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Quantitative Evaluation of Acoustic Concentration of NASH Rat Liver Using Statistical Analysis Models for Echo Amplitude Envelope

エコー振幅包絡線統計モデルを用いたNASHラット肝臓の音響濃度の定量評価

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1. Introduction

Ultrasound quantitative diagnostic methods are proposed in decades, and some methods are already using in clinical study and actual diagnosis. These quantitative diagnostic methods are sometime divided to two groups from object of estimation. One of the object is tissue elasticities, and the other is scatterer properties. Our group have developed some echo analysis techniques that focused on the estimation of the scatter properties.

Ultrasonography is often used for diagnose liver diseases. Ghoshal[1)] and Ho[2)] have been proposed some tissue characterization analysis methods for fatty liver and fibrosis liver. The aim of our study is the detection of non-alcoholic steatohepatitis (NASH) on the early disease stage. NASH liver has complex tissue structure that of the fibers and fatty tissue are mixed in the liver. In the current, it is difficult to distinguish NASH from simple fatty liver by ultrasound, and histology also. Because it cannot understand what either of fat and fiber is the main cause of these diseases. Additionally, it is difficult to do the high-precision analysis of ultrasound echo signal that observed by actual ultrasound clinical scanner. Because the echo data was accumulate as the result of some signal processing such as sensitivity time control, complementation in three dimensions, and etc.

In this study, RF signal can be acquired as ultrasound echo signal from small samples of excised rat livers without complex signal processing. Single element concave transducers with high frequency ultrasound (f >15 MHz) were used to data acquisition to do the high-precision analysis with high resolutions.

2. Materials and methods

A) Animal model

The objects are Slc:SD male rats grown at the animal facility in our laboratory from age of 6 weeks. Normal (control) liver rat are fed normal diet. Fibrosis liver rats are injected carbon tetrachloride and olive oil (1×10^3 mml per 1 g of rat weight) in their back under anesthesia. This injection are done twice a week until an age of 19 weeks. NASH liver rats are made by same injection and fed a high calorie diet (DIO P.D 60% Energy for Fat-blue), fatty food. Three rats were used for each case of liver condition. All animal protocols are approved by animal experiment committee of Chiba University.

B) RF echo signal acquisition

RF echo signal data were acquired from freshly excised rat liver. A liver lobe of each rat liver was put into a water tank that filled degassed water at the measurement. The water temperature in the tank was controlled as the same as room temperature (25 ℃ ±2 ℃). The time of 15 min is required for the scanning of each liver lobe sample.

Ultrasound data were acquired with a focused single element transducer (V328, Olympus NDT) that had an aperture of 9.5 mm and focal length of 19.2 mm. The transducer had a center frequency of 14.4 MHz and a -6 dB bandwidth was 8.85 MHz. The transducer was excited by a pulser/receiver unit (Panametrics 5800, Olympus NDT). The echo signal of 1 scan line was digitized at 250 MS/sec with 8-bit digitizer (Wave runner 6030-I, LeCroy). The distance between scan line was 30 μm that is a third part of the lateral resolution of the ultrasound beam.

C) Analysis with Nakagami distribution

The Nakagami distribution is one of probability density distributions (PDF) that generalized from Rayleigh distribution, and is given by the following equation.[3)]

$$f(x) = \frac{2\mu^{\mu}x^{(2\mu-1)}}{\Gamma(\mu)\Omega^{\mu}}\exp\left(-\frac{\mu}{\Omega}x^2\right)U(x)$$

In the Nakagami distribution, Γ and U are gamma function and the unit step function, respectively. This PDF has two parameters which are shape parameter μ and scaling parameter Ω. μ and Ω are obtained from following equations.

$$\Omega = E(X^2), \qquad \mu = \frac{[E(X^2)]^2}{E[X^2 - E(X^2)]^2}$$

Nakagami distribution can be divided into three modes from the value of μ. In the case for μ <1, μ =1 and 1< μ, they are called pre-Rayleigh, Rayleigh, and Post-Rayleigh, respectively. The PDF of echo amplitude obey to Rayleigh distribution when scatterers are sufficient density and homogeneous. If the scatterer density is lower than case of Rayleigh, the PDF is defined as pre-Rayleigh.

The statistical analysis of the amplitude envelope in each RF signal of rat liver with three dimensional region of interest (3-D ROI). The size of 3-D ROI is 300 μm (100 sample points) in depth *540 μm (18 lines) in lateral *540 μm (18 lines) in slice.

3. Results

Figure 1 shows examples of histology of representative samples in each rat liver model. NASH model liver contains both fat droplets and fibers. Fibrosis model liver contains only fibers.

Figure 2 shows the mean and the standard deviation of estimated Nakagami μ parameters in all data sets. It is shown Nakagami μ parameter is higher than other cases in NASH model. However, in the result of statistical test (*t*-test), there are no significant differences between three models.

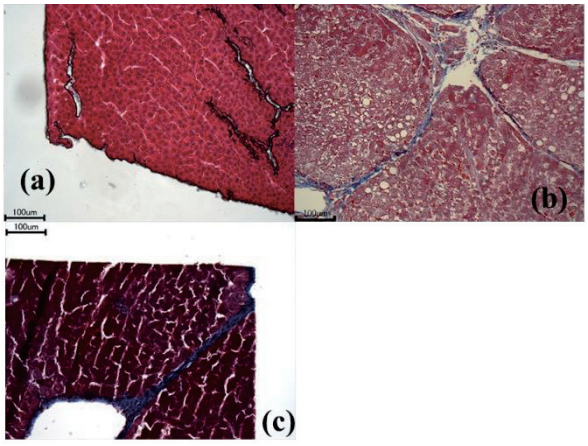

Fig. 1 Histology of isolated livers (a)Normal (H&E-staining) (b)NASH(Azan-staining) (c)Fibrosis(Azan-staining)

4. Discussion

Nakagami μ parameter of NASH model was higher than normal model. It was the same tendency of fatty liver study[1] which is used 20 MHz center frequency. Estimated Nakagami μ parameter in normal model and fibrosis model were the same. It was different tendency with latest study which was used 6.5 MHz center frequency.[2] The relationship between previous studies and our work cannot directly compared, because used frequency were different in each study. Because the Nakagami μ parameter relate to relationship between number of scatterer per resolution cells.[4]

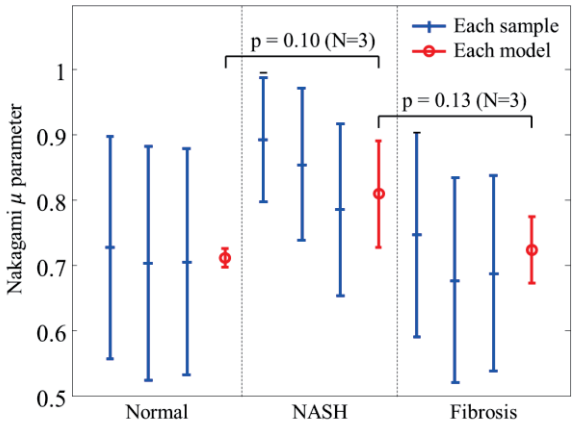

Fig. 2 Estimated Nakagami μ values. Center mark and error bar show mean and standard deviation, respectively.

In the current results, it has been possible to detect the characteristics of fat, however, it is difficult to find the characteristics of fiber. It is considered 15 MHz center frequency is too high for fibers detection in rat liver cases.

5. Conclusion

The statistical echo amplitude envelope analysis using Nakagami distribution was applied to three types of rat livers. The value of Nakagami μ parameter was higher than control and fibrosis liver in NASH liver case. It shows the fat is one of the big factor to define the characteristics of echo signal in 15 MHz. It is required to confirm the frequency dependency of the analysis with Nakagami distribution in future work.

Acknowledgment

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