Master Thesis

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Modeling and flow control for a left ventricular assist device

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Abstract

Contents

List of Symbols

Abbreviations

A-V!	**A-V!**
BTD	Bridging to decision
BTR	Bridging to recovery
BTT	Bridging to transplantation
BVAD	Biventricular Assist Device
CO	Cardiac Output
CVDs	Cardiovascular Diseases
CVS	Cardiovascular System
DT	Destination therapy
EDV	End-diastolic volume
ESV	End-systolic volume
HR	Heart rate
HTx	Heart transplantation
IMACS	International Mechanically Assisted Circulatory Support
INTERMACS	Interagency Registry for Mechanically Assisted Circulatory Support
LVAD	Left Ventricular Assist Device
MCS	Mechanical Circulatory Support
RWTH Aachen	Rheinisch-Westfälische Technische Hochschule Aachen
SL!	**SL!**
SV	Stroke Volume
VADs	Ventricular Assist Devices
WHO	World Health Organization

1 Introduction

1.1 Motivation and goal

1.2 Struture of the thesis

2 Medical Fundamentals

Comprehension of the physiological functionality of the human heart and the cardiovascular system is an important prerequisite to the work addressed in this thesis. Therefore the basics of these topics will be explained in this chapter.

2.1 Cardiovascular System

The fundamental task of the cardiovascular system is to supply all organs with blood. The system is divided into two components. The systemic circulation and the pulmonary circulation. As shown in Figure 2.1, which represents the percentage distribution of the blood over the circulatory system, the systemic circulation is supplying blood flow to all tissues and organs except the lung. Due to this, it is also referred to as the greater circulation. [Hal16]

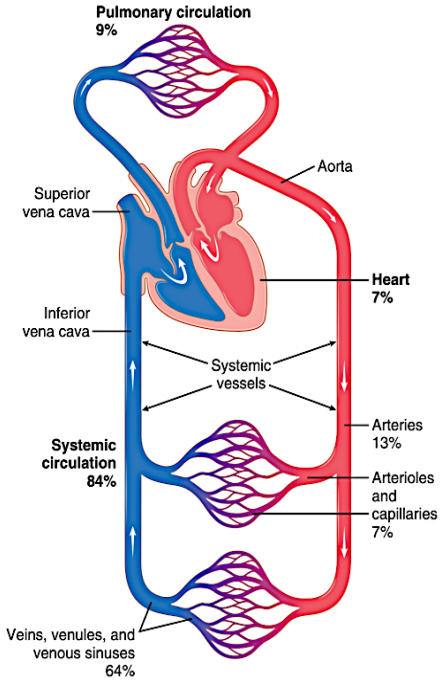

Figure 2.1: Blood distribution in the circulatory system [Hal16].

The center of the cardiovascular system is the heart. The heart itself consists of two mechanical pumps, which are functionally connected in series but are united in one organ. It is separated into two sides, which themselves are divided into an atrium

and a ventricle each. The atria act as weak primer pumps needed to provide blood flow to the ventricles.[SLH11] Both, the atria and the ventricles are surrounded by the myocardium, which acts as the working muscle of the heart. Through the contraction of the myocardium, blood is pumped into the circulatory system.[SK07] The left ventricle is pumping oxygenated blood through the aorta into the systemic circulation. There, the oxygen stored in the blood is delivered to the organs. The blood, now low in oxygen, is then led into the right atrium through the inferior and superior vena cava. From the right atrium, the deoxygenated blood then enters the right ventricle and afterwards is directed into the pulmonary circulation via the pulmonary artery. After the blood is oxygenated in the lungs, it is returned to the left atrium through the pulmonary vein.[SLH11] In addition to the atria and the ventricles each side of the heart has an atrioventricular (A-V) valve, as well as a semilunar (SL) valve. The A-V valve of the left heart is called the mitral valve, the one of the right heart is referred to as the tricuspid valve. The aortic valve and pulmonary valve are the SL valves of the left and right heart, respectively.[SK07] Figure 2.2 provides a graphic overview of the anatomy of the heart and the course of blood flow through the heart.

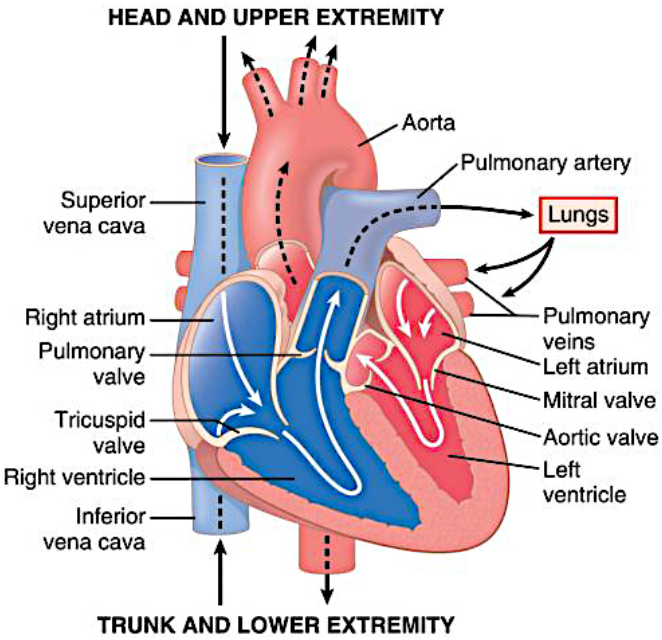

Figure 2.2: Anatomy of the human heart [Hal16].

The amount of blood pumped through the two sides of the heart is equal at all times. This value is called cardiac output (CO). It is calculated through by multiplying the heart rate (HR) and the stroke volume (SV). For an average adult at rest, with a

heart rate of approximately $70min^{-1}$ and a stroke volume of 70 ml, this leads to

$$CO = HR \times SV = 70min^{-1} \times 70ml = 5\frac{l}{min} \tag{2.1}$$

In case of maximum physical load, the cardiac output can increase as high as $20\frac{l}{min}$, for a stroke volume of 110 ml and a heart rate of $190min^{-1}$. [SLH11]

The cardiac cycle describes the events that occur during the time-span of one heartbeat. It is triggered by an electrochemical action potential originating from the sinus node. The cycle is divided into four phases. Figure 2.3 illustrates these action phases and events of the cardiac cycle for the left ventricle. During the period of isovolumic

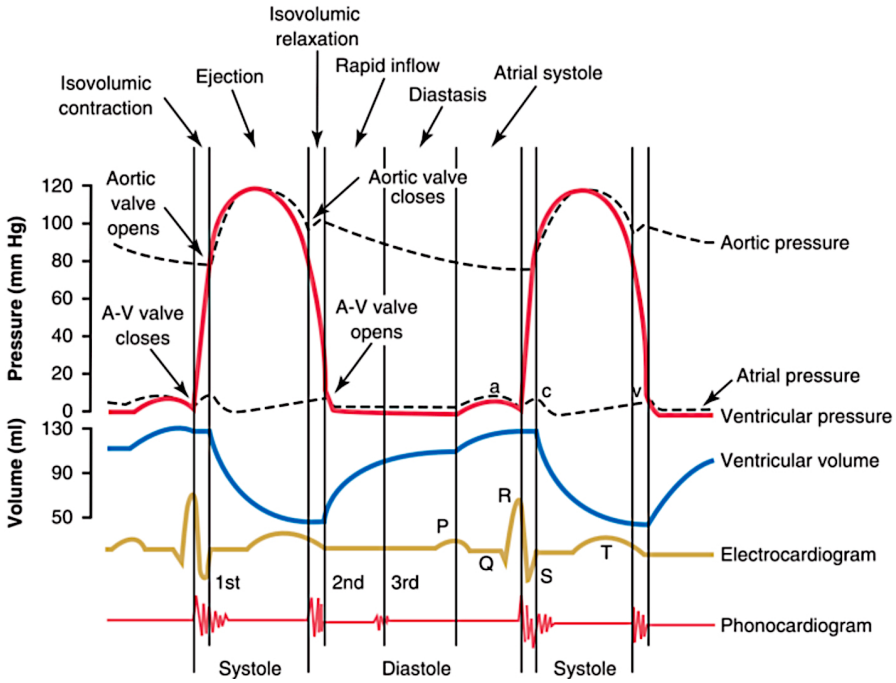

Figure 2.3: Action phases of the cardiac cycle based on the example of the left ventricle [Hal16].

contraction, the ventricular pressure increases. For the left ventricle, the pressure increases from about 4-6 mmHg to 80 mmHg. The values for the right ventricle are much lower. This increase is happening as a direct result of the ventricular contraction. The A-V valves, as well as the SL valves, are closed during this process. This leads to a constant blood volume in the ventricles. As soon as the ventricular pressure exceeds the arterial pressure the pulmonary and aortic valves open and blood can flow into the aorta and the pulmonary artery. This phase is called ejection phase, as the blood is ejected into the circulatory system. The period of isovolumic

contraction in combination with the ejection phase is called systole.[SLH11] During the systole the blood volume in the ventricle decreases by 55-60%, resulting in an end-systolic volume (ESV) of about 40-50 ml [Hal16]. Due to the contraction of the myocardium, the ventricular pressure keeps increasing for a while before decreasing again as the relaxation of the myocardium sets in. As soon as the outflow of the blood ends, the semilunar valves close, initiating the period of isovolumic relaxation. During this period pressure in the ventricles is decreasing, while the blood volume is constant. When the pressure in the atrium exceeds the ventricular pressure, the A-V valves open and blood is flowing into the ventricles until the pressure levels are balanced.[SLH11] This phase is referred to as the period of rapid filling of the ventricles. Combined with the isovolumic relaxation it represents the diastole. The end-diastolic volume (EDV) is about 110-120 ml.[Hal16] While, at rest, the diastole lasts about twice as long as the systole, above a heart rate of $150 min^{-1}$, the two phases are about equal [SLH11].

The pumping mechanism of the left ventricle can be illustrated well using a pressure-volume diagram (P-V diagram). For the construction of the P-V diagram first the relationship between the left ventricular volume and the ventricular pressure during diastole and systole, as displayed in Figure 2.4a, has to be discussed. The blue

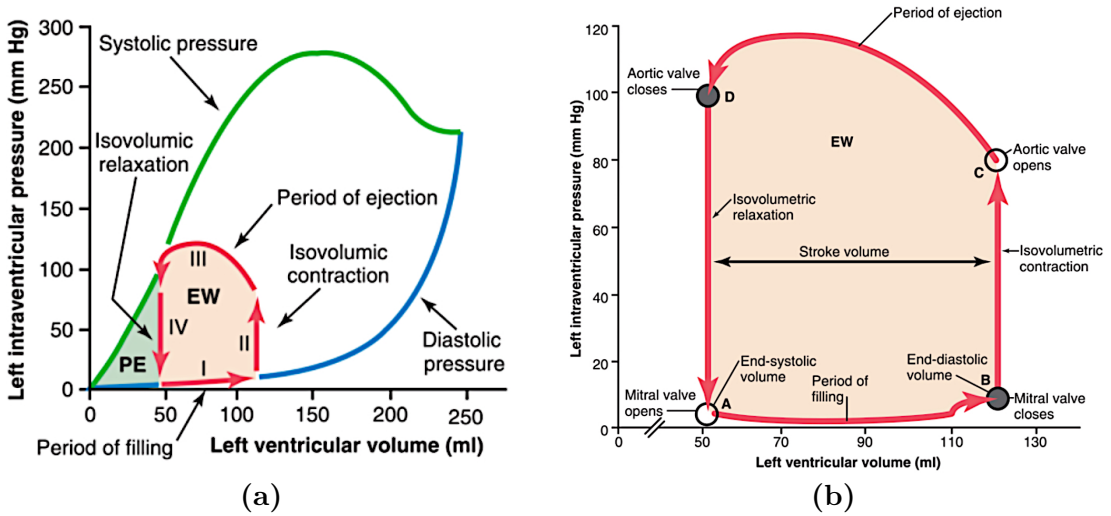

Figure 2.4: (a)Working diagram of the left ventricle with the P-V diagram. (b) Close-up P-V diagram. [Hal16]

curve representing the *diastolic pressure* is calculated by gradually filling the heart with higher blood volumes and then measuring the diastolic pressure just before ventricular contraction occurs. It is describing the heart's mechanical properties when the myocardium is in a relaxed state. The green curve in Figure 2.4a, named

systolic pressure, is plotted by measuring the systolic pressure over varying filling volumes for constant ventricle volumes. The red lines in Figure 2.4a and Figure 2.4b indicate the cardiac cycle and its four action phases, as described above. The line between points A and B in Figure 2.4b depicts the period of rapid filling. The isovolumic contraction is represented through line II in Figure 2.4a, respectively between points B and C in Figure 2.4b. The ejection phase is represented through III in Figure 2.4a and the line referred to as IV represents the period of isovolumic relaxation. The area of the work diagram, marked with EW in Figure 2.4 is a measure of the work done by the heart. Knowledge of the P-V diagram is an important prerequisite in understanding myocardial diseases, such as heart failure. [SLH11]

2.2 Heart failure

In the case of heart failure, the heart is unable to provide the required amount of blood flow to the cardiovascular system in order to supply all organs and tissue with oxygen. Heart failure does not directly represent a disease but rather a clinical syndrome. Nevertheless, the symptoms of different forms of heart failure are very similar and eventually manifest themselves in a decreased cardiac output. One acute consequence of heart failure, for example, is the feeling of shortness of breath. In the long term, however, severe heart failure can also lead to muscle weakness and a lack of concentration.
According to [SLH11], heart failure can be attributed to either systolic dysfunction or diastolic dysfunction. In systolic dysfunction, there is either a limitation of contractility or an impairment of the ejection phase sequence. Causes may include prolonged pressure stress, also called hypertension, or restriction of oxygen supply due to coronary artery disease. Furthermore, cardiac arrhythmias or a heart attack can lead to systolic dysfunction. In diastolic functional impairment, the dysfunction is evident in the course of the filling phase. This can be triggered, among other things, as a result of reduced compliance of the myocardium due to hypertrophy or fibrosis.
For the treatment of heart failure, drug therapy using beta-blockers is initially targeted in most cases. However, if this is not successful, the use of ventricular assist devices can be a useful alternative in order to relieve the heart and provide sufficient blood flow. [SLH11]

3 Technical Fundamentals

Not only the medical background covered in the previous chapter, but also knowledge of the technology of mechanical heart support technologies, such as ventricular assist devices is essential for this work. Since the main part of this thesis addresses the implementation of flow control algorithms for a left ventricular assist device, the basics of control theory and a introduction on iterative learning control will be presented here as well.

3.1 Ventricular Assist Devices

The World Health Organization (WHO) names cardiovascular diseases (CVDs) as the global number one cause of death. In 2016 about 17.9 million people died from CVDs, which represent 31% of all global death that year.[Wor20] Despite the fact that heart transplantation (HTx) still is the gold standard for treatment of patients with terminal heart failure [Sch10] ventricular assist devices (VADs), as a kind of mechanical circulatory support (MCS) technology, are becoming more and more important in treating patients with CVDs. This is due both to the fact that this disease pattern is becoming more significant due to demographic change and to the increasing shortage of donor organs.[DMH19]

3.1.1 Technology

Since the first artificial blood-pump has been implanted in 1963 [LHH$^+$63] technology of VADs has improved significantly.
The general aim of ventricular assist devices is to provide mechanical support in pumping blood through the human body with the heart remaining inside the patients body. Assistance can either be implemented to support the heart in a counter pulsation approach, working synchronous to the heart cycle, or as an asynchronous support. Despite there being several types of VADs, all of them are working according to the same principle. Blood is taken from the circulatory system through the pumps inlet and ejected at another location via the outlet of the pump.[LW16]
VADs are differentiated by three criteria: the localization of the device inside the human body, the flow profile and the implantation strategy.
Regarding the localization of the assistance there are three types of VADs. With around 93% of all implemented devices the most commonly used ones are the left

ventricular assist devices.[DMH19] LVADs are placed inside the left ventricle, from where they are pumping blood into the aorta [GSL+03]. The second localization option is given by placing the device as a support for the right ventricle. These devices are therefore called right ventricular assist devices (RVADs). RVADs are positioned such that blood is taken from the right atrium and ejected into the pulmonary artery. [DMH19] In some cases RVADs in combination with the aforementioned LVADs are used to build a biventricular assist device (BVAD). This type of heart support is mainly used for more severe heart diseases with a high risk of developing right heart failure. [SH19]
The flow profile as the second criterion for VAD distinction is represented through pulsatile and continuous flow devices. The most commonly known type of pulsatile device is a pneumatically driven pump ventricle. [LW16] However, according to the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) over 95% of all implanted devices are continuous flow devices [KPK+17]. These in their most commonly used form are electrically driven rotational blood pumps. A technological difficulty with these devices is the high probability of blood damage due to small gaps and very high rotational speed. In exchange for this problematic these devices enable a dynamic adaption to the patients physiological needs by being able to quickly adjusting parameters like the motor current. The possibility of keeping track of these signal characteristics furthermore makes it possible to detect malfunctions such like misplacement of the pump. [LW16]
Implantation of the VADs can be performed in one of three ways: paracorporeal, intracorporeal or percutaneous [DMH19]. For VAD systems which follow a paracorporeal approach, only the in- and outflow cannulas are located inside the human body. The cannulas are connecting the pump, which is located outside the body, with the ventricle and the vessels. Due to the pump being placed outside of the patients body, these systems provide the option for pediatric MCS. For most other systems this is not possible due to the device being to big to fit inside a child's body. [SBL19] One example for paracorporeal systems are the aforementioned pneumatically driven pump ventricles [LW16]. As far as the other two criteria for VAD differentiation are concerned, all combinations of localization and flow control are possible [SBL19]. As an example of a percutaneous device, [DMH19] names the Impella 2.5, which is a rotary blood pump with continuous flow used for left ventricular assistance.

3.1.2 Therapeutic objective

Traditionally the therapeutic goals of VAD treatment can be divided into three categories: *bridging to transplantation* (BTT), *bridging to recovery* (BTR) and *destination therapy* (DT). However in some cases also the classification into *bridging to decision* (BTD) and *bridging to transplantability* are mentioned as well. The decision

INTERMACS Score	NYHA	Patient condition	Survival time
1	IV	critical cardiogenic shock	hours
2	IV	increasing catecholamine demand	days
3	IV	stable under inotropics	a week
4	IV	frequent decompensation	weeks-month
5	IV	rest discomfort/ not resilient	weeks-month
6	IV	rest discomfort/ merely resilient	month
7	IIIb	merely resilient	one year survival rate: 50-70%

Table 3.1: Relation between INTERMACS Score, NYHAc-classification, patient condition and approximate survival time based on [Eif18]

for one of these goals is based on the type of CVD and the condition the patient is in, when receiving VAD assistance.[KSS+11] An overview on the relation between the INTERMACS Score, the New York Heart Association(NYHA)-classification and the patient's condition is presented in Table 3.1. The INTERMACS Score, which is based on data from patients which have received VAD treatment, links the need for a VAD and the appropriate time frame in which the devices needs to be implanted. It is of high importance in the decision of the therapeutic objective for VAD treatment. [DMH19]
The goal of *bridging to transplantation* has a big relevance with patients in NYHA-IV Stadium which are showing hemodynamical instability. Due to a heart transplantation being the desired final treatment for these patients there must be no contraindication to HTx. In case the patient does show a contraindication, such as malignant tumors or an uncontrollable sepsis, the therapeutic objective changes from BTT to DT. In order for a treatment with a VAD as destination therapy being indicated all conservative treatment options need to be exhausted. Due to the ever-growing shortage of donor organs DT as a therapeutic approach in patients with heart insufficiency will become more relevant in the future even in cases usually suited for heart transplantation. [DMH19] There may occur some cases, in which at first a contraindication for HTx exists, which later on may dissolve. These indicate a therapy based on a *bridging to transplantability* goal. [KSS+11]
The indication for a *bridging to recovery* approach is twofold. Either the patient shows heart failure as a result of ischemia reperfusion damage or due to infectious genesis. In the first case the myocardium usually is able to recover within a few days, whereas in the second one the potential and the time necessary for recovery depends on how badly the tissue is damaged. In either scenario a weaning from the VAD is an essential part of therapy. [DMH19]
If a patient is admitted in cardiogenic shock and medical treatment is not sufficient,

VAD type		Therapeutic objective	
LVAD	93%	DT	40%
BVAD	4%	BTD	30%
TAH	2%	BTT	29%
unknown	0.1%	others (BTR,...)	1%
RVAD	0.05%		

Table 3.2: Percentages of VAD types and thearapeutic objectives in mechanical heart supports based on [DMH19].

bridging to decision becomes a relevant form of therapy. By providing the patient with a VAD, a more accurate assessment of the patient's condition is possible. Based on this, the decision on further treatment can be thought through more thoroughly. [KSS+11] Table 3.2 illustrates the proportions of different VAD types and therapeutic goals using the International Mechanically Assisted Circulatory Support (IMACS) register.

3.2 Control Theory

3.2.1 PI Controller

Chien Hrones Reswick

3.2.2 Iterative Learning Control

4 Modeling and Identification

4.1 Sputnik VAD

The Sputnik VAD is an axial-flow blood pump, developed in a cooperative project of the National Research University of Electronic Technology, OJSC Zelenograd Innovation-Technology Center of Medical Equipment, FSBI "Academician V.I. Shumakov Federal Research Center of Transplantology and Artificial Organs", Ministry of Health of Russian Federation, DONA-M LLC and BIOSOFT-M LLC in 2009. [ST15]
This device is used for left ventricular assistance in patients with acute heart failure. The therapeutic objective in implantation of a Sputnik VAD is bridging to transplantation. The VAD is able to pump up to 10 liters of blood per minute with a continuous flow profile. The implantable pump weighs about 200 g, has a length of 81 mm and a maximum diameter of 34 mm. It consists of a moving and a stationary part. The moving part, the impeller, which is a rotor with four blades, contains a permanent NdFeB-magnet which is actuated by a brushless DC motor. The rotor spins clockwise with speed values between 4000-10000 rpm. An overview of the pumps specification is presentet in Table 4.1 The stator is located inside a titanium

Blood flow	0-10 L/min
Rotational speed	4000-10000 rpm
Length	81 mm
Diameter	34 mm
Weight	200g

Table 4.1: Specifications of Sputnik VAD

housing with a 16 mm diameter. The stationary part of the pump consists of a flow straightener with three stationary blades and a flow diffusor with three twisted blades. The flow straightener is located in front of the rotor and straightens the incoming blood flow into the rotor. Behind the rotor, the blood is directed into the diffusor. Figure 4.1 depicts a cross-section of the Sputnik VAD and identifies it's individual components. The connection between the pump and the cardiovascular system is performed using in- and outflow cannulas, a felt ferule and vascular prosthesis which is sewed to the aorta. [ST15] The Sputnik VAD is powered using two lithium-ion batteries, fully loaded providing enough energy for up to eight hours of system support. The maximum charging time for the batteries is less than five hours. During this time the batteries can either be exchanged by another set of batteries or

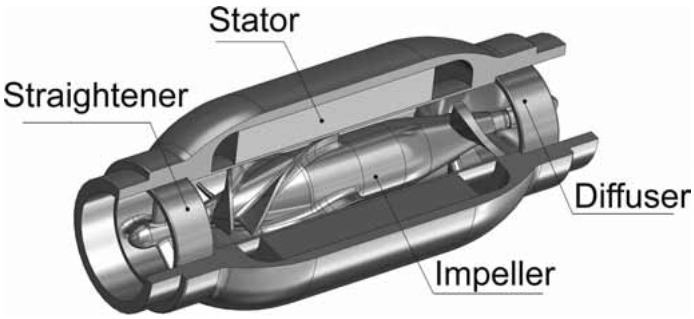

Figure 4.1: Cross-section of the Sputnik VAD from [ST16]

the system can be powered through connection to an AC network. A microprocessor-based driving unit is used to regulate the pump speed, manage the power supply and store parameter data. It is connected percutaneously to the pump with a up to 170 cm long and 5 cm wide lead. [ST15]

4.2 Hardware in the Loop Test Bench

4.3 System Identification

5 Implementation of Flow Control

5.1 Controller Design

5.1.1 PI Controller

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5.1.2 Iterative Learning Control

5.1.3 Iterative Learning Control with varying iteration length

5.2 Evaluation of Controllers

6 Conclusion and future work

A Appendix

Bibliography

[DMH19] Dashkevich, A ; Michel, S ; Hagl, C: Indikationsstellung und Therapieziele der mechanischen Kreislaufunterstützung. In: *Medizinische Klinik-Intensivmedizin und Notfallmedizin* 114 (2019), Nr. 5, S. 452–458

[Eif18] Eifert, S: Perkutane und chirurgische Optionen der mechanischen Kreislaufunterstützung in der Therapie der terminalen Herzinsuffizienz. In: *Der Anaesthesist* 67 (2018), Nr. 5, S. 321–325

[GSL+03] Grabellus, F. ; Schmid, C. ; Levkau, B. ; Stypmann, J. ; Scheld, H. ; Baba, Hideo A.: Myokardiale Veränderungen unter mechanischer linksventrikulärer Unterstützungstherapie. In: *Der Pathologe* 24 (2003), Nr. 2, S. 83–90

[Hal16] Hall, John E.: *Guyton and Hall Textbook of Medical Physiology, Jordanian Edition E-Book*. Elsevier, 2016

[KPK+17] Kirklin, James K. ; Pagani, Francis D. ; Kormos, Robert L. ; Stevenson, Lynne W. ; Blume, Elizabeth D. ; Myers, Susan L. ; Miller, Marissa A. ; Baldwin, J. T. ; Young, James B. ; Naftel, David C.: Eighth annual INTERMACS report: Special focus on framing the impact of adverse events. In: *The Journal of Heart and Lung Transplantation* 36 (2017), 2020/08/05, Nr. 10, S. 1080–1086

[KSS+11] Krabatsch, T ; Schweiger, M ; Stepanenko, A ; Drews, T ; Potapov, E ; Pasic, M ; Weng, Y ; Huebler, M ; Hetzer, R: Fortschritte bei implantierbaren mechanischen Kreislaufunterstüzungssystemen. In: *Herz* 36 (2011), Nr. 7, S. 622

[LHH+63] Liotta, Domingo ; Hall, C.William ; Henly, Walter S. ; Cooley, Denton A. ; Crawford, E.Stanley ; DeBakey, Michael E.: Prolonged assisted circulation during and after cardiac or aortic surgery: Prolonged partial left ventricular bypass by means of intracorporeal circulation. In: *The American Journal of Cardiology* 12 (1963), Nr. 3, S. 399 – 405. – ISSN 0002–9149. – Symposium on Cardiovascular-Pulmonary Problems Before and After Surgery Part I

[LW16] *Kapitel* Herzunterstützungssysteme. In: Leonhardt, Steffen ; Walter, Marian: *Medizintechnische Systeme: Physiologische Grundlagen,*

Gerätetechnik und automatisierte Therapieführung. Berlin, Heidelberg : Springer Berlin Heidelberg, 2016. – ISBN 978–3–642–41239–4, S. 107–144

[SBL19] Sponga, Sandro ; Benedetti, Giovanni ; Livi, Ugolino: Short-term mechanical circulatory support as bridge to heart transplantation: paracorporeal ventricular assist device as alternative to extracorporeal life support. In: *Annals of cardiothoracic surgery* 8 (2019), 01, Nr. 1, S. 143–150

[Sch10] Schüller, Annika: Das Kunstherz – Möglichkeiten der mechanischen Kreislaufunterstützung (VAD). In: *intensiv* 18 (2010), Nr. 03, S. 138–147

[SH19] Shehab, Sajad ; Hayward, Christopher S.: Choosing Between Left Ventricular Assist Devices and Biventricular Assist Devices. In: *Cardiac failure review* 5 (2019), 02, Nr. 1, S. 19–23

[SK07] Schiebler, Theodor H. ; Korf, Horst-W: *Anatomie: Histologie, Entwicklungsgeschichte, makroskopische und mikroskopische Anatomie, Topographie*. Springer-Verlag, 2007

[SLH11] Schmidt, Robert F. ; Lang, Florian ; Heckmann, Manfred: *Physiologie des Menschen mit Pathophysiologie*. Springer-Verlag, 2011

[ST15] Selishchev, Sergey ; Telyshev, Dmitry: Ventricular assist device Sputnik: Description, technical features and characteristics. In: *Trends in Biomaterials and Artificial Organs* 29 (2015), Nr. 3, S. 207–210

[ST16] Selishchev, Sergey ; Telyshev, Dmitry: Optimisation of the Sputnik-VAD design. In: *The International journal of artificial organs* 39 (2016), 09. http://dx.doi.org/10.5301/ijao.5000518. – DOI 10.5301/ijao.5000518

[Wor20] World Health Organization: *Cardiovascular diseases (CVDs)*. https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds), Zuletzt besucht am 06.08.2020