Ultrasonographic Tissue Signature for Shistosomal Liver and Other Related Liver Pathologies

Ahmed M. Badawi*, Ahmed M. Hashem, Ahmed S. Derbala*, Aly Hendawi**, Abou-Bakr M. Youssef*, and Mohamed F. Abdel-Wahab****

*** Cairo University, Faculty of Engineering**

**** Cairo University, Faculty of Medicine**

Abstract— Ultrasound imaging is a non-invasive, sensitive method in the diagnosis of hepatic shistosomiasis, yet it is a subjective one. It is difficult to differentiate properly diffuse liver diseases during the early changes from normal pathology by visual inspection from the ultrasound images. In this study, 180 cases of bilharzial, cirrhotic, normal, and mixed liver pathologies are analyzed for clinical investigations, ultrasound measurements, pathological, and biochemical measurements.

The B-mode images are captured and analyzed for first and second order textural parameters, speckle parameters, attenuation parameter. The statistics done for various groups of pathologies indicated a significant differences between different groups. An unsupervised clustering algorithm is applied to the cirrhotic group to find subclasses of cirrhosis. The results of clustering showed a good match with that of pathological findings. This work can assist the sonographer to quantitatively and efficiently differentiate between diffuse liver diseases.

INTRODUCTION

Tissue characterization is a term that usually refers to the quantitative estimation of tissue or image features leading to a more accurate distinction of normal and abnormal tissues; the results of tissue characterization are quantitatively interpreted using numerical values. It aims to provide additional information about tissues not available by viewing ordinary images of the ultrasound B-scan. Thus; gained information are quantitative and is far less operator dependent than the usual B-scan images.

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 of medical diagnosis. 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. The physician has rely on detection of inhomogeneities between echo amplitudes received from the neighboring areas of the image. Such an approach is, of course, subjective and consequently problematic in itself. Moreover, in certain cases the disease attacks the entire tissue area, say, entire liver (diffuse liver diseases). Then, the ultrasonic image will be homogeneous (see figure 1), and as a result the diagnosis is sometimes difficult [1-8].

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 for these features is texture homogeneity. Its presence or absence can be widely debated between different experienced sonographers. Another feature is texture echogenicity 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 provides low diagnostic accuracy (around 70%) [1,,3,9-19]. Therefore the physicians may have to use further invasive methods such as the pathology investigation of 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 [9-12]. The quantitative analysis of using ultrasound signals as an aid to the diagnosis of diffuse disease has been described by many researchers [2-7 ,9-20].

The quantitative parameters measured for ultrasound tissue characterization are broad categories extracted from pulse-echo data (gray scale B-mode image). These are:

1-Image textural parameters: These are mean gray level (*MGL*), gray level variance (*VAR*), and five of the relevant gray level histogram *percentiles*. Co-occurrence matrix parameters, such as contrast (*CON*), entropy (*ENT*), correlation (*COR*), and angular second moment (*ASM*) [10].

2-Speckle Parameters: These are mean scatterer separation (d), diffuse and specular scatterer intensity (I_d,I_s), specular standard deviation (σ_s) and a few other related parameters [20].

3-Acoustic Parameters: These are attenuation coefficient (*ATTEN*) and the backscattering coefficient (*BSC*) [2,5,7,20,21].

DATA ACQUISITION AND METHODOLOGY

The following was done for the studied subjects:

1- Medical History and clinical examination.

2- Urine and stool examination for schistosomiasis ova.

0-7803-2940-6/95/$4.00

3- Liver function tests Serum bilirubin, ALT, and AST.
4- A blood sample is taken, serum is separated and kept frozen at (-40 °C). Collected serum samples are examined for: HBV seromarkers namely HBsAg, anti HBc and anti Hbs. For HBsAg positive cases, HBeAg + DNA polymease is done.
-HCV seromarker namely anti HCV (2 nd generation ELISA). For positive cases PCR is done .
-Serum procollagen III peptide (PIIIP) levels by RIA.
5- Conventional ultrasound examination stressing on:
* *Liver* size (in ML and MCL), texture, and hepatic veins.The diameter of 3 peripherally located portal tracts is measured and a mean is taken.
* *Spleen* size (taking its 3 dimensions) and echogenicity.
* Presence or absence of ascites.
6- Needle liver biopsy is taken for fit patients (satisfactory Prothrombin time and Concentration); sections taken are stained by conventional haematoxlin and eosin stains, periodic acidschiff and Masson trichrome (specific for fibrous tissue).
7- **Tissue characterization analysis steps:**

A) Image acquisition for the liver, 2 scans are acquired (subcostal and mid-line sections taking the caudate lobe) at 3.5 Mhz, images are corrected for TGC, diffraction and focusing of the beam using AIUM phantom[11-19], then a region of interest (R01) is taken, at least 2x2cm (64*64 pixels), for which different tissue characterization parameters are extracted.

B)Tissue characterization parameters extraction
The ROI is analyzed for the following parameters:

I- **Textural parameters:**

a) Histogram parameters
1) Mean gray level (MGL): defines the average gray levels in the region.
2) Image variance: defines the deviation of the echoes from the MGL.
3) Five different percentiles (0.1, 0.3, 0.5, 0.7, 0.9): defines the percent of all the gray levels reached at this level .
b) Co-Ocurrence matrix parameters
4) Contrast(CON): defines the coarseness of the texture
5) Entropy (ENT): defines the homogeneity of the texture
6) Correlation (CORR): defines the linnearity of the relationship of the gray levels
7) Angular second moment (ASM): defines the clustering of gray levels and different gray level transitions

II- **Acoustic parameters:**

8) Attenuation coefficient(a): defines the decay of the echoes levels with depth and frequency and is given in dB/cm Mhz
9) Back-scattering coefficient Mu(180): defines the amount of back-scattered power with respect to the incident.

III- **Speckle parameters:**

10) Speckle separation (d): defines the distance between which the speckles are ordered (ordering of structure)
11) Diffused intensity of scatters (Id): define the contribution of small scatterers to the image.
12) Specular intensity of scattereres: defines the contribution of large structure of scatterers to the image.

RESULTS AND CONCLUSION

The number of subjects studied are 40 shistosomal periportal fibrosis with various stages, 60 cirrhosis+chronic active hepatitis, 40 mixed livers and 40 normal livers. Their clinical, ultrasound findings are summarized in tables III, IV. Patients with cirrhosis showed more signs of liver cell failure and shrunken livers while schistosomal cases had more prevalent splenomegaly or history of splenectomy.
Conventional ultrasound findings are shown in Table IV.

Liver biopsy are done for all the patients. Cirrhosis was not present in pure shistosomal cases and periportal fibrosis granuloma were not seen in cirrhotic cases.
All the tissue characterization parameters statistics for all pathologies are tabulated in table I, II. The significance of every parameter in various group is clear. These parameters could be used to assist quantitatively the sonographer for accurate differentiation of diffused diseases.

An unsupervised clustering algorithm (self-organization Kohonen network) was applied to the cirrhotic group (60 cases) to determine how many subclasses could the cirrhotic class be divided into. The input vectors selected to include the following parameters (MGL, VAR. PER0.9, CONT, ENT, ATTEN, B.SC., d, PIIIP). The input vector is of 9^{th} dimension. The Kohonen self-organization feature map is a two layered network that can organize a topological map from a random starting point[22,23,24]. The resulting map shows the natural relationships among the patterns that are given to the network. Incoming patterns are classified by the units that activate in the competitive layer. Similarities among patterns are mapped into closeness relationships on the competitive layer grid. After training is complete, pattern relationships and groupings are observed from the competitive layer. When an input pattern is presented to the network at the input layer , the second layer units then sum their inputs and compete to find a single winning unit. The law that governs the updating of the weights is as follow:

$$w_{ji}(t+1) = w_{ji}(t) + \eta(t)[i(t) - w_{ji}(t)] \qquad (1)$$

where $w_{ji}(t)$ is the weight of the neuron ji in the map at iteration t, i(t) is the input at iteration t, $\eta(t)$ is the learning coefficient at iteration t. The winning neurons in the competitive layer are updated in the neighborhood of the winning neuron whose minimum distance is measured as:

$$d_{jp}(t) = \sum_{i=1}^{n_i} [i_i(t) - w_{ji}(t)]^2 \qquad (2)$$

where $d_{jp}(t)$ is the distance to neuron j for the t^{th} iteration of pattern p. Taking the size of the map to be 81 neurons, the learning rate is taken to be 0.2, for 1500 iteration, the size of initial neighborhood is taken as a fraction 0.5 of whole competitive layer. After training, the 60 input vectors of cirrhosis were classified into 3 main clusters. The output of these cluster were compared to the pathology of the cases, the error was 3.3% two cases were misclassified with respect to the

pathology. The three cluster are early cirrhosis, mild cirrhosis, and active cirrhosis.

In conclusion it was found that: - Ultrasonographic tissue characterization could add other information not readily available by conventional ultrasonography for diagnosis of diffused liver pathologies e.g.:

- Superadded hepatitis or cirrhosis on expectedly pure schistosomal cases.

- Degree of periportal fibrosis even early could be verified.

- The subclassification of liver cirrhosis could assist to diagnose variable degrees of cirrhosis.

This analysis could be used for the future work to monitor the progress of cirrhosis, and measure the effect of chemotherapy and various fibrinolytic agents.

REFERNCES

[1] Kossof G: Display techniques in ultrasound pulse echo investigations. JCU 2:61, 1974.

[2] Kevin J. Parker, Robert M. Lerner, Robert C. Waag, "Comparison of techniques for invivo attenuation measurements", IEEE Tran. on BME, vol. 35, NO. 12, Dec. 1988.

[3] Gosnik, B. B., Lemon, S.K., Scheible, W., Leopold, G. R., "Accuracy of ultrasonography in diagnosis of hepatocellular diseases", AJR, 133, 19-23, 1979.

[4] Chung-Ming Wu, Yung-Chang Chen, and Kai-Shang Hsieh, "Texture Features for Classification of Ultrasonic Liver Images.", IEEE Trans. on Medical Imaging, Vol. 11, NO. 2, June 1992.

[5] Roman Kuc, "Clinical Application of An Ultrasound Attenuation Coefficient Estimation Technique for Liver Pathology", IEEE Trans. on Biomedical Engineering, vol. BME-27, NO. 6, June 1980.

[6] Robert C. Waag,"A review of tissue characterization from ultrasonic scattering", IEEE Trans. on BME.,vol.31,NO.12, DEC. 1984.

[7] Kevin J. Parker, Robert M. Lerner, Robert C. Waag, "Comparison of techniques for invivo attenuation measurements",
IEEE Transaction on MBE, vol. 35, NO. 12, Dec. 1988.

[8] Oosterveld BJ, Thijssen JM, "Texture in Tissue Echograms Speckle or Information?" J Ultrasound Med 9:215-229, 1990.

[9] A. M. Youssef, A. A. Sharawi, IEEE symposium on ultrasound in philadelphia 1990 "K-sodata clustering analysis for diffuse liver disease".

[10] D. Sclaps, U. Rath, J. F. Volk, I. Zuna, A. Lorentz, K. J. Lehmann, D. Lorentz, G. V. Kaick, W. J. Lorentz, "Ultrasonic tissue characterization using a diagnostic expert system". In bacharach, S. L. edn. :Information processing in medical imaging, p. 343, Martinus Nijhoff, Dordecht, 1886.

[11] A. M. Youssef, A. A. Sharawi, Ahmed M. Badawi, IEEE symposium on ultrasound,philadelphia 1990, "Ultrasound velocity in cervix uteri for the diagnosis of cervical incompetence".

[12] A. M. Badawi, Salim M. Emara, A. M. Youssef, "Fuzzy reasoning in ultrasound tissue characterization of diffuse liver diseases", ICECS', IEEE 94, Dec., pp. 89-97.

[13] A. M. Badawi, Salim M. Emara, A. M. Youssef , "Ultrasound tissue characterization of diffuse liver diseases using fuzzy rules", IFSICC 94, Mar., pp. 288-289.

[14] A. M. Badawi, Ahmed M. Hashem, A. M. Youssef, M. F. Abdelwahab , "Invivo quantification of motion in liver parenchyma and its application in shistosomiasis tissue characterization", SPIE'95, Feb., vol. 2424 pp. 602-610.

[15] S. M. Emara A. M. Badawi, A. M. Youssef, "Fuzzy similarity measures for ultrasound tissue characterization", SPIE'95, Feb., vol. 2424 pp. 556-566.

[16] A. M. Badawi, A. M. Youssef, Annual Meeting of Egy. Society of Gastro. and Egy. Soc. of Ultras., December 1992,"Effect of Static Compression on the Acoustical and Textural Parameters of the Liver with Correlation to Diffuse Diseases".

[17] A. M. Badawi, A. M. Youssef, Annual Meeting of Egy. Soc. of Gastro. and Egy. Soc. of Ultrasonography, December 1992,"Tissue Characterization of Diffuse Liver Diseases Using Neural Nets".

[18] Yasser M. Kadah, Aly A. Farag, Abou-Bakr M. Youssef, Ahmed M. Badawi, ANNIE Nov. 93 St. Louis, Missouri,"Statistical and Neural Classifiers for Ultrasound Tissue Characterization"

[19] Yasser M. Kadah, Aly A. Farag, Abou-Bakr M. Youssef, Ahmed M. Badawi, SPIE Sept. 93 at Boston, Massachusetts,"Automatic Tissue Characterization from Ultrasound Imagery".

[20] Insana M. F, Wagner R. F., Garra B. S. et al,"Analysis of Ultrasound Image Texture via Generalized Rician Statistics", Opt Eng. 225:743, 1986

[21] Nicholas D, "Evaluation of Backscattering Coefficients for Excised Human Tissues, Results, Interpretation and Associated Measurement", Ultrasound Med Biol 8:17,1982

[22] Judith E. Dayhoff, "Neural Network Archeitectures An Introduction", Chap. 9, The Kohonn Feature Map.

[23] Teuvo Kohonen, "The self-Organizing map", Proc. of IEEE, vol. 78, No. 9, Sept. 1990, pp.1464-1480.

[24] Russell C. Eberhart, Roy W. Dobbins,"Neural Network PC tools", Academic Press.

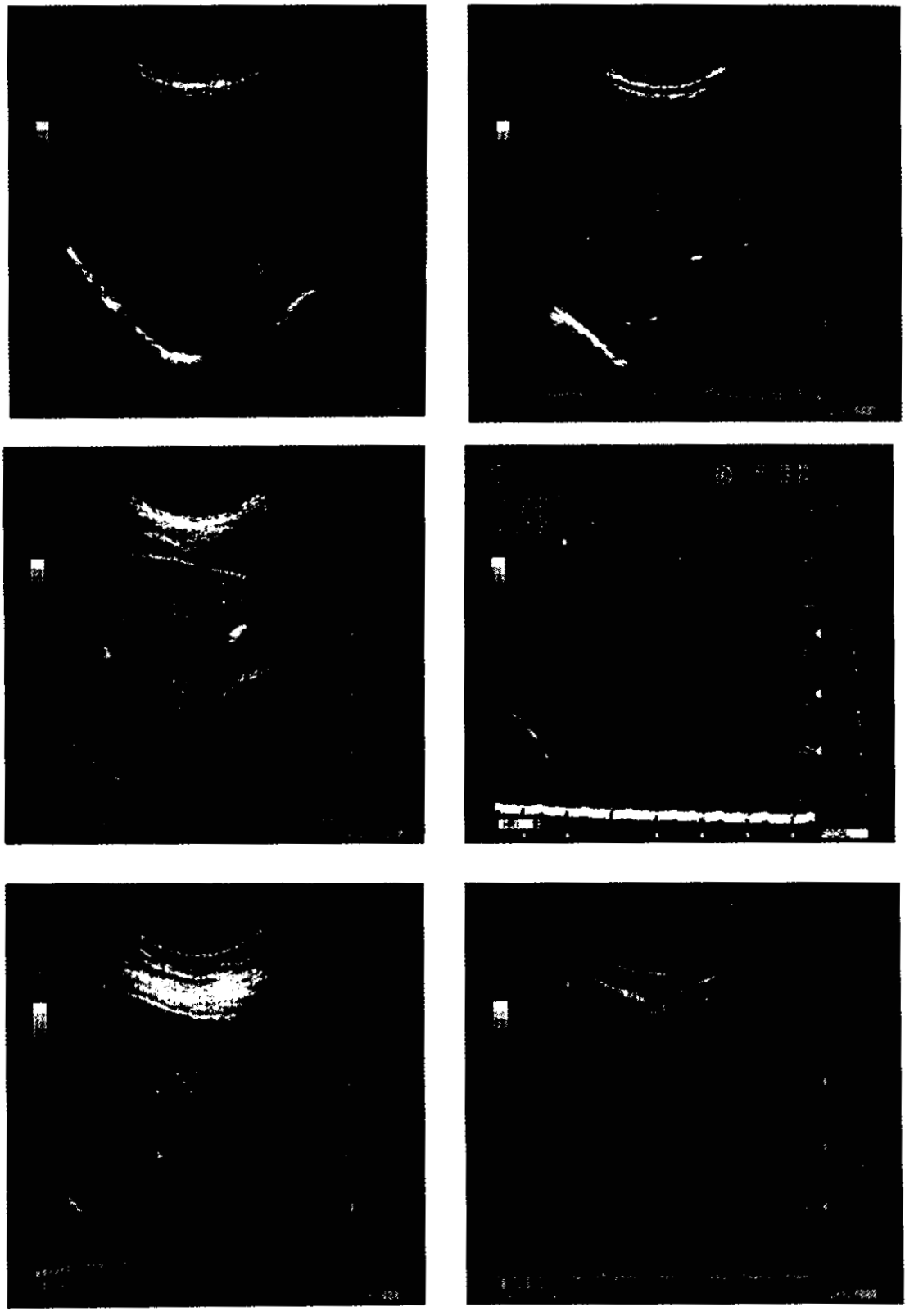

FIGURE 1. B-MODE IMAGES FOR NORMAL, B1, B2, EARLY CIRR., MILD CIRR., AND MIXED LIVERS (LEFT TO RIGHT)

TABLE I
STATISTICS FOR TISSUE CHARACTERIZATION PARAMETERS FOR DIFFERENT LIVER PATHOLOGIES

Params.	μ_b	σ_b	p-value	μ_c	σ_c	p-value	μ_m	σ_m	p-value
MGL	24.6	4.2	0.04	26.45	5.7	0.0082	25.88	4.63	0.0083
VAR	22.3	4.6	0.0002	35.3	6.22	0.0033	31.2	5.71	0.003
PER0.9	31.8	4.74	0.021	33.58	6.198	0.00286	33.32	5.55	0.0001
B.SC	0.003784	0.00041	0.0004	0.00399	0.00045	0.00021	0.00385	0.00055	0.00266
CONT	53.6	12.2	0.00054	58.49	16.2	0.0057	59.86	18.14	0.00019
ASM	0.00365	0.00107	0.244	0.00392	0.00137	0.2	0.00525	0.00123	0.688
ENTR	5.907	0.2449	0.00137	5.982	0.335	0.0036	6.0399	0.2911	0.000018
CORR	0.1151	0.088	0.626	0.095	0.066	0.7	0.135	0.108	0.277
ATTEN	0.561	0.090	0.00033	0.531	0.067	0.0012	0.5465	0.056	9*10E-6
d	2.4	0.8	0.0288	2.79	0.58	0.02	2.5	0.9	0.019
Id	55.3	19.9	0.65	53.8	24.11	0.84	55.7	27.5	0.68
Is	510.4	223.3	0.927	656.6	382.8	0.12	612.7	367.1	0.25
PIIP	6.642	1.167	6*10E-8	7.39	1.686	5*10E-8	7.254	1.674	3*10E-7

Note: b stands for shistosomal(bilharzial), c for cirrhosis, m for mixed, n for normal liver pathologies

TABLE II
STATISTICS FOR TISSUE CHARACTERIZATION PARAMETERS FOR SHISTOSOMAL CASES(GRADE I,II)

Params.	μ_{b1}	σ_{b1}	p-value	μ_{b2}	σ_{b2}	p-value	μ_n	σ_n
MGL	24.58	4.3	0.0581	25.26	3.73	0.036	21.2	2.21
VAR	20.1	3.5	0.038	23.5	4.2	0.012	18.2	4.1
PER0.9	31.5	4.9	0.0427	33.4	3.36	0.0176	28.3	3.6
B.SC	0.0037	0.00042	0.0035	0.00385	0.00046	0.00108	0.00341	0.00033
CONT	52.5	12.1	0.00157	60.32	12.6	0.00092	41.3	8.9
ASM	0.0037	0.00111	0.334	0.00334	0.00077	0.2364	0.0043	0.00117
ENTR	5.893	0.252	0.00343	5.993	0.232	0.022	5.647	0.282
CORR	0.121	0.087	0.485	0.077	0.093	0.608	0.1022	0.0921
ATTEN	0.555	0.0916	0.00093	0.598	0.084	0.00012	0.4721	0.039
d	2.377	0.782	0.0348	2.545	1.08	0.042	1.9	0.55
Id	53.88	20.1	0.669	64.4	18.5	0.29	52.5	22.2
Is	532.0	218.5	0.239	376.4	229.1	0.23	504.6	196.2
PIIP	6.768	1.221	1.65*10E-7	5.966	0.508	2.2*10E-4	3.47	0.711

Note: The black-bordered cells are not significant (p-value>0.5), b1,b2 stands for shistosomal grade I, II

TABLE III
CLINICAL FINDINGS IN STUDIED SUBJECTS

	Shisto. %	Mixed %	Cirr. %
General:			
- Jaundice	0	20	28.2
- Palmar erthema	0	20	20.5
- Spider navei	0	5.6	7.7
- Pollar	7.7	8.6	0
- LL edema	0	2.8	7.7
Abdominal:			
- Hepatomegaly	19.2	5.6	33.3
- Shrunken Liver	0	0	7.7
- Splenomegaly	34.6	61.5	30.8
- Splenectomy	3.8	0	0
* Hepatosplenomegaly	23.1	46.2	25.7
* Ascites	0	14.5	17.9
ALT elevation	26.9	57.1	41.1

TABLE IV
ULTRASOUND FINDINGS IN STUDIED SUBJECTS

	Shisto. %	Mixed %	Cirr. %
* Hepatomegaly	30.7	25.7	30.7
* Shrunken liver	0	2.9	7.7
* Liver Texture			
- Homogeneity	100	0	0
- Early coarsness	0	25.7	20.5
- Coarseness	0	61.5	51.3
- Brightness	0	8.7	28.2
* Portal tract thickening			
2.5≤3.0 mm	15.4	17.1	0
3.0-4.9 mm	69.2	77.1	0
5.0-6.9 mm	15.4	2.8	0
≥ 7 mm	0	0	0
* Hepatic vein attenuation	0	60	66.6
* Splenomegaly	65.4	88.6	64.1