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Proceedings of Symposium on Ultrasonic Electronics, Vol. 33 (2012) pp. 245-246
13-15 November, 2012

Experimental study for active path block in a capillary flow by using microbubbles aggregation

微小気泡の凝集現象を利用した人工血管での狭小流路塞栓のための実験的検討

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1. Introduction

It is known that microbubbles form their aggregations under ultrasound exposure. By using the microbubbles aggregation, the effects of ultrasound therapy would be expected due to increase temperature elevation accelerates in thermal therapy [1-2] and degree in sonoporation. However, there was a problem of side effect because microbubbles spread in human body with bloodstream. Therefore, we have ever reported our attempts to control microbubbles using the primary and secondary Bjerknes force to elucidate the conditions in sound pressure, central frequency of ultrasound, and flow velocity for active path selection in water flow [3]. Also we investigated trapping in blood flow of microbubbles using artificial blood vessels with a simple shape [4]. However, because of the difficulty to produce a capillary-mimicking artificial blood vessel, the behavior of aggregations in a capillary, e.g., a probability to obstruct bloodstream, a destruction of the aggregation, etc, has not been predicted. If there is the possibility that the aggregations might obstruct entire vessels, it can be applied as a novel therapeutic method of an artificial embolisation near the target area of a tumor. Meanwhile, microbubbles aggregation should be controlled to prevent to enter unwanted area. In this paper, we describe the experiment to investigate the size of microbubbles aggregation and the possibility to block the paths.

2. Experiment

We used the microbubbles Sonazoid® and prepared the following two types of artificial blood vessels, which were the straight path model and the capillary model.

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2.1 Size of microbubbles aggregation

By using a straight model we have calculated of the size of microbubbles aggregation under various conditions of ultrasound emission. And to evaluate area of the aggregation, we established a square region of interest in the observation area [4].

2.2 Induction of aggregation and path block

Also a capillary model was used for active path block by making use of aggregation. **Fig. 1** and **Fig. 2** show the experimental setup. The inflow path of 2 mm was repeatedly divided into two lower courses to constitute the artificial capillary until 16 paths, where the minimum diameter was 0.50 mm. In this experiment, we prepared two focused ultrasound transducers. One is to produce the microbubbles aggregations in the middle of the inflow, and the other is to propel the aggregation and induce to an objective path, where these central frequencies were 5 MHz (T_{ag} and T_{in}). The maximum sound pressures and of T_{ag} and T_{in} were set from 300 kPa to 500 kPa. The flow velocity was set at 20 mm/s. In addition we also used colored water to visualize path block and flow variations in the artificial capillary model.

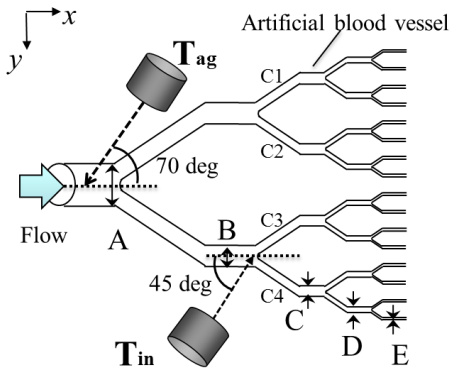

Fig. 1 Experimental setup of *x-y* plane

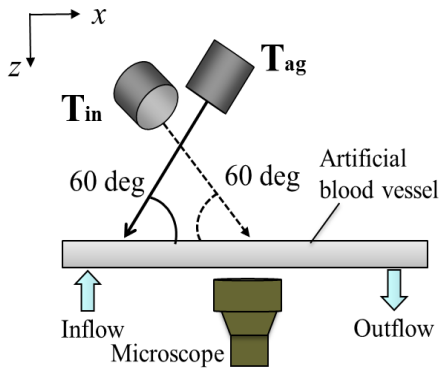

Fig. 2 Experimental setup of *x*-*z* plane

4. Results and Discussion

As the result of the size of aggregations, it increased according to the exposure time of ultrasound emission, where the several small aggregations were gradually coalesced. In 20 s of ultrasound exposure, the area of microbubbles aggregation was about than 1 mm^2. Though the size of aggregation increased in proportion to sound pressure and inversely to the flow velocity, it was independent to the central frequency. **Fig. 3** shows the map of percentage in through rate and path block due to aggregations, when ultrasound of T_{ag} (300 kPa) was shut in 20 s, while ultrasound of T_{in} was emitted with 300 kPa. To elucidate the destinations of the aggregations, **Fig. 4** shows the through rate of aggregations in paths C1 to C4. More flown aggregations were inducted to path C3 where higher sound pressure of T_{in} indicated higher probability in active path selection. Because the destination of an aggregation is originally random, we have confirmed that the aggregation is controlled to a desired path by using an ultrasound for induction. This indicates that there is possibility to control the location of path block.

Fig. 5 shows the probability of path block from the paths B to E, when ultrasound of T_{ag} was also shut at 20 s, while sound pressure of T_{in} was mitted with 300 kPa. The probability of path block in paths D and E was more than that in paths B and C, which result is reasonable because the area of cross sections in paths B and C were 1.56 and 0.79 mm^2, respectively, considering above-mentioned size of an aggregation of 1 mm^2.

5. Conclusions

In this study, we observed the behavior of microbubbles aggregation in a capillary flow. We confirmed the possibility of active path block by using aggregations. Furthermore, the more aggregations were inducted to the desired path when an ultrasound for induction was set. These results indicate that commercially available microbubbles, which is used as contrast agent for diagnosis, can be applied for a novel therapy.

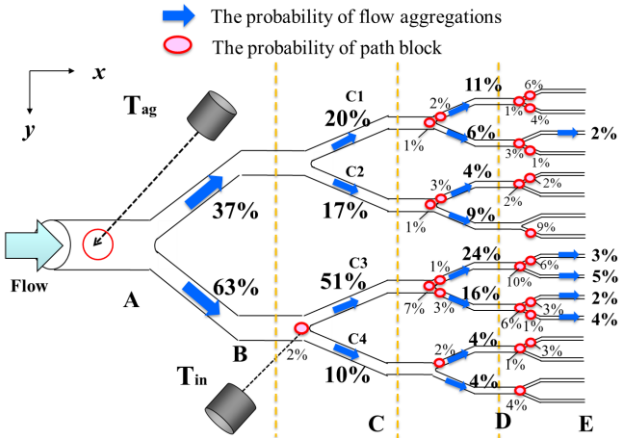

Fig. 3 The map of percentage in through rate and path block due to aggregations (T_{ag} and T_{in} were 300 kPa, after T_{ag} was shut in 20 s)

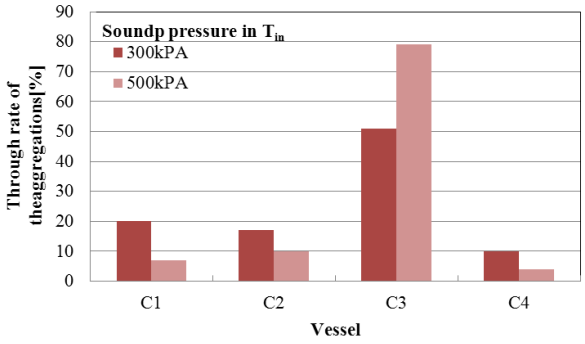

Fig. 4 The through rate of aggregations in paths C

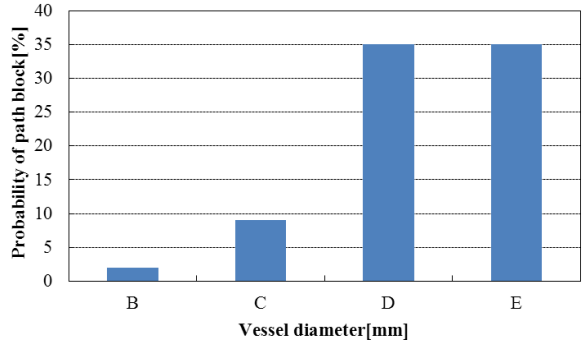

Fig. 5 The probability of path block from the paths B to E with sound pressure T_{in} of 300 kPa.

Acknowledgment

This work was supported by the Japan Society for the Promotion of Science (JSPS) through the Funding Program for Next Generation World-Leading Researchers (NEXT Program).

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