Quantitative estimation of liver fibrosis considering effect of resolution of ultrasound in B-mode image

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Summary
We have been developing an evaluation method of liver fibrosis using ultrasound images to realize quantitative diagnosis of hepatitis. To evaluate liver fibrosis quantitatively, we have focused on a probability density function of the echo amplitude. Then, a multi-Rayleigh distribution model expressed by combination of Rayleigh distributions with different variances has been proposed. This multi-Rayleigh distribution model enabled us to extract fibrosis parameters from a B-mode image. However, the B-mode image is affected by a resolution of the ultrasound; therefore, the fibrosis parameters estimated from the B-mode images deviate from their true values. In this paper, we examined the effect of the resolution of the ultrasound by computer simulation. As a result, we could see that the estimated fibrosis stage becomes smaller and the estimated amount of the fibrotic tissue becomes a little larger than their true values. Then, we tried to compensate the effect of the resolution. We showed the possibility that we could correct the estimated fibrosis parameters to their true values by considering the relationship between the estimated fibrosis parameters and the resolution size of the ultrasound.

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1. Introduction

We have been developing a quantitative diagnostic method of hepatitis using ultrasound image. The diagnosis using an ultrasound image is noninvasive and easily performed compared with other imaging diagnostic methods, such as X-ray computed tomography (CT) or magnetic resonance imaging (MRI). However, a high level of skill and experience is needed for an operator to read the ultrasound image so that it is difficult to evaluate quantitatively especially in an initial stage of liver fibrosis. Therefore, the quantitative diagnostic method of hepatitis using the ultrasound image is strongly required.

To evaluate the liver fibrosis quantitatively, we measured the acoustical properties of liver tissue [1–3], modeled the tissue structure of liver fibrosis, and examined the relationship between biological tissue structures and ultrasound images [4–6]. From the knowledge obtained through these studies, a method of quantifying the stage of diffuse liver disease has been demonstrated [7–10] and the quantitative evaluation of the degree of liver fibrosis has been examined [11–17].

To evaluate liver fibrosis quantitatively, analyzing a probability density function (PDF) of the echo amplitude is effective [18–20]. To express the PDF of the echo amplitude from tissue of liver fibrosis, we proposed a multi-Rayleigh distribution model which is composed of several Rayleigh distributions with different variances [21–24]. This multi-Rayleigh model enabled us to extract the fibrosis parameters from a B-mode image.

When we make the B-mode image by a ultrasonic beam, their appears an effect of a resolution of the ultrasound. Because the resolution of the ultrasound has the width for 3-dimensional direction, the fibrotic tissue spreads in the B-mode image. Therefore, the fibrosis parameters estimated from the B-mode image deviate from their true values. In the previous study, we evaluated the diagnostic method based on the multi-Rayleigh model with considering the effect of the ultrasonic beam width which is the resolution for a lateral direction, and evaluated the effect of the ultrasonic beam width quantitatively [25].

In this study, we examined the effect of the resolution of the ultrasound considering the width for lateral and axial direction and tried to correct the estimated fibrosis parameters to their true values. First, we describe the amplitude distribution model of liver fibrosis and the estimation method for extracting the
fibrosis parameters from the PDF of the echo amplitude. Then, we examine the effect of the 2-dimensional resolution of the ultrasound for the quantitative estimation method of liver fibrosis based on the multi-Rayleigh model. Finally, we evaluate a relationship between the estimated fibrosis parameters and the size of the resolution to correct the estimated parameters to their true values.

2. Extraction of fibrosis parameters using the multi-Rayleigh distribution model

When many scattered points are distributed randomly and homogeneously, such as in normal liver tissue, the PDF of the echo amplitude can be approximated by a Rayleigh distribution. On the other hand, in an inhomogeneous medium, such as a fibrotic liver, the PDF of the echo amplitude deviates from the Rayleigh distribution. It is considered that a fibrotic liver is composed of various tissues, such as normal and fibrotic tissues. We proposed a multi-Rayleigh distribution model that is modeled using a combination of Rayleigh distributions with different variances. The Rayleigh distribution is given by

\[ p(x) = \frac{2x}{\sigma^2} \exp\left(-\frac{x^2}{\sigma^2}\right), \tag{1} \]

where \( x \) and \( \sigma^2 \) are the echo amplitude and the variance of the echo amplitude, respectively.

The multi-Rayleigh distribution model with two components is given by

\[ p_{\text{mix}}(x) = (1 - \alpha)p_{\text{low}}(x) + \alpha p_{\text{high}}(x), \tag{2} \]

where \( p_{\text{high}}(x) \) is the Rayleigh distribution with a high variance (fibrotic tissue), \( \sigma_{\text{high}}^2 \), and \( p_{\text{low}}(x) \) is the Rayleigh distribution with a low variance (normal liver), \( \sigma_{\text{low}}^2 \). \( \alpha \) (0 ≤ \( \alpha \) ≤ 1) is the mixture rate of the Rayleigh distribution with a high variance. Therefore, the model parameters are the variance ratio \( (\sigma_{\text{high}}^2/\sigma_{\text{low}}^2) \) and the mixture rate \( (\alpha) \). The variance ratio and mixture rate are related to the fibrosis stage and the amount of fibrotic tissue, respectively. To determine the fibrosis parameters, variance ratio and mixture rate from the echo amplitude, it is necessary to establish the multi-Rayleigh distribution model that expresses the PDF of the echo amplitude. We use the expectation maximization (EM) algorithm [26] to estimate the parameters of the multi-Rayleigh distribution model.

3. Evaluation of effect of the resolution of the ultrasound on quantitative diagnosis

In this section, we examine the effect of the resolution of the ultrasound. When the tissue structure is observed using a scanning ultrasound beam, the B-mode image is affected by the resolution of the ultrasound. Even if the reflection target is a point, the ultrasound image of the point spreads owing to the width of the resolution so that the B-mode image of the tissue structure differ from that of an actual tissue structure. This effect also appears in the PDF of the echo amplitude calculated from the B-mode image; therefore, the fibrosis parameters in Eq. 2 estimated from the B-mode image changes according to the resolution size of the ultrasound.

To examine the effect of the resolution of the ultrasound, we perform a simulation in which we estimate the fibrosis parameters from B-mode images while changing the ratio between the fibrotic tissue size and the resolution size.

3.1. Scatterer distribution model

We used a scatterer distribution model by combining the scatterer distribution of normal and fibrotic tissues shown in Fig. 1. The lateral and axial resolution of the ultrasound is determined by the ultrasonic beam width and pulse width, respectively; therefore, the effect of the resolution for lateral and axial direction appears in the each direction’s change in the tissue structure. For this reason the scatterer distribution model was composed of normal liver and rectangular fibrotic tissues. By using this model, the change in the tissue structure appears only in the lateral and axial direction, and thus we can examine the effect of the resolution of the ultrasound specifically. In this paper, we use the 2-dimensional scatterer distribution model so that we need not to consider the resolution for a slice direction. Since the PDF of the echo amplitude becomes a Rayleigh distribution at a density higher than 10 scattered points per point spread function (PSF), the scatterer density of the normal liver is 10 points/PSF. In the fibrotic tissue, the number of scatterers is larger than that in the normal liver, and the variance ratio, which is one of the fibrosis parameters, corresponds to the scatterer density ratio of normal tissue to fibrotic tissue. In this study, we set the variance ratio at 5 by setting the scatterer density of the fibrotic tissue at 50 points/PSF. In addition, we set the mixture rate by changing the area of the fibrotic tissue. In this study, we set the mixture rate at 0.1.

In order to examine the relationship between the size of the fibrotic tissue and resolution size, we divide fibrotic tissue and establish new scatterer distribution models that have the different size of the fibrotic tissue, as shown in Fig. 1. In these models, each size of the fibrotic tissue is proportional to the resolution size which is approximated as a rectangle. In addition, these scatterer distribution models are established only by division so that the number of scatterers, the set fibrosis parameters, and the relative positions of scatterers in each tissue do not change.
Therefore, we can examine the relationship between the fiber size and the resolution size of the ultrasound specifically.

3.2. Ultrasound simulation

We calculate B-mode images of the scatterer distribution models using Field II, which is a tool for ultrasonic simulation [27,28]. The scatterer distribution model was located 30 to 40 mm from the transducer. The lateral size of the scatterer distribution model was 40 mm. The scatterers’ reflection coefficients are identical. The center frequency is 5.0 MHz and the sampling frequency is 100 MHz. The focal position moves dynamically from 20 to 40 mm at 1 mm intervals to control ultrasonic beam width in an image.

Figure 2(a) shows the scatter distribution model, and Fig. 2(b) shows the B-mode image calculated from Fig. 2(a). The normalized fiber size $F_s/\text{Rs}$, which is the fiber size divided by the resolution size of the ultrasound, are (i) 10, (ii) 2.5, (iii) 1.25, and (iv) 0.63. From Fig. 2, we can see that the fibrotic tissue blurred at the border between the fibrotic tissue and normal liver, and as the fiber size becomes smaller, the border of tissues becomes more obscure.

3.3. Estimated fibrosis parameters

From Fig. 2, we estimated the fibrosis parameters based on the multi-Rayleigh model. At each fibrotic tissue size, five B-mode images were calculated using five different patterns of randomly distributed scatterers, and the fibrosis parameters were estimated from them, respectively. Figure 3 shows the mean values and the standardized deviations of the estimated fibrosis parameters by error bars. In Fig. 3, the $x$-axis is the normalized fiber size $F_s/\text{Rs}$. When the fiber size corresponds to the resolution size, the $F_s/\text{Rs}$ equals to 1. Figure 3(a) shows the estimated variance ratio (fibrosis stage), and Fig. 3(b) shows the estimated fiber mixture rate (amount of the fibrotic tissue). From Fig. 3, we can see that by the effect of the resolution, the estimated variance ratio becomes smaller and estimated mixture rate becomes a little larger than their true values (setting values) when the fiber size becomes smaller. The fibrosis parameters can be estimated stably when the fiber size becomes larger than about one-half of the resolution size ($F_s/\text{Rs} > 0.5$) though the estimated fibrosis parameters deviate from their true values. The unsteadiness of the fibrosis parameters when the fiber size becomes smaller than about one-half of the resolution size ($F_s/\text{Rs} < 0.5$) is not because of the effect of the resolution but because of the estimation method based on the multi-Rayleigh model. In the condition that the fiber size becomes smaller than about one-half of the resolution size, the PDF of the echo amplitude can be modeled by a single Rayleigh distribution model. However, the multi-Rayleigh model tried to divide the PDF into two Rayleigh distribution models with different variances so that the estimated fibrosis parameters can take several values.

4. Examination of method to compensate the effect of the resolution

In this section, we examine the method to compensate the effect of the resolution of the ultrasound.

4.1. Compensation procedure for the effect of the resolution

In the previous section, we clarified that the effect of the resolution was related to the relationship between the fiber size and the resolution size. Considering this relationship, we tried to correct the estimated fibrosis parameters to their true values in the following procedure.

1. We make B-mode images from a same scatterer distribution model with each ultrasound beam which has a different beam width.
2. We estimate the fibrosis parameters from each B-mode image made by the procedure 1.
3. We estimate the fibrosis parameters when the beam width equals to 0 from the relationship between the estimated fibrosis parameters and the beam width.
4.2. Results of compensation in the simulated image

By ultrasonic simulation, we made the B-mode images which have different beam widths. We changed the ultrasound beam width by changing the F-number on a dynamic focus. Figure 4 shows the scatterer distribution model. The setting variance ratio is 5 and the setting mixture rate is 0.1. Figure 5 shows the B-mode images calculated from Fig. 4 with different beam widths. The beam widths are (a) 2.5 mm, (b) 2.0 mm, and (c) 1.5 mm.

Then, we estimated the fibrosis parameters from Fig. 5. Figure 6 shows the relationship between the estimated fibrosis parameters and the ultrasound beam width. In Fig. 6, the x-axis is the beam width and the y-axis is (a) the estimated variance ratio and (b) the estimated mixture rate. From Fig. 6, we can see that as small as the beam width becomes, the estimated fibrosis parameters approach to their true values when the beam width equals to 0.

To estimate the fibrosis parameters when the beam width equals to 0, we approximated the change of the estimated fibrosis parameters. We show the estimation results on Fig. 6. From this extrapolation results, we can estimate the fibrosis parameters when the beam width equals to 0. The estimated variance ratio and the estimated mixture rate when the beam width equals to 0 are 4.75 and 0.10, respectively. The
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5. CONCLUSIONS

We examined the effect of the 2-dimensional resolution of the ultrasound for quantitative estimation method of liver fibrosis using ultrasound image. By the effect of the resolution of the ultrasound, the estimated variance ratio (fibrosis stage) becomes smaller than its true value and the estimated fiber mixture rate (amount of fibrotic tissue) becomes a little larger than its true value. The effect of the resolution is related to the relationship between the fiber size and the resolution size. A quantitative evaluation of the compensation method is a future work.

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References