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Observation of spatial-temporal dynamics of bubble cavitation during high-intensity ultrasound exposure

強力超音波照射中の気泡キャビテーションの時空間的ダイナミクスの観測

Ren Koda†, Takumu Origasa, Toshitaka Nakajima, and Yoshiki Yamakoshi (Grad. School of Science and Technology, Gunma Univ.)
江田廉†，折笠拓夢，中嶋俊貴，山越芳樹 (群馬大院　理工）

1. Introduction

The *in vivo* bubble cavitation application, such as sonoporation and drug delivery, is a promising method to enhance permiablity of the drugs. For the understanding of the mechanism of bubble cavitation, several methods have been investigated using various techniques. Recently, a multi-element detector like an ultrasound array is used for acoustic detecting methods include active cavitation mapping (ACM) and passive cavitation mapping (PCM)[1]. In general, PCM, which are performed by passively recording acoustic emissions from cavitation bubbles, can be employed to provide a 2-D spatial mapping of cavitation activity during ultrasound exposure. However, not only spatial resolution but also highly temporal resolution is required because bubble cavitation includes signals from highly time-resolved dynamics relative to the fundamental frequency of US such as the nonlinear oscillation of bubbles and bubble destruction.

We have been proposed a time-resolved measurement method for a secondary US wave irradiated by bubble cavitation by using generally utilized US imaging equipment[2]. By the method, better than 1mm spatial resolution and sub-μs order time resolution monitoring are achieved by using two images (S- and T-images). However, since these two images are obtained using a conventional color Doppler imaging instrument, the measured data is limited information compared to the RF signal. Moreover, the RF-signals include more information potentially by applying visualization algorithm.

In this study, a beamforming method is applied to ultrasound RF signals in order to obtain holographic image which contain bubble cavitation signal. A novel measurement method of bubble cavitation, which has temporal resolution of sub-micro second and spatial resolution of sub-mm, is proposed and the bubble cavitation signal source is reconstructed by holographic US wave back-propagation.

2. Reconstruction of holographic image by back-propagation

We consider a case where microbubbles exist in only high intensity focused US wave (Pumping wave) focal point area. In holographic image reconstruction, we consider the wave back-propagation signals radiated from bubble located at *x*-position and at certain fixed depth.

When the secondary US signal irradiated from a certain positon x is described as $g(x,t)$, the receiving signal at ith element of the liner array probe is estimated as

$$f_i(\eta_i, t) = K\int_x F\left(g\left(x, t-\frac{r}{c}\right)\right)dx \qquad (1)$$

where r is a distance between the bubble position and the positon of the ith element of the linear array probe. η_i is a distance of ith element from the center of the probe. K is an electronic coefficient, F is a receiving characteristic factor of the linear probe, c is sound speed.

By wave back-propagation, sound pressure distribution along the x-axis is obtained as follow,

$$g_r(x,t) = \sum_i f_i\left(\eta_i, t+\frac{r}{c}\right) \qquad (2)$$

The amplitude information is estimated by quadrature detector output signals.

3. Results

We observed holographic images for microbubble Sonazoid suspension which was injected to a small hole in an agarose gel. A concave transducer was adopted for Pumping US irradiation. The center frequency of Pumping US was set at 2.5 MHz. The irradiation time of Pumping US was set to 10μs. As the US equipment for recording RF signal, an ultrasound platform (RSYS0003, microsonic Co.,Ltd., Japan) with an imaging US linear array probe (7.5MHz; Probing US) was adopted. The RF signals acquired by 16 elements (ch1-ch16) of the linear probe are recorded via A/D converter (31.25MHz sampling). The signals are digitized with

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e-mail: koda@gunma-u.ac.jp

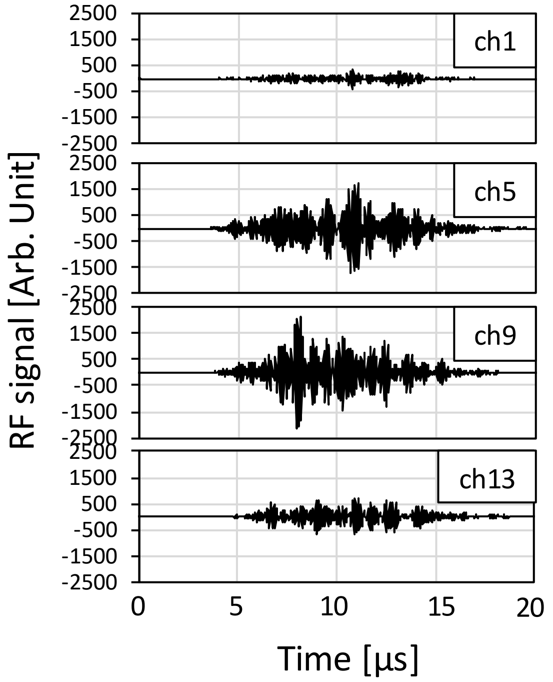

Fig.1. RF signals recorded by ch1, ch5, ch9, ch13, respectively.

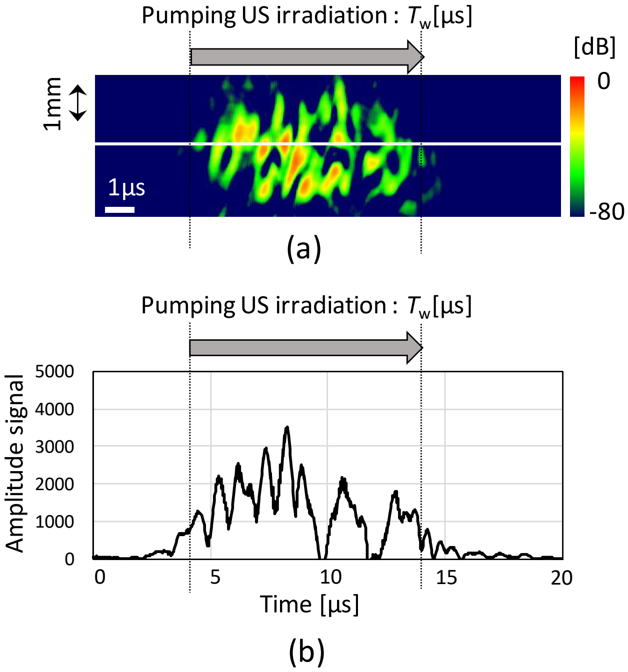

Fig.2. Reconstructed holographic image of amplitude signal (a), 1-D amplitude signal after beamforming (b)

12 bit precision and stored in text files for image reconstruction. The images are reconstructed by holographic US wave back-propagation.

Fig.1 shows several RF signals acquired by the linear array probe during Pumping US wave irradiation. Within 16 elements of the linear probe, RF signals recorded by ch1, ch5, ch9, ch13 are shown. When Pumping US is synchronized with the irradiation timing of Probing US, a bubble cavitation signals (BCS) are measured within the length of RF signal which is sampled in 1024 points. The sound pressure of Pumping US is 1.0MPa. The concentration of Sonazoid suspension is 8.0x10^{-3} µL/ml. The signals are filtered by IIR band pass filter. The range of frequency band limitation is between 5.0 - 10.0 MHz. Since the central frequency of Probing US is chosen to be much higher than that of Pumping US in order to suppress the US wave, which is propagated directly from the Pumping US transducer, the harmonic frequency component caused by bubble cavitation is recorded.

Figs.2(a) and 2(b) show a holographic image and the 1-D amplitude of RF signal after the application of beamforming method. The sound pressure of Pumping US is 0.5MPa. The concentration of Sonazoid suspension is 8.0x10^{-3} µL/ml. In Fig.2(a), the horizontal and the vertical axis of the image indicate time and *x*-position, respectively. We clearly see the temporal and spatial development of secondary US signal in the image. The succession of signal pattern in lateral direction is observed. Although further research is needed, it may be considered the cause of the succession in *x*-direction is not by bubble movement but by lateral propagation of secondary US by nonlinear oscillation or destruction of bubbles. In addition, intermittent pattern in time direction is observed. This cause is thought to be by bubble destruction and bubble cloud formation. In Fig.2(b), the 1-D amplitude signal is obtained by analyzing the white line in Fig.2(a). This signal fluctuates as a result of the movement, nonlinear oscillation, cloud formation, and destruction of bubbles. Although, in order to measure the bubble destruction signal, sub-µs-order time resolution, which is achieved by the proposed method, is insufficient, bubble nonlinear oscillation can be measured by the proposed method.

4. Conclusions

In this study, we proposed a temporal and spatial resolved observation of microbubble cavitation signal measurement method. We applied a beamforming method to ultrasound RF signals which contain bubble cavitation signal in order to reconstruct holographic image. From the holographic image reconstruction, lateral propagation of secondary US in the bubble cavitation is observed.

References

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2. R. Koda, Y. Izumi, H. Nagai, and Y. Yamakoshi, Jpn. J. Appl. Phys. **56**, 047201 (2017).