Using Texture Analyses of Contrast Enhanced CT to Assess Hepatic Fibrosis

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Authors: N. Daginawala¹, B. Tischler¹, K. Buch², H. Yu¹, B. Li¹, J. A. Soto¹, S. Anderson¹, ¹Boston, MA/US, ²Westborough, MA/US
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Aims and objectives

Hepatic fibrosis results from chronic insults such as viral hepatitis, alcohol, and non-alcoholic fatty liver disease (NAFLD). Cirrhosis is characterized by advanced hepatic fibrosis with scarring and formation of regenerative nodules. Patients with cirrhosis are at increased risk of developing complications such as portal hypertension, liver failure, and the development of hepatocellular carcinoma, among others. Therefore, the early detection and staging of fibrosis and cirrhosis is of great clinical importance as this may lead to timely diagnosis and the initiation of appropriate therapeutic regimens.

The current gold standard for staging of fibrosis is with percutaneous biopsy which has several limitations to consider including that it is invasive, is subject to inter and intra-observer variability, and is subject to sampling error due to heterogeneous distribution of fibrosis in the liver. (1-3) Given the limitations of percutaneous biopsy, the development of non-invasive methods of evaluating hepatic fibrosis with the ability to distinguish between lower and higher grades of hepatic fibrosis is of significant clinical importance, as they yield the potential for repeatable assessments with minimal risk and patient discomfort. Therefore, a variety of noninvasive methods, including the use of serum markers, ultrasound-based transient elastography, and MR-based imaging approaches have been evaluated and shown promise in their ability to diagnose and stage fibrosis [4-6]. To date, when compared to other imaging-based approaches such as ultrasound-based transient elastography or MRI, the reported applications of CT imaging to the assessment of hepatic fibrosis have been markedly fewer. [7] However, CT offers unique advantages, including its nearly ubiquitous availability, whole organ imaging capacity, and when compared to MRI, relatively low cost and fewer on page contraindications.

Texture analysis allows for the quantitative analysis of a wide range of morphologic and physiologic properties of living tissues, including complex texture features that are not visible to the human eye. Texture analysis of biomedical imaging data has been widely employed in the analysis of a number of different pathologies and organ systems such as the liver, thyroid, breasts, kidneys, prostate, heart, brain, and lungs [8-11]. Given the advantages of CT imaging and the strengths of texture analyses in biomedical imaging, this study aims to evaluate the utility of texture analyses of contrast-enhanced CT images in evaluating the degree of liver fibrosis in patients with chronic liver disease.
Methods and materials

The institutional review board approved this retrospective study. For this study, patients who had non-targeted ultrasound-guided liver biopsies performed within 6 months of a portal venous phase contrast-enhanced CT examination of the abdomen between December 2005 and April 2013 were included. Patients were excluded from the study if biopsy showed tumor or granulomatous involvement of the liver. The pathology reports of the 83 patients meeting our inclusion criteria were queried in our institutional electronic medical record to identify the results of each individual’s ultrasound-guided percutaneous liver biopsy. The degree of fibrosis which had been reported for each patient, graded on a scale from 0-6 and based on the Ishak fibrosis scoring were recorded for each patient.

Using a dedicated AW workstation (GE Healthcare, Cleveland, OH), a single radiologist (blind) manually segmented five 1.25 mm thick axial images at the level of the porta hepatis. The visualized vessels within the segmented portions of the liver were identified by the radiologist and manually omitted from the final segmented liver image (Figure 1). Following segmentation, an in-house developed, MATLAB-based texture analysis program was employed to extract 42 texture features (Table 1) from each segmented volume of liver. 13 histogram features, 5 gray level co-occurrence matrix (GLCM) features, 11 gray-level run-length (GLRL) features, 4 gray level gradient matrix (GLGM) features, and 9 Laws features, were computed and averaged over the 5 images per patient.

Histopathologic grades of hepatic fibrosis (Ishak Fibrosis Staging Scale) were correlated with texture parameters after stratifying the patients into two analysis groups comparing Ishak scale 0-2 with 3-6 and 0-3 with 4-6. A classification and regression tree analysis (CART) was performed to find texture features most correlated with the grade of hepatic fibrosis. Using the 9- neighborhood standard deviation, average CT number, and Laws features texture parameters low level of fibrosis (0-2) versus high levels of fibrosis (3-6) were correlated and sensitivity, specificity, and positive predictive value were calculated. Similarly, the mean gradient, mean attenuation coefficient, and Laws features texture parameters were used to correlate low to moderate level fibrosis (0-3) versus higher levels of fibrosis (4-6).
Images for this section:

![Contrast enhanced portal venous phase axial image of the liver with a fibrosis score of 0 (right) and 6 (left) after segmentation on the AW workstation. Texture analysis was able to correctly distinguish textural differences in the normal and cirrhotic liver.](image)

**Fig. 1:** Contrast enhanced portal venous phase axial image of the liver with a fibrosis score of 0 (right) and 6 (left) after segmentation on the AW workstation. Texture analysis was able to correctly distinguish textural differences in the normal and cirrhotic liver.

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<table>
<thead>
<tr>
<th>Histogram features</th>
<th>gray level co-occurrence matrix</th>
<th>gray-level run-length</th>
<th>gray level gradient matrix</th>
<th>Laws features</th>
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<tr>
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<td>short run emphasis</td>
<td>mean</td>
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<td>contrast</td>
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<td>skewness</td>
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<td>run percentage</td>
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<td>Laws feature 5</td>
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<tr>
<td>harmonic mean</td>
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<td>Laws feature 6</td>
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<tr>
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<td>high gray-level run emphasis</td>
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<td>Laws feature 7</td>
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<tr>
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<td>Laws feature 9</td>
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<tr>
<td>IQR</td>
<td>long run high gray-level emphasis</td>
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<td>test</td>
<td>entropy</td>
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**Table 1:** List of the 42 texture parameters falling into 5 different categories that were evaluated.
Results

Our patient population consisted of 83 patients with hepatic fibrosis scores as follows: 16 patients with a score of 0, 18 patients with a score of 1, 15 patients with a score of 2, 11 patients with a score of 3, 2 patients with a score of 4, and 5 patients with a score of 5, and 16 patients with a score of 6. (Figure 2)

CART analysis found that the 9- neighborhood standard deviation, average CT number, and Laws features texture parameters (Figure 3) were most correlated with the ability to distinguish patients with low levels of fibrosis (0-2) versus high levels of fibrosis (3-6) and demonstrated a sensitivity of 97%, specificity of 94%, and PPV of 92%. Additionally, for distinguishing low to moderate level fibrosis (0-3) versus higher levels of fibrosis (4-6) CART analysis demonstrated the mean gradient, mean attenuation coefficient, and Laws features texture parameters (Figure 4), obtained a sensitivity of 82%, specificity of 98%, PPV of 95%. (Table 2)
Fig. 2: Distribution of fibrosis scores. 83 patients were included with fibrosis scores ranging from 0 to 6.

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Fig. 3: CART decision tree comparing low level of fibrosis (0-2) versus high levels of fibrosis (3-6) demonstrates the 9- neighborhood standard deviation (std.9), average CT number (mean), and Laws features (L6) texture parameters correlate best with histopathologic fibrosis score.

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Fig. 4: CART decision tree comparing low to moderate level fibrosis (0-3) versus higher levels of fibrosis (4-6) demonstrate the mean gradient (MGR), mean attenuation coefficient (Mean), and Laws features (L5) texture parameters correlate best with histopathologic fibrosis score.

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<table>
<thead>
<tr>
<th>Fibrosis Score</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
</tr>
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<tr>
<td>0-2 vs 3-6</td>
<td>97%</td>
<td>94%</td>
<td>92%</td>
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<tr>
<td>0-3 vs 4-6</td>
<td>83%</td>
<td>98%</td>
<td>95%</td>
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Table 2: Sensitivity, specificity, and positive predictive value (PPV) of texture parameters in predicting liver fibrosis using classification and regression tree analysis (CART) on contrast enhanced CT.

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Conclusion

In patients with chronic liver disease, grading of fibrosis levels is of great clinical importance to guide therapy and assess prognosis. Texture analysis of contrast enhanced CT offers a promising alternative to the current gold standard of biopsy as it offers a noninvasive and repeatable method of assessment. Visual assessments of images by the human eye alone are subject to interobserver variability. Texture analysis offers a potential avenue to detect subtle texture features not perceived by the human eye and offers a quantitative approach to analyzing these differences. The results reported in this study demonstrate the potential utility of contrast-enhanced CT for this application. Specifically we found a sensitivity of 97%, specificity of 94%, and a PPV of 92% for discriminating patients with low levels of hepatic fibrosis from those with high levels of fibrosis and a sensitivity of 82%, specificity of 98%, PPV of 95% for discriminating patients with low to moderate levels of fibrosis from higher levels using a CART analysis approach. Further studies involving refining such techniques has the potential of further increasing accuracy, perhaps allowing for the highly accurate staging of fibrosis.
References


