NORMALIZED INDEX OF HEMOLYSIS EVALUATION OF AN IMPLANTABLE CENTRIFUGAL BLOOD PUMP FOR LONG TERM VENTRICULAR ASSISTANCE

Eduardo G.P. Bock, eduardo_bock@yahoo.com.br
Faculdade de Engenharia Mecânica da Universidade Estadual de Campinas, Cidade Universitária, Barão Geraldo, Campinas, SP.
Instituto Dante Pazzanese de Cardiologia, Av. Dr. Dante Pazzanese, 500 – Ibirapuera 04012-180, São Paulo, SP.

Pedro Ivo Antunes, pedrougo_85@hotmail.com
Instituto Dante Pazzanese de Cardiologia, Av. Dr. Dante Pazzanese, 500 – Ibirapuera 04012-180, São Paulo, SP.

Giuliano Gentile Padilha da Silva, giuliano.gentile@gmail.com
Instituto Dante Pazzanese de Cardiologia, Av. Dr. Dante Pazzanese, 500 – Ibirapuera 04012-180, São Paulo, SP.

Juliana Leme, leme_juliana@yahoo.com.br
Instituto Dante Pazzanese de Cardiologia, Av. Dr. Dante Pazzanese, 500 – Ibirapuera 04012-180, São Paulo, SP.

Daniel F. Legendre, legendre@terra.com.br
Instituto Dante Pazzanese de Cardiologia, Av. Dr. Dante Pazzanese, 500 – Ibirapuera 04012-180, São Paulo, SP.

Jeison W. G. Fonseca, jeison_f@yahoo.com
Instituto Dante Pazzanese de Cardiologia, Av. Dr. Dante Pazzanese, 500 – Ibirapuera 04012-180, São Paulo, SP.

José F. Biscegli, jose_biscegli@baxter.com
Instituto Dante Pazzanese de Cardiologia, Av. Dr. Dante Pazzanese, 500 – Ibirapuera 04012-180, São Paulo, SP.

Denys E. C. Nicolosi, denys@neurotrend.com.br
Instituto Dante Pazzanese de Cardiologia, Av. Dr. Dante Pazzanese, 500 – Ibirapuera 04012-180, São Paulo, SP.

Aron J. P. Andrade, aandrade@fajbio.com.br
Instituto Dante Pazzanese de Cardiologia, Av. Dr. Dante Pazzanese, 500 – Ibirapuera 04012-180, São Paulo, SP.

Antonio Celso F. Arruda, celso@fem.unicamp.br
Faculdade de Engenharia Mecânica da Universidade Estadual de Campinas, Cidade Universitária, Barão Geraldo, Campinas, SP.

Abstract. *A new implantable centrifugal blood pump for long term ventricular assistance is being developed and tested. This pump is made of Titanium alloy and uses ceramic double pivot bearing system to achieve longer durability. Hemolisys is an important parameter that must be evaluated in every new blood pump. Normalized Index of Hemolysis (NIH) is the main value to measure the blood damage calculated from Plasma Free Hemoglobin (PFH) as described by ASTM F1841 and ASTM F1830. A closed mock loop was assembled to evaluate NIH in pump. This circuit was composed by a flexible reservoir, two PVC tubes with 3/8" of diameter and 0.5 m of length, pressure monitor, ultrasonic flow meter, and Labview virtual instrument. Each test was performed during six hours pumping 5.0 L/min at 100 mmHg of pressure head and 37ºC of temperature, and seven blood assays were collected and evaluated. The PFH was measured with Catachem Kit (Catachem Inc., Bridgeport, USA). The mean NIH value was 0.0054 mg/100L. This value is considered excellent compared with values found in literature. In Vivo tests will be performed as future work.*

Keywords*: Left Ventricle Assist Devices, Centrifugal Blood Pumps, Normalized Index of Hemolysis, Plasma Free Hemoglobin.*

1. INTRODUCTION

A centrifugal blood pump was developed with a unique impeller design concept. This feature was called dual impeller because it allies a spiral-shaped cone with vanes to improve blood flow characteristics around the top inflow area, which often originates blood clot due to stagnant flow, Fig. 1. Previous series of studies demonstrated significant advantages of a spiral-shaped impeller design providing axial characteristics to flow (Andrade, 1996). The axial force component can avoid the stagnant flow formation. Therefore, this principle can help to avoid thrombus related with blood stagnation (Yamane, 2004). This work presents the studies of wear evaluation in double pivot bearing system, hydrodynamic performance tests with mock loop circuit and preliminary normalized hemolysis tests.

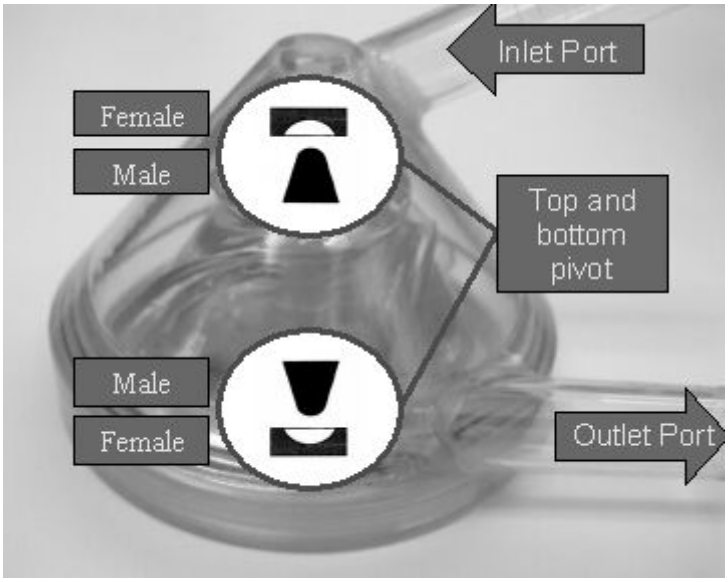

Figure 1. The new centrifugal blood pump is shown with a double pivot bearing system.

The double pivot bearing system has been used and studied in the last decade showing simplicity and reliability. Recent studies estimated particles release from a centrifugal pump with a system composed by Alumina ceramic (Al_2O_3) and Ultra high molecular weight polyethylene (UHMWPE), Fig. 1. The double pivot bearing system was tested under severe conditions showing very small risk to release debris particles from pump to blood (Takami, 2006).

In order to verify the possibility of different materials application, wear tests were made with double pivot bearings. Mainly, two types of wear are found in this application, abrasive wear and surface fatigue. Previous tests with this system were performed in pumps working in mock loop circuits. In order to study the wear in each component of double pivot bearing, a wear station was assembled when the wear phenomenon could be measured isolated.

Performance tests were made as In Vitro studies in order to characterize pump's hydraulic performance curves. These tests can provide important information about the pump's capability and function. The curves generated can be used as a diagram to predict which rotation is necessary to provide differential pressure allied to flow (Takami, 1997a). The performance tests compared two different types of pump's inlet port, a 45º and a 30º of inlet angle. Finally, two isolated normalized tests of hemolysis with human blood were performed to have a preliminary result producing 4 values of Normalized Index of Hemolysis. It was obtained by variation of Free Plasma Hemoglobin (PFH) measured by a tetramethylbenzidine (TMB) assay method, the PFH kit (Catachem, Bridgeport, USA).

2. MATERIALS AND METHODS

2.1. Wear evaluation in double pivot bearing system

A wear tests station was assembled with purpose of measure isolated wear rate in outside pump conditions. This way, it was possible to vary the shear stresses in consequence of charge applied to system, Fig. 2.

The main idea was to evaluate wear rate in Double Pivot Bearing system with a mass approach. This way, it's possible to quantify the bearing's material debris released in blood during pump's function.

Adapting a mill machine, the wear tests station was assembled with rotation controller, water lubrication, depth controller and applied charge measurement system. The wear tests were divided in three steps. In first step, all bearings were weighted in a precision scale with divisions of 0.1 mg. After this, each pair of male and female bearing was tested. Two types of pairs were tested, ceramic-polymeric pairs and ceramic-ceramic pairs. After finished tests, the pairs were weighted again to measure the wear loss in mass.

The polymers chosen were Nylon, UHMWPE, and Teflon (PTFE) because their low frictional coefficients. The ceramics chosen were Zirconium dioxide (ZrO_2), Silicon nitride (Si_3N_4), Alumina (Al_2O_3) and Carbon. All pieces tested had surfaces polished and roughness controlled to assure an average of 0.1 mm to 0.5 mm. Each test was performed under the following conditions: room temperature 21ºC, 40,000 revolutions, 1.0 Kgf of charge applied at 4,000 rpm.

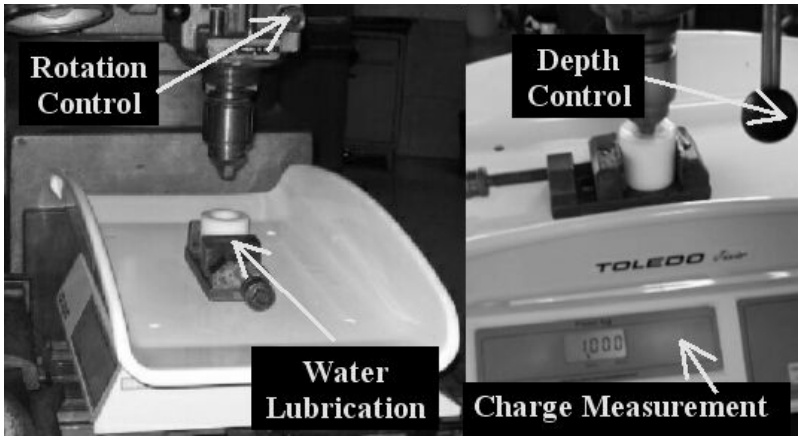

Figure 2. The proposed wear tests station assembled in a vertical milling machine (left) with charge measurement system (right).

2.2. Hydrodynamic performance tests with mock loop circuit

Initial performance tests were made to study the Dual Impeller in a mock loop circuit. A performance tests station was assembled, Fig. 3, with one hang flexible reservoir sac (Flexible Sac, 3M, USA), two pressure probes, one pressure monitor, one ultrasonic flow meter with 3/8" probe (Transonic Systems, Ithaca, USA), the complete system, pump and controller, acquisition PCI slot and a laptop with Labview software (National Instruments, Austin, USA).

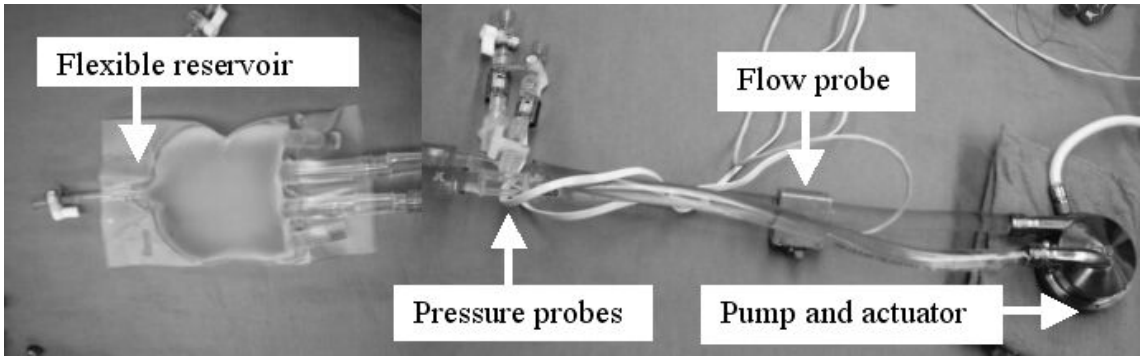

Figure 3. Simple Mock Loop Circuit used during performance tests.

The Mock Loop Circuit was set with a water solution with 37 % of Glycerin to simulate the blood viscosity. The hang flexible reservoir was filled with 0.4 L and placed 0.5 m above pump. The pressure gages were connected 0.3 m from pump inlet and pump outlet, respectively. The ultrasonic flow meter transducer was located 0.15 m from pump outlet. Total length of tubing from inlet/outlet of pump to reservoir sac was 2.0 m. Tubing should be horizontal to table for easily load setting with the screw clamp. Any air was removed from mock loop before the data acquisition (Hansen, 2006). Two pumps were tested in this station with different inlet angles, 45º and 30º of inlet's angle, Fig. 4.

Seven rotation speeds were mapped for each pump with this test. The rotations chosen were 1200, 1400, 1600, 1800, 2000, 2200 and 2300 rpm. Two coordinated points collected by software form a curve for each rotation. The last rotation (2300 rpm) was chosen because its proximity with maximum designed speed for pump's actuator. During the maximum rotation data acquisition it is possible to realize how the flow decreases in motor's fixed voltage.

With screw clamp open, the first point collected was the maximum flow for 1200 rpm. Closing the screw clamp and increasing system load, system total resistance, the flow decreases and the second point was collected in the next 0.5 L/min multiple and, this way, successively until achieve 0.0 L/min when screw clamp is totally closed. Then, follow up to get the second curve (1400 rpm) and others.

Figure 4. Pump one with inlet port angle of 30º and pump two with inlet port angle of 45º.

2.3. Normalized hemolysis tests

According to ASTM Standard Practices F1830 and F1841, the hemolysis test was divided in five steps: collection and preparation of blood, mock loop setup, six hours test, Plasma Free Hemoglobin (PFH) measurement, and Normalized Index of Hemolysis (NIH) calculation. Blood was drawn from a human volunteer using a large bore needle into a 0.5 L blood bag which heparin to avoid clot formation during the harvesting procedure. No negative pressure in excess of 100 mmHg was applied there and the blood was refrigerated between 2 to 8º C.

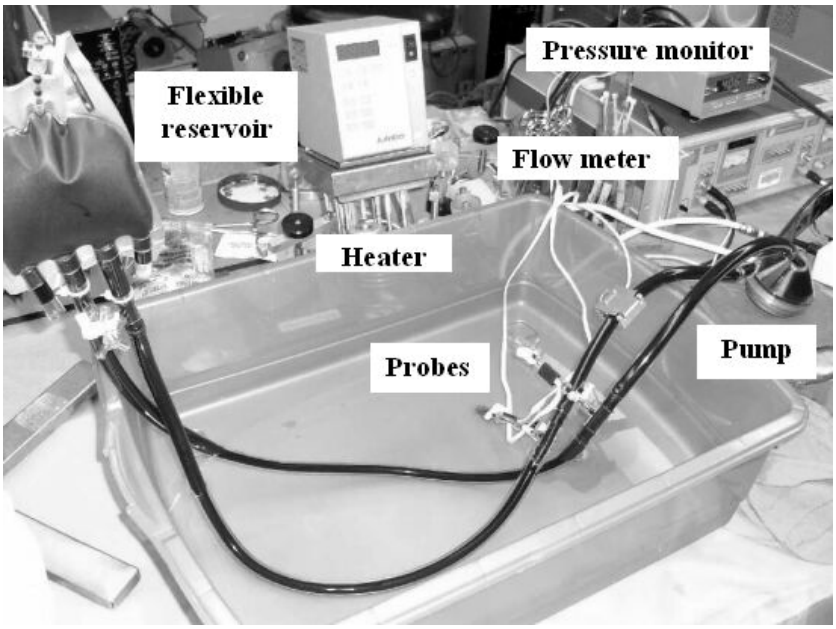

Figure 5. Mock Loop Circuit used during NIH tests.

A test loop was assembled with 2 m of flexible 3/8" polyvinyl chloride tubing, a flexible reservoir with sampling port, an ultrasonic flow meter with probe, a thermistor with thermometer and the blood pump, Fig. 5. This circuit was first filled with phosphate buffered saline and then, filled with blood. This blood had the hematocrit range between 28 to 32 % controlled by hemodilution and temperature 37 ± 1ºC. The pump revolution was adjusted to provide 5 ± 0.25 L/min flow rate. A screw clamp positioned at outlet side was applied to produce the required conditions for left heart assist application, 100 mmHg. In each six hours test, seven samples were collected T0, T1, T2, … T5 and T6, and their respective PFH was measured.

3. RESULTS

3.1. Materials Ranking

The results of wear evaluation in different materials tested were sorted by percentage loss of mass and a ranking list of ten best results is shown, Table 1. Values express the total loss of mass caused by wear in pairs and its percentage of pair total weight.

Table 1. Ranking of materials under wear tests.

	Male bearing	Female bearing	Wear loss (g)	Percentage (%)
1st	Silicon Nitride	Silicon Nitride	0,0001	0,00585412
2nd	Alumina	UHMWPE§	0,0001	0,00610575
3rd	Carbon	UHMWPE§	0,0001	0,00724901
4th	Carbon	Nylon	0,0001	0,01005227
5th	Alumina	PTFE£	0,0002	0,01346257
6th	Silicon Nitride	Nylon	0,0002	0,01831837
7th	Carbon	PTFE£	0,0002	0,01941936
8th	Alumina	Nylon	0,0003	0,02059449
9th	Zirconium Dioxide	UHMWPE§	0,0003	0,02715454
10th	Zirconium Dioxide	Nylon	0,0006	0,05052206

§ UHMWPE: Ultra-high molecular weight Polyethylene ; £ PTFE: Poly-tetra-fluorethylene, Teflon.

3.2. Performance Curves

One graph was plotted with each pump curves superposed in order to better understanding differences between both hydrodynamic performances, Fig. 6.

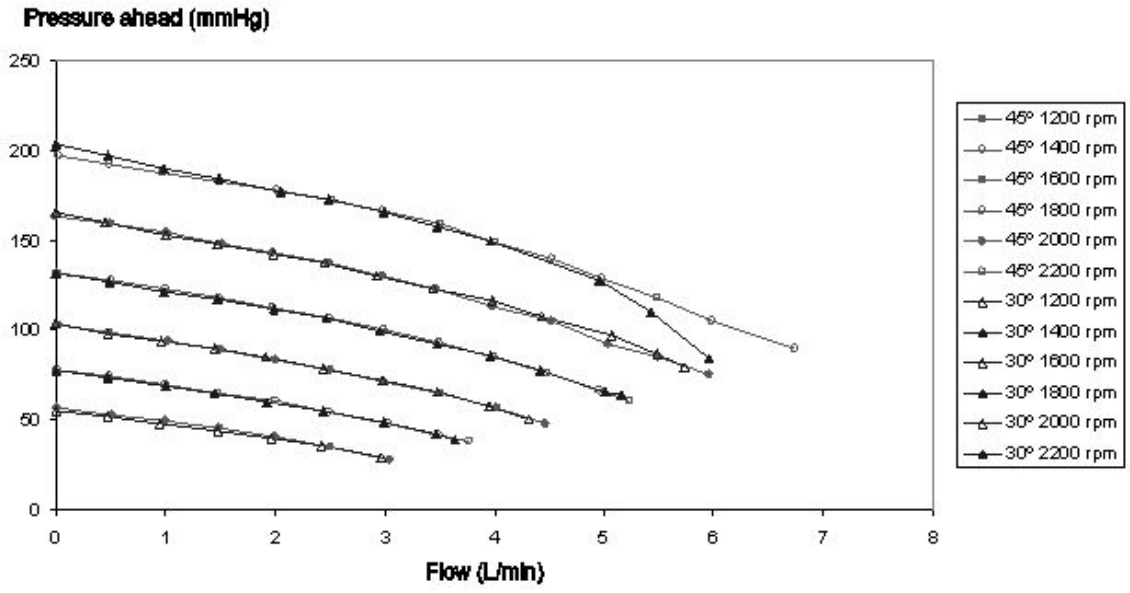

Figure 6. Performance Curves showing Hydrodynamic Characteristics for both pumps tested.

3.3. PFH releasing

A PFH value was measured for each sample. With this PFH variation in time T0, T1, T2, ... T5 and T6, a graph was plotted representing hemoglobin releasing in plasma during the experiment, Fig. 6. This progressive alteration in PFH levels in blood is caused by trauma imposed by pump. A trend line was added to compare data distribution.

4. DISCUSSION

As described in previous studies the bearing composed by Alumina and UHMWPE showed the best results in wear evaluation trials with ceramic-polymeric pairs (Takami, 1997b). However, the pair manufactured only with Silicon Nitride, tested in ceramic-ceramic trials, had the lower mass loss. Pivot bearing systems composed only by ceramic are know to have higher vibration during pumping applications instead of shock absorption experienced in ceramic-polymeric pivot bearing systems (Takami, 2006) and (Takami, 1997b).

The pump with inlet angle of 45º showed best performance results comparing with other pump, built with inlet angle of 30º. This slight difference among curves is highlighted in rotations beyond 1800 rpm when the curves from 45º pump decrease pressure ahead versus flow. Inlet port's angle is a problem to deal when designing centrifugal blood pumps especially eccentric inlet pumps as Dual Impeller Pump (Andrade, 1997), (Bock, 2005) and (Nosé, 1998).

As described by several authors, NIH for LVAD should be between 0.004 mg/100L to 0.02 mg/100L to be considered satisfactory and anti-traumatic blood pump. After calculations, the preliminary hemolysis tests showed a NIH value of $0.0054 \pm 2{,}46.10^{-3}$ mg/100L (Andrade, 1996), (Takami, 1997a), (Bock, 2005) and (Nosé, 1998).

5. CONCLUSIONS

In order to avoid vibration problems, the pair composed by Alumina and UHMWPE, also second best result in ranking, was chosen to be the materials of Double Pivot Bearing system. Dual Impeller Centrifugal Blood Pump had proven to be a feasible LVAD. The hydraulic characteristics are similar to other established, durable and reliable devices. This pump is now ready for accurate hemolysis verification and then in vivo studies. The hemolysis studies will be repeated to provide better statistical data in a future undergoing work but it can be also an indicator of good development status because NIH found is close to 0.004 mg/100L minimum mark.

6. ACKNOWLEDGEMENTS

The authors are grateful to all colleagues from Baylor College of Medicine (BCM), Institute of Energetic and Nuclear Researches (IPEN) and Adib Jatene Foundation (FAJ) as well as CNPq and Capes by partially support of this research.

7. REFERENCES

Andrade, A.J.P., Biscegli, J.F., Dinkhuysen, J. et al., 1996, "Characteristics of o blood pump combining the centrifugal and axial pump principles", Artificial Organs, Vol.20, pp. 605-612.

Andrade, A.J.P., Biscegli, J.F., Nosé, Y. et al., 1997, "Flow visualization studies to improve the spiral pump design", Artificial Organs, Vol.21, pp. 680-685.

Bock, E., Fonseca, J.W.G., Andrade, A.J.P. et. al., 2005, "A new concept of centrifugal blood pump using pivot bearing system: the conversion of the spiral pump inlet port", Proceedings of Technology Meets Surgery International, Vol.1, Sao Paulo, Brazil.

Hansen, E., Bock, E., Nosé, Y. et al., 2006, "Miniaturized all-in-one rpm-controllable actuator for gyro centrifugal blood pump", Proceeding of 52nd ASAIO Annual Conference, Vol. 1, Chicago, USA.

Nosé, Y., 1998, "Design and Development Strategy for the Rotary Blood Pump", Artificial Organs, Vol.22, pp. 438-446.

Takami, Y., Andrade, A.J.P., Nosé, Y. et al., 1997a, "Eccentric inlet port of the pivot bearing supported Gyro centrifugal pump", Artificial Organs, Vol.21, pp. 312-317.

Takami, Y., Nakazawa, T., Nosé, Y. et al., 1997b, "Material of the double pivot bearing system in the Gyro C1E3 centrifugal pump", Artificial Organs, Vol.21, pp. 143-147.

Takami, Y., 2006, "In Vitro Study to Estimate Particle Release from a Centrifugal Blood Pump", Artificial Organs, Vol.30, pp. 371-376.

Yamane, T., Miyamoto, Y., Yamazaki, K. et al., 2004, "A Comparative Study between Flow Visualization and Computational Fluid Dynamic Analysis for the Sun Medical Centrifugal Blood Pump", Artificial Organs, Vol.28, pp. 458-466.

8. RESPONSIBILITY NOTICE

The authors are the only responsible for the printed material included in this paper.