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An Ultrasonic Scoring System for the Diagnosis of Chronic Liver Diseases

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Abstract — This paper describes a new ultrasonic scoring system based on the texture characteristics of ultrasonic liver images. This system generates an ultrasonic disease severity (UDS) score that is highly correlated with the computer morphometry (CM) score obtained from the evaluation of liver fibrosis based on the biopsy specimens. Essentially, UDS score is with great resemblance to CM score in the statistical presentation. Therefore, UDS score is defined mathematically referring to CM score as the scoring basis. As a result, UDS can faithfully reflect the disease progression that is determined conventionally based on the evaluation of liver fibrosis. Promising results have been obtained in experimental studies, and it will currently undergoes extensive clinical experiments.

Key words: Chronic liver disease, Ultrasonic scoring system, Ultrasonic disease severity, Computer morphometry score, Ultrasonic liver image.

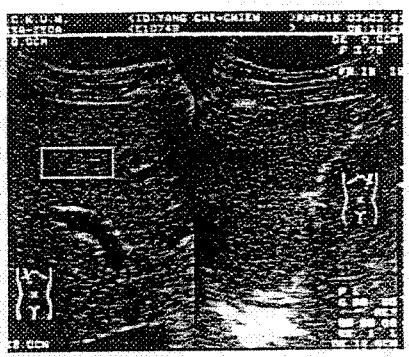
1. Introduction

B-mode liver sonogram, the most frequently used diagnostic ultrasonic modality, produces gray-scale images from echo signals arising from pulsed ultrasound beam propagating through soft tissues. The ultrasonic scans are highly operator and instrument dependent because the characteristics of ultrasonic image are closely related to the attenuation and scattering properties. Therefore, current liver sonography is still a qualitative, or at best semi-quantitative image modality. Visual criteria of diagnosing diffused liver diseases are widely used, however, generally confusing and extremely subjective. It depends on the physicians to observe certain tissue characteristics, such as texture coarseness, echogenicity and smoothness of inferior edge, from the liver images and to compare them in order to diagnose the liver states [1]. For some liver diseases, their tissue characteristics are very similar, thereby, the diagnostic accuracy using visual interpretation is estimated to be around 72% [2, 3]. This result does not yet produce a conclusive diagnosis. Therefore, physicians have to further examine with other invasive methods, typically the liver needle biopsies. Liver biopsy is the standard clinical routine for diagnosing chronic liver diseases and for guiding and monitoring treatment. But, there are associated morbidity (3%) and mortality (0.03%). Therefore, developing a reliable, non-invasive and quantitative ultrasonic scoring system for evaluating histological changes in ultrasonic liver image is highly promising in diagnosing and monitoring chronic liver diseases.

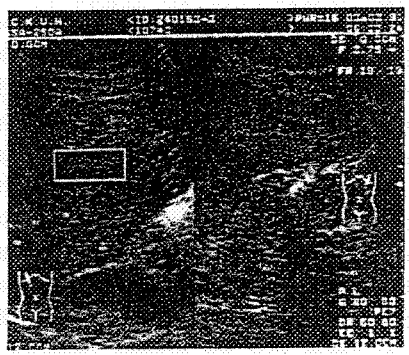
Echotexture of liver was reported to be a standard for assessing the liver states in clinical diagnosis [3]. However, the measurement of liver echotexture was always subjective based on the physician's observation. Therefore, many texture descriptors had been developed to measure the echotexture of liver [4-9]. These texture descriptors consisted of texture energy, co-occurrence matrix, fractal dimension, texture spectrum, statistical feature matrix and texture feature coding method. In [9], we compared the classification capability among the above-mentioned texture descriptors for classifying three liver states that are normal, hepatitis and liver cirrhosis. Figures 1-3 illustrate examples of these cases. Experiments with ninety ultrasonic liver images revealed that features generated from co-occurrence matrix and texture feature coding method were effective for classifying the three liver states. As a result, the two texture descriptors are used here to establish the ultrasonic scoring system.

The key of establishing the ultrasonic scoring system is to find the powerful texture features that can reflect the progression of liver disease. From the histological view, the progression of liver disease mainly reflects in the amount of fibrosis of the liver specimens. In the recent decade, Knodell's score was widely used to measure liver fibrosis [10]. It only recorded five numerical scores for staging liver fibrosis based on the physician's observation. Obviously, it was not enough to develop a quantitative progression index for liver disease. In [11,17], we proposed a quantitative index, called computer morphometry

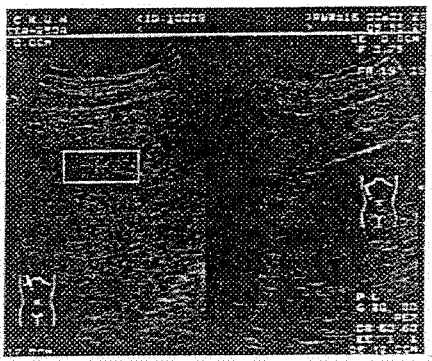
(CM) score, that was more reliable and effective than the conventional Knodell's score for evaluating the amount of liver fibrosis. Thus, the CM scores are used herein as the criteria for selecting powerful texture features from the above-mentioned texture descriptors.



1. Liver B-scan ultrasonic images for a normal cases displaying a homogeneous texture of liver and more smoothness of the inferior surface.



2. Ultrasonic scans for a liver hepatitis. Distinguishing this case from the normals and liver cirrhosis is quite difficult.



3. An ultrasonic image case of liver cirrhosis with a coarse echotexture and rough inferior surface.

As mentioned previously, the CM score is closely related to the progression of liver disease. Thus, it is a good indicator to develop the ultrasonic scoring system for assessing the ultrasonic liver images. A powerful ultrasonic scoring system should generate the disease severity score that matches the corresponding CM score as closely as possible. To establish the correlates between the selected texture features and the corresponding CM score, the quadratic equations of the selected texture features are defined mathematically based on the CM scores in the training stage. The scoring criterion of assessing the ultrasonic liver image is the minimization the variation between the observed texture features and the estimated texture features estimated by quadratic equations. The severity scores generated herein are called ultrasonic disease severity (UDS) score. Besides, the intervals of UDS scores in different liver states are also determined as the standards for classification. Experiments with forty test images demonstrate that the UDS scores generated from this system are significantly correlated with the CM scores of corresponding biopsy specimens. In addition, one hundred and twenty ultrasonic liver images are used to test the classification capability. The resulting correct classification rate reaches as high as 86.7%. These results reveal the possibility to replace the invasive needle biopsy examination by using the system presented herein.

2. Materials and methods

2.1. Powerful Texture Features Selection

The major morphological change of the progression of chronic liver diseases is that the collagen fibers are increasingly presented in liver specimens. Therefore, the amount of liver fibrosis is a powerful index to quantitatively assess the chronic liver diseases. In the literature, echotexture was also reported to be very powerful for evaluating diffuse liver disease [3]. Thus, if we can establish the correlation between the measurements of echotexture and the amount of fibrosis in liver specimens, sonography will become an effective and non-invasive tool in the systematic assessment of chronic liver diseases. In [9], we found the co-occurrence matrix method and texture feature coding method are powerful texture descriptors for classifying the chronic liver diseases. Therefore, the two texture descriptors are used to establish the correlates with the pathological fibrosis measurement.

Entries of the co-occurrence matrix are transitions between all pairs of two gray levels [5]. The gray-level transitions are calculated based on two parameters, displacement d and angular orientation θ. More precisely, let i and j be two gray levels and $N_{d,\theta}(i,j)$ denote the number of transitions between two pixels whose gray levels are i and j with d-pixels apart and angular orientation θ. In other words, $N_{d,\theta}(i,j)$ is the number of pixel-pairs at locations (x,y) and (w,z) satisfying the following conditions; $G(x,y)=i, G(w,z)=j, \|(x,y)-(w,z)\|=(d,\theta)$ where $\|(x,y)-(w,z)\|=(d,\theta)$ is a distance measure to describe the distance between two pixels of spatial locations at (x, y) and (w, z) with d-pixels apart and along angular orientation θ. Normalizing $N_{d,\theta}(i,j)$ yields the probability or the relative frequency of the gray-level transition

$$p(i,j|d,\theta)=\frac{N_{d,\theta}(i,j)}{N} \quad (1)$$

where N is the number of total gray-level transitions in the co-occurrence matrix.

Based on the gray-level co-occurrence matrix, Haralick [5] proposed fourteen feature measures for texture analysis, four of which listed below have been proven to be useful for the detection of diffuse and malignant liver diseases [12]. Therefore, we use the four texture features to develop the ultrasonic scoring system.

a) Contrast (CON):

$$CON=\sum_{i,j\in G}(i-j)^2\times p(i,j|d,\theta) \quad (2)$$

b) Angular Second Moment (ASM):

$$ASM=\sum_{i,j\in G}p^2(i,j|d,\theta)\cdot \quad (3)$$

c) Entropy (ENT):

$$ENT=-\sum_{i,j\in G}p(i,j|d,\theta)\log\{p(i,j|d,\theta)\} \quad (4)$$

d) Correlation:

$$COR=\frac{\sum_i\sum_j[(i\cdot j)\cdot p(i,j|d,\theta)-\mu_x\mu_y]}{\sigma_x\sigma_y} \quad (5)$$

where μ_x and σ_x are the mean and standard deviation of the row sum of the co-occurrence matrix and μ_y and σ_y are the mean and standard deviation of the column sum of the co-occurrence matrix.

Besides, we also proposed an approach called texture feature coding method (*TFCM*) for classifying ultrasonic liver images [9]. *TFCM* is a coding scheme which transforms an image into a feature image whose pixels are represnted by texture feature numbers. The texture feature number of each central pixel (x,y) is generated based on the gray-level changes of its eight surrounding pixels. The eight surrounding pixels can be decomposed into the first-order and second-order connectivities. The first-order connectivity contains four pixels immediately adjacent to the central pixel and the second-order connectivity are the other four pixels diagonally adjacent to the central pixel. The $\alpha(x,y)$ is used to indicate types of the gray-level gradient variation of the first-order connectivity, whereas the gradient variation type of $\beta(x,y)$ is defined in the second-order connectivity. The texture feature number *(TFN)* is encoded by $TFN(x,y)=\alpha(x,y)\times\beta(x,y)$ whose values range from 0 to 41. The higher the texture feature number is, the greater change in gray-level gradient will occur. The ideas of gray-level histogram and co-occurrence matrix are employed in *TFCM* to define the texture feature number histogram and texture feature co-occurrence matrix based on Eqs. (6) and (7).

$$p_\Delta(n)=\frac{N_\Delta(n)}{N},\quad n\in\{0,1,2,\ldots,41\} \quad (6)$$

$$p_\Delta(i,j|d,\theta)=\frac{N_{\Delta,d,\theta}(i,j)}{N_t} \quad (7)$$

where Δ is the tolerance of gray-level gradient variation. In Eq. (6), the $N_\Delta(n)$ is the number of occurrence of the texture feature number n and N is the total number of pixels in the feature image. In Eq. (7), the $N_{\Delta,d,\theta}(i,j)$ is defined similarly as in Eq.(1), i and j are texture feature numbers and N_t is the total number of *TFN* transitions.

In [9], we defined eight texture features from the texture feature number histogram and texture feature number co-occurrence matrix. Four of them listed below had been proven to be powerful for classifying the liver states.

a) Coarseness: $Coarse=\sum_{\Delta=0}^{R}p_\Delta(41)$ were R is a positive integer. (8)

b) Homogeneity: $Hom=\sum_{\Delta=0}^{R}p_\Delta(0)$ (9)

c) CodeEntropy:

$$CEntropy = -\sum_{i=0}^{41}\sum_{j=0}^{41} p_\Delta(i,j|d,\theta)\log p_\Delta(i,j|d,\theta) \quad (10)$$

d) Gray-Level Resolution Similarity:

$$GLRS = \sum_x \sum_y \sum_{i=0}^{41}\sum_{j=0}^{41} \frac{p(i,j;x,y)}{1+(i-j)^2} \quad (11)$$

where $p(i,j;x,y)$ is defined as the joint probability of the pixel (x, y) with $TFN = i$ when $\Delta = 0$ and $TFN = j$ when $\Delta = 3$.

The disease severity of chronic liver disease is reflected by the amount of liver fibrosis of the biopsy specimens. Therefore, it is necessary to develop an objective system for measuring the amount of liver fibrosis. In [11], we developed an automatic image analysis system, which consisted of a microscope, a computer-driven slide-driver, and the software for image acquisition, processing and data analysis. The image analysis procedures included color model selection, histogram-based normalization, clustering, moment-persevering thresholding and ranking filter for tissue characterization. In addition, the computerized motor driver and the x-y directional stage were designed and installed to move specimens on an optical microscope and to compute the fibrosis index. The system was capable of computing the percentage of fibrous area to the complete liver tissue area as an index for assessing the amount of liver fibrosis. The index is called computer morphometry (CM) score. In [17] we found that the CM score was superior to the conventional Knodell's score for evaluating the liver fibrosis. The pathological CM score is used for selecting the powerful texture features.

In [12], we found that the disease changes of ultrasonic liver texture are more sensitive on features of the co-occurrence matrix with 3 or 4-pixels apart along the angular directions of 0^0 or 90^0. Thus, we use the two displacements along the two directions to obtain four co-occurrence matrices. Sixteen texture features can be extracted from these matrices. In addition, four texture features by texture feature coding method are also adopted. Four texture features ($|r| \geq 0.85$), that are significantly correlated to CM scores, are selected as the most powerful features for establishing the ultrasonic disease scoring system. They are $GLRS(d=1,\theta=0^0)$, $Entropy_{(d=1,\ \theta=0^0,\Delta=3)}$, $COR_{(d=1,\theta=90^0)}$ and $ASM(d=4,\theta=0^0)$. Experimental results with forty samples show that the resulting severity scores generated from this system are highly correlated with CM score more than the ones designed by other texture features.

2.2. Ultrasonic Disease Scoring System

In the literature, the texture features were only used to construct a classification system for clustering the three liver states [14]. The widely used texture classification methods including the minimum-distance classifier, Bayesian estimation, k-nearest neighboring classifier and neural network have been reported to be useful in these studies. However, they only classified test samples into the three disease states. No quantitative measurement of disease severity has yet been generated for assessing the progression of the chronic liver disease. As mentioned above, the liver disease progression can be perceived and evaluated based on the amount of liver fibrosis. Among conventional methods of liver fibrosis measurement, the CM score is most reliable and accurate method [11]. Therefore, the proposed scoring system is designed referring to the corresponding CM scores. For this purpose, a system of quadratic equations is used to define the correlation between the texture features and the corresponding CM scores. The designed details are described as follows.

Forty training samples, including the ultrasonic images and their needle specimens, are used to establish the ultrasonic scoring system in the training stage. The selected texture features and its corresponding CM score of the i-th training sample are evaluated and defined as $< f_{1,i}, f_{2,i}, f_{3,i}, f_{4,i} >$ and t_i. The quadratic equations of selected texture features with respect to the corresponding CM score are defined in Eq. (12).

$$\begin{aligned} f_{1i} &= a_1 t_i^2 + b_1 t_i + c_1 \\ f_{2i} &= a_2 t_i^2 + b_2 t_i + c_2 \text{ ,i=1,2,..,40} \\ f_{3i} &= a_3 t_i^2 + b_3 t_i + c_3 \\ f_{4i} &= a_4 t_i^2 + b_4 t_i + c_4 \end{aligned} \quad (12)$$

These coefficients a_j, b_j, c_j are determined using the least square estimation based on Eq. (13).

$$X = (T^t T)^{-1} T^t F \quad (13)$$

where

$$X = \begin{bmatrix} a_j \\ b_j \\ c_j \end{bmatrix}, \quad T = \begin{bmatrix} t_1^2 & t_1 & 1 \\ t_2^2 & t_2 & 1 \\ . & . & . \\ . & . & . \\ t_{10}^2 & t_{10} & 1 \end{bmatrix}, \quad F = \begin{bmatrix} f_{j,1} \\ f_{j,2} \\ . \\ f_{j,i} \\ . \\ . \\ f_{j,10} \end{bmatrix}, \quad for\ j = 1,2,3,4.$$

The quadratic equations defined in Eq.(12) are used to derive a disease severity score for assessing the ultrasonic liver image. The resulting score is called ultrasonic disease severity (UDS) score. The assessment criterion of image **X** is based on the minimization of square error between the texture features of **X** and the estimated texture features obtained by the quadratic equations. The square error term is defined as Eq. (14).

$$SE = \sum_{i=1}^{4} [g_i - (a_i u^2 + b_i u + c_i)]^2, \quad (14)$$

where the $< g_1, g_2, g_3, g_4 >$ are the texture features of **X**.

Differentiating of Eq.(14) with respect to the variable u, we obtain the root u of Eq. (15) as UDS such that the square error term is minimized.

$$2(\sum_{i=1}^{4} a_i^2)u^3 + 3(\sum_{i=1}^{4} a_i b_i)u^2 + (2\sum_{i=1}^{4} a_i c_i + \sum_{i=1}^{4} b_i^2 - 2\sum_{i=1}^{4} g_i a_i)u + (\sum_{i=1}^{4} b_i c_i - \sum_{i=1}^{4} g_i b_i) = 0 \quad (15)$$

3. Experimental results and discussion

In this study, we have successfully developed an ultrasonic scoring system to assess the severity of the chronic liver disease. The system integrates the techniques of texture analysis with pathological CM score measurement. In this system, all programs are encoded by Visual C++ version 4.0 with a Pentium personal computer under MS-Windows 95 environment. The system provides user-friendly interfaces and efficient computation for real-time clinical evaluation. Forty training samples with ultrasonic images and corresponding needle specimens are collected from forty patients in whom thirteen of them are normals, nineteen are chronic hepatitis and eight are with liver cirrhosis. These training samples are used to select the powerful texture features, and then to establish the quadratic equations of texture features based on CM scores in the ultrasonic scoring system. The resulting quadratic equations are used to derive the UDS scores of liver images in sequential assessment. Additionally, in the conventional clinical diagnosis, physicians always classify the ultrasonic liver image into the one of three liver states. To provide the standards for classification, the forty training images are also used to determine the severity intervals of UDS score for different liver states according to their medical records. The intervals of UDS scores in different liver states are determined by the ANOVA and point-bisexual correlation analysis. The results are normal: 2.8832 ± 1.668, liver hepatitis: 5.9296 ± 1.554 and liver cirrhosis: 13.8257 ± 2.632. The thresholds of UDS for three different disease states are 4.54 (normal ~ liver hepatitis) and 9.62 (liver hepatitis ~ cirrhosis) based on the normal distributions with equal standard variation.

Forty ultrasonic images and their corresponding needle specimens are used as the test samples to analyze the stability and accuracy of the proposed scoring system. Three independent physicians, blind to the disease severity of patients, are requested to assess these test images by using the proposed system. The Kendall coefficient of concordance W, under 99%confidence level is used to test the system's reliability.

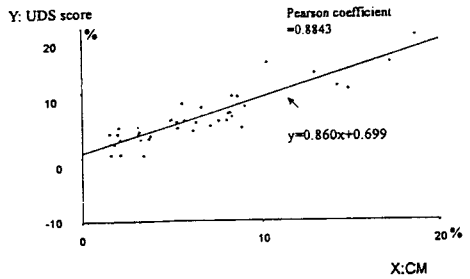
$$W = \frac{\sum_{i=1}^{N} X_i^2 - \frac{(\sum_{i=1}^{N} X_i)^2}{N}}{\frac{1}{12} k^2 (N^3 - N)} \quad (16)$$

N and k are the number of patients and the number of physicians, X_i is the sum of UDS scores determined by the three independent physicians for the i-th patient. The Kendall coefficient of concordance is only 0.1353. It reveals that the system provides stable assessment.

The accuracy of UDS score is verified by comparing with the pathological CM scores. The Pearson correlation coefficient, r_{xy}, between the UDS scores and CM scores is computed by Eq (17).

$$r_{xy} = \frac{\frac{\sum (X - \bar{X})(Y - \bar{Y})}{N-1}}{\sqrt{\frac{\sum (X - \bar{X})^2}{N-1}} \sqrt{\frac{\sum (Y - \bar{Y})^2}{N-1}}} \quad (17)$$

where the two severity score values are recorded by X and Y.



4. The relationship between ultrasonic disease score and computer morphometry score

Figure 4 displays the correlation between the results of UDS scores and CM scores under 95% confidence level. The correlation coefficient is 0.8843 ($p<0.001$). The significant correlation reveals that the proposed UDS scores can faithfully reflect to CM scores that is an important factor to assess the progression of chronic liver disease. In other words, the UDS score is a powerful and stable index for assessing the ultrasonic liver images. The results also reveal that the system of quadratic equations is an appropriate correlate between the selected texture features and the corresponding CM scores. It is still interesting topics to define the best correlates between texture features and CM scores in the further such that the resulting ultrasonic system is most effective.

To demonstrate the above-mentioned four texture features are the best candidates, we select other texture features as feature sets for developing the scoring system. Let scoring system A be designed with texture feature set A ($GLRS_{(d=1,\ \theta=0^0)}$ and COR $(d=4,\theta=90^0)$), System B be designed by texture feature set B (features of set A with $CEntropy_{(d=4,\theta=90^0)}$). System C be designed by texture feature set C (features of set B with $ASM_{(d=4,\theta=90^0)}$). System D be designed by texture feature set D (features of set C with $COR(d=3,\theta=0^0)$) and system E be designed by six texture feature set E (features of set D with $ASM(d=4,\theta=0^0)$). Table 1 shows the correlation between the UDS scores generating from these scoring systems and the corresponding CM scores. From this table, we find that UDS scores generated by system C has largest correlation coefficient among these systems. Additional texture features are combined with feature set C can not make the resulting scoring system more effective. Thus, we confirm that the above-mentioned four selected features are best candidates for establishing ultrasonic scoring system.

In the clinical diagnostic practices, the ultrasonic liver images are usually classified into the three disease states. The effective scoring system should avoid the misclassification, especially the false-negative misclassification. The false-negative rate is the probability of the misclassification that the patients indicate as normal or mild disease while the actual diagnosis are more severe disease. High false-negative rate represents a danger to the patients when physicians use this scoring system. One hundred and twenty ultrasonic liver images, verified by needle biopsy, are used to test the discrimination capability. The classification results are listed in Table 2. From the experimental result we find that the negative-false rate is only 8.33% and the correct classification rate is 86.7%. It is many superiors to the conventional method utilized by the co-occurrence matrix or texture feature coding method [9].

4.Conclusion and summary

In this paper, a quantitative ultrasonic scoring system is proposed based on the characteristics of echotexture of liver. The system does not only generate quantitative indices to assess the disease progression but also classify the ultrasonic liver images. The quantitative indices are called the ultrasonic disease severity (UDS) scores. In conventionally clinical diagnosis, the amount of liver fibrosis is one of the key factors to assess the progression of chronic liver disease. The CM scores were reported to be a powerful index to measure the amount of liver fibrosis on the biopsy specimen. Thereby, the system proposed herein is designed referring to the CM score as the scoring basis. Experimental results demonstrate that the UDS score generated from this system is significantly correlated with corresponding CM score. In other words, the resulting UDS score can faithfully reflect the disease progression of chronic liver disease. It is possible to be alternative for assessment the disease progression instead of the needle biopsy examination. Additionally, in the clinical diagnostic practices, the ultrasonic liver images are always classified into the three liver states that are normals, liver hepatitis and liver cirrhosis. To provide the standards for classification, the intervals of UDS of different disease states are also determined. One hundred and twenty samples are used to test the classification capability. The correct classification rate reaches around 86.7%. It is reveal that the proposed system has great potential to become a valuable clinical tool for liver diagnosis in the future. Besides, several

characteristics of liver tissues have been used to evaluate the degree of diffuse parenchyma liver disease, including the smoothness of liver surface, echogenicity, echotexture and backscattering parameters [15, 16]. However, this system proposed herein only use the information of echotexture. In further studies, it is still interesting topic to enhance this system's performance by integrating other features of the tissue characteristics.

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Table 1. The correlation coefficient between CM scores and UDS scores generated by different scoring system with different texture feature sets. The texture features of set A are GlRS($d=1,\theta=0^0$) and COR($d=4,\theta=90^0$), set B are set A with CEntropy($d=4,\theta=90^0$), set C are set B with ASM($d=4,\theta=90^0$), set D are set C with COR($d=3,\theta=0^0$) and set E are set D with ASM($d=4,\theta=0^0$). Obviously, the scoring system with texture feature set C has best capability of assessment.

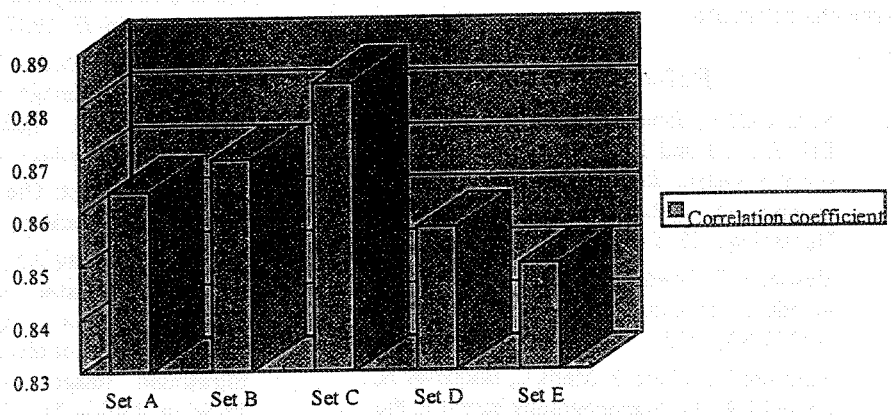

Table. 2. The confusion matrix of forty test patients is listed. The left column indicates the true liver states of the test samples while the upper row indicates the corresponding classification results. Correct classification rate is 86.7%. The false-negative rate is only 8.33%.

	Normal	Hepatitis	Cirrhosis
Normal	37	2	1
Hepatitis	5	32	3
Cirrhosis	1	4	35