Exploring Texture-Based Parameters for Noninvasive Detection of Diffuse Liver Diseases and Liver Cancer from Ultrasound Images

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Abstract : Non-invasive, image based detection of diseases is one of the most important issues in the nowadays research of biomedical images, because it prevents from some serious problems, that could be generated by the invasive techniques and could be dangerous for the patients. Texture is a fundamental visual property of the tissue providing a lot of information concerning its pathological state. Thus, we developed specific methods for texture analysis and recognition, for automatic and semi-automatic detection of some liver diseases from ultrasound images, in order to assist the medical personal in establishing a diagnostic in non-invasive way. We also performed some studies concerning the relevance of these parameters in the case of various liver diseases.

Key-Words: - Textural parameters, Diffuse liver diseases, Cancer, Data Mining, Automated diagnosis

1. Introduction

Liver cancer is considered one of the most frequent causes of mortality in the entire world. The hepatocellular carcinoma (HCC) is one of the primary malign liver tumors, with hepatic origin, such as the hepatoblastoma, colangiocarcinoma and hepatic sarcoma [1]. One of the non-invasive methods for HCC diagnosis is the ultrasonography. This method can be optimized through computerized methods of echographic image processing. Beside the features analyzed by the medical specialists, that can be noticed with the eyes, the specific methods for image analysis can provide subtle information, like those referring to the textural features of the hepatic parenchyma – first and second order statistics of the grey levels, multi-scale features, the fractal dimension, features referring to the structure and distribution of microstructures, to the bi-dimensional shape of the contour, respectively to the tri-dimensional aspect of the tumor. Other important category is that of diffuse liver diseases, such as steatosis – which imply the accumulation of fat in hepatocytis (liver cells); hepatitis – implying the inflammation and degradation of the hepatic tissue, resulting in fibrosis or necrosis, and, finally, the cirrhosis, implying the presence of the fibrosis and necrosis, but also the nodules formation, usually preceding cancer. Properties like the grey levels mean variance, coarseness and second order statistics like entropy, homogeneity, contrast, correlation, based on the Grey level co-occurrence matrix (GLCM), but also the fractal index can provide the information which is necessary for diffuse liver diseases characterization and distinction.

We apply texture-based features in order to describe and to compare the main pathological stages of the liver – steatosis (fat accumulation), fibrosis (liver tissue degradation) [10], [11] and liver tissue reorganization (nodules and tumors formation). We will study all these cases from the point of view of the texture-based features (first and second order statistics, respectively the fractal index) .

2. Visual appearance of liver tissue in ultrasound images in various pathological stages

Ultrasound images are formed as the result of ultrasounds propagation from the transducer in the human body and from the human body back to the transducer. They are obtained through echography

and map the structure of the human organs and the appearance of the organs tissue on the computer screen. Ultrasounds meet interfaces in their way, corresponding to the surfaces of various organs and are reflected by these interfaces. Ultrasound images are characterized through echogenicity, that correspond to the average of the grey levels in the image; high echogenicity means an increased value of the average of the grey levels. The main property of the ultrasound images consists in the fact that the echogenicity decreases as a function of deepness, as a result of ultrasounds attenuation. In both cases of steatosis and fibrosis, the main characteristic is the increased echogenicity of the liver tissue. More advanced, computerized analysis is needed, in order to make an accurate distinction between these two stages. First and second order statistics are also useful, because they describe the distribution of the grey levels in the region of interest. In the case of the liver tissue reorganization, when nodules and tumors [1] appear, the main visual characteristic is the inhomogeneity. In order to distinguish various types of tumors, in a more detailed manner, texture-based analysis is necessary. First and second order statistics, as well as fractals, are useful for the description of the grey levels distribution and structure in the region of interest. Malign tumors have a complex structure and a rich vascularization.

2.1. Appearance of liver tissue in the case of diffuse liver diseases in ultrasound images

Diffuse liver diseases are defined through global transforms of the liver tissue, the entire area of the liver being affected. Steatosis means fatty liver infiltration, so that the liver's echogenicity increases, because of the increase of the number of interfaces; the liver's volume also increases, the vessels become hardly observable and the left kidney becomes apparently transonic, comparatively to the hepatic parenchyma. Hepatitis is characterized through the liver inflammation. Cirrhosis is a diffuse liver disease characterized through the association of fibrosis, regeneration nodules and hepatocitar necrosis, with hepatic structure alteration. The tissue homogeneity decreases due to the nodules.[1] Thus, diffuse liver diseases induce some specific modifications of the properties of ultrasound images, which can be analyzed by using computerized, texture-based methods. [10]

2.2. Liver tumor appearance in ultrasound images from incipient to advanced stage

The diseases that precede hepatocellular carcinoma are frequently viral hepatitis, of type B or C, or cirrhosis; all these conditions can change the ADN structure in the hepatocities. The alcohol and metabolism problems transmitted on the hereditary paths can constitute, as well, favoring factors for the birth of the hepatocellular carcinoma. Concerning the histological precursors of the hepatocellular carcinoma, these are nodules with a high degree of dysplasia, but not all nodules of this type evolve in hepatocellular carcinoma. Some researchers [15] have observed that only those nodules that had regular contour were dangerous. In the incipient stage, the hepatic tumors appear as lesions – regions having a different texture than that of normal liver tissue, being of small dimensions. The little structures of HCC type can appear as hiper or hypo-echogenic nodules. The aspect can be also hypo-echogenic with a hyper-echogenic hallo; or, in some cases, hyper-echogenic center with a hipo-echogenic halo. Starting from this moment, the presence of a rich, anarchic vascularization is noticed in this region. As the tmors increase, eterogenity becomes the most important textural attribute, because of the fibrosis, necrosis and active growing sub-regions of the tumors.

3. Existing methods for liver pathological state evaluation from ultrasound images

Methods for evaluating the pathological state of the liver tissue usually compute some texture-based features and then use a classification method in order to decide a diagnostic; another possibility is to use data-mining methods in order to find hidden relations between these parameters.

3.1. Diffuse liver diseases detection

Initially, first order statistics were used for liver's tissue characterization. Kazuo proposed a method based on grey level histograms; he computed the grey level histogram width, GLHW, a measure denoting the difference between the highest and lowest grey level and also the number histogram bars [8]. Other first order statistics which have been

used are the mean (average) grey level and the first percentile of the grey level distributions [7]. The first order statistics were found not enough for a complete characterization of the properties of the liver tissue in order to differentiate between diffuse liver diseases.

Then, second order statistics based on the Grey Level Co-occurrence Matrix (GLCM) were used [18]. Features like the GLCM mean, GLCM variance, homogeneity, entropy, angular second moment, contrast, correlation were computed, then a classification method like k nearest neighbor (k-nn), Support Vector Machine (SVM) or Artificial Neural Networks (ANN) was applied. Cavouras implemented a decision tree, in order to differentiate between normal and ab-normal liver (first stage), steatosis and cirrhosis (second stage), respectively different degrees of steatosis and cirrhosis (last stage). In order to perform classification at each stage, the Multilayer Perceptron (MLP) was used [21]. Transform based methods were also used, in order to analyze the signal modifications generated by the diffuse liver diseases. The wavelet transform was used in [13]. Another approach is based on features like the spatial grey level dependence matrices, the Fourier spectrum, the grey level difference statistics and the Laws texture energy measures, considered not good enough in order to provide the expected speed and accuracy of the results. Features based on the fractal Brownian motion model are used instead, proving a 90% accuracy [19]. Other texture-based features used for diffuse liver diseases characterization in ultrasound images are the attenuation and backscattering coefficient, run-length matrices and RF signal parameters [7].

3.2. Existing methods for cancer detection

Cancer [1] recognition implies both the localization of the tumor and the recognition of its nature (benign or malignant, type of malignant or benign tumor). Localization can be made by expert methods, which can directly segment the malignant tumor, or by medical persons, who can detect by their own eyes the suspect regions and then further image-based analysis is needed in order to establish the type and nature of this tumor. In order to perform segmentation, probabilistic methods, based on maximum-likelihood estimation, were used in combination with textural features as the second order statistics of the 3D co-occurrence matrix [3]. Active-contour models like genetic-snakes [2], geometric level-set methods [5] and deformable B-Spline curves [17] were also used in combination with features like the second order statistics of GLCM [2] and form-factors [5]. In order to perform recognition of the texture in a certain region of interest and to classify the hepatic lesions, GLCM based features like the GLCM mean, GLCM variance, skewness, contrast, angular second moment, entropy, correlation and run-length matrix based features like the run length distribution, long run emphasis (LRE), low grey level run emphasis (LGRE), high grey level run emphasis (HGRE) were used in combination with an artificial neural network and then with a linear classifier.[16]. Wavelet transform was used in [20] for scale-insensitive recognition of benign and malignant liver tumors. Fractal-based methods like box-counting method that evaluated the complexity of contour lines and the complexity of pixel values distribution, respectively the Hurst coefficient were used in [6] in order to differentiate salivary gland tumors. Radio-Frequency (RF) parameters were used for texture characterization, for prostate cancer detection [9].

4. Proposed methods

Our intention is to characterize the liver tissue in the region of interest using properties like echogenicity, homogeneity, contrast, roughness, granularity, but also to surprise the complexity of the local and global structure of the grey levels using fractals. All these features are relevant both for the characterization of the global properties of the tissue in the case of diffuse liver diseases and for the description of the properties of the regions with malignant tumors. Distinguishing elementary texture structures (texels), using clustering methods, could be also useful.

4.1. GLCM second order statistics

The Grey Level Cooccurence Matrix (GLCM) is a pixel-based well known statistic, which provides information like the texture contrast, homogeneity, entropy, energy, correlation. Thus, it computes, for each possible pair of grey levels (g1, g2), the number of pairs of pixels, having intensities g1 and g2 which are situated from each other at a distance

given by a specified displacement vector (dx, dy). [4]

$$C_D(g_1,g_2) = \#\{((x,y),(x',y')) : f(x,y)=g_1, f(x',y')=g_2, x=x'+dx, y=y'+dy\} \quad (1),$$

where #S is the size of the set S.
In practice, the GLCM probability is used:

$$p(g_1,g_2) = \frac{C_D(g_1,g_2)}{\sum_{g1,g2} C_D(g_1,g_2)} \quad (2)$$

The most important second order statistics computed using GLCM, are:

- ***Contrast:***

$$Contrast = \sum_i \sum_j (i-j)^2 p(i,j) \quad (3)$$

- ***Entropy***

$$Entropy = \sum_{i,j} p(i,j) \log p(i,j) \quad (4)$$

- ***Local homogeneity***

$$local\_\hom og = \sum_i \sum_j \frac{1}{1+(i,j)^2} p(i,j) \quad (5)$$

Other features that could be useful are texture energy, correlation, variance, cluster shade and cluster prominence.

4.2. Fractals

Fractals provide a measure of the complexity of the grey level structure in a certain region of interest, having the property of self-similarity at different scales. In the texture analysis case, the purpose is that of defining the structure of the basic cell, the texel, and also the global structure of the texture, resulted by the repetition of these texels. Every texture, characterized through the intensity I, can be represented as a reproduction of the copies of some basic elements, scaled with a factor r:

$$I=N^D \quad (6),$$

equivalent with

$$D = \frac{\log N}{\log(1/r)} \quad (7)$$

D is the fractal dimension of the texture having the intensities of its pixels I. One of the ways to express the fractal dimension is the Hurst coefficient, described in [14].

4.3. Our new approach using the above described methods

We computed first order statistics like the gray level mean, then the Gray Level Co-occurrence Matrix and the second order statistics on small squares (10 pixels side), towards the deepness of the image, on the central line of the region of interest, usually, inside of the left liver lobe. The direction was chosen accordingly to the decrease of the mean grey level, due to the attenuation of the ultrasounds. The grey level mean and second order statistics like contrast, homogeneity, entropy, variance, texture energy, resulted by the Gray Level Co-occurrence Matrix were computed towards the deepness of the image and plotted as a function of deepness. These plots were also compared with similar plots, representing features measured on ultrasound images with HCC in various situations (incipient HCC, diffuse HCC, encefaloid HCC).
The fractal dimension was estimated applying the Hurst method and the autocorrelation was also computed on the region of interest selected by the user. In order to distinguish diffuse liver diseases from ultrasound images, a k-nearest neighbor method was applied using as features the plots of the gray level mean and of the second order statistics previously mentioned. The user has to select a new image for classification; the features (second order statistics of GLCM) are computed on the new image and plotted in the specified direction. The new plots are compared with the plots in the training set, using the above mentioned recognition method .

4.4. Evaluating parameters influence for each class

In order to study the influence of the second order statistics on each class of images (for diffuse liver diseases – steatosis, hepatitis, cirrhosis, respectively for liver cancer) we use Bayesian Networks [22]. These are probability based networks that establish the causal relationship between the data. The edges that link the items (the child nodes with their parents) have associated values corresponding to the conditional probabilities of parent node's values, given the child node values. We used the Weka data-mining instrument, version 3.5, for this evaluation [23]. In the case of steatosis, it resulted

that the textural parameters that best characterize this disease are the mean gray value, respectively the angle of the plot for mean gray value, built as mentioned before. The figure bellow illustrates the influence of the slope of average of gray levels on stheatosis.

Probability Distribution Table For slope_avgg

stheatosis	'(-inf--0.02042]'	'(-0.02042-inf)'
yes	0,823	0,177
no	0,081	0,919

Fig. 1. Probability distribution table for the slope of average gray level in the case of steatosis, computed using Bayesian Networks

In the case of cirrhosis, it resulted that the textural parameters that best characterize this disease are the mean gray value, texture energy and entropy.

Probability Distribution Table For entropy

cirrhosis	'(-inf-52.342173]'	'(52.342173-inf)'
yes	0,242	0,758
no	0,919	0,081

Fig. 2 Probability distribution table for the slope of entropy in the case of cirrhosis, computed using Bayesian Networks

4.5. Finding hidden knowledge

In order to identify degrees of steatosis, which are difficult to detect by medical personal, we applied clustering methods on a dataset representing textural parameters of steatosis, measured for 50 different patients. The X-means clustering method of Weka data-mining instrument detected two clusters that are best separated by the mean gray level parameter: 93% of the items belonging to the first cluster, have the mean gray level bellow 80, while 83% of the items of the second cluster, and have a mean gray level above 80. It results that homogeneity is a relevant parameter in detecting different degrees of steatosis.

In order to identify degrees of cirrhosis we applied the same clustering procedure. Two clusters were detected two clusters, best separated by the homogeneity parameter: 95% of the items belonging to the first cluster have the homogeneity bellow 130, while 91% of the items of the second cluster have homogeneity above 130.It results that homogeneity is a relevant parameter in detecting different degrees of cirrhosis.

5. Other experimental results

Applying the k – nearest-neighbor method using the GLCM second order statistics as features, we obtained the following recognition rates: 86% for normal liver, 90% for steatosis, 85% for hepatitis and 50% for cirrhosis. The values of the second order statistics are relevant for the textural properties of the tissue, having a great contribution in distinguishing the various pathological states of the liver. Plotting the mean grey level as a function of deepness, in various situations, we notice that it has a positive slope in the case of normal liver and a negative slope in the diffuse liver diseases case, with the most drastically decrease in the case of steatosis.

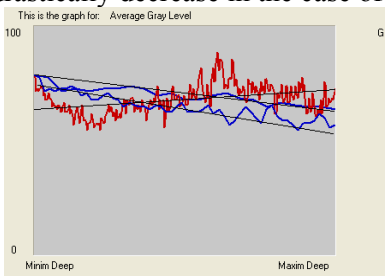

Fig. 3. Comparison between the plots of the mean (average) grey level in the cases of normal liver (positive slope), steatosis (negative slope, down) and hepatitis (negative slope, up)

The Hurst fractal index is usually small for normal liver and diffuse liver diseases (lower than 0.15) and higher inside of the tumor, (higher than 0.20), so it contributes to the detection of liver cancer.

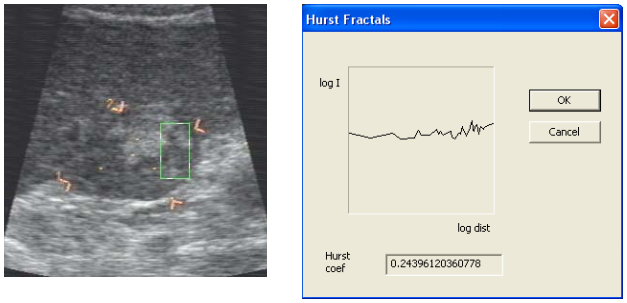

Fig.4. Plot and value (0.24) of the Hurst coefficient (right image) computed on the selected region inside of the tumor, as seen in the left image

6. Conclusions

The applied methods and the experimental analysis denote that the echogencity is higher in the case of steatosis, compared with the other liver states; tissue structure is inhomogen in the case of cirrhosis and very complex in the case of tumors (low

homogeneity, high contrast and high fractal index). The data mining methods like bayesian networks and also the clustering methods were very helpful in order to find hidden knowledge within our data. Because, inside of the tumor, the vascularization is also complex, edge based statistics like edge frequency could be also helpful. In order to improve the recognition rate, we will use more performing recognition methods like artificial neural networks (ANN). SOM method and k-means clustering method are also considered to be used for the unsupervised detection of tumor regions.

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