Usefulness of Attenuation and Backscattering Coefficients in Investigating Complex Non-alcoholic Steatohepatitis from Ultrasound Images, Preliminary Results

Sergiu Nedevschi[1], Cristian Vicas[1], Delia Mitrea[1] Monica Lupsor[2], Mircea Grigorescu[2], Radu Badea[2]
[1] Technical University of Cluj-Napoca, [2] 3'rd Medical Clinic Cluj Napoca
sergiu.nedevschi@cs.utcluj.ro

Diagnosing liver non-alcoholic steatohepatitis (NASH) using non invasive procedures is challenging because the visual aspects in US imaging between healthy and affected liver are very much alike. Attenuation, backscattering coefficients along with the correlation coefficient and fit error are employed to determine the behaviour of the US beams into the liver tissue. The values of these coefficients generate features for a support vector classifier. It is investigated the role of each pathology component in altering the studied features. The possibility of using these features in clinical practice is also investigated. The results are promising, implemented methods can detect steatosis from US images with Area Under Curve value of 0.92. Identifying steatosis grades yields lower results because of the influence of the fibrosis.

1 Introduction

In literature the attenuation and backscattering coefficients were used to differentiate between healthy and affected liver [1][2][3]. Liver tissue is affected by several pathological modifications (steatosis, fibrosis, lobular inflammation etc). Our work studies the usefulness of these coefficients in evaluation of diffuse liver pathologies. Patients (investigated using liver biopsy and US imaging) are divided in groups. These groups are compared one by one by training a classification algorithm. Groups are chosen in such a way that, if possible, only a certain pathology (or pathology grade) varies between them. The resulting discrimination rates give us information about how much the studied pathology influences the coefficients. In this paper is proposed the use of two other features in order to increase the detection accuracy. The relevance of all these coefficients is also investigated. The final goal of our research is to train a classifier (or a meta-classifier) that will be able to recognize the steatosis grade regardless of the associated pathologies.

2 Methods

The coefficients are calculated on the B-mode ultrasound image. A straight line is fitted on all US images in such a way that it avoids major artefacts as in Figure 1 [2]. Two values are computed, the gray level of the pixel along the line and the depth of that pixel. The gray level is computed by averaging *n* pixels to the left and right of the line. The value *n* is a parameter for the algorithm and takes values of 7, 11 and 15 pixels.

Linear regression by least-squares approximation is applied to these values. The slope represents the attenuation coefficient and the offset (intercept) represents the backscattering coefficient. The new proposed features are the correlation coefficient r^2 and the fitting error (Figure 2).

Support Vector Machines algorithm is used as a classifier [4]. Classification performance is measured using the Cohen's Kappa statistic computed as shown in Figure 3. [5].

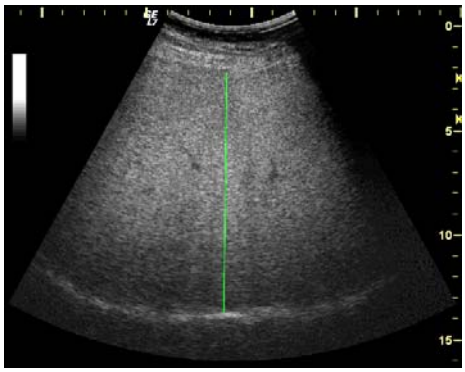

Fig 1. An ultrasound image with a straigt line fitted in such a way that it avoids artefacts

$$r = \frac{N\sum_i x_i y_i - \sum_i x_i \sum_i y_i}{\sqrt{\left[N\left(\sum_i x_i^2\right) - \left(\sum_i x_i\right)^2\right]\left[N\left(\sum_i y_i^2\right) - \left(\sum_i y_i\right)^2\right]}}$$

$$s^2 = \sum \frac{(y_i - (a + b \cdot x_i))^2}{n-1}$$

Fig 2. Correlation coefficient r and fitting error s^2. a and b are the coefficients of the regression line ($y=a+bx$) ; n is the number of points

$$K = \frac{P(a) - P(e)}{1 - P(e)}$$

Fig 3. Computing Cohen's Kappa statistic: *P(a)* is the relative observed agreement among rates and *P(e)* is the probability that agreement is due to chance.

Using 10 fold Cross Validation the mean and standard deviation for K is computed for each dataset. The relevance of the studied features is calculated using correlation-based feature evaluation [4].

From over 800 examined patients only 96 have NASH pathology and are suited for this study. Ultrasound images are acquired from the right lobe. Brunt score, fatty infiltration grade and fibrosis stage are recorded. A group of 22 clinically healthy patients were investigated using only ultrasound.

3 Results

Patients were grouped in such a way that only a pathological aspect varies between them. This is done in order to establish the discrimination power of implemented methods when applied to certain pathology. Not all the pathology grades could be evaluated because of the reduced patient volume. Another grouping was established in such a way that the patients share a common pathology grade (i.e. the same Brunt score) regardless of other pathologies. 465 comparisons were made. In the following are presented the most significant results. The detection rates of the Brunt scores with respect to normal lot are revealed in Table 1. The discrimination rates between various Brunt grades are lower because of the influence of steatosis and fibrosis.

Tab 1. Comparison between normal lot and Brunt grades.

Comparison case	Kappa
Normal – Brunt 1	0.7
Normal – Brunt 2	0.85
Normal – Brunt 3	0.99
Brunt 1 – Brunt 2	-0.01
Brunt 2 – Brunt 3	0.16

Next, the Brunt lots were divided according to the steatosis grades and fibrosis stages.

In Table 2 is shown the influence of fibrosis and fatty infiltration over steatohepatitis grade detection. In the first row is presented the discrimination rate between Brunt score 1 and Brunt score 2. The discrimination is almost 0. In the following two rows are the results after keeping only patients having fibrosis stage 2 and fatty grade 2 respectively. One can note that the discrimination rates are improved. In the second row (where the fibrosis stage is kept constant) the fatty can vary among the groups. In the third row, the fatty grade is kept constant and the fibrosis stage can vary. The fact that the discrimination rates are higher when only the fatty grade varies between groups indicates that the fatty infiltration is the best detected pathology by the methods presented here. Other lot divisions were performed but they have reduced patient volume. For this reason, no clear rule can be deduced on how fibrosis stages affect Brunt score detection, but it is clear that coexisting pathologies affect the detection rates.

Tab 2. The influence of fibrosis stage and fatty infiltration in steatohepatitis grade detection.

Comparison case	Kappa
Brunt 1 – Brunt 2	-0.01
Brunt 1 Fibrosis 2 – Brunt 2 Fibrosis 2	0.5
Brunt 1 Fatty 2 – Brunt 2 Fatty 2	0.2
Brunt 2 – Brunt 3	0.16
Brunt 2 Fibrosis 1 - Brunt 3 Fibrosis 1	0.75

Steatosis has the most important effect and it is investigated further. In Table 3 are the detection rates of steatosis. These detection rates are better than those from Brunt score.

Tab 3. Detection of steatosis (fatty infiltration) grades.

Comparison case	Kappa
Normal – Fatty 1	0.65
Normal – Fatty 2	0.9
Normal – Fatty 3	1
Fatty 1 – Fatty 2	0.34
Fatty 2 – Fatty 3	0.29

The next part focuses on detecting fatty infiltration and fatty infiltration grades. In addition to kappa statistic, Receiver operating characteristic curves are raised and the AUC (Area under Curve) is computed.

The 118 patients were divided in two groups, healthy patients and affected patients (having fatty infiltration ≥ 1). First group has 22 patients and the second has 91 patients. 5 patients have brunt score ≥ 1 but no fatty infiltration and they were excluded. 60 parameter sets for SVM algorithm were tested. 30 parameters were applied using a polynomial kernel and 30

using a RBF kernel. Using 10 fold cross-validation and 66% of the data, the best parameter combination was determined. The rest of the data (33%) was used to infer the kappa statistic. The process was repeated 5 times and the mean kappa value was recorded. A value of K=0.69 and AUC=0.928 was found. These results indicate that the methods presented here could be used in clinical practice in order to detect patients affected by fatty infiltration.

Another clinically important decision is to discriminate between low fatty infiltration and severe steatosis. We divided the patients in low fatty (grade 0,1) and high fatty (grade 2,3)

The kappa value was computed using the procedure described above. The computed values were: K=0.67 and AUC=0.919.

We investigated the discrimination rates between steatosis grades. The patients were divided in groups having steatosis grade 0 (healthy patients) 1,2 and grade 3. Kappa and AUC values were computed as described above. The results are presented in Table 4.

Tab 4. The discrimination between various fatty infiltration grade

Computed statistic	Value
Kappa statistic	0.37
AUC for healthy lot	0.923
AUC for steatosis grade 1	0.703
AUC for steatosis grade 2	0.701
AUC for steatosis grade 3	0.83

Another division was performed according to fatty infiltration grade but we include only the patients having low fibrosis stage. The results are presented in Table 5.

Tab 5. The discrimination between various fatty infiltration grade at patients having low fibrosis stage (0,1)

Computed statistic	Value
Kappa statistic	0.46
AUC for healthy lot	0.919
AUC for steatosis grade 1	0.788
AUC for steatosis grade 2	0.726
AUC for steatosis grade 3	0.928

Another aspect of interest is the relevance of the implemented features. Correlation-based feature evaluation in combination with 10 fold cross-validation on the entire patient lot was performed. From each fold the relevant features are noted. In Table 6 are the features that appear relevant in all folds.

Tab 6. The feature relevance computed on entire patient lot

Feature
Slope computed at 7 pixels
Offset computed at 7 pixels
R^2 computed at 7 pixels
Slope computed at 15 pixels
Offset computed at 15 pixels
R^2 computed at 15 pixels

4 Discussion

Over 450 comparison cases were investigated in order to evaluate the impact of fatty and fibrosis on US image. The hepatocyte ballooning, inflammation and necrosis have their effect

on the US image, but steatosis has the most important impact.

The reduced patient volume didn't allow investigating all pathology combinations.

More patients have to be investigated in order to assess the impact of these pathological modifications on the ultrasound image.

Implemented methods can be used to discriminate between healthy patients and patients with fatty infiltration with high accuracy. Also, these methods allow distinguishing between various steatosis grades but with lower accuracy.

Fibrosis alters the absorption of US waves. Detection rates of fatty grades are higher when only the patients having lower fibrosis stages are considered. It is supposed that the fibrosis could increase the scattering of the US waves and its effect overlaps with the effect of fatty. Unfortunately the number of patients having higher fibrosis grade (2 or 3) was low and no relevant conclusions could be inferred.

Attenuation, correlation coefficient and backscattering are the most significant features in detecting fatty infiltration and steatohepatitis.

5 Conclusions

Attenuation, backscattering and correlation coeficients can be successfuly employed to distinguish between normal liver and moderate/severe steatohepatitis.

Fibrosis along with fatty infiltration affects the behaviour of US wave into the liver tissue. The effect of fibrosis on implemented features is lower than the effect of steatosis but this effect increases with the fibrosis stage. Even if the number of patients having high fibrosis stage was not significant, we can say that one should consider the fibrosis stage when discriminating the steatosis grades.

Proposed coefficients increase the detection accuracy and allow us to discriminate between various steatosis grades even when there are overlapping pathologies.

The results show that it is possible to assess the steatosis and steatohepatitis grade based on US images. New features have to be considered [6], features that could indicate the fibrosis stage. More patients have to be investigated in order to clearly determine the impact of each pathology grade over the liver tissue.

Acknowledgement

This work was sponsorised by the Romanian National Authority for Scientific Research as part of the CEEX program FINALISM 94/31.07.2006 and SIDEF 71/17.07.2006.

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