The performance of the attenuation coefficient computed on the ultrasonic image in quantifying steatosis in chronic liver disease, compared to the classical US examination

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Aims and objectives

- Hepatic steatosis is a frequent histological finding in patients with chronic liver diseases (CLD).
- The current "gold standard" for evaluating steatosis is liver biopsy, but it is invasive and may result in severe complications [1]. Furthermore, liver biopsy also has potential sampling errors and cannot be readily repeated for adequate patient follow-up [2].
- Ultrasonography (US) is the most commonly noninvasive imaging modality used for evaluating hepatic steatosis [3], but it cannot establish with certainty the degree of fatty infiltration and also cannot differentiate steatosis from fibrosis.
- We aim to evaluate the performance of a new parameter - attenuation coefficient (AC) computed on the US image in quantifying steatosis in CLD, compared to classical US examination.
Methods and materials

- 682 consecutive histological proven CLD patients (508 HCV, 74 HVB, 100 NASH) examined at Regional Institute of Gastroenterology and Hepatology, University of Medicine and Pharmacy Cluj-Napoca, Romania, were prospectively included in this study.
- All of them underwent percutaneous liver biopsy (LB) for grading and staging the disease.
- The epidemiological data and the biological parameters were determined on the same day as the LB.

Ultrasound exam

- Each patient was submitted to an abdominal ultrasound exam by means of a GE Logiq 7 device, using a 5.5 MHz convex probe, one day before the LB.
- We observed the classical US criteria for the hepatic steatosis diagnosis (hepatomegaly with increased echogenicity and posterior attenuation of the ultrasound). Considering the existence of this modification, it was performed a semi quantitative determination of the steatosis:

1. Mild steatosis - slow increase of hepatic echogenicity, with normal visualization of diaphragm and intrahepatic vessels' wall
2. Moderate steatosis - moderate increase of hepatic echogenicity, with difficult visualization of diaphragm and intrahepatic vessels' walls
3. Severe steatosis - highly increased hepatic echogenicity, with no visualization of diaphragm, of intrahepatic vessels' walls and the posterior part of right hepatic lobe

Computing the image coefficients

- The examination protocol was built to acquire the maximum amount of information from the tissue level, with as little "noise" as possible overlaid to this process. Once the setting took place, it was used for all the examined patients.
- For each patient, US images were acquired from the right lobe through intercostal spaces.
- The images were saved on the ultrasound machine hard disk in DICOM format and further processed using a special soft designed by the Technical University of Cluj-Napoca.
- On each US image, a straight line was fitted so as to avoid artefacts. This line represents the ultrasound beam path into the liver tissue and it has to be as parallel as possible to the US rays, preferably vertical. The fitted line is the region of interest (fig.1).
The grey level values for each point along this line are calculated by averaging 7 horizontal pixels (the pixel under the line and three more pixels from each side) [4]. For each point of the line, two values were stored: the average grey level computed as above and the depth (in millimeter units) (fig.2).

As a measure of ultrasonic attenuation, linear regression by least-squares approximation was applied to this dataset. The slope of this line (in grey-level units per mm) represents the attenuation coefficient [5].

**Histological study**

- liver biopsy was performed by using the TruCut technique with a 1.8 mm (14G) diameter automatic needle device - Biopty Gun (Bard GMBH, Karlsruhe, Germany).
- liver biopsy specimens were fixed in formalin and embedded in paraffin
- the slides were evaluated by a single expert pathologist
- only biopsy specimens with more than 6 intact portal tracts were eligible for evaluation.
- Liver fibrosis stage and necroinflammatory activity grade were evaluated according to the Metavir scoring system in all patients, except those with NASH, evaluated according to the Brunt system [6-8].
- **Steatosis** was categorized in all patients by visual assessment as:
  1. S0 - none
  2. S1 - steatosis in <33% of hepatocytes
  3. S2 - steatosis in 33% to 66% of hepatocytes
  4. S3 - steatosis in > 66% of hepatocytes.

**Statistical analysis**

- statistical analysis was performed using the SPSS software version 15.0 (SPSS Inc., Chicago, IL, USA)
- attenuation coefficient (AC) data were expressed as mean values.
- differences in mean values were tested by one-way analysis of variance (ANOVA) and Kruskal-Wallis test; relationships between the parameters were characterized using the Spearman correlation coefficients.
- the diagnostic performance of AC was assessed using sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), likelihood ratios (LR) and receiver operating characteristic (ROC) curves. Optimal cut-off values for AC were chosen to maximize the sum of sensitivity and specificity, and positive and negative predictive values were computed for these cut-off values.
Images for this section:

**Fig. 1:** Ultrasound image of the right lobe at 16 cm. The mean grey levels are computed along the white line.

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Fig. 2: The graphic representation of the average grey level in relation to depth

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Results

# Baseline characteristic of patients

- most patients were female (58.47%)
- median age: 46.62 years
- the mean size of the liver biopsy sample: 11.14 mm
- mean number of portal spaces: 12.15.

# Correlation between the attenuation coefficient and different histological parameters

- In univariate analysis, AC values were significantly correlated with steatosis, balloning and lobular inflammation, but there was no significant correlation with activity or fibrosis.
- Among the histopathological factors correlating with AC, the multivariate analysis found steatosis as the only factor influencing independently AC in CLD patients (table 1)

# The mean values of AC for each steatosis grade

The differences were statistically significant between all the steatosis grades, except S2 vs S3 (table 2, Fig. 3).

# AC cut-off values

Table 3 shows the optimal cut-off values as well as the corresponding sensitivity, specificity, positive and negative predictive values.

Fig.4 shows the ROC curves according to different steatosis grade thresholds: S0 versus S1, S2 and S3 patients (S#1), S0 and S1 versus S2-S3 patients (S#2) and S0-S1-S2 versus S3 (S3).

# The comparative value of the classical ultrasonography and the attenuation coefficient in steatosis grading

- The major benefits of using the attenuation coefficient are the important increase of the classical US specificity and positive predictive values for the steatosis grading (table 4)
Table 1: Univariate and multivariate analysis of histopathological factors independently influencing the AC values in CLD patients

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<table>
<thead>
<tr>
<th>Factors</th>
<th>Correlation coefficient (Spearman)</th>
<th>p</th>
<th>Multivariate analysis (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steatosis</td>
<td>-0.454</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fibrosis (Metavir)</td>
<td>-0.010</td>
<td>0.214</td>
<td>-</td>
</tr>
<tr>
<td>Necroinflammatory activity (Metavir)</td>
<td>-0.030</td>
<td>0.220</td>
<td>-</td>
</tr>
<tr>
<td>Fibrosis (Brunt)</td>
<td>-0.024</td>
<td>0.897</td>
<td>-</td>
</tr>
<tr>
<td>Ballooning (Brunt)</td>
<td>-0.210</td>
<td>0.033</td>
<td>0.9457</td>
</tr>
<tr>
<td>Lobular inflammation (Brunt)</td>
<td>-0.247</td>
<td>0.009</td>
<td>0.5672</td>
</tr>
</tbody>
</table>

Table 2: The mean values of AC for each steatosis grade

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<table>
<thead>
<tr>
<th>AC</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>S0</td>
<td>-0,0011</td>
<td>0,0917</td>
<td>-0,2705</td>
<td>0,4593</td>
</tr>
<tr>
<td>S1</td>
<td>-0,0556</td>
<td>0,0859</td>
<td>-0,3356</td>
<td>0,2193</td>
</tr>
<tr>
<td>S2</td>
<td>-0,1214</td>
<td>0,0922</td>
<td>-0,3386</td>
<td>0,0905</td>
</tr>
<tr>
<td>S3</td>
<td>-0,1411</td>
<td>0,1032</td>
<td>-0,3174</td>
<td>0,1248</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AC cutoff value</th>
<th>( \geq S1 ) (S0 vs S123)</th>
<th>( \geq S2 ) (S01 vs S23)</th>
<th>S3 (S012 vs S3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Se (%)</td>
<td>( \leq -0,0471 )</td>
<td>( \leq -0,0821 )</td>
<td>( \leq -0,1474 )</td>
</tr>
<tr>
<td>Sp (%)</td>
<td>50,73</td>
<td>79,66</td>
<td>66,67</td>
</tr>
<tr>
<td>+LR</td>
<td>92,72</td>
<td>76,47</td>
<td>91,60</td>
</tr>
<tr>
<td>-LR</td>
<td>6,96</td>
<td>3,39</td>
<td>7,93</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>0,53</td>
<td>0,27</td>
<td>0,36</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>88,8</td>
<td>43,1</td>
<td>32,0</td>
</tr>
<tr>
<td>AUROC</td>
<td>0,790</td>
<td>0,853</td>
<td>0,845</td>
</tr>
</tbody>
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Table 3: Performance of AC in steatosis grading.

- **Se (%)**: 61.47, 50.73, 0.0001
- **Sp (%)**: 84.84, 92.72, <0.0001
- **PPV (%)**: 82.28, 88.8, 0.0009
- **NPV (%)**: 39.63, 62.4, <0.0001

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<th>S012 vs S3</th>
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<tr>
<td><strong>Usual US</strong></td>
<td>68.64</td>
<td>79.66</td>
<td>69.44</td>
</tr>
<tr>
<td><strong>AC</strong></td>
<td>70.39</td>
<td>76.47</td>
<td>87.85</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td>&lt;0.0001</td>
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Table 4: The comparative value of the classical ultrasonography and the attenuation coefficient in steatosis grading.

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**Fig. 3:** The mean values of AC for each steatosis grade

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![Graphs showing sensitivity vs. 100-specificity for different steatosis grade thresholds](image)

**Fig. 4:** The ROC curves according to different steatosis grade thresholds

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Conclusion

The use of attenuation coefficient computed on the US image could substantially improve the ability of the usual US for the assessment of steatosis grade. The attenuation coefficient could be used to develop an imaging method for the detection of liver steatosis that is less operator dependent.
Personal information

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