

Risk Management to Validation VAD design

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Abstract: Implantable Ventricular Assist Devices (VAD) used as heart failure advanced therapy have adverse events, including VAD malfunction. A method for improving the reliability of VAD through a risk analysis and inherent safety recommendations for bench-tested VAD is proposed. The result is presentation of an algorithm to validate VAD design. The method provides constant verification by monitoring operating variables which when compared to a standard behavior curve provides data that allow prediction of failures. Thus, in the project life cycle a continuous improvement of the reliability of VAD projects is possible.

Keywords: Decision support and control; Identification and validation; Model formulation, experiment design.

1. INTRODUCTION

The term Mechanical Circulatory Support Device (DSCM) defines blood pumps used to assist or replace the left or right ventricles or both, and are known as Left Ventricular Assist Device (LVAD), Right Ventricular Assist Device (RVAD), or Biventricular Device (BVD), and the term Ventricular Assist System (VAS) can also be used (Deng and Naka, 2007).

There are two fundamental types of artificial heart, one that provides an extra ventricle to help pump blood to the body, which is called the Ventricular Assist Device (VAD), which is the focus of this work, and the total artificial heart. (CAT) which is a replacement for the whole heart that can be implanted in the body after the failed heart is removed (Deng and Naka, 2007)(Kyo, 2014) (Tozzi *et al.*, 2017).

SCM implantation has proven to be a successful option for treating patients with heart problems, i.e. it can be implanted to ensure that the patient can wait until receiving a heart transplant, VAD or VAS, and In this case, this practice is

known as a “bridge to transplant” (PPT), or when the patient has a high transplant rejection rate, the device is implanted as a permanent solution, and in this case, this practice is known as “Destination Therapy” (TDD) (Kyo, 2014)(Yost *et al.*, 2016)(Murala and Si, 2017).

Research by the International Society of Lung and Heart Transplantation (ISLHT) and Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) has shown that after SCM implantation some of the patients who received the device did not reach a very long life expectancy, which is related to adverse events such as infection, bleeding, neurological dysfunction, respiratory failure, device malfunction and thromboembolism (John *et al.*, 2010)(Theisz, 2012)(Kirklin *et al.*, 2015)(Kirklin *et al.*, 2017)(Cowger *et al.*, 2017)(Chambers *et al.*, 2017)(Dias *et al.*, 2018)(Mavroudis, Kirklin and DeCampli, 2018). Similar adverse events were analyzed by researchers who performed 895 VAD implants at three medical institutions from 2004 to 2013 and were divided into: (i) implantation techniques and anatomical restrictions; (ii) patient-related factors such as degree of infection, bleeding, and adequacy of

anticoagulation; (iii) mechanical configurations of VAD; and (iv) device design and manufacturing (Starling *et al.*, 2014). The four related factors previously have a complex interaction that affects device reliability. Of the factors presented, it can be observed that the third and fourth, refer to the design, mechanical configuration and manufacture of the VAD. From these data, the search for information for a better understanding of adverse events in ADLs has been deepened, as the research carried out by INTERMACS, which today has a database collected from approximately 185 hospitals, which have already performed more than 22,866 implants (Kirklin *et al.*, 2017). This entity relies on the cooperative efforts of clinicians, scientists, manufacturers and government entities to survey failures in VADs (Khazanie *et al.*, 2016)(Murala and Si, 2017). In recent surveys 17,633 continuous-flow VAD implants, from 2012 to 2016, there were 5398 deaths, and survival rates were distributed (Kirklin *et al.*, 2017), as shown in Table 2. Research indicates that the main major adverse events following VAD implantation in the first occurrence are infection, bleeding, device malfunction, stroke, and death (Kyo, 2014)(Prinzing *et al.*, 2016)(Kirklin *et al.*, 2017).

Table 1. Survival Rates in Streaming VADs from 2012 to 2016

Percentage	Period
95%	To 1 month
81%	For 12 months
70%	For 24 months
59%	For 36 months
49%	For 48 months
21%	For 96 months

One of the studies involving 145 hospitals and 6,885 patients who received some type of VAD, from 2006 to 2012, of the 594 cases using pulsed-flow VAD 119, the equivalent to 20%, presented device malfunction. For the 5,358 cases in which continuous flow VAD was used, 660, the equivalent of 12.3%, presented malfunction (Kirklin *et al.*, 2013). For 2442 readmissions, according to the INTERMACS database, 8% of the causes of readmission were due to VAD malfunction (Kirklin *et al.*, 2012)(Dembitsky and Adamson, 2014).

According to a survey conducted by IMACS (International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support) from January 2013 to December 2016, with continuous flow pumps, equivalent to 13,618 of the implanted patients, the amount of malfunction in VADs were 233 cases, equivalent to 2% of death cases (Mavroudis, Kirklin and DeCampi, 2018). Despite technological improvements, VADs still have a worrying participation in the survival rate of patients implanted with VADs (Theisz, 2012)(Kyo, 2014)(Mozaffarian *et al.*, 2016)(Kirklin *et al.*, 2017).

The increasing longevity of patients transplanted with VADs as a target therapy recently justifies the development of features that improve the robustness and reliability in the life cycle of these devices (Yang, 2007)(Goldstein *et al.*, 2018)(Cowger *et al.*, 2017). The life cycle of a product are all

phases from conception to deactivation of a product (Klespitz, Biro and Kovacs, 2016)(IEC 61508-1, 2010). For the medical device risk management standard, ISO 14971, the life cycle of a product is all stages of a health product's life, from initial design to decommissioning and disposal (ABNT ISO 14971, 2009). Robustness, in turn, is defined as the ability of a product to perform its intended function consistently in the presence of variables that have adverse effects on the intended function, which is difficult to control (Yang, 2006)(Modarres, Kaminskiy and Krivtsov, 2017). This technique is very suitable for improving reliability at low cost over a short period of time over specified conditions of use within a statistical engineering methodology that demonstrates the statistical accuracy of the project (Yang, 2006).

Failure modes can be verified through a risk analysis to determine the cause-effect of the failures, which favours the treatment and management of these failures (Yang, 2006)(Modarres, 2006) guidelines that favour the implementation of a program in the life cycle of these devices (ABNT ISO 14971, 2009)(Theisz, 2012). By using appropriate risk analysis tools chosen according to the available design data, the causes and effects can be analyzed, favouring the treatment of these causes and effects (Modarres, 1993)(Modarres, 2006)(ABNT NBR ISO 31000, 2009)(Proenca *et al.*, 2017)(Aven and Zio, 2018).

Failure handling with the implementation of inherent safety concepts has been employed in chemical, petrochemical and nuclear processes, incorporating active safety barriers to prevent hazardous events from occurring, reducing hazards, causes and amount of people exposed to the effects (Kletz and Amyotte, 2010). International standardization standards have been designed to support processes and products where a large number of quality management, risk, information security, product testing and medical device specific application systems can be found. IEC 61508-4, for example, adopts the use of safe fault and inherent safety principles applied to safety-related electrical, electronic, and programmable electronics systems (IEC 61508-4, 2010). Implementing inherent safety as a barrier to fault handling directly impacts the reliability level of a device or process.

The proposed method aims to improve the reliability of the VAD through a risk analysis and safety recommendations inherent to the VAD project, which after the changes is tested on the bench. The test allows a verification of the VAD's functionality, through the reliability and risk data. The data that is detected provides information for decision making, allowing comparison with expected or determined values, with the desired reliability.

2. PROPOSED METHOD

In the detailing of the method will be described the protocols and tools that will be used to carry out the experimental research.

In these steps 1 through 4, risk analysis assesses project reliability, production, or testing, allowing the project to be validated in step 5 "Project Validation". This last step ensures

the inherent reliability of the device, validating the design, allowing future verification to verify the reduction of adverse events arising from the malfunction of these devices. The collected data provide a statistical treatment that favours the adjustment of actuator control parameters on the test bench, so that the “Bench Test Procedure” can be adjusted (Dias *et al.*, 2018)(Dias *et al.*, 2017).

2.1 Method for Research Project Cycle

The inherent reliability is not simple to be achieved in time-varying equipment (Li, Cui and Yi, 2016; WHO, 2018)(Zhang, 2017), as is the case with a VAD, so a cyclical process has been devised five steps as proposed in Figure 1. The steps are described in detail in the following sections. A VAD design characterization, step 1, is built on demand requirements, which is evaluated in step 2 “Risk Analysis” in such a way that it provides sufficient reliability for the production of rapid prototyping as provided in step 3 “PETG VAD samples” from a bench test and inspection device in step 4 “Bench Tests”. Step 5 “VAD Design Validation” can be performed by applying the design improvement indicator method from the failure data obtained.

2.1.1 VAD Project Characterization

The characterization of the VAD Project is the detailing of design data related to its dimensions, components, operating variables and functionality to perform its required functions.

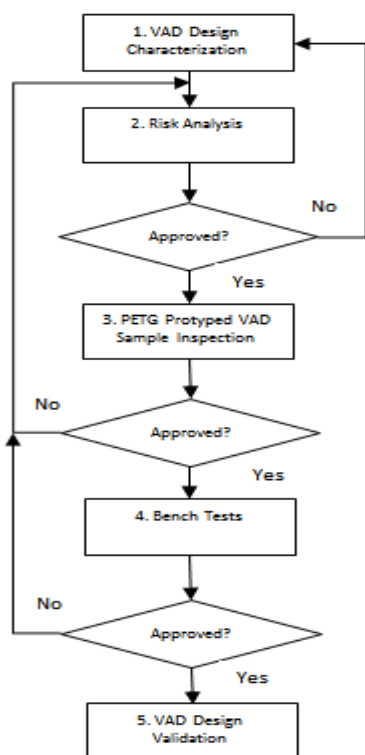


Fig. 1. Research Project Cycle Method Algorithm

2.1.2 Risk Analysis

Initially, hazards and their causes are identified by using an appropriate tool such as Cause and Effect Analysis (CEA), Preliminary Hazard Analysis (PHA) or Fault Tree Analysis (FTA), Failure Mode Analysis and Effects (FMEA), and, Bow Tie Analysis as available information. After assessing the causes of the hazards, the consequences are assessed and the hazard categories are designated, thereby prioritizing the recommendations or measures proposed for improving safety and qualitatively assessing the hazards encountered.

The Risk Analysis (RA) of the product or process will follow the use of appropriate forms and procedures for its systematization, according to the step and available information. The main tool and methodology to be used will be Preliminary Hazard Analysis (PHA).

2.1.3 PETG Prototyped VAD Sample Inspection

The step consists in the inspection of PETG prototyped VAD samples, based on protocols for the surface or roughness analysis procedure.

The procedure refers to the operating instructions for Taylor Hobson's 3D TS CCI 3000 - Non-Contact Surface Profiling Systems contained in the User's Guide. Operating instructions are required for the parameters: profile depth P_t ; cut λ_c ; ripple height W_t ; average roughness R_a and R_q ; roughness depth R_z and R_{max} ; R_{sk} and R_{ku} ; peak height R_p and R_v ; depth of base roughness R_{3z} ; material rate R_{mr} and t_p ; R_k , R_{pk} , R_{vk} , M_{r1} , M_{r2} ; R_{sm} , $R_{\Delta q}$; peak count R_{pc} , H_{SC} . The monitoring of the roughness parameters allows an analysis of wear variations, in the 3D of the surface peaks, and, consequently, the component failure tendency. In this way, with application of predictive statistics, for example a Weibull Distribution.

2.1.4 Bench Tests

The test bench proposed in this work is composed of two tanks (T1 and T2) that are responsible for the storage of the fluid that travels through the system (Figure 2). The fluid is transported from tank T1 to tank T2.

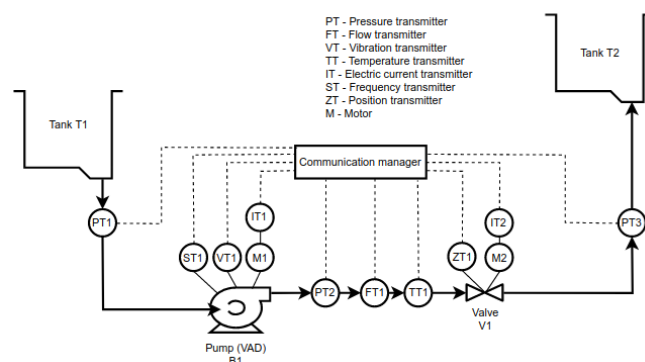


Fig. 2. VAD In Vitro Test Bench Process Diagram and Instrumentation

The transport is carried out from a pump (P1), which imposes energy on the system. During the test bench operation process, sensors are used to collect the main variables

involved in the system to provide decision support to the operator (Figure 3). The test bench has sensors that collect fluid pressure at tank outlet T1, engine M1 rotation of pump P1, pump vibration P1, electric motor current M1 of pump P1, fluid pressure at the outlet of pump P1, fluid flow at pump outlet P1, fluid temperature at pump outlet P1, position of motor M2 of valve V1, electric current at motor M2 of valve V1 and pressure of fluid at the inlet of tank T2. To perform, the test bench has an M1 motor responsible for the rotation control of the pump P1 and an M2 motor responsible for the position control of the valve V1 that allows the flow control of the fluid. To collect the data emitted by the sensors and impose the new references to the actuators, a communication manager is necessary for distribution of the information.

In the development of the proposed control system, it is approached the concept that the test bench does not have an on-board control and monitoring system. In this way, the control system acts on a remote server that collects information from the test bench sensors for monitoring information on mobile / desktop devices.

For monitoring, the communication manager is responsible for reading the data emitted by the sensors from the test bench and publishing them from the physical event manager to the collection and storage processes in the database. For data access, users can perform request / response requests to request the data stored in the database and make decisions about the operation of the test bench. All collection, storage, monitoring and command features are centralized in the use-case manager. This module is responsible for controlling the information demanded by sensors, actuators and users.

For the validation of the VAD project it is necessary that the analyzed variables remain within a standard curve. For this the device is allocated on the test bench to perform the standard curve survey. Independent variables (rotor speed and flow) are manipulated with progressive adjustment of values, while observing the behavior of dependent variables (pressure, vibration, temperature, and energy consumption). The behavior collection cycle, (values) of the dependent variables, starts with the fixed rotation speed for all flow variations. For each flow variation, the respective values of the dependent variables are collected. Once all flow scales have been traversed; and the reading of the dependent variables, already cited, collected. A new adjustment is made to the rotor speed variable and a new cycle is started. The information system includes a pre-programmed schedule for performing tests on devices, for example: it has speed set-up ranges and flow variations. Upon completion of the pre-set test, the device is able to perform the following tests. Gathering information during this step is useful for improving the standard curve of this type of device. Once the various standard curve tests have been performed for the same type of device, the database, with knowledge of the behavior of dependent and independent variables, will be used to observe deviations in subsequent test phases.

It is important to note that the standard curve is unique for each device type, i.e. a single curve for all devices of the same type. All behavior of the device under test is stored in a database, allowing the study of failure trends.

Since, for all test situations, device behavior data is stored, this allows you to evaluate fault trends. An analysis of the collected failure data using statistical tools provides a prediction of failures for VAD. This allows future devices under test to be evaluated for fault predictability, providing useful information for decision-making ahead of faults. The decisions are designed to favor the reliability and longevity of the device's life under test under conditions that may represent an ideal perfusion to a human being. Decisions are made by the operator who tracks alerts and fault ratings, even remotely interfering.

VAD design validation is possible from the verification of the failure data obtained, which can be done by applying the design improvement index, Equation (1) from the handling and data collection, and diagnostic and prognostic analysis, which is detailed in the following items.

DII presents a relationship between the design impact of preventive or control measures implemented to reduce risk (RII) plus the impact of these measures on project reliability (IMC) plus the TSMII indicating the level of safety. Inherent attributed to preventive measures.

$$DII = RII + RLII + TSMII (1)$$

DII - Project Improvement Index;

RII - Risk Improvement Index;

RLII- Reliability Improvement Index; and,

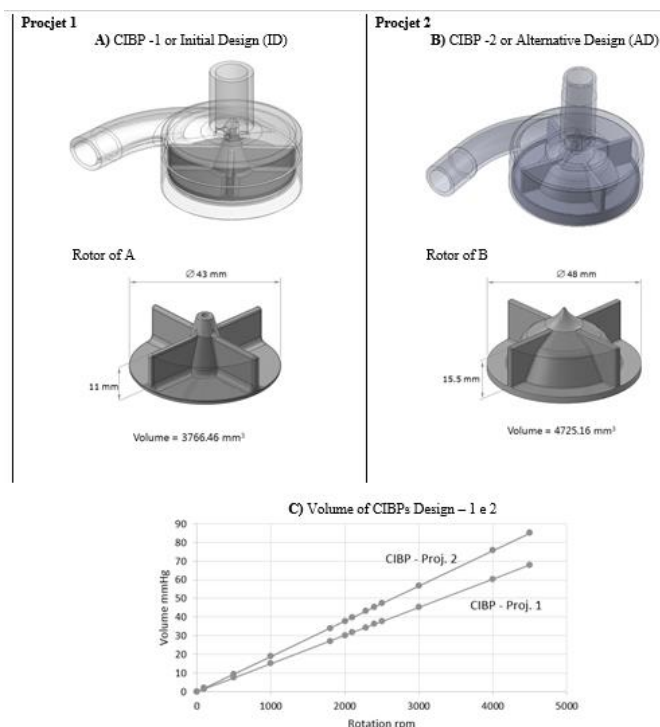


Figure 3. Design of CBPIs 1 and 2 for volume analysis

2.1.5 VAD Design Validation

TSMII - Total Security Measures Improvement Index.

3. RESULTS

The VAD - 1, Figure 3, was submitted to the cyclic method of reliability improvement, starting from bench tests (4. Bench Test) and sent for analysis (2. Risk Analysis). With the result of the risk analysis, there was an improvement in the design between the "A" rotor and the "B" rotor, with an increase in volume between blades from 3,766.46 mm³ to 4,725.16 mm³, as shown between the Project 1 and Project 2 of Appendix A. With this, it is possible to obtain a volume gain with the same rotation of the pump, for example with the rotation of 4000 rpm, shown in figure "C", of the same Appendix A. That is, with a rotation of 3,150 rpm, the same volume can be obtained in Project 2 as in Project 1. Thus, the lower rotation, initially, allows a reduction in friction, throughout the life cycle of the rotor that will allow an increase in its longevity. The Table 2 presents the results of the risk analysis of the VAD Design, having an indication of failure (or problem) to be solved, the "frictional wear of moving parts" in the components: rotor, bearing and bearing cradle. The analysis had the following causes: load on the rotor, bearing and bearing cradle; speed rotor; required flow rate; and bearing material and cradle. The effects observed were: "Mean Time to Failure" reduced compared to intended; unexpected rotor shutdown or locking and loss of pump performance against desired flow.

To improve the reliability of the design, measures were proposed to reduce the risk and increase the reliability with inherent safety concept, described below: i) analyze the volume between the rotor ends; ii) design and analyze pump curves to compare them to numerical models and verify their effectiveness and efficiency; iii) analyze surface and roughness before and after use of CIBP during bench testing to check for wear on moving parts; iv) make a design update with the suggested recommendations and v) analyze the reduction of failures in relation to the evolution of wear of moving parts.

Table 2 – Preliminary Hazards Analysis (PHA) applied to VAD Design

Risk	Cause of Failure	Failure Effect	Proposed Actions
Rotor lock	•Load on rotor, bearing and bearing cradle	•MTF reduced	i) Analyze of volume between rotor fins for optimization of flow. ii) Elaborate and analyze the effectiveness of pump curves (RPM x Pressure x Flow). iii) Analyze surface (roughness) before the test and after the test and determine wear of moving parts between the BSI projects 1 and 2. iv) Review project with relation (RPM x Pressure x Flow). v) Analyze and predict faults from the evolution of the wear of the moving parts between the BSI project 1 and 2.
	•Speed (RPM) x Volume	•Rotor stop / lock	
	•Required flow (aortic flow)	•Loss of income	
	•Bearing and cradle material		

4. CONCLUSIONS

The algorithm of the proposed method allows a risk analysis of the initial design with an adequacy using inherent safety concepts and later bench testing. This made it possible to validate the VAD, developed by the university's research group. Appendix A, presents the improvement of reliability with the reduction of the speed, for example from 4,000 rpm to 3,150 rpm, for the same volume, reducing the friction of the engine. The management of data variation obtained from the comparison with the standard curve allows an indication of the trend of failures, which helps in the design review.

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