Cardiovascular medical devices performance under microgravity conditions

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***Abstract*— This article is intended to analyze the performance regarding the occlusion of medical devices for congenital cardiopathies PDA-R and ASD-R through a cardiac emulator subjected to Microgravity conditions compared to the results obtained with earth gravity. The experiment is basically to comparatively determine the occlusion percentage of the aforementioned devices. Such results were obtained at the Drop Tower, property of ZARM (Center of Applied Space Technology and Microgravity).**

Important terms – Nitinol, ASD-R, PDA-R, Microgravity,

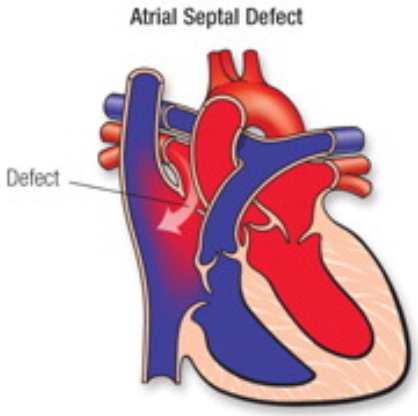
I. INTRODUCTION

In order to establish a proper context for this experiment, it is necessary to start by giving certain previous definitions:

• **ASD Device**.- The ASD (Atrial Septal Defect) is one of the cardiac defects to be simulated in this research. It is mainly characterized by having an open communication (hole) in the interauricular wall "Septum" of the heart (wall separating both auricles) as shown in Figure-1. Such communication allows oxygen-rich blood ready to be transported throughout the whole body, to be contaminated with oxygen-poor blood and so the patient's body does not receive enough oxygen. At the same time it is important to say that this defect also produces collateral damage such as erratic flow inside the cardiac cavities and lung-related problems. [1]

Figure-1

Atrial Septum Defect



(Source. American Heart Association, 2016)

There are several methods to measure the ASD diameter; transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), angiocardiography and intracardiac echocardiography (ICE)[2], among others. The importance of measuring the defect is due to the standard criteria for selecting the size of the occluding device during research. Table-1 shows defect diameters and device sizes for a 270 patient's sample.

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[1] Human Malformations and Related Anomalies. Page 572

[2] Echocardiography-Guided Interventions. Page 2

Table-1

Defect sizes and ASD-R occluding device

	Group I (n = 142)	Group II (n = 128)
Age [Yr]	15.3 ± 14.9 (2.0-72)	20.9 ± 16.8 (3.2-66)
Body weight [Kg]	35.1 ± 18.6 (12-86)	45.3 ± 17.3 (13-79)
Qp / Qs	2.2 ± 1.0 (1.1-5.4)	2.1 ± 1.1 (1.0-5.6)
Defect size [mm] TTE	12.9 ± 5.6 (3.3-30)	14.0 ± 5.9 (2.5-30)
TEE	14.2 ± 6.4 (3.0-30)	14.3 ± 7.3 (3.0-31.7)
Angiography	15.2 ± 6.6 (4.5-35.7)	15.4 ± 7.3 (2.7-35.1)
Device size [mm]	16.5 ± 7.6 (7.0-38)	19.4 ± 8.4 (5.0-38)

(Source. Sizing of Atrial Septal Defects by Intracardiac Echocardiography for Device Closures, 2008, Chien J,Hwang B , Fu Y, Lee P)

From Table-1 the existence of a range from 2.7-35.1[mm] diameter for the ASD-R defect and a device range from 7.0-38[mm] diameter was determined.

Devices used during this research were provided by PFM S.R.L., a company dedicated to "Design, production, commercialization and sale of Class III devices for congenital cardiopathies" and according to Nit-Occlud® ASD-R's instruction manual the ASD-R defect's diameter is measured with a transesophageal ultrasound and a balloon catheter. According its manual, the minimum and maximum ASD-R occlusion diameter is 6 and 30[mm], as shown in Figure-2.

Figure-2

Parameterization for the selection of ASD-R device

Catalog No.	Stent (mm)	Disc (mm)	Margin (mm)	ASD Diameter (mm)
160208	8	16	4,0	De 6 a 7
160210	10	19	4,5	De 7,1 a 9
160212	12	22	5,0	De 9,1 a 11
160214	14	24	5,0	De 11,1 a 13
160216	16	28	6,0	De 13,1 a 15
160218	18	30	6,0	De 15,1 a 17
160220	20	33	6,5	De 17,1 a 19
160222	22	35	6,5	De 19,1 a 21
160224	24	38	7,0	De 21,1 a 23
160226	26	42	8,0	De 23,1 a 25
160228	28	44	8,0	De 25,1 a 27
160230	30	47	8,5	De 27,1 a 30

(Source. Instruction for use ASD-R_Rev09, 2014, PFM SRL)

In this respect and in order to determine the performance of the ASD-R device, the pulmonary-systemic ratio was quantified. It is calculated with several methods such as the oxymetric technique, Doppler echocardiography, MRI, etc[3]. Such ratio is ideally 1. However, when there is a gap between left and right atrium, this value changes to 2.2±1.0 (Table-1).

[3] Quantification of the pulmonary and systemic circulation: Qp/Qs. What is it, how it's calculated and what is it used for. Page 1

• **PDA Device**.- The second cardiac defect to be studied during this research is known as PDA (Patent Ductus Arteriosus). This is a problem occurring immediately right after birth in some babies since there is an abnormal blood flow between the two main arteries connected to the heart, aorta and pulmonary. This can be seen in Figure-3. Before birth, these two arteries are connected through a blood vessel called "Ductus Arteriosus", an essential component of the fetal blood flow. After some minutes or in some cases days after birth, this vessel should close. However, 10% of gestations before 30 weeks[4], this small communication does not manage to properly occlude, exposing the heart to a lot of tension and raising the blood pressure in the pulmonary arteries[5].

Table-2

Defect and PDA-R Occluding device sizes

Authors (study time)	#Pts	PDA sizes [mm]	Occlusion method	Closure% at the last follow-up
Azun 1996 (not reported)	43	Not reported	Coil	3 months: 86%
Tometzki et al. 1996 (1994-1995)	71	2.0 (1-5)	Coil	6 months: 98%
Celiker et al. 1997 (1994-1995)	52	3.2 (1-6.5)	Coil	1 month: 94%
Thanopoulos et al. 2000 (1997-1999)	43	3.9 (2.2-8)	ADO	1 day: 100%
Galal et al. 2001 (1994-1998)	272	2.55 (0.2-7)	Coil	6 months: 79%
Pass et al. 2004 (1999-2002)	439	2.6 (0.9-11.2)	ADO	1 year: 99%
Wang et al. 2006 (1995-2000)	350	2.7 ± 1.2	Coil ADO	3 months: 96%
Jang et al. 2007 (1999-2005)	117	4.0 (3-8)	ADO BD Coil	General: 97%
Gudausky et al. 2008 (2000-2005)	132	1.7 ± 1.0	Coil ADO	6 months: 95%
Azhar et al. 2009 (2000-2004)	121	2.9 (1-10)	Coil ADO	General: 98%
Children's Hospital Boston (2005-2009)	168	2.6 (1.0-6.0)	Coil ADO	General: 95%
Total	1808	Average 2.7 (0.2-11.2)	Coil BD ADO	General average: 94.0%

(Source. To Close or Not Close, 2010, Fortescue E, Lock E, Galvin T)

According to the Nit-Occlud® PDA-R's instructions manual, the following measures of the defect should be taken in order to select the device, as shown in Figure-4.

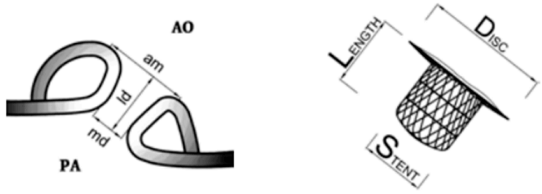
[4] Intensive Care Nursery House Staff Manual. Page 99

[5] Echocardiography in Pediatric and Adult Congenital Heart Disease. Page 214

Figure-4

Parameterization for the selection of the PDA-R device

Reference number	Suggested prescription for the PDA diameter (mm)	Stent (mm) S	Disc (mm) D	Length (mm) L	Implantation sheath Nit-Occlud® (F)
160102	2	4	8	6,5	6
160103	3	5,5	10	7	6
160104	4	7	12	8,5	6
160105	5	8,5	14	9,5	6
160106	6	10	16	11	8
160107	7	11,5	18	12	8
160108	8	13	20	13,5	9



(Source. Instruction for use ASD-R_Rev09, 2014, PFM SRL)

In Figure-4, md represents the minimum diameter.

It must be considered that for the choice of the device the following equation is necessary (Equation-1):

$$S = md \times (\text{from } 1{,}5 \text{ to } 2) \quad (1)$$

Where S is the S_{TENT} that is measured in mm and it's shown in Figure-4.

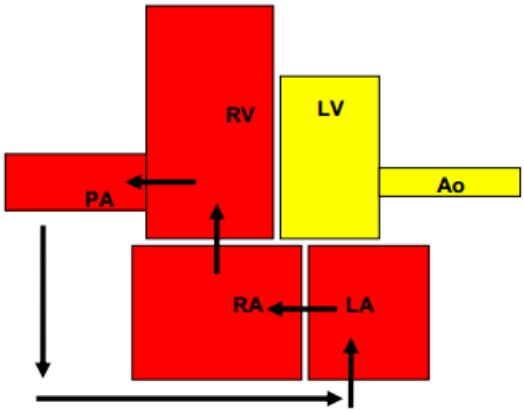
For the choice of the device's diameters to be used, it is necessary to specify the concept of left-to-right shunting and the pulmonary-systemic ratio, being the parameters of the recirculated pulmonary flow. Meaning that one part of the pulmonary venous blood does not go through systemic circulation. The Q_p:Q_s ratio is considered 1:1 for healthy people while it is lower than 1 when there is a right to left shunt and higher than 1 when there is a left to right shunt as shown in Figure-5 for the case of the ASD. As there are pathologies such as PDA or ASD, this ratio's value is different from 1 and it depends on the defect's diameter. The larger the diameter the bigger the shunt and therefore, the ratio moves away from Q_p:Q_s = 1:1.

This is why devices treating pathologies affecting the Qp:Qs ratio in a greater proportion were chosen, that is, devices with larger diameters in PDA-R and ASD-R respectively.

II. Experimentation

Figure-5

Blood flow inside the heart chambers



(Source. Secundum Atrial Septal Defect in the Adult, 2009, Lund University-Department of Cardiology)

Therefore, according to previous data about defect's and device's size, the following diameters were chosen (Table-3).

Table-3

Defect's and device's sizes for the analysis of experimental performance

Device	ASD-R	PDA-R
Defect's diameter	29mm	10,30mm
Allowed range	27,1-30 mm	8,0-12mm
Device's size	30	8

(Source. Home-made, 2015)

Similarly, it must be established that the heart's emulator for the analysis of congenital cardiopathies was designed based on an actual human heart's dimensions. Table-4 shows the main initial specifications for the aforementioned design:

Table-4

Cardiac specifications

Internal diameter [mm]	50-60
Area [cm^2]	<200
Volume [ml]	122-158

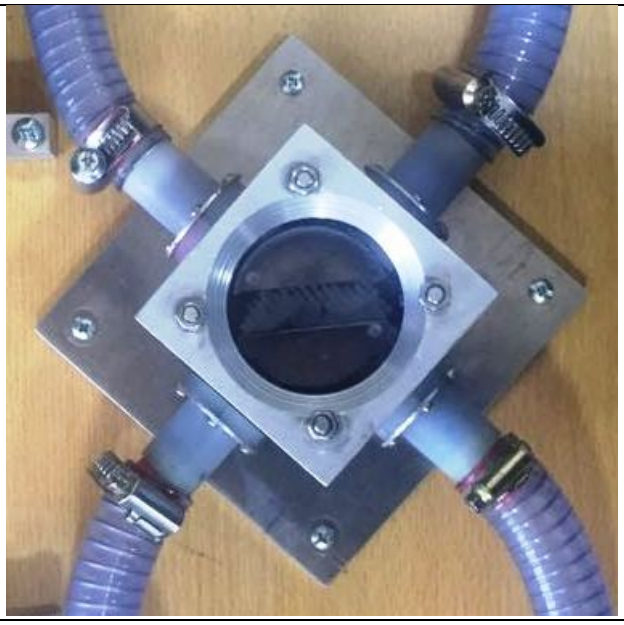
(Source. On the Weight and Dimensions of the Heart: In Health and Disease, Thomas B. Peacock, 2011)

The cardiac emulator was manufactured from machined Teflon[6], a metallic base and finally, an upper translucent acrylic cap for internal observation as shown in Figure-6. This

[6] Röchling, Engineering Plastics, Ijasa. Page 4

emulator has two chambers divided by a wall. It is built with individual volumetric dimensions; first the auricles for the ASD device's defect as well as a high precision reproduction of the aorta and pulmonary arteries for the PDA device's defect.

Figure-6
Cardiac Emulator

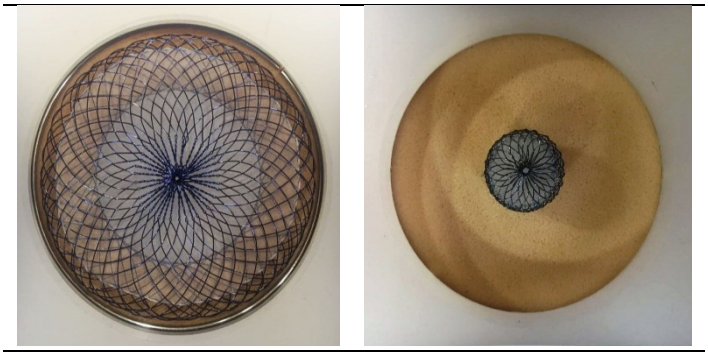


(Source. Photograph of the experiment, 2016)

In order to achieve the separation between the aforementioned heart chambers, a wall was manufactured from the same Teflon. This wall's main feature is to be able to withstand an ASD defect as well as a PDA defect as shown in Figure-7. In addition, this wall has a mechanical structure designed to hold a piece of EVA rubber (chosen to emulate the heart's internal tissue due to its texture and thickness). Finally, this piece has an orifice corresponding to the expected size of the defect.

Figure-7
Separation wall

"Septum" with ASD "Ductus" with PDA



(Source. Photograph of the experiment, 2015)

In search of getting results closer to reality; a research was held in order to obtain a human blood-like liquid. In this regard and considering our main objectives, the most important parameters to be taken in account were viscosity and blood density:

Viscosity is determined by the plasma's viscosity, that is, the percentage of total volume of blood made of red cells and their mechanical properties. Red cells have a unique mechanical behavior that may be erythrocyte deformability, referring to the ability of red cells to deform under certain amount of force without breaking; and erythrocyte aggregation, referring to the formation of red cells under low or null flow conditions, resulting from the attracting forces between erythrocytes. For this reason, the blood works as a non-Newtonian fluid and it is thicker at the end of each diastole and less thick at the peak of each systole[7].

In this way, it can be determined that the normal viscosity range of blood at 37[ºC] is between 2.8 [m2/s] and 3.8 [m2/s][8].

Density is defined as total mass units per volume units. However, there is another concept of density related to water; called specific gravity. The specific gravity of pure water is 1[g/ml], while that of total blood is 1,050[g/ml]. The exact value depends on the amount of blood cells diluted in the solution of blood plasma.

In venous blood, the density is higher when the person is standing than when it is sitting. In these cases, the density may increase up to 1,025[g/ml]. The density of individual blood cells changes according to the type of cells, in an interval between 1,115[g/ml] for erythrocytes and 1,070[g/ml] for certain leucocytes[9].

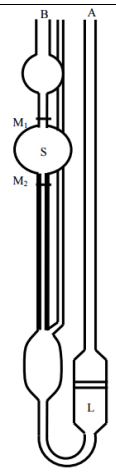
Therefore, considering the aforementioned characteristics of blood, the laboratory tests managed to obtain a liquid that could emulate human blood as much as possible. However, it is important to say that in order to observe the operation of an occluding cardiac device in microgravity, the liquid's viscosity

[7] Physical Parameters of Blood as a Non-Newtonian Fluid. Page 232
[8] Hemodynamical Flows: Modeling, Analysis and Simulation. Page 93
[9] The Physics Factbook

is more important than its density. Considering that, the intention is to emulate the blood flow through the implanted device in order to determine if it can adequately occlude the defect.

The Ostwald's viscometer was used to run some tests, whose diagram can be seen in Figure-8. A defined amount of liquid is introduced in the viscometer at compartment L and then, by suction, it passes to bulb S until the level of the liquid reaches an M1 marking. After that, the liquid is drained until the level reaches an M2 marking as we use a chronometer to measure time. The viscometer is cleaned in order to repeat the procedure with the reference liquid. Consequently, t1 and t2 are obtained and the viscosity of the liquid is calculated through Equation-1.

Figure-8
Ostwald's Viscometer



(Source: https://www.upo.es/depa/webdex/quimfis/docencia/basesFQ/Pract/cuatroycinco.pdf, 2015)

$$\frac{\eta_1}{\eta_2} = \frac{\rho_1 t_1}{\rho_2 t_2} \qquad (2)$$

A mix of distilled water and propylene glycol in different proportions was used. Using Equation-1 the ideal mix for simulating blood was obtained, 80% distilled water and 20% propylene glycol. Besides, the obtained density was also approximate.

As a validation of the system it is important to say that a real laboratory comparison has been made between the previously determined solution and real human blood with the Ostwald's viscometer.

The final results of the blood emulator are shown in Table-5:

Table-5
Blood emulator

Parameter	Theoretical data	Emulator
Density	1,050 [g/ml]	1 [g/ml]
Viscosity	2,8 – 3,8 [m^2/s]	3 [m^2/s]

(Source. Hemodynamical Flows: Modeling, Analysis and Simulation, 2008)

Thus, by defining the aforementioned characteristics and in search to determine certain factors in microgravity conditions, comparing data in earth conditions, the following hypothesis was established: Hypothesis-H1: "The cardiovascular medical devices subjected to microgravity conditions show a better performance with regard to their defect's occlusion capacity compared to what was obtained in earth gravity conditions".

1. **Performance.** Thanks to the high speed camera (500fps) located in the Launch Capsule and focusing on this experiment, the occlusion's capacity of the device was determined. It was possible to analyze the flow of the blood emulator thanks to the air transportation through bubbles that allowed clearly visualizing with the help of image processing software, the occlusion's percentage of devices.

It is necessary to highlight the device's performance comparison between earth gravity and microgravity conditions. Also, there were additional tests that can be seen in Table-6, in microgravity as well as in gravity.

Table-6
Tests for performance analysis

Test code	Earth gravity	Microgravity	Defect	Device's size
GT1-151124	X		ASD	Center 30
GT2-151125	X		PDA	Stent 8
GT3-151126	X		ASD	Without device
GT4-151127	X		PDA	Without device
MT1-151124		X	ASD	Center 30
MT2-151125		X	PDA	Stent 8
MT3-151126		X	ASD	Without device
MT4-151127		X	PDA	Without device

(Source. Home-made, 2016)

For the comparison of the results of devices' performance the variation on the Q_p:Q_s ratio was considered. This is

calculated by applying several methods, being the Fick[10] method the most common, as shown in Equation-3:

$$Q_p : Q_s = \frac{SAO_2 - MVO_2}{PVO_2 - PAO_2} \quad (3)$$

Where SAO_2, MVO_2, PVO_2 and PAO_2 are the oxygen content in systemic arterial, systemic mixed venous, pulmonary venous and pulmonary arterial blood.

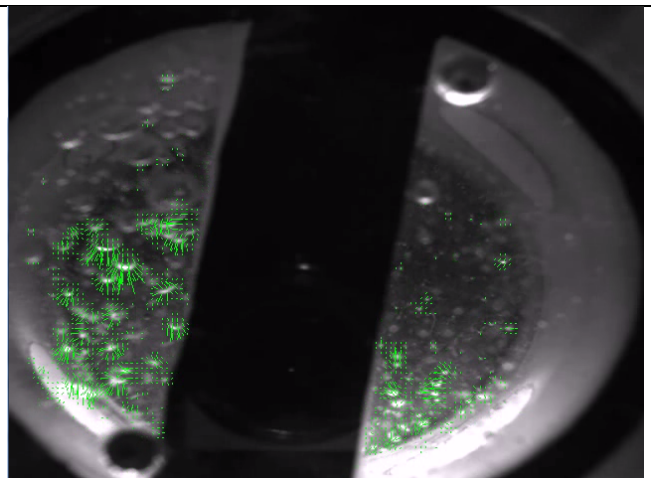
However, the previous expression needs the values of 4 spots in the heart. For the current case, only the 2 areas of the heart involving the defect were emulated. Therefore, it is not possible to calculate the Q_p:Q_s ratio but it is possible the estimation of the variation percentage depending on the occlusion level between the emulator's chambers. Considering a complete occlusion, the Q_p:Q_s ratio would be 1:1 and any flow between chambers would change this value.

As there are two tests, both in earth gravity and microgravity, it is possible to establish the improvement percentage for the occlusion of the device between both trials considering the initial derivation of fluids only with the defect. Therefore, the flow between chambers should be quantified.

For this purpose, the trials' videotapes are available. They were processed through artificial vision algorithms in Simulink. *Optical Flow* function block were used, which estimates the velocity of a moving object; for this case, bubbles velocities at both sides of the camera were determined. Thus, it is possible to estimate the flow and consequently the derivation or shunt of the defect, as well as the occlusion percentage of devices (Figure-9).

Figure-9

Processing of flow estimation



(Source. Snapshot of the image processing, 2016)

[10] Estimating cardiac output. Utility in the clinical practice. Available invasive and non-invasive monitoring. Page 1

Figure-9 shows the image of the camera after processing. Bubbles can be observed with flow inside heart chambers (green-colored). On the left side, there is a larger amount of green indicators since the flow is initiated through the activation of the pump in this chamber. It must be said that liquid is not pumped in the right chamber in order to keep the blood emulator as static as possible; in presence of the defect, a part of the left fluid manages to transport itself inside the right chamber and mix. Thus, the amount of flow indicators is always lower at the right side, as shown in Figure-10.

Figure-10

Binarization of the flow lines

(Source. Snapshot of the image processing, 2016)

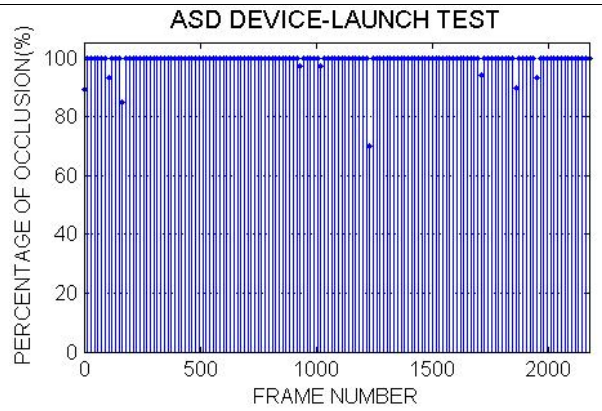
Thus, Figure-10 shows the binarized image of the flow indicators in both chambers of the emulator. At a glance, it can be seen that the indicators in the right chamber are less than those of the left chamber. So, it is possible to establish the derivation and occlusion percentage depending on the case (defect or device) through percentage calculation with equations 4 and 5:

$$\%\ derivation = \frac{Number\ of\ pixels\ (right)}{Number\ of\ pixels\ (left)} \quad (4)$$

$$\%\ occlusion = 100 - \frac{Number\ of\ pixels\ (right)}{Number\ of\ pixels\ (left)} \quad (5)$$

Figure-11

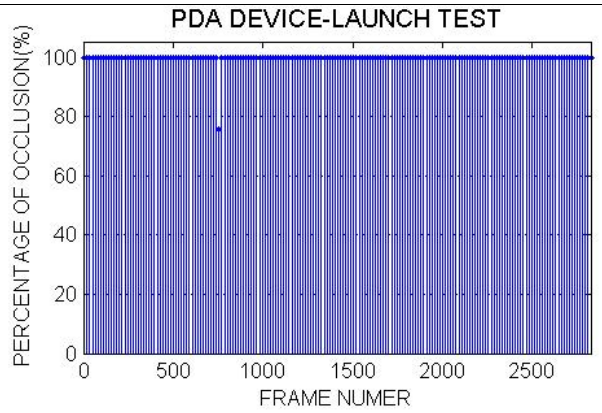
Occlusion percentage for the ASD device in microgravity



(Source: Home-made. Processing result, 2016)

Figure-12

Occlusion percentage for the PDA device in microgravity



(Fuente: Home-made. Processing result, 2016)

Figure-11 and Figure-12 show data about occlusion percentage when processing frame by frame and applying equation-5. It is evident that the average of the occlusion percentage is close to 100% and so, the final occlusion percentage is the average of the occlusion percentage obtained from each frame.

One should remember that first, results in earth gravity conditions were obtained and then compared with the Microgravity results, as described in Table-7:

Table-7

Derivation and occlusion percentage results

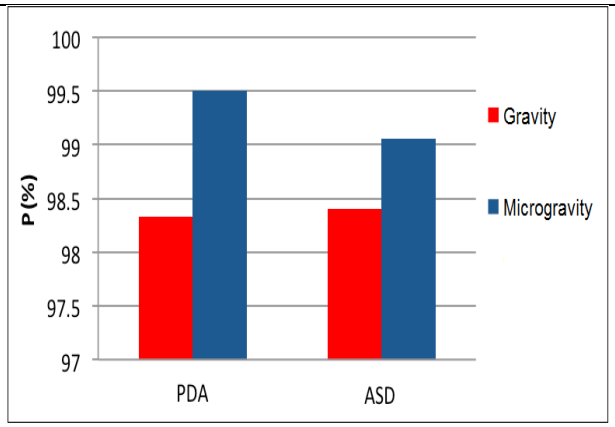
Test code	Earth gravity	Microgravity	Derivation [%]	Occlusion [%]
GT1-151124	X		1.60	98.40
GT2-151125	X		1.67	98.33
GT3-151126	X		26.39	73.61
GT4-151127	X		45.16	54.84
MT1-151124		X	0.94	99.06
MT2-151125		X	0.051	99.949
MT3-151126		X	25.81	74.19
MT4-151127		X	44.15	55.85

(Source. Home-made, 2016)

Considering a strict sense regarding the devices performance, the most important variable about the efficacy of cardiovascular devices is the previously obtained occlusion percentage. Besides, highlighting that the sample size is very small, it is necessary to make the analytic comparison of results shown in Table-7, from which the results comparison was established through Figure-13.

Figure-13

Occlusion percentage comparison between earth gravity and microgravity



(Fuente: Home-made. Processing result, 2016)

It is clearly evident a derivation reduction in microgravity conditions in the defect trials; while the occlusion percentage increases in the trials with PDA and ASD medical devices.

This behavior is explained when applying the Bernoulli's principle[11] (Equation-6).

$$P_1 + \frac{1}{2}\rho V_1^2 + \rho g h_1 = P_2 + \frac{1}{2}\rho V_2^2 + \rho g h_2 \qquad (6)$$

Where $P_1\ y\ P_2$ are pressures, ρ is density, $V_1^2\ and\ V_2^2$ are velocities, $h_1\ and\ h_2$ are heights and lastly g is gravity. In Equation-6 there are parameters that may be eliminated in microgravity since gravity is negligible at any point of the fluid. So, the total pressure gets reduced to Equation-7.

$$P_{TOTAL} = P + \frac{1}{2}\rho V^2 \qquad (7)$$

When eliminating a component, the total pressure is decreased and at the same time, since P is a constant as well as density; the fluid's velocity is also decreased. Consequently, the derivation percentage decreases and the occlusion percentage increases. (Figure-13).

Therefore, Hypothesis-H1 has been proved when corroborating that, comparatively, the cardiovascular medical devices subjected to microgravity conditions have a greater performance regarding their capacity for defect's occlusion, compared to that capacity in earth gravity conditions.

III. Conclusions

By means of several tests in both earth gravity and microgravity conditions, respective comparisons and experiment analysis; it was concluded that an ASD or PDA medical device obtains a higher occlusion percentage in microgravity conditions (better performance). The image analysis could show the percentage of fluid that goes through the occluding device and it was analytically corroborated that this value is lower in earth gravity conditions.

Considering that the occlusion is the most important characteristic in order to study an ASD or PDA cardiovascular device, it can be probed that such devices have a proper occluding performance in space conditions of microgravity. This assertion opens the door to a more profound study about cardiac medical devices for their application in human beings subjected to space conditions; being the cornerstone from which we could start to run performance tests of medical devices and biomaterials for the new space age of humanity.

[11] Bernoulli's principle. Page 16

References

[1] K.W.K. Yeunga, K.M.C. Cheunga, W.W. Lua, C.Y. Chungb, Materials Science and Engineering A, 383 (2004) 213–218.

[2] Peltonen M., Lindroos K., Kallio M.: Journal of Alloys and Compounds 460, 2008.

[3] Human Malformations and Related Anomalies. Published by Oxford University. Roger E. Stevenson, Judith G. Hall. 2005.

[4] Echocardiography in Pediatric and Adult Congenital Heart Disease. Benjamin W. Eidem, Frank Cetta, Patrick W. 2012.

[5] Biophysics & Biophysical Chemistry. Academic Publishers. 2002.

[6] Hemodynamical Flows: Modeling, Analysis and Simulation. Giovanni P. Galdi, Rolf Rannacher, Anne M. 2008.

[7] The Physics Factbook. Glenn Elert. 2004.

[8] On the Weight and Dimensions of the Heart: In Health and Disease. Thomas B. Peacock. 2015.

[9] Chien J, Hwang B,Fu Y,Lee P,Hsieh K, Jan S,"Sizing of Atrial Septal Defects by Intracardiac, Echocardiography for Device Closures",p 399-401,J Chin Med Assoc, 2008 Taipei,Taiwan.

[10] PFM S.R.L., "Instruction for use", ASD-R_Rev09,2014, Bolivia

[11] Thilén U, "Secundum Atrial Septal defect in the adult", Lund University-Department of cardiology, Lund,Swedwn, 2009

[12] Fortescue E, Lock E, Galvin T, McElhinney, "To Close or Not to Close", Congenit Heart Dis,p 354-365,2010

[13] PFM S.R.L., "Instruction for use", PDA-R_Rev18, 2014, Bolivia

[14] Echocardiography-Guided Interventions. Frank E. Silvestry. 2009

Cuantificación de la circulación pulmonar y sistémica: Qp/Qs. Qué es, cómo se calcula y para qué sirve. Lo que el radiólogo debe saber. C. Marín Rodríguez. 2015

[15] Rochling, Plásticos Para Ingeniería. Ijasa. 2006.

[16] Estimating cardiac output. Utility in the clinical practice. Available invasive and non-invasive monitoring. X. García. 2011

[17] Principio de Bernoulli. Carlos Isaac Torres Jarrín. 2011.