System overview of the fully implantable destination therapy—ReinHeart-total artificial heart

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Abstract

OBJECTIVES: Owing to the lack of suitable allografts, the demand for long-term mechanical circulatory support in patients with biventricular end-stage heart failure is rising. Currently available Total Artificial Heart (TAH) systems consist of pump units with only limited durability, percutaneous tubes and bulky external equipment that limit the quality of life. Therefore we are focusing on the development of a fully implantable, highly durable destination therapy total artificial heart.

METHODS: The ReinHeart-TAH system consists of a passively filling pump unit driven by a low-wear linear drive between two artificial ventricles, an implantable control unit and a compliance chamber. The TAH is powered by a transcatheter energy transmission system. The flow distribution inside the ventricles was analysed by fluid structure interaction simulation and particle imaging velocimetry measurements. Along with durability tests, the hydrodynamic performance and flow balance capability were evaluated in a mock circulation loop. Animal trials are ongoing.

RESULTS: Based on fluid structure interaction simulation and particle image velocimetry, blood stagnation areas have been significantly reduced. In the mock circulation loop the ReinHeart-TAH generated a cardiac output of 5 l/min at an operating frequency of 120 bpm and an aortic pressure of 120/80 mmHg. The highly effective preload sensitivity of the passively filling ventricles allowed the sensorless integration of the Frank Starling mechanism. The ReinHeart-TAH effectively replaced the native heart’s function for animals for up to 2 days.

CONCLUSIONS: In vitro and in vivo testing showed a safe and effective function of the ReinHeart-TAH system. This has the potential to become an alternative to transplantation. However, before a first-in-man implant, chronic animal trials still have to be completed.

Keywords: Total Artificial Heart TAH • Fully implantable • Heart failure • Quality of life

INTRODUCTION

Owing to the lack of suitable allografts, the demand for long-term mechanical circulatory support, and especially Total Artificial Heart (TAH) therapy in patients with biventricular end-stage heart failure is rising [1]. In the context of Destination Therapy, the drive unit of the TAH has to be highly durable, though compact and powerful enough to replace the native heart’s function. Furthermore, due to the well-known risk for infection [2], percutaneous drivelines that are commonly used for energy supply of the drive unit should be replaced by a transcatheter energy transmission (TET) system and, in terms of sufficient patient mobility, bulky external equipment should be avoided. Finally, since the native heart is completely excised, reliable real-time monitoring of pump flow should be ensured. With more than 1300 implants, the established TAH is the accredited Syncardia TAH (Syncardia Systems Inc., Tucson, AZ, USA). Nevertheless, its pneumatic drive requires a percutaneous driveline and the control unit could be optimized regarding noise. We introduce the ReinHeart-TAH, a fully implantable Destination Therapy TAH system with a high degree of preload sensitivity that allows the integration of physiologic flow control. Here, we provide an update on the current state of development based upon report results from in vitro testing, anatomical fitting studies and ongoing animal trials.

DEVICE DESCRIPTION

System

The design requirements for the ReinHeart-TAH are the complete implantability of the major components of the system and a high durability of the drive- and control unit, facilitating a maintenance-free operation for at least 5 years. To meet these requirements, an electrically powered low-wear linear drive was designed [3]. The required mean power of less than 20 W is transmitted transcatheterly. Figure 1 shows a scheme of the entire TAH.
Pump unit. The pump unit (Fig. 1A) is the central element of the TAH system. It replaces the native heart anatomically and functionally. The pump unit consists of a drive unit surrounded by two artificial ventricles. With a diameter of 87 mm and a height of 90 mm, it has a weight of 940 g and a volume of 550 ml at the current state of development. Each ventricle is separated from the drive unit by a polyurethane membrane that generates pulsatile blood flow by an inward movement. Two inflow cuffs connect the pump unit to the left and the right atrium and two outflow grafts to the aorta and the main pulmonary artery. Four mechanical heart valves (St. Jude Medical, Inc., St. Paul, MN, USA) facilitate unidirectional blood flow.

A detailed view of the pump is shown in Fig. 3. Drive unit: The linear drive features four coils on a bobbin and magnets. This bobbin can either be pulled into the magnetic field or pushed out of it by the variation of the coil current. The resulting movement is guided by one central axle and can eject the left and right ventricle alternatively, unlike the concurrently ejecting ventricles of the native heart. A position-sensing system detects the position along this central axle. The monitoring system also includes a sensor for the temperature of the drive unit. Inside the bobbin, durable connection springs provide the electrical connection to the coils. Bobbins and springs are the only moving parts of the drive unit, a feature that ensures low wear and therefore high durability. The pusher plates mounted on each side are not fixed to the membranes. This allows a preload sensitive filling of the chambers avoiding suction events. Artificial ventricles: Each MABS (a styrene copolymer) ventricle houses two mechanical valves and one polyurethane membrane. The membrane separates the blood-filled side of the ventricles from the inside of the drive unit. The ventricles are designed to provide a maximum stroke volume of 60 ml and can be rotated around the central axis of the pump unit in order to compensate for any anatomical misalignments. The orientation of the inlets and outlets can be easily adapted to the individual anatomy of the TAH recipient.

Prostheses: We developed primary sealed cuffs and grafts that can be easily attached to the inlet and outlet of each ventricle by a common snap connector. These consist of a well suturable, sprayed material that has an adapted compliance, in contrast to commercially available vascular prostheses. Compared with
the latter [5], our prostheses do not require a sealing process during the operation.

**Implantable controller.** The purpose of the implantable controller (Fig. 1B) is: (1) to power and control the pump unit and compliance chamber; (2) to provide status information of the pump unit and compliance chamber; (3) to provide a battery as a backup in case of a TET system failure. It consists of a printed circuit board, which includes the power and communication electronics, as well as four battery cells. Three microplugs are used to connect the pump unit, the compliance chamber and the TET coil. A microcontroller acquires the data of the position-sensing system inside the pump unit to detect the position of the coil bobbin. The power electronics then distribute current to the motor coils to generate a sinusoidal movement that leads to pulsatile pump cycles. The batteries to power the pump unit are charged by the TET system. They can support the device for about 45 min at full capacity, in case of a disconnected TET system, e.g. for body care.

**TET system.** The TET system (Fig. 1C) transmits electrical energy from the external to the internal coil. Thus it powers all implantable components (Fig. 2). The subcutaneously implanted coil is connected to the implantable controller and has a diameter of 70 mm. The annular external coil has an inner diameter of 70 mm and an outer diameter of 100 mm. The 70 mm cut-out of the external coil facilitates the alignment of the internal and external coil. Owing to the optimal coupling between the coils, power losses are remarkably low and local heating is minimized. The TET system is able to support the TAH up to a distance and misalignment of 30 mm.

**Compliance chamber.** The compliance chamber (Fig. 1D) allows for a controlled filling of the ventricles. It is connected to the pump unit and its operation is controlled by the implantable controller. It prevents suction events and regulates balance between left and right ventricular output by diminishing sharp pressure peaks in the drive unit. An integrated pump adjusts air pressure and supports movement of the polyurethane membranes.

**External user interface and batteries.** The purpose of the external user interface (Fig. 1E) is: (1) to deliver operational data of the TAH system; (2) to enable adjustment of all clinical relevant parameters; and (3) to control the energy transmission of the TET system. The external coil of the TET system and the external battery packs (Fig. 1F) are connected to the user interface. The whole system is either powered by a power cord for stationary use (current state of development) or by an externally worn battery pack (Fig. 1F) for mobile use. In the battery mode, the use of two battery packs with a weight of below 1 kg each and a total support time up to 12 h is planned. With a third battery pack as a backup, the support time can be extended to 18 h.

**METHODS**

**Anatomical fitting studies**

Virtual and cadaver fitting studies were performed, aiming to optimize the inlet- and outlet configuration of the TAH system [6]. The TAH surface model was virtually placed into the three-dimensional image data of 27 end-stage heart failure patients from either sex. The pump unit was aligned with the atrioventricular and aorta, pulmonary artery, left and right atrium and surrounding organs was evaluated. The results were used to iteratively optimize the valves’ position and orientation inside the ventricles.

**Fluid structure interaction simulation and particle image velocimetry**

The pumping process of the TAH system was modelled within a fully coupled three-dimensional time-dependent fluid structure interaction (FSI) simulation [7]. We focused on the motion pattern of the polyurethane membranes and analysed the resulting flow distribution inside the pump. In addition, by calculating the percentage of blood remaining in the ventricles from the last pump cycle, we simulated washout for different valve orientations [8]. The flow distribution was additionally analysed by a stereo particle image velocimetry-system (Stereo-PIV, e.g. [9]). Flow was captured as vectors of velocity in several measurement planes of the ventricle. Furthermore, we investigated two different orientations of the mechanical heart valves and compared shear-stress development between single- and bileaflet mechanical valves.

**Durability tests**

The polyurethane membranes and connection springs are the critical components of the system. They were investigated under
physiological conditions, but at increased operational frequency. To test the durability of the complete TAH system under constant physiological conditions, a system durability tester was designed.

Mock circulation loop

To test the hydrodynamic performance of the TAH, we developed a mock circulation loop. This is a hydraulic model that simulates the cardiovascular system including systemic and pulmonary resistance, arterial and pulmonary compliance, right and left atrium, bronchial shunt and venous return [10]. Arterial resistances, compliances and venous volume are electrically adjustable, thus enabling the simulation of a wide range of physiological and pathophysiological conditions. Two tubing flow sensors (20PXL; Transonic Systems, Ithaca, NY, USA) measure systemic and pulmonary flow and four pressure sensors (DPT-9009; Codan, Lensahn, Germany) measure aortic pressure (AoP), pulmonary arterial pressure (PAP), and left atrial (LAP) and right atrial pressure (RAP). The mock circulation loop can be coupled with a software model that implements autoregulatory controls of the cardiovascular system. A hardware in a loop platform (DS1103 dSPACE, Paderborn, Germany) runs the real-time simulation and enables control of the TAH.

Animal trials

The TAH system is currently being tested in a chronic bovine model. Following typical excision of the native heart [5], the inflow cuffs are sutured to the remnants of the left and the right atrium and anastomosis of the outflow grafts with the aorta and the main pulmonary artery is performed. Finally, the pump unit is connected with the grafts, inserted into the thorax and connected to the control unit and the compliance chamber. At the current state of development, the control unit and compliance chamber for the animal trials are still external.

RESULTS

Anatomical fitting

As described by Fritschi et al. [6], in a virtual study, the distance between the valve centres proved to be relatively uniform between male and female patients. The cranial-caudal and the ventral-dorsal distances of male patients was about 10% higher than those for female patients. With the exception of the ventral-dorsal distance and the distance between the mitral and aortic valve, all other parameters deviate less than 10% from results taken from the literature. Figure 4 shows the virtual fitting of a male patient. The contour of the ventricles is highlighted in the CT slices. The three-dimensional reconstruction shows the pump unit in the orthotropic position.

Fluid structure interaction and particle image velocimetry

Figure 5 shows flow distribution for a top view plane of the ventricle as estimated by FSI simulation and PIV measurements. The
first column shows the positions of the pusher plate over the phase of the pump cycle. The second to fourth columns show the velocity fields documented in one slice of the ventricle during a simulation without valves, with valves and for the experimental measurements, respectively. All measurements were performed under standard conditions (operating frequency: 120 bpm, aortic pressure: 120/80 mmHg). The simulation without valves tended to overestimate velocities, whereas the simulation with valves

Figure 5: Comparison of the flow distribution for the FSI simulation and PIV measurement. (B–E) Velocity fields of the FSI simulation without valves (left), with valves (middle) and PIV measurement (right) in one slice (A) for different positions of the pusher plate (charts). FSI: fluid structure interaction; PIV: particle image velocimetry. (Reprinted from [8] with permission from Wichtig Publishing.)
showed a high level of agreement to experimental data. To determine washout performance, the ratio of residual blood volume in the ventricle to current blood volume was calculated over time. In cases of suboptimal valve orientation 99.4% of blood was washed out after 3 pump cycles, whereas in cases of optimal valve orientation 99.88% [8].

Mock circulation loop

After connecting the TAH to the mock loop, we simulated different haemodynamic scenarios (rest, exercise) by adapting the mock loop parameters and the TAH beat rate. Under a constant compliance chamber pressure and without any physiological control of the TAH, pressures (aortic pressure, pulmonary artery pressure, left atrial pressure, right atrial pressure) and flow values were documented and analysed at different beat rates. Figure 6 shows the resulting pressure- and flow curves. The systemic atrial compliance of the mock loop was set from 1.26 ml/mmHg for the resting and 1.11 ml/mmHg for the exercising patient. The resulting aortic pressure was 102/85 mmHg for the resting and 104/60 mmHg for the exercising scenario. At rest, aortic flow of the TAH was 4.8 l/min at a beat frequency of 100 bpm. The mean aortic pressure was 93 mmHg and the mean pulmonary arterial pressure 14.2 mmHg. At a higher beat frequency of 150 bpm for the exercising scenario, aortic flow was 6.5 l/min and the mean aortic and pulmonary arterial pressure 80 mmHg and 13.6 mmHg, respectively.

To evaluate hydrodynamic performance of the TAH, mock loop parameters were set to physiological pressures. The TAH system was controlled manually and compliance chamber pressure was adapted as needed in order to provide complete filling. The beat rate was gradually set from 95 bpm to 155 bpm and the resulting cardiac output was measured. Figure 7 shows the performance curve of the TAH under physiological aortic pressures. At a beat rate of 110 bpm, aortic flow was 5 l/min. Under a beat rate of 155 bpm cardiac output was 7.5 l/min.

Further results

In the first durability tests, critical components such as the connection springs and the membranes performed adequately; they are currently undergoing testing with accelerated frequency under physiological conditions. So far, the springs have been tested for 440 million cycles and the membranes for 250 million cycles, corresponding to a calculated duration of 7 years and 4 years, respectively; both tests are still ongoing.

In a bovine model the TAH effectively replaced the native heart’s function for up to 2 days (Fig. 8). TAH flow and vascular pressures were normal. In total, 12 animal trials have been
performed. The complexity and invasiveness of the operation in a bovine model required a significant learning curve. The reasons for termination were bleeding, pulmonary and technical problems with a decreasing incidence and gastric problems with an increasing incidence with longer trial duration. The major objective of the ongoing trial is to validate long-term haemocompatibility and to finalize an automatic flow control system.

**DISCUSSION**

The TAH performed satisfactorily in vitro and in vivo. The fitting study of the pump unit showed the advantage in the use of prostheses to connect the TAH ventricles to the vascular system. The inlet cuffs can be adapted to individual anatomical geometries. Since a kinking prosthesis would worsen the hydrodynamic performance, the outlet grafts have to be cut to a length as short as anatomically possible. To optimize other implanted components, the combined approach of virtual and cadaver studies is planned.

The simulated washout performance revealed that 99.4% of blood was washed out of the ventricles within 3 pump cycles, thus reducing the risk of clot formation. The PIV experiments showed a reduction in shear stress when bileaflet valves were used. Therefore, these valves were chosen for all in vitro and in vivo experiments. In the animal trial, a free plasma haemoglobin concentration of 38 mg/dl after 24 h is feasible. However, haemolysis has to be further analysed in future animal trials with a longer duration.

The membranes and connection springs are the moving parts of the pump unit, and hence critical to its durability. These two components showed promising mechanical stability in the durability tests for 4 and 7 years, respectively. In addition, the durability of the complete TAH system is determined within the TAH system durability testing. The testing procedure is based on a formerly published manuscript about TAH testing [11]. The hydrodynamic validation of this testing procedure was already performed.

The TAH showed a good haemodynamic performance in vitro and in vivo. The preload sensitivity was confirmed through the mock circulation loop experiments. Figure 7 depicts a linear relation between beat rate and flow. It implies a good control of the cardiac output by adapting the beat rate with parallel physiological control.

The next step of the ongoing animal trials is to extend the trial duration with the current pump unit. Bleeding and breathing problems have been eliminated by the learning curve in the operation process. The complex bovine gastric physiology can also present challenges during the animal trials. In parallel, a weight reduction of this pump unit to 800 g is planned for the future. The implantation of the control unit and the TET system during an animal trial is also scheduled for the end of this year.

**Limitations of the model and comparison with the state of the art**

Though full implantability and the TET system sound promising, the TAH system still has to prove functional in 90-day animal trials. Despite the pneumatic drive, the Syncardia TAH is still the only satisfying TAH. In comparison, our pump unit has a greater volume. Along with the additional implantable components, our surgical procedure is much more complex. On the other hand, the void space between the Syncardia ventricles might not be filled by pericardium and lungs; this can become a source of infection due to accumulation of clots and debris. These complications can be avoided with the complete pump unit and fixed ventricles of our TAH system.

The outer coil of the TET system can be misaligned or even disconnected. In case of a disconnection event, the internal battery provides power for up to 45 min. Without the external gear, we think this duration time is sufficient for body care of the patient. The planned support time of up to 12 h using two external battery packs is comparable to state of the art LVAD and TAH systems.

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**REFERENCES**


