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In vivo Application of Fatty Liver Progression Assessment Method by Double Nakagami Model

ダブル仲上モデルによる脂肪肝進行度評価法の生体内応用

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1. Introduction

The envelope statistical analysis is one of the quantitative ultrasound (QUS) technique for assessment of the fatty liver diseases The analysis of the human liver echo data using Nakagami probability density function (PDF) model confirmed the correlation between Nakagami parameter μ and hepatic fat fractions indicating fat mass[1]. Double Nakagami PDF model, which is combinated two Nakagami PDF models, enabled to detect early stage of fatty liver owing to RF data acqiusition using high frequency ultrasound (>10 MHz) [2].

In this study, double Nakagami PDF model was applied to *in vivo* rat liver data using an clinical ultrasonic scanner with high frequency linear array probe, and the performance of the discrimination between normal and fatty liver was examined.

2. Methods

2.1 *in vivo* rat liver experiment

The measurement objects were 6 rats (Slc:SD, male) those are assumed to be normal and fatty liver models: 2 normal (13 weeks) and 4 fatty liver model rats (15 weeks). The fatty liver model rats were produced by feeding high fata/high cholesterol diet. The experimental protocol was approved by the Animal Experiment Committee of Chiba University.

A clinical ultrasound scanner (LOGIQ S8, GE healthcare) equipped with a high-frequency linear-array probe (ML6-15, GE healthcare) were used for acquisition of RF data from *in vivo* rat livers. The linear array probe was fixed on the rat under the anesthesia using a probe holder. The sampling frequency was 50 MHz. The center frequencies were variable as 9, 11, 13, and 15 MHz. Three different cross sections were measured from each rat. A typical frame was analyzed per each rat without the body motion caused by breathing.

2.2 Amplitude envelope statistical analysis

Nakagami and double Nakagami PDF models were compared in this study. Nakagami PDF model is given as[3].

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

where Γ is gamma function, μ and ω are related to the number density of scatterers and the echo signal energy, respectively. Amplitude envelope statistics are classified accoding to the value of the Nakagami parameter μ. The cases where $\mu < 1$, $\mu = 1$, and $\mu > 1$ are called as pre-Rayleigh, Rayleigh, and post-Rayleigh statistics, respectively. These parameters were estimated using the maximum likelihood method.

Double Nakagami PDF model assumes that the echo signal from fatty liver is mainly composed of normal liver structures and lipid droplets. Its equation is defined as

$$p_{mix}(x) = (1-\alpha)p_L(x|\mu_L,\omega_L) + \alpha p_F(x|\mu_F,\omega_F), \qquad (2)$$

where p_L and p_F were PDFs represented by Nakagami model of the normal liver structures and lipid droplets, respectively. Nakagami parameter μ_F corresponds to the number density of lipid droplets. The parameters $\alpha\omega_F$ are related to the energy of the echo signal from the fatty component.

The parameters of double Nakagami PDF model were optimazed based on the Kullback-Leibler (KL) divergence. The parameter μ_L was fixed at mean value of parameter μ of normal rat liver for each frequency. The parameters μ_F, ω_F, and α were optimazed based on the KL divergence, given as

$$D_{KL}(p||p_{mix}) = \sum_{i=0}^{\infty} q(x_i)\log\frac{q(x_i)}{p(x_i)}, \qquad (3)$$

where $q(x_i)$ and $p(x_i)$ are the probability density of the echo amplitude envelpe and double Nakagami PDF model, respectively. The cost function of D_{KL} was solved using “fminsearch” function in MATLAB (The MathWorks Inc.).

Analysis area was manually selected with excluding blood vessels. The size of ROI was five times (2 mm in depth and 4 mm in lateral) in each

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resolution cell, and the ROI was scanned by 80% overlap in each direction.

3. Results and discussion

Figure 1 shows the mean and standard deviation of estimated parameters of three section for each rat liver by each frequency. Both parameters μ and μ_F of the fatty liver was higher than that of the normal liver. Also as compared between **Figs. 1(a) and 1(b),** parameters μ and μ_F were obtained with same relationship. Because the value of μ_F was closer to 1 than parameter μ, double Nakagami PDF model agreed with the theory where hyperechoic scatterers exist with high number density. Therefore, the parameter μ_F is considered to be superior to parameter μ for absolute evaluation of scatterer structure.

Figure 1(c) shows the result of $\alpha\omega_F$ at each rat using different frequencies. The parameter $\alpha\omega_F$ of the fatty liver was also larger than that of the normal liver. The parameter $\alpha\omega_F$ has possibility to evaluate the fat mass. Hence, the use of both parameters μ_F and $\alpha\omega_F$ may be possible to characterize the degree of fatty liver progression with *in vivo* data that cannot be evaluated by only Nakagami PDF model.

4. Conclusion

Double Nakagami PDF model was applied to in vivo datasets of normal and fatty rat livers. As the result, Nakagami parameter μ and μ_F related with the scatterers number density have the same relationship on both normal and fatty models. Moreover, $\alpha\omega_F$ related to the energy of fatty component also discriminates the difference between normal and fatty liver. Therefore, the use of the parameters μ_F and $\alpha\omega_F$ may allow the assessment of fatty liver progression focusing on lipid droplets density and mass.

In future works, the quantitative analysis of fatty liver progression will be performed. Furthermore, it is also necessary to assess the relationship between fatty liver progression and double Nakagami parameters.

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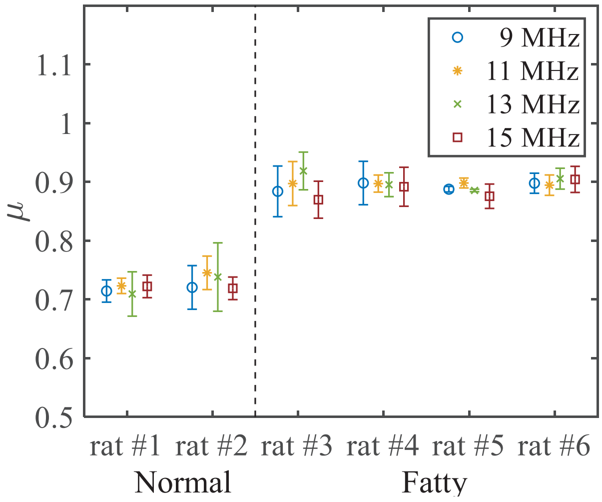
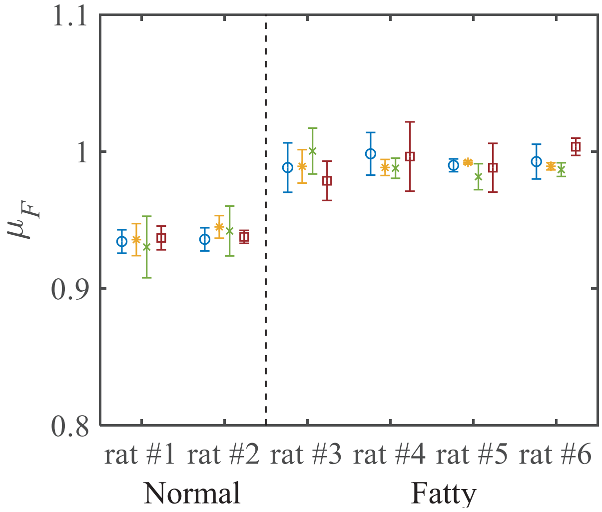
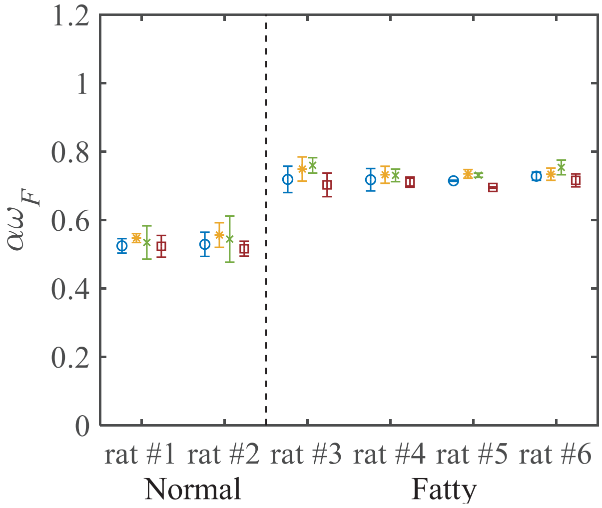


(a) Parameter μ of Nakagami PDF model



(b) Parameter μ_F of double Nakagami PDF model



(c) Parameter $\alpha\omega_F$ of double Nakagami model

Fig. 1 Estimated QUS parameters from normal and fatty livers.