Computer Aided Diagnosis for Breast Lesions in Ultrasound Images Under Non-Extensive Tsallis Entropy

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Abstract

This paper presents a methodology to study breast lesions captured from ultrasound (US) devices. One of the main problems behind this theme is the separation of the lesion from their background in order to further extract their features, allowing a better automatic analysis later. Previous works have shown that by considering such images as non-extensive physical systems allows implementation of specific algorithms which facilitates the lesion separation. Then, as Tsallis entropy has appeared as a promise theory underlining non-extensive systems, in this paper we propose a recursive algorithm, based on this theory, in order to apply optimal threshold for breast lesion ultrasound image segmentation. A fundamental issue about segmentation methods that use Tsallis statistics is the setting of the parameter $q$, also called non-extensivity parameter. Recently, we introduced a method for automatic computation of $q$ value in general natural images. Now, our strategy is to use this automatic computation combined with two levels of Tsallis segmentation, specific for breast lesion ultrasound images. Then, experimentally, we show that our methodology properly extracts the lesion from the background allowing application of specific heuristics which delimit the lesion core for further analysis of the following three different lesion features: circularity, contrast and acoustic shadow/reinforcement. We meet the medical literature when we show that malignant lesions have high acoustic reinforcement behavior and benign ones have smoothing circularity as well. Our experiments have achieved optimal values for a data base of 250 images, and objective index rates that are better than those reported in the current literature under the same conditions. Two of these indices are: Sensitivity = 1.0 and Specificity = 1.0, which are reached when we use acoustic shadow/reinforcement as the main lesion’s feature. The malignant/benign classification is accomplished through a SVM classifier with a B-Spline kernel.

Key words: CAD systems; Tsallis Statistics; Breast Ultrasound Images
Introduction

In the early 21st century, breast cancer remains one of the most common diseases among women around the world. Although the rate of new cases has increased since the 80s, according to the American Cancer Society [40] the mortality rate has decreased by 2.3% since 1990. This fact may be a consequence of early diagnosis, which in turn has received considerable attention from the technological development of hardware and software as well.

There are many different types of breast cancer, with different stages (spreading), aggressiveness, and genetic makeup. Therefore, diagnosis and treatment vary greatly depending on those factors. Whether it is malignant or benign, breast lesions have visual characteristics that differentiate themselves in terms of morphology as well as in terms of superficial tissue, including texture and luminance distribution. In morphological terms, usually benign lesions tend to be oval, spherical and ellipsoidal, and malignant lesions tend to be more invasive, lobular and spiculated. In terms of superficial tissue, benign lesions tend to be more homogeneous and dense due to the strong presence of liquid, while malignant lesions tend to be more heterogeneous due to the high probability of developing calcification. Unfortunately, both types of lesions may mimic each other making diagnosis a hard challenge.

Diagnostic ultrasound is recognized as a safe, cost-effective, and highly flexible imaging modality capable of providing clinically relevant information about most parts of the body in a rapid and cost-effective fashion [16, 45].

However, the accuracy of diagnosis still heavily depends on the experience and skill of the radiologist and the quality of the involved equipment. Although it is a fact that the three-dimensional ultrasound has a higher quality of response than the corresponding bi-dimensional, manufacture and improvements of 2D devices are still in turn due to the low cost and effectiveness of this technology.
A few decades ago, with the improvement of digital equipment and the development of techniques for image processing, mainly associated with Computer Vision, the war against breast cancer has gained a powerful ally: the so-called Computer Aided Diagnosis (CAD), which is a computational system to assist radiologists in the interpretation of medical images [14, 6, 23].

A CAD system combines elements from artificial intelligence and digital image processing. When coupled to an ultrasound CAD it can help the image analysis and cancer detection. But even under great development of the current methods for prevention and detection of breast cancer, about 60% of the biopsies has to be proven not indicated. This number is alarming considering that in many cases an invasive biopsy may aggravate the lesion and also starts a metastasis. This fact further highlights the importance of developing techniques for automatic classification and analysis of images in CAD systems.

Despite of the development of CAD systems, radiologists must indicate the image area to be analyzed. Then, an automated system splits the image into main regions, selects from them the specific region of interest (ROI) and extracts features for further computation of tissue properties and morphological aspects. Finally, based on selected features, a classifier is used to indicate the likelihood of the ROI to be a benign or malignant lesion.

The partition of image into main regions of interest is a fundamental step known in Computational Vision area as *image segmentation*. Specifically in ultrasound images, this task is even more challenging since it involves issues of low resolution, low signal to noise ratio, and ill-defined borders.

In [32, 35, 31], it was suggested that medical images such as ultrasound or x-ray can be well segmented with the use of non-extensive entropy. This type of entropy arose in the late 80’s in statistical mechanics as a generalization of the (BGS) Boltzmann-Gibbs-Shannon entropy [41, 42]. In 2004, Albuquerque and colleges [1] presented the first algorithm based on non-extensive entropy for image segmentation, showing its efficiency for mammography segmentation. This work was extended in [35, 31, 32] for ultrasound
images with promising results and suggesting that the spatial and temporal characteristics involved in breast images can achieve an adequate segmentation with the use of Tsallis entropy.

The main feature of the Tsallis entropy is the introduction of the parameter $q$, called the non-extensivity parameter. From the viewpoint of the image analysis, the variable $q$ is associated with the amount of information contained in each image. Therefore, the computation of the $q$ parameter becomes a fundamental challenge.

This paper has the following four contributions. First, based on the recursive non-extensive algorithm proposed in [30] for general natural images, we propose to use the same idea to the present context of breast images. This is valid since the considered algorithm has achieved good results when the authors consider four luminance levels in their data base. In the present medical image context, we have ultrasound images with a main central core (generally representing a tumor), a thinning border around the this core (generally transition tissue between tumor region and other masses), and regions representing other breast organs. Then, since we have in this kind of image two until four regions of investigation, it is interesting to see how the algorithm proposed in [30] behaves in our ultrasound data base. Second, we present heuristics to select the ROI among the main computed regions. The improvement in efficiency related to other general segmentation algorithm will allow a more reliable extraction of three specific breast lesion features: circularity, acoustic shadow/reinforcement and contrast. Therefore, allowing a more precise classification to be further carried out in experiments. Third, we show, through ideal objective indices, that our results meet the medical literature. Finally, we propose to use as similarity measure between feature vectors representing breast images, the recently proposed Kullback-Leibler divergence under non-extensive Tsallis statistics, introduced in [3]. We show that it gives us a new control parameter improving the final classification results.
Related Works

For a complete review of important papers about breast ultra-sound images in the last decade see [17].

We can find several techniques for classification of breast lesion from ultrasound devices, say: Bootstrap [15], Support Vector Machine (VM) [7] and Neural Networks [12, 11, 26]. Nevertheless, these classifiers are main dependent on the chosen features, which are defined by radiologists before diagnostic exam. These characteristics are very dependent on the tumor profile such as geometric features, texture and grayscale patterns, as well as the features surrounding the lesion. These features together with the classifiers determine the efficiency of the CAD software.

Sawaki et al. [37] proposed a CAD system using fuzzy inference for breast ultra-sound and adopted six different criteria to classify lesions such as: shape, border, edge shadows, internal echoes, posterior echoes, and halo. However, their system accuracy, sensitivity and specificity were only 60.3%, 82.1% and 42.9%, respectively.

Texture framework in ultrasound image processing goes back to more than two decades. Garra et al. [21] analyzed the breast lesions using a co-occurrence matrix of ultrasound images to represent their texture information. Chen et al. [12] proposed an autocorrelation coefficients to analyze the same texture information. Since their implementations were presented on a smaller set of data, there is a fundamental weakness with texture-based strategies. The settings of ultrasound machine parameters have to be fixed for acquiring data. On the contrary, if ultrasound parameter setting changed, the CAD performance was very unstable (Chen et al. [11]). Moreover, a CAD system trained by images from one ultrasound machine needs to be trained again for a different device due to different image resolution and image quality. Hence, Chen et al. [11] proposed nearly setting-independent features based on shape information. Their system was very robust and powerful because the statistical data using ROC curve were all greater than 0.95. Chang
et al. [8] also used six shape features in their analysis, including factor, roundness, aspect-ratio, convexity and solidity. Note that all these strategies were used on 2-D ultrasound device. As a result, the shape and structure information of the breast lesions could not be reconstructed, and consequently may be not possible to determine the growth of the cancer and its spatial relationships. Recently, 3-D ultrasound (Chang et al. [5]) has shown promising signs that overcome the limitations of traditional 2-D devices and allow physicians to view anatomy in 3-D interactively, instead of assembling the sectional images in their minds. Chang et al. proposed an application of autocorrelation matrix running difference structures. They have studied pixel relation analysis techniques for use with 3-D breast US images and compares its performance to 2-D versions of images. They found that the features from only some slices were enough to provide good diagnostic.

Due to the speckle noise, artifacts and also low-intensity regions – generally from blood vessels – it is not an easy task to extract the features from the US images by a common image-processing technique (Cheng et al. [10]). One main reason is that the pixels in the tumor may have a lower level of intensity than the surrounding normal tissue (Cheng et al. [9]). Then, Chen et al. [12] presented a work where they suggest that the 2-D normalized autocorrelation coefficients are suitable to reflect the inter-pixel relations within an image and make it possible to differentiate benign and malignant breast masses. Different tissues have significantly different pixel relations in US images.

The correlation between neighboring pixels within the 2D images is an important feature of the tumor. A study based on the pixel relation analysis techniques was developed by Chen et al. ([12], [19], [13]). They have used normalized autocorrelation coefficients to reflect the inter-pixel correlation within a region. In order to generate similar autocorrelation characteristics for tumor regions under different brightness but with a similar pixel relation, the autocorrelation coefficients are further modified into mean-removed auto-covariance coefficients. In their work, these auto-covariance coefficients for each breast tumor image are found and taken as inter-pixel relation features in order to distinguish the differences between benign and malignant tumors.
The spiculation feature is mostly used to diagnose the breast tumors using 3-D US. In the later study by Rotten et al. [36], the coronal section in the 3-D US allows precise demonstration of the tissue surrounding the central lesion. A converging pattern of the peripheral tissue is highly suspicious of malignancy. The converging pattern is a spiculation in which alternating hypoechoic and hyperechoic lines radiating in multiple directions from the mass into the surrounding tissue. This feature is well seen on mammograms, and malignancy cannot be excluded based on this finding. In their experiments, 91% (53 of 58) of malignant tumors and 6% (8 of 128) of benign tumors have spiculation. Although there are several successful spiculation detection techniques on mammograms (Karssemeijer and teBrake [24]; Kobatake and Yoshinaga [25]; Vyborny et al. [44]; Liu et al. [27]), the automatic spiculation detection on US images is not easily implemented due to the speckle noise.

Chen et al [14]. develop a computer-aided diagnosis (CAD) algorithm with setting independent features and artificial neural networks to differentiate benign from malignant breast lesions. All performance comparisons were based on paired-sample t-tests. The proposed CAD algorithm could effectively and reliably differentiate benign and malignant lesions. The proposed morphologic features were nearly setting independent and could tolerate reasonable variation in boundary delineation. Their proposed CAD algorithm was composed of three essential components, namely, feature extraction, feature selection, and classification. To relax the constraints on the system settings, the morphologic features rather than the regional features were adopted. The potential dependence of the morphologic features on the contour extraction process was minimized by capturing important topologic properties of the lesions, which may not vary drastically with the delineated contour. Feature selection was necessary to alleviate dimensionality [18]. A set of essential morphologic features that yield a best performance was selected on the basis of stepwise logistic regression [20]. Classification was accomplished with a multilayer feed-forward neural network (MFNN) [46] on the basis of the essential morphologic features. Then, seven morphologic features were extracted from each lesion to account
for three important sonographic features: shape, contour, and size. Five of these morphologic features were developed by including the number of substantial protuberances and depressions, lobulation index, elliptic-normalized circumference, elliptic-normalized skeleton, and long axis to short axis ratio. The other two features were clinically useful indicators: depth-to-width ratio and size of the lesion.

**Breast Lesion Characteristics**

The edges or borders of breast masses can be circular, microlobulares, indistinct or spiculated [28]. The shape can be oval, lobular or irregular. A spicular border is a strong indication for malignancies, while a circular border is a strong indication of a benign lesion. However, these are only indicators, not necessarily determine the presence or absence of carcinoma. Some benign masses such as postoperative scars, necrotic fat, hematomas, stellar radial forms or abscesses may mimic malignant lesions. On the other hand, some malignant lesions such as invasive ductal carcinoma, fibrosarcoma, lymphoma, primary or secondary pseudo-lymphoma, and metastases may be similar to benign masses. An ultrasound or MRI exam is thus only an auxiliary evaluation. A lesion in the breast may be definitively classified as malignant only after a histological or cytological analysis. However, both benign and malignant lesions may have the following characteristics: circular or oval, star or spiculated, calcified, or any combination of these four. A complete study about the breast tumors under the ultrasound view can be see in [28].

*Circular/Oval and Spicular/Star Lesions*

Once that benign lesions are often made up of liquids (e.g.: cysts or fibroadenomas) they are normally found in ellipsoidal shape, being wider than high. For this reason, they also have a better compressibility in relation to malignant. But fibroadenomas usually also have a thin capsule around the lesion.
On the other hand, malignant lesions usually have high density and increased calcification, which impart to them a less compressive character. They are also more lobular and randomly oriented non-aligned along the breast structures. The invasive nature, density and slightly compressive malignant lesions cause these lesions to have low circularity and are higher than wide, generally compressing both the parenchyma and the estrogen around the breast.

In turn, spicules or stellate lesions have a central solid tumor with radiating structures and poorly defined borders. Many breast cancers have spicules forms, although specula lesions with few or very small specula are difficult to observe. In a truly spiculated lesion the largest diameter of the radiation tends to occur on the margin of the tumor.

The larger the central tumor, the longer are the spicules. If the spicules reach the skin, muscles, or the halo region, it results in shrinkage and thickening at the skin. If a dense central tumor is identified, it is often an indication of malignancies. In turn, benign masses have very different power, but post-surgical fibrosis, fat necrosis, abscesses and hematomas can mimic lesion spicules; and invasive lobular carcinomas or very small invasive ductal can be difficult to be observed.

**Calcification**

Breast calcifications are deposits of calcium that is mobilized from the blood into the tissues, then suffering several pH transformations, settling in the form of calcium salts. There are two types of calcifications: those composed of calcium oxalate dihydrate - which are acidic calcifications with polyhedral shape and occurring in 10 to 15% of cases. The other type results from the deposition of calcium phosphate in tissue necrosis or products of secretion and contributes over 70% of cases visualized in mammography.

Since the calcification results in decreased fluid in the lesions, they generate sound artifacts that produce areas of low attenuation of sound, producing an effect known as
acoustic enhancement, allowing sound to pass through the lesion and best highlighting the areas below the lesion. This is an indication of malignance.

On the other hand, a benign lesion tends to have a watery dense central core (e.g. cysts and fibroadenomas) which are anechoic regions, and as such hinder the passage of sound or fully reflects, creating a darkened region below the lesion more than the regions around, becoming difficult to visualize these shaded regions. Due to creating a darkened area below the lesion, this process is a sound artefact known as acoustic shadowing and is an indication of benign lesion.

In our work, we consider both information of shape and texture, as well as information to improve the efficiency of the proposed method for automatic tumor analysis and classification. Specifically, the acoustic shadow/reinforcement is of utmost importance, since it has the best results in the studied database.

Information Theory of Non-Extensive Entropy

The traditional equation for entropy, over a probability density function \( p(x) \), also called Boltzmann-Gibbs-Shannon entropy (BGS), is defined as:

\[
S = - \sum_i p_i \ln(p_i)
\]

Generically speaking, systems that can be described by Equation (1) are called extensive systems and have the following additive property: Let \( A \) and \( B \) be two random variables, with probability densities functions \( A = (a_1, \ldots, a_n) \) and \( B = (b_1, \ldots, b_n) \), respectively, and \( S \) be the entropy associated with \( A \) or \( B \). If \( A \) and \( B \) are independent, under the context of the Probability Theory, the entropy of the composed distribution\(^1\) verify the

\(1\) we define the composed distribution, also called direct product of \( A = (a_1, \ldots, a_n) \) and \( B = (b_1, \ldots, b_n) \), as \( A \times B = \{a_i b_j\}_{i,j} \), with \( 1 \leq i \leq n \) and \( 1 \leq j \leq n \)
so called additivity rule:

\[ S(A + B) = S(A) + S(B) \]  \( (2) \)

For nearly three decades, this rule has been used by several researchers of computer vision system to find an optimal threshold in order to separate the foreground from the background of gray scale images [4, 38]. The general idea, historically by T. Pun [29], consider the histogram of gray scale with \( L \) bins a symbol source, with all symbols statistically independent.

This traditional form of entropy is well known and for years has achieved some success in explaining various phenomena if both the effective microscopic interactions and the effective spatial microscopic memory are short-ranged. Roughly speaking, when the system does not have this behavior, the standard formalism becomes only an approximation, and some kind of extension appears to be necessary. A more complete review of this theory can be found in [41, 42, 43].

Recent developments based on the concept of non-extensive entropy, also called Tsallis entropy or \( q \)-entropy, has generated a new interest in the study of the Shannon entropy to Information Theory. [39]. Tsallis entropy is a new proposal for the generalization of BGS traditional entropy applied to non-extensive physical systems.

The non-extensive characteristics of Tsallis entropy have been applied through the inclusion of a parameter \( q \), which generates various mathematical properties [43]. The Tsallis entropy is defined as follows:

\[ S_q(p_1, \ldots, p_k) = 1 - \frac{\sum_{i=1}^{k} p_i^q}{q - 1} \]  \( (3) \)

where \( k \) is the total number of possibilities of the whole system and the real number \( q \) is called the entropic index (or non-extensive parameter) that characterizes the degree of system non-extensivity.

In the limit \( q \to 1 \), Equation (3) meets the traditional BGS entropy defined by Equation
These features give the q-entropy more flexibility to explain various physical systems, which can not be properly explained by the traditional BGS formalism. Then, this new kind of entropy does not fail to explain the traditional physical systems since it is a generalization.

Furthermore, a generalization of some theory may suppose the violation of one of its postulates. In the case of the generalized entropy proposed by Tsallis, the additive property described by Equation (2) is violated in the form of Equation (4), which apply if the system has a non-extensive characteristic. In this case, the Tsallis statistics is useful and the $q$-additivity describes better the composed system. In our specific case, the experimental results section show that it is more convenient consider the systems studied in this work as non-extensive.

$$S_q(A * B) = S_q(A) + S_q(B) + (1 - q)S_q(A)S_q(B)$$  \hspace{1cm} (4)

In this equation, the term $(1 - q)$ stands for the degree of non-extensivity. Note that, as stated before, when $q \to 1$, this equation meets the traditional Equation (2).

Recently, Albuquerque and colleagues [1] have proposed an algorithm using the q-entropy formalism to general image segmentation. Their idea was almost the same as that proposed by T. Pun but under the new formalism suggested by Tsallis. Suppose an image with $L$ gray levels. Let $P = \{p_1; p_2; \ldots ; p_L\}$ be the probability distribution of these levels. So, it would be two probability distributions, one for the foreground ($P_A$) and one for the background ($P_B$). We can find a partition at luminance level $t$, which separates the pixels of $P$ into two new partitions $P_A$ and $P_B$. In order to maintain the constraints $0 \leq P_A \leq 1$ and $0 \leq P_B \leq 1$, we normalized the two distributions as:

$$P_A : \frac{p_1}{p_A}, \frac{p_2}{p_A}, \ldots, \frac{p_t}{p_A}$$

and

$$P_B : \frac{p_{t+1}}{p_B}, \frac{p_{t+2}}{p_B}, \ldots, \frac{p_L}{p_B}$$

where $p_A = \sum_{i=1}^{t} p_i$ and $p_B = \sum_{i=t+1}^{L} p_i$. 

13
Now, following Equation (3), we can calculate the a priori Tsallis entropy for each distribution as $S_A = \frac{1 - \sum_{i=1}^{t} (\frac{p_i}{p_A})^q}{q-1}$ and $S_B = \frac{1 - \sum_{i=t+1}^{L} (\frac{p_i}{p_B})^q}{q-1}$, respectively. Now, considering the pseudo-additive property given by Equation (4), for two statistically independent systems, we can compute:

$$S_{A*B}(t) = \frac{1 - \sum_{i=1}^{t} (\frac{p_i}{p_A})^q}{q-1} + \frac{1 - \sum_{i=t+1}^{L} (\frac{p_i}{p_B})^q}{q-1} + (1 - q) \frac{1 - \sum_{i=1}^{t} (\frac{p_i}{p_A})^q}{q-1} \sum_{i=t+1}^{L} (\frac{p_i}{p_B})^q$$

(5)

To accomplish the task of segmentation, in the work proposed by Albuquerque and colleagues [1], the measure of information between two classes (foreground and background) is maximized. In this case, the luminance level $t$ is considered as the optimal threshold value ($t_{opt}$), which can be achieved with a cheap computational effort of

$$t_{opt} = \arg \max[S_A(t) + S_B(t) + (1 - q)S_A(t)S_B(t)]$$

(6)

Note that the value $t$ that maximizes Equation (6) depends mainly on the entropic parameter $q$. So far in the literature the $q$-value that generates $t_{opt}$ is not explicitly calculated and must be found empirically. In this paper, one of our main contributions is an algorithm to automatically compute an acceptable a priori $q$-value. This idea was first suggested in [30] for segmentation of general natural images. Now, we suggest this idea under the specific context of breast lesions in ultrasound devices.

**The Extended Kullback-Leibler Divergence**

The BGS entropy is close related to another kind of entropy, the well known relative entropy, also called *Kullback-Leibler Divergence* ($D_{KL}$), which is a measure of statistical divergence between two probability distributions $P = \{p_1, p_2, \ldots, p_n\}$ and $P' = \{p'_1, p'_2, \ldots, p'_n\}$, defined as:

$$D_{KL}(P : P') = \sum_{i} p_i \cdot \log \frac{p_i}{p'_i}$$

(7)
The Kullback-Leibler divergence can be naturally estimated through replacing the conventional Shannon formalism by the Tsallis formalism. In the recent work L. Borland et al. [3] generalized the Kullback-Leibler gain of information to the non-extensive statistics. This extended divergence is defined as:

$$D_{KL_q}(P : P') = \sum_{i} \frac{p^q}{q-1} \cdot (p_i^{1-q} - p_i'^{1-q})$$

(8)

In the present work, we use the $D_{KL_q}$ divergence to measure the information between two regions in order to quantify malignant and benign differences among them.

**Computation of the $q$ index**

Consider the background and foreground as independent physical systems. The very celebrated strategy of T. Pun [29] for image segmentation was to use the property of additivity (Equation (2)) of extensive systems to find the optimal threshold between the two systems. This fact is based on the idea that the maximum possible amount of information is transferred when the global maximum entropy is achieved by adding the individual entropies of each system. The same argument holds for non-extensive systems. However, the formalism used here is according to Equation (5), where $t$ is the optimal threshold that maximizes the self-information.

As stated before, the Tsallis formalism is a generalization of Shannon entropy, meeting the traditional system when $q \to 1$ only. Thus, we can conclude that the $q$-entropy can capture both the extensive and non-extensive behaviors. Thus, it is reasonable to investigate the entropic segmentation approaches for breast ultrasound images in both contexts. Later, we will show that, for our database, we get better segmentation performance (in terms of output from the CAD system) under non-extensive formalism.

Of course, the usage of a new parameter has an extra computational price to pay, and each image or region, independent of its type, may demand for different values of $q$ (including
Figure 1. $S_q/S_{max}$ as a function of $q$ range. The lower value, corresponding to $q = 0.46$, is the optimal $q$ used for initial segmentation (Fig. 2-middle).

$q = 1.0$) in order to achieve maximization of information. Thus, it is interesting to evaluate the value of entropy for each image under a range of $q$; e.g.: considering sub-extensive systems where $q \leq 1.0$.

From the point of view of Information Theory as lower the maximum entropy $S_q$ produced by some $q$ value related to the theoretical maximum entropy $S_{max}$ of a physical system (in this case, a breast cancer image) larger is the self-information contained in the system. This is the well known principle of Information Theory and leads to the idea that the optimal $q$ value can be achieved by minimizing the $S_q/S_{max}$ ratio. Then, before applying the proposed formalism stated by Equation (6), we compute the optimal $q$ value underlining the image. This is accomplished according to the method proposed in [30] as the following. For each discrete $q$ value in the range $[0.01, 0.02, ..., 2.0]$ we get the optimal $q$ as that which minimizes the $S_q/S_{max}$ ratio. In this paper we work with the hypothesis that each ultrasound image is a whole extensive system, and also consider that its internal
region also behaves as independent physical system as well. This assumption states that may be different values of $q$ for each image or region that best segment it.

**A Multi-Segmentation Non-Extensive Algorithm**

In order to apply different $q$ values to segment different image regions, and to achieve the main regions in a image, we carried out two levels of segmentation based on the formalism presented in section before. Initially, we compute the $q$ value by minimizing $S_q/S_{\text{max}}$ and apply the Equation (6) to get a first optimal $t_{\text{opt}}$ threshold obtaining a first level of segmentation separating background ($R_B$) from foreground ($R_F$). Then, for each region found ($R_B$ and $R_F$) we compute new $q$ values, treating $R_B$ and $R_F$ as different physical systems, and apply the algorithm again, obtaining two new $t_{\text{opt}}$ values as well. Thus, we can find up to four intensity levels to partition the images. This is a general algorithm presented first in [30] for general natural images, and now we apply in breast lesion segmentation. Fig. 2 shows an example. Fig. 2-left is the original image, and Fig. 2-middle is its first level of segmentation into two regions ($R_B$ and $R_F$), achieved with the optimal $q = 0.46$, which corresponds to the minimal value of the curve of Fig. 1 ($S_q/S_{\text{max}}$). Following the same idea for $R_B$ and $R_F$ regions, we compute new $q$ values by minimizing new $S_q/S_{\text{max}}$ curves and achieve two new optimal thresholds $t_{\text{opt}}$. This is the second level of segmentation. The final segmentation result can be seen in the Fig. 2-right. In this case we found $q = 0.15$ for $R_B$ and $q = 0.73$ for $R_F$, suggesting sub-extensive system behavior for all regions.

**The Proposed Methodology**

This section explains how to use the proposed non-extensive multi-segmentation algorithm with the proposed automatic procedure to compute $q$ for feature extraction suitable for a subsequent binary classification between malignant/benign lesion. In particular, we
Figure 2. (left image) a original breast image; (middle image) the first segmentation with $q = 0.46$ achieving $R_B$ and $R_F$; (right image) the final segmentation with $q = 0.15$ and $q = 0.73$ for the previous $R_A$ and $R_F$, respectively.

show how to take advantage of the proposed multi-segmentation algorithm and how it can be adapted into a CAD system in order to extract the breast lesion features.

In the first step of our methodology, we apply the non-extensive algorithm for splitting a breast image (Fig. 2-left) into two regions, $R_F$ and $R_B$, then applying again the non-extensive algorithm, now achieving independent segmentations inside $R_F$ and $R_B$ regions (Fig. 2-right).

This non-extensive multi-segmentation approach with automatic calculation of the parameter $q$ splits the ultrasound image until 4 discrete gray levels which (for better visualization in this paper) are labeled with gray intensities: 255, 160, 80 and 0. Thus, after the second level of segmentation, the result will look like Fig. 2-right. The criterion for labeling is the following.

According to Section about calcification as more watery is a lesion less it will be echogenic and thus tend to appear in darker tones in the ultrasound images (e.g. the central circular and dark region of Fig. 2-left). The same could be applied to regions around the lesion, such as those made by fat and lymphatic or venal channels. Since the central core regions (and also those around) are those of greatest interest in this work, we choose to label them with intensity value 255. For simplicity, in our work we call the central lesion as core, its border around as border and the border’s branches as branches.

The border tends to be less watery than the core, and therefore is more echogenic appear-
ing less darkened in the ultrasound. So, after a second level of segmentation, the border stands out from the lesion as well as from the regions of organs and channels so far. So, we chose to label the border in a second level of segmentation with intensity value 160. Finally, the clearest regions in the original image (those more echogenic than the other and usually corresponding to organs around the lesion) are chosen to receive the two remaining luminance levels 80 and 0 (e.g. Fig. 2-left).

In the diagnosis of breast cancer, initially the most important regions to be observed are the suspected cores (labeled 255) and borders (labeled 160). There are basically two cases that can be observed in a process of segmentation based on thresholding. The first one has a well-defined central core wrapped by an also well defined border, which in turn may have branches reaching regions to other more distant organs. An example can be seen in Fig. 2. The second case, shown in Fig. 3, appears when the lesion is a mixture of two cores: one watery (less echogenic and dark) and another calcified (echogenic and clear).

The Fig. 3-a is an original image where we can see the darker core (region pointed by the left arrow) and the calcified core (region pointed by the right arrow). The segmentation with non-extensive entropy can separate these two cores such as in (Fig. 3-b). However, it becomes a problem since the lesion is truly made by two cores (as shown Fig. 3-c). This second case is particularly difficult to analyze in an automatic fashion (and even subjectively), since calcified lesions are not well defined and may also be branched. On the other hand, from the point of view of diagnosis, it is important to analyze both the lesion as a whole (the two cores together) besides two cores individually.

But if only one level of segmentation is carried out, possibly one core will be incorporated into the foreground and the other into the background, and only one core (say, the foreground) will be further evaluated, probably leading to misdiagnosis. Besides, the highlighted regions in Figs. 2-right and 3-b may contain structures that do not belong to the lesion. Therefore, the next stage should be able to properly distinguish the two cores as well as merge them as a single lesion if it is demanded. In this work, we implement
After step 1, there are only pixels labeled with the four intensity values: 255, 160, 80 and 0. Initially, we take pixels labeled only with values 255 and, in step 2, we apply the following heuristic. Let $p_i = 255$ and $p_j = 255$, $i \neq j$, be two pixels in a region $R_F$ after application of the non-extensive segmentation over an image $I$ with diameter $D$ and size $N$. The objective of step 2 is clustering the $R_F$ region according to the distance between its pixels. This is accomplished through the following rule. $p_i$ and $p_j$ belong to the same cluster in $R_F$ if the Euclidean distance $d(p_i, p_j)$ is less than a threshold $T \leq D$. This heuristic splits pixels with value 255 in a set of clusters $\mathbb{K}$. For all $C_k \in \mathbb{K}$, we define $P_a^k = |C_k|/N$ the probability of cluster $C_k$ in $I$. We also define $P_c^k = 1 - d(pc^k, pm)/D$
(where $pc^k$ is the geometric center of the cluster $C_k$ and $pm$ is the geometric center of $I$) the probability of $pc^k = pm$. Note that $0 \leq P^k \leq 1$ since $d(\cdot, \cdot)$ has an upper bound $D$. Thus, we suppose that the cluster $C_k$ is the likely region of interest if: $\forall p_i, p_j \in C_k$, $d(p_i, p_j) < T$ and $P^k = P^a_k + P^c_k = \max\{P^a_i + P^c_i\}, i = 1, 2, \ldots, |K|$. Now, we denote the $C_k$ with this property as $R_p(I)$. It completes the step 2 of the algorithm.

Then, step 3 takes $R_p(I)$ (a region of interest found in step 2) as a seed point from where the area around (those labeled with intensity 160) will be inflating (through morphological dilating) then further investigated by searching for a region with greater accuracy to be the breast lesion region. We denote the region around $R_p(I)$ as $R_r(I)$. Then, geometrically $R_p(I) \in R_r(I)$. Examples of $R_p(I)$ are given in Fig. 3-c ($L = 255$) and the central white regions in Fig. 4-b and e.

Inflating the seed region $R_p(I)$ is equivalent to properly merge $R_p$ and a subset of $R_r$ that corresponds to lesion’s border. The obtained inflated region is conventionally called by $R_c(I)$. Our strategy to reach $R_c(I)$ is to dilate the seed region $R_p$ taking $R_r(I)$ as an upperbound. This is accomplished by performing a loop of a pair of the following morphological operations dilation of $R_p +$ intersection with $R_r$. In our experimental tests will be necessary to carried out less than 10 iterations for any database images. Since the morphological dilation operation is an effect proportional to the frontier being inflated, the $R_p$’s edge – that within $R_r$ – inflates faster near the center of $R_r$ than in the borders and branches. It means that $R_p$ tends to grow through filling $R_r$ but will not strongly escaping by its branches. Examples of these results can be seen in images of Fig. 4-c and 4-f. Previous works show that it is very important to analyze $R_p(I)$ region in order to get an good diagnosis based on this important region. In our experiments, we will show that the diagnosis is sometimes more accurate when $R_c(I)$ is then considered instead of $R_p(I)$.

Working with $R_c$ instead of $R_p$ gives several advantages. First, we can evaluate the lesion as a whole, which includes calcified locations or watery at the same time, which are
features suggesting carcinoma, cysts or fibroadenomas lesions. Also, we can accurately can trace region’s scope bellow of lesion, where we can find evidences for acoustic shadow (characteristics of benign lesions) or acoustic enhancement (characteristics of malignant lesions). This is precisely in accordance to section about breast lesion calcification, showed before.

Two new examples are presented in Fig. 4. Figs. 4-a and d are the original images. Figs. 4-b and e present the results after step 2. In Fig. 4-b there is a main core $R_p$ (labeled $L = 255$) wrapped with a border $R_r$ (labeled $L = 160$) with branches connecting regions far from the main core which do not belong to lesion; and in Fig. 4-e there is two adjacent main cores $R_p$ and $R_r$ (labeled $L = 255$ and $L = 160$). Finally, Figs. 4-c and 4-f show the corresponding inflated $R_c(I)$ regions, respectively.

![Figure 4](image)

Figure 4. Step 4: (a) and (d) Original images; (b) Main core of the lesion $R_p$ ($L = 255$) and $R_r$ with branches connecting distant regions ($L = 160$); (e) region $R_p$ ($L = 255$) is incomplete due to calcifications generating a second core region $R_r$ ($L = 160$); (c) and (f) Final main regions $R_c$s after inflating respective $R_p$ regions.

Regarding $R_c$, step 4 computes the smallest convex polygon inscribing $R_c$. This is ac-
complished throughout a convex-hull implementation [2]. Two examples corresponding to Fig. 4-c and 4-f are shown in Figs. 5-a and b. The computation of convex-hull allows for the precise determination of the region below the lesion, where acoustic-shadow or acoustic-enhancement features can be found, as stated earlier.

Figure 5. Convex-hull after step 4: (a) corresponding to lesion of Fig. 4-a; and (b) Fig. 4-d, respectively. The dotted bounded region is called the Below the Region of Lesion (BRL).

After the four previous steps, we extract features of the Region of Interest (ROI), now called \( R_c(I) \). Based on the section about lesion characteristics, we define three features which are more likely to be the most discriminating between benign and malignant lesions: 

- **Circularity (CT)**: The first characteristic considered in this study is the circularity. According to the section on lesion characteristics, benign lesions are more circular compared to malignant ones. In order to calculate the CT, we first compute the geometric center \( GC \) of \( R_c \) and then the histogram distribution of radii from \( GC \) to the boundary of \( R_c \). As a reference point, we also compute the average histogram circularity \( CT_m \) of all ultrasound images in the database. Thus, the final feature \( CT \) for an ultrasound image \( I \) with histogram circularity \( CT_i \) is computed as \( D_{KL}(CT_m : CT_i) \) divergence (Section 1, Equation (8)).

- **Acoustic Shadow/Reinforcement (SR)** and **Contrast (CS)**: Additional features are explored in our study.
• Acoustic Shadow/Acoustic Reinforcement (SR): In accordance to section about lesion characteristics, benign lesions tend to generate acoustic shadows and malignant lesions tend to generate acoustic reinforcements, both below the lesion region \( R_c \) (remember it includes \( R_p \) and \( R_r \)) (see BRL regions in Fig. 5). In our proposed method we use the lower boundary of the convex-hull of \( R_c \) to find the BRL region. Then we compute the gray scale cumulative (on the right) histogram \([22]\) of BRL region in order to estimate the acoustic shadow/reinforcement of corresponding lesion. At diagnosis exam time, if we observe an unimodal histogram with a peak on the left, the BRL region will be an acoustic shadow. On the other hand, if we observe an unimodal histogram with a peak on the right, the BRL region will be an acoustic reinforcement. As a reference point we compute an ideal cumulative histogram (on the right) as \( H_{cm} = [0, 0, \ldots, 1] \). Let \( H_{ci} \) be the cumulative histogram of an ultrasound image \( I \). The final SR of \( I \) is then computed as \( D_{KL_q}(H_{ci} : H_{cm}) \) divergence (Section 1, Equation (8)).

• Contrast (CS): In accordance to section about calcifications, a ROI of a lesion (\( R_p \) or \( R_r \)) may have several spots of calcification, which appear as small whitish dots or speckle noises. This combination of localized calcified (common in malignant lesions) nearly to anechoic regions so much affects the contrast inside ROI. Thus, we take the difference of luminance patterns around the neighborhood of a pixel \( p(x, y) \) as the measure of contrast between the pixel \( p(x, y) \) and its 8-connected neighbors taken from the co-occurrence matrix of ROI \([22]\). For a \( CC(i, j) \) entry of the co-occurrence matrix, let \( CSV(i, j) \) be the contrast vector calculated as \( CSV(i, j) = |i - j| \cdot CC(i, j)/|ROI| \), where \( |ROI| \) is the total ROI’s area. Let \( CSV_m \) be the average contrast vector of all images’s ROI of all ultrasound images in the database, and \( CSV_i \) be the contrast vector of the ROI of some ultrasound image \( I \). The CS of \( I \) is then computed as \( D_{KL_q}(CSV_m : CSV_i) \) divergence, Equation (8)) between their respective contrast vectors.
Experimental Results

In order to test our proposed method we have used a 50 pathology-proven cases database – 20 benign and 30 malignant – Each case is a sequence of 5 different image views of the same lesion. Then, we have tested 100 images of benign lesion and 150 of malignant ones. Since the detection of a malignant lesion between five images of the same case indicates a malignant case, it is reasonable to consider 250 different cases. Then, for each image \(i\) from the database, we compute a \(n\)-dimensional feature vector, according to the previous terminology presented for our methodology.

In this work, the three features outlined above will be analyzed in order to determine the most discriminant one(s). Therefore, firstly, it is interesting to observe the discriminant power of each one individually. Thus, to observe the circularity behavior of the data base, we compute the average histogram of radii (according to the previous circularity definition \(CT\)) for all benign lesions (defined \(CT_b\)) and for all malignant lesions (defines \(CT_m\)). A comparison of the two mean histograms can be seen in Fig. 6. To plot Fig. 6

![Figure 6. Comparison between benign and malignant average histograms of raddi.](image)
we sampled the radii between 100-bin (horizontal axis) and plot the probability value for each bin in the vertical axis. We can observer that the mean histogram for benign lesions \((CT_b)\) has a peak nearby 0.1 while the average histograms for malignant lesions \((CT_m)\) has a peak nearby 0.2, which indicates smaller radii (on average) for benign lesions.

Also, the Shannon entropy for the \(CT_b\) histogram is around 2.693 while for \((CT_m)\) is around 3.06. Since as higher the entropy proportional to disorder, it can be concluded that the variation of radii to malignant tumors is higher than for corresponding benign, which is in accordance to the statements in section about calcifications.

The second feature studied is the Acoustic Shadow/Reinforcement \((SR)\). In this case, the comparison of the average histogram for benign \((SR_b)\) and malignant \((SR_m)\) can be seen in Fig. 7. The curves are very distinguishable, which gives to \(SR\) a better discriminant power than the circularity averages showed in Fig. 6. In this figure, we have sampled

![Figure 7. Comparison of mean vector for acoustic shadow/reinforcement SRs between benign \((SR_b)\) and malignant \((SR_m)\) distributions.](image)

the 256 traditional gray scale histogram to 140 only in order to better visualization. In addition, another interesting behavior can be observed. The pattern for average lumi-
nance ($SR_m$) for malignant lesions is strongly unimodal, with marked peak on the right which very suggesting regions with higher luminance levels than for benign lesions ($SR_b$). This behavior is a clear evidence of acoustic enhancement (in accordance with medical literature). On the other hand, in the case of average pattern for benign images, we can see a histogram of average luminance ($SR_b$) with a more heterogeneous pattern. Since the acoustic shadow may appear anywhere below the lesion, the pattern $SR_b$ is more indicative of a benign one.

The third studied feature is $CS$. Here, also we take the average of all contrast vectors for benign ($CS_b$) and malignant ($CS_m$) lesions. In this case, the comparison is carried out through the contrast vector, which is the inline co-occurrence matrix. However, this matrix has $255 \times 255 = 65025$ cells, which can be difficult to visualize. Then, we resample this feature into 100 entries only. The corresponding 100-bin co-occurrence entries can be seen in Fig. 8 according to the definition of previous section. In this figure each value in the x-axis represents a pair of $|i - j|$ coordinates from the co-occurrence matrix multiplied by the probability that $|i - j|$ co-occurs in a 8-connected neighborhood. Thus, as higher and more concentrated are the peaks, the larger is the amount of contrast patterns $|i - j|$ occurring. Thus, according to Fig. 8 we conclude that benign patterns have almost the same contrast as malignant ones. But when we measure Shannon entropy for both histograms (9.402 for $CS_b$ and 9.41 for $CS_m$) we see that the contrast distribution for malignant lesions has a dispersion slightly greater than for benignant, suggesting a more heterogeneous behavior for malignants.

The curves shown in Figs. 6-8 suggest some guesses about the discriminant power of each features but are not conclusive. Therefore, we performed a series of classification experiments that combine the three measured feature and their respective objective indices.

Since our data base is small we have improved the results through a cross-validation method. Then, these ultrasonic images are randomly divided into five groups. We first set the first group as a testing group and use the remaining four groups to train the
Figure 8. Comparison of mean vectors contrast for benign $CS_b$ and malignant $CS_m$ lesions.

SVM. After training, the SVM is then tested on the first group. Then, we set the second group as a testing group and the remaining four groups are trained and then the SVM is tested on the second. This process is repeated until all five groups have been set in turn as testing group.

For each test, to estimate the performance of our methodology, we have gotten the following nine objective indices: true positive (TP), true negative (TN), false positive (FP), false negative (FN), accuracy (AC), sensitivity (SEN), specificity (SPC), positive predictive value (PPV) and negative predictive value (NPV). In all experiments we have used a SVM classifier (as suggested by [33, 34]) with a b-spline kernel. We summarize all the experiments in Table 1. Figura 9 present a comparison between these five combinations in the ROC (Receiver Operating Characteristic) curves, which provides tools to select possibly optimal models and to discard suboptimal ones independently from (and prior to) training. The formulas for these indices are as follows:

- TP = True Positive
- TN = True Negative
- FP = False Positive
- FN = False Negative
- Accuracy = (TP+TN)/(TP+TN+FP+FN)
- Sensitivity = TP/(TP+FN)
- Specificity = TN/(TN+FP)
- Positive Predictive Value = TP/(TP+FP)
- Negative Predictive Value = TN/(TN+FN)
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Table 1

Summary of all experiments presenting the nine objective indices for five different combinations of lesion features. CT, CS and SR stand for Circularity, Contrast and Acoustic Shadow/Reinforcement, respectively. CT+CS stand for combination of Contrast and Circularity; and CT+CS+SR are all feature lesions together.

to specifying) the cost context or the class distribution. ROC analysis is related in a direct and natural way to cost/benefit analysis of diagnostic decision making and are well known and used in context of medical imaging. A ROC curve is a graphical plot of the sensitivity, or true positives, vs. (1 - specificity), or false positives, for a binary classifier system as its discrimination threshold is varied. The ROC can also be represented equivalently by plotting the fraction of true positives (TPR = True Positive Rate) vs. the fraction of false positives (FPR = False Positive Rate). Also known as a Relative Operating Characteristic curve, because it is a comparison of two operating characteristics (TPR vs. FPR) as the criterion changes.
Firstly, we observe the influence of $CT$ feature in the SVM classifier. The objective indices are in the first column of Table 1. It indicates that $CT$ feature is an important feature for malignance recognition but should be combined with other features in order to achieve better performance. This conclusion is in accordance with medical literature since several carcinomas and cysts may mimic each other leading to low $CT$ value. In the ROC curve of Fig. 9 it has $Az = 69.74$ area.

As in the case of $CT$ we also observe $CS$ feature individually in terms of the objective indices. Now, we can see these indices in the second column of Table 1. This performance is quite equals to $CT$ since all the other indices achieve similar values. These indices suggest a considerable feature for visual classification, however will be not conclusive. In the ROC curve of Fig. 9 it has $Az = 57.27$ area.

In the third column of Table 1, we present the $SR$ feature individually. It achieves a perfect performance alone. This is no surprising due to the histogram behavior is very much different according to Fig. 7. It is also in accordance with medical literature explained in section about lesion characteristics. It is confirmed by the ROC curve of Fig. 9 as IT has $Az = 100$ area.

Now, we consider both $CT$ and $CS$ as a combination feature. The nine objective indices are shown in the fourth column of Table 1. The $AC = 0.64$ index value suggest a better general performance than $CT$ and $CS$, individually, despite it has a similar $Az = 69$ area in the ROC curve of Fig. 9.

Finally, we observed the $SR$ feature influence. In this case, we obtain also a good result when combined it with $CT$ and $CS$ in a three-dimensional feature vector. In this case, we have the objective index values in the fifth column of Table 1. This result is also in accordance with Fig. 7 as well as with section about lesion features, indicating a strong discriminant power of $SR$ feature in order to separate malignant from benign lesions. For this case, the $Az = 98.55$ area in the ROC curve of Fig. 9 confirms the performance.
Comments and Conclusions

This paper presents a methodology based on non-extensive entropy to separate breast lesions of ultrasound images from the background with automatic calculation of the $q$ parameter. We test our methodology in a 250 image database of 50 patients considering three features (one morphological and two textured): circularity, acoustic shadow/reinforcement and contrast. Our experimental tests show that the acoustic shadow/reinforcement is the best discriminant feature and circularity must be combined with contrast in order to improve the CAD performance. The circularity feature was extracted from $R_p$ region instead of $R_c$, which indicates that the central core plays an important role to quantify the lesion circularity. On the other hand, the acoustic shadow/reinforcement as well as the contrast must be extracted from the $R_c$ area instead of the central core $R_p$ alone, indicating that both calcified regions as well as watery ones must be combine one each other in order to quantify malignance or benign behavior.

While the heuristics of steps 2 and 3 are not generic, regions $R_p$, $R_c$ and $R_r$ were not
possible to estimate properly without these heuristic implementations combined with non-extensive entropy. The results also show that it is adequate to separate the images into four regions. To accomplish this task it is necessary to consider the images as non-extensive physical systems.

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