Chapter 8:
In vitro end in vivo experience with the PUCA-II, a single-valved pulsatile catheter-pump

Abstract

The Pulsatile Catheter (PUCA) pump is a trans-arterial pulsatile ventricular assist device that can be used for short-term left ventricular support. The separate inflow and outflow valves in the first version of the device (PUCA-I) were replaced by a single inflow/outflow valve in the last PUCA pump version (PUCA-II). The new combined valve was tested during in vitro (mock circulation) and in vivo experiments for valve leakage, flow resistance, and thrombus formation.

During the in vitro experiments a maximum valve leakage of 6% during ejection and 21% during aspiration was found. The maximum flow resistance coefficient (K) was 4.

The animal experiments demonstrated that the PUCA-II could be positioned within a few minutes into the left ventricle without X-ray guidance and without using a vascular graft. Thrombi were not found in the combined valve after total pump time of 3 hours, which proved the good washout of the valve. Initial experiments to position the pump in the right ventricle through the pulmonary artery were successful and contributed to the development of a new application for the device.

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Introduction

The Pulsatile Catheter (PUCA) pump is an intraventricular blood pump that can be used as a short-term (up to 3 days) left ventricular assist device (LVAD). The device consists of an extracorporeally placed pneumatically driven single-port membrane pump connected to a reinforced valved indwelling catheter. The PUCA pump is ECG triggered, aspirates blood from the left ventricle (LV), and ejects it into the ascending aorta during the diastolic phase.

To prevent high shear stresses, the PUCA pump is driven at low pump frequencies. ECG triggered pump modes of 1:2, 1:3 or 1:4 (pump action : heart action) allow the pump to fill itself during two or more heart actions, and the pump volume is ejected during the diastolic phase of the following heart action. As a consequence left ventricular and aortic pressures are largely influenced by the pump because of the direct ventricular unloading and the generated counterpulsation effect. This phenomenon has been demonstrated in computer simulation studies[1], mock circulation studies[2] as well as in animal studies[3]. In case of severe cardiac arrhythmia or signal disorders, the pump driver switches automatically to an untriggered mode.

The first version of the PUCA pump (PUCA-I) was presented in 1993 at the ISAO-ESAO congress in Amsterdam[4]. Separate inflow and outflow valves were implemented in the tip of the PUCA-I catheter to guide the blood from the ventricle towards the membrane pump and from the membrane pump to the aorta. The pump was activated electro-hydraulically or pneumatically.

Although the PUCA-I showed promising results, animal studies demonstrated that the ultra-thin catheter and the external outflow valve became often damaged during pump insertion. Some outflow valves showed thrombus formation after two hours of pumping. To overcome these problems the catheter and the valve system have been redesigned. By changing the reinforcement wire the flexibility of the catheter was strongly improved. Pneumatic activation of the membrane pump was chosen to allow optimal performance during ECG synchronous mode. However, the most significant difference between PUCA-I and PUCA-II is the valve system: the separate inflow and outflow valves of the PUCA-I were replaced by a combined inflow/outflow valve in PUCA-II (patent pending).

This article describes the design and the in vitro and in vivo experiments with PUCA-II: an ultra-thin 21 French (Fr) single-valve catheter connected to a 50 ml single-port membrane pump. The positioning of the catheter into the left ventricle, without X-ray guidance and without using a vascular graft, was examined in 3 animal experiments. In two animals the possibility to use the PUCA pump as a right

ventricular assist device (RVAD) was tested by introducing a shortened PUCA-II catheter into the right ventricle (RV) via the pulmonary artery. Two types of the PUCA-II will be derived from the tested 21 Fr prototype: an 18 Fr and a 24 Fr version. The 18 Fr PUCA pump is meant to operate under closed chest conditions and have to be introduced into the LV via the axillary artery. This version can generate a pump flow of approximately 2 L/min. The 24 Fr version can be used under open-chest conditions and can be inserted directly into the aorta or pulmonary artery. The 24 Fr PUCA pump can generate a pump flow of 4-5 L/min.

Methods

Valve design

The new combined valve is composed of a tubular valve housing that can be integrated in the catheter. The valve housing has a lateral opening that allows blood to pass to the aorta and a valve leaflet that turns around an axis. In aspiration position the valve leaflet closes the opening between the valve housing and the aorta, allowing blood to be aspirated only from the ventricle. In ejection position the valve leaflet closes the distal opening of the housing (towards the left ventricle) allowing blood to be ejected into the aorta (Fig. 1).

Fig. 1. The combine inflow/outflow valve (patent pending) during aspiration (above) and during ejection (below) used in PUCA-II VAD.

Optimal valve openings and outflow angles were analyzed from numerical modelling studies[5]. The valve leaflet enables proper closing of the outflow orifice

(ejection phase), while a 0.5 mm opening between the valve housing and the valve leaflet remains when the valve is in the aspiration position. The valve leaflet hardly passes the outside of the valve housing during pump ejection. A smooth and tight connection between the catheter and the valve housing, as well as between the catheter and the catheter/membrane pump connector is realized by gluing the metal parts to the polyurethane catheter.

Valve leakage, measured in a mock circulation, was defined as:

$$\text{Aspiration leakage}\,(\%) = \frac{Q_1 - Q_2}{Q_1} * 100$$

$$\text{Ejection leakage}\,(\%) = \frac{Q_2}{Q_1} * 100$$

Q_1 = mean flow (L/min) at proximal end of the valve (pump side)
Q_2 = mean flow (L/min) at distal end of the valve (ventricle side)

Flow resistance coefficient *K* and valve leakage were measured in a mock circulation (Fig. 2) that consisted of two reservoirs: one representing the aorta (reservoir 1) and one representing the left ventricle (reservoir 2). A 12 cm long inflow tube with the same inner diameter as the PUCA-II catheter connected reservoir 1 with reservoir 2, thus mimicking the distal part of the PUCA catheter. A second tube with a length of 28 cm connected reservoir 1 with the membrane pump. The valve was placed in reservoir 1 between the free ends of the two tubes mentioned. Water/glycerol mixture was used as blood mimicking fluid. A pressure of 100 mm Hg was set in the mock aorta as mean aortic pressure (valve afterload); a pressure of 60 mm Hg was set in the mock ventricle as LV systolic pressure (valve preload). Reservoir 2 was filled by reservoir 1 using an open overflow system. Ultrasound flow probes (Transonic Systems Inc., Ithaca, USA) and pressure transducers (Baxter, USA) were positioned at the proximal and distal ends of the valve.

The flow resistance coefficient *K* was defined as:

$$K = \frac{2\Delta P}{\rho * v^2}$$

ΔP = pressure difference over the valve (Pa)
v = mean velocity (m/sec)
ρ = blood density (1060 kg/m^3)

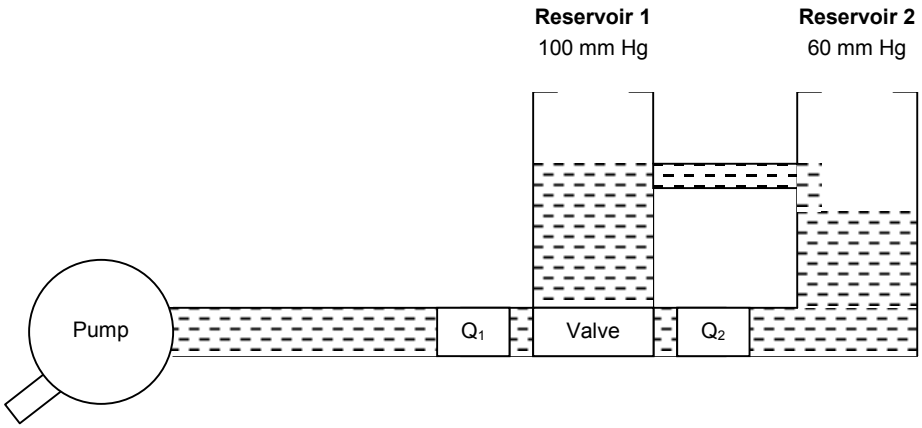

Fig. 2. Schema of the mock-circulation used for in vitro measurements.

The valve leakage and resistance coefficient were measured at a full-fill / full-empty pump mode using a pneumatic driver (UTAH Heart driver: Artificial Heart Research Laboratories, Salt Lake City, USA). The full-fill/full-empty pump mode was reached at a pump frequency of 32 beats/min, generating a pump flow of 1.7 L/min. Catheter flows (Q_1 – proximal from the valve; Q_2 – distal from the valve) were measured during pump aspiration and during pump ejection. All measurements have been performed in triplicate.

Flow visualization

For flow visualization studies the same pump configuration was used as in the in vitro measurements. For practical reasons the valve and the connecting tubing were placed in an open reservoir instead of in a mock circulation. Ink was injected in the proximal part of the catheter (pump side) and the pump ejection was recorded from a regular video camera. The recorded outflow patterns were compared with the outflow patterns simulated by a finite element method model[5].

Animal experiments

For initial open chest animal experiments with the single-valved catheter, a 40 cm long, 21 Fr. PUCA-II catheter (6 mm inner diameter) was made from nickel-titanium reinforced Tecothane® (Thermedics, Inc., Woburn, Mass., USA) with a wall thickness of 0.3 mm. A stainless steel tip was integrated into the distal end of the catheter to prevent inflow obstruction during blood aspiration. The combined inflow/outflow valve was positioned 12 cm from the distal end of the catheter in the LVAD version. To test the possibility for right ventricular support, a PUCA pump catheter with combined valve located 6 cm from the distal end was made. The proximal end of the catheter in both LVAD and RVAD versions was integrated in a

connector that enabled a tight connection between the catheter and a 50 ml single-port membrane pump (Polymedica, Aachen, Germany; Fig. 3).

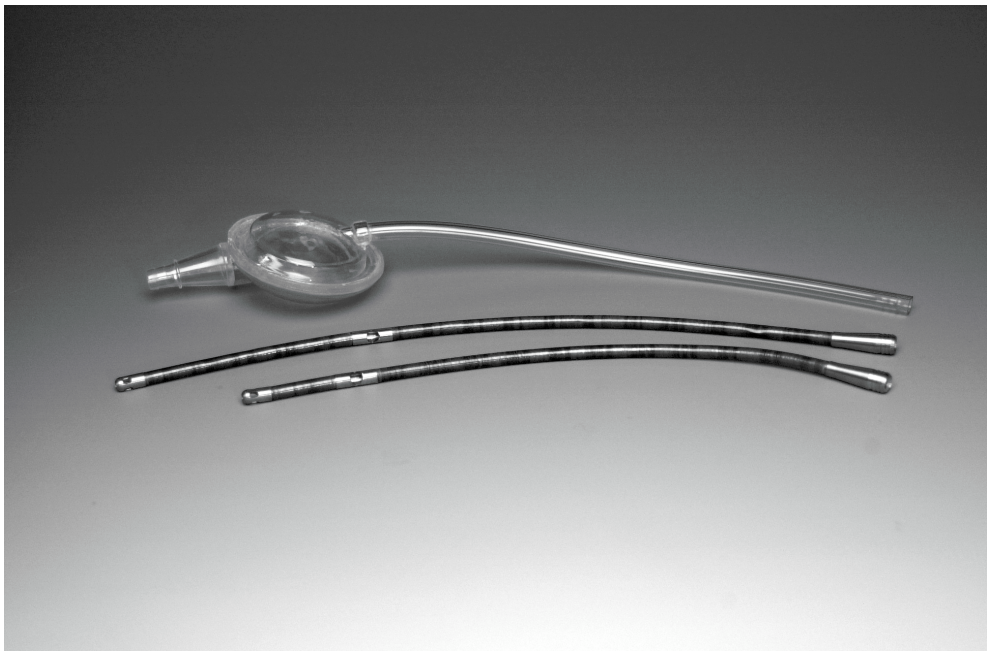

Fig. 3. The RVAD version (below) and the LVAD version (middle) of the PUCA-II with the 50 ml single-port driving membrane pump (Polymedica, Aachen, Germany; above).

Inside the tip of the PUCA-II a balloon catheter was inflated to prevent blood passage through the valve during the surgical introduction, and for monitoring pressure wave patterns to control the positioning of the PUCA pump tip[6]. Two circular sutures (4/0 Prolene) were placed in the thoracic aorta and were subsequently secured by tourniquets. Through a small incision in the aorta, the PUCA pump was introduced into the LV. The tourniquets were tied to control the bleeding. The pressure patterns derived from the tip of the balloon catheter confirmed the position of the PUCA-II tip into the LV[6]. The balloon catheter was then removed, the PUCA pump catheter was de-aired and connected to the membrane pump. The pump was activated using a Datascope Intra-Aortic Balloon Pump (IABP) driver (Datascope Corp., Oakland, N.J., USA) at a pump frequency of 40 beats per minute (bpm). The same procedure was repeated in the pulmonary artery to position a short-tip PUCA pump catheter into the right ventricle and to obtain right ventricular (RV) support.

The PUCA-II was tested as LVAD for 2 hours in 3 sheep, and as RVAD and biventricular assist device (BiVAD) for 1 hour in 2 sheep.

After the end of all animal experiments the catheters were removed and the valves were checked macroscopically for thrombus formation.

Results

In vitro measurements

Table 1 presents the percentage valve leakage during ejection and aspiration, and the flow resistance coefficient *K*.

Valve leakage was about three times higher during pump aspiration in comparison to pump ejection. The measured parameters of valve 1 and valve 2 were in the same range

Fig. 4. Flow visualisation during PUCA-II ejection: the ink is ejected under an angle of ± 45^0 with the valve housing. The distal part of the catheter is ink free.

Flow visualization

With the video set-up the valve action and the change in flow directions could be monitored well. Although the photo's taken from these video images were with low contrast, figure 4 shows that during pump ejection the valve leaflet closed the distal part of the catheter and the water/glycerol mixture was ejected through the "aortic" valve opening under an angle of ± 45^0 with the valve housing.

Animal experiments

The introduction of the PUCA pump tip into the aorta and the passage of the valve through the small opening in the aorta was performed easily and without complications. There was no blood loss through the valve during the insertion. The positioning of the catheter's tip into the LV was performed under pressure guidance only; X-ray monitoring was not necessary.

The introduction of the catheter into the pulmonary artery and the positioning of the catheter's tip into the RV were performed without complications as well.

Although the Datascope driver could displace balloon gas volumes that equalled the volume of the membrane pump, no full-fill/full-empty modes were obtained. Left and right pump flows was estimated at 1.2-1.4 L/minute.

Macroscopic examination of the valves showed that all valves tested were free of thrombi.

Valve number	Preload (mm Hg)	Afterload (mm Hg)	Pump flow (L/min)	Ejection leakage (%)	Aspiration leakage (%)	Resistance coefficient (*K*)
1	60	100	1.7	6	21	4
2	60	100	1.7	5	17	3

Table 1. Mean ejection leakage (%), aspiration leakage (%) and resistance coefficient *K* of PUCA-II measured in mock circulation.

Discussion

The *K*-values demonstrate that the opening of the valve does not generate high flow resistance. The percentages of leakage during the ejection phase are acceptable. A small amount of leakage keeps the blood behind the valve moving, thus preventing the formation of stagnating zones. The valve leakage during aspiration (i.e., aspiration from the aorta instead of the LV) was rather high (17-21%). Improving the accuracy of the manufacturing technique can decrease this

leakage to acceptable values. It is planned to limit valve leakage during aspiration to <10%.

The flow visualization studies demonstrated the usefulness of our computer simulation models. The content of the membrane pump was ejected through the "aortic" valve opening under an angle of ± 45^0 with the valve housing, which is in line with the results obtained with our finite element model studies. The flow visualization proved that the flow-jet will not be focussed at the aortic wall, but in the direction of the aortic flow, thus avoiding damage of aortic intima.

Thrombi were not found in the combined valve in both LVAD and RVAD experiments, which proves that the design of the combined valve enables a good wash out.

The fact that a full-fill/full-empty pump mode could not be realized was due to the driving system used. The IABP driver is designed to displace a limited volume of gas through a thin catheter and to fill and to empty the intra-aortic balloon in a very short period of time. Based on previous experiences with pneumatic drivers we expect that the IABP driver can be adapted to the requirements of the PUCA pump system.

In comparison with the indications for use of the IABP[7] it is expected that the PUCA pump can be used under the same circumstances. Unlike the true blood pumps, however the IABP depends on residual LV function and therefore has only minor effects in patients with profound heart failure[8]. The PUCA pump in fact combines the direct LV unloading effect of the Hemopump (Medtronic, Inc., Minneapolis, MN, USA) with the counterpulsation effect of IABP, a combination that has proven to provide an excellent support for the ischemic, failing heart[9]. Like the Hemopump, the PUCA pump cannot be used in cases that the catheter cannot pass the aortic valve (e.g. severe valve stenosis or mechanical valve prosthesis).

Micro-axial blood pumps can generate non-pulsatile blood flows up to 10 L/minute. A certain amount of pulsatility can be generated by these pumps when intermittent pump speeds are used, but the quality of the pulse generated from the PUCA pump is obviously superior to that of non-pulsatile pumps[3].

The working principle of the Modified Assist Device (MAD) and the Heart Ranger developed by Imanchi et al[10,11] and the intra aortic cannula pump[12] are all based on the PUCA pump concept. The main difference between the pumps mentioned and the PUCA-II is the fact that they all use a dual-valve system.

In the previous experiments with the dual-valve version of the PUCA pump we used a vascular graft sutured to the aorta to prevent valve damage during the

introduction of the catheter. The present study proved that the single-valve PUCA-II can be inserted directly into the aorta and that vascular graft is not necessary. The introduction technique, comparable with the technique used for aorta cannulation for heart-lung bypass, allows the PUCA pump to be inserted into the aorta within few minutes. The correct position of the catheter-tip into the ventricle is verified by pressure control. The method is easy, inexpensive, does not require X-ray guidance, and therefore avoids radiation of patient.

Reducing the distance between the catheter tip and the combined valve a right ventricular application for the PUCA-II was developed. This first in vivo experiments with the PUCA pump as a RVAD demonstrated that the short-tip catheter could be introduced into the RV via the main pulmonary artery in the same way as the LVAD version: without vascular graft and without X-ray guidance. Further animal experiments are needed to study the influence of the right ventricular as well as biventricular support with the PUCA pump on the pulmonary and systemic circulation.

In previous studies we described the influence of the LV support with the PUCA pump on myocardial oxygen consumption and coronary flow patterns[2,3]. Although we do not expect that the single-valve catheter will behave differently from the dual-valve version, further experiments are needed to prove this and to study biocompatibility properties of the pump before bringing the PUCA-II into a clinical trial.

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