Chapter 9:
General discussion

Congestive heart failure (HF) is a growing health problem with a high mortality rate\(^1\). Two major groups of HF patients can be distinguished: HF patients with sufficient responds and HF patients with insufficient responds to pharmacological therapy. The last group includes patients with potency for myocardial recovery (e.g., patients with cardiogenic shock after heart surgery or myocardial infarction) as well as end-stage HF patients. The most effective non-pharmacological therapy, heart transplantation, is limited due to the shortage of donor hearts. Mechanical Circulatory Support Systems (MCSS) can support or replace the pump-function of the failing heart, and can stabilize or even improve the condition of those patients\(^2\).

The Pulsatile Catheter (PUCA) pump is VAD that can be used as a Left Ventricular Assist Device (LVAD). The device has unique place in the group of Ventricular Assist Devices (VAD) because:

- The PUCA pump is a trans-arterial assist device, i.e., the device-catheter can be introduced into the left ventricle (LV) via a superficial artery (e.g., axillary artery) or via the ascending thoracic aorta. The open-chest introduction of the PUCA pump does not require a vascular graft to be previously sutured to the aorta. The last technique, comparable with the technique used for aorta cannulation for heart-lung bypass, allows the PUCA pump to be inserted into the left ventricle within minutes. As known, the short-term VAD’s are nearly always applied in cardiac emergencies (acute myocardial infarction, postcardiotomy cardiogenic shock, weaning from heart-lung machine, etc.). Therefore the introduction technique used for application of a short-term VAD is extremely important: an easy, fast, and safe introduction technique guarantee that the ventricular assist can start as soon as possible, and thus increase significantly the chance of myocardial recovery. Initial experiments to position the PUCA pump into the right ventricle through the pulmonary artery were successful and contributed to the development of a new application for the device.

- The correct position of the PUCA pump into the ventricle can be verified by pressure control\(^3\). The standard peripheral implantation technique for trans-arterial blood pumps (e.g., the Hemopump) requires X-ray control\(^4\). Using pressure control, the tip of the pump-catheter can be positioned accurately just
within the LV outflow tract, thereby avoiding contact with arrhythmogenic cardiac tissues by penetrating too deep into the LV. The technique is inexpensive, uses widely available equipment (bedside monitor), does not require X-ray guidance, and in this way avoids radiation of patient and staff. Trans-esophageal echography could be used during assist to verify the position of the catheter tip in the LV and to control the valve performance.

- The PUCA pump is the only trans-arterial LVAD that combines direct LV unloading with pulsatile flow on counterpulsation basis. The PUCA pump in fact combines the direct LV unloading effect of the Hemopump (Medtronic, Inc., Minneapolis, MN, USA) with the counterpulsation effect of Intra-Aortic Balloon Pump (IABP), a combination that has proven to provide an excellent support for the ischemic, failing heart. However, the Hemopump generates a non-pulsatile flow, which is less desirable than the pulsatile flow. Moreover, due to the presence of unique single-valve, the PUCA pump can be temporary switched off and kept in place without backflow from aorta to LV. If the Hemopump is switched off a backflow occurs. The IABP, unlike the true blood pumps, depends on the residual LV function and therefore has only minor effects in patients with profound hemodynamic compromise.

- The separate inflow and outflow valves in PUCA-I have been replaced by unique combined inflow/outflow valve in PUCA-II. The valve leaflet is the only moving part in the PUCA pump system (except the membrane in the membrane pump self). The last reduces significantly the risk of mechanical breakdown as well as the hemolysis during assist. The lack of thrombus formation in the valve after animal tests demonstrated a good valve washout.

The PUCA pump is indicated for a short-term (up to 3 days) LV support in patients with acute ventricular failure after heart operation, myocardial infarct, acute myocarditis, or as prophylactic in patients with mild heart failure during non-cardiac operations or high-risk Percutaneous Trans-luminal Coronary Angioplasty (PTCA). Reducing the distance between the catheter tip and the combined valve a right ventricular application for the PUCA pump was developed. The initial animal experiments 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. Further animal experiments are needed however to study the influence of the right ventricular as well as biventricular support with the PUCA pump on the pulmonary and systemic circulation.

The potential market for the PUCA pump can be calculated from the market of IABP. The indications for use of PUCA pump as LVAD are comparable with the indications for use of IABP. As known, about 200,000 IABP disposable sets are
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sold per year worldwide. In about 10% of the cases the LV support with the IABP fails and a LV support with other LVAD is required. The combination between relative low price, easy introduction, direct ventricular unloading with pulsatile flow on counterpulsation basis, and the simple control makes the PUCA pump a first-choice LVAD. Therefore it can be estimated that about 20,000 PUCA pumps could be sold per year only as LVAD.

The numerical simulation studies showed high similarity with the results obtained during the in vitro and in vivo tests of the PUCA pump\textsuperscript{10}. This leads to two major conclusions:

- The numerical simulation is a useful tool for testing of new PUCA pump prototypes that can save time, money, and experimental animals.

- The numerical simulation can be clinically used to chose the optimal PUCA pump configuration (catheter diameter, membrane pump volume, etc.), to chose the optimal driving mode for each individual patient depending of the actual hemodynamic values, as well as to predict the effect of the chosen PUCA pump configuration on the patient’s hemodynamic.

LV assist with the PUCA pump decreases significantly LV myocardial oxygen consumption (LV MVO\textsubscript{2}) and optimises the coronary flow in healthy animals\textsuperscript{11}. However, before pre-clinical trials, the PUCA pump should be tested in animals during acute heart failure conditions. Therefore, two animal models have been developed: an animal model of coronary sclerosis and a model of acute LV heart failure. The idea behind the first model was to develop an atherosclerotic plaque in the animal coronary artery and in this way to develop myocardial ischemia and consequently angina pectoris during exercise (pacemaker-induced tachycardia). Although undoubtedly successful in the development of selective coronary atherosclerosis\textsuperscript{12}, the model was not able to develop within the period of 4 weeks a plaque that can lead to myocardial ischemia. Therefore we concluded that this model could be used to study atherogenesis as well as for investigations of mechanical properties of the coronary arteries, but the model is unsuitable for testing of the PUCA pump during acute heart failure conditions. Long-term experiments should be performed to study the progress of the developed plaques and their effects on the myocardial blood supply. The second model was more successful. Combining a mild coronary stenosis with mild pacemaker-induced tachycardia an acute LV heart failure was developed. The technique used proved to be safe and the coronary constrictor allows fine-tuning of the demand ischemia. The model will be used in the following experiments with the PUCA pump to study the effect of the device during acute LV heart failure.
The PUCA pump is almost ready for the first pre-clinical trials. However, some preceding steps are still ahead:

- The PUCA pump should be tested for hemolysis, thrombus formation, and mechanical failures during chronic animal experiments. Although the PUCA pump is indicated for short-term ventricular support (up to 3 days), the device should be tested for safety reasons during 10-14 days support. After the experiments, all animals should be terminated and examined for thromboembolic complications. The catheter, the valve, and the membrane pump should be checked for mechanical damage as well as for thrombus formation.

- Cadaver studies should be performed in order to obtain the optimal distance between the catheter’s tip and the valve in the RVAD version of the PUCA pump.

- Animal experiments should be performed to study the influence of the right ventricular as well as biventricular support with the PUCA pump on the pulmonary and systemic circulation.

- The production technique of the combine valve should be improved in order aspiration valve leakage (i.e., aspiration from the aorta instead from the left ventricle during the aspiration phase) to be decreased below 10%.

- The Datascope-driver, used for driving the membrane pump, should be adapted according to the requirements of the PUCA pump in order full-fill / full-empty modes to be obtained.

- Different sterilization methods for the PUCA pump should be tested (e.g., γ-radiation, ethylene oxide, etc.) in order to select a method with minimal interaction with the PUCA pump material.

References


