TEXTURE BASED APPROACH FOR BUILDING THE IMAGISTIC MODEL OF HEPATOCELLULAR CARCINOMA

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Abstract: The purpose of this paper is to present a method elaborated in order to build the imagistic textural model of hepatocellular carcinoma, focused on the exhaustive set of textural features and the associated textural parameters. Methods like Bayesian Belief Networks and Decision Trees are used in order to learn and evaluate the relevance of the features. Thus, the relevant textural features are selected and their specific characteristics are determined. The possibility of automatic recognition is also studied by applying classification on the textural features and by computing the recognition rates of various classifiers.

Keywords: ultrasound image analysis, texture, relevant feature selection, accuracy, reliability evaluation, pattern recognition, hepatocellular carcinoma

1. INTRODUCTION

Liver chronic diseases constitute an important public health issue. The evolution of diffuse liver diseases is variable, but it has generally long term. Whatever the nature of the liver aggression, it seems to follow a pattern characterised by the successive stages: inflammation (at the beginning), necrosis, fibrosis, regeneration (cirrhosis), dysplasia, and hepatocellular carcinoma (at the end). Hepatocellular carcinoma (HCC) is the most frequent malignant liver tumor, so we study in this paper the possibilities to characterize it. The fundamental visual properties of malignant liver tumors, and also of hepatocellular carcinoma, which can be noticed by human eye from ultrasound images, are: the irregular-shaped, often vague contours, the complex structure of vessels and the heterogeneity of the tissue, but these properties are not enough in order to do an accurate diagnosis, so a more subtle analysis is required. Computerized methods, which extract information from medical images, are being widely studied nowadays in order to replace the old methods through a new, non-invasive technology. Thus, virtual biopsy tends to replace the old, traditional one, and this requires the development of adequate, computer-vision based methods, in order to obtain an accurate imagistic model of the malignant tumors. Texture is a fundamental visual property which is essential especially in tissue characterization and in pathological structures recognition. Texture-based methods are implemented in association with classifiers in order to perform automatic tumor differentiation for various kinds of organs (Chikui et al., 2005), (Yoshida et al., 2003), (Madabhushi et al., 2005). However, the relevance of the textural features and their statistical values for malignant liver tumors are not determined systematically through scientific, specific, automatic methods. We aimed to do this in our research, by using the following learning-based methods: the Bayesian Belief Networks and the Decision Trees. The relevance of each textural feature and their statistical values for the class of HCC will be the specific parameters of the textural imagistic model for this class. The elaboration of the imagistic textural model of HCC required three phases: (1) *the specification phase*, consisting in the *definition* of the data models and steps used for model generation; (2) *the model generation (implementation) phase* and (3) the *model validation phase*. Concerning

the model generation phase, two steps are necessary: an *image analysis step*, consisting in the computation of the textural features and in the identification of the set of relevant textural features; then a *learning step,* in which we obtain some specific features like the mean, the variance, the maximum, the minimum value of the textural features and their probability distribution. At the end, there is a validation phase, in which we evaluate the generated model. We aim, in this way, to put in evidence the fundamental imagistic, textural properties of the hepatocellular carcinoma and also to correlate them with its visual properties, perceived by the human eye.

2. TUMORS ASPECT IN ULTRASOUND IMAGES

In order to compare the results provided by the computer-vision based methods with the visual aspect of the hepatocellular carcinoma that can be noticed in ultrasound images, it is useful to know what the visual properties of the HCC are in its various evolution stages. Hepatocellular carcinoma (HCC) is one of the most frequent malignant tumors of liver (75% of the liver cancer cases). Other well known malignant liver tumors are hepatoblastoma (7%), cholangiocarcinoma and cystadenocarcinoma (6%). As we previously mentioned, HCC evolves from cirrhosis, after a restructuring phase at the end of which dysplasic nodules (future malignant tumors) result. In incipient phase, HCC appears like a small region having a different texture than the other parts of the tissue and a diameter of about 1.5 cm to 2 cm. In the case of an evolved HCC, the essential textural attribute is that of heterogeneity, due to the co-existence of regions with necrosis and fibrosis, and of regions with active growths [13]. HCC is also characterized through a very complex structure of vessels. It can present one of the following forms: a clearly delimited, encephaloid form, a nodular multicentric form, or a diffuse form (Badea et al., 2000).

3. EXISTING METHODS FOR COMPUTER BASED TUMOR RECOGNITION

Concerning the textural analysis of the malignant tumors, the goal is to extract imagistic features in order to establish the differences of malignant tumors versus other types of tissues, independently of noise, artefacts, scale and orientation. Thus, methods like the Grey Levels Co-occurrence Matrix (GLCM) (Valckx et al., 1997) and its second order statistics, the Run Length Matrix parameters (Sujana et al., 1996), as well as multi-scale methods are widely used in the field of computer-based tumor recognition from biomedical images. In (Sujana et al., 1996) the authors compute the first order statistics (the mean grey level and the variance of grey levels), the Gray Level Co-occurrence Matrix second order parameters and the Run-Length Matrix parameters which are used in association with an Artificial Neural Networks based classifier, as well as with a classifier based on Linear Discriminants. The accuracy obtained by using Linear Discriminants was 79.6%, while using neural networks, a recognition rate of 100% was obtained. Fractal-based methods are used in (Chikui et al., 2005) in order to distinguish the salivary gland tumors from ultrasound images. Algorithms like 2D and 3D Box-Counting, respectively the Hurst coefficient method, are implemented in order to compute the fractal index. These methods proved to be useful in order to distinguish the malignant tumors from pleomorphic adenoma, the value of the fractal index being correlated with the tissue structure complexity. Wavelet transform was also implemented in order to analyze the values of the textural parameters at multiple resolutions. In (Yoshida et al., 2003) the goal was that of extracting, using the Wavelet transforms, some basic elements, having a well defined pattern of grey levels. The method provided good results concerning the differentiation between malignant and benign liver lesions, the accuracy, measured as the area under the ROC curve (A_z) being approximately 0.90. From the multi-resolution methods class, the Gabor transform was also implemented in (Madabhushi et al., 2005) and provided good results in combination with the GLCM second order parameters and the Bayesian classifier for prostate malignant tumor recognition from 3D MRI images. Thus, textural parameters were widely used and provided satisfying results for the purpose of malignant tumors recognition in the cases of various organs. Concerning the detection of hepatocellular carcinoma from ultrasound images, the relevance of the textural features, the correlation between them and their specific, statistical values were not studied yet.

4. THE PROPOSED METHOD: THE IMAGISTIC TEXTURAL MODEL OF HCC

The goal of our work is to present a *method elaborated in order to build the imagistic textural model of HCC* for the future purposes of semi-automatic and automatic diagnosis.

4.1. Definition and specifications for the imagistic textural model of HCC.

Texture is an essential attribute in malignant tumors characterization and recognition. Based on this fact, our purpose is to build a textural imagistic model for HCC, in order to support the process of non-invasive, computer based semi-automatic and automatic diagnosis. This model will consist in the relevant textural features and the specific, statistical values of them, able to characterize the HCC with maximum accuracy.

The imagistic textural model of HCC will be centred on the following parameters:

- The relevance of each textural feature in HCC characterization, determined by using the Bayesian Belief Networks method during the first filtering

stage, then the Decision Tree method at the second level.

- The maximum, minimum and mean values of the textural features, as well as the standard deviation of these values, determined from a large enough number of cases representing the class of HCC.
- The probability distribution for the values of the textural features in the case of HCC (Witten et al., 2005).

The mathematical description of the imagistic textural model is given bellow.

Let F be the space of textural features, containing a number of n such features.

$$F = \{f_i\}_{i=1,..,n} \quad (1)$$

Then, the textural imagistic model of the tumor, TM, consists in a collection of vectors V_{fi}, associated with each relevant textural feature f_i, containing the specific values that characterize each analyzed class.

$$TM = \{V_{f_i}\}_{i=1,..,n} \quad (2)$$

In our case, we start with an initial feature space consisting in a set of textural features, like the average of grey levels, minimum grey level, maximum grey level, the GLCM second order parameters, edge-based statistics, the fractal Hurst coefficient and the entropy computed on three components of the image obtained by applying the wavelet transform at the first level of decomposition.

$$\begin{aligned} F = \{&\text{avg\_grey, max\_grey, min\_grey, GLCM\_contrast,} \\ &\text{GCLCM\_local\_homogeneity, GLCM\_corellation,} \\ &\text{GLCM\_energy, GLCM\_entropy, GLCM\_variance,} \\ &\text{Edge\_frequency, Edge\_contrast, Hurst\_coefficient,} \\ &\text{W1\_entropy, W2\_entropy, W3\_entropy}\} \end{aligned} \quad (3)$$

The relevant features will be selected from these textural features during model generation. The vectors of the imagistic textural model consist in the specific parameters, associated with the relevant textural features, previously mentioned and given bellow, where *Min* (the minimum value), *Max* (the maximum value), *Mean* (the mean value) and the *Standard Deviation* are real numbers; the *Relevance* is an *integer,* representing the level of the textural parameter in the decision tree. The *Probability Distribution* is a vector of intervals, each interval having associated a certain probability.

$$\begin{aligned} V_f = [&Min, Max, Mean, St.Deviation, \text{Re}levance, \\ &\text{Pr}obability\ Distrib.] \end{aligned} \quad (4)$$

As we mentioned before, the *model generation (implementation) phase* consists in two steps: *the image analysis* step and *the learning step*.

At the end, *the validation* of the obtained textural imagistic model of HCC is due.

In a forerunner step, the image classes are built for HCC and non-HCC categories, the textural parameters are computed on each of these images, and stored then in a database. During the ***image analysis step*,** we use texture-based methods for feature extraction, like the Grey Levels Co-occurrence Matrix (GLCM) and its second order parameters, the Hurst fractal index, edge-based statistics, and respectively the entropy parameter computed on the images resulted after applying the Wavelet transform. Then, Bayesian Belief Networks and Decision Trees are applied in order to determine the relevance of the textural features, the relevant features are separated from the non-relevant ones and the final set of features for the imagistic textural model is established. During the *learning step*, the statistical values like the minimum, maximum, mean value and the standard deviation are learned on a large enough number of samples; the probability distributions per class are also determined for each textural feature. Specific methods for automatic, supervised learning that involve the analysis of the features relevance and of the probabilistic influence between the features, like Bayesian Belief Networks and Decision Trees are used during the model generation phase. During *validation*, we take into account only the final feature space obtained in the previous phase, using its elements as inputs for classifiers like Bayesian Belief Networks, Decision Trees and Neural Networks, in order to evaluate the recognition rate in each case. The validation is being done on a new set of images (the test set), different from the training set. The subset of obtained relevant textural features is also compared with other textural features subsets obtained by using alternative methods for feature selection.

4.2. Description of the methods used in the imagistic textural model generation and validation phases

4.2.1.Texture-based methods for image analysis.

The texture-based methods that we apply and analyze in this work are shortly described bellow.

- **The Grey Levels Co-occurrence Matrix**

The Grey Levels Co-occurrence Matrix (GLCM) provides, through the values of the second order parameters, useful information about the visual properties of the tissue like echogenicity, homogeneity and contrast. It computes, for each possible pair of grey levels ($g1$, $g2$), the number of pairs of pixels, having intensities $g1$ and $g2$, being in a spatial relationship given by a specified displacement vector $(\vec{dx}, \vec{dy})$.

$$\begin{aligned} &C_D(g_1, g_2) = \#\{((x,y),(x',y')): \\ &f(x,y) = g_1, f(x',y') = g_2, |x - x'| = dx, \\ &|y - y'| = dy, \text{sgn}(dx \cdot dy) = \text{sgn}((x - x') \cdot (y - y'))\} \end{aligned} \quad (5)$$

where #S is the size of the set S.

The scalar value of $\vec{dx}$, denoted by dx, is the horizontal distance between the two pixels of the considered pair belonging to the 2D image, while the scalar value of $\vec{dy}$, denoted by dy, is the vertical distance between the same two pixels (Clausi et al., 2002).

In practice, the GLCM probability is used. In our implementation, we computed the GLCM probability matrix by considering $dx = 2$ and $dy = 1$, because due to the nature of the ultrasound image, the grey level intensity decreases with the deepness, so we wanted to surprise very accurately the grey level differences in the vertical direction. The second order parameters (Haralick features) that we compute from GLCM, considered as being able to best characterize the tumor tissue from the point of view of the grey levels distribution, are: *contra*st, *variance*, *local homogeneity*, *correlation*, *energy* and *entropy* (Clausi et al., 2002), (Valckx et al., 1996) .

- **Edge-based statistics**

The edge-based statistics like edge-frequency and edge-contrast also provide useful information concerning the complexity of grey-levels structure, as they compute the relative number of separations between regions with different intensity values and also the relative amount of the difference between these regions (Wu et al., 1992). Edge contrast measures the differences in intensity level between neighbouring pixels, while edge frequency refers to the amount of edge pixels in the area of interest.

- **The Hurst Fractal Coefficient**

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. Every texture, characterized through the intensity I, can be represented as a reproduction of the copies of N basic elements, scaled with a certain factor.

$$I=N^D \tag{6}$$

where D is the fractal dimension of the texture.
One of the ways to express the fractal dimension is the Hurst coefficient, computed through a specific algorithm, described in (Parker, 1996).

- **The Wavelet Transform**

The Wavelet Transform performs the decomposition of the signal spectrum in components having various frequencies, thus giving the possibility of analyzing the signal at various resolutions and of scale-insensitive methods development. The decomposition is made around the basic frequency of the spectrum. The expression of the decomposition through the Wavelet Transform is the following (Parker, 1996):

$$W_{f(x)}(m,n)=\frac{1}{\sqrt{s}}\int_{-\infty}^{\infty} f(x)w_{m,n}(x)dx \tag{7}$$

where $w_{m,n}(x)$ has the following expression:

$$w_{m,n}(x)=g\left(\frac{x-n}{m}\right)=\frac{1}{\sqrt{|m|}}\psi\left(\frac{x-n}{m}\right) \tag{8}$$

Here, ψ is the wavelet basic function, (mother wavelet); it usually takes the form of a sinusoid, giving the name of the transform. In practice the Haar function is used more often (Parker, 1996). We also consider here the Haar function as the basis for the Wavelet transform. For implementation, we use the discreet form of the Wavelet decomposition formula. We extract the signal component, and then we compute the entropy value for each component, using the expression (Stollnitz et al., 1995):

$$Entropy=-\sum_{x=1}^{N}\sum_{y=1}^{M}|I(x,y)|\log_2|I(x,y)| \tag{9}$$

4.2.2. Pattern classification methods used during learning and evaluation

The values of the textural features described above are used as inputs for classifiers like Bayesian Belief Networks, Decision Trees and Neural Networks (Duda et al., 2000), in order to analyze both their relevance and the recognition rates obtained.

In order to analyze the relevance of the textural features, a hierarchy of two classifiers is used:

- In the first stage, the Bayesian Belief Networks are used and a ***yes/no*** answer is obtained concerning the existence of any probabilistic influence between the values of textural features and the values of the class parameter. The features for which the answer was "***yes***" are included in the final set of relevant features. A Bayesian Belief Network with a single layer is implemented, the purpose being that of analyzing the inflence among the textural features and the class parameter.
- In the second stage, the relevant textural features obtained in the first stage are considered as inputs for the Decision Trees method, and they are assigned a relevance value, equal with the level of the textural feature in the Decision Tree. If a textural feature is not part of the Decision Tree, it will be assigned a value of -1 for its relevance. Bayesian Belief Networks are also used in order to learn the probability distribution per class of each textural feature. (Witten et al., 2005). The recognition rates, obtained by using the group the relevant textural features, are analyzed, for the future purpose of automatic recognition.

The software instrument Weka 3.5 is used for pattern recognition and parameters exploration (Witten et al., 2005). The Bayesian Belief Networks, the Decision Trees method (J48 algorithm from Weka 3.5, corresponding to the well known C4.5 algorithm), as well as the Multilayer Perceptron method are used for this purpose, in order to evaluate the imagistic textural model. For Bayesian Belief Networks, K2 search method with BMAEstimator were selected (Boukaert, 2004); for Multilayer Perceptron, the 'a' value, predefined in Weka 3.5, and having the significance a = (number of attributes + number of classes)/2, was chosen for the number of hidden nodes from the single hidden layer. Thus, a reasonable number of hidden nodes resulted, to get a satisfying accuracy and also to avoid overtraining. Concerning the learning rate, a value of 0.1 was chosen and a value of 0.9 was set for the momentum (Duda et al., 2000); the J48 algorithm with pruning was used in the same environment and a minimum number of two examples was set for the terminal nodes.

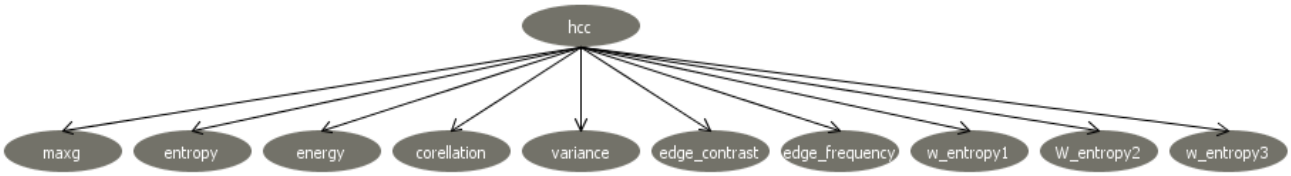

Figure 1. The Bayesian Belief Network showing the dependencies between the class parameter and the textural features

5. EXPERIMENTS CONCERNING THE IMAGISTIC TEXTURAL MODEL OF HCC

First, a set of 100 images for each class (HCC and non-HCC) was gathered and a training set was built. The non-HCC class consisted of images of cirrhotic liver, cirrhosis being the disease that precedes HCC. The images were taken under the same orientation conditions and under the same settings of the echographic device, at 5.5 MHz.

During the *image analysis* step, the methods for texture analysis were applied on regions of interest of rectangular shape and size of 50x50, selected inside the tumor for HCC class, and anywhere inside the liver for the non-HCC class. The values of these textural features were computed and stored. The Bayesian Belief Networks and the Decision Trees were applied in two stages in order to determine the subset of relevant textural feature and their probability distribution. The Bayesian Belief Network, containing the relevant grey-level based features and edge-based statistics determined in the first stage is illustrated in Figure 1. From the first stage, the following textural features resulted as being relevant and were included in the textural imagistic model of HCC: the maximum of grey levels, the GLCM features entropy, energy, correlation, variance; edge frequency, edge contrast and the entropies on the first three wavelet components of the image. They were considered as inputs for the Decision Tree method. The structure of the Decision Tree obtained by applying the J48 method of Weka 3.5, illustrates that the GLCM energy (situated on the 1st level), edge contrast (on the 2nd level) the maximum grey level (situated on the 3rd level) and edge frequency (on the 4th level) are the most relevant features. *During the learning step*, the relevant textural features were considered and their specific, statistical values were learned.

From the probability distribution for the GLCM energy parameter, obtained with Weka 3.5, after applying Bayesian Belief Networks, illustrated in Table 1, it results that it takes, in the case of HCC, low values situated in the interval (0, 0.000736] with the probability of 0.893, and in the case of non-HCC it takes high values situated in the interval (0.000736, ∞) with a probability of 0.992**.**

Table 1. The probability distribution for energy

HCC	(0, 0.000736]	(0.000736, ∞)
Yes	0.893	0.107
No	0.008	0.992

A part of the textural imagistic model for the class of HCC, containing two of the most relevant features and their specific values, is illustrated in Table 2.

In the previous table, P is the probability value associated to the given interval; thus, the most probable interval of variation for the considered textural feature is provided; it is derived from the probability distribution per class learned using the Bayesian Belief Networks.

During the *validation* phase, the test set was built containing 100 images per class (HCC and cirrhotic liver), taken under the same conditions as the images in the training set. The classification methods of Bayesian Belief Networks, Decision Trees and Multilayer Perceptron of Weka 3.5 were applied on the textural features determined as being relevant during the learning phase. The cross validation method with 100 folds was chosen. Using Bayesian Belief Networks, the recognition rate was 91.74 %, the sensitivity was 88.3%, the specificity was 95.9% and the area under the ROC curve was 0.977. With Multilayer Perceptron the accuracy was 97.247%, the sensitivity was 96.7%, the specificity was 98% and the area under the ROC curve was 0.983. With Decision Trees (J48 algorithm) the recognition rate was 89.90%, the sensitivity was 91.7%, the specificity was 87.8% and the area under the ROC curve was 0.943. Alternatively, *Exhaustive Search* combined with *CFS (Correlation-Based Feature Selection) subset evaluation* (Hall et al., 2003), (Witten et al., 2005) was applied in Weka 3.5. in order to compare the features selected through this method with our subset of relevant features. The following subset was selected by Weka: minimum grey level, variance, entropies computed on the first and third wavelet

Table 2. The statistical values for the most relevant textural features

HCC	Min	Max	Mean	Most Probable Interval
GLCM Energy	0	0.002	0.001	(0, 0.00073], P=0.893
Max Grey Level	50	133	84.1	[77.5, ∞) P= 0.598

subimages from the first level of decomposition, edge contrast and edge frequency. Thus, the intersection done between the two feature subsets contain 6 features, which is 60% of our subset and 85.7% of the second subset.

5. CONCLUSIONS

As the experimental results demonstrate, the textural features are adequate for HCC representation and recognition. GLCM based features, as well as edge-based features and multi-resolution features are important for HCC characterization and recognition. In association with Decision Trees and Bayesian Belief Networks, they are suitable for building the imagistic model of HCC, as the results of applying the classification methods on the relevant textural parameters are satisfying, being around 90%. Concerning the correlation with the visual features, the importance of the maximum grey level is explained through the fact that the HCC tumors are hyperechogenic in most of the images. Features like GLCM entropy, GLCM variance, edge contrast and edge frequency confirm the complex structure in grey levels and in local features, as expected in the case of a malignant tumor. Since energy was found correlated with entropy through a logarithmic curve, the energy parameter was also found relevant. The relevance of the GLCM correlation denotes the existence of a mutual dependence between the grey levels from the malignant tumor tissue, being thus a subtle property.

The experiments will be further improved by collecting larger sets of items per class, belonging to a bigger number of patients, in order to obtain more reliable results and to diminish the error rates. Other types of pathological structures, like other malignant tumors, benign tumors, healthy liver tissue and liver tissue affected by other diffuse liver diseases will be considered as well for the non-HCC class. Also, other feature selection specific methods (Jain et al., 2000) will be elaborated and tested, the results of these methods will be compared and the best feature selection method will be established in order to obtain the best imagistic textural model. The mutual dependencies and the kind of influences between the textural features will also be analyzed using methods like Bayesian Belief Networks with multiple layers or by regression, in order to exclude the redundant parameters, to improve the speed and the accuracy.

The method will be extended for incipient HCC recognition and also for HCC prediction through the detection of the advanced cirrhosis phase that precedes HCC.

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