J Artif Organs (2014) 17:373–377
DOI 10.1007/s10047-014-0787-8

BRIEF COMMUNICATION

Artificial Heart (Basic)

Influence of a novel electrocardiogram-synchronized rotational-speed-change system of an implantable continuous-flow left ventricular assist device (EVAHEART) on hemolytic performance

Satoru Kishimoto · Kazuma Date · Mamoru Arakawa · Yoshiaki Takewa · Takashi Nishimura · Tomonori Tsukiya · Toshihide Mizuno · Nobumasa Katagiri · Yukihide Kakuta · Daisuke Ogawa · Motonobu Nishimura · Eisuke Tatsumi

Received: 21 April 2014 / Accepted: 16 August 2014 / Published online: 2 September 2014

Abstract We developed a novel controller for a continuous-flow left ventricular assist device (EVAHEART) that can change the pump's rotational speed (RS) in synchronization with a patient's myocardial electrocardiogram (ECG) with the aim of facilitating cardiac recovery. We previously presented various applications of this system in animal models, but there remained a concern that the repeated acceleration and deceleration of the impeller may induce additional hemolysis. In this study, we evaluated the blood trauma and motor power consumption induced by our system in a mock circulation. We evaluated our system with a 60-bpm pulse frequency and a variance between the high and low RSs of 500 rpm (EVA-P; $n = 4$). The continuous modes of EVAHEART (EVA-C; $n = 4$) and ROTAFLOW ($n = 4$) were used as controls. The pumps were examined at a mean flow rate of 5.0 ± 0.2 L/min against a mean pressure head of 100 ± 3 mmHg for a 4-h period. As a result, the normalized indexes of the hemolysis levels of EVA-P and EVA-C were 0.0023 ± 0.0019 and 0.0023 ± 0.0025, respectively, and their difference was not significant. The estimated mean motor power consumptions of EVA-C and EVA-P were 6.24 ± 0.33 and 7.19 ± 0.93 W, respectively. When a novel ECG-synchronized RS-change system was applied to EVAHEART, the periodic RS change with a 500-rpm RS variance did not affect the hemolysis at a 60-bpm pulse frequency.

Keywords Hemolytic performance · Implantable left ventricular assist devices · Pulsatile flow · EVAHEART · Electrocardiogram-synchronized rotational-speed-change system

S. Kishimoto (✉) · K. Date · Y. Takewa · T. Tsukiya · T. Mizuno · N. Katagiri · Y. Kakuta · E. Tatsumi
Department of Artificial Organs, National Cerebral and Cardiovascular Center Research Institute, 5-7-1 Fujishiro-dai Suita, Osaka 565-8565, Japan
e-mail: kishimoto.satoru.ri@mail.ncvc.go.jp

S. Kishimoto · M. Nishimura
Department of Organ Regeneration Surgery, Division of Surgery, University of Tottori, Tottori, Japan

M. Arakawa
Department of Cardiovascular Surgery, Saitama Medical Center, Jichi Medical University, Saitama, Japan

T. Nishimura
Department of Cardiovascular Surgery, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan

D. Ogawa
Sun Medical Technology Research Corporation, Nagano, Japan

Introduction

We developed a novel driving system for an implantable continuous-flow left ventricular assist device (CF-LVAD) (EVAHEART; Sun Medical Technology Research Corp., Nagano, Japan), which can change the pump's rotational speed (RS) in synchronization with a patient's myocardial electrocardiogram (ECG). We have previously shown that this system can improve the arterial pulsatility, enhance myocardial perfusion, control the native heart load, and provide a greater likelihood of aortic valve opening in large animal models [1–8]. These findings indicate that this ECG-synchronized RS-change system will be highly beneficial for patients with severe heart failure for a cardiac functional recovery. However, there remains a concern that the repeated acceleration and deceleration of the impeller may induce additional hemolysis. In this study, we evaluated the blood trauma induced by our driving system in a

mock circulation to ensure that the system is safe for clinical application.

Materials and methods

Pumps

The ECG-synchronized RS-change system of EVAHEART is achieved by periodically changing the command RS by detecting R-wave on the ECG. In this study, we used a pulse generator (Medtronic 5330; Medtronic, Minneapolis, USA) to provide an artificial R-wave and EVAHEART was operated with a basic command that increases the RS in 30 % of each R–R interval and decreases the RS in the residual 70 % (EVA-P; $n = 4$). We set the pulse frequency to 60 bpm and the variance between the high and low RSs to 500 rpm. The pumps were operated at a mean flow rate of 5.0 ± 0.2 L/min against a mean pressure head of 100 ± 3 mmHg. To compare the hemolysis levels, the continuous modes of EVAHEART (EVA-C; $n = 4$) and ROTAFLOW (MAQUET GmbH & Co. KG, Rastatt, Germany) (ROTAFLOW; $n = 4$) were used as controls.

Test circuits and conditions

The mock loops consisted of polyvinyl chloride (PVC) tubes, a PVC soft reservoir, and a pump head (Fig. 1). The total length of the mock circuits was 140 cm, and they were filled with 600 mL of aseptically collected fresh bovine blood, including a 45-mL acid citrate dextrose solution (ACD-A solution; Terumo Corp., Tokyo, Japan). The bovines were used in accordance with the guidelines of the Committee on Animal Studies at the National Cerebral and Cardiovascular Center, and the National Cerebral and Cardiovascular Center Animal Investigation Committee approved the study. The blood temperature was maintained at 37 ± 1 °C using a water bath. The flows were measured using an ultrasonic flow detector (Transonic TS401 and a 1/2 in. flow probe; Transonic System Inc., Ithaca, NY, USA), and the pressures derived from the inflow and outflow tracts were monitored using a polygraph system (RM-7000; Nihon Koden Corp., Tokyo, Japan). These data were recorded using the LabChart 5 software (ADInstruments, Bella Vista, NSW, Australia).

Measurement and analysis

Hemolysis performance

Blood samples were collected immediately after the pump's condition stabilized and at 30 min intervals over a 4-h period. The plasma-free hemoglobin levels were measured at an outside company (SRL Inc., Tokyo, Japan), and the normalized index of hemolysis (NIH) was

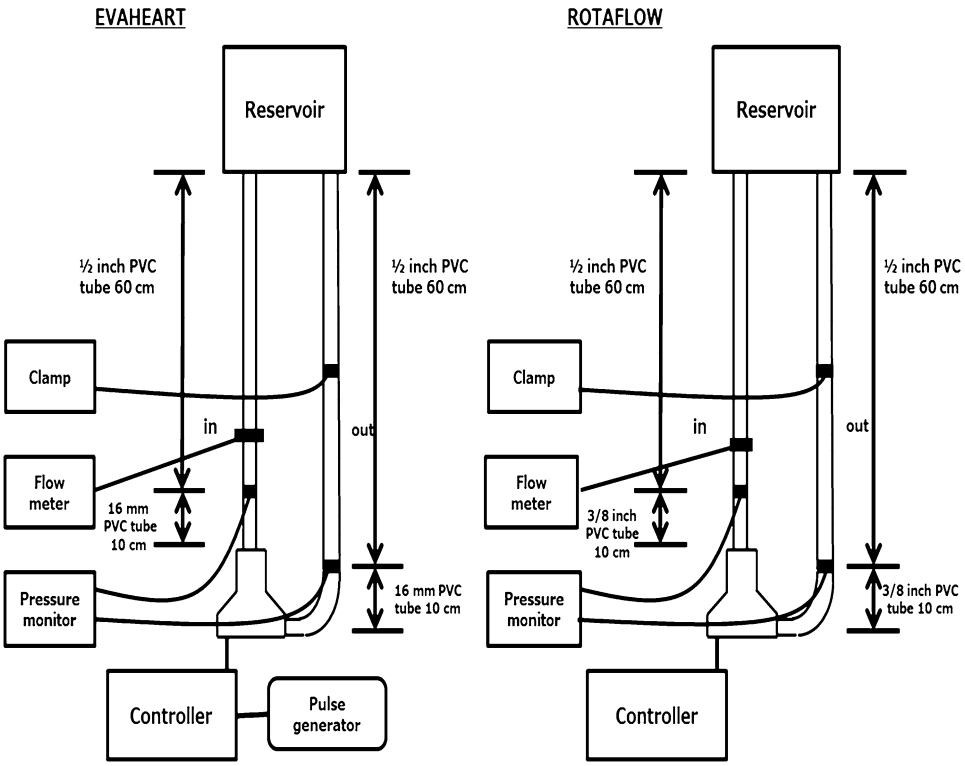

Fig. 1 Schematic drawing of each test loop

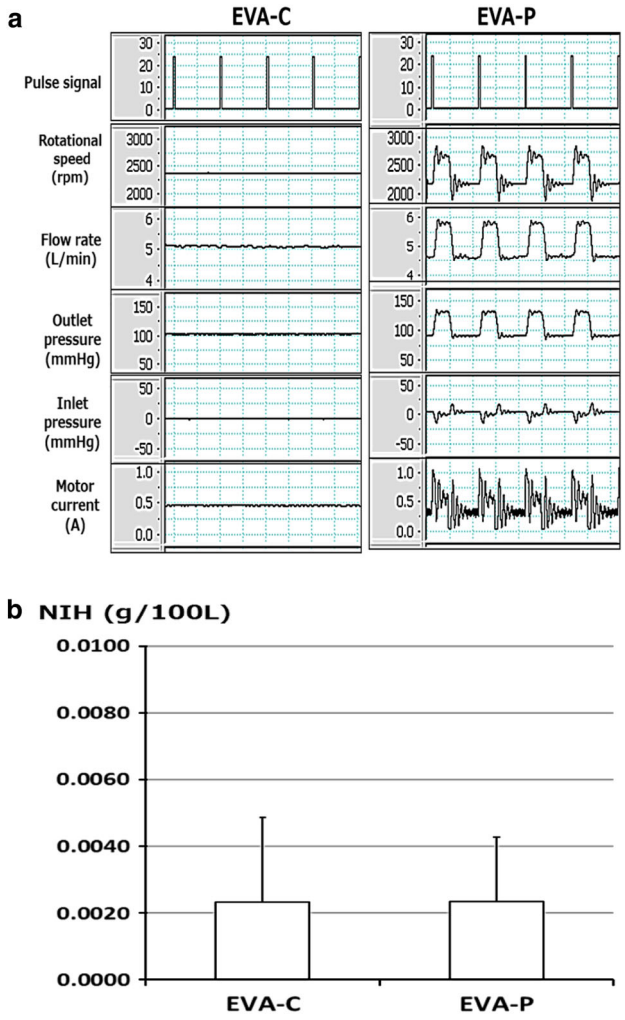

Fig. 2 **a** Sample waveforms for the actual rotational speed, flow rate, pressure, and motor current of EVAHEART in continuous (EVA-C) and electrocardiogram-synchronized rotational-speed-change (EVA-P) modes for the test conditions. The flow rate of EVA-P changed from 4.5 ± 0.1 to 5.9 ± 0.2 L/min. The pulse amplitude was approximately 50 mmHg. **b** Results of hemolysis testing showing no significant difference in the normalized index of hemolysis (NIH) levels between the EVAHEART continuous (EVA-C) and electrocardiogram-synchronized rotational-speed-change (EVA-P) modes

calculated according to American Society for Testing Materials (ASTM) standards using the following formula [9]:

$$\text{NIH (g/100 L)} = \Delta\text{Pf Hgb} \times V \times (100 - \text{Hct})/100 \times 100/(Q \times T),$$

where ΔPf Hgb (g/L) is the increased concentration of plasma-free hemoglobin, Hct (%) is the hematocrit of the blood sample, V (L) is the priming volume of the circuit, Q (L/min) is the blood flow rate during testing, and T (min) is the total time of testing.

We defined ΔPf Hgb as the difference in the values at 240 and 0 min. The value at 240 min was calculated using a line that best fits the data of the Pf Hgb concentration versus time plot [10].

Motor power consumption

We also focused on the motor power consumption of EVA-P because the heat generated by excessive motor power consumption might increase the blood temperature and lead to hemolysis [11].

The test results are expressed as the mean ± SD and were analyzed for significant differences using a paired t test. A probability value of <0.01 was considered significant.

Results

Flow and pressure generation

The required RS for EVA-P to achieve our test conditions was 2679 ± 11 rpm in the high-RS phase and 2169 ± 7 rpm in the low-RS phase. The flow for EVA-P changed by approximately 1.5 L/min during a cycle, and a pulse pressure of approximately 50 mmHg was generated under our test conditions (Fig. 2a). The required RSs for EVA-C and ROTAFLOW were 2352 ± 17 and 2083 ± 21 rpm, respectively.

Hemolytic performance

The NIH levels of EVA-P, EVA-C, and ROTAFLOW were 0.0023 ± 0.0019, 0.0023 ± 0.0025, and 0.0010 ± 0.0009 g/100 L, respectively. No significant differences were noted between EVA-P and EVA-C (Fig. 2b).

Motor power consumption

The mean motor current of EVA-P was approximately 15 % higher than that of EVA-C (0.42 ± 0.02 A vs. 0.48 ± 0.06 A). As the EVAHEART control voltage was 15 V, the estimated mean motor power consumptions of EVA-C and EVA-P were 6.24 ± 0.33 and 7.19 ± 0.93 W, respectively.

Discussion

Our study had two major findings. First, a periodic RS change with a 500-rpm RS variance did not affect the hemolysis at a 60-bpm pulse rate when an ECG-synchronized RS-change system was applied to the EVAHEART implantable CF-LVAD. Second, approximately 1 W of

additional power consumption was needed for operation for the periodic RS change.

Several studies have evaluated the hemolysis levels of the mode of periodic RS change (pulsatile mode) of centrifugal pumps [12–14]. Kono et al. [14] proposed that the pulsatile mode of a magnetically suspended centrifugal pump at almost the same conditions as ours did not increase hemolysis. Tayama et al. [12] investigated the pulsatile mode of Gyro C1E3 for various conditions. They showed that the hemolysis results in the pulsatile mode of Gyro C1E3 were comparable to or better than those in the continuous mode and found that a relatively slow beating rate, a proper pulse amplitude, and proper usage of a pump with excellent hemolysis performance were the important factors in avoiding excessive blood cell damage. Our results are in line with those reports. The system of periodic RS change in EVAHEART with excellent hemolysis performance did not affect hemolysis for our test conditions.

The main concern related to the system of periodic RS change in continuous-flow pumps is the creation of an appropriate pulse amplitude, which is defined by the pump characteristics and the variance between the high and low RSs. We have started experiments using our ECG-synchronized RS-change system in conscious large animal models and have confirmed that a difference between the high and low RSs of 500 rpm is sufficient [6]. Thus, we defined the 500 rpm variance between the high and low RSs as the basic setting to evaluate the hemolysis characteristic of our system. In this paper, EVA-P was operated at approximately 2700 rpm in the high-RS phase. Generally, a high RS might affect the hemolysis; however, our results indicate that the difference between the RS of EVA-C and the RS of the high-RS phase of EVA-P does not significantly affect.

The estimated mean motor power consumption of EVA-P was 7.19 ± 0.93 W. If all the energy generated by the motor were transmitted to the blood, approximately 1 W of additional power consumption would be involved in the production of heat in EVA-P. In this study, the circulation blood was maintained at 37 ± 1 °C using a water bath. Thus, the relationship between the motor power consumption and the blood temperature could not be verified. Yamazaki et al. [15] evaluated EVAHEART (in continuous mode) in calf models, and they stated that EVAHEART operated with a power consumption of 8–10 W, and there were no hemolysis observed. The range of motor power consumption observed in our study seemed to be within the allowable range.

The limitations of our study were that we did not evaluate a higher RS variance and higher pulse rate [13].

Conclusions

When an ECG-synchronized RS-change driving system was applied to the EVAHEART implantable CF-LVAD, the periodic RS change with a 500-rpm RS variance did not affect the hemolysis at a 60-bpm pulse rate.

Conflict of interests The authors have no conflicts of interest to disclose.

References

1. Ando M, Nishimura T, Takewa Y, Yamazaki K, Kyo S, Ono M, et al. Electrocardiogram-synchronized rotational speed change mode in rotary pumps could improve pulsatility. Artif Organs. 2011;35:941–7.
2. Ando M, Takewa Y, Nishimura T, Yamazaki K, Kyo S, Ono M, et al. A novel counterpulsation mode of rotary left ventricular assist device can enhance myocardial perfusion. J Artif Organs. 2011;14:185–91.
3. Kishimoto Y, Takewa Y, Arakawa M, Umeki A, Ando M, Nishimura T, et al. Development of a novel drive mode to prevent aortic insufficiency during continuous-flow LVAD support by synchronizing rotational speed with heartbeat. J Artif Organs. 2013;16:129–37.
4. Umeki A, Nishimura T, Ando M, Takewa Y, Yamazaki K, Kyo S, et al. Change of coronary flow by continuous-flow left ventricular assist device with cardiac beat synchronizing system (native heart load control system) in acute ischemic heart failure model. Circ J. 2013;77:995–1000.
5. Umeki A, Nishimura T, Ando M, Takewa Y, Yamazaki K, Kyo S, et al. Alteration of LV end-diastolic volume by controlling the power of the continuous-flow LVAD, so it is synchronized with cardiac beat: development of a native heart load control system (NHLCS). J Artif Organs. 2012;15:128–33.
6. Arakawa M, Nishimura T, Takewa Y, Umeki A, Ando M, Adachi H, et al. Alternation of left ventricular load by a continuous-flow left ventricular assist device with a native heart load control system in a chronic heart failure model. J Thorac Cardiovasc Surg. 2014. doi:10.1016/j.jtcvs.2013.12.049. (Epub ahead of print).
7. Ando M, Nishimura T, Takawa Y, Ogawa D, Yamazaki K, Kashiwa K, et al. A novel counterpulse drive mode of continuous-flow left ventricular assist device can minimize intracircuit backward flow during pump weaning. J Artif Organs. 2011;14:74–9.
8. Ando M, Nishimura T, Takewa Y, Kyo S, Ono M, Taenaka Y, et al. Creating an ideal "off-test mode" for rotary left ventricular assist devices: establishing a safe and appropriate weaning protocol after myocardial recovery. J Thorac Cardiovasc Surg. 2012;143:1176–82.
9. ASTM. ASTM F1841-91. Standard practice for assessment of hemolysis in continuous flow blood pumps. 2005.
10. Sobieski MA, Giridharan GA, Ising M, Koenig SC, Slaughter MS. Blood trauma testing of CentriMag and RotaFlow devices: a pilot study. Artif Organs. 2012;36:677–82.
11. Araki K, Taenaka Y, Masuzawa T, Wakisaka Y, Nakatani T, Akagi H, et al. In vitro performance in centrifugal blood pumps. Jpn J Artif Organs. 1994;23:898–903.
12. Tayama E, Nakazawa T, Takami Y, Ohtsubo S, Ohbayashi Y, Andrade AJ, et al. The hemolysis test of Gyro C1E3 pump in pulsatile mode. Artif Organs. 1997;21:657–9.
13. Tayama E, Niimi Y, Takami Y, Ohashi Y, Ohtsuka G, Glueck JA, et al. Hemolysis test of a centrifugal pump in a pulsatile mode:

the effect of pulse rate and RPM variance. Artif Organs. 1997;21: 1284–7.
14. Kono S, Nishimura K, Yamada T, Oonishi T, Tsukiya T, Akamatsu T, et al. In vivo and in vitro evaluation of the pulsatile mode of a magnetically suspended centrifugal pump. ASAIO J. 1997;43:M580–4.
15. Yamazaki K, Kihara S, Akimoto T, Tagusari O, et al. EVA-HEART: an implantable centrifugal blood pump for long-term circulatory support. Jpn J Thorac Cardiovasc Surg. 2002;50: 461–5.