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Experimental evaluation of quantitative technique for hepatitic fibrosis using ultrasonic phantom
肝線維化評価手法のファントムによる実験的検討

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1. Introduction

To realize a quantitative diagnosis of liver disease, we have examined the relationship between the change of liver tissue and ultrasound images, and have developed the quantitative estimation method of liver fibrosis[1-4]. It is important to evaluate the validity of this technique using clinical ultrasound images [5]. However, in case of clinical data, we could not observe images at a continuous stage of disease progression. In addition, a true value of the amount of fibrotic tissue in diseased liver is uncertain. If we represent a continuous stage of liver desease using a phantom, the relationship between ultrasound images and biological tisuue can be clarified. In this paper, we present the basic experimental evaluation results about the accuracy of quantitative technique for hepatitic fibrosis using an ultrasonic phantom.

2. Relationship between disease progression and change of the probability density function

Echo images of homogeneous tissue with high scatterer density, such as normal liver tissue, have many granular patterns that are called speckle pattern. It is known that the probability density function (PDF) $p(x)$ of original signal amplitude x of the echo images can be approximated by Rayleigh distribution given by

$$p(x) = \frac{x}{\sigma^2}\exp\left(-\frac{x^2}{2\sigma^2}\right), \qquad (1)$$

where σ is shape parameter of the distribution.

As the liver disease progresses, fibrous tissue, which is a stronger scattering medium than that of normal liver tissue, increases. The PDF of echo signals gradually deviates from Rayleigh distribution with fibrosis progression. In order to express this deviated PDF, we have proposed an amplitude distribution model for liver fibrosis in which the distribution function is modeled by a combination of Rayleigh distributions with low variance ${\sigma_{\mathrm{low}}}^2$ (normal tissue) and high variance ${\sigma_{\mathrm{high}}}^2$ (fibrotic tissue).

The PDF of the amplitude distribution model of a fibrotic liver, $p_{\mathrm{mix}}(x)$, is given by

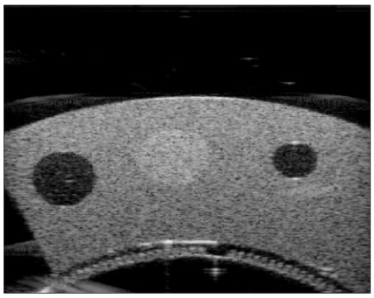


Fig. 1 RF image of phantom

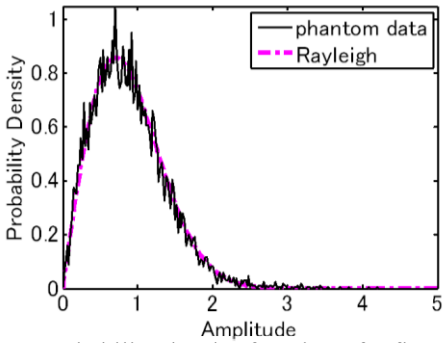


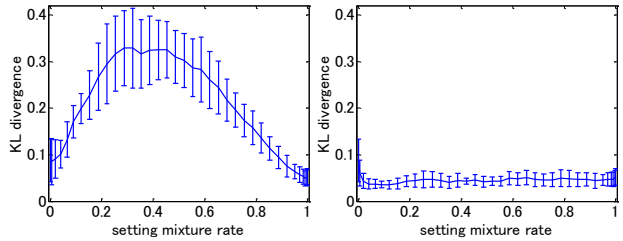
Fig. 2 Probability density function of reflected signal from phantom

$$p_{\mathrm{mix}}(x) = (1-\alpha)p_{\mathrm{low}}(x) + \alpha p_{\mathrm{high}}(x), \qquad (2)$$

where $p_{\mathrm{low}}(x)$ and $p_{\mathrm{high}}(x)$ are the Rayleigh distributions with a low variance (normal liver) and a high variance (fibrotic tissue) respectively, and α is a mixture rate of the Rayleigh distribution with a high variance. From the observed statistical properties, we can estimate the variance ratio $({\sigma_{\mathrm{high}}}^2/{\sigma_{\mathrm{low}}}^2)$ and the mixture rate as an inverse problem.

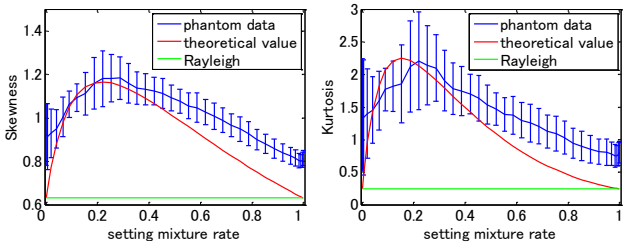
3. Quantitative characteristics of disease progression model

Figure 1 shows a phantom used for the experimental evaluation of the quantitative technique. Since the phantom has dense scattering points enough to generate speckle pattern, the PDF of a homogenous part can be approximated by Rayleigh distribution, as shown in **Fig. 2**. This phantom consists of three scatterer parts with a high, middle and low density. We used two parts with a high and middle density in this experimental evaluation. As a region of interest (ROI) crosses the boundary between different density parts, we can



(a) Rayleigh (b) amplitude distribution model

Fig. 3 KL divergence



(a) (b)

Fig. 4 Skewness(a) and kurtosis(b)

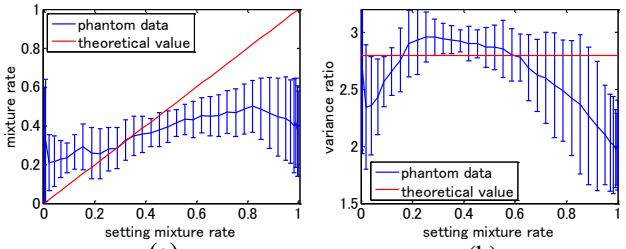
vary a ratio of the high variance part in the ROI (setting mixture rate) in the amplitude distribution model from 0 to 1. We obtained the parameters of the proposed quantitative diseased model from reflected signal in the ROI, and estimated the accuracy of obtained parameters.

Figure 3 shows results to evaluate the difference between obtained data PDF and approximation PDF functions with changing a mixture rate, using Kullback–Leibler (KL) divergence. KL divergence is a measure of the difference between two distribution functions, that is given by

$$D_{KL}(P \parallel \mathrm{Q}) = \sum_{x} P(x) \log \frac{P(x)}{Q(x)}, \qquad (3)$$

where P and Q are discrete stochastic variables. In **Fig. 3**, $P(x)$ is PDF of obtained data. $Q(x)$ is Rayleigh distribution (**Fig. 3 (a)**) or amplitude distribution model (**Fig. 3 (b)**). Generally, it is considered that two distributions are almost equal if KL divergence is less than 0.1. As shown in **Fig. 3 (a)**, the PDF of the obtained data deviates from Rayleigh distribution with changing a setting mixture rate. On the other hand, the PDF is well approximated by amplitude distribution model as shown in **Fig. 3 (b)**.

Figures 4(a) and **(b)** show skewness ($\mathrm{E}[(x-u_x)^3]/\sigma_x^3$) and kurtosis ($\mathrm{E}[(x-u_x)^4]/\sigma_x^4 - 3$) of obtained phantom data as a function of setting mixture rate, where E is the expectation value, u_x and σ_x are the mean and standard deviation of x respectively. Skewness and kurtosis are the statistical pamameters that can be stably calculated from the measured data. A theoretical curve is plotted as shown in **Fig. 4** by red line. Althouth the calculated skewness and kurtosis roughly agree with the theoretical value, there are large



(a) (b)

Fig.5 Estimation of mixture rate (a) and variance ratio(b)

differences at mixture rates of near 0 or larger than 0.6. This difference may be caused by a slight disagreement between PDF of the measured data and Rayleigh disrtibution at a setting mixture rate of 0 or 1.

Figure 5 shows the estimated variance ratio and mixture rate of amplitude distribution model. The variance ratio and the mixture rate can be estimated from the observed statistical parameters, skewness and kurtosis as an inverse problem. The estimated variance ratio and mixture rate agree well with predicted values (red lines) at setting mixture rate ranging from 0.2 to 0.6.

4. Conclusions

We presented the basic experimental evaluation results about the accuracy of quantitative technique for hepatitic fibrosis using an ultrasonic phantom. As a ROI crossed on the boundary between two scatterer areas with diferent densities in a phantom, we expressed the change from normal tisuue to fibrotic tissue of the liver disease. The probability density function is modeled by a combination of Rayleigh distributions with low variance and high variance. It is found that the PDF can be well approximated by amplitude distribution model, and that the parameters of amplitude distribution model can be estimated relatively well at a mixture rate of below 0.6. We will evaluate quantitative characteristics of disease progression model using a phamtom with nodule structure.

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