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Fuzzy logic algorithm for quantitative tissue characterization of diffuse liver diseases from ultrasound images

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Abstract

Computerized ultrasound tissue characterization has become an objective means for diagnosis of liver diseases. It is difficult to differentiate diffuse liver diseases, namely cirrhotic and fatty liver by visual inspection from the ultrasound images. The visual criteria for differentiating diffused diseases are rather confusing and highly dependent upon the sonographer's experience. This often causes a bias effects in the diagnostic procedure and limits its objectivity and reproducibility. Computerized tissue characterization to assist quantitatively the sonographer for the accurate differentiation and to minimize the degree of risk is thus justified. Fuzzy logic has emerged as one of the most active area in classification. In this paper, we present an approach that employs Fuzzy reasoning techniques to automatically differentiate diffuse liver diseases using numerical quantitative features measured from the ultrasound images. Fuzzy rules were generated from over 140 cases consisting of normal, fatty, and cirrhotic livers. The input to the fuzzy system is an eight dimensional vector of feature values: the mean gray level (MGL), the percentile 10%, the contrast (CON), the angular second moment (ASM), the entropy (ENT), the correlation (COR), the attenuation (ATTEN) and the speckle separation. The output of the fuzzy system is one of the three categories: cirrhosis, fatty or normal. The steps done for differentiating the pathologies are data acquisition and feature extraction, dividing the input spaces of the measured quantitative data into fuzzy sets. Based on the expert knowledge, the fuzzy rules are generated and applied using the fuzzy inference procedures to determine the pathology. Different membership functions are developed for the input spaces. This approach has resulted in very good sensitivities and specificity for classifying diffused liver pathologies. This classification technique can be used in the diagnostic process, together with the history information, laboratory, clinical and pathological examinations.

Keywords: Tissue characterization; Liver; Diffuse disease; Ultrasound parameters; Fuzzy logic

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1. Introduction

Pulsed-echo ultrasound is a non-invasive technique capable of visualizing an internal structure of soft tissues and as such it is considered to be an extremely important and valuable tool for medical diagnosis [1]. However, despite their importance, existing ultrasonic systems have a number of important shortcomings. The main problem stems from the fact that presently the diagnosis is, usually, of qualitative nature [2,3]. The physician has to rely on detection of inhomogeneities between echo amplitudes received from the neighboring areas of the image [4]. Such an approach is, of course, subjective and consequently problematic in itself. Moreover, in certain cases the disease attacks the entire tissue area, say the entire liver (diffuse liver diseases) [5]. Then, the ultrasonic image will be homogeneous as shown in Fig. 1, and as a result the diagnosis is sometimes difficult [6–9].

Visual criteria for diagnosing diffused liver diseases are in general confusing and highly subjective because they depend on the sonographer to observe certain textural characteristics from the image and compare them to those developed for different pathologies to determine the type of the disease. An example of such features is texture homogeneity. Its presence or absence can be widely debated between different experienced sonographers. Another feature is texture brightness which can be a matter of argument in marginal cases. Moreover, some of the diseases are highly similar in their diagnostic criteria, which tend to confuse the sonographers even more.

The visual criteria provide low diagnostic accuracy (around 70%) [5,10]. Therefore, the physicians may have to use further invasive methods such as ultrasonically guided needle biopsy. Although this technique is considered to be the golden test for diagnosis, it has the disadvantage of being invasive and more importantly, it may cause a great risk of cancer spread if it cuts through a localized cancer area [11]. The quantitative analysis of ultrasound signals as an aid to the diagnosis of diffuse disease has been described by many researchers [6–9]. The quantitative parameters obtained from pulse-echo data (gray scale B-mode image) can be divided in four broad categories:

1.1. Image textural parameters

These are mean gray level (MGL), gray level variance (VAR), and five of the selected relevant gray level histogram percentiles (PER 0.1–PER 0.9) to have a reduced set of obtained feature vector. Co-occurrence matrix parameters, such as contrast (CON), entropy (ENT), correlation (COR), and angular second moment (ASM) [5].

1.2. Speckle parameters

These are mean scatterer separation ($\bar{d}$) diffuse and specular scatterer intensity (I_d, I_s), specular standard deviation (σ_s) [12].

1.3. Radiofrequency parameters

These are attenuation coefficient (ATTEN) and the backscattering coefficient (BSC) [2,13].

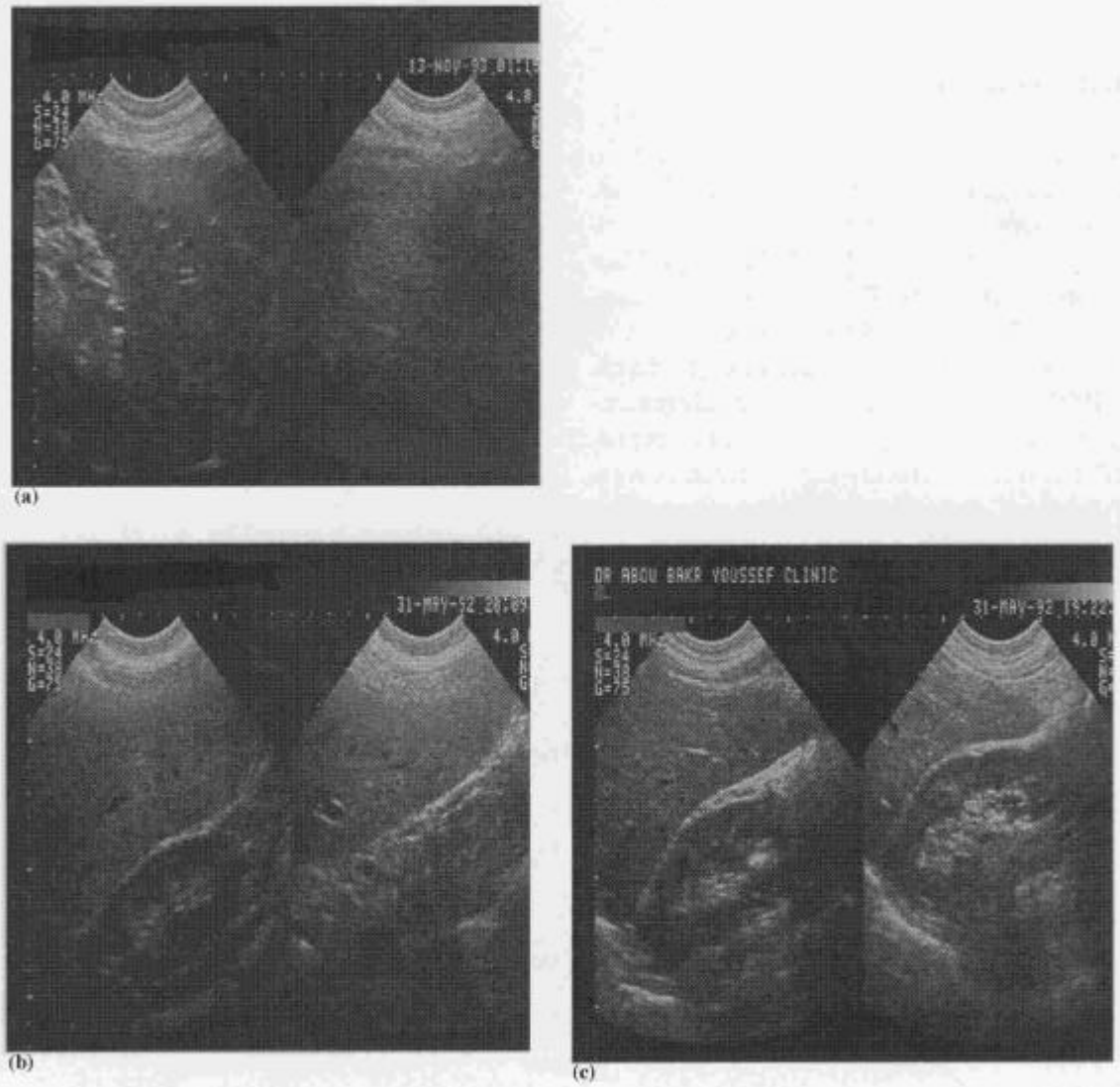
1.4. Autoregressive parameters

These are normally 6×6 autoregressive model matrix derived from the selected region of interest (ROI, normally 50×50 pixels) [14,15].

There are over 40 parameters but only the most significant parameters will be used for classification. All parameters were evaluated

using correlation measurements as to have a reduced set of uncorrelated parameters, and to mark those parameters which correlate the strongest to the different pathologies [16]. Eight parameters were selected: MGL, PER0.1, CON, ENT, COR, ASM, ATTEN, and $\bar{d}$ The clustering of the three pathologies was previously done using statistical methods (k nearest neighbor) [11], neural networks [17–19], and category learning networks [16,20].

In our tissue characterization system, there is an overlap of classes in the parameter space, hence no linear discriminant function can fit the boundaries between different classes.



(a) (b) (c)

Fig. 1. (a) Normal B-mode ultrasound image captured at 4 MHz. (b) Fatty B-mode ultrasound image captured at 4 MHz. (c) Cirrhotic B-mode ultrasound image captured at 4 MHz.

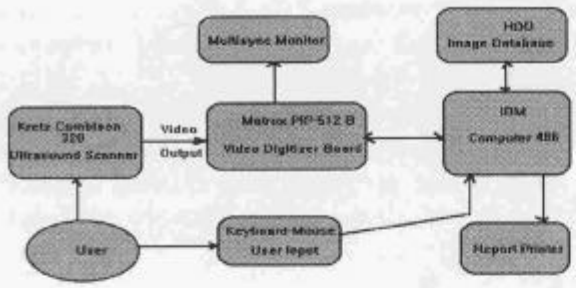


Fig. 2. Block diagram for the quantitative tissue characterization system (QTCS).

2. Data acquisition

In the data acquisition system shown in Fig. 2, the video output of a Kretz-320 mechanical sector ultrasound scanner was connected to a Matrox PIP-512 frame grabber card on an IBM-386 PC. The image is captured in 512 × 512 pixels with a resolution of 8 bits/pixel. Software was developed to define the ROI and to extract all the aforementioned parameters [16].To obtain reproducible results, the following parameters were standardized for all tissue characterization parameters [16,19]:

1. Ultrasound machine settings: e.g. TGC, FOCUS, FREQUENCY, and ZOOM controls, which can change the overall image gain and produce zooming effects and hence influences the image statistics in an unpredictable way. Moreover, the frequency of ultrasound waves used must be the same since the attenuation is frequency dependent.
2. ROI shape, size and location: to obtain reliable statistics, there must be at least 1000 pixels in the ROI, the shape was taken to be rectangular for easy computations. To avoid the distorting effects in ultrasonic wave patterns such as side lobes and grating lobes, the ROI is selected at the center line of the image, and then corrected for diffraction and focusing of the ultrasound beam [2].

3. Materials and methods

The B-mode images are acquired at 4 MHz, digitized, and corrected for diffraction and focusing. Then, the eight significant parameters are extracted from the image. A needle BIOPSY is obtained for every patient. The medical decision was made based on the history information, laboratory measurements, clinical biopsy, and clinician experience.

This protocol was followed for a set of 140 cases for the three pathologies: normal, fatty, and cirrhotic livers. The set of 140 vectors was divided into two sets: one set to derive the fuzzy rules, the other to test the performance of the system using the previously generated rules, see Table 1. This was done to test the system and derive the sensitivity and specificity of the developed fuzzy system for the different pathologies.

Fuzzy logic provides an algorithm which can convert linguistic rules into a decision strategy [21]. The set of linguistic description

Table 1
Number of cases for generating rules and testing for the three pathologies

	Normal		Cirrhosis		Fatty	
	Rules	Test	Rules	Test	Rules	Test
Number	23	13	30	27	30	17

rules is based on expert knowledge. From this set of rules, the inference mechanism will provide a linguistic decision.

The generalized modus ponens (GMP) plays an important role in this process. The simplest form of GMP is

fact 1: x is A'

fact 2: IF x is A THEN y is B

consequence: y is B'

where A, B, A', B' are fuzzy sets and x, y are linguistic variables. Several methods of inference mechanisms are based on this form of approximate reasoning. The most important inference mechanism is the compositional rule of inference suggested by Zadeh [21]. The general form of this compositional operator is denoted by sub star composition [22]. $y = x \circ R$, where $\circ$ presents the compositional operator and R is a fuzzy relation represented by any fuzzy implication function. The fuzzy rule in the form of 'IF x is A and y is B THEN z is C', is a fuzzy relation R defined as follows:

$$\mu_R \underline{\Delta} \mu_{(A \text{ and } B \to C)}(u, v, w) = [\mu_A(u) \text{ and } \mu_B(v)] \to \mu_C(w)$$

where A and B, are fuzzy sets $A \times B$ in $U \times V$ and $R \underline{\Delta}$ (A and B) $\to C$ is a fuzzy implication in $U \times V \times W$.

Nearly 40 distinct fuzzy implication functions have been described in the literature [22,23]. The most well-known fuzzy implication function is described by Mamdani and Larsen and listed in [22].

In recent years many techniques of medical diagnosis have attempted to model the relation between the diseases and symptoms using fuzzy logic [24–28]. In our approach the medical knowledge is represented by a fuzzy relation R between the ultrasound characteristic features and pathologies. Thus, given the fuzzy set S of the measured features calculated from the ultrasonic image, the fuzzy set D of possible pathology can be inferred by the compositional rule of inference, $D = S \circ R$.

We extracted the fuzzy relation R from numerical data using the method suggested by Wang and Mendel [29]. As shown in Table 1, there are 83 cases to derive the fuzzy rules and 57 cases to test the system. This data set is for the three different pathologies, normal, fatty and cirrhotic livers.

3.1. Rules extraction steps

As shown in Table 1 the data were divided into two sets, one to extract the rules and the other to test the rule-based system. The steps for rules extraction are:

3.1.1. Step 1

Assume the domain intervals for each parameter, where the domain interval of a variable means that most probably this variable will lie in this interval (the value of the variable is allowed to be outside this domain). Divide each domain interval into three regions denoted by high, low, and medium. Assign each region a certain fuzzy membership function. We have chosen three forms of membership functions, the triangle form, the trapezoidal form and the bell form. By adjusting the ranges of the membership functions, it was found that the bell shape is the best shape to be selected. This is because the judgment of the physicians on the parameters is not so sharp (the bell shape extends from 0 to ∞ for positive crisp values). Also we have found good results using the bell shape and easy calculations. The equation of the bell form used in the analysis is given as follow

$$\mu_s(s) = e^{-[(s-\bar{s}_m)^2/2\sigma^2]}$$

where μ_s denotes the membership function of a fuzzy value as shown in Fig. 3.

Choosing the fuzzy singleton ($\bar{s}_m$) for each fuzzy set depends on two criteria: (1) statistical basis; and (2) expert knowledge.

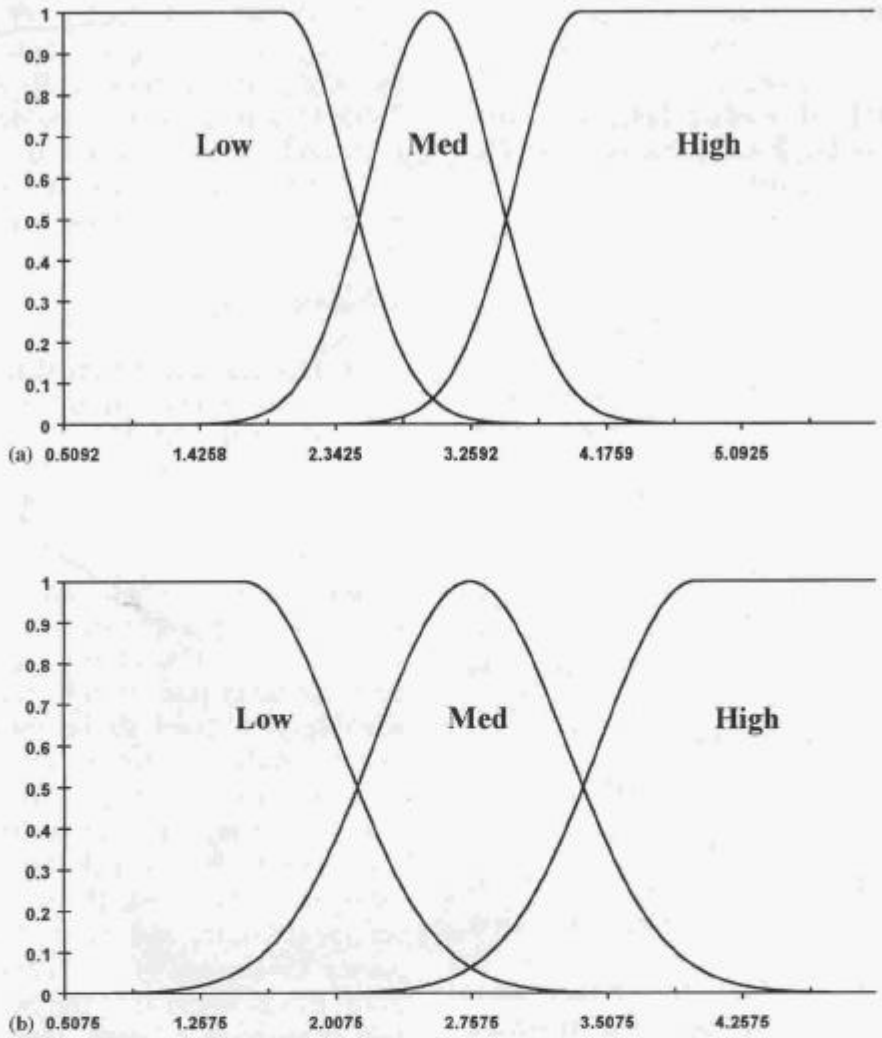


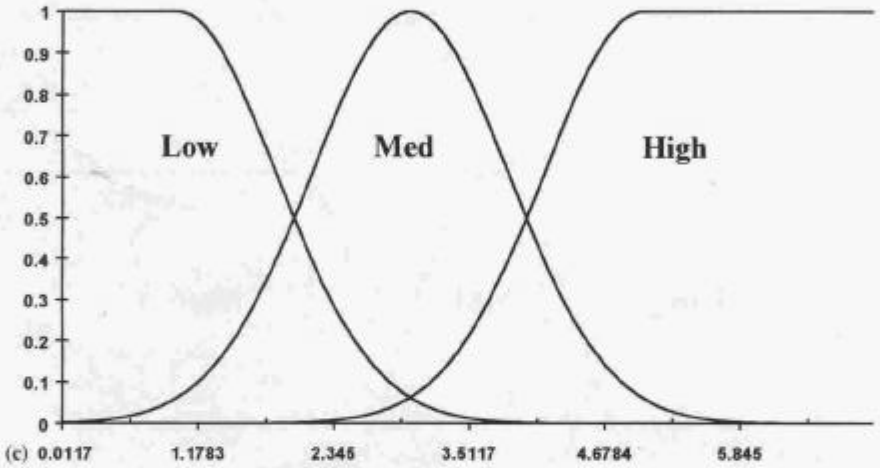
Fig. 3. (a) Membership functions for mean gray level (MGL). (b) Membership functions for 0.1 Percentile (0.1 PER). (c) Membership functions for contrast (CON). (d) Membership functions for entropy (ENT). (e) Membership functions for angular second moment (ASM). (f) Membership functions for correlation (COR). (g) Membership functions for attenuation (ATTEN). (h) Membership functions for Speckle separation ($\bar{d}$).

The bell form of the membership function given above is taken for the fuzzy value *Med*. For the *Low* value if $s < \bar{s}_l$, then μ_s equals to 1. For the *High* value if $s > \bar{s}_h$ then μ_s equals to 1.

Since we have only three pathologies and the size of the input space is eight, we have chosen only three regions for each variable because the high resolution is not required in this case to take a decision. The crossover point was set to be at 0.5 as shown in Fig. 3. In this sense a dominant rule always exists and is associated with the degree of belief greater than 0.5. The output which is a linguistic variable called the pathology, has three fuzzy values named normal, fatty and cirrhosis.

3.1.2. Step 2

First, determine the membership degrees for each of the given parameters MGL_i, $PER0.1_i$, CON_i, ENT_i, COR_i, ASM_i, ATT_i and d_i in all the different regions. For example MGL_1 has degree 0.8 in *High*, 0.3 in med and 0.09 in *Low*. Then, we assign the maximum degree of the three to the given parameter i.e. MGL_1 is *High*. Finally, obtain a rule from one pair of desired input–output data. e.g. the rule generated for the data ((MGL = 2.6, PER0.1 = 1.6, CON = 1.313, ENT = 5.113, COR = 0.682, ASM = 0.0084, ATT = 0.7782, d = 1.44), fatty) has the form: IF ((MGL is *Med*) and (PER0.1 is *Low*) and (CON is *Low*) and (ENT is *Med*) and (COR is *High*) and (ASM is *Low*) and (ATTEN is *High*) and (d is *Low*)) THEN pathology is fatty.



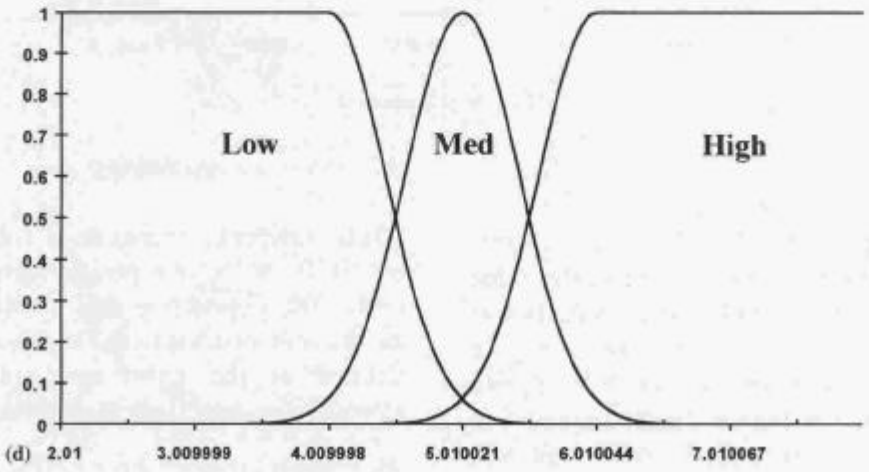
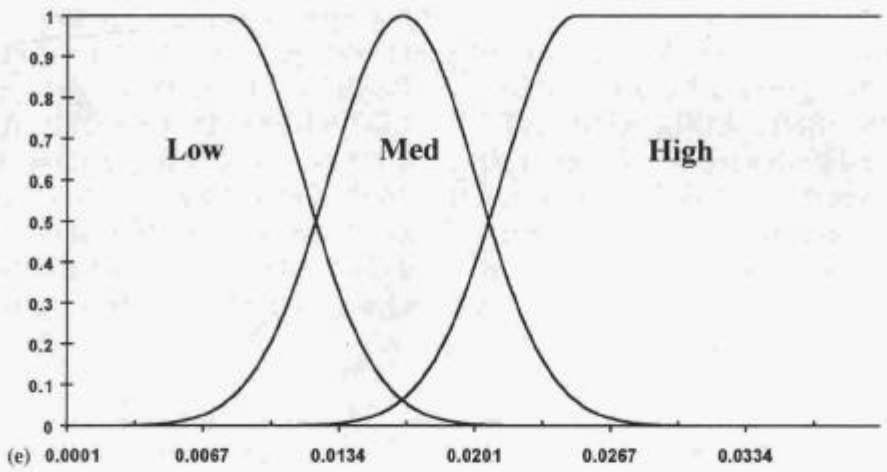


Fig. 3. (*Continued*)



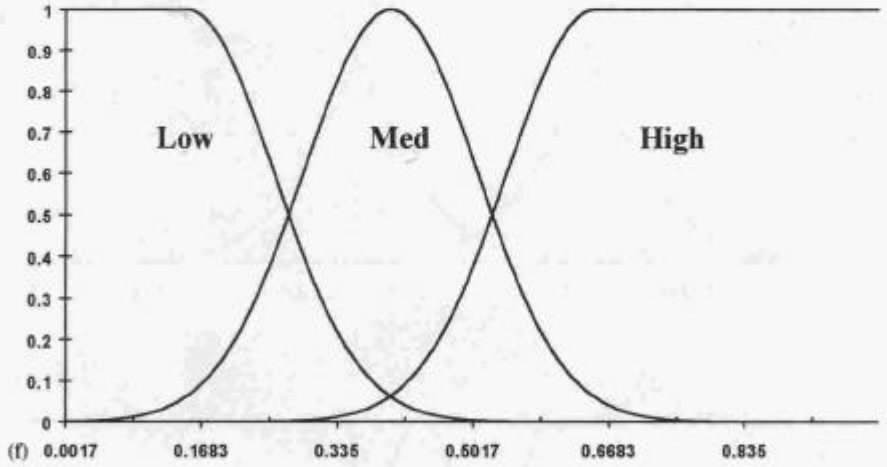


Fig. 3. (*Continued*)

3.1.3. Step 3

Rules validation: as every case generates one rule, it is probable that there will be some conflicting rules, i.e., rules that have the same IF part but have different THEN part. In our case no conflicted rules were reported, in future if this case happened we will append the rule having the higher degree of belief to our rule base system and the other rule will be excluded.

3.2. Inference mechanism

The inference mechanism used was based on SUP. MIN compositional rule of inference. The connective *and* is commonly used as the *min* operator, while the connective or defined as the *union* operator. The firing strength for each rule is as follows:

$$\alpha_{R_i} = \mu_{\mathrm{MGL}_{Ri}}(\mathrm{mgl}) \wedge \mu_{\mathrm{PER.1}_{Ri}}(\mathrm{per.1})$$

$\wedge\ \mu_{\mathrm{CON}_{Ri}}(\mathrm{con}) \wedge \mu_{\mathrm{ASM}_{Ri}}(\mathrm{asm}) \wedge \mu_{\mathrm{COR}_{Ri}}(\mathrm{cor})$

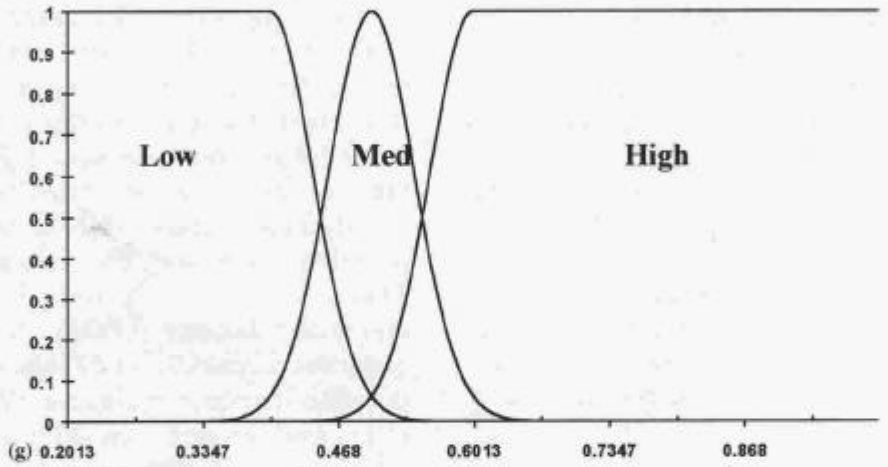
$\wedge\ \mu_{\mathrm{ENT}_{Ri}}(\mathrm{ent}) \wedge \mu_{\mathrm{ATTEN}_{Ri}}(\mathrm{atten}) \wedge \mu_{d_{Ri}}(d)$

where i runs along all the cases, $\wedge$ is the minimum operator. For each class of the three pathologies, we use the max operator for the firing strength corresponding to this class.

$$\alpha_p = \max(\alpha_{\mathrm{normal}}, \alpha_{\mathrm{fatty}}, \alpha_{\mathrm{cirrhosis}})$$

where p denotes the pathology and the decision is made based on α_p Finally we select among the three classes of pathologies, the one with the highest value, and consider the new case to belong to the corresponding class. By experience if α_p is less than 0.5 for an unknown case, the confidence will be low for decision.

The confidence of an unknown tested case characterized by its crisp data will be low



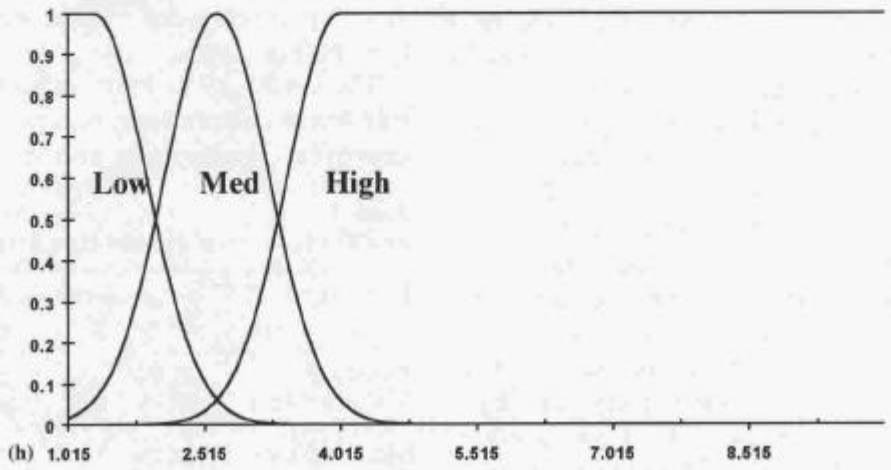


Fig. 3. (*Continued*)

($\alpha_p < 0.5$) if its data is far from that data used to generate the rules. As long as the data of an unknown case is close to the data used for generation of any of the rules, the firing strength of the corresponding pathology, α_p will be greater than 0.5.

If the firing strength α_p is less than the selected threshold (0.5), the decision will not be made based only on the previously extracted rules, however, after it is pathologically investigated, and correctly diagnosed, then the generated rule for this case is appended to the rule base. If there are two equal firing strength then the decision will be made for probability of both pathologies at the same time. For example if the firing of cirrhosis and fatty are the same and both > 0.5 then the clinician will go to the history information that can decide if the patient is fat or if he has a history of factors that may induce cirrhosis such as alcohol intake and so he will decide which of these two pathologies to take into consideration for his decision.

4. Results

The system was developed using 140 cases, these cases were classified into two sets one to generate the rules while the other to test the system (see Table 1). In the first stage of developing this system, for any new case (defined by a crisp data and pathologically diagnosed), this data is used to generate a new rule which appended to our data base rules. The number of generated rules till now presented a good match between the decision from the system and the pathology examinations. The illustration of the membership grades for all the significant parameters used in our analysis is shown in Fig. 3a–h. The number of rules is growing every day by appending a pathologically investigated and correctly diagnosed cases. Although the maximum number of the rules for (eight) inputs and three fuzzy values is (3^8), the number of cases used to generate the rules till now presented a good performance, matched with the clinicians supports and examinations.

Table 2
Results of fuzzy rule-based classification

Pathology	Training set	Test set
Specificity	100%	92%
Sensitivity for cirrhosis	100%	94%
Sensitivity for Fatty	100%	96%

The results of classification of different liver pathologies using our proposed fuzzy rule based system are shown in Table 2. The results of our previous work [19] using minimum distance classification, Bayes quadratic classification, voting k-NN classification and neural networks classification are shown in Tables 3–6 for comparison. The results for minimum distance (Table 3) and Bayes quadratic classification (Table 4), are lower than the subjective evaluation (70%) from the ultrasound images even after normalization for the data set. The results of voting k-NN classification (Table 5) and neural network classification (Table 6) are higher than the subjective evaluation from ultrasound images. We found that our fuzzy rule based system is much more specific and sensitive to liver pathologies.

The sensitivity to liver cirrhosis using fuzzy rule based classification is higher than neural networks classification and other classifica-

Table 3
Results of minimum distance classification

Pathology	Before normalization	After normalization
Specificity	29.4%	23.5%
Sensitivity for Cirrhotic	23.5%	0%
Sensitivity for Fatty	41.2%	76.5%

Table 4
Results of Bayes quadratic classification

Pathology	Before normalization	After normalization
Specificity	86.5%	56.8%
Sensitivity for Cirrhotic	16.2%	0%
Sensitivity for Fatty	70.3%	91.9%

tion techniques. The sensitivity to fatty liver using fuzzy rule based classification is comparable to voting k-NN classification and neural networks classification. Also we have the highest specificity using fuzzy rule based classification. The great advantage of this fuzzy rule based system analysis is its close nature to the subjective classification used by ultrasonographer where they diagnose liver using ultrasound by observing some of these parameters and write a linguistic clinical report with sentences such as 'liver parenchyma brightness is hyperechoic (high MGL), texture is heterogeneous (high ENT) and texture is coarse (high CON)'.

Table 6
Results of neural networks single perception classification

Pathology	Training set	Test set
Specificity	86.7%	88.3%
Sensitivity for cirrhosis	95.0%	91.7%
Sensitivity for fatty	100%	96.7%

5. Conclusions

The results of this work revealed the potential value for considering the idea of fuzzy reasoning in quantitative tissue characterization (QTC) of diffused liver diseases. The specificity and sensitivity for diagnosis of diffused liver diseases is much higher than the statistical classification techniques and is comparable to the neural networks techniques. This potential value could be used for an on-line diagnosis of the pathology, and minimize the risk of taking needle Biopsy from the patient. This approach has proven very powerful role in the differentiation of early cirrhosis from normal. The proposed system can be suggested for diffusely diseased organs like spleen, thyroid and kidney. The proposed system can be easily implemented on ultrasound machines hardware.

Table 5
Results of Voting k-NN classification

	Before normalization			After normalization		
k	Specificity	Sens. cirh.	Sens. fatty	Specificity	Sens. cirh.	Sens. fatty
1	94.1%	100%	94.1%	88.2%	100%	100%
2	100%	100%	93.3%	88.9%	100%	100%
3	81.3%	82.4%	94.1%	62.5%	94.1%	93.8%
4	84.6%	100%	94.1%	63.6%	93.3%	93.8%
5	82.4%	94.1%	94.1%	53.3%	87.5%	93.8%
6	75.0%	92.3%	94.1%	53.8%	100%	93.8%
7	80.0%	88.2%	100%	53.3%	87.5%	88.2%
8	78.6%	88.2%	94.1%	53.8%	86.7%	88.2%
9	81.8%	88.2%	94.1%	60.0%	93.3%	88.2%

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