Verification of Amplitude Envelope Analysis Model for NASH Liver Evaluation

NASH 肝評価における振幅包絡特性解析モデルの適用性の検証

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1. Introduction

Some of amplitude envelope statistics analysis techniques has been employed as quantitative ultrasound (QUS) methods to evaluate tissue properties of livers. The relationships between the statistical parameters of the analysis models and liver fibrosis or hepatic steatosis grades were reported[1,2]. On the other hand, the main requirement in clinical practice is the quantitative diagnosis of non-alcoholic steatohepatitis (NASH) which has both fat and fiber present in the liver and has a strong tendency to become cancerous.

In this study, we applied the multi-Rayleigh (MRA) model, which has been proposed as an evaluation model for liver fibrosis, to clinical data sets of human liver inckuding sinple steatosis, fibrosis, and NASH acquired with an clinical ultrasound scanner. The possibility of distinguishing of amount of fibrous tissue and lipid droplets in each diseased liver was evaluated.

2. Materials and methods

2.1 Clinical dataset

A total of 204 human liver echo dataset acquired using a clinical ultrasound scanner at Chang Gung Memorial Hospital, Taiwan, were used for the statistical amplitude envelope analysis. The dataset was divided into four groups based on fat mass assessed by liver biopsy: Healthy (< 5 %), Mild (5 - 33%), Moderate (33- 66 %), and Severe (> 66 %). A clinical ultrasound scanner (Model3000, Terason) equipped with a convex array probe (Model5C2A, Terason) was used to acquire RF data. The center frequency and the sampling frequency were 3.5 and 30 MHz, respectively.

2.2 Amplitude envelope analysis

The amplitude envelope probability distribution of the echo signal from a dense and uniformly distributed scatterer medium can be approximated by the Rayleigh model, given as,

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

where x is amplitude envelope, σ^2 is echo signal energy.

As fibrosis progresses, the provability density function (PDF) deviates from the Rayleigh distribution by changing to a heterogeneous tissue structure due to the formation of fibrous tissue and nodules. MRA model combining multiple Rayleigh distributions was proposed to evaluate the statistical properties of echo signals from cases with advanced fibrosis.

$$p_{mix}(x) = \alpha_L p_L(x) + \alpha_M p_M(x) + \alpha_H p_H(x) \quad (2)$$

In eq.2, $p_*(x)$ are the probability densities of independent echo signals from three types of scatters with different scatter densities or scattering intensities and are defined as Rayleigh PDFs with different scale parameters σ_*^2. The number of components of the Rayleigh distribution used in the estimation was determined from the moments representing the statistical properties of the echo signal. This method allows the MRA model to evaluate the number of components that correspond to the tissue structure[3].

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The analysis area was selected manually, except for the blood vessels. A region of interest (ROI) was scanned into the scan-converted image, and MRA parameter estimation was performed with 80% overlap with the analysis in the adjacent ROI. The size of the ROI was set to be three times the resolution cell (5.7 mm in depth, 7.2 mm in lateral).

As liver fibrosis parameters, the mixed ratio of high-dispersion Rayleigh distribution $R_m(\alpha_H)$ and the power ratio $R_v(\sigma_H^2/\sigma_M^2)$ of the echo signal with normal tissue were analyzed in a combined manner. The healthy liver structure filter (HLSF) method[4] was applied to extract the regions reflecting the characteristics of echo signals from fibrous tissues. The area ratio of the non-Healthy areas and the non-Healthy parameter R_v were used as evaluation parameters.

3. Results and Discussion

In parameter estimation, regions determined to have significant modeling errors in the MRA model were identified mainly in cases of fatty liver, and these regions were defined as non-MRA. **Figure 1** shows the area of non-MRA relative to the analyzed area at each steatosis stage. This result confirmed the statistically significant difference between the Healthy group and the other fatty liver groups. In particular, the difference between the Mild and Moderate/Severe groups was significant, suggesting that the screening identification of Moderate and Severe fatty liver is possible.

Figure 2 shows the mean and standard deviation of liver fibrosis parameters for different fatty liver groups and fibrosis progression levels. **Figs. 2(a)** shows a statistically significant difference between F0, in which fibrosis had not progressed, and F1 – F4, in which fibrosis had progressed. This result suggests that liver fibrosis parameters reflect the characteristics of fibrous tissue in early fatty liver. On the other hand, there was no significant difference between F0 and F1 – F4 clinical data in **Figs. 2(b) – (c)**. In moderate and severe fatty liver groups, the characteristics of lipid droplets were more dominant than those of fibrous tissue, and the evaluation results were similar to a medium with a dense and homogeneous distribution of scatterers.

4. Conclusion

The MRA model was applied to clinical data sets. The result suggested the possibility of identifying of fatty liver from PDF shape even in cases that the echo amplitude envelope characteristics do not fit the model conditions. Furthermore, in early fatty liver, liver fibrosis parameters could be used to evaluate the fibrosis progression.

In future works, the relationship between the scatterer distribution and the evaluation parameters in more detail will be examine by computer simulations and human data sets observed by higher frequency ultrasound.

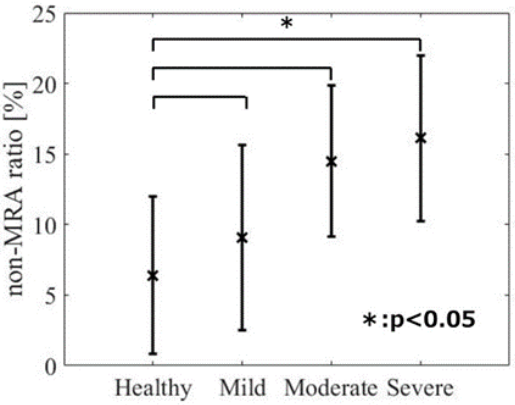

Fig. 1 non-MRA ratio for each steatosis stage.

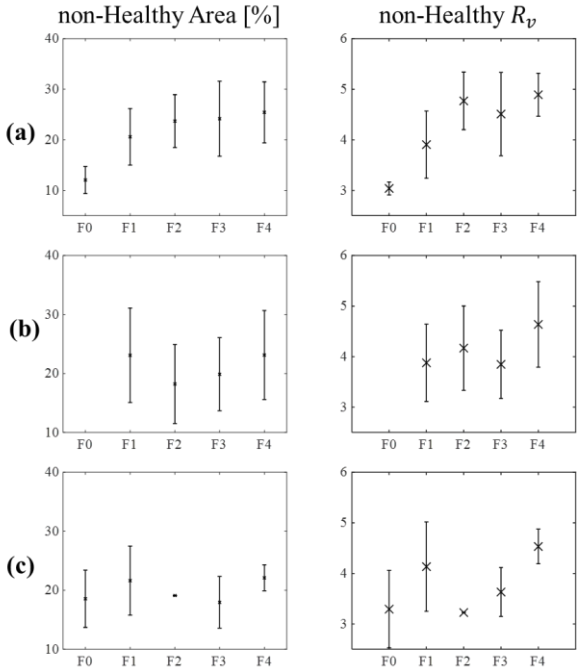

Fig. 2 Estimated liver fibrosis parameters for each fatty group. (a)-(c) are showing the results of Mild, Moderate, and Severe group, respectively.

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