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THOUGHTS & PROGRESS

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Prevention of thrombus formation in blood pump by mechanical circular orbital excitation of impeller in magnetically levitated centrifugal pump

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Abstract

Background: Mechanical circulatory support devices, such as left ventricular assist devices, have recently been used in patients with heart failure as destination therapy but the formation of thrombus in blood pumps remains a critical problem. In this study, we propose a mechanical antithrombogenic method by impeller excitation using a magnetically levitated (Maglev) centrifugal pump. Previous studies have shown that one-directional excitation prevents thrombus; however, it is effective in only one direction. In this study, we aimed to obtain a better effect by vibrating it in a circular orbit to induce uniform changes in the shear-rate field entirely around the impeller.

Methods: The blood coagulation time was compared using porcine blood. (1) The flow rate was set to 1 L/min, and applied excitation was at a frequency of 280 Hz and amplitude of 3 μm. (2) Moreover, the effect was compared by varying the frequency, amplitude, and direction of the excitation. In this experiment, the flow rate was set to 0.3 L/min.

Results: (1) The thrombus formation time was 77 min without excitation and 133 min with excitation, which was 1.7 times longer. (2) The results showed no difference between (280 Hz, 3 μm) and (50 Hz, 16 μm) circular orbital excitations, and no directional difference, with thrombus formation of 2.5 times longer under all conditions than that without excitation.

Conclusion: In the case of simple reciprocating excitation, the time was approximately 1.2 times longer. This indicated that the circular orbital excitation is more effective.

KEYWORDS

antithrombogenicity, circular orbit, intelligent function, magnetic bearing, vibration of impeller

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1 | INTRODUCTION

Mechanical circulatory support devices, such as left ventricular assist devices (LVADs), are commonly used as destination therapies (DTs) in patients with heart failure.[1] As the number of DTs increases, it is expected that the LVADs will be used for a longer period. Therefore, the survival rate of patients depends on the durability of the device, which needs to be improved.[2]

The new generation blood pumps possess enhanced durability and reduced risk of thrombosis and hemolysis.[3–5] However, thrombosis, which causes cerebral infarction or myocardial infarction, remains a problem.[6] Although antithrombotic agents can be administered to prevent thrombosis, serious side effects, such as cerebral hemorrhage or bleeding are still unresolved. In addition, there are situations in which antithrombotic agents cannot be used, such as immediately after surgery or when bleeding occurs. Even though many studies have been conducted on detecting the thrombus,[7–12] the prevention techniques have not been sufficiently investigated.

In a previous study, we developed a method to prevent thrombus formation by the simple reciprocating excitation of a magnetically levitated (MagLev) impeller.[13] This technology is innovative in that it is expected to be a new method of anticoagulation control regardless of the patient's condition. This study develops a control method to obtain further antithrombogenic properties by circular orbital excitation. This method requires only a change in the impeller displacement control system; therefore, it can be applied to MagLev impellers that can control planar two degrees of freedom. To evaluate the antithrombotic function, we demonstrated that coagulation time was prolonged using porcine blood in in-vitro experiments.

2 | MATERIAL AND METHOD

2.1 | Principle behind the antithrombogenic method

Blood coagulation begins when platelets adhere to a foreign surface, and it is expected that the high-frequency oscillation of the blood contact surface can prevent the coagulation process by altering the local blood flow. The shear velocity field on the impeller surface is changed to prevent adhesion. To achieve this, we used a MagLev centrifugal blood pump, which comprises a six-vane impeller, top and bottom housings, and a motor unit with magnetic bearings to levitate and rotate the impeller.[14]

In a previous study, the excitation was applied in one direction for thrombus prevention. Detailed control systems for magnetic levitation and excitation have been reported previously as well.[13] If the impeller is excited in a circular orbit, a superior thrombus prevention effect to that of reciprocating excitation can be expected. The target levitation value of the MagLev impeller, which can be controlled in planar two degrees of freedom (one is defined as the X-direction and the other as the Y-direction), is set as follows: a sine wave was set in the X-direction, and a cosine wave in the Y-direction was used to perform circular orbital excitation.

2.2 | Antithrombogenic experiment with and without excitation

In the in-vitro experiment, the blood coagulation times with and without excitation were compared using porcine blood (Tokyo Shibaurazoki Co., Ltd., Tokyo, Japan). Figure 1A,B illustrate the circulatory loop, which consists of a blood pump, reservoir, ultrasonic flowmeter (SONOFLOWCO.55/120, SONOTEC), thermostatic bath, and clamp. The temperature of the thermostatic bath was maintained at 37 ± 0.3°C. The circuit was filled with 600 ml of blood; the pump speed was set to 2000 rpm, and the flow rate was adjusted to 1.0 ± 0.05 L/min. Activated whole clotting time (ACT) was measured while protamine was added, and excitation was initiated when it reached 200 ± 20 s. During excitation, ACT was measured every 30 min to control it at approximately 200 s.

The impeller excitation conditions are listed in parts (A) and (B) of Table 1. The experiments were conducted under conditions (A) without excitation and condition (B) with an excitation frequency of 280 Hz and radius of 3 μm. To detect thrombus formation, circular orbital excitation was stopped temporarily, and the impeller was excited in one direction. Then, the phase difference, ϕ, between the displacement and supplied current was measured every 10 min for a duration of 60 s. A thrombus was detected when the phase difference, ϕ, increased by 2° or more.[15,16]

2.3 | Antithrombogenic experiment with different conditions

The influence of the excitation conditions on thrombus prevention was evaluated via in-vitro experiments using porcine blood. Parts (C) to (E) of Table 1 list the excitation conditions used in this experiment. Under condition

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(C), the experiment was conducted without excitation for control purposes. Conditions (D) and (D′) have the same frequency and radius (280 Hz, 3 μm) but opposite directions of rotation, as shown in Figure 1C. When the excitation is counterclockwise (CCW), its direction is the same as that of the rotation direction. Conversely, when the excitation is clockwise (CW), its direction is opposite to that of the rotation direction. In condition (E), the impeller was excited at a frequency of 50 Hz and a radius of 16 μm; thus, the shear rate, γ_{rms} was the same as that in condition (D).

The setup was the same as that described in the previous subsection, except for the blood temperature, which was directly measured by inserting thermocouples in the circulatory loop and controlled by the thermostatic bath at 37 ± 0.3°C. The circuit was filled with 250 ml of blood; the pump speed was set to 2000 rpm, and the flow rate was adjusted to 0.3 ± 0.05 L/min. The excitation was initiated, and protamine was added for 5 min to achieve an ACT of 160 s. The phase difference, ϕ, was measured every 2 min for a duration of 30 s.

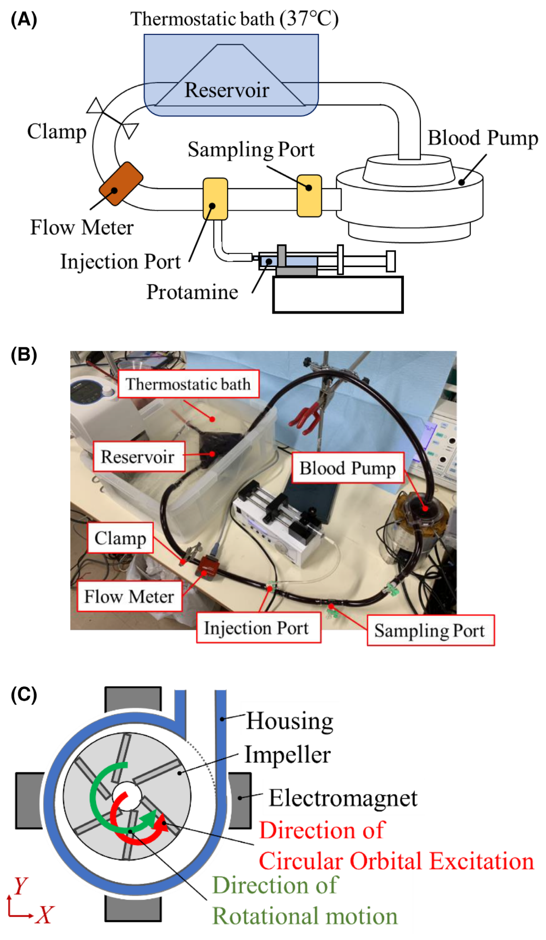

FIGURE 1 Mock circulation loop used in the experiments showing the direction of rotation and excitation (A) configuration of mock circulatory loop (B) image of mock circulatory loop (C) top view of the impeller and housing. The direction of each round arrow indicates a positive direction.

3 | RESULTS

3.1 | Antithrombogenic experiment with and without excitation

Figure 2 demonstrates the phase difference, ϕ, and ACT until blood coagulation. The average blood coagulation times were 77 and 133 min without and with excitation, respectively, and the *t*-test revealed a significant difference between the two. Thus, it was confirmed that excitation prolonged the blood coagulation time by 1.7 times. As shown in the photographs of the impeller and housing captured after the experiment, a small thrombus was observed in all the experiments.

3.2 | Antithrombogenic experiment with different conditions

Figure 3 shows the average coagulation time for each excitation condition. Compared with condition (C), the blood

TABLE 1 Experimental conditions

Conditions	(A) Without excitation	(B) With excitation	(C)	(D)	(D′)	(E)
Frequency (Hz)	0	280	0	280	280	50
Amplitude (μm)	0	3	0	3	3	16
Direction			–	CCW	CW	CCW
RMS of shear rate γ_{rms} (s^{-1})	17 700	17 700	17 700	17 700	17 700	17 700
RMS of shear acceleration γ_{rms} (s^{-2})	0	21 900	0	21 900	21 900	3700
Rotational speed of impeller (rpm)	2000	2000	2000	2000	2000	2000
Flow rate (L/min)	1.0	1.0	0.3	0.3	0.3	0.3

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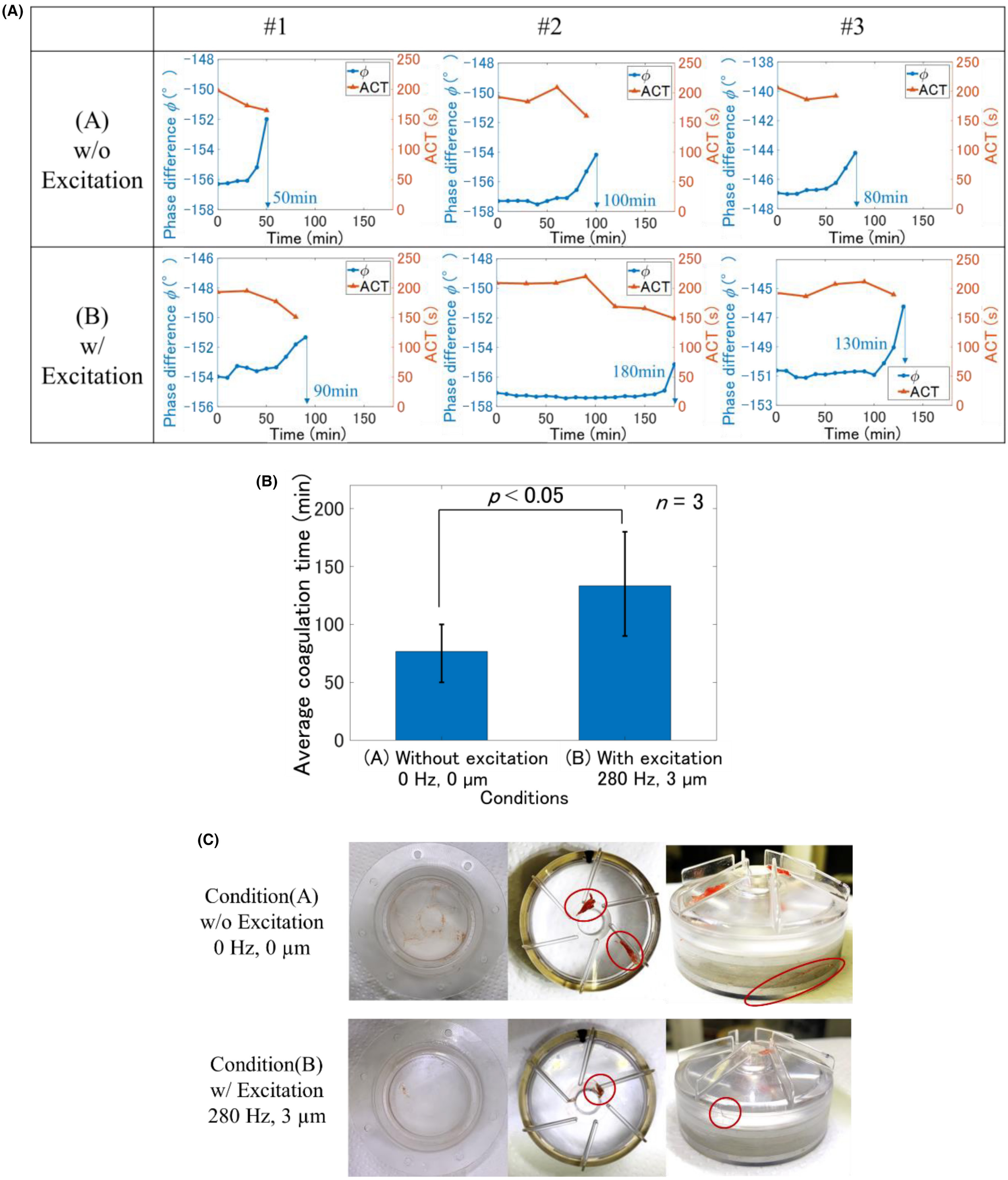

FIGURE 2 Result of the experiment. The pump speed and flow rate were 2000 rpm and 1 L/min, respectively. Additionally, ϕ was measured every 10 min, and the experiment was terminated when ϕ increased by more than 2° from the average of the first three measurements. (A) Phase difference and ACT in each experiment (B) average coagulation time with and without excitation (C) image of the housing and impeller.

coagulation time increased by 2.8 times in condition (D), 2.4 times in condition (D′), and 3.0 times in condition (E). The *t*-test proved that the time for blood coagulation with conditions (D), (D′), and (E) was significantly different from that with condition (C).

4 | DISCUSSION

The blood coagulation time with excitation increased by 2.7 times or more compared to that of without excitation owing to impeller excitation regardless of applied

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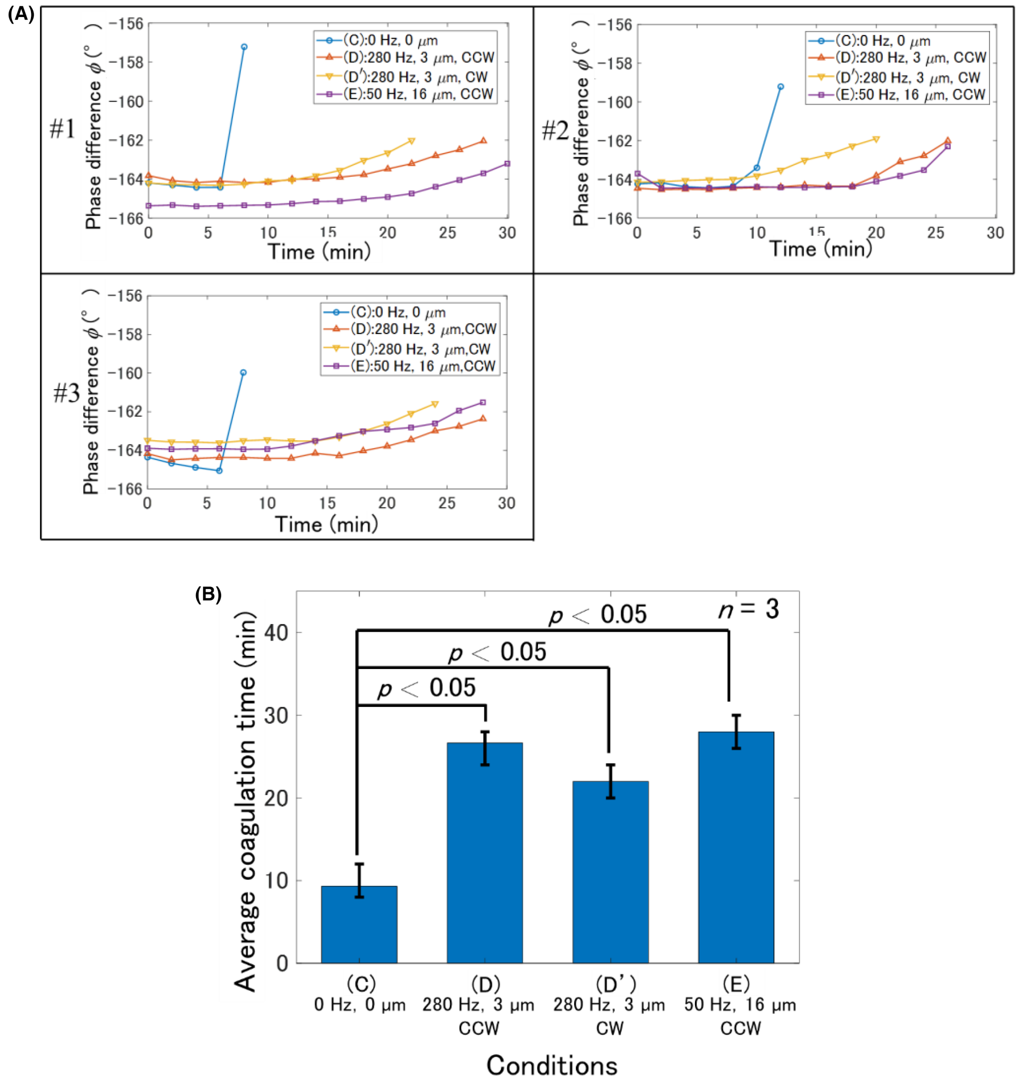

FIGURE 3 Results under varying vibration conditions. The pump speed and flow rate were 2000 rpm and 0.3 L/min, respectively. (A) Phase difference and ACT in each experiment (B) average coagulation time with different conditions.

TABLE 2 Experimental conditions of the previous study

Conditions	(F)	(G)	(H)
Frequency (Hz)	0	280	70
Amplitude (μm)	0	2.5	10
RMS value of shear rate, γ_{rms} (s^{-1})	17 700	17 700	17 700
RMS value of shear acceleration, γ_{rms} (s^{-2})	0	18 200	4560

frequency and radius. This suggests that an appropriate value or threshold for shear acceleration exists for thrombus prevention. The shear accelerations provided in this study were greater than the threshold value under all conditions, which may have led to similar results.

Table 2 lists the conditions for the antithrombogenic properties by reciprocating excitation in a previous study. The results of the two experiments are compared in Figure 4. Moreover, the blood coagulation times were normalized by the results of the control conditions (C) and (F) in Figure 4A,B, respectively. Conditions (C) and (F) signify the control condition for this study and the previous study, respectively. The circular orbital motion is more effective than simple reciprocating excitation for thrombus prevention. It can be assumed that two-directional excitation can provide a uniform change in the shear velocity throughout the impeller perimeter.

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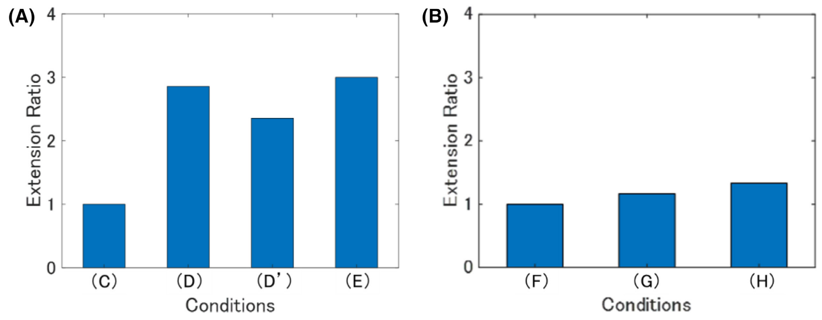

FIGURE 4 Comparison between the rates of blood coagulation prolongation times between the previous and this study. Conditions (C) and (F) are the control conditions without excitation in this study and the previous study, respectively. (A) Circular orbital oscillation (B) simple reciprocal oscillation.

5 | CONCLUSIONS

In this study, we proposed a method for preventing thrombus formation by applying circular orbital motion to the impeller of a MagLev blood pump. We confirmed that changes in the shear field around the impeller inhibited blood coagulation and exhibited a more effective antithrombogenic effect than unidirectional excitation did. The blood coagulation time did not show the considerable difference for different excitation conditions, implying that the shear acceleration threshold could be assumed for antithrombogenic properties.

AUTHOR CONTRIBUTIONS

All authors have contributed to this research and approved submitting the final manuscript. Kohei Hatakenaka: design of experiments, acquisition and analysis of data, and drafting the manuscript. Wataru Hijikata: conception of the study and drafting of the manuscript. Tatsuki Fujiwara, Katsuhiro Ohuchi, and Yusuke Inoue: design of experiments, acquisition, and analysis of data.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest with the contents of this article.

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