Control of a thin catheter bending at bifurcation points in artificial blood vessel by using acoustic radiation force*

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Abstract— **In this paper, control of a thin catheter bending by using acoustic radiation force was carried out to develop precise and noninvasive surgery in small blood vessel. First, it was elucidated that the acting force to a thin catheter made from perfluoroalkoxy (PFA) copolymer could be obtained from the cantilever equation in the effective range, where the displacement of the catheter divided by the cube of the length of the catheter was less than 1.0x10^{-5} mm^{-2}. Next, under the above cantilever theory, acoustic radiation force acting to the catheter was measured in the condition of the continuous ultrasound radiation. Furthermore, it was observed that the force depended on the ultrasound frequency. We confirmed that the force was obtained in the practical condition by the experiment and controlled it bending in artificial blood vessel including multiple bifurcations. It was suggested that the therapy using thin catheter and ultrasound is fully promising.**

I. Introduction

Nowadays, catheter is not only used in medical therapy, but also studied for minimally invasive surgery. For instance, examination of coronary stenosis, coronary balloon angiography and endovascular stent therapy, are still seemed high-level catheter applications. In an application of embolization therapy for liver cancer, which is an injection of substances to block the blood flow to cancer cells in the liver, the catheter has to be come close to the target as much as possible. As the importance of less invasive therapies increases, the requirement of the role of catheter will become important for micro surgery. Using a thin catheter, of which width is less than 500 μm, it must be expected that more various applications of the clinical catheter though the capillary expands. However, because the width of a metal guide-wire, which is used with the conventional catheter therapy using X-ray [1], is at least 400 μm, it is difficult to apply to smaller vessel less than 1 mm. Therefore, we have considered a method of active control of the thin catheter by using acoustic radiation force to contribute a precise and noninvasive surgery in tumor blood vessels.

The acoustic radiation force is generated where acoustic energy density gap occurs at the interface along ultrasound propagation. We have studied a new therapeutic application using microbubble controlled by ultrasound radiation force, e.g. active path selection [2,3], trapping [4,5], and forming aggregation [6] of microbubbles using artificial blood vessels, where microbubbles containing anticancer drug are delivered to a desired target in the blood vessel. If the catheter could come closer to the target tissue, the drug in microbubbles will be delivered more reliably and accurately to the point where drug density will be locally increased.

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It is well known that the acoustic radiation force is independent to ultrasound frequency when the interface is quite larger than the wavelength and where diffraction effect can be ignored. On the other hand, because the size of a microbubble is smaller than the wavelength, acoustic radiation force strongly depends on the frequency [2,6]. Thus it is important to investigate theoretically and experimentally the force on a thin catheter with a width of several 100 μm versus frequency because the width of the catheter is near the wavelength. In this paper we describe our preliminary attempt for active control of thin catheter by acoustic radiation force to show the feasibility of this method.

II. Principle

Before measuring the acoustic radiation force acting on a thin catheter, the relationship between an external force and a displacement of the catheter should be elucidated. Figure 1 shows the model of a thin catheter, which has outer radius of r_0, inner radius of r_i, balk elasticity of E_l and the original length of L_0, is fixed on a rigid body.

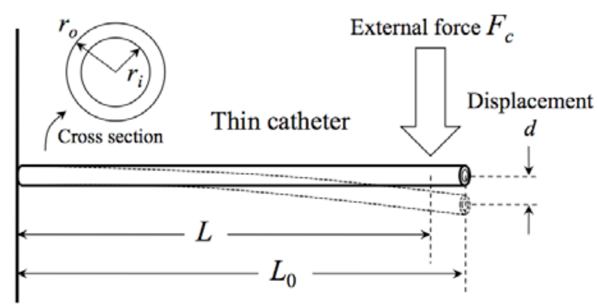

Figure 1. A model of thin catheter to adopt cantilever theory.

When the external force propels near the end of the catheter to bend it, the cantilever theory [7], which is used in material technology, predicts that the relationship between the external force F_c and the displacement d as

$$F_c = \frac{3E_l d}{L^3} \cdot \frac{\pi}{4}\left(r_0{}^4 - r_i{}^4\right), \quad (1)$$

where L ($L < L_0$) indicates the distance from the rigid body to the point where the external force is applied. Since all parameters except the length L depend on the fabrication of the catheter, F_c can be regarded in proportion to d/L^3, which indicates that longer catheter requires less force to obtain a certain displacement. However, it is very important to investigate the effective ranges of the parameter d/L^3

experimentally because there must be limitation of this relationship where the displacement would saturate in spite of the increase of external force.

Next we consider that the catheter is propelled by acoustic radiation force. When an object, which dimension is larger than the wavelength in an acoustic field, acoustic radiation force F_a to propel the object in the direction of propagation is expressed using Langevin equation [8] as eq. (2), where the cylinder shape of the catheter was taken into account to calculate the acoustic radiation force. Here the surface of the catheter is assumed to reflect ultrasound.

$$F_a = \iint \frac{p_z^2(x,y)}{2\rho c^2} dxdy , \quad (2)$$

where $p_z(x, y)$ indicates the acoustic pressure distribution at the distance z from the transducer, x-axis corresponds the axis of the catheter, and y-axis is in the direction of the width of the catheter. In this study, since the width of the catheter $2r_o$ is small enough, the integration was executed along the x-direction to obtain the acoustic radiation force acting on the catheter as eq. (3).

$$F_a = \frac{r_o}{\rho c^2} \int p_z^2(x) dx . \quad (3)$$

Though eq. (3) does not include the effect of frequency, there is a possibility of frequency dependence of acoustic radiation force on a thin catheter when the order of wavelength is larger than the size of the catheter. Thus it is important to investigate the acoustic force using multiple frequencies experimentally.

III. EXPERIMENT

A. Application of cantilever theory to thin catheter

We prepared a thin catheter made of perfluoroalkoxy (PFA) copolymer, which has the outer radius r_o = 200 µm and the inner radius r_i = 50 µm, balk elasticity was measured as E_l = 600 MPa. The catheter reflects ultrasound in water because its sound speed is 1520-40 m/s and the density is 2 g/cm^3. The original catheter is transparent and easily bent by hand. We have prepared several catheters with different lengths.

Here, when ultrasound is exposed on the catheter to be bent as shown in Fig.1, the external force F_c cannot be measured directly using a conventional measurement because it is too small in µN order. Thus we considered an experimental setup shown in Fig. 2 and carried out the following procedure. First, two catheters with the lengths with L_1 and L_2 ($L_1 < L_2$) are placed in parallel with connecting the both ends by thread without the slack. The basement of the catheter 1 is fixed on a rigid body whereas the catheter 2 is fixed on a vehicle, which is movable in the direction perpendicular to the original axis of the catheters. Then the vehicle moved to right as shown in Fig. 2, both catheters are bent. If both catheters satisfy the cantilever theory of eq. (1), and the displacements in both catheters are measured as d_1 and d_2, respectively, the following equation should be fulfilled.

$$\frac{d_1}{L_1^3} = \frac{d_2}{L_2^3} . \quad (4)$$

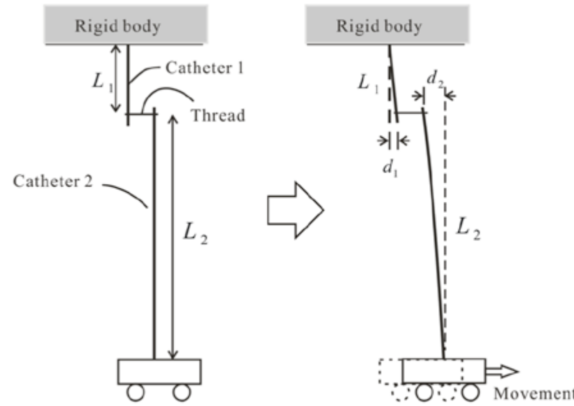

Figure 2. A setup for measurement to measure effective range of cantilever theory.

Under the above assumption, by defining the following evaluation function, the effective ranges, where the cantilever theory is applicable, will be estimated. In the range where *err* in eq. (5) is regarded to be close to 1.0, the effective force F_c is directly converted from the displacement of the catheter using eq. (1).

$$err = \left(\frac{L_1}{L_2}\right)^3 \frac{d_2}{d_1} . \quad (5)$$

As shown in Fig. 2, both axes of chosen two catheters are placed horizontally on a table, where the microscope (Omron KH-7700) was used to measure the displacements in both catheters according to the motion of the vehicle.

B. Investigation of frequency dependency of acoustic radiation force on thin catheter

After the effective ranges where the cantilever theory was applied, we investigated the frequency dependence of acoustic radiation force using the same catheter, which was placed in the bottom of a tank with filled degassed still water with the rigid body as shown in Fig. 3. The displacement of the catheter was observed immediately upon exposure of ultrasound and measured using the above-mentioned microscope, which was set beneath the bottom of the water tank. Between the catheter and the transducer there is a thin cellophane film to prevent the effect of sound flow with the distance from the catheter. The catheter was located in the distance of L_h = 50 mm from the bottom of the tank, and in the distance of L_f = 80 mm from the ultrasound transducer (TD) with L_p = 5 mm. The axis of the transducer was adjusted to make the intersection point in the distance of L_s = 4 mm from the tip of the catheter. Water temperature was kept to be 26 degree C through the experiment. We used ultrasound transducers including a flat ceramic disc to emit plane sinusoidal ultrasound, which central frequencies of continuous wave ranged in 2, 3, 7, and 10 MHz to compare the dependence of frequency, where the sizes of beam spots (half width of the sound pressure distribution) were 7.5, 5.0, 4.0, and 3.5 mm, respectively.

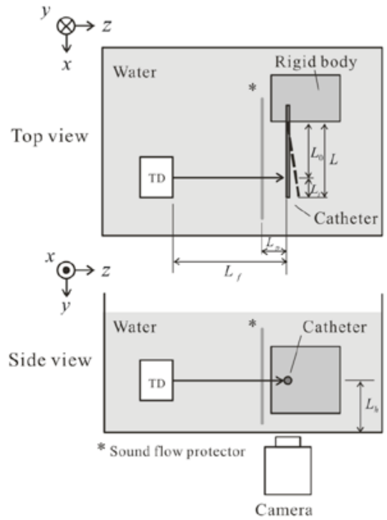

Figure 3. System configuration to measure displacement of catheter using acoustic radiation force.

IV. RESULTS

A. Estimation of effective range of the cantilever theory

To investigate the effective range where the cantilever theory can be applied, we prepared two catheters, whose lengths are different, to apply to the experiment in Fig. 2. The length of L_2 was varied to be 39, 44, 48, and 52 mm, respectively, by fixing the length of L_1 to be 30 mm because of the detection resolution of displacement using the microscope. Figure 4 shows the relationship between the displacements of d_1 and d_2, where parameters are the length of L_2, which includs four times experiments for each length. The solid lines indicate the proportional lines with the slope of L_2^3/L_1^3 in eq. (4) for each length of L_2. According to the increase of the displacement of d_1, the displacements data of d_2 became apart from the proportional lines gradually [9], which suggests that the conditions near the proportional lines indicate an effective range of the cantilever theory.

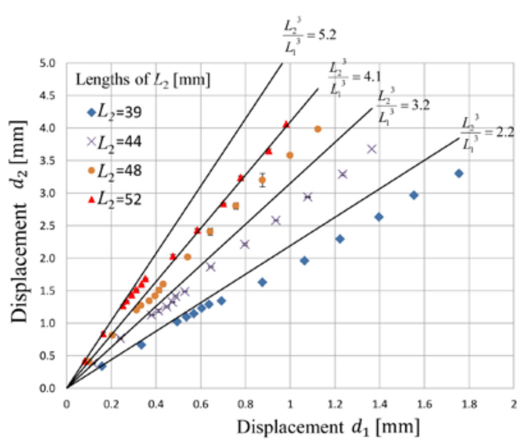

Figure 4. Relationship between displacements of two catheters according to the length of catheter.

Figure 5 shows the variation of evaluation function of *err*, which was defined as eq. (5), versus the displacement of d_2. The value of *err* decreased in inverse proportion to the displacement of d_2, in which solid line indicates the fitting curve when the length of L_2 was 48 mm. Here we established a threshold, where the effective range should fulfills $0.95 < err < 1.05$. Calculating linear approximation lines using several point near $err = 0.95$, we have obtained the maximum displacements of d_2 according to the value of L_2^3, which indicates the limitation of the cantilever theory, and the result is shown in Fig. 6. Then the relationship between d_2 and L_2^3 showed linear to indicate that the effective range was given where the ratio of d_2/L_2^3 is less than 1.0 x 10^{-5} mm^{-2}, which is the slope of the solid line in Fig. 6.

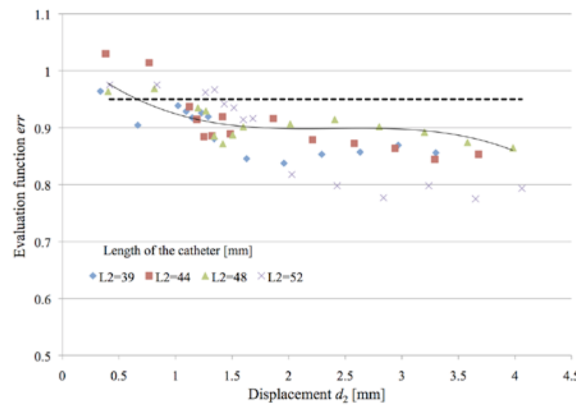

Figure 5. Variation of evaluation function versus displacement of catheter.

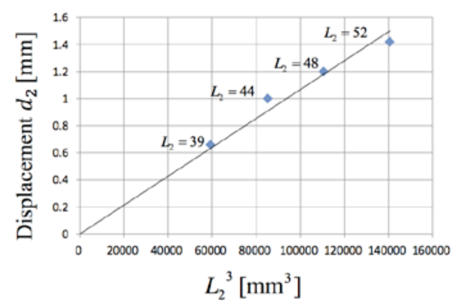

Figure 6. Maximum displacement d_2 versus the value of L_2^3, which indicates the limitation of the cantilever theory with 5% assurance.

B. Investigation of frequency dependency of acoustic radiation force

Using the result in the previous section, we have estimated the acoustic radiation force on a thin catheter for active control of the catheter. Figure 7 shows the relationship between calculated acoustic radiation force F_c [μN], which was derived from the actual displacement, and peak acoustic pressure [kPa], which was measured before this experiment shown in Fig. 4. Because these results included the displacements using 4 kinds of lengths of L = 39, 44, 48 and 52 mm, this graph shows independency in the length of the catheter. However, the result obviously shows the dependencies on the frequency despite the acoustic pressures were the same, since there is no term of frequency in eq. (2). Because the actual wavelengths of ultrasound were 750, 500, 210 and 150 μm with frequency of 2, 3, 7, and 10 MHz, respectively, there is a possibility that the width of the catheter $2r_o$ = 400 μm does not satisfy the assumption of Langevin equation.

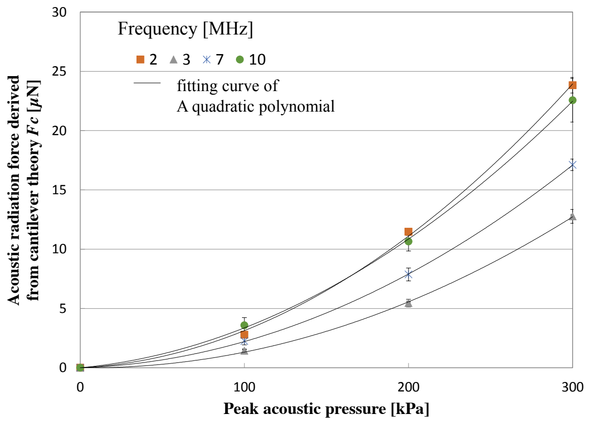

Figure 7. Relationship between acoustic radiation force and peak acoustic pressure on thin catheter.

Figure 8 shows the comparison of the force F_c and F_a, calculated from eqs. (1) and (3), respectively, with the parameters of frequency. There seems to be a correlation between two forces on each frequency. These two values, which were derived from different preconditions, ranged in several 10 μN order but did not correspond perfectly. The reason of that is considered as the difference in the surface shape of the catheter, where the former was considered as a cylinder, as the latter was a plane, which should be studied in the future research.

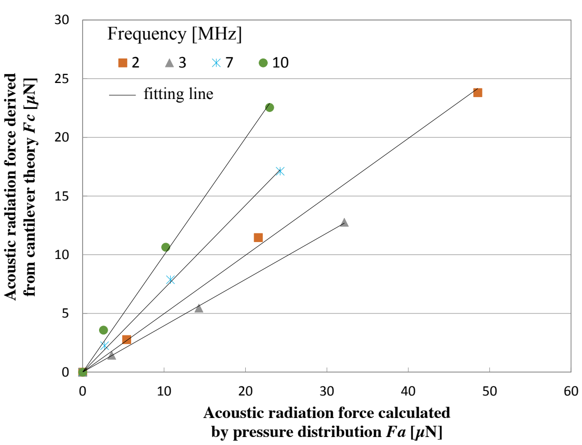

Figure 8. Relationship of acoustic radiation forces calculated from cantilever theory and sound pressure distribution.

C. Control of thin catheter bending in artificial blood vessel

Figure 9 shows captured images of the microscope when two different continuous ultrasound waves were applied on a thin catheter in the artificial blood vessel, which was made of poly(ethylene glycol) [2-6] and had two bifurcations with minimum inner diameter of 1 mm. Let us notice that the catheter is invisible due to its high transparency, thus the presence of the catheter has to be confirmed by inner diameter, which is visible due to light refraction of air inside. The catheter was inserted from the bottom of the image to be bent by the ultrasound radiation (the peak sound pressure of 500 kPa and the central frequency of 7 MHz) from the right at the Y-form bifurcation. After passing the first bifurcation, the catheter was pushed manually until reaching the second bifurcation, where the tip of the catheter was bent by ultrasound radiation (the peak sound pressure of 600 kPa and the central frequency of 10 MHz) from the lower left. Here the catheter was confirmed to be bent at two points with the displacements, which satisfied the cantilever theory. Similarly acoustic radiation forces were calculated from the displacements as long as d_2/L_2^3 is in the effective range of the cantilever theory.

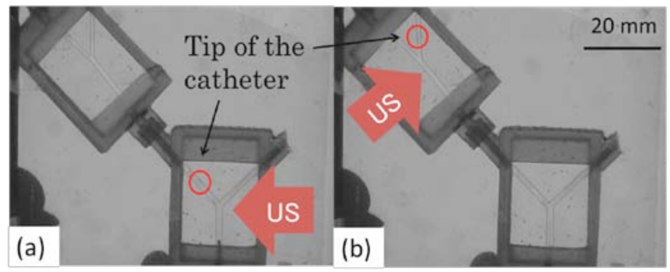

Figure 9. The demonstration of thin catheter bending and inserting through (a) first and (b) second bifurcations of artificial blood vessel under exposure of continuous ultrasound.

V. Conclusion

In this paper we have elucidated the method to measure acoustic radiation force on a thin catheter with a width of 400 μm using cantilever theory and compared with simulation derived from acoustic pressure distribution. Before measuring acoustic radiation force we estimated the effective range where the cantilever theory can be applied, which was the ratio of d/L^3 is less than 1.0 x 10^{-5} mm^{-2}. Then we compared acoustic radiation forces between the result of the cantilever theory and the calculation of acoustic pressure distribution. As the result, we showed the dependence of acoustic radiation force on frequency, where the higher frequency had an advantage to control a thin catheter. Furthermore, we have confirmed the bending control of the catheter with specified ultrasound parameters. Because estimated condition of ultrasound emission was safe for human, the practical realization of endovascular therapy using ultrasound and a thin catheter is fully promising.

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