

Detecting HCC Tumor in Three Phasic CT Liver Images with Optimization of Neural Network

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Abstract—The aim of this work is to build a model based on tissue characterization that is able to discriminate pathological and non-pathological regions from three-phasic CT images. With our research and based on a feature selection in different phases, we are trying to design a neural network system with an optimal neuron number in a hidden layer. Our approach consists of three steps: feature selection, feature reduction, and classification. For each region of interest (ROI), 6 distinct sets of texture features are extracted such as: first order histogram parameters, absolute gradient, run-length matrix, co-occurrence matrix, autoregressive model, and wavelet, for a total of 270 texture features. When analyzing more phases, we show that the injection of liquid cause changes to the high relevant features in each region. Our results demonstrate that for detecting HCC tumor phase 3 is the best one in most of the features that we apply to the classification algorithm. The percentage of detection between pathology and healthy classes, according to our method, relates to first order histogram parameters with accuracy of 85% in phase 1, 95% in phase 2, and 95% in phase 3.

Keywords—Feature selection, Multi-phasic liver images, Neural network, Texture analysis.

I. INTRODUCTION

HEPATOCELLULAR Carcinoma (HCC), the most common primary liver tumor, accounts for 85-90% of primary liver cancer. It is the third most common cause of cancer death and the fifth most common cancer worldwide. The traditional methods to differentiate normal liver tissues from abnormal ones are largely depending on the radiologist experience. Thus Computer-Aided Diagnosis (CAD) systems based on image processing and artificial intelligence techniques have aroused a lot of interest, since they can provide constructive diagnosis suggestions to clinicians for decision-making [1]. Only seldom physicians use 3 phasic CT images for detecting HCC tumor in the liver. The first series of CT scanning is performed during the arterial phase, which takes place 20 to 30 seconds after the injection of the contrast agent. This is the time period when the majority of the contrast agent is flowing through the hepatic artery. The second series of CT scanning is taken from 60 to 70 seconds after the initiation of the infusion, when the majority of the contrast agent is flowing through the hepatic portal vein. This set of CT is defined as the portal-venous phase (PVP). A third scanning is often performed during the equilibrium phase (10

– 20 minutes after the infusion) when the contrast agent is equally concentrated in the hepatic artery and portal vein.

In recent years, a lot of researches and papers have focused on this area, but most of them considered non-enhanced CT images [1]-[3]. Only in some cases, researchers have chosen to work on enhanced CT images. In [4], SVM and Dipolar Decision Tree algorithms have been applied to Multiphase CT images with respectively 90% and 99% precision in RLM features. In [5], a neural network has been applied to multiphase CT images to detect normal and abnormal, cyst-other disease, and carcinoma hemangioma. In the same paper, a first watershed algorithm has been used to extract the region of the liver. For registration of liver SIFT algorithm was used, then the operation of extracting the ROI based on Gabor wavelet Transformation was performed. For the feature extraction, a Scattergram (Scattergram is known as two-dimensional histogram of spatial variation and is constructed from a pair of images) has been employed. In the first order histogram, the following metrics has been used as first order statistical feature (General Moments, absolute moment, entropy) and temporal feature extraction (Relative signal intensity, Intensity changing trend, Signal Enhancement Ratio). For classification purposes, the researchers used a neural network with a percentage of accuracy in phase 1: 97.97%, phase 2: 98.51%, and phase 3: 97.53%. In [6], texture features have been employed such as first order statistics (histogram statistics, Grey Tone Difference Matrix (GTDM)), and second order statistics such as GLCM, Gabor filter, Laws texture energy measures, classifying 3 parts in CT images such as Liver, Kidney and Spleen. After detecting each part in the CT, J4.8, Boosting and SMO have been applied and the results compared. In [7], the use of three feature classes such as first order statistics (Moments, central moments, absolute moments and entropy), second order statistical features (such as angular second moment, Contrast, Inverse difference moment, Entropy) and temporal Signal Tendency Feature (such as Relative signal intensity, Intensity changed Tendency) was preferred. In this case, the classification has been obtained through SVM for a full feature set with an accuracy of 92.42% in pre-contrasted, 90.9% in arterial phase, 95.45% in portal phase and 89.39% in delayed phase for normal, Cyst-other disease, and carcinoma hemangioma. Considering the above, in this paper we try to find an answer to the following questions. Can we design a new system to improve the result of previous works with a new approach? Can we examine the effect of the number of neurons in a hidden layer on the performance of a NN classifier? As can be seen in all previous works, the researchers used the same

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features for all 3 phases as an input to classification algorithms. However, we started thinking that with the injection of liquid, the highest-ranking features capable of explaining the classes in each phase could change. The development of such a system implies two major steps. The first step consists in finding the best features to describe the pathology and healthy part in the liver. The second step implies a correct classification of the desired tissue. In Section II, we will describe our experience regarding data, explaining how to get images, and talking about feature selection methods and classification. In Section III, we will discuss the results and future work.

In the next section, we will briefly explain the proposed neural network application and show the results of the classification algorithm with different calculation parameters. This will be followed by a discussion of the results obtained.

II. EXPERIMENTAL WORK

A. Image Acquisition

Abdominal enhanced CT images (3 phase images) have been taken with 512*512 pixels size and 8-bit gray-level from 8 patients affected by HCC tumor. The position, size and extent of tumors were defined in CT images by an expert radiologist. In each phase, for each patient, 5 slices that better show the situation of tumor were selected. In the liver two classes can be distinguished, healthy class and pathological class. In each slice, we took one window from the healthy part and one window from the pathological part. According to article [4] a 13 by 13 pixels window size has been chosen as the one related to minimum classification error rate for HCC tumor. At the end, we obtained a dataset consisting of 80 samples (40 samples for the healthy part and 40 samples for the pathological part). As usual when dealing with abdominal district, all images need to be calibrated in the range [L: 50, W: 350] as a default in Dicom work software.

B. Feature Selection and Reduction

As regards feature selection, we used Mazda software version 4.6. This software is free and available on [8]. Six feature classes were taken into account as Statistical features, Run Length Matrix, Co-occurrence matrix, Auto regression matrix, Wavelet, and Gradient. Table I shows the details of each feature class employed in this research.

The run-length matrix-based parameters were computed 4 times for each ROI in vertical, horizontal, 45-degree, and 135-degree directions. The co-occurrence matrix-based parameters were computed up to 20 times, for $(d,0)$, $(0,d)$, (d,d) , $(d,-d)$ where the distance d can take values of 1, 2, 3, 4, and 5.

All features were normalized according to +/- 3 Sigma criterions.

In conclusion, 270 features were extracted from 120 images (40 samples in each phase).

By using discriminant analysis, a feature ranking was applied independently to each feature class. Then, considering the high dimensionality of data and related sensitivity of neural networks, feature reduction was employed. This

allowed us to get better results as regards classification algorithms. The 10 highest relevant features capable of discriminating the classes in each CT phase were selected as input to classification algorithm. For features such as AR model, Histogram features, and gradient where the number of measures is less than 10, we did not apply any reduction. The feature selection algorithm can be applied only to features such as RLM, Wavelet, and COM in order to reduce the number of input features to an algorithm.

TABLE I
 TEXTURE PARAMETERS COMPUTED IN MAZDA

Name of Feature	Sub-Features	Number of Features Used
Histogram	-mean	9
	-variance	
	-skewness	
	-kurtosis	
	-1-%percentile	
	-10-%percentile	
RLM	-50-%percentile	20
	-90-%percentile	
	-99-%percentile	
	-mean	
	-variance	
Gradient	-skewness	5
	-kurtosis	
	-percentage of pixel with nonzero gradient	
	-run length nonuniformity	
	-grey level nonuniformity	
	-long run emphasis	
Co-occurrence matrix	-short run emphasis	219
	-fraction of image in run	
	-Angular second moment	
	-contrast	
	-correlation	
	-sum of squares	
	-inverse different moment	
	-sum average	
	-sum variance	
	-sum entropy	
AR Model	-entropy	5
	-difference variance	
	-difference entropy	
	- θ_1	
	- θ_2	
	- θ_3	
Wavelet	- θ_4	12
	- σ	
Total number of features used:		270

For feature ranking and feature selection, we apply mutual information criterion. Mutual information is a measure of dependence between two or more random variables. In the case of two random variables X and Y , this is defined as follows [8]:

$$MI(X, Y) = H(X) + H(Y) - H(X, Y),$$

where H is the entropy. We can infer that random variable X stores values of texture features, while Y stores the classification label as assigned in the training/test dataset. Then, a large value of mutual information between texture feature X and class category variable Y means that this feature carries information about class membership (its values are

correlated with given class categories). As a consequence, such a feature is useful for classification. On the other hand, when class category does not depend on the feature value X, mutual information is very low or equals to zero since $H(X,Y)=H(X)+H(Y)$ for independent variables [8].

TABLE II
 RESULT OF FEATURE RANKING WITH MUTUAL INFORMATION

Phase 1 Feature Ranking	Phase2 Feature Ranking	Phase3 Feature Ranking
Histogram Features		
Perc.50%-0.351	Perc.90%-0.646	Perc.90%-0.571
Mean-0.350	Perc.50%-0.58	Mean-0.510
Perc.10%-0.308	Mean-0.581	Perc.99%-0.484
Perc.01%-0.185	Perc.99%-0.558	Perc.50%-0.470
Perc99%-0.148	Perc.01%-0.403	Perc.10%-0.324
Perc.90%-0.108	Perc.10%-0.383	Perc.01%-0.283
Variance-0.084	Skewnes-0.077	Skewness-0.142
Skewness-0.069	Kurtosis-0.037	Kurtosis-0.123
Kurtosis-0.045	Variance-0.017	Variance-0.063
RLM		
45dgr_LnREph0.12	135dgr_LngREmph0.11	135dgr_LngREmph-0.101
Vertl_ShREmp-0.12	45dgr_LngREmph0.063	45dgr_LngREmph-0.063
45dgr_RLNUni0.1	Horz_Fraction-0.056	Horz_Fraction-0.056
45dgr_Fraction-0.1	45dgr_shrtREmp-0.046	45dgr_shrtREmp-0.046
Vertl_RLNUni0.093	Horz_LngREmph-0.043	Horz_LngREmph-0.043
45dgr_shrtREp0.09	45dgr_RLNonUni-0.04	45dgr_RLNonUni-0.042
Vert_Fraction-0.08	45dgr_Fraction-0.041	45dgr_Fraction-0.041
Vertl_LngREph0.07	Horzl_RLNonUni0.040	Horzl_RLNonUni0.040
135dr_LnREph0.07	Horzl_ShrtREmp-0.038	Horzl_ShrtREmp-0.038
135dr_RLNUn-0.06	135dr_Fraction-0.037	135dr_Fraction-0.037
COM		
S(1,-1)Contrst-0.37	S(3,-3) SumOfSqs-0.21	S(2,-2) Contrast-0.229
S(1,-1)DiFEnt-0.288	S(3,-3)DiFVarnc-0.200	S(1,0) Correlat-0.218
S(1,-1)DiFVar0.282	S(0,4)SumOfSqs-0.169	S(1,1)DiFVarnc-0.211
S(1,-1)Correlat-0.26	S(5,-5)SumVarnc0.169	S(2,0)Contrast-0.208
S(1,-1)SumVar0.20	S(1, 1)SumEntrp-0.155	S(1, 1)Correlat-0.208
S(0,3)DiFEntrp-0.19	S(4,-4)SumOfSqs-0.149	S(0,1)DiFEntrp-0.205
S(2,-2)Correlat-0.19	S(0,5) SumVar- 0.143	S(4,-4)SumVarnc-0.202
S(0,2)SumVar0.18	S(2,0)Contrast-0.133	S(1,1)DiFEntrp-0.191
S(0,2)DiFEntrp-0.17	S(3,-3)Contrast-0.129	S(2,0)Correlat-0.175
S(2,-2)Contrst-0.17	S(3,0)SumOfSqs-0.126	S(1,1) Contrast0.175
Wavelet		
WavEnHL_s-3-0.31	WavEnLL_s3-0.303	WavEnHL_s-3-0.293
WavEnLH_s-30.21	WavEnHL_s3-0.283	WavEnLH_s-3-0.233
WavEnHH_s-30.18	WavEnLL_s2-0.274	WavEnHH_s-3-0.230
WavEnLH_s-10.17	WavEnLL_s1-0.184	WavEnLH_s-2-0.149
WavEnHL_s-20.16	WavEnLH_s30.164-	WavEnHL_s-3-0.146
WavEnLL_s-2-0.16	WavEnLH_s1-0.148	WavEnLL_s-1-0.126
WavEnLL_s-3-0.15	WavEnHH_s1-0.082	WavEnLL_s-1-0.119
WavEnLL_s-1-0.13	WavEnHH_s3-0.046	WavEnLL_s-2-0.103
WavEnHH_s-10.07	WavEnHH_s-2-0.04	WavEnHH_s-2-0.091
WavEnHH_s-20.06	WavEnLH_s-2-0.03	WavEnHH_s-1-0.079
Gradient		
GrNonZeros-0.085	GrMean-0.039	GrMean-0.138
GrMean-0.082	GrNonZeros-0.036	GrVariance-0.089
GrSkewness-0.032	GrSkewness-0.027	GrSkewness-0.072
GrVariance-0.027	GrVariance-0.017	GrNonZeros-0.044
GrKurtosis-0.019	GrKurtosis-0.009	GrKurtosis-0.036
AR model		
Teta2-0.100	Sigma-0.119	Teta4-0.157
Teta1-0.097	Teta3-0.094	Sigma-0.088
Sigma-0.096	Teta1-0.081	Teta2-0.078
Teta4-0.021	Teta2-0.072	Teta-0.067
Teta3-0.019	Teta4-0.044	Teta-0.034

Table I reports features as calculated by Mazda software.

The result of feature ranking with mutual information algorithm and the associated feature selection results are

shown in Table II. In this table, only the 10 highest-ranking features are shown together with the associated MI value.

As can be seen in Table II, each phase has its own feature ranking. This means that after the injection of contrast liquid, the texture in the pathological and healthy part of the liver has changed over time.

A mutual information algorithm may be also applied to the features that do not need any reduction for input in algorithm such as AR model, Gradient and histogram features. This algorithm can be used to show the different ranking in each phase.

On this point, we can observe that some features classes give rise to large MI values, while some other features have low values. For instance, histogram features, COM and wavelets show, in general, larger values than the other parameter classes. In particular, the absolute highest values are those obtained by histogram features in phase 2 and 3.

In the next section, we will briefly explain the proposed neural network application. We will also show and discuss the results of the classification algorithm with different calculation parameters.

C. Classification and Results Discussion

Neural Network applications in Computer-Aided Diagnosis represent the main stream of computational intelligence in medical imaging [10]. The penetration and involvement of these applications are almost comprehensive for all medical problems because neural networks have the nature of adaptive learning from input information and, by using a suitable learning algorithm, they can improve following the variety and change of input content. Furthermore, neural networks have the capability of optimizing the relationship between inputs and outputs via distributed computing, training, and processing. This leads to reliable solutions as desired by the specification, while medical imaging provides the most important tool for facilitating such inspection and visualization. Many researches in the field of medical images have been done which benefit from neural network, such as image segmentation, edge detection, and image registration. More details on previous works regarding neural networks in medical images are reported in [10]. A large amount of research has been conducted on CT liver images with the aim of detecting tumors or other pathological signs. In [9], the researchers used neural network for non-enhanced CT images in order to discriminate small hemangiomas, the most common non-cystic benign lesions, from metastases, which represent the vast majority of malignant hepatic lesions. In [1], they suggest to employ a computer-aided diagnostic system to characterize CT focal liver lesions. Here a hierarchical approach consisting of three sequentially placed feed-forward networks has been applied, where the first NN classifies into normal or pathological liver regions. The pathological liver regions are characterized by the second NN as cyst or other disease. The third NN classifies other diseases into hemangioma or hepatocellular carcinoma. In [11], the researchers used neural network to discriminate liver disease from non-enhanced CT images. In this case, a sigmoid radial

basic function has been employed in neural network with growing and pruning algorithm (SRBFNN-GAP). This led to a new method capable of discriminating cyst, hepatoma, cavernous hemangioma and normal tissue. ANN is an information processing system, which is inspired by the models of biological neural networks [10]. An adaptive system changes its structure or internal information flowing through the network during the training phase. ANN is widely used in many areas because of its features, such as a strong capacity of nonlinear mapping, a high accuracy for learning, and a good robustness. As regards the development of a NN model, the researcher should pay attention to the number of hidden neurons, number of hidden layers, number of training, type of training algorithm. Actually, our research shows the results gathered from the effect of number of neurons on hidden layers and number of training time.

One of the major challenges in the design of neural network is the fixation of hidden neurons with minimal error and highest accuracy. The quality of prediction made by the network is measured in terms of the generalization error.

Generalization performance varies over time as the network adapts during training. The numbers of hidden neurons that we used for our work is chosen according to the paper presented in [12], because of its simplicity, scalability, and additivity. The number of hidden neurons is $N_h = (n + n_0 - 1) / 2$ where n is the number of inputs; n_0 is the number of outputs. In this paper, we used a neural network toolkit in Matlab R2014a.

We employed a 2-layer (one hidden layer) NN for classification of normal and pathological part. The neural network has been applied with 2 and 5 neurons in hidden layer and with different time of training to design a neural network model. The training set was made of 75% of total data (56 observation samples). For test set and validation, 15 % of data observation (12 samples) has been used. Each set is changed and randomly chosen every time in each learning repetition. Tables III-VIII show the results of neural network algorithms.

According to Tables III-VIII, the best classification result depends on the histogram features in all 3 phases. Precision is 85% with 5 neurons in hidden layer in phase 1, 95% with 2 neurons in hidden layer in phase 2 and 95% with 5 neurons in phase 3. Other features did not achieve as good results for tumor detection.

Another conclusion that can be inferred from these tables is that histogram features and wavelet features improve their performances in various phases, thus proving the above argument. Injection of contrast is useful for discriminating parenchyma and HCC tumors.

According to [13], Hepatocellular Carcinomas are often easier to detect on delayed phase images than on portal venous images, and detectability and characterization are improved by adding delayed phase imaging to the biphasic CT examination. According to this aspect, this work represents a confirmation that with the third phase better results of detection may be achieved for all considered features.

TABLE III
 RESULTS OF NEURAL NETWORK ON HISTOGRAM FEATURES

Number of Phase	Number of Training Time	Number of Neurons in Hidden Layer	
		2	5
Phase1	1	51.2	67.5
	2	62.5	58.8
	3	50.0	85.0
	4	62.5	53.8
	5	67.5	77.5
Phase2	1	91.3	93.8
	2	92.5	92.5
	3	93.8	92.5
	4	95.0	93.8
	5	95.0	76.3
Phase 3	1	50.0	95.0
	2	87.5	93.8
	3	88.8	85.0
	4	88.8	87.5
	5	81.3	76.3

TABLE IV
 RESULTS OF NEURAL NETWORK ON RLM FEATURES

Number of Phase	Number of Training Time	Number of Neurons in Hidden Layer	
		2	5
Phase1	1	67.5	50.0
	2	46.3	50.0
	3	53.8	63.7
	4	63.7	68.8
	5	50	65.0
Phase2	1	63.7	53.8
	2	50.0	57.5
	3	56.3	50.0
	4	55.0	52.5
	5	50.0	50.0
Phase 3	1	50.0	66.3
	2	47.5	76.3
	3	56.3	53.8
	4	50.0	50.0
	5	48.8	52.5

TABLE V
 RESULTS OF NEURAL NETWORK ON GRADIENT FEATURES

Number of Phase	Number of Training Time	Number of Neurons in Hidden Layer	
		2	5
Phase1	1	56.3	71.3
	2	60.0	46.3
	3	60.0	53.8
	4	47.5	65.6
	5	62.5	56.3
Phase2	1	58.8	56.3
	2	50.0	65.0
	3	57.5	48.3
	4	58.8	57.5
	5	60.0	62.5
Phase 3	1	58.8	58.3
	2	56.3	60.0
	3	60.0	67.5
	4	61.3	61.3
	5	65.0	67.5

TABLE VI
 RESULTS OF NEURAL NETWORK ON COM FEATURES

Number of Phase	Number of Training Time	Number of Neurons in Hidden Layer	
		2	5
phase1	1	70.0	73.8
	2	85.0	75.0
	3	76.3	73.8
	4	76.3	67.5
	5	65.0	68.8
Phase2	1	72.5	72.5
	2	62.5	70.0
	3	78.8	72.5
	4	67.5	67.5
	5	75.0	70.0
Phase 3	1	73.8	67.5
	2	65.0	75.0
	3	53.8	68.8
	4	83.8	79.5
	5	62.5	80.0

TABLE VII
 RESULTS OF NEURAL NETWORK ON AR MODEL FEATURES

Number of Phase	Number of Training Time	Number of Neurons in Hidden Layer	
		2	5
Phase1	1	70.0	71.3
	2	46.3	58.8
	3	66.3	61.3
	4	53.8	47.8
	5	66.3	61.3
Phase2	1	51.2	52.5
	2	58.8	66.3
	3	57.5	72.5
	4	55.0	70.0
	5	52.5	55.0
Phase 3	1	53.8	51.2
	2	66.3	57.5
	3	62.5	65.0
	4	56.5	60.0
	5	70.0	68.8

TABLE VIII
 RESULTS OF NEURAL NETWORK ON WAVELET FEATURES

Number of phase	Number of Training time	Number of Neurons in Hidden Layer	
		2	5
Phase1		80.0	72.5
	1	70.0	76.3
	2	77.5	77.5
	3	70.0	75.0
	4	75.8	72.5
Phase2	1	72.5	85.0
	2	60.0	87.5
	3	78.8	75.0
	4	68.8	80.0
	5	65.0	70.0
Phase 3	1	82.5	86.3
	2	68.8	81.3
	3	78.8	77.5
	4	83.8	65.0
	5	60.0	81.3

III. CONCLUSION AND FUTURE WORKS

The highest accuracy in detection of tumor part with respect to healthy part can be obtained through histogram features, with the accuracy of detection in phase 1: 85% with 5 hidden neurons, in phase 2: 95% with 2 hidden neurons and in phase 3: 95% with 5 hidden neurons. In Table VIII, the wavelet features also show that with the injection of contrast liquid better results can be achieved as regards the detection of tumor (the best result of tumor detection belongs to phase 3). On the other hand, Gradient feature, AR model, and COM feature show that first phase has better ability to detect tumor. The second place belongs to wavelet features with 80% percentage of detection in phase 1, 85% in phase 2 and 86.3 % in phase 3. In this paper we showed that in contrasted CT images, with the injection of liquid each phase texture changes. Therefore, the feature ranking that could discriminate class of tumor and class of healthy is different.

In this paper, a research work for the choice of appropriate feature selection methods has been described in the context of HCC tumor analysis from Triphasic CT volumes. With the purpose of tissue characterization, each feature class has been considered independently from one another, in order to understand their information content and their ability to describe a parametric tissue model. The results are strictly in accordance with some of the practical observations reported in previous works, as described before. It is clear that classification results could benefit from the multi-temporal analysis that can be achieved when considering the integrated use of two or three phases at the same time. A comprehensive analysis of the information content carried by each phase is also the basis for the future research work our lab is carrying on about data fusion. It is, in fact, our opinion, that an integrated visualization of the three phases could help medical diagnosis, improving sensitivity and specificity when dealing with huge amount of data as in the considered acquisition modality.

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