

## Accuracy Verification of Amplitude Envelope Analysis Models for Fatty Liver Assessment

脂肪肝評価における複数の振幅包絡特性解析モデルの精度比較

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### 1. Introduction

The amplitude envelope analysis is one of the powerful tools to provide QUS (Quantitative ultrasound) parameters. In particular, the evaluation using mixture model, which is represented by the addition of statistical models, is highly accurate in the assessment of fibrosis and fatty liver<sup>[1][2]</sup>. The double Nakagami (DN) PDF model enables the evaluation focusing on lipid droplets in rat liver data acquired with single element with center frequency of 15 MHz. However, it has not been examined whether the DN PDF model can be applied to the echo data acquired at the low frequency (i.e. < 10 MHz) used in abdominal ultrasound examination to provide a high-level diagnosis.

In this study, we applied the DN PDF model to echo data of human liver acquired at low frequency, and verified the accuracy of the QUS parameters. Besides, we discussed further possibility of fatty liver assessment method by DN PDF model.

### 2. Materials and methods

#### 2.1 Clinical dataset

A total of 204 cases of human liver echo dataset acquired using a clinical ultrasound scanner at Chang Gung Memorial Hospital, Taiwan was used for amplitude envelope analysis. The dataset was divided into four groups based on fat mass assessed by liver biopsy: healthy (< 5 %), mild (5 - 35 %), moderate (35 - 70 %) and Severe (> 70 %).

A clinical ultrasound scanner (Model3000, Terason) equipped with a convex array probe (Model5C2A, Terason) were used for acquisition of RF data. The center frequency and the sampling frequency were 3.5 and 30 MHz, respectively.

#### 2.2 Amplitude envelope analysis

The Nakagami PDF is the basic method used for fatty liver assessment, and given as<sup>[3]</sup>.

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

where  $\Gamma$  is gamma function,  $\mu$  and  $\omega$  are related to the number density of scatterers and the echo signal energy, respectively. Amplitude envelope statistics are classified according to the value of the Nakagami parameter  $\mu$ . The cases where  $\mu < 1$ ,  $\mu = 1$ , and  $\mu > 1$  are called as pre-Rayleigh, Rayleigh, and post-Rayleigh statistics, respectively.

DN PDF model is expressed as a mixture model of the Nakagami PDFs as following equation.

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

In eq. 2,  $p_L$  and  $p_F$  are Nakagami PDFs representing normal liver structures and lipid droplets, respectively. The parameter  $\mu_F$  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 parameter  $\mu_L$  was fixed at mean value ( $\mu_L = 0.84$ ) of parameter  $\mu$  of healthy human liver in this study. Three parameters  $\alpha$ ,  $\mu_F$  and  $\omega_F$  were optimized using Nelder-Mead method. The optimization was based on Kullback-Leibler (KL) divergence. The parameter  $\omega_L$  was calculated from estimated parameters and following constraint equation.

$$\omega_L = \frac{1 - \alpha\omega_F}{1 - \alpha} \quad (3)$$

Analysis area was manually selected with excluding blood vessels. The ROI was scanned on the scan-converted image. Namely, the ROI for analysis was set to that the actual physical size is constant anywhere in the analysis region. Therefore, the appearance shape and size of scanning line information differs depending on places. The size of ROI was three times the resolution cell in each direction (5.7 mm in depth and 7.2 mm in lateral), 80 % overlapping with the analysis at the adjacent ROI.

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### 3. Results and Discussion

**Figure 1** shows the parametric images of DN PDF model parameters for each disease state. The areas where both parameters were high values locally increased with the increase in fat mass. Also as compared between **Figs. 1(a) – (d)** and **1(e) – (h)**, the textures of the parametric images of  $\mu_F$  and  $\alpha\omega_F$  were different. This indicates that the amount and distribution of fat are locally different.

**Figure 2** shows the mean and standard deviation of estimated QUS parameters for each steatosis stage. N represents the number of cases used to calculate the statistics. The Nakagami parameters  $\mu$  and  $\mu_F$  had different correlations to steatosis stage. Parameter  $\mu_F$  was higher than 1 in healthy liver group. In the case of low resolution, DN PDF model agreed with the theory where hyperechoic scatterers exist with high number density even in early fatty liver. In contrast,  $\alpha\omega_F$  tended to decrease, but no significant difference was confirmed. Because the size of the lipid droplet was small compared to the resolution cell, a slight difference in  $\alpha\omega_F$  between steatosis stage was detected. According to these results, the estimated parameters  $\mu_F$  and  $\alpha\omega_F$  have possibility to evaluate number density of lipid droplets and fat mass, respectively. However, it is difficult to evaluate fatty liver with each parameter.

In a previous study, healthy liver structure filter (HLSF) method has been proposed in which the non-healthy area is easily visualized by analyzing parameters of DN PDF model in a complex way using a polar coordinate system<sup>[4]</sup>. It may be possible to present additional information about lipid droplets by applying HLSF method to clinical data acquired at low frequency.

### 5. Conclusion

DN PDF model was applied to clinical datasets. As the result, the parameters  $\mu_F$  and  $\alpha\omega_F$  of DN PDF model were obtained with different relationship and may be related to the number density of lipid droplets and fat mass, respectively.

In future works, the fatty liver assessment method focusing on lipid droplets will be examined by applying HLSF method to this result.

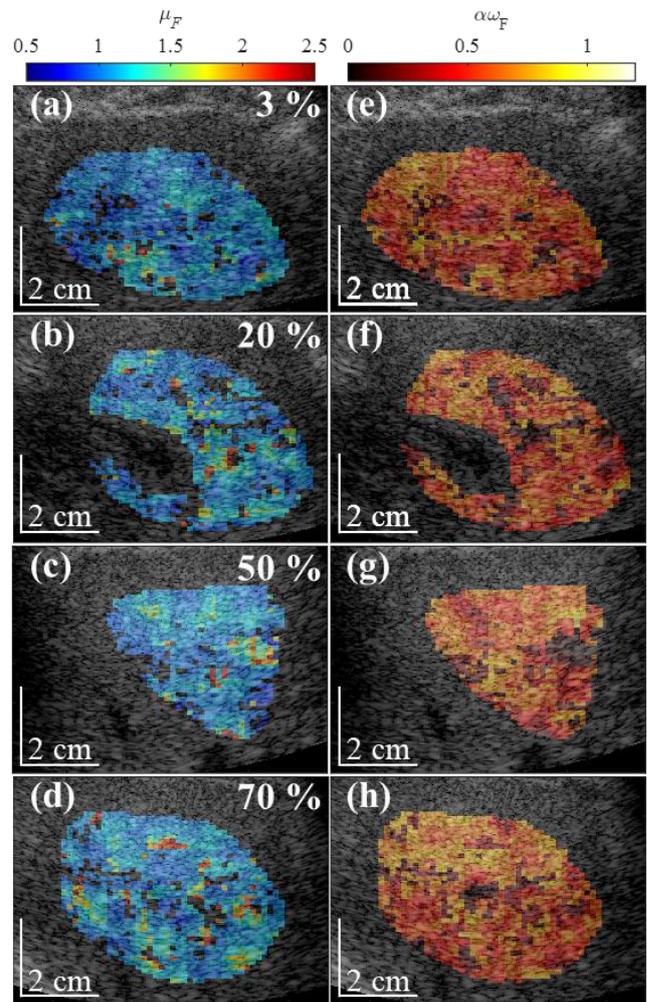


Fig. 1 Representative parametric images of parameters  $\mu_F$  and  $\alpha\omega_F$  for each disease state.

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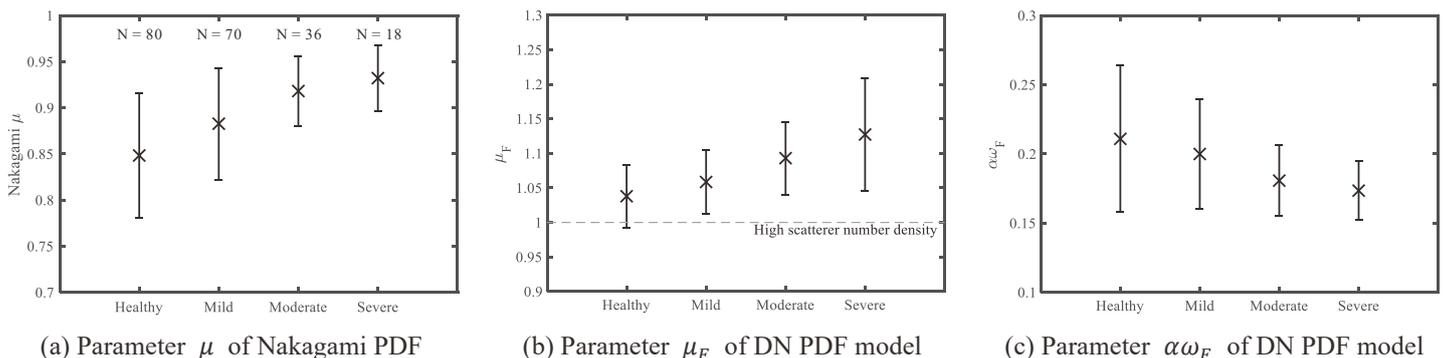


Fig. 2 Estimated QUS parameters for each steatosis stage.