3J4-1

Application of Super-resolution Technique to Spatiotemporal Observation of Bubble Cavitation
超解像技術の気泡キャビテーションの時空間観測への適用

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1. Introduction

The *in vivo* bubble cavitation application, such as sonoporation and drug delivery, is a promising method to enhance permeablity of the drugs. We have proposed an image reconstruction technique that enables both temporal- and spatial-resolved observation of bubble cavitation dynamics using the back propagation of the acoustic cavitation emission (ACE) signal [1]. Alothough this method has an excellent temporal resolution of sub microseconds, its spatial resolution is almost same as that of general ultrasound imaging devices. As bubble clouds show complicated motion owing to Bjerknes forces, the spatial resolution is insufficient to observe bubble cavitation dynamics within a single blood vessel.

Many researches have been reported on super-resolution technique in the optical imaging field. One of them is called structured illumination microscopy (SIM) [2], which uses exitation light with periodic pattern along specified directions. By utilizing the interference between the observation signal and the periodic signal, super-resolution imaging that exceeds the resolution limit can be realized.

In this study, high resolution bubble cavitation observation is performed by combining SIM with the bubble cavitation observation method. In our method, virtual periodic signals are used instead of periodic illumination.

2. Application of super-resolution technique

Fig. 1 shows a schematic diagram of the proposed method. The high intensity ultrasound is irradiated to microbubbles. When bubble cavitation occurs, an ACE signal is generated. The signal is received by the array elements on the linear probe, and the RF data is recorded by the ultrasound imaging device. The temporal- and spatial-resolved image of the bubble cavitation is reconstructed by ultrasound wave back propagation. The reconstructed image consists of a signal with the point spread function (PSF) convolved. Therefore, the original signal is estimated from the known PSF, and super-resolution processing is applied to the estimated original signal. It is assumed that the PSF has an intensity distribution in the range of $\pm k_c$ in Fourier space. Here, k_c is a cutoff frequency determined by the aperture width of the linear probe and the wavelength. To obtain a super-resolution image, we use three 1-D periodic signals that are phase-shifted by $2\pi/3$ with the spatial frequency k_0 in the x-axis direction. This cause interference with the spatial frequency of the original image and the periodic signal, and then, the super resolved image has information of spatial frequency higher than k_c.

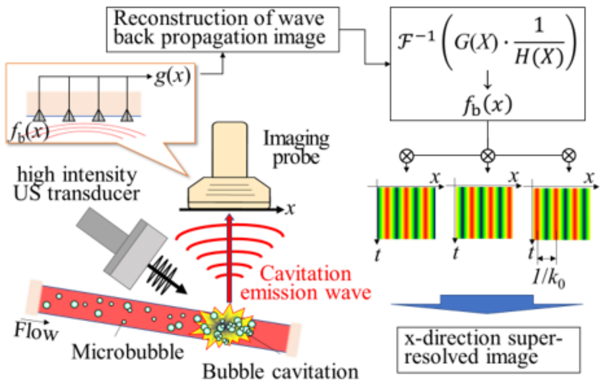

Fig. 1 Overview of proposed method.

The periodic signal is expressed as

$$fill_{\mathrm{i}}(x) = 1 + \cos(k_0 x + \varphi_{\mathrm{i}}) \tag{1}$$

Here, the index i shows the i-th shift of the phase(i=1,2,3), φ_{i} indicates the phase shift($\varphi_{\mathrm{i}} = (2\pi/3)i$).The observation signal phase-modulated by this periodic signal is

$$g_{\mathrm{i}}(x) = \{fill_{\mathrm{i}}(x)\cdot f_{\mathrm{b}}(x)\} * h(x) \tag{2}$$

where $f_b(x)$ is the original signal of bubble cavitation, $h(x)$ is PSF, and the asterisk denotes convolution. Since the observed signal shifts $\pm k_0$ in Fourier space due to interference with the periodic signal, the super-resolution signal contains sum and difference components with respect to k_0. Therefore, the PSF of the super-resolution image (PSF_{SIM}) becomes the weighted addition of the components shifted by $\pm k_0$ from the original PSF. The super-resolution PSF is expressed as follows using γ.

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$$H_{\mathrm{SIM}}(X) = H(X) + \gamma H(X - k_0) + \gamma H(X + k_0) \quad (3)$$

Therefore, the super-resolution observation image in Fourier space is

$$G_{\mathrm{SIM}}(X) = F_{\mathrm{b}}(X) \cdot H_{\mathrm{SIM}}(X) \quad (4)$$

Fig. 2 shows the PSFs intensity distribution in Fourier space before and after super-resolution and the 1-D plot in real space. The cut-off frequency of the super-resolution image is extended to $\pm(k_c+k_0)$. By selecting k_0 so that $k_0 \cong k_c$, the band width range becomes $\pm 2k_c$. Therefore, the spatial resolution in the real space can be expected to be approximately twice in the x-axis direction.

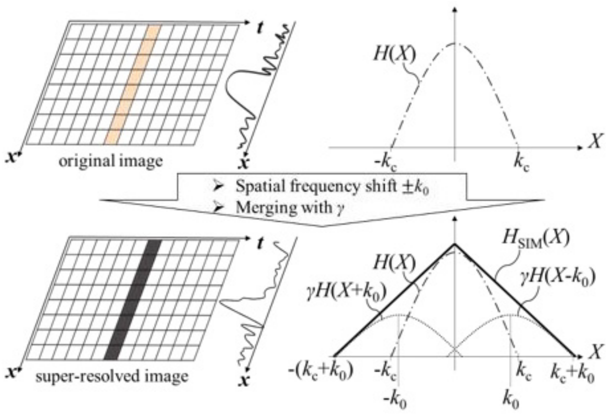

Fig. 2 1-D distribution of bubble cavitation image and PSFs intensity distribution in the spatial frequency space.

3. Results

The spatial resolution in the x-axis direction of the proposed method was confirmed by simulating the convolution of the PSFs and the impulse input. **Fig. 3** shows the simulation results of the conventional method and the proposed method. From **Fig. 3**, the half width of the conventional method is 0.52 mm, and the half width of the proposed method using super-resolution technique is 0.27 mm. These results indicate that the spatial resolution was improved by about 1.93 times.

We applied the proposed method to a bubble cavitation observation experiment using microbubble Sonazoid injected to a small hole (diameter: 2 mm) in an agarose gel. The high intensity ultrasound irradiates to bubbles with a sound pressure of 1.0 MPa and a central frequency of 2.5 MHz. The concentration of suspension of microbubbles was 1.2×10^7 /mL. To record RF signals, an ultrasound platform (RSYS0003, microsonic Co.,Ltd., Japan) with an imaging US linear array probe (7.5 MHz) was adopted.

Figs. 4(a) and 4(b) show typical bubble cavitation observation images obtained by the conventional method and the proposed method. Although some noise appears in the super-resolution image, the spatial resolution in the x-axis direction is improved. The improved spatial resolution provides information on the fine cavitation intensity distribution within the diameter of the bubble-injected hole.

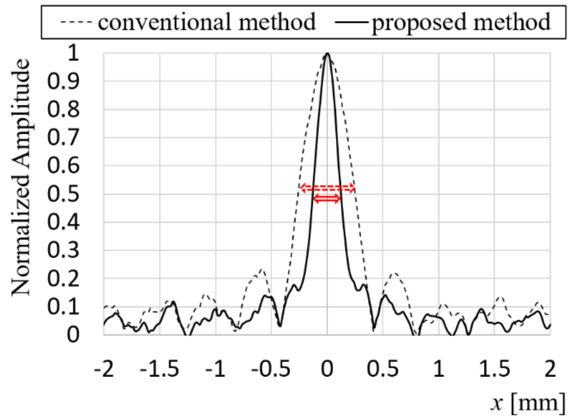

Fig. 3 Comparison of simulation results obtained by conventional and the proposed method.

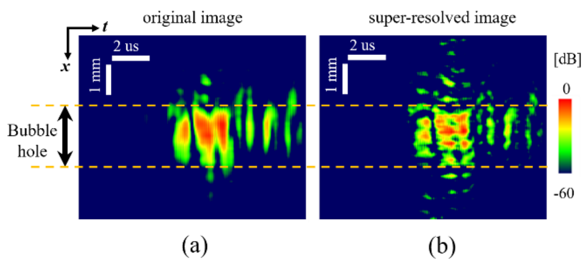

Fig. 4 Typical bubble cavitation observation images. (a) original image (b) super-resolved image

4. Conclusion

In this study, we applied the super-resolution technique using interference with periodic signals to bubble cavitation observation images. As results, the resolution in the x-axis direction was improved about twice, and the cavitation distribution inside the blood vessel could be observed.

References

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2. S. Hayashi and Y. Okada: Molecular Biology of the cell. **26** (2015) 1575.