Proceedings of Symposium on Ultrasonic Electronics, Vol. 36 (2015)
5-7 November, 2015

Evaluation of statistical analysis models for envelope amplitude of liver based on histology

病理像に基づく肝エコー包絡振幅統計解析モデルの評価

Mikito Ito[1†], Kenji Yoshida[2], Mori Shohei[3], Hiroyuki Hachiya[3], Tadashi Yamaguchi[2]
([1]Grad. School Eng., Chiba Univ.; [2]Center for Frontier Medical Engineering, Chiba Univ.; [3]Tokyo Inst. Tech.)
伊藤幹人 [1†]，吉田憲司 [2]，森翔平 [3]，蜂屋弘之 [3]，山口匡 [2] ([1] 千葉大院工, [2] 千葉大 CFME, [3] 東工大)

1. Introduction

We have investigated the relationship between the progress of liver fibrosis and the probability density function of echo envelope amplitude. Although the parameters of some statistical analysis models show sensitivity for the fibrosis grade in related study, the relationship between the tissue structures and the parameters of statistical analysis models have not been linked definitely because many factors can be considered as cause in change of the echo properties. To interpret the influence which complexity of the tissue structure gives in echo properties, the echo which reflected real tissue structure based on histology were tried by simulation and the statistical analysis was performed in this study.

2. Materials and methods of computer simulation based on histology

Figure 1 shows the schematic image of the simulation setup (a) and the emitted sound field with used transducer for simulation (b). Echo simulation was performed with Field II (Tech. Univ. of Denmark) based on calculation of spatial impulse responses in MATLAB [1]. A concave transducer with a single element, a diameter at 20 mm, and an elevation focus at 50 mm was simulated. The transmission and reception frequency was 5.0 MHz, and the sampling frequency was set to 50 MHz. The speed of sound was assumed to be 1540 m/s. Simulation echo data was acquired from the scattering field at 0.5 mm beam intervals in the lateral and slice, which was equivalent to half of lateral point spread function for this transducer.

The size of the scattering field was 50 mm × 50 mm × 20 mm, and scatterers were placed inside this domain. The scattering properties such as number density and scattering amplitude of each scatterer were defined from *tissue maps* which were manufactured from 20 pieces of consecutive histology. The consecutive histology were made from an excised liver from an autopsy sample of fibrosis liver, which was offered from Chiba University Hospital. After sliced at 4 μm in every

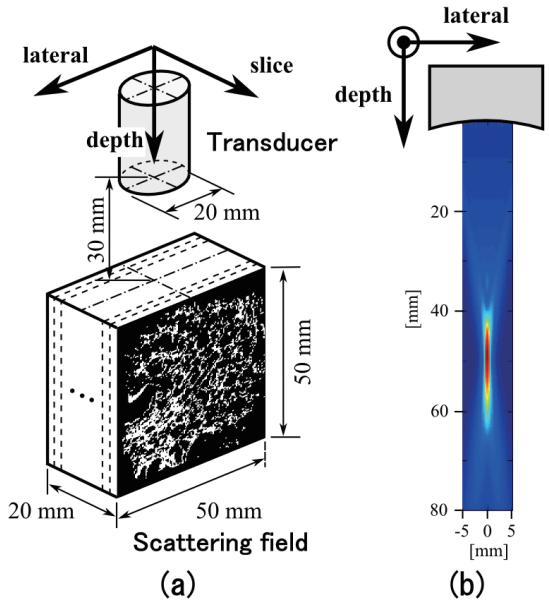

Fig. 1 (a) Schematic image of the simulation setup (b) Emitted sound field with used transducer for simulation

1 mm, they were stained by Azan staining to observe the fibrotic tissue by light microscopy. By performing threshold processing stained histology after performing thinning and interpolation, the *tissue maps* classified into 'fibrotic' or 'normal' were defined. The size of each voxel was about 0.4 mm × 0.4 mm × 0.4 mm. With corresponded to a spatial position and the class of the *tissue maps*, the scattering properties of each scatterer placed at random in the scattering field were defined. **Table I** shows the scattering properties of each class in this study. In addition, the size of the region of interesting (ROI) was 15 mm × 15 mm × 15 mm for the statistical analysis.

Table I The scattering properties of each class in the *tissue maps*

No.	Number density [per voxel]		Scattering amplitude	
	'fibrotic'	'normal'	'fibrotic'	'normal'
1	1	0	N(0,1)	0
2	1	1	N(0,1)	0.2 ×N(0,1)
3	1	1	N(0,1)	0.4 ×N(0,1)

3. Statistical analysis

For the echo simulation data, the relationship between the tissue structures based on histology and the parameters of statistical analysis model was investigated. In this study, the multi-Rayleigh model, which has high sensitivity to the fibrosis grade [2], was examined for echo simulation data based on histology. The concept of this model is based on Rayleigh distribution. In homogeneous medium with high number density of the scatterers, it is known that the probability density function (PDF) $p(x)$ of echo amplitude x can be approximated by the Rayleigh distribution given by

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

where σ^2 is a scale parameter representing the variance in the echo amplitude envelope. With represented by mixture two Rayleigh distribution with different parameters of σ^2 , multi-Rayleigh model is given by

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

where $p_{\mathrm{L}}(x)$ and $p_{\mathrm{H}}(x)$ are the Rayleigh distribution with low variance($\sigma^2=\sigma_L^2$, normal tissue) and high variance($\sigma^2=\sigma_H^2$ fibrotic tissue), respectively. α $(0\le\alpha\le1)$ is the mixture rate of the Rayleigh distribution with a high variance. This mathematical model has a major advantage in such as a correspondence to the physical state of liver fibrosis compared to other models [2-3].

4. Results

Figure 2 shows the scattering fields used for the echo simulation, the simulated B-mode images, and the results of the statistical analysis in the ROI. In addition, **Table II** shows the ratio of the scattering amplitude R_{fib} in the *tissue maps* given by

$$R_{\mathrm{fib}}=\frac{\text{the scattering amplitude of 'fibrotic'}}{\text{the scattering amplitude of 'normal'}}, \qquad (3)$$

and the parameters of the multi-Rayleigh model in the ROI. In the simulated B-mode image of No. 1, the fibrotic tissue structures were clearly. When the ratio of the scattering amplitude R_{fib} becomes close to 1, which means oncoming of homogeneous medium, the visibility of the tissue structures becomes lower in B-mode. In addition, for the statistical analysis using the multi-Rayleigh model, the $\sigma_{\mathrm{H}}^2/\sigma_{\mathrm{L}}^2$ decreases with a tendency of R_{fib} as shown in Table II. On the other hand, the rate of the 'fibrotic' voxels to 'normal' voxels was 0.30. For the statistical analysis using multi-Rayleigh model, the mixture rate α were close to this value in case of

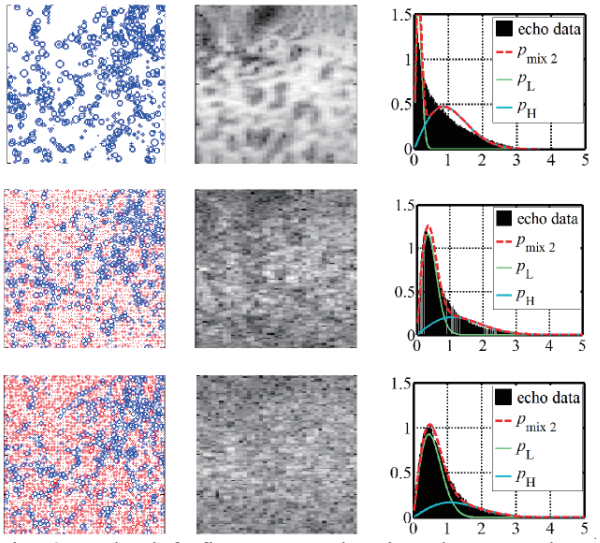

Fig. 2 The left figures are showing the scattering fields used for echo simulation. The size and the color of the circles means the scattering amplitude and the classes of the *tissue maps*, respectively. The circle with blue and red are classified into 'fibrotic' and 'normal', severally. The center and right figures are showing simulated B-mode images and results of analysis (the PDF and estimated multi-Rayleigh model) in the ROI, respectively. The upper, middle, and lower are model of No. 1, No. 2, and No. 3, severally.

Table II The ratio of the scattering amplitude in the *tissue maps*, and the parameters of the multi-Rayleigh model in the ROI

No.	R_{fib}	α	$\sigma_{\mathrm{H}}^2/\sigma_{\mathrm{L}}^2$
1	∞	0.67	50.0
2	5	0.37	10.7
3	2.5	0.30	5.60

that the visibility of the tissue becomes lower in B-mode such as No. 2 and No. 3.

4. Conclusion

To accurately interpret the relationship between the tissue structure and the echo properties, the statistical analysis for envelope amplitude was performed for the simulation data based on histology. The result showed that the parameters of multi-Rayleigh model can represent the tissue characteristic in case of unclear tissue structure in B-mode images. In future work, the influence of the other properties such as number density will be examined for echo simulation. In addition, the influences of the sound field such as the difference of the sound pressure in depth should be considered.

References

1. J. A. Jensen and N. B. Svendsen: IEEE Trans. Ultrason., Ferroelec., Freq. Contr. **39** (1992) pp 262-267.
2. S. Mori *et al*: Jpn. J. Appl. Phys. **54** (2015) 07HF20.
3. T. Yamaguchi and H. Hachiya, J. Mech. Med. Ultrason. **37** (2010) 155