [129:256]. The formula to evaluate breast density is the sum of white pixels divided by the sum of white pixels and dark pixels. The obtained value is close to zero. Nevertheless, there is space for further research on this issue.

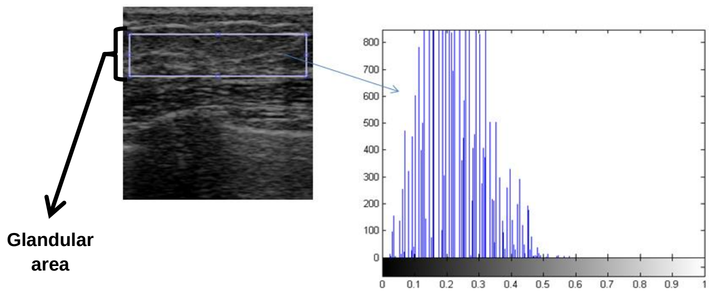


Figure 2.7 - Selected area in the breast glandular area and the respective image histogram.

2.5.2 Fuzzy C-Means in ultrasound images

Fuzzy c-means segmentation of an image was used to convert an input image into two segments to represent the dark area in one cluster and the white area in another. For a selected area that represents the glandular area of the breast ultrasound image, the fuzzy c-means algorithm is applied.

As observed in Figure 2.8, the two clusters cannot be identified clearly, and the center of the clusters represented by "O" and "X" are close, which indicates that it is not possible to extract the two features for further classification.

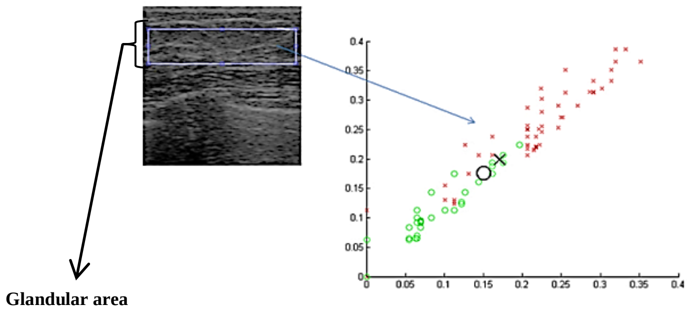


Figure 2.8 - Fuzzy C- Means applied to the selected breast area.

2.5.3 Gray-level co-occurrence matrix in ultrasound images

To calculate the gray-level co-occurrence matrix for a grayscale image, the MATLAB® *graycomatrix* [90] package is used to evaluate the following values:

- Contrast – Provides the measure of the intensity between each pixel and its neighbor. If the value of contrast is zero, it means there is no variance in grayscale intensity.
- Homogeneity - Returns a value that measures the closeness of the distribution of elements, each element in relation to an element in the diagonal. Large values of homogeneity mean that the image contains similar levels of gray.
- Correlation - Returns a measure of how each pixel is correlated with the neighboring pixels.

In this case, four gray-level co-occurrence matrixes are calculated, i.e., for angles 0º, 45º, 90º and 135º. Two gray levels are considered.

The calculations of the contrast, homogeneity and correlation are performed for a set of 85 breast ultrasound images, and the obtained results are similar, which suggests that the images have a lower contrast range between 0.000 and 0.035. There is a weak variance in the grayscale intensity. The correlation is close to one and ranges from 0.875 to 1.000, which means that the pixels are strongly correlated, and a high value for the homogeneity, which ranges from 0.300 to 0.749, indicates that the image contains similar levels of gray, which makes these features unsuitable for further classification.

Figure 2.9 provides an example illustrating this situation. Based on this example, it is difficult to analyze the ultrasound images with these methods.

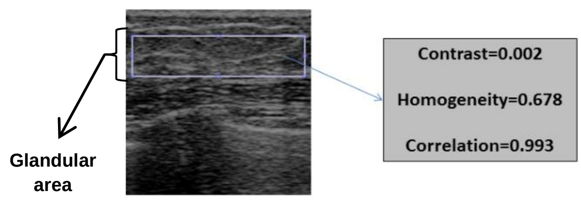


Figure 2.9 - Results from gray-level co-occurrence matrix in the selected area.

2.6 Conclusions

In this paper, the relevance of breast density as a risk factor and the gravity associated with breast cancer are discussed. Several studies have analyzed breast density with other risk factors and concluded that breast density may be considered a risk that is as relevant as the other known risks. For this reason, the assessment of breast density value is important. Quantitative and qualitative approaches for evaluating breast density are also discussed.

For mammography, several algorithms are used to obtain, in most cases, a qualitative assessment of breast density. However, few algorithms exist for ultrasound images. Three of the methods that have previously been applied to mammography were applied to ultrasound images. Although the obtained results are not satisfactory, they may be a starting point for further research on the assessment of breast density in ultrasound images.

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Chapter 3

Semiautomatic and Automatic Methods for Evaluating Breast Density in Ultrasound Images[2]

Abstract

Objective: Breast density is a risk factor for breast cancer, but the commercially available ultrasound systems do not provide an estimation of breast density. The objective of this study is to propose and evaluate four algorithms for estimating breast density in ultrasound images.

Materials and Methods: A set of 85 breast ultrasound images is analyzed. Manual evaluation of breast density over this set was performed by two radiologists, including two distinct evaluations by the first radiologist at different times. The proposed algorithms are used to obtain estimates of breast density.

Results: For the quantitative analysis, an interval was defined for each image, which was limited by the lowest and highest values of the three radiologist evaluations. The percentage of the breast densities within the interval over the set of images was evaluated for the four algorithms. For the qualitative BIRADS assessment corresponding to the quantitative evaluation of the breast density, the percentages of the number of classifications for each algorithm that reached 3 hits or at least 2 hits of the classification based on the three radiologist observations were evaluated over the set of images.

Conclusion: Algorithms with automatic thresholding (BDthrAuto and BDComboAuto) are more accurate, according to the radiologist evaluations, than are the corresponding algorithms based on the half division of the grayscale interval (BDthr128 and BDCombo128). However, semiautomatic

[2] This chapter consists of the version submitted for possible publication of the following article: Oliveira A, Pereira M., Moutinho J., Freire M.M. Semiautomatic and Automatic Methods for Evaluating Breast Density in Ultrasound Images, submitted for publication in an international journal. Available at: http://www.di.ubi.pt/~mario/Angela2.pdf.

algorithms (BDthr128 and BDthrAuto) lead to better estimates of breast density compared with automatic algorithms (BDCombo128 and BDComboAuto), which makes the BDthrAuto algorithm a good candidate for computer-based breast density estimation.

Keywords: Breast density; breast ultrasound image; breast density evaluation; computer-aided analysis; algorithm for breast density evaluation.

3.1 Introduction

There are several factors that affect the risk of breast cancer. In studies conducted by the American Cancer Society [1] and the European Cancer Organization [2], risk factors for breast cancer have been found, including age, lifestyle, hereditary factors, exposure to ultraviolet light, exposure to toxins, hormone treatments and, more recently, breast density.

Breast density varies from woman to woman, depending on the breast composition, which includes both glandular and fat tissue. Therefore, in medical exams such as mammography or breast ultrasound, breast tissue presents itself differently: darker regions indicate fat tissue, and clearer regions indicate glandular tissue. Breast density depends on factors such as the number of children, weight and age. Breast density is considered a risk factor, and it has been considered a relevant factor in several studies. Since the study of J. Wolfe in 1976 [3], several studies have established a relationship between the density of the mammary gland and the risk of breast cancer [4-15].

The currently available ultrasound systems do not provide a numerical evaluation of breast density to radiologists, so breast density is roughly estimated by the radiologist through visual observations of the ultrasound image. There are some approaches to this classification [3], which, in most cases, depend on the skills of the radiologist, who, being unable to perform a uniform assessment, may require the support of a computer to obtain more objective results.

Several studies have proposed quantitative approaches based on computer-assisted methods for breast density evaluation in mammography using histograms [16-22], thresholding [23-32], clustering or texture analysis techniques [33-38] for feature extraction and thus the further classification of breast tissue. Some of those techniques, specifically clustering or texture analysis, were also implemented for density estimation in breast ultrasound images. Fuzzy c-means has been shown to be unsuitable for feature extraction in ultrasound images because the division into two clusters does not show clearly determined dense and fatty tissues; thus, it does not provide significant information. Using the gray-level co-occurrence matrix that results from the average of the four covariance matrices for 0°, 45°, 90° and 135°, the maximum and minimum values of some relevant features for the set of 85 ultrasound images considered in this study range between: 0.000 and 0.035 for Contrast, 0,300 and 0,749 for Homogeneity, 0.875 and 1.000 for Correlation, and 0.983 and 1.000 for Energy, which makes these features unsuitable for further classification.

To obtain a better understanding of the clinical history of patients, breast density may be relevant. The use of ultrasound systems for cancer detection and diagnosis has increased due to the portability, convenience and low cost associated with ultrasound [39]. However, the commercially available ultrasound systems do not provide an estimated value of breast density, primarily due to the complexity of obtaining a reliable value.

The image produced by ultrasound is not always presented in the same way because it is sensitive to the manipulation and skills of the radiologist. Therefore, it is important to be able to manipulate an ultrasound image to obtain satisfactory values for breast density. The objective is to obtain a value that is as close as possible to the value of breast density; however, this process is hampered by ultrasound images because different types of breast conditions may allow significant freedom in obtaining images of the breast.

Ultrasound has been used in human body imaging for over half a century, but only a few methods have been proposed for evaluating breast density in ultrasound images. Those methods that exist only allow a qualitative assessment and are targeted for 3D images.

Chen et al. proposed [40, 41] a qualitative classification of breast density. In this method, each breast imaging requires three steps and overlapping, and the breast must be submerged in water to obtain 3D whole breast images. Other methods have been proposed, which present volumetric estimation in 3D breast images, such as the method proposed by Chang et al. [42] or the work developed by Moon et al. [43], which compares the density analysis using automated whole breast ultrasound (3D) and magnetic resonance imaging.

Ultrasound is one of the most widely used imaging technologies in medical diagnosis, but the difficulty of analyzing images makes it difficult to determine the breast density. Therefore, this paper addresses this problem. We propose four algorithms for evaluating breast density in ultrasound images by using original images without any preprocessing or removing the speckle noise.

3.2 Methods

3.2.1 Study population and image acquisition

The set of 85 images analyzed in this paper was obtained from patients who had already been diagnosed and treated in Cova da Beira's Hospital in Covilhã, Portugal, with disease evolution for the period 2007-2013. These ultrasound images make no reference to the patient's identification.

Experimental data were acquired using LOGIQ Book XP, a high-performance, multipurpose hand-carried imaging system. The ultrasound images are structural images based on the reflection of a sonographic imaging ultrasound device that was used in the B-mode on the walls tissues, as illustrated in Figure 3.1a), and it is a two-dimensional ultrasound presentation of the produced echo in a single plane. The intensity of the echo is represented by the modulation of the brightness.

A digital image can be considered a large array of discrete dots, each of which has an associated brightness. The algorithms herein proposed aim to evaluate the density of breast in ultrasound images. The evaluation is based on the number of occurrences of black and white in the ultrasound images, considering the division of the interval of 256 possible gray intensity values of the grayscale image. The proposed algorithms consider the original images without applying a filter or pre-processing or removing the speckle noise. The speckle noise analysis approach adopted in each situation depends heavily on the applications. The main objective is to improve the image quality while maintaining both the outlines and the structural information when the noise is softened by a grainy texture. Considering the region of interest for visual interpretation, smoothing may be less desirable and is not used in this study.

3.2.2 Conversion of the image to grayscale

We can describe a monochromatic image as a mathematical function of light intensity and its value at any point of spatial coordinates proportional to the brightness or gray level image at that point. The intensity of a monochrome image point is in the range [0:1]. A conversion of the original image into a grayscale is performed before image acquisition in the algorithms.

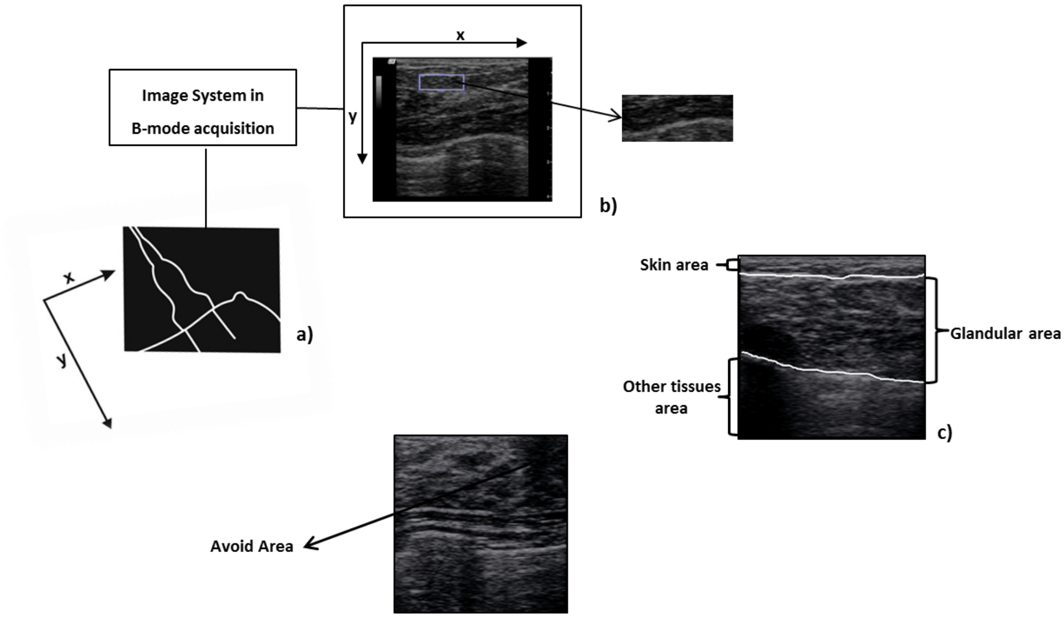


Figure 3.1- a) Identification of breast ultrasound image areas; **b)** B-mode image acquisition; **c)** Manual selection of the region of interest; **d)** Avoided area when the selection is made.

3.2.3 Selection of the region of interest

The glandular area of a breast in an ultrasound image is the area marked in Fig. 1c). The radiologist analyzes an image in which the mammary gland is not selected and in which the skin area and other tissues must be excluded. Selecting the region of interest in the first two algorithms is a manual procedure, so the radiologist selects a rectangular image area that has more relevance to the breast density evaluation, as shown in Figure 3.1b). The size of the selected area and the starting point depend on the area of interest that the radiologist considers important, and he/she can resize and adjust it by resizing or repositioning the drawn box and avoiding areas where eco affects the image, as illustrated in Figure 3.1d). This image generates a grayscale matrix, and from this point forward, all computations are made with the matrix resulting from the selected rectangular image, as represented in Fig. 1c). This process of selection was repeated three times in different parts of the glandular area of the image to reduce the variability of the evaluated breast density, and the following processing is performed for these three selections.

3.2.4 Normalization of the array values

Performing the analysis of the two-dimensional array of each grayscale image shows that the maximum value of the two-dimensional array is significantly smaller than 1, so the two-dimensional array is normalized by dividing each element by its maximum value to normalize all values in the range [0:1]. First, the maximum value of the two-dimensional array is computed. Second, all values of the two-dimensional array are divided by the maximum value. The new normalized two-dimensional array is the input for computing the breast density value.
The concentration of points in the first half of the histogram reveals that the original image is too dark and may produce poor results.

3.2.5 Estimation of breast density with the interval of the gray intensity split in half thresholding (BDthr128Algorithm)

The breast tissue is composed of glandular tissue and fatty tissue, which are represented in ultrasound images by whiter and darker zones, respectively. Therefore, considering the original ultrasound image (I) that was converted to grayscale (I1) and with the normalized two-dimensional array (A1) resulting from the grayscale image for each image region of interest, a respective image histogram (H1) is computed. The histogram range for a grayscale image is [1:256]. Therefore, the range is split into two subintervals [1:128] for pixels that are counted as dark pixels, called Blacks, which represent the fat tissue, and [129:256] for pixels that are counted as white pixels, called Whites, which represent the glandular tissue. For the sub-range [1:128], the value of the histogram in this range is counted and added to a sum, and the total sum is divided by the total number of values in this range. The same is then done for the sub-range [129:256] to count the white values. After analyzing all values of the histogram for each half of the range, breast density is computed by calculating the sum of Whites divided by the sum of both Blacks and Whites multiplied by one hundred.

Finally, the breast density is given by the mean of the breast densities (Di, i=1, 2, 3) of the three selected images. This procedure is described in the flowchart of Figure 3.2.

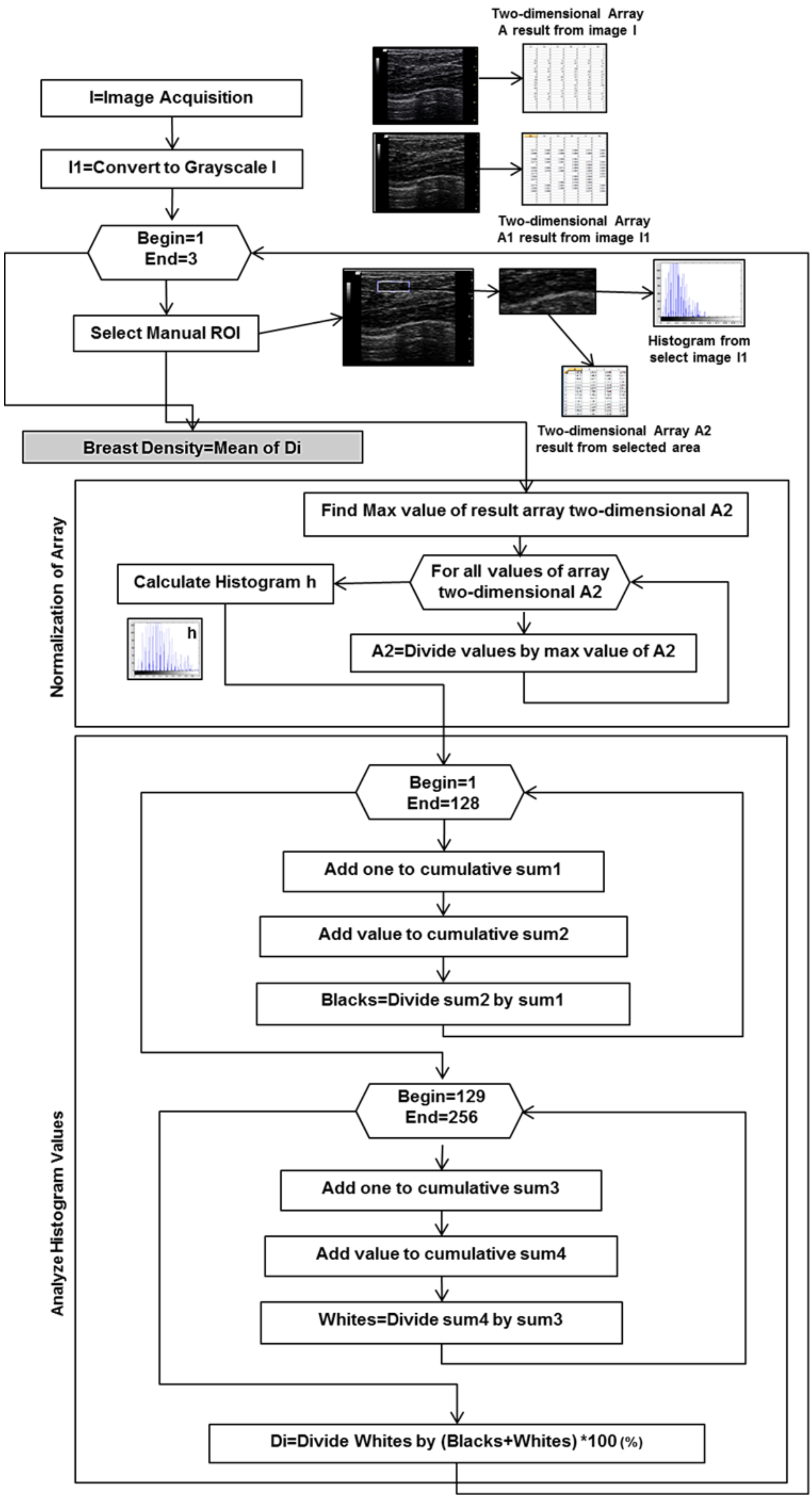


Figure 3.2 - Flowchart of the BDthr128 algorithm.

3.2.6 Estimation of breast density with automatic thresholding of the interval of the gray intensity values (BDthrAuto Algorithm)

In this algorithm, the difference from BDthr128 is the division of the interval [1:256]. Instead of splitting the interval in half, the division is automatic and depends on the values of the histogram that were obtained when selecting the ultrasound images. The procedure is similar to the BDthr128 algorithm, but the cumulative histogram is calculated before calculating the sum of the values corresponding to glandular tissue (Blacks) and the ones corresponding to fatty tissue (Whites). The median value (thr) is calculated for the array with the values generated by the histogram (H1). The first value above (thr) is (thr1). This is the value (thr1) from which the division of the interval [0:256] into two subintervals is performed: [0: thr1] and [(thr1 +1), 256]. From this point forward, the procedure is the same as defined in the BDthr128 algorithm, as shown in the flowcharts of Figure 3.2 and Figure 3.3.

Finally, as in BDthr128 algorithm, the breast density is given by the mean of the breast densities (Di, i=1, 2, 3) of the three selected images. This procedure is described in the flowchart depicted in Figure 3.3.

3.2.7 Automatic estimation of breast density (BDCombo128 and BDComboAuto Algorithms)

The third and fourth algorithms use the Breast Ultrasound images Gland Segmentation (GD) method for gland selection that was proposed by Braz et al. [44], which isolates the mammary gland without the intervention of radiologists and evaluates the breast density in a fully automatic mode.

The manual selection of the region of interest presented in BDthr128 and BDthrAuto algorithms is replaced by the application of the GD method. However, after applying the GD method, it is necessary to perform an additional procedure to remove the skin area and thus obtain solely the mammary gland area. The resulting image corresponds to image I1. From image I1, the one-dimensional array A is produced with all of the values from image I1. The procedures Normalization Array and Analyze Histogram Values of the BDthr128 and BDthrAuto algorithms are then applied. The new algorithms are BDCombo128 and BDComboAuto, which result from the BDthr128 and BDthrAuto algorithms, respectively, and are executed separately. The complete procedure related to the automatic estimation of breast density is illustrated in Figure 3.4.

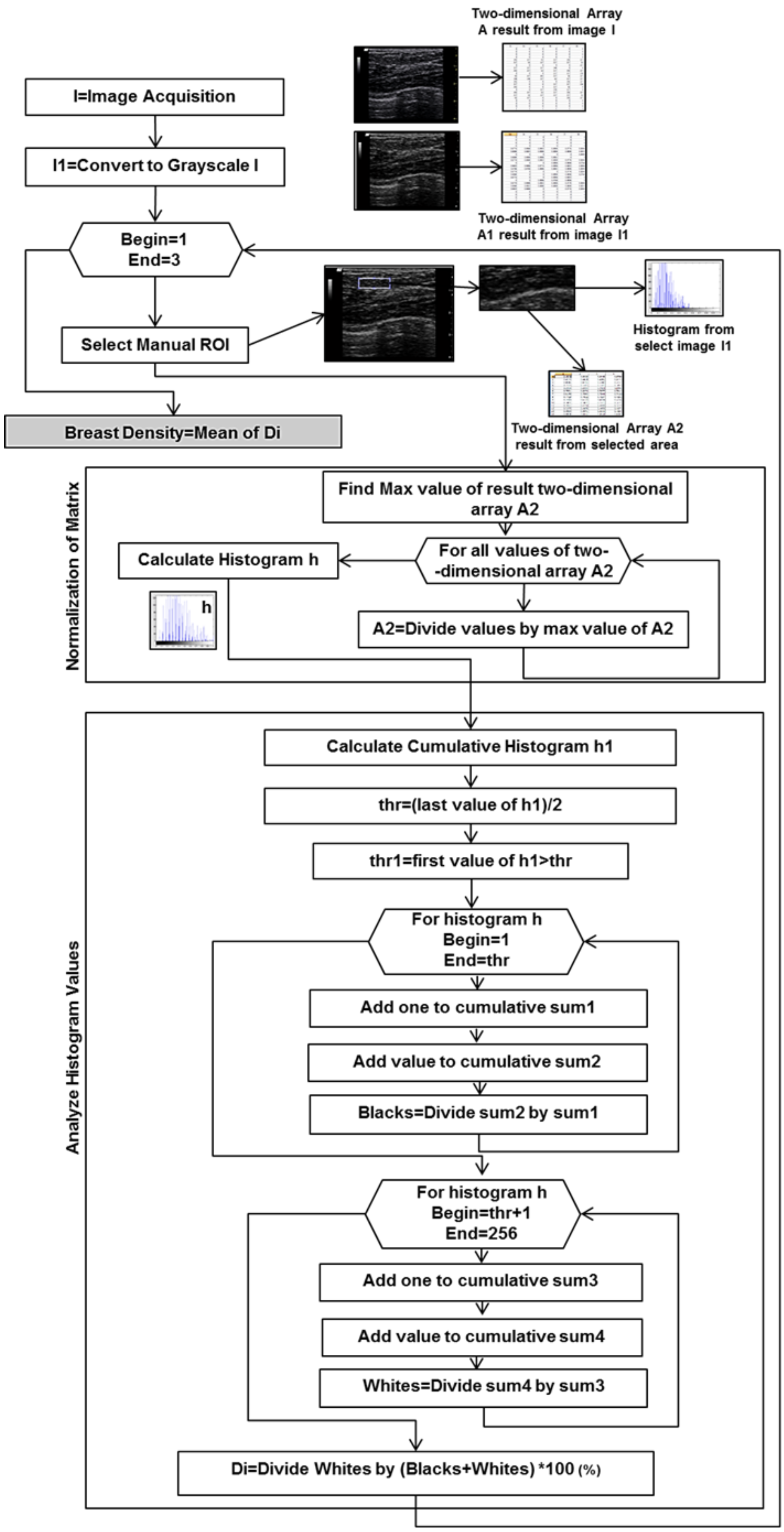


Figure 3.3 – Flowchart of the BDthrAuto algorithm.

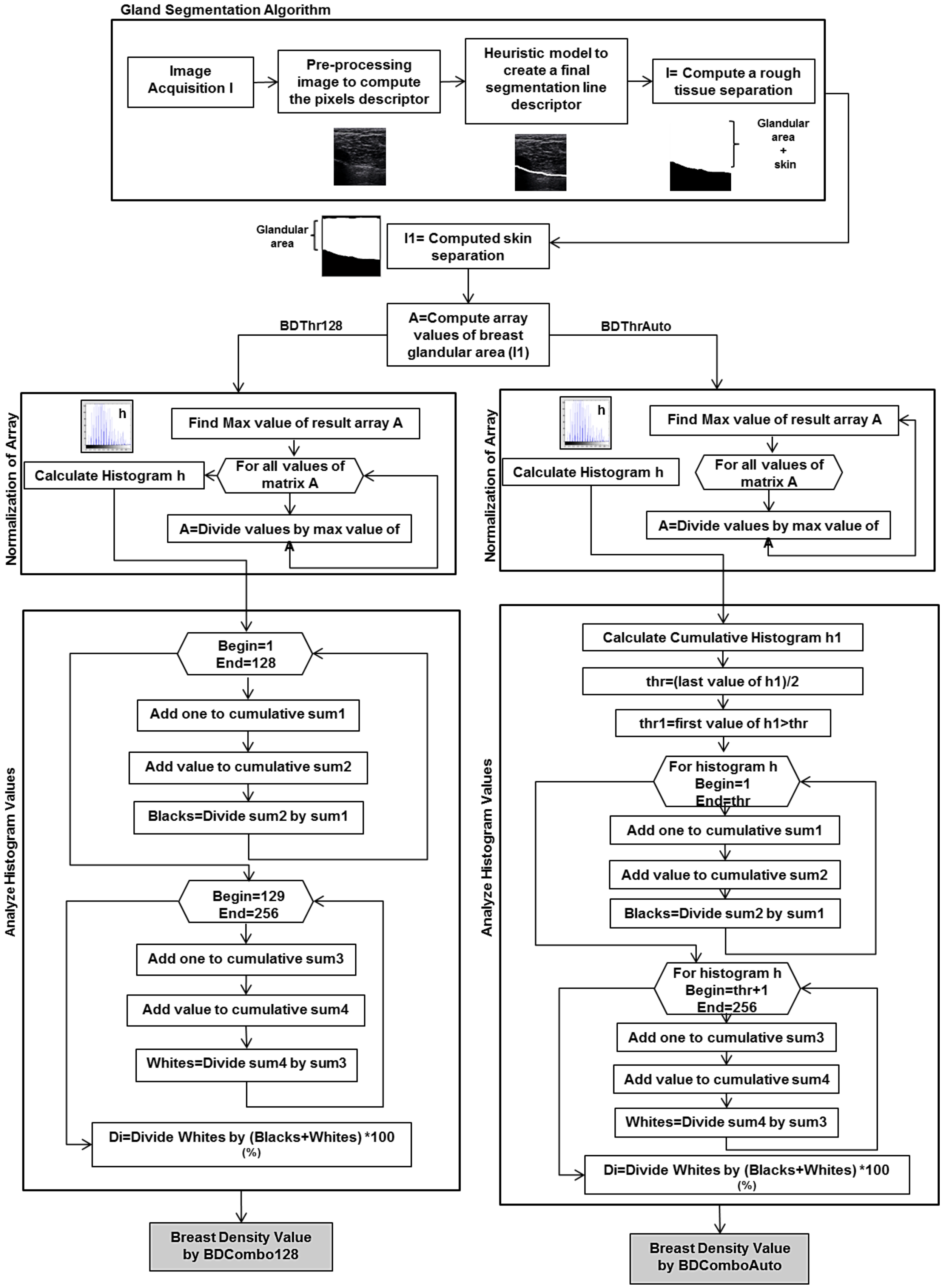


Figure 3.4 - Flowchart of the BDCombo128 and BDComboAuto algorithms.

3.3 Results and discussion

The four proposed algorithms were implemented in MATLAB and were applied to the set of 85 breast ultrasound images. Table 3.1 shows the values of breast density obtained using the BDthr128 and BDthrAuto algorithms considering the three rectangular image selections made in 11 breast ultrasound images, in which the last three images contain breast nodules. Nodules change local conditions in breast tissue through the compression, vascularization or swelling of the area; therefore, the algorithms have focused, in this phase, on images without nodules because the conditions of the mammary gland change the density values and breast density must be measured in areas that are not affected by nodes. To obtain correct breast density values, it is not always possible to obtain areas with the scale required to make the three selections necessary. Table 3.1 shows the manual classification of breast density performed by two radiologists: the evaluation of the first radiologist (RE 1A), the evaluation of the first radiologist twenty days after the first evaluation (RE 1B), and the evaluation of the second radiologist (RE 2). These ratings were made at different times and were performed by direct visual observation by the radiologists before algorithms were applied to the images. The selection of images in the breast ultrasound images can be performed by technicians who know the location of the glandular area and does not necessarily have to be performed by radiologists.

The densities for the proposed algorithms are related to the values obtained with each of the selections D1, D2 and D3. We compare the average of these three partial densities with the corresponding breast density value provided by the radiologists.

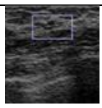
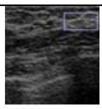
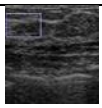
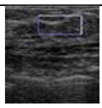
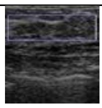
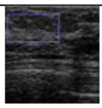
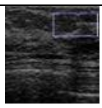
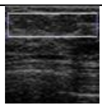
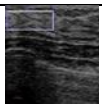
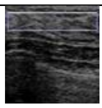
The results obtained with BDCombo128 and BDComboAuto algorithms are also presented in Table 3.1 and are compared with the values provided by the radiologists.

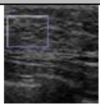
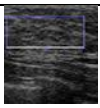
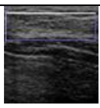
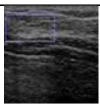
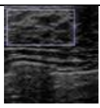
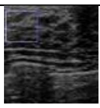
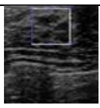
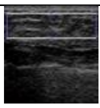
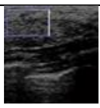
Table 3.2 shows the remaining results for the next 74 images, excluding the illustrations of the selections shown in Table 1.

Based on the results provided in the previous section, the assessment of breast density by radiologists is subjective because it changes from radiologist to radiologist and may change every time that the same radiologist makes an assessment of the breast density for a given ultrasound image. This fact is revealed by analyzing the assigned ratings and is illustrated in the chart presented in Figure 3.5a) and in Tables 3.1 and 3.2.

For the same breast ultrasound image, ratings varied by up to 30%, especially when the radiologist is different. When the observations are made twenty days apart by the same radiologist, there are also variations that reach 20% differences.

Table 3.1 - Breast density values for a sample of 11 images provided by radiologists and obtained using the BDthr128 and BDthrAuto algorithms for the three selected images as well as the values obtained using the BDCombo128 and BDComboAuto algorithms.

Images	Selections		Density Obtained with BDthr128 Algorithm		Density Obtained with BDthrAuto Algorithm		RE1A (%)	RE1B (%)	RE2 (%)	Density Obtained with BDCombo128 Algorithm (%)	Density Obtained with BDComboAuto Algorithm (%)
			Values (%)	MEAN (%)	Values (%)	MEAN (%)					
		**D1**	40.2		41.8						
I1		**D2**	37.9	**44.3**	39.7	**43.5**	**40**	**30**	**30**	**40.3**	**43.1**
		**D3**	54.7		49.1						
		**D1**	33.1		38.2						
I2		**D2**	20.4	**26.5**	31.7	**35.0**	**40**	**35**	**40**	**27.3**	**35.3**
		**D3**	26.1		35.2						
		**D1**	25.1		33.5						
I3		**D2**	18.2	**22.3**	28.7	**31.0**	**25**	**30**	**30**	**17.9**	**28.8**
		**D3**	23.6		30.9						
		**D1**	64.7		55.3						
I4		**D2**	51.4	**58.0**	49.7	**51.4**	**50**	**60**	**75**	**49.1**	49.1
		**D3**	57.8		49.3						

Images	Selections		Density Obtained with BDthr128 Algorithm		Density Obtained with BDthrAuto Algorithm		RE1A (%)	RE1B (%)	RE2 (%)	Density Obtained with BDCombo128 Algorithm (%)	Density Obtained with BDComboAuto Algorithm (%)
			Values (%)	MEAN (%)	Values (%)	MEAN (%)					
I5		**D1**	33.4	**28.5**	37.8	**36.3**	**40**	**30**	**45**	**10.4**	**20.7**
		**D2**	22.0		34.7						
		**D3**	30.2		36.5						
I6		**D1**	40.3	**47.4**	45.7	**48.3**	**40**	**40**	**75**	**37.1**	**43.0**
		**D2**	48.8		48.4						
		**D3**	53.1		50.7						
I7		**D1**	29.7	**32.5**	35.1	**36.7**	**30**	**35**	**40**	**19.4**	**25.6**
		**D2**	37.6		40.2						
		**D3**	30.2		34.8						
I8		**D1**	17.5	**18.9**	29.6	**30.4**	**35**	**30**	**45**	**18.2**	**31.4**
		**D2**	20.9		31.6						
		**D3**	18.2		30.1						
I10		**D1**	50.1	**67.9**	49.8	**56.1**	**55**	**60**	**80**	**41.6**	**43.7**

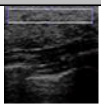
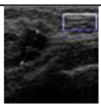
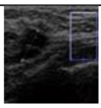
Images	Selections		Density Obtained with BDthr128 Algorithm		Density Obtained with BDthrAuto Algorithm		RE1A (%)	RE1B (%)	RE2 (%)	Density Obtained with BDCombo128 Algorithm (%)	Density Obtained with BDComboAuto Algorithm (%)
			Values (%)	MEAN (%)	Values (%)	MEAN (%)					
		**D2**	74.5		58.1						
		**D3**	79.0		60.5						
I9		**D1**	39.5	**32.0**	42.9	**37.1**	**40**	**40**	**25**	**19.6**	**20.9**
		**D2**	29.1		38.2						
		**D3**	27.3		30.2						
I11		**D1**	18.7	**17.9**	33.1	**30.4**	**30**	**20**	**35**	**10.9**	**23.9**
		**D2**	18.8		29.3						
		**D3**	16.3		28.7						

Table 3.2 - Values of breast density for the next 74 images provided by radiologists and obtained with the BDthr128, BDthrAuto, BDCombo128 and BDComboAuto algorithms.

Images	Density Obtained with the BDthr128 Algorithm				Density Obtained with the BDthrAuto Algorithm				RE 1A (%)	RE 1B (%)	RE 2 (%)	Density Obtained with the BDCombo128 Algorithm (%)	Density Obtained with the BDComboAuto Algorithm (%)
	D1 (%)	D2 (%)	D3 (%)	MEAN (%)	D1 (%)	D2 (%)	D3 (%)	MEAN (%)					
I12	63.9	63.8	65.7	**64.5**	52.3	52.1	54.1	**52.8**	**50**	**60**	**80**	**67.6**	**57.0**
I13	40.9	27.8	25.0	**31.2**	44.6	36.9	36.4	**39.3**	**40**	**35**	**35**	**19.1**	**30.6**
I14	25.0	20.6	30.7	**25.4**	32.2	33.2	37.5	**34.3**	**25**	**40**	**45**	**24.9**	**23.2**
I15	22.6	30.5	23.4	**25.5**	34.1	40.1	35.4	**36.5**	**40**	**50**	**60**	**28.5**	**36.2**
I16	39.4	42.1	36.6	**39.4**	42.2	45.9	42.0	**43.4**	**50**	**60**	**70**	**24.4**	**35.4**
I17	14.6	25.7	21.3	**20.5**	28.1	39.2	31.8	**33.1**	**45**	**30**	**45**	**20.2**	**31.4**
I18	28.6	27.5	37.2	**31.1**	36.0	35.1	42.8	**38.0**	**50**	**35**	**40**	**28.1**	**34.1**
I19	18.3	19.1	25.7	**21.0**	31.5	31.9	36.5	**33.3**	**40**	**35**	**35**	**22.3**	**30.5**
I20	18.5	20.9	30.4	**23.3**	28.1	31.6	37.3	**32.3**	**30**	**30**	**28**	**17.4**	**27.4**
I21	24.7	30.3	16.3	**23.8**	33.8	36.8	28.6	**33.1**	**40**	**40**	**25**	**17.5**	**27.6**
I22	17.5	21.1	18.8	**19.1**	31.3	32.9	31.5	**31.9**	**35**	**40**	**30**	**17.3**	**30.6**
I23	43.2	32.6	51.6	**42.5**	45.2	41.5	50.5	**45.7**	**50**	**50**	**65**	**36.9**	**44.0**
I24	41.5	35.1	42.3	**39.7**	43.4	42.4	43.5	**43.1**	**45**	**50**	**60**	**29.4**	**39.2**
I25	30.6	32.8	40.3	**34.6**	39.6	40.8	43.1	**41.2**	**40**	**45**	**45**	**25.5**	**34.3**
I26	35.0	32.1	41.2	**36.1**	41.2	36.2	45.5	**40.9**	**40**	**40**	**50**	**28.8**	**35.1**
I27	26.7	24.7	31.2	**27.5**	31.7	29.8	37.1	**32.9**	**30**	**25**	**30**	**22.3**	**30.6**
I28	28.0	27.4	28.5	**28.0**	37.6	37.4	36.9	**37.3**	**30**	**40**	**55**	**22.1**	**34.8**
I29	16.5	24.8	17.2	**19.5**	31.2	36.2	30.3	**32.6**	**30**	**40**	**35**	**20.8**	**29.5**
I30	52.0	57.2	53.6	**54.3**	49.5	51.2	50.4	**50.4**	**55**	**50**	**65**	**39.6**	**46.8**
I31	17.9	22.3	19.7	**20.0**	32.2	34.9	31.9	**33.0**	**25**	**30**	**40**	**19.1**	**31.1**
I32	27.2	25.0	24.0	**25.4**	33.7	33.9	32.2	**33.3**	**30**	**25**	**35**	**30.3**	**35.1**
I33	44.3	58.0	35.3	**45.9**	45.2	50.9	40.2	**45.4**	**45**	**40**	**60**	**30.6**	**36.9**
I34	37.1	31.9	43.5	**37.5**	40.5	39.0	45.2	**41.6**	**45**	**50**	**45**	**33.6**	**36.9**
I35	47.2	50.0	44.9	**47.3**	47.8	47.8	46.1	**47.2**	**45**	**50**	**55**	**44.3**	**47.4**
I36	61.0	63.4	56.8	**60.4**	52.5	52.6	56.8	**52.1**	**50**	**60**	**55**	**48.9**	**48.9**
I37	37.9	44.5	37.8	**40.0**	43.6	46.1	42.9	**44.2**	**45**	**55**	**45**	**29.7**	**38.0**
I38	58.4	67.2	52.1	**59.2**	51.5	54.7	50.2	**52.2**	**50**	**50**	**55**	**48.9**	**48.9**
I39	39.7	41.6	54.9	**45.4**	41.8	42.8	50.8	**45.1**	**30**	**30**	**40**	**33.9**	**37.4**
I40	18.8	20.1	27.1	**22.0**	32.2	32.0	37.6	**33.9**	**25**	**30**	**30**	**21.2**	**31.6**
I41	28.1	26.2	36.7	**30.3**	35.7	34.1	42.6	**37.5**	**25**	**30**	**25**	**28.5**	**35.2**
I42	24.5	20.6	33.4	**26.2**	36.1	31.7	38.9	**35.6**	**25**	**25**	**20**	**22.1**	**32.9**
I43	32.3	31.4	24.6	**29.4**	41.6	40.3	36.2	**39.4**	**30**	**30**	**38**	**25.1**	**37.3**
I44	25.5	21.0	31.5	**26.0**	33.8	32.0	36.8	**34.2**	**30**	**25**	**20**	**23.8**	**33.0**
I45	56.0	65.7	49.7	**57.2**	49.2	53.1	49.3	**50.6**	**45**	**50**	**60**	**49.8**	**49.8**
I46	57.4	56.1	64.2	**59.2**	54.0	52.5	55.2	**53.9**	**45**	**50**	**75**	**63.6**	**56.5**
I47	16.7	18.2	18.8	**17.9**	31.0	30.2	33.7	**31.6**	**35**	**30**	**45**	**18.1**	**31.3**
I48	18.2	27.5	28.2	**24.6**	26.9	37.3	36.2	**33.5**	**30**	**30**	**30**	**16.7**	**26.6**
I49	51.6	42.4	62.5	**52.2**	51.0	45.5	58.5	**51.7**	**45**	**40**	**65**	**42.5**	**45.4**
I50	39.4	42.2	35.0	**38.9**	44.1	47.0	40.2	**43.8**	**35**	**30**	**55**	**25.3**	**34.2**
I51	62.0	45.0	67.3	**58.1**	55.0	45.8	57.8	**52.9**	**50**	**40**	**65**	**37.2**	**39.3**
I52	42.1	36.3	45.1	**41.2**	45.1	42.8	46.8	**44.9**	**50**	**40**	**45**	**39.4**	**44.1**

Images	Density Obtained with the BDthr128 Algorithm				Density Obtained with the BDthrAuto Algorithm				RE 1A (%)	RE 1B (%)	RE 2 (%)	Density Obtained with the BDCombo128 Algorithm (%)	Density Obtained with the BDComboAuto Algorithm (%)
	D1 (%)	D2 (%)	D3 (%)	MEAN (%)	D1 (%)	D2 (%)	D3 (%)	MEAN (%)					
I53	41.1	38.4	43.7	**41.1**	43.0	44.8	44.6	**44.1**	**45**	**35**	**30**	**31.2**	**37.0**
I54	32.4	42.8	30.8	**35.3**	40.9	44.5	39.5	**41.6**	**40**	**30**	**35**	**37.2**	**39.3**
I55	34.0	30.4	39.6	**34.7**	40.4	36.1	43.9	**40.1**	**35**	**25**	**52**	**30.5**	**36.2**
I56	26.8	28.6	24.2	**26.5**	35.3	36.6	34.4	**35.4**	**35**	**25**	**55**	**25.1**	**35.5**
I57	25.7	23.9	29.0	**26.2**	32.7	32.4	35.3	**33.5**	**25**	**20**	**45**	**25.4**	**32.6**
I58	25.9	27.4	26.7	**26.7**	36.1	37.5	36.1	**36.6**	**40**	**35**	**70**	**21.6**	**34.2**
I59	15.8	23.8	18.3	**19.3**	29.8	35.3	29.4	**31.5**	**20**	**20**	**40**	**15.0**	**26.7**
I60	21.6	22.6	20.4	**21.5**	30.1	33.5	29.9	**31.2**	**20**	**30**	**55**	**17.7**	**27.7**
I61	33.2	53.9	49.1	**45.4**	43.5	51.1	48.9	**47.8**	**40**	**40**	**75**	**37.1**	**43.0**
I62	27.2	32.9	17.4	**25.9**	36.1	37.5	30.0	**34.5**	**35**	**30**	**70**	**27.2**	**35.5**
I63	23.9	28.4	23.1	**25.1**	37.3	36.5	35.2	**36.3**	**35**	**30**	**45**	**18.0**	**30.3**
I64	17.6	23.1	17.5	**19.4**	32.3	36.6	29.3	**32.7**	**35**	**25**	**40**	**18.2**	**29.3**
I65	31.8	30.5	30.9	**31.1**	37.8	36.1	37.0	**37.0**	**40**	**30**	**48**	**30.7**	**36.1**
I66	44.2	60.1	34.1	**46.1**	45.1	52.9	40.2	**46.1**	**45**	**45**	**65**	**45.7**	**48.1**
I67	31.1	35.4	27.3	**31.3**	35.5	39.3	33.0	**36.0**	**45**	**40**	**36**	**49.2**	**49.2**
I68	38.6	36.1	43.2	**39.3**	42.3	40.2	44.8	**42.4**	**50**	**50**	**46**	**33.6**	**36.9**
I69	50.0	50.6	44.5	**48.4**	47.4	48.1	46.1	**47.2**	**40**	**40**	**75**	**48.7**	**48.7**
I70	61.3	64.5	55.3	**60.4**	53.1	54.2	49.7	**52.3**	**50**	**50**	**75**	**55.5**	**52.1**
I71	34.3	43.2	32.7	**36.7**	37.6	45.0	39.2	**40.6**	**40**	**25**	**40**	**44.1**	**47.2**
I72	35.7	42.4	35.6	**37.9**	40.5	43.7	40.6	**41.6**	**40**	**60**	**45**	**34.9**	**40.9**
I73	51.8	57.8	51.9	**53.9**	50.4	50.8	49.9	**50.4**	**45**	**60**	**55**	**49.6**	**49.6**
I74	34.3	39.9	34.2	**36.1**	37.6	41.3	36.9	**38.6**	**35**	**40**	**40**	**27.4**	**33.1**
I75	20.5	20.7	23.3	**21.5**	30.4	31.5	31.8	**31.2**	**25**	**20**	**20**	**22.9**	**31.4**
I76	28.7	26.2	32.3	**29.1**	35.2	34.8	37.4	**35.8**	**25**	**25**	**30**	**31.6**	**35.5**
I77	19.9	21.9	28.4	**23.4**	33.2	29.2	35.7	**32.7**	**20**	**20**	**30**	**23.5**	**33.5**
I78	25.3	23.7	27.6	**25.5**	34.9	34.7	37.5	**35.7**	**30**	**20**	**25**	**27.2**	**35.6**
I79	16.9	12.7	20.1	**16.6**	26.4	25.4	29.2	**27.0**	**30**	**25**	**15**	**24.7**	**33.1**
I80	53.8	58.2	51.2	**54.4**	49.3	51.4	50.2	**50.3**	**45**	**50**	**65**	**49.3**	**49.3**
I81	60.0	57.2	66.7	**61.3**	53.6	53.6	56.6	**54.6**	**40**	**60**	**70**	**63.5**	**56.6**
I82	16.0	20.0	16.9	**17.6**	31.9	31.5	29.1	**30.8**	**25**	**30**	**20**	**21.1**	**32.8**
I83	18.2	18.5	31.1	**22.6**	27.4	30.9	36.3	**31.5**	**20**	**30**	**40**	**12.3**	**27.2**
I84	59.3	41.4	57.8	**52.8**	54.1	45.9	54.1	**51.4**	**40**	**45**	**60**	**51.2**	**50.7**
I85	37.2	39.4	34.5	**37.1**	40.8	44.7	39.3	**41.6**	**35**	**35**	**55**	**22.9**	**32.3**

Variation equal to or greater than 10% occurs in 32.9% of the observations of the same breast ultrasound image made by the same radiologist. For the observations made by different radiologists, variation equal to or greater than 10% occurs in 71.8% of the observations, which reveals the subjectivity of the observations and the inherent problems in the method.

Both BDthr128 and BDthrAuto algorithms require human intervention. To analyze the results produced by these two algorithms, the maximum and minimum values of the observations of each ultrasound image made by radiologists and are considered to define a range of values [minValue, maxValue], where minValue is the lowest value of the three radiologist observations and maxValue is the highest value of those observations. Considering the breast density value obtained for each of these algorithms, for each analyzed image, it was verified that the obtained values for breast density were within the specified range, as illustrated in Figure 3.5b).

For the BDthr128 algorithm, 56% of the breast density estimates fall within the interval [minValue, maxValue], whereas for the BDthrAuto algorithm, the percentage of breast density estimates within the interval is 73%. This result demonstrates that the second algorithm is more accurate than the first algorithm according to the radiologist evaluations of the breast density.

We also describe the application of an algorithm that isolates the mammary gland in the BDthr128 and BDthrAuto algorithms, which results in the BDCombo128 and BDcomboAuto automatic algorithms. The procedure used to analyze the breast density results for both algorithms was the same as defined for the BDthr128 and BDthrAuto algorithms, as previously described and illustrated in Figure 3.5c).

After considering the range with the maximum and minimum for each of the observations of breast density for the same image, 28% of the values obtained by applying the algorithms are within the range for the BDCombo128 algorithm and 42% of the values from the BDComboAuto algorithm are within the range, which indicates that the algorithms that use automatic thresholding have better performance according to radiologist evaluation.

Another approach considers a qualitative assessment, the Breast Density Classification according to the BI-RADS lexicon [45, 46]:

- BIRADS type 1 – The breast is of almost entirely fat; thus, glandular tissue is < 25%;
- BIRADS type 2 – There is scattered fibroglandular tissue in the breast; thus, glandular tissue is in the interval [25%, 50%];
- BIRADS type 3 – Fibrous tissue is prevalent throughout the breast but is not clustered together; thus, glandular tissue is in the interval [51%, 75%];
- BIRADS type 4 – The breast contains >75% glandular and fibrous tissue.

A few examples of this conversion are illustrated in Table 3.3.

To contextualize the obtained values for the four proposed algorithms in this qualitative evaluation, the charts in Figure 3.6 a), b) and c) were created to illustrate the distribution of the values. Considering the three radiologist observations for each image, according to the qualitative assessment, 3 hits were obtained over the set of 85 images in 28 images (32.94%) for the BDthr128 algorithm and 41 images (48.24%) for BDthrAuto algorithm. At least 2 hits were obtained for 59 images (69.41%) for the BDthr128 algorithm and 73 images (85.88%) for the BDthrAuto algorithm. For BDthr128, there are 13 images (15.29%) that have no hits with the radiologist observation, whereas for BDthrAuto, no such situation occurs because each classification coincides with at least one of the observations made by radiologists. For the BDCombo128 and BDComboAuto algorithms, 3 hits were obtained in the entire set of 85 for 21 images (24.71%) with the BDCombo128 algorithm and for 40 images (47.06%) with the BDComboAuto algorithm. At least 2 hits were obtained for 49 images (57.65 %) with the BDCombo128 algorithm and 67 images (78.82%) with the BDComboAuto algorithm. For BDCombo128, there are 26 images (30.59 %) that have no hits with the radiologist observations, whereas for BDComboAuto, there are 3 images (3.53%) with no hits.

Table 3.3 – Values of breast density provided by radiologists and by the algorithms BDthr128, BDthrAuto, BDCombo128 and BDComboAuto with their conversion in BIRADS lexicon.

Images	Density Obtained with				RE 1A (%)	RE 1B (%)	RE2 (%)	BIRADS lexicon conversion						
	BDthr128 Algorithm (%)	BDthrAuto Algorithm (%)	BDCombo128 Algorithm (%)	BDComboAuto Algorithm (%)				BDthr128	BDthrAuto	BDCombo128	BDComboAuto	RE1A	RE1B	RE2
I1	44.3	43.5	40.3	43.1	40	30	30	2	2	2	2	2	2	2
I2	26.5	35.0	27.3	35.3	40	35	40	2	2	2	2	2	2	2
I3	22.3	31.0	17.9	28.8	25	30	30	1	2	1	2	2	2	2
I4	58.0	51.4	49.1	49.1	50	60	75	2	2	2	2	2	3	3
I5	28.5	36.3	10.4	20.7	40	30	45	2	2	1	1	2	2	2
I6	47.4	48.3	37.1	43.0	40	40	75	2	2	2	2	2	2	3
I7	32.5	36.7	19.4	25.6	30	35	40	2	2	1	2	2	2	2
I8	18.9	30.4	18.2	31.4	35	30	45	1	2	1	2	2	2	2
I9	64.5	52.8	67.6	57.0	50	60	80	3	3	3	3	2	3	3
I10	67.9	56.1	41.6	43.7	55	60	80	3	3	2	2	3	3	3
I11	32.0	37.1	19.6	20.9	40	40	25	2	2	1	1	2	2	1
I12	31.2	39.3	19.1	30.6	40	35	35	2	2	1	2	2	2	2
I13	17.9	30.4	10.9	23.9	30	20	35	1	2	1	1	2	1	2

The prevalence or the proportion of breast images with “3 hits” and “2 hits” is given by the total number of hits for each condition divided by the number of ultrasound images. The results are shown in Table 3.4 for the four algorithms in this study.

These algorithms perform manipulation of arrays and the complexity time is polynomial, or O(nk), where k is constant and k and n are integers. According to Cobham [47], such algorithms are considered viable and efficient. This paper intends to show a simple but effective way to compute an estimate value for breast density compared with the values assigned by radiologists.

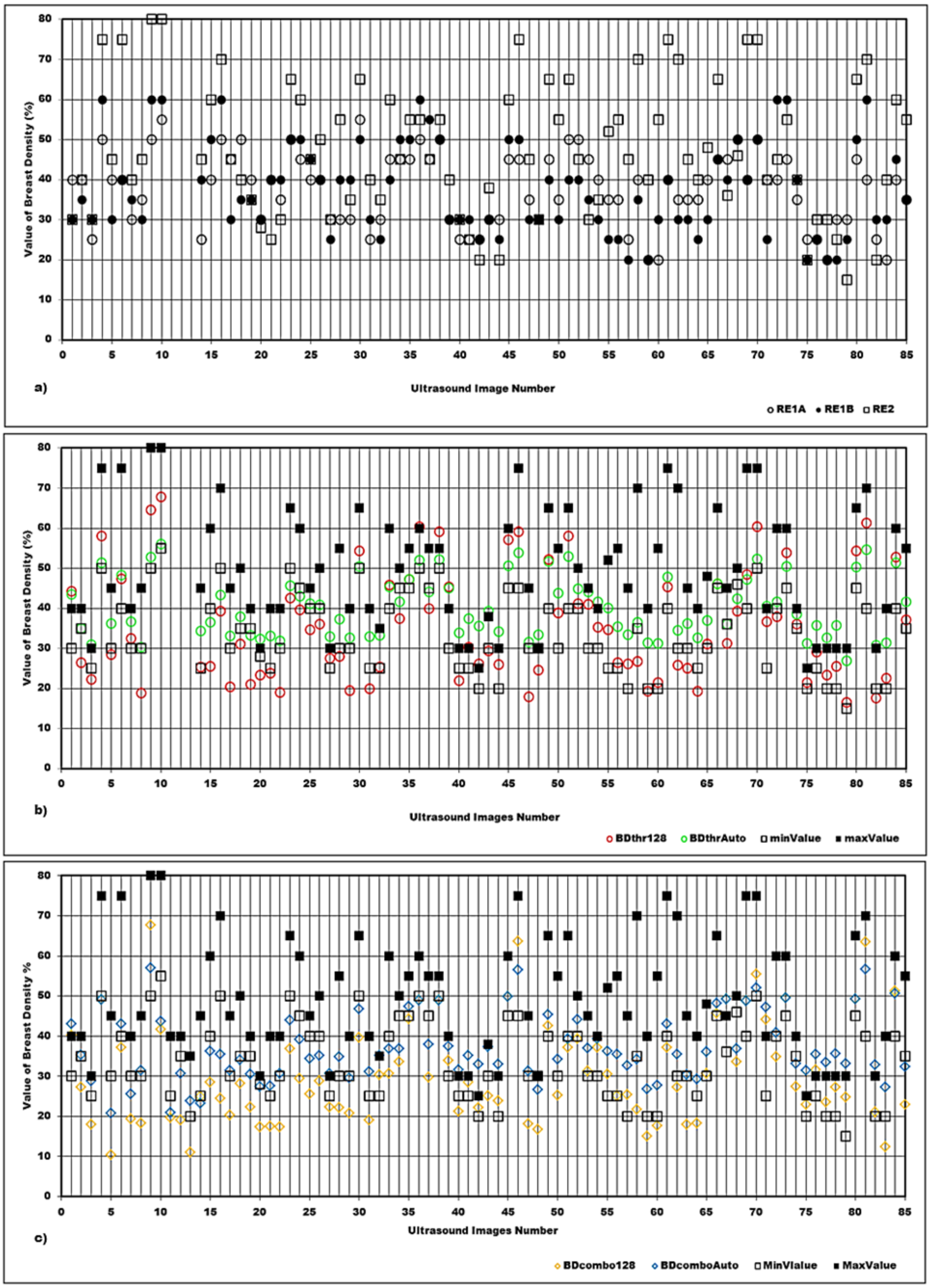
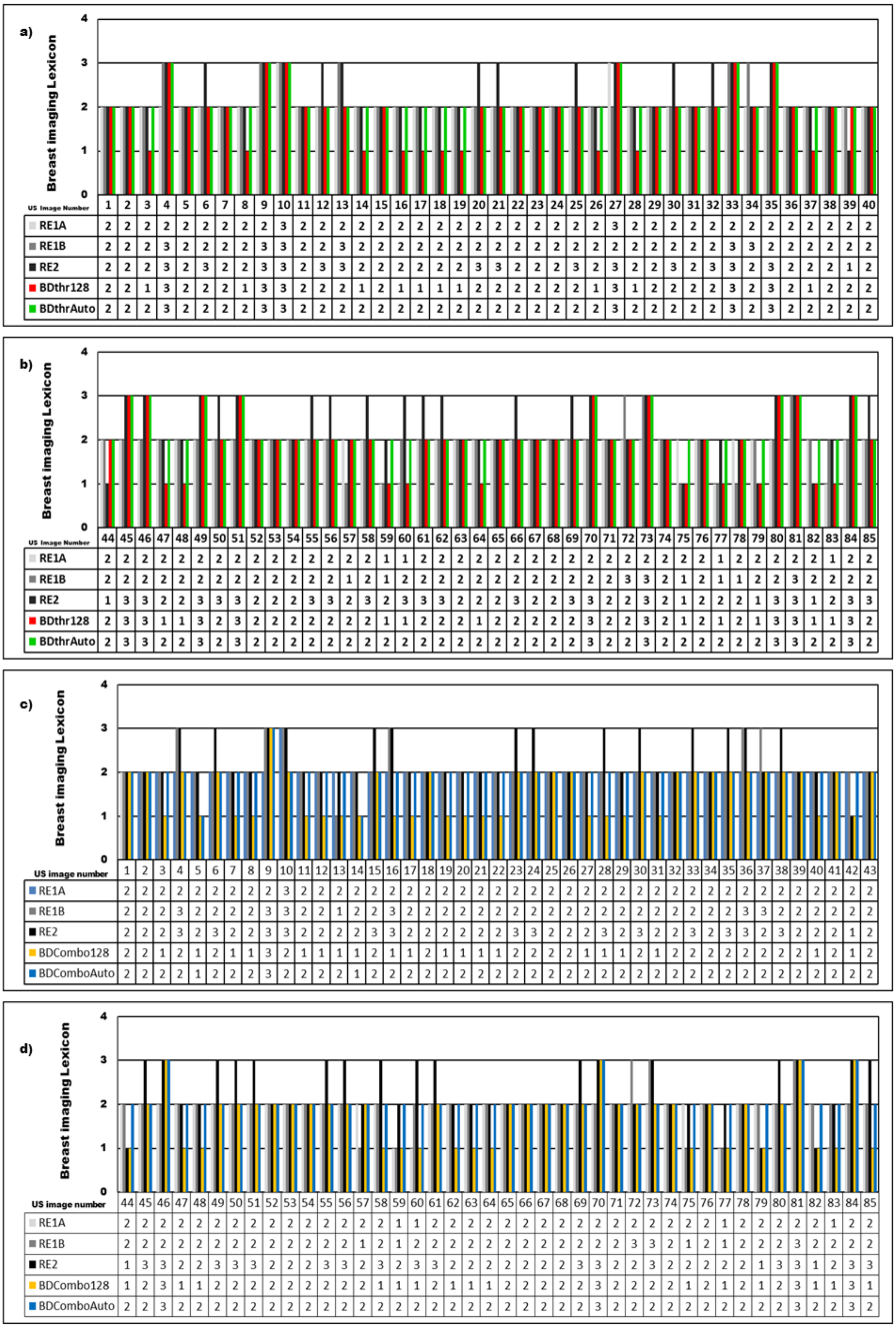


Figure 3.5– Comparison of the breast density of breast ultrasound images for a) Breast density values provided by the radiologists; b) BDthr128 vs BDthrAuto vs min value among the three radiologist classifications for each image and the max value of the classifications; c) BDCombo128 vs BDComboAuto vs the min value among the three radiologist classifications for each image and the max value of the classifications.



a)

US Image Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
RE1A	2	2	2	2	2	2	2	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2
RE1B	2	2	2	3	2	2	2	2	3	3	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3	2	2	2	2	2	2
RE2	2	2	2	3	2	3	2	2	3	3	2	3	3	2	2	2	2	2	2	3	3	2	2	2	3	2	3	2	2	3	2	3	3	2	3	2	2	2	1	2
BDthr128	2	2	1	3	2	2	2	1	3	3	2	2	2	1	2	1	1	1	1	2	2	2	2	2	2	1	3	1	2	2	2	2	3	2	3	2	1	2	2	2
BDthrAuto	2	2	2	3	2	2	2	2	3	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	2	2	2	2	2	3	2	3	2	2	2	2	2

b)

US Image Number	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85
RE1A	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	1	2	2
RE1B	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	3	3	2	1	2	1	1	2	2	3	2	2	2	2
RE2	1	3	3	2	2	3	3	3	2	2	2	3	3	2	3	2	3	3	3	2	2	2	3	2	2	3	3	2	2	3	2	1	2	2	2	1	3	3	1	2	3	3
BDthr128	2	3	3	1	1	3	2	3	2	2	2	2	2	2	2	1	1	2	2	2	1	2	2	2	2	2	3	2	2	3	2	1	2	1	2	1	3	3	1	1	3	2
BDthrAuto	2	3	3	2	2	3	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	2	2	3	2	2	2	2	2	2	3	3	2	2	3	2

c)

US image number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43
RE1A	2	2	2	2	2	2	2	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
RE1B	2	2	2	3	2	2	2	2	3	3	2	2	1	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3	2	2	2	2	2	2
RE2	2	2	2	3	2	3	2	2	3	3	2	2	2	2	3	3	2	2	2	2	2	2	3	3	2	2	2	3	2	3	2	2	3	2	3	3	2	3	2	2	2	1	2
BDCombo128	2	2	1	2	1	2	1	1	3	2	1	1	1	1	2	1	1	2	1	1	1	1	2	2	2	2	1	1	1	2	1	2	2	2	2	2	2	2	2	1	2	1	2
BDComboAuto	2	2	2	2	1	2	2	2	3	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2

d)

US image number	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85
RE1A	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	1	2	2
RE1B	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	3	3	2	1	2	1	2	2	2	3	2	2	2	2
RE2	1	3	3	2	2	3	3	3	2	2	2	3	3	2	3	2	3	3	2	2	2	2	2	2	2	3	3	2	2	3	2	2	2	2	2	1	3	3	1	2	3	3
BDCombo128	1	2	3	1	1	2	2	2	2	2	2	2	2	2	1	1	1	2	1	1	1	2	2	2	2	2	3	2	2	2	2	1	2	1	2	1	2	3	1	1	3	1
BDComboAuto	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	2	2	2	2	2	2	2	2	2	2	3	2	2	3	2

Figure 3.6– Comparison of the breast qualitative classification for breast ultrasound images for a) BDthr128 vs BDthrAuto vs qualitative classification for ultrasound images 1-43; b) BDthr128 vs BDthrAuto vs qualitative classification for ultrasound images 44-85; c) BDthr128 vs BDthrAuto vs qualitative classification for ultrasound images 1-43; d) BDthr128 vs BDthrAuto vs qualitative classification for ultrasound images 44-85.

Table 3.4 - Prevalence of the results of the set of BD algorithms for qualitative classification.

		Algorithms	Hits with radiologists evaluations		Prevalence	
			3 hits	At least 2 hits	For 3 hits	For 2 hits
Ultrasound Images	Total= 85	BDthr128	28	59	0.33	0.69
		BDthrAuto	41	73	0.48	0.86
		BDCombo128	21	49	0.25	0.58
		BDComboAuto	40	67	0.47	0.79

3.4 Conclusions

The subjectivity observed in radiologist evaluations shows how important it is to obtain computer-based estimates for breast density to reduce this subjectivity. In this paper, four algorithms were proposed to estimate the breast density in ultrasound images. The first and second semiautomatic algorithms, BDthr128 and BDthrAuto, convert an image from a breast ultrasound to grayscale and normalize the corresponding two-dimensional array of the image by using the histogram to estimate the value of breast density. The third and fourth algorithms, BDCombo128 and BDComboAuto, have as a starting point an algorithm that isolates the mammary gland. However, this algorithm does not remove the corresponding skin area. This deficiency was eliminated, and the automatic steps of the first and second algorithms were applied, which resulted in two automatic algorithms. In both analyses, the results obtained with the algorithms BDthrAuto and BDComboAuto, which were derived from an automatic threshold, have the best coincidence with the values assigned by radiologists for each breast ultrasound image. The qualitative assessment shows better results compared with the quantitative evaluation. This was expected because of the interval width of each BIRADS type, which has a larger amplitude. The semiautomatic algorithms have better performance than the automatic algorithms because the region of interest is chosen manually, thereby revealing results that are closer to the results provided by radiologists.

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Chapter 4

New Methods for Evaluation and Classification of Breast Density in Ultrasound Images Using Otsu Threshold[3]

Abstract

Objectives: Breast density is a risk factor for breast cancer. Currently, the breast density in ultrasound images is roughly evaluated by radiologists using direct visual observation of the images. In this paper, we propose two methods for the computer-based evaluation and classification of breast density in ultrasound images using Otsu thresholding.

Dataset and methods: A set of 82 breast ultrasound images is analyzed. Manual evaluation of breast density over this set was made by two radiologists, including two distinct evaluations of the first radiologist in different periods. Two new algorithms for the estimation of breast density are specified: a semiautomatic algorithm with manual selection through three rectangular boxes of the glandular area with Otsu thresholding (BDthrOtsu); and an automatic algorithm with automatic segmentation of breast glandular area and with Otsu thresholding (BDComboOtsu).

Results: The proposed algorithms are applied to a set of 82 images, and both quantitative (breast density estimation) and qualitative (classification according to the BIRADS lexicon) assessments were performed. The percentage of the breast densities within the interval of the three radiologist evaluations of the set of 82 images was evaluated for the proposed algorithms with Otsu thresholding. These results are compared with the results obtained with the two semiautomatic algorithms and the two automatic algorithms to estimate the breast density. Moreover, regarding the qualitative BIRADS, the percentage of the number of classifications for each algorithm achieving the 3 hits and at least 2

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hits of the classification based on the three radiologist observations was evaluated for the set of images.

Conclusions: For quantitative assessment, semiautomatic algorithms for the estimation of breast density using Otsu thresholding and automatic thresholding (BDthrOtsu and BDthrAuto) perform better to the radiologist evaluations than the algorithm based on the half division of the grayscale interval (BDthr128); nevertheless, the algorithm using automatic thresholding (BDthrAuto) has better performance than the algorithm using Otsu Thresholding (BDthrOtsu). Regarding automatic algorithms (BDCombo128, BDComboAuto and BDComboOtsu), the algorithm using Otsu thresholding leads to better estimates of the breast density than the other algorithms. For qualitative assessment, both semiautomatic algorithms using Otsu thresholding and automatic thresholding (BDthrOtsu and BDthrAuto) have similar performance according to the radiologist classifications, and both algorithms perform better than the corresponding algorithm based on the half division of the grayscale interval (BDthr128). Regarding automatic algorithms (BDComboOtsu, BDComboAuto and BDCombo128), the algorithm using Otsu thresholding leads to better classifications than the other two, but when values of prevalence are considered, both BDComboOtsu and BDComboAuto algorithms lead to similar results.

Keywords: Breast ultrasound; Breast density; Histogram threshold methods; Algorithm for breast density evaluation; Computer aided analysis.

4.1 Introduction

Breast density has been recognized as a strong risk factor for breast cancer [1-8]. Therefore, it is important to determine the correct estimates of breast density, but commercially available ultrasound equipment does not provide this value. If no other type of medical diagnosis equipment is used, it is up to radiologists to make an assessment of breast density, which has been shown to be quite subjective.

Due to the importance of breast density, several algorithms have been proposed to evaluate breast density in mammograms [9-24] and few in ultrasound images [25-30]. However, and despite the clinical interest in breast ultrasound, it has been difficult to accurately evaluate breast density based on ultrasound images.

Recently, Oliveira et al. proposed in [31] four algorithms based on histogram and gray level thresholding to estimate the value of the breast density. Two are semiautomatic algorithms, BDthr128 and BDthrAuto, where the selection of the region of interest is determined by radiologists through three rectangular boxes in the glandular area of the image. The other two algorithms are fully automatic, BDCombo128 and BDComboAuto. These automatic algorithms include an algorithm for segmentation of breast glandular area [32], which includes skin, together with a procedure for skin removal and similar histogram analyses and thresholding methods as were used in BDthr128 and BDthrAuto algorithms.

After image acquisition and grayscale conversion without any preprocessing method, the selection of the region of interest is made manually for BDthr128 and BDthrAuto, resulting in a two-dimensional array from the selected portion of the image. Regarding BDCombo128 and BDComboAuto algorithms, after the application of the gland segmentation algorithm and skin separation, a one-dimensional array is obtained. For these four algorithms, the normalization of the array values is performed. In the analysis of each array, it was verified that the maximum value was significantly smaller than 1; therefore, the array was normalized by dividing each element by the maximum value of the array.

Given a grayscale image, its histogram consists of the histogram of its gray levels, that is, a graph indicating the number of times each gray level occurs in the image. Based on this fact and on the range of the histogram [1:256], the range was split into two subintervals: [1:128] for pixels counted as black pixels and [129:256] for pixels counted as white pixels in BDthr128. Breast density is determined by the division of the sum of whites and the sum of the blacks and whites.

BDthrAuto is based on histogram thresholding but considers an automatic threshold based on the cumulative histogram, and the threshold (thr) was defined by the range of the intervals: [1:thr] and [(thr+1):256]. After obtaining the normalized array, histogram thresholding of the BDthr128 and BTthrAuto algorithms was applied, respectively, to the BDCombo128 and BDComboAuto algorithms.

In this paper, we investigate two new variants of those previous four algorithms by replacing their thresholding algorithms, based on the half division of the grayscale interval and automatic thresholding, with an Otsu thresholding algorithm, resulting in a semiautomatic algorithm for the estimation of breast density with manual selection of the regions of interest in the glandular area and with Otsu thresholding, called the BDthrOtsu algorithm, and an automatic algorithm with automatic segmentation of the breast glandular area with Otsu thresholding, called the BDComboOtsu algorithm. The Otsu method was proposed by Nobuyuki Otsu in 1979 [33] and has been widely used in computer visualization and image processing to automatically perform clustering-based image thresholding. This algorithm computes a gray level histogram threshold, which can be used to convert an intensity image to a binary image normalized within intensity values that lie in the range [0, 1].

In the remainder of this paper, we specify both BDthrOtsu and BDComboOtsu algorithms and present their evaluation quantitatively in terms of the estimation of breast density and qualitatively in terms of the classification using BIRADS lexicon. A comparison with the performance of the other four previously proposed algorithms is also provided.

4.2 Dataset and methods

4.2.1 Image acquisition and dataset

Ultrasound images considered in this study were acquired using a LOGIQ Book XP, a high performance multipurpose hand-carried imaging system. The set of 82 breast ultrasound images analyzed in this study was obtained from patients with disease that was already diagnosed and treated in Cova da Beira's Hospital in Covilhã, Portugal, during the period 2007 – 2013. The set of 82 images make no reference to any patient's identification.

The manual classification of breast density in each image was based on direct visual observations of two radiologists, where were considered as a reference. The two evaluations of the first radiologist using the same set of images were also considered, with the second evaluation being performed twenty days after the first one.

4.2.2 Specification of the semiautomatic algorithm using Otsu thresholding (BDthrOtsu algorithm)

After image acquisition, the proposed algorithms require the conversion of the original acquired image I into a grayscale image IM. The Otsu method was applied to each selected rectangular image from the region of interest. In a typical breast ultrasound image, the skin appears at the top, glandular area in the middle and other tissues at the bottom of the image as shown in Figure 4.1a. The radiologist may select the most representative area from the glandular area, as illustrated in Figure 4.1b, avoiding areas of echo that affect the image. Three rectangular image samples from the glandular area in the original image were obtained to reduce the variability of the breast tissue.

For the Otsu method, we use the *graythresh* function from MATLB® [34], which chooses the threshold to minimize the variance of the black and white pixels, formulated as discriminant analysis. A particular criterion function was used as a measure of statistical separation and to define a *level* as being the argument to another function of MATLAB®, *im2bw* [35], which converts the grayscale image into a binary image; in the output image, all pixels with luminance greater than *level* are replaced by a value of one, and all of the other pixels are replaced by a value of zero. The result of this procedure application in the three selections, IM_i, i=1, 2 and 3 of grayscale image is shown in Figure 4.1c.

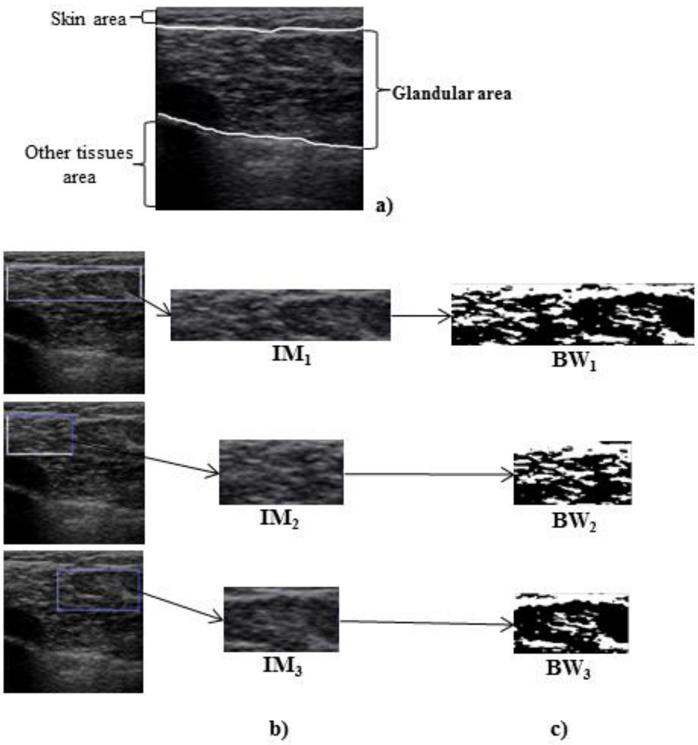


Figure 4.1 - Region of interest of breast ultrasound images: a) identification of breast glandular area; b) the selection was made manually by the radiologist; c) image result from the Otsu threshold.

Then, the two-dimensional array M_i, with i=1, 2 and 3, of those image selections is computed. Such a two-dimensional array is made up of only zeros and ones, and for each two-dimensional array, the sum of ones was calculated, where ones correspond to the white area, i.e., fatty tissue, and zeros correspond to the black area, i.e., glandular tissue.
The breast density is calculated for each selected image IM_i, i=1, 2, and 3, by applying the following formula:

$$D_i = \frac{sum\ of\ ones}{number\ of\ rows\ of\ Mi*number\ of\ columns\ of Mi},\ i = 1,2,3 \qquad (1)$$

The final breast density was given by:

$$Density\ (\%) = mean(D_i) * 100,\ i = 1,2,3 \qquad (2)$$

The full procedure, called BDthrOtsu, is illustrated in the flowchart of Figure 4.2.

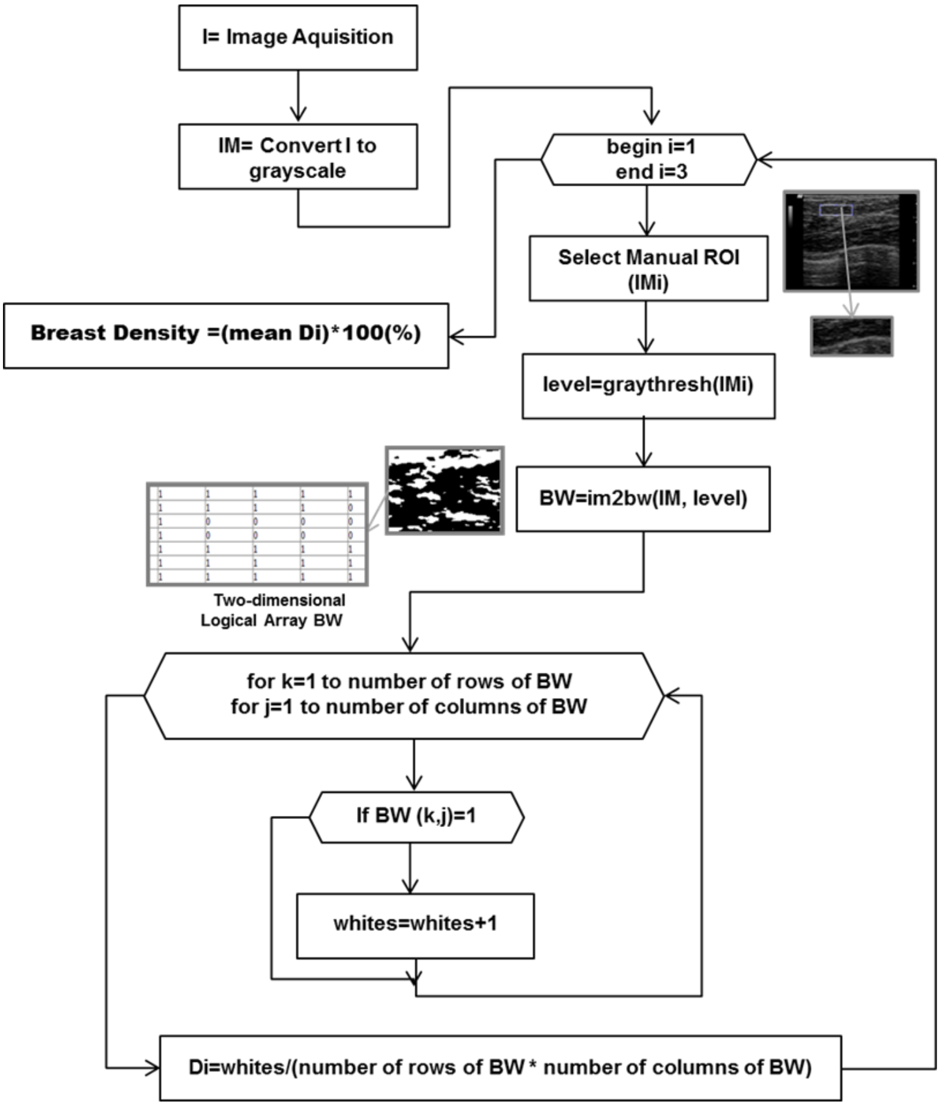


Figure 4. 2 – Flowchart of the BDthrOtsu algorithm.

4.2.3 Specification of the automatic algorithm using Otsu thresholding (BDComboOtsu algorithm)

In this method, the input image is obtained using the Gland Segmentation Algorithm, as illustrated in Figure 4.3. It is necessary to compute the skin separation to obtain just the glandular area, resulting in an array A. To implement the Otsu method, the *graythresh* function from MATLB® [34] was applied to the array A, and *level* was defined for the argument to the *im2bw* function of MALLAB® [35]. The BW one-dimensional array is an array compound of ones and zeros, and the method for calculating the breast density is similar to the method used in the BDthrOtsu algorithm, but for a one-dimensional array. All values equal to one were found and summed, and the result was divided by the length of the BW array, so that the final formula for calculating breast density was as follows:

$$Density\ (\%) = \frac{sum\ of\ ones}{length\ of\ BW\ array} * 100 \qquad (3)$$

The entire procedure, called BDComboOtsu, is illustrated in the Figure 4.3 flowchart.

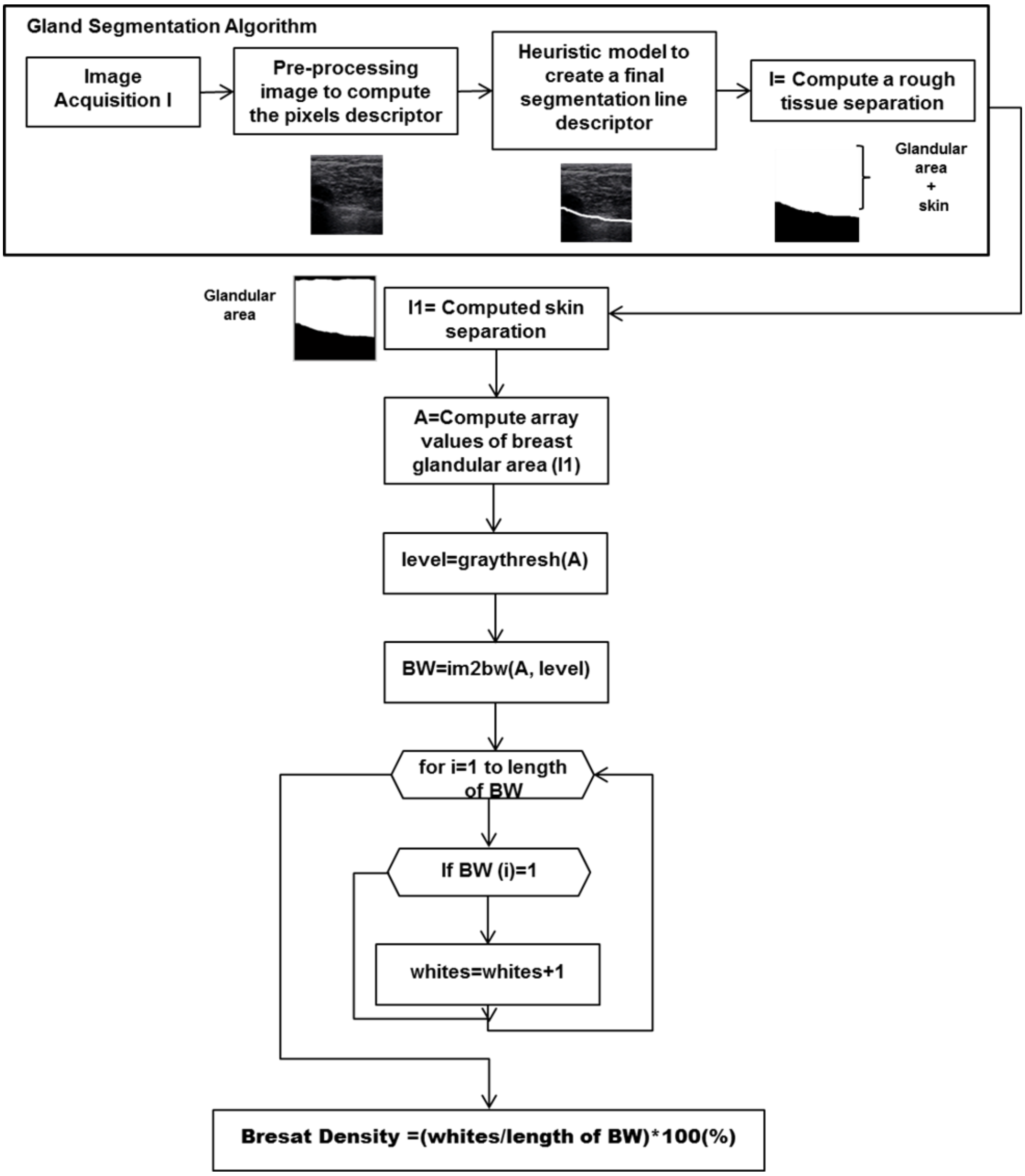


Figure 4.3- Flowchart of the BDComboOtsu algorithm.

4.3 Results and discussion

The values for breast density obtained with the previously mentioned algorithms using the set of ultrasound images were compared with the three evaluations of breast density performed by radiologists; two of those evaluations were performed by the same radiologist twenty days apart. For the quantitative evaluation, an interval was defined where the minimum value corresponded to the lowest value of the three radiologist observations and the maximum value corresponded to the highest value of those observations. For example, considering observations 1, 2 and 3 by radiologists with the values of 30, 35 and 50, respectively, the interval set would be [30, 50]. For the performance evaluation of each algorithm, it was verified whether the estimate of breast density obtained by each algorithm for each image was within the above interval. The qualitative analysis is based on the BIRADS lexicon [36, 37] and is based on converting each breast density value in the corresponding BIRADS type. Therefore, for type one, we considered breast density values smaller than 25%, for type two, values larger or equal than 25% and smaller or equal than 50%, for type three values larger than 50% and smaller or equal than 75%, and finally type four for values larger 75%.

Table 4.1 and Table 4.2 show the breast density values obtained with semiautomatic algorithms BDthr128, BDthrAuto and BDthrOtsu. The mean of the three breast densities obtained for each rectangular selection D1, D2 and D3 is compared with the values provided by the radiologists. Table 4.3 shows the values of breast density obtained with the automatic BDCombo128, BDComboAuto and BDComboOtsu algorithms.

The evaluation of the breast density performed by the first radiologist is represented by RE 1A, the second evaluation by this radiologist performed twenty days after the first evaluation is represented by RE 1B, and the evaluation of the second radiologist is represented by RE 2. The assessment of breast density by radiologists is subjective, and this fact is evidenced by the values presented in Tables 4.1, 4.2 and 4.3. The rectangular selection in the breast ultrasound images can be performed by technicians who know the location of the glandular area and does not necessarily have to be performed by a radiologist.

The breast density values obtained with the BDthrOtsu algorithm are compared with the values obtained with BDthr128 and BDthrAuto algorithms and with the maximum and minimum values of the radiologist observation range for the set of 82 images, as illustrated in the Figure 4.4 chart. For the BDthr128 algorithm, 51.2% of cases fall within the interval; for the BDthrAuto algorithm, the value is 69.5% for the same range, and for the BDthrOtsu algorithm, the value is 64.6% indicating that the BDthrAuto algorithm has better performance than the other two according to the radiologist evaluation of the breast density.

Table 4.1- Values of breast density provided by radiologists and obtained with BDthr128, BDthrAuto and BDthrOtsu algorithms for ultrasound images 1-41.

Images	Density Obtained with the BDthr128 Algorithm				Density Obtained with the BDthrAuto Algorithm				RE 1A (%)	RE 1B (%)	RE 2 (%)	Density Obtained with the BDthrOtsu Algorithm			
	D1 (%)	D2 (%)	D3 (%)	MEAN (%)	D1 (%)	D2 (%)	D3 (%)	MEAN (%)				D1 (%)	D2 (%)	D3 (%)	MEAN (%)
I1	40.2	37.9	54.7	**44.3**	41.8	39.7	49.1	**43.5**	**40**	**30**	**30**	46.0	47.7	50.6	**48.1**
I2	33.1	20.4	26.1	**26.5**	38.2	31.7	35.2	**35.0**	**40**	**35**	**40**	38.1	40.5	36.5	**38.4**
I3	25.1	18.2	23.6	**22.3**	33.5	28.7	30.9	**31.0**	**25**	**30**	**30**	34.7	37.9	34.2	**35.6**
I4	64.7	51.4	57.8	**58.0**	55.3	49.7	49.3	**51.4**	**50**	**60**	**75**	57.4	61.0	54.8	**57.8**
I5	33.4	22.0	30.2	**28.5**	37.8	34.7	36.5	**36.3**	**40**	30	**45**	39.0	46.8	31.9	**39.2**
I6	40.3	48.8	53.1	**47.4**	45.7	48.4	50.7	**48.3**	**40**	**40**	**75**	30.5	44.2	29.3	**34.7**
I7	29.7	37.6	30.2	**32.5**	35.1	40.2	34.8	**36.7**	**30**	**35**	**40**	35.9	38.6	39.0	**37.8**
I8	17.5	20.9	18.2	**18.9**	29.6	31.6	30.1	**30.4**	**35**	**30**	**45**	31.5	34.3	29.0	**31.6**
I9	63.9	63.8	65.7	**64.5**	52.3	52.1	54.1	**52.8**	**50**	**60**	**80**	52.7	50.5	48.3	**50.5**
I10	50.1	74.5	79.0	**67.9**	49.8	58.1	60.5	**56.1**	**55**	**60**	**80**	60.5	53.9	58.3	**57.6**
I11	25.0	20.6	30.7	**25.4**	32.2	33.2	37.5	**34.3**	**25**	**40**	**45**	35.8	38.3	38.6	**37.6**
I12	22.6	30.5	23.4	**25.5**	34.1	40.1	35.4	**36.5**	**40**	**50**	**60**	38.0	40.3	36.5	**38.3**
I13	39.4	42.1	36.6	**39.4**	42.2	45.9	42.0	**43.4**	**50**	**60**	**70**	44.8	46.9	42.3	**44.7**
I14	14.6	25.7	21.3	**20.5**	28.1	39.2	31.8	**33.1**	**45**	**30**	**45**	35.4	28.4	45.8	**36.5**
I15	28.6	27.5	37.2	**31.1**	36.0	35.1	42.8	**38.0**	**50**	**35**	**40**	39.5	36.1	42.5	**39.4**
I16	18.3	19.1	25.7	**21.0**	31.5	31.9	36.5	**33.3**	**40**	**35**	**35**	35.5	32.0	38.6	**35.4**
I17	18.5	20.9	30.4	**23.3**	28.1	31.6	37.3	**32.3**	**30**	**30**	**28**	27.5	32.8	32.7	**31.0**
I18	24.7	30.3	16.3	**23.8**	33.8	36.8	28.6	**33.1**	**40**	**40**	**25**	35.3	38.7	30.8	**35.0**
I19	17.5	21.1	18.8	**19.1**	31.3	32.9	31.5	**31.9**	**35**	**40**	**30**	28.5	31.1	36.4	**32.0**
I20	43.2	32.6	51.6	**42.5**	45.2	41.5	50.5	**45.7**	**50**	**50**	**65**	47.8	48.6	48.3	**48.2**
I21	41.5	35.1	42.3	**39.7**	43.4	42.4	43.5	**43.1**	**45**	**50**	**60**	42.1	35.3	42.6	**40.0**
I22	30.6	32.8	40.3	**34.6**	39.6	40.8	43.1	**41.2**	**40**	**45**	**45**	46.2	40.7	40.8	**42.6**
I23	35.0	32.1	41.2	**36.1**	41.2	36.2	45.5	**40.9**	**40**	**40**	**50**	42.0	36.6	33.7	**37.4**
I24	26.7	24.7	31.2	**27.5**	31.7	29.8	37.1	**32.9**	**30**	**25**	**30**	36.4	31.0	43.5	**37.0**
I25	28.0	27.4	28.5	**28.0**	37.6	37.4	36.9	**37.3**	**30**	**40**	**55**	42.2	40.1	38.0	**40.1**
I26	16.5	24.8	17.2	**19.5**	31.2	36.2	30.3	**32.6**	**30**	**40**	**35**	26.1	30.1	25.9	**27.4**
I27	52.0	57.2	53.6	**54.3**	49.5	51.2	50.4	**50.4**	**55**	**50**	**65**	36.4	45.3	46.4	**42.7**
I28	17.9	22.3	19.7	**20.0**	32.2	34.9	31.9	**33.0**	**25**	**30**	**40**	29.0	33.0	30.2	**30.7**
I29	27.2	25.0	24.0	**25.4**	33.7	33.9	32.2	**33.3**	**30**	**25**	**35**	43.4	43.7	39.8	**42.3**
I30	44.3	58.0	35.3	**45.9**	45.2	50.9	40.2	**45.4**	**45**	**40**	**60**	47.8	55.9	46.0	**49.9**
I31	37.1	31.9	43.5	**37.5**	40.5	39.0	45.2	**41.6**	**45**	**50**	**45**	47.7	38.9	54.8	**47.1**
I32	47.2	50.0	44.9	**47.3**	47.8	47.8	46.1	**47.2**	**45**	**50**	**55**	49.2	49.0	45.9	**48.0**
I33	61.0	63.4	56.8	**60.4**	52.5	52.6	56.8	**52.1**	**50**	**60**	**55**	52.5	51.5	46.3	**50.1**
I34	37.9	44.5	37.8	**40.0**	43.6	46.1	42.9	**44.2**	**45**	**55**	**45**	43.2	44.6	51.2	**46.3**
I35	58.4	67.2	52.1	**59.2**	51.5	54.7	50.2	**52.2**	**50**	**50**	**55**	55.5	62.1	52.5	**56.7**
I36	39.7	41.6	54.9	**45.4**	41.8	42.8	50.8	**45.1**	**30**	**30**	**40**	47.9	42.4	49.1	**46.5**
I37	18.8	20.1	27.1	**22.0**	32.2	32.0	37.6	**33.9**	**25**	**30**	**30**	29.9	31.2	41.0	**34.0**
I38	28.1	26.2	36.7	**30.3**	35.7	34.1	42.6	**37.5**	**25**	**30**	**25**	37.7	35.5	40.4	**37.8**
I39	24.5	20.6	33.4	**26.2**	36.1	31.7	38.9	**35.6**	**25**	**25**	**20**	37.5	23.0	41.2	**33.9**
I40	32.3	31.4	24.6	**29.4**	41.6	40.3	36.2	**39.4**	**30**	**30**	**38**	32.3	41.6	32.2	**35.4**
I41	25.5	21.0	31.5	**26.0**	33.8	32.0	36.8	**34.2**	**30**	**25**	**20**	37.2	31.8	43.1	**37.4**

Table 4. 2 - Values of breast density provided by radiologists and obtained with BDthr128, BDthrAuto and BDthrOtsu algorithms for ultrasound images 42-82.

Images	Density Obtained with the BDthr128 Algorithm				Density Obtained with the BDthrAuto Algorithm				RE 1A (%)	RE 1B (%)	RE 2 (%)	Density Obtained with the BDthrOtsu Algorithm			
	D1 (%)	D2 (%)	D3 (%)	MEAN (%)	D1 (%)	D2 (%)	D3 (%)	MEAN (%)				D1 (%)	D2 (%)	D3 (%)	MEAN (%)
I42	56.0	65.7	49.7	**57.2**	49.2	53.1	49.3	**50.6**	**45**	**50**	**60**	56.7	62.1	50.9	**56.6**
I43	57.4	56.1	64.2	**59.2**	54.0	52.5	55.2	**53.9**	**45**	**50**	**75**	53.5	52.1	44.5	**50.1**
I44	16.7	18.2	18.8	**17.9**	31.0	30.2	33.7	**31.6**	**35**	**30**	**45**	29.7	32.2	29.9	**30.6**
I45	18.2	27.5	28.2	**24.6**	26.9	37.3	36.2	**33.5**	**30**	**30**	**30**	27.7	41.2	33.3	**34.1**
I46	51.6	42.4	62.5	**52.2**	51.0	45.5	58.5	**51.7**	**45**	**40**	**65**	51.7	47.8	53.2	**50.9**
I47	39.4	42.2	35.0	**38.9**	44.1	47.0	40.2	**43.8**	**35**	**30**	**55**	47.3	48.5	43.8	**46.5**
I48	62.0	45.0	67.3	**58.1**	55.0	45.8	57.8	**52.9**	**50**	**40**	**65**	58.9	51.9	55.7	**55.5**
I49	42.1	36.3	45.1	**41.2**	45.1	42.8	46.8	**44.9**	**50**	**40**	**45**	46.0	43.5	48.0	**45.8**
I50	41.1	38.4	43.7	**41.1**	43.0	44.8	44.6	**44.1**	**45**	**35**	**30**	41.4	34.7	43.3	**39.8**
I51	32.4	42.8	30.8	**35.3**	40.9	44.5	39.5	**41.6**	**40**	**30**	**35**	46.0	37.1	48.8	**44.0**
I52	34.0	30.4	39.6	**34.7**	40.4	36.1	43.9	**40.1**	**35**	**25**	**52**	42.2	37.2	43.5	**41.0**
I53	26.8	28.6	24.2	**26.5**	35.3	36.6	34.4	**35.4**	**35**	**25**	**55**	38.7	38.8	38.2	**38.5**
I54	25.7	23.9	29.0	**26.2**	32.7	32.4	35.3	**33.5**	**25**	**20**	**45**	36.8	30.1	36.6	**34.5**
I55	25.9	27.4	26.7	**26.7**	36.1	37.5	36.1	**36.6**	**40**	**35**	**70**	39.4	40.7	38.4	**39.5**
I56	15.8	23.8	18.3	**19.3**	29.8	35.3	29.4	**31.5**	**20**	**20**	**40**	26.8	30.8	23.9	**27.2**
I57	21.6	22.6	20.4	**21.5**	30.1	33.5	29.9	**31.2**	**20**	**30**	**55**	36.5	40.0	31.6	**36.0**
I58	33.2	53.9	49.1	**45.4**	43.5	51.1	48.9	**47.8**	**40**	**40**	**75**	31.4	33.1	32.3	**32.3**
I59	27.2	32.9	17.4	**25.9**	36.1	37.5	30.0	**34.5**	**35**	**30**	**70**	37.8	45.3	32.1	**38.4**
I60	23.9	28.4	23.1	**25.1**	37.3	36.5	35.2	**36.3**	**35**	**30**	**45**	42.5	42.5	40.0	**41.7**
I61	17.6	23.1	17.5	**19.4**	32.3	36.6	29.3	**32.7**	**35**	**25**	**40**	31.8	35.7	31.9	**33.2**
I62	31.8	30.5	30.9	**31.1**	37.8	36.1	37.0	**37.0**	**40**	**30**	**48**	36.9	37.8	41.4	**38.7**
I63	44.2	60.1	34.1	**46.1**	45.1	52.9	40.2	**46.1**	**45**	**45**	**65**	53.7	51.8	42.5	**49.3**
I64	31.1	35.4	27.3	**31.3**	35.5	39.3	33.0	**36.0**	**45**	**40**	**36**	37.3	39.3	40.0	**38.9**
I65	38.6	36.1	43.2	**39.3**	42.3	40.2	44.8	**42.4**	**50**	**50**	**46**	47.9	43.0	53.9	**48.3**
I66	50.0	50.6	44.5	**48.4**	47.4	48.1	46.1	**47.2**	**40**	**40**	**75**	52.8	42.6	47.9	**47.7**
I67	61.3	64.5	55.3	**60.4**	53.1	54.2	49.7	**52.3**	**50**	**50**	**75**	50.4	54.5	46.0	**50.3**
I68	34.3	43.2	32.7	**36.7**	37.6	45.0	39.2	**40.6**	**40**	**25**	**40**	45.5	47.1	44.9	**45.8**
I69	35.7	42.4	35.6	**37.9**	40.5	43.7	40.6	**41.6**	**40**	**60**	**45**	42.6	45.3	48.2	**45.4**
I70	51.8	57.8	51.9	**53.9**	50.4	50.8	49.9	**50.4**	**45**	**60**	**55**	56.3	62.5	51.4	**56.7**
I71	34.3	39.9	34.2	**36.1**	37.6	41.3	36.9	**38.6**	**35**	**40**	**40**	48.6	46.1	48.9	**47.9**
I72	20.5	20.7	23.3	**21.5**	30.4	31.5	31.8	**31.2**	**25**	**20**	**20**	29.4	29.6	39.3	**32.8**
I73	28.7	26.2	32.3	**29.1**	35.2	34.8	37.4	**35.8**	**25**	**25**	**30**	38.0	38.1	38.2	**38.1**
I74	19.9	21.9	28.4	**23.4**	33.2	29.2	35.7	**32.7**	**20**	**20**	**30**	37.2	28.6	43.7	**36.5**
I75	25.3	23.7	27.6	**25.5**	34.9	34.7	37.5	**35.7**	**30**	**20**	**25**	31.7	31.3	32.7	**31.9**
I76	16.9	12.7	20.1	**16.6**	26.4	25.4	29.2	**27.0**	**30**	**25**	**15**	37.3	40.6	41.8	**39.9**
I77	53.8	58.2	51.2	**54.4**	49.3	51.4	50.2	**50.3**	**45**	**50**	**65**	56.7	48.9	50.4	**52.0**
I78	60.0	57.2	66.7	**61.3**	53.6	53.6	56.6	**54.6**	**40**	**60**	**70**	55.5	50.4	44.0	**50.0**
I79	16.0	20.0	16.9	**17.6**	31.9	31.5	29.1	**30.8**	**25**	**30**	**20**	30.8	33.4	30.2	**31.5**
I80	18.2	18.5	31.1	**22.6**	27.4	30.9	36.3	**31.5**	**20**	**30**	**40**	27.0	41.0	32.4	**33.4**
I81	59.3	41.4	57.8	**52.8**	54.1	45.9	54.1	**51.4**	**40**	**45**	**60**	52.7	43.8	53.6	**50.0**
I82	37.2	39.4	34.5	**37.1**	40.8	44.7	39.3	**41.6**	**35**	**35**	**55**	45.0	48.3	42.8	**45.4**

Table 4.3- Values of breast density provided by radiologists and obtained with the BDCombo128, BDComboAuto and BDComboOtsu algorithms.

Images	Density Obtained with the Algorithm		RE 1A (%)	RE 1B (%)	RE 2 (%)	Density Obtained with the Algorithm
	BDCombo128	BDComboAuto				
I1	40.3	43.1	40	30	30	45.9
I2	27.3	35.3	40	35	40	38.9
I3	17.9	28.8	25	30	30	34.4
I4	49.1	49.1	50	60	75	54.4
I5	10.4	20.7	40	30	45	26.6
I6	37.1	43.0	40	40	75	46.0
I7	19.4	25.6	30	35	40	36.8
I8	18.2	31.4	35	30	45	32.8
I9	67.6	57.0	50	60	80	52.2
I10	41.6	43.7	55	60	80	50.7
I11	24.9	23.2	25	40	45	36.0
I12	28.5	36.2	40	50	60	39.4
I13	24.4	35.4	50	60	70	44.8
I14	20.2	31.4	45	30	45	36.0
I15	28.1	34.1	50	35	40	44.2
I16	22.3	30.5	40	35	35	33.9
I17	17.4	27.4	30	30	28	35.1
I18	17.5	27.6	40	40	25	30.3
I19	17.3	30.6	35	40	30	28.4
I20	36.9	44.0	50	50	65	46.9
I21	29.4	39.2	45	50	60	40.5
I22	25.5	34.3	40	45	45	41.3
I23	28.8	35.1	40	40	50	39.1
I24	22.3	30.6	30	25	30	33.8
I25	22.1	34.8	30	40	55	38.3
I26	20.8	29.5	30	40	35	30.2
I27	39.6	46.8	55	50	65	37.7
I28	19.1	31.1	25	30	40	36.0
I29	30.3	35.1	30	25	35	39.9
I30	30.6	36.9	45	40	60	44.5
I31	33.6	36.9	45	50	45	44.9
I32	44.3	47.4	45	50	55	50.1
I33	48.9	48.9	50	60	55	52.0
I34	29.7	38.0	45	55	45	45.1
I35	48.9	48.9	50	50	55	54.8
I36	33.9	37.4	30	30	40	44.1
I37	21.2	31.6	25	30	30	35.9
I38	28.5	35.2	25	30	25	43.6
I39	22.1	32.9	25	25	20	38.1
I40	25.1	37.3	30	30	38	40.5
I41	23.8	33.0	30	25	20	36.9

Table 4.4 - Values of breast density provided by radiologists and obtained with the BDCombo128, BDComboAuto and BDComboOtsu algorithms for images 42 to 82.

Images	Density Obtained with the Algorithm		RE 1A (%)	RE 1B (%)	RE 2 (%)	Density Obtained with the Algorithm
	BDCombo128	BDComboAuto				
I42	49.8	49.8	45	50	60	53.7
I43	63.6	56.5	45	50	75	51.5
I44	18.1	31.3	35	30	45	32.8
I45	16.7	26.6	30	30	30	35.7
I46	42.5	45.4	45	40	65	50.3
I47	25.3	34.2	35	30	55	41.9
I48	37.2	39.3	50	40	65	47.2
I49	39.4	44.1	50	40	45	49.2
I50	31.2	37.0	45	35	30	41.9
I51	37.2	39.3	40	30	35	44.6
I52	30.5	36.2	35	25	52	40.6
I53	25.1	35.5	35	25	55	38.5
I54	25.4	32.6	25	20	45	36.3
I55	21.6	34.2	40	35	70	36.7
I56	15.0	26.7	20	20	40	33.8
I57	17.7	27.7	20	30	55	33.6
I58	37.1	43.0	40	40	75	46.0
I59	27.2	35.5	35	30	70	40.0
I60	18.0	30.3	35	30	45	40.4
I61	18.2	29.3	35	25	40	34.4
I62	30.7	36.1	40	30	48	40.2
I63	45.7	48.1	45	45	65	53.0
I64	49.2	49.2	45	40	36	53.1
I65	33.6	36.9	50	50	46	45.1
I66	48.7	48.7	40	40	75	46.3
I67	55.5	52.1	50	50	75	52.8
I68	44.1	47.2	40	25	40	51.0
I69	34.9	40.9	40	60	45	42.2
I70	49.6	49.6	45	60	55	53.5
I71	27.4	33.1	35	40	40	39.0
I72	22.9	31.4	25	20	20	36.9
I73	31.6	35.5	25	25	30	41.0
I74	23.5	33.5	20	20	30	39.3
I75	27.2	35.6	30	20	25	42.5
I76	24.7	33.1	30	25	15	37.0
I77	49.3	49.3	45	50	65	53.1
I78	63.5	56.6	40	60	70	51.6
I79	21.1	32.8	25	30	20	33.5
I80	12.3	27.2	20	30	40	30.4
I81	51.2	50.7	40	45	60	52.4
I82	22.9	32.3	35	35	55	46.9

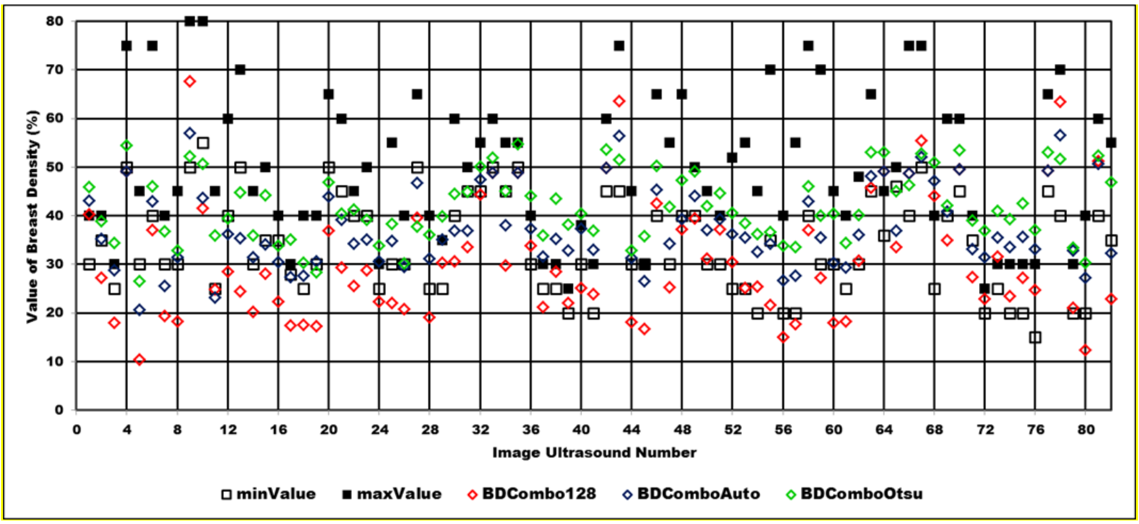


Figure 4.4- Comparison of breast densities of ultrasound images for BDthr128 vs BDthrAuto vs BDthrOtsu vs minimum and maximum values among three classifications by radiologists for each image.

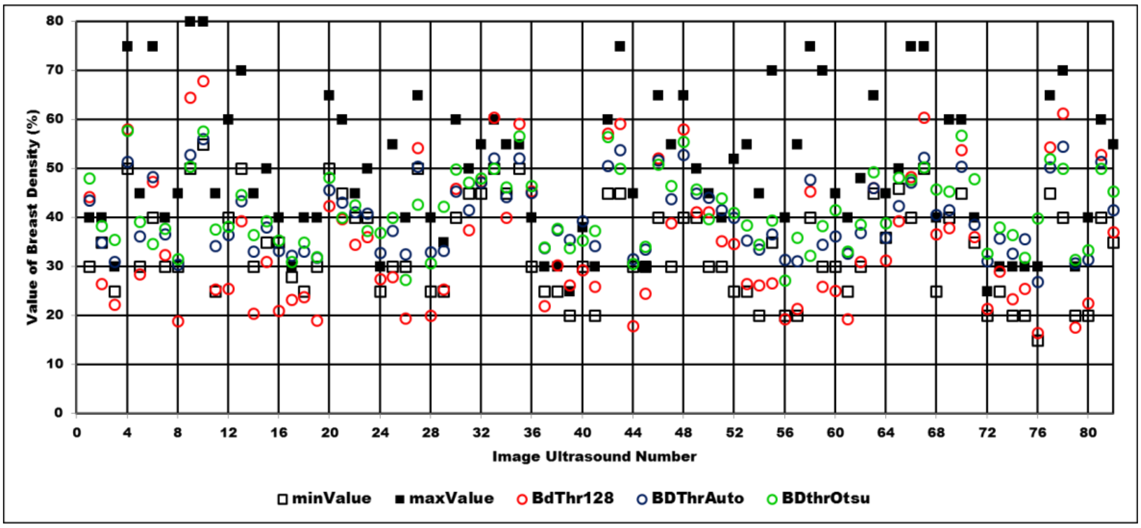


Figure 4.5 - Comparison of breast densities of ultrasound images for the BDCombo128 vs BDComboAuto vs BDComboOtsu vs minimum and maximum values among three classifications by radiologists for each image.

Figure 4.5 shows the breast density obtained with the BDCombo128, BDComboAuto and BDComboOtsu automatic algorithms and the maximum and minimum values of the radiologist observation range for the set of 82 images. The procedure used for the analysis of the results of the breast density obtained with the automatic algorithms is the same previously used for the semiautomatic algorithms. Taking into account the range with the maximum and minimum for each of the radiologist observations of the same image over the set of 82 images, the results obtained by the automatic algorithms are as follows: 31.7% of the values are within the range for the BDCombo128 algorithm, 48.8% of the values are within the range for the BDComboAuto algorithm and 61.0% of the values are within the range for the BDComboOtsu algorithm, showing the algorithm that uses Otsu thresholding performs better according to the radiologist evaluations.

Table 4.5 summarizes the values obtained with BDthr128, BDthrAuto, DBDthrOtsu semiautomatic algorithms and BDCombo128, BDComboAuto and BDComboOtsu, automatic algorithms according quantitative radiologists evaluation.

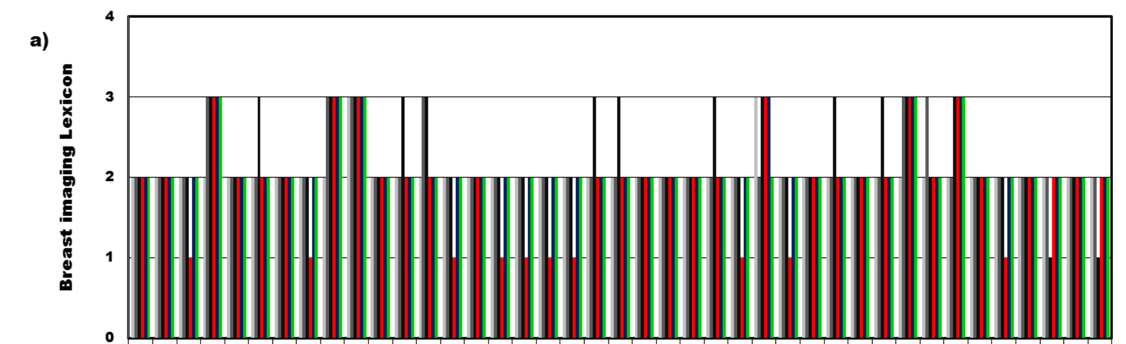
Table 4. 5 – Quantitative values obtained with the six algorithms developed according to radiologist evaluation.

Type	Algorithms	Accuracy with radiologist defined range (%)
Semiautomatic	BDthr128	51.2
	BDthrAuto	**69.5**
	BDthrOtsu	64.6
Automatic	BDCombo128	31.7
	BDComboAuto	48.8
	BDComboOtsu	**61.0**

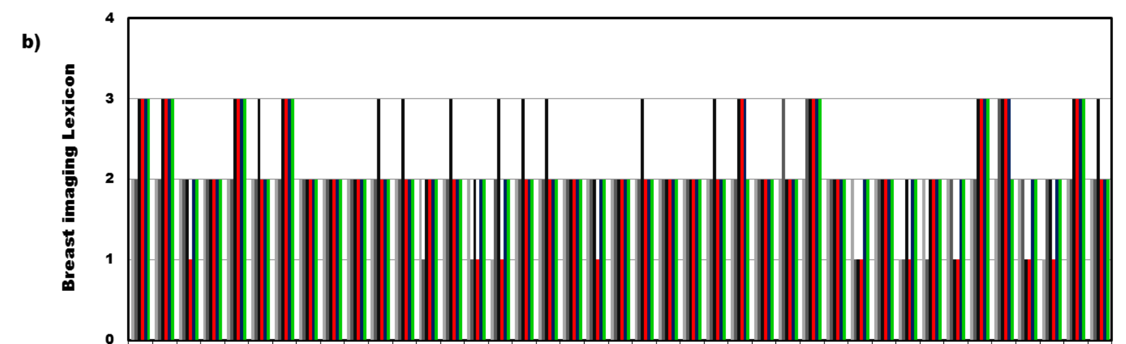
A qualitative assessment, according to the BI-RADS lexicon [36, 37] was also considered, where the values of breast densities observed by radiologists were classified according to the qualitative BIRADS lexicon. Taking into account these classifications, the algorithms for the estimation of breast density are evaluated based on the number of three hits or at least two hits with the three values of breast density provided by the radiologists for each image over the set of 82 images. Thus, the BDthr128 algorithm reached 26 images with 3 hits (31.7%), the BDthrAuto algorithm reached 38 images (46.3%), and the BDthrOtsu algorithm reached 38 images (46.3%). For at least 2 hits, the BDthr128 algorithm reached 56 images (68.3%), the BDthrAuto algorithm reached 70 images (85.4%), and the BDthrOtsu algorithm reached 70 images (85.4%).

Regarding the BDthr128 algorithm, there were 12 images (14.6%) that achieved no hits according to the radiologist observations whereas for the BDthrAuto and BDthrOtsu algorithms, this never occurred because there was always a coincidence with at least one of the observations made by the radiologists, as shown in Figure 4.6. The automatic algorithms performed as follows for 3 hits: the BDCombo128 algorithm reached 19 images (23.2%), the BDComboAuto algorithm reached 35 images (42.7%), and the BDComboOtsu algorithm reached 36 images (43.9%). For at least 2 hits, the BDAuto128 algorithm reached 45 images (54.9%), the BDComboAuto algorithm reached 68 images (82.9%), and the BDComboOtsu algorithm reached 65 images (79.3%).

Regarding the BDCombo128 algorithm, there were 23 images (28.0%) that exhibited no hits according to the radiologist observations, whereas for the BDComboAuto algorithm, there were 3 images (3.7%), and for the BDComboOtsu algorithm there were 23 images (2.4%) with no hits, as shown in Figure 4.7.



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41
RE1A	2	2	2	2	2	2	2	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2
RE1B	2	2	2	3	2	2	2	2	3	3	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3	2	2	2	2	2	2	2
RE2	2	2	2	3	2	3	2	2	3	3	2	3	3	2	2	2	2	2	2	3	3	2	2	2	3	2	3	2	2	3	2	3	3	2	3	2	2	2	1	2	1
BDthr128	2	2	1	3	2	2	2	1	3	3	2	2	2	1	2	1	1	1	1	2	2	2	2	2	2	1	3	1	2	2	2	2	3	2	3	2	1	2	2	2	2
BDThrAuto	2	2	2	3	2	2	2	2	3	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	2	2	2	2	2	3	2	3	2	2	2	2	2	2
BDthrOtsu	2	2	2	3	2	2	2	2	3	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	2	3	2	2	2	2	2	2



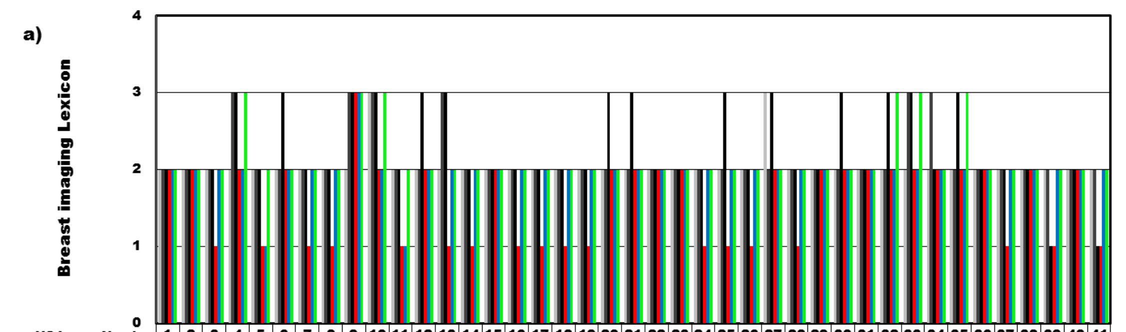
	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82
RE1A	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	1	2	2
RE1B	2	2	2	2	2	2	2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	3	3	2	1	2	1	1	2	2	3	2	2	2	2
RE2	3	3	2	2	3	3	3	2	2	2	3	3	2	3	2	3	3	3	2	2	2	3	2	2	3	3	2	2	3	2	1	2	2	2	1	3	3	1	2	3	3
BDthr128	3	3	1	2	3	2	3	2	2	2	2	2	2	2	1	1	2	2	2	1	2	2	2	2	2	3	2	2	3	2	1	2	1	2	1	3	3	1	1	3	2
BDThrAuto	3	3	2	2	3	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	2	2	3	2	2	2	2	2	2	3	3	2	2	3	2
BDthrOtsu	3	3	2	2	3	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	2	2	2	2	2	2	3	2	2	2	3	2

Figure 4.6 - Comparison of qualitative classification of breast density in ultrasound images for BDthr128 vs BDthrAuto vs BDthrOtsu vs qualitative classification resulting from the radiologist evaluations of ultrasound images for: a) 1-41; b) 42-82.

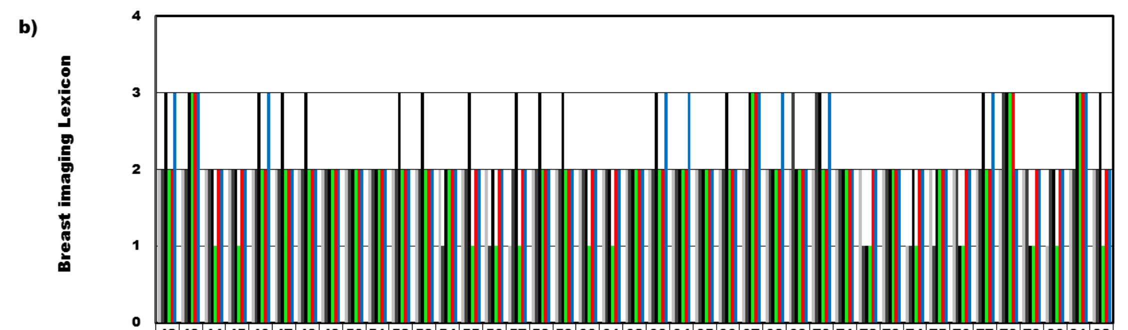
Table 4.6 shows the prevalence for the classification of the breast density, with prevalence given by:

$$Prevalence = \frac{Total\ of\ hits}{Total\ of\ ultrasound\ images} \qquad (4)$$

According to Cobham [38], algorithms performing the manipulation of the arrays have a complexity polynomial time, or O(nk), with k constant and k, n integer. Such algorithms are considered viable and efficient.



US Image Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41
RE1A	2	2	2	2	2	2	2	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2
RE1B	2	2	2	3	2	2	2	2	3	3	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3	2	2	2	2	2	2	2
RE2	2	2	2	3	2	3	2	2	3	3	2	3	3	2	2	2	2	2	2	3	3	2	2	2	3	2	3	2	2	3	2	3	3	2	3	2	2	2	1	2	1
BDCombo128	2	2	1	2	1	2	1	1	3	2	1	2	1	1	2	1	1	1	1	2	2	2	2	1	1	1	2	1	2	2	2	2	2	2	2	2	1	2	1	2	1
BDComboAuto	2	2	2	2	1	2	2	2	3	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
BDComboOtsu	2	2	2	3	2	2	2	2	3	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3	2	3	2	2	2	2	2	2



US Image Number	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82
RE1A	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	1	2	2
RE1B	2	2	2	2	2	2	2	2	2	2	2	2	1	2	1	2	2	2	2	2	2	2	2	2	2	2	2	3	3	2	1	2	1	1	2	2	3	2	2	2	2
RE2	3	3	2	2	3	3	3	2	2	2	3	3	2	3	2	3	3	3	2	2	2	3	2	2	3	3	2	2	3	2	1	2	2	2	1	3	3	1	2	3	3
BDCombo128	2	3	1	1	2	2	2	2	2	2	2	2	2	1	1	1	2	2	1	1	2	2	2	2	2	3	2	2	2	2	1	2	1	2	1	2	3	1	1	3	1
BDComboAuto	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	2	2	2	2	2	2	2	2	2	2	3	2	2	3	2
BDComboOtsu	3	3	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3	2	2	3	3	2	3	2	2	2	2	2	2	3	2	2	2	3	2

Figure 4.7 - Comparison of qualitative classification of breast density in ultrasound images for BDCombo128 vs BDComboAuto vs BDComboOtsu vs qualitative classification resulting from the radiologist evaluations of ultrasound images for: a) 1-41; b) 42-82.

Table 4.6- Prevalence of the results of the breast density algorithms for qualitative classification.

	Algorithms	Hits with radiologists evaluations		Prevalence	
		For 3 hits	At least 2 hits	For 3 hits	At least 2 hits
Ultrasound Images Total =82	BDthr128	26	56	0.32	0.68
	BDthrAuto	38	70	0.46	0.85
	BDthrOtsu	38	70	0.46	0.85
	BDCombo128	19	45	0.23	0.55
	BDComboAuto	35	68	0.43	0.83
	BDComboOtsu	36	65	0.44	0.79

Table 4.7 shows a summary of the values obtained with BDthr128, BDthrAuto, DBDthrOtsu semiautomatic algorithms and BDCombo128, BDComboAuto and BDComboOtsu, automatic algorithms for qualitative classification according to radiologists evaluation.

Table 4.7 – Qualitative values obtained with the six algorithms developed according to radiologists evaluation.

Type	Algorithms	Accuracy with radiologist BIRADS lexicon (%)	
		For 3 hits	At least 2 hits
Semiautomatic	BDthr128	31.7	68.3
	BDthrAuto	**46.3**	**85.4**
	BDthrOtsu	**46.3**	**85.4**
Automatic	BDCombo128	23.2	54.9
	BDComboAuto	42.7	82.9
	BDComboOtsu	**43.9**	**79.3**

Conclusions

Two new algorithms for breast density evaluation were proposed using Otsu thresholding. The performances of these two algorithms have been evaluated quantitatively and qualitatively and their results are compared with the results of the other two semiautomatic and two automatic algorithms for the evaluation of breast density.

Regarding quantitative assessment, semiautomatic algorithms based on Otsu thresholding and automatic thresholding (BDthrOtsu and BDthrAuto) perform better according to the radiologist evaluations than the algorithm based on the half division of the grayscale interval (BDthr128). Nonetheless, the algorithm using automatic thresholding (BDthrAuto) has better performance than the algorithm using Otsu Thresohlging (BDthrOtsu). Regarding the automatic algorithms (BDCombo128, BDComboAuto and BDComboOtsu), the algorithm using Otsu thresholding led to better estimates of breast density than the other two algorithms.

For qualitative assessment, both semiautomatic algorithms using Otsu thresholding and automatic thresholding (BDthrOtsu and BDthrAuto) have similar performance according to the radiologist classifications, and both algorithms have better performance than the corresponding algorithm based on the half division of the grayscale interval (BDthr128). Regarding the automatic algorithms (BDComboOtsu, BDComboAuto and BDCombo128), the algorithm using Otsu thresholding led to better classifications than the other two algorithms, but both the BDComboOtsu and BDComboAuto algorithms led to similar performance in terms of prevalence.

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Chapter 5

Conclusions and Future Work

This chapter presents the main conclusions that resulted from the research described in this thesis. Furthermore, it discusses a few research topics related to the work developed in the doctoral program that may be addressed in the future.

Breast cancer is considered one of the most serious types of cancer and is one of the major causes of mortality in women; however, a few men are also affected by this disease.

Several research studies have considered the risk factors for breast cancer; the most evident of these is to have been born a woman. However, among the various risk factors, breast density has been increasing in importance.

Recently, in the United States, a law was passed that requires radiologists to communicate breast density values to their patients when this value is high, so that they can perform additional tests at the patients' request; several working groups have sought to publish study findings on this topic on the web including correct information for radiologists and patients. This fact demonstrates the importance of breast density.

Regular examinations are advised for women mainly after 40 years of age because age is another major risk factor; the older a woman, the greater is the risk of breast cancer. The most commonly performed exams in addition to clinical examination are mammography and breast ultrasound. The use of breast ultrasound has increased because of the advantages compared to mammography, such as the cost, convenience of the examination, and portability of the equipment.

The evaluation of breast density using computer-aided systems based on image processing is not simple because the texture of breast tissue is highly variable. In mammography images, this variability is not problematic, which allows a more effective evaluation. Several studies and methods have been developed as a result, orienting the results to a qualitative classification in international classification systems such as BIRADS. Regarding breast ultrasound, this evaluation is not as effective as with mammographic images. Some preliminary work on the use of extracted mammogram features in ultrasound images for the evaluation of the breast density led to the conclusion that the methods

that work effectively for feature extraction in mammograms do not reach satisfactory results when used in breast ultrasound images.
Thus, given that the focus of this thesis was to develop a method to estimate breast density, new algorithms were investigated based on thresholding. Thresholding seems to be the most effective method based on breast image characteristics and respective image matrices. However, it was necessary to perform a more detailed analysis of the values of the array to determine the range of values and how a thresholding application could be accomplished. The specification of these algorithms is presented in Chapter 3 of this thesis. Chapter 4 also presents two new algorithms for breast density evaluation that use Otsu thresholding.

The proposed algorithms are semiautomatic and automatic. The semiautomatic algorithms, BDthr128, BDthrAuto and BDthrOtsu, consider three rectangular manual image selections in different parts of the glandular area of the breast ultrasound images to reduce the variability and consider the original images without the application of any filter or image pre-processing. For the automatic algorithms, BDCombo128, BDComboAuto and BDComboOtsu, an automatic algorithm was used to extract the glandular area instead of manual selections.

In semiautomatic algorithms, after making the selection, the image was converted into a grayscale image, and all the values were within the range [0, 1]. The resulting two-dimensional array for each selection was normalized because the range of values was concentrated in most cases on the lower values of the interval [0, 1]. The same occurred with the values from the one-dimensional array resulting from the gland segmentation algorithm.

The first algorithm, BDthr128, calculated the breast density based on the interval of gray intensity split in half thresholding, with predefined values. The second algorithm, BDthrAuto, evaluated the breast density based on automatic thresholding of the interval of gray intensity values. The third and fourth algorithms, BDCombo128 and BDComboAuto, used a one-dimensional array before normalizing the BDthr128 and BDthrAuto thresholding, respectively. The fifth algorithm, BDthrOtsu, calculated the breast density based on Otsu thresholding without normalizing the two-dimensional array. In the sixth algorithm, Otsu thresholding was applied to the one-dimensional array resulting from the application of gland segmentation to the breast images.

The results obtained with the algorithms were compared with the values provided by the radiologists who performed a manual breast density classification. Two radiologists performed the evaluations at different time points using direct visual observation before the application of the algorithms to the images. We compared the average of the three partial densities for the semiautomatic algorithms and the results of the automatic algorithms with the corresponding values of breast density provided by the radiologists.

The subjectivity verified in radiologist evaluations show how important it is to obtain computer-based estimates for breast density to reduce this subjectivity. Subjectivity was present in the radiologist observations because for the same breast ultrasound image, the ratings varied by up to 30% based on different radiologists and up to 20% for observations made by the same radiologist separated by twenty days.

To analyze the results produced by the algorithms, the maximum and minimum value of the observations of each ultrasound image by radiologists were considered and a range of values [minValue, maxValue] were defined where mimValue is the lower value of three radiologist observations and maxValue is the highest value of those observations. Considering the breast density value for each of these algorithms, for each analyzed image, whether the obtained values for breast density were or were not within the specified range was determined.

A qualitative evaluation was also performed. An interval was defined where the minimum value corresponded to the lowest value of the three radiologist observations and the maximum value corresponded to the highest value of those observations. The qualitative analysis was based on the BIRADS lexicon and was performed by converting each value of breast density in the corresponding BIRADS type.

The semiautomatic algorithms showed better performance than the automatic algorithms because the choice of the region of interest was performed manually, revealing results closer to the results provided by radiologists. Nevertheless, for the three automatic algorithms proposed, BDthrAuto performs better than BDthr128 and BDthrOtsu according to the radiologist evaluation of the breast density. For the automatic algorithms and considering the quantitative assessment, the BDComboOtsu algorithm has better performance than the other two; however, the difference was minimal for both BDComboAuto and BDComboOtsu if qualitative assessment is considered.

Thus and as a conclusion, breast density may be evaluated using the BDthrAuto semiautomatic algorithm or the BDComboOtsu algorithm, with similar results to the radiologist’s findings.

For future work, we intend to test the proposed algorithms in larger sets of breast ultrasound images, including more images with breast nodules because it is necessary to obtain areas with the scale required to perform the three selections of the glandular area. We also intend to investigate the accuracy of the segmentation of the breast glands because it may improve the performance of the semiautomatic algorithms regarding automatic algorithms, namely in images with many irregularities in the gland region. We also plan to validate the results obtained with our algorithms applied to ultrasound images with the results obtained with similar algorithms for mammography in the same women.

The integration of these algorithms into ultrasound systems is a mid-term objective, although it is ambitious given the policy of the companies currently operating in the market. However, this might contribute to the early diagnosis of breast cancer.