Wavelet Analysis of Liver Fibrosis

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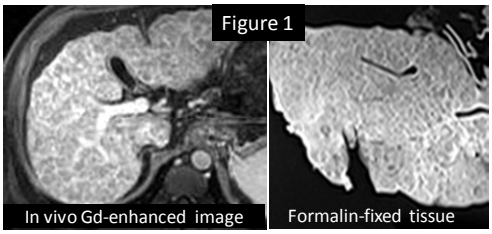
Introduction: Chronic liver disease (CLD) due to Hepatitis B/C infection or non-alcoholic steatohepatitis (NASH) is a major health problem in the USA and worldwide [1]. The first manifestation of CLD is liver inflammation, which can progress to fibrosis and liver cancer. Fibrosis is characterized by structural changes in the liver due to the deposition of collagen and staging is important for patient management. Staging of liver fibrosis requires a biopsy which is an invasive procedure with associated morbidity, cost, and sampling errors. Magnetic Resonance Elastography (MRe) has been proposed as an alternative to biopsy. The technique yields a measurement of the liver stiffness as a surrogate of fibrosis [2]. MRe requires specialized equipment, training of the personnel performing the procedure, and the measure of liver stiffness may not be sensitive to early stages of fibrosis. The goal of this study is to investigate if the structural changes that occur in the liver due to fibrosis can be detected by a localized frequency analysis of the liver images using wavelets.



Methods: The study was performed in ex-vivo liver samples fixed in 10% formalin. We have observed that treatment of ex-vivo tissue with formalin imparts signal characteristics to fibrotic structures that resemble the signal enhancement observed at the delayed phase of Gd contrast-enhanced images in vivo. The similarities between Gd-enhanced in vivo images and the images of the formalin-fixed ex vivo tissue for advanced cases of fibrosis are shown in Fig. 1.

Images of three ex-vivo tissue samples representing a normal liver, a liver with intermediate fibrosis, and a liver with advanced fibrosis were acquired on a 3T Siemens scanner using a T1-weighted 3D gradient echo sequence (TR/TE/α=15ms/2.38ms/40^o). Data were acquired with high spatial resolution (0.35 mm^3) and at resolutions closer to typical clinical resolutions. 2-D stationary wavelet analysis using a 5-level dyadic decomposition was performed on representative slices of each of the three tissues. The Daubechies orthogonal wavelet with one vanishing moment [3] was used. Mean value of the absolute wavelet coefficients in each subband was used to quantify signal energy in each subband.

Results: Figure 2(top) shows high resolution images of the tissue samples. It is clear from the zoomed region for each tissue that there are structural differences between the advanced and normal cases. There are high frequency structures in the tissue with advanced fibrosis whereas the normal tissue has a smoother appearance. The intermediate case has areas of localized disease associated with high frequency structures as well as areas with a smoother appearance.

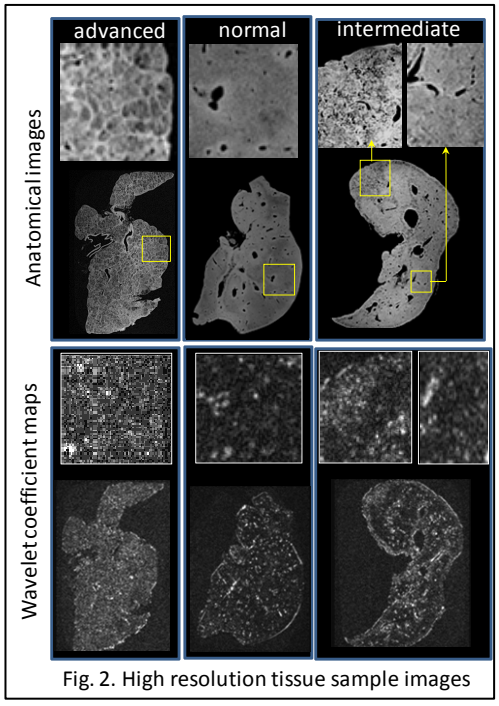


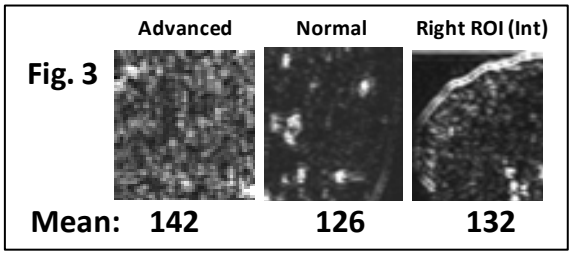
Fig. 2. High resolution tissue sample images

Figure 2(bottom) shows the corresponding level 1 (highest spatial frequency content) wavelet subband for the HL orientations. The tissue with advanced fibrosis has larger coefficients (higher intensity) throughout compared to the normal tissue, where only regions around blood vessels show large coefficients. The intermediate tissue shows areas with larger coefficients localized in different regions of the tissue. These correspond to the regions with structural features similar to the advanced fibrotic tissue. Other areas have lower coefficient values and these correspond to areas with smoother appearance similar to the normal tissue.

Table 1	Mean of absolute wavelet coefficient			
	Advanced	Normal	Intermediate	
			Left-ROI	Right- ROI
Level 1	133.3	97.3	129.9	110.1
Level 2	339.3	254.4	364.8	324.7
Level 3	709.5	564.6	715.7	886.6
Level 4	1121.1	1275.9	1249.1	1443.8
Level 5	1708.3	2821.2	1681.1	2975.0

Table 1 shows the mean of the absolute value of the wavelet coefficients for the HL orientation for various levels. In level 1 (highest frequency content) the structural features associated with disease have a higher mean than the structures associated with normal tissue. As the frequency content is shifted to low frequencies (higher decomposition levels in the wavelet analysis) the pattern is reversed, as expected.

The results shown above were obtained for tissue samples imaged at high resolution because structural features are better depicted in the anatomical images. A wavelet analysis on lower resolution images showed the same trend as the high resolution samples. The HL wavelet subband for level 1 for the selected regions within the three tissues are shown in Fig. 3 together with the means of the absolute values of the wavelet coefficients. The data were acquired with a resolution of 0.74x1.0x1.0 mm^3, which is attainable in a clinical setting. Note that that the tissues corresponding to advanced and intermediate disease have higher wavelet coefficients compared to the normal tissue.



Conclusions: A wavelet analysis was performed in ex vivo tissue samples that mimic Gd-enhanced in vivo images. The results showed that regions containing high frequency structures can be isolated with wavelets and parameters derived from the analysis can be used to classify tissues. The approach presented here can be adapted for clinical applications by adjusting imaging parameters (timing parameters and spatial resolution) for maximum contrast between fibrotic structures and normal tissue. The method can be of great values for the characterization of liver fibrosis.

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References: [1] Kim WR, Hepatology 2002; 36: 227; [2] Kim D, Radiology 2013; 268: 411; [3] Daubechies I, SIAM 1992.