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RESEARCH ARTICLE

IN-VITRO SIMULATION TEST METHODOLOGY OF THE VALVULOPLASTY EMBOSSING BALLOON SYSTEM: AN INNOVATIVE APPROACH TO AORTIC VALVE STENOSIS TREATMENT

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Abstract

Cardiac stroke is the most leading cause of death these days. The frequency of heart defects are being diagnosed more and more frequently these days. A variety of heart diseases exist, each with its own causes, symptoms and treatments. Cardiovascular diseases (CVDs), are a group of conditions that affect the heart and blood vessels. They are the leading cause of death globally. Aortic stenosis is one of such vascular heart disease. Aortic stenosis is a condition characterized by narrowing of heart's aortic valve, making it harder for blood to flow from the heart into the aorta and onward to the rest of the body. The Valvuloplasty Embossing Balloon is a novel device designed to relieve aortic stenosis by dilating the stenotic valve using a controlled inflation mechanism. This study presents an in-vitro simulation testing of a developed Valvuloplasty Embossing Balloon System and evaluates the performance of the balloon system. In-vitro simulation test is performed using aortic arch simulation model. Before progressing to clinical trials or further regulatory evaluation, this in-vitro test results helps to evaluate the Valvuloplasty Embossing Balloon performance. Research results demonstrate the efficacy and reliability of the proposed methodology, offering valuable insights for further development and optimization of the balloon system.

Introduction:-

Under normal circumstances the left ventricle pumps blood to the aorta and and subsequently to the systemic circulation. Aortic stenosis (AS) is a progressive condition characterized by the narrowing of the aortic valve. Due to this narrowing of the aortic valve blood flow is restricted which may results in cardiac issues. If the aortic stenosis remains untreated it can result in heart failure, arrhythmias or sudden cardiac death (2019, pp. Chambers, JohnB). This condition is commonly associated with aging, calcification, or congenital defects.

Invasive valve replacement surgery has long been the standard treatment for severe AS. In order to overcome, the high-risk nature of surgery, particularly for elderly or comorbid patients, the less invasive procedures such as balloon valvuloplasty was developed. Valvuloplasty embossing balloon are the vital device to treat aortic stenosis. It involves the use of a catheter-mounted balloon that is inserted into the stenotic valve and inflated to widen the valve opening (2018, pp. Akahori, Hirokuni)

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The Valvuloplasty Embossing Balloon is a specialized medical device designed to perform valvuloplasty by inflating within a stenotic valve, stretching it open to allow for better blood flow. The Embossing Balloon comes in various sizes, allowing it to be tailored to the specific anatomy of the patient and the severity of the stenosis.

This research aims to evaluate the performance of the in-house developed Valvuloplasty Embossing Balloon in an in-vitro aortic arch simulation model. To ensure the system's safety, efficacy, and durability, it undergoes rigorous in-vitro testings. In-vitro studies serve as a critical preliminary step in evaluating the feasibility of novel developed medical devices before in-vivo trials. For in-vitro simulation study silicone based aorta arch simulation model was used that replicated human aorta. The current research study depicted the performance of a balloon's expansion in order to assure aortic stenosis before it undergoes in-vivo trials.

Objective of In-vitro Simulation:-

Before progressing to pre-clinical or clinical applications it is crucial to conduct, in vitro simulation tests for medical device's validation purposes. The methodology for the Valvpuloplasty Embossinig Balloons in in-vitro simulation testing shows that the balloon demonstrates performance by ensuring dilation of valves and effective navigation through complex aortic structures in a simulated environment. It also discusses the devices functionality under conditions mimicking settings to guarantee the safety and accuracy of the procedure whilst highlighting the balloon systems durability, over multiple usage cycles.

Literature Review:-

In-vitro simulation has been widely used in the development and testing of medical devices, particularly in the field of vascular interventions. The methodologies for simulating human physiology, especially for heart and vascular systems, are well-documented in several studies. The studies, presented comprehensive guidelines on the management of valvular heart disease, providing foundational insights for device testing protocols (2017, pp. HelmutBaumgartner, VolkmarFalk). It also focused on the management strategies for valvular heart conditions, highlighting the importance of precision and safety in device deployment (2017, pp. Nishimura, Rick A)

The first percutaneous transcatheter implantation of an aortic valve prosthesis, which set a precedent for using minimally invasive devices like clot retrieval systems. Their research focuses on the difficulties encountered when navigating structures – a problem that modern clot removal technologies also tackle (Cribier et al., 2002).

As people grow older aortic valve narrowing gets worse, over time. It used to be that surgery was the way to treat narrowing of the aortic valve but now using a balloon to widen the aortic valve has become the first choice, for treating congenital aortic narrowing (AS).

Materials & Methods:-

The objective of an in-vitro simulation test methodology for the Valvuloplasty Embossing Balloon was to assess the device's performance in a controlled laboratory environment, simulating the conditions of the human aorta arch. The tests evaluated the balloon's ability to navigate complex aortic anatomy, dilate stenotic valves, and maintain durability during multiple inflation-deflation cycles.

It is a model made of silicone which resembles the entire anatomical architecture of the aorta, the arch and the branching arteries within physiological conditions of the human body. As far as in vitro experiments are concerned, they usually consist of Anatomical Replication and Circulation Simulation

The Anatomical Replication is the aortic arch model composed of the aortic root, ascending aorta, aortic arch, and descending aorta. To imitate the difficulties created by complex aortic structure, the branching arteries including the brachiocephalic trunk, left common carotid and left subclavian arteries are also included in the model.

Circulatory System Simulation depicts fluids having viscosity and pressure profiles similar to blood are passed through the model to create conditions which mimic the circumstances present during the valvuloplasty procedure.

Materials/Tools:-

1. **Valvuloplasty Embossing Balloon:** The primary device being tested.
   a) Key Device Specifications

- **Embossing Element Material**: Nitinol
- **Embossing Element Design :** Anchor head and zig-zag strut at proximal and distal end with Serpentine link at intermediate region
- **Ballon Material: Nylon**
- **Soft Tip**: Pebax
- **Balloon Diameter (mm):** 14.0, 16.0, 18.0, 20.0, 23.0, 25.0
- **Usable Balloon Length (mm):** 40 -45
- **Usable catheter length:** 130 cms
- **Sheath compatibility:** 14 F

2. **Aortic Arch Simulation Model:** A flexible, anatomically accurate model of the human aortic arch, including the ascending aorta, aortic arch, and descending aorta.
3. **Perfusion System:** Used to simulate blood flow through the aortic arch model.
4. **Pressure Monitoring Sensors:** To record real-time pressure changes during the procedure.
5. **Guidewire and Catheter Insertion Tools:** For assisting the passage of the balloon catheter into the aorta.

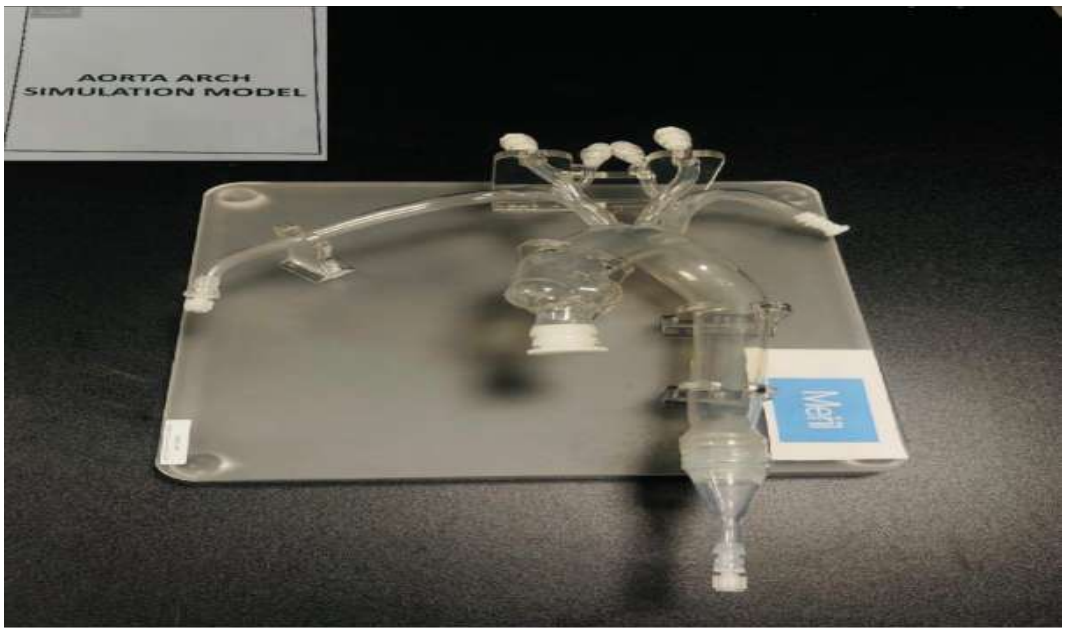

Figure 1:- Aorta Arch Simulation Model.

Experimental Procedure:
Preparation of the Aorta Arch Simulation Model:
Model Setup:
The aortic arch model was established using flexible materials like silicone, so that it can mimic the human aortic structure incorporating the stenosed aortic valve. The model was mounted onto a test rig in order to be securely positioned and easily insert the balloon catheter inside.

Simulating Stenosis:
The model also has a module that depicts a stenosed aortic valve. For purposes of the scenario, this valve can be rotated to reflect aortic stenosis from mild, moderate and on up to severe.

Fluid System:
A pulsatile flow system is developed for the purpose of simulating blood flow and pressure levels that are experienced in the human body. Saline solution, appropriate for realism in hemodynamic conditions, is then pumped around the aorta model.

Procedure Testing:
The aortic arch model was used to test the experimental maneuvers, including the guidewire insertion and catheterizations, and the device deployment. Each of these steps was done in a laboratory.

1. **Simulation Monitoring**:

Measurement of physiological parameters including pressure was also done continuously.

2. **Repetition and Validation**:

Procedures were repeated multiple times to validate the reproducibility and accuracy of the simulated interventions.

Simulation Procedure:
Access and Entry Point: Introduction of the Balloon Catheter Access Through a Peripheral Artery
It begins with vascular access from a peripheral artery, most from the femoral artery located in the groin in most individuals. Although it is not shown on the model, the femoral artery is the point of entry of the catheter into the bloodstream in the direction towards the heart. Being of the size to allow accommodation to the catheter and balloon system, the femoral artery provides relatively direct access to the aorta.

Guidewire Insertion:
Pass a guidewire from the outside that passes through the valve and into the aorta arch model. This mimics the process in human procedures when guiding the balloon catheter to the appropriate location.

Balloon Catheter Placement:
The Valvuloplasty Balloon Catheter is placed down the guidewire and gently placed in the stenosed valve.

Ascending the Aorta
Once the catheter passes through the femoral artery, the catheter is carefully turned upwards towards the descending aorta. Then the catheter moves into the ascending aorta, which is the lower part of the curved aortic arch represented in the model. Ascending aorta is so important because it brings the catheter closer to the aortic valve, which is the target site for any intended treatment. This part of the path is essential, therefore, to ensure that the catheter is tracking the correct course as it approaches the heart and the arch of the aorta.

Navigation Through the Aorta: Traversing the Aortic Arch
The Aortic Arch: A Complex Pathway
The aortic arch is one of the central anatomy parts of the vascular system, and the curved path that connects the ascending aorta with the aorta descending. This makes the aortic arch a challenging pathway through which the catheter would need to pass into the heart within the valvuloplasty procedure. The arch comprises a curved structure that carries blood outward from the heart to the rest of the body, making it an important pathway through which the catheter needs to pass in order to reach the aortic valve.

The model shows the complex geometry of the aortic arch: its normal curvature poses a difficulty in the aspect of reachability. This portion of the procedure requires the catheter manipulation on the part of the operator not to cause damage to the walls of the vessel, nor push into the branching arteries that branch from the arch.

The Three Branching Arteries
There are three key arteries that branch off from the aortic arch:
1.Brachiocephalic Artery (Innominate Artery): The first major branch that feeds blood to the right arm and head.
2. Left Common Carotid Artery: The second branch, that feeds the left side of the head and neck.
3. Left Subclavian Artery: The third one feeding blood to the left arm.
Branches to be avoided

It is designed to move across these branches because it along the curvature of the arch aorta. It then very carefully handles the catheter so as not to enter any of the branching arteries by mistake. This is tricky and simulates the real life in a patient's vasculature.

Approaching the Aortic Valve: Preparing for Deployment
Descending Toward the Aortic Valve:
Having negotiated the aortic arch successfully, the catheter advances along the descending aorta and reaches the aortic valve. In aortic stenosis patients, this valve is narrowed, and the balloon catheter will have to cross over this area.

This is the most critical part of the treatment. Ensuring the balloon gets into a proper position in the narrowed valve, it will be effective in the treatment procedure. The Valvuloplasty Balloon is slowly introduced to the stenotic area and is set to be deployed.

Figure 2:- Deployment of Valvuloplasty Embossing Balloon System.

Deployment of the Valvuloplasty Balloon: Treating the Stenosis
Balloon Inflation:
Once the catheter is in position, the balloon is gradually inflated using a controlled saline or contrast solution. In the in-vitro setup, sensors measure and record the pressure applied to the balloon, as well as the pressure exerted by the stenosed valve.

Embossing Mechanism:
The system's unique embossing mechanism ensures that the balloon expands uniformly and specifically targets the stenotic valve without overstretching surrounding tissues. The in-vitro setup allows researchers to monitor the precision of this embossing process.

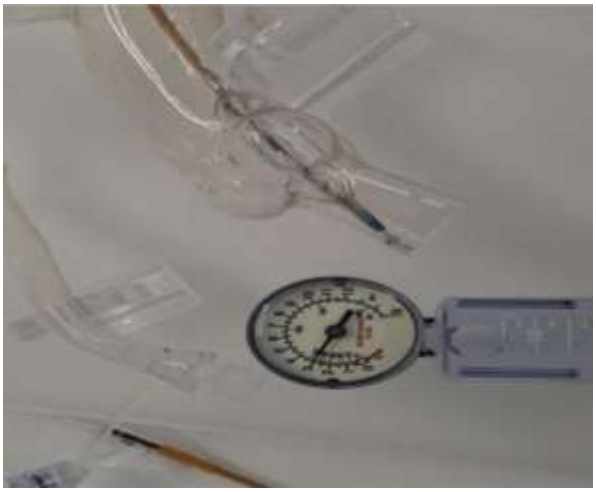

Figure 3:- Balloon Inflation.

Valve Area Expansion:
As it inflates with inflation during inflation, the balloon inflation stretches the valve's leaflets or the narrowed portion of the valve; as it does so, the valve opens wider, relieving the obstruction caused by the stenosis. The radial force exerted by the balloon pushes the valve cusps apart, increases the valve opening, and allows more free flow of blood from the heart into the aorta.

Balloon Deflation and Removal
Balloon Deflation:
Once the desired expansion of the valve has been achieved, the balloon is slowly deflated. This step is carefully monitored to ensure that the balloon contracts without causing any harm to the valve or surrounding tissues.

Balloon Extraction:
After deflation, the balloon catheter is gently removed from the model via the same guidewire that was initially placed. It carefully retracted through the aortic arch, descending aorta, and back out of the model through the the chosen access point.

Post-Procedure Analysis
Visual Inspection:
After the procedure, the aortic valve model is closely examined to identify any potential damage or structural changes. This includes checking for tears in the valve, overstretching, or signs of mechanical stress induced by the balloon.

Durability Testing:
Repeated cycles of inflation and deflation was performed to test the durability and longevity of the balloon system under prolonged use. This simulates real-life clinical conditions where the device may be used multiple times or for extended durations.

Results:-

Table 1:- Test Parameters and Observations.

Sr. No.	Test Parameter	Observation
01	Kink Free Navigation	There was no evidence of kinking or deformation of the catheter, even when subjected to bends.
02	Performance Under Stress:	The catheter was subjected to increased force when maneuvering through challenging anatomical models. Even under higher forces, the system maintained its kink resistance, ensuring consistent balloon positioning during valve dilation.
03	Smooth Guidewire Tracking	The catheter tracked smoothly over the guidewire and through the simulated vascular pathway. Even in models replicating complex, narrow aortic arches, the system exhibited excellent trackability.
04	Guidewire-Catheter Interaction	There was minimal friction between the guidewire and the catheter, which facilitated easy advancement through the model. This feature helps in reducing the overall procedural time and improving accuracy in positioning the balloon.
05	Balloon Performance and Durability	No balloon ruptures or mechanical failures were observed during high-pressure inflation tests, confirming the device's durability
06	Balloon Deflation Efficiency	Complete Deflation: There was no residual inflation or balloon deformation during the deflation process. The balloon collapsed uniformly and easily, making extraction straightforward and safe.

Kink-Free Navigation:
The catheter negotiated a difficult aortic anatomy easily without kinking or deformation. Such characteristics are an important factor for efficient passage over the aortic arch.

Kink resistance means the balloon catheter continues uninterrupted to reach the stenotic valve to facilitate

avoidance of procedural complications typically encountered with tortuous vasculature. navigation promotes stabilization of the balloon to allow for proper positioning and delivery of effective treatment.

Performance Under Stress:
Under simulated insertion through tight and curved aortae elevated forces were shown as consistent performance by the device in structural integrity. In such models, if this is not the case, high forces can cause strain to structures or deformation of a less strong device. In this case, the system tended to preserve both its shape and functional consistency.

Easy Guidewire Tracking:
The catheter had a smooth passage over the guidewire; there was minimum friction, which minimized insertion forces while increasing control over movement of the catheter within the simulation model.

Smooth guidewire tracking correlates with lesser procedural time and accuracy as the operator can focus more on correct placement and inflation and less on fighting resistance from the catheter.

Guidewire-Catheter Interaction:
The interaction of guidewire-catheter saw minimal friction thus allowing smooth advancement through the model and improving manipulation of the device. Low friction reduces procedural time, increases accuracy, and improves overall safety by reducing sudden jerks or hesitations in catheter movement that may potentially damage vascular structures.

Balloon Performance and Durability:
High-pressure inflation tests demonstrated that the balloon could withstand the pressures required for effective stenosis dilation without bursting or mechanically failing.

Durability testing entails repeated inflation-deflation cycles mimicking true clinical conditions and thereby showing the feasibility of multiple uses of the balloon.

Efficiency of Balloon Deflation:
Post-inflation, the balloon fully deflated uniformly without residual inflation or deformation. The uniform deflation of the balloon facilitated easy extraction without danger to the catheter in balloon extraction.

Efficiency in the process of deflation is paramount to prevent complications like entrapment or damage upon removal of the balloon from the valve tissue post-procedure.

Results demonstrated precise and uniform valve dilation, successful navigation through the aortic arch, and stable balloon performance under high-pressure conditions. The results confirmed the device's robustness, safety, and reliability under various challenging in-vitro conditions. These features make the system highly suitable for real-world clinical application, offering both safety and effectiveness for the treatment of aortic valve stenosis.

Discussion:-

The results of the in-vitro simulation tests are promising for the clinical potential of the Valvuloplasty Embossing Balloon. Its ability to navigate complex aortic anatomy without kinking, combined with its precision in dilating stenotic valves, addresses some of the primary limitations of earlier devices.

The results obtained for the Valvuloplasty Embossing Balloon are promising to reduce the incidence of restenosis even further and improve patient outcomes through homogeneous dilation, as well as minimizing the level of mechanical stress at the valve. The laboratory in-vitro simulation ensured the safety and performance of the device under controlled conditions.

Conclusion:-

Aortic stenosis, presenting as narrowing of the aortic valve, prevents blood from flowing from the heart to the other parts of the body, causing symptoms like short breath, chest pain, and in serious cases, heart failure. Valvuloplasty Embossing Balloon is an advanced medical device that promises to bring about revolution in the treatment of

valvular heart disease, especially in the case of aortic stenosis. Its successful in-vitro simulation tests have shown the capability of this device in providing safe, effective, and minimally invasive relief to aortic stenosis patients. The journey of the device toward pre-clinical application would make a significant difference in the quality of patient outcomes and quality of life by offering advanced, high-performance solutions for valvuloplasty procedures. The Valvuloplasty Embossing Balloon is an important tool in the treatment of aortic stenosis; by allowing careful passage up the aortic arch to position the balloon within the stenotic valve and inflate the balloon to relieve the stenosis restores blood flow from the heart to the body, it is invaluable to practice with an aortic arch model toward the development of the fine skills that define the skill of these complex procedures. Design is the enabler for success. The design is highly robust and flexible, allowing the pressures needed to distend a stenotic valve without causing damage to other tissue structures. Its embossing technology enables the balloon to accept the anatomy of the valve so that an evenly spread force will be transferred once inflated. This therefore reduces the risk of valve rupture or regurgitation wherein the valve fails to close, and blood is flowing backward. In summing up, Valvuloplasty Embossing Balloon is the way to the future of valvular heart disease treatments. Its minimal invasion and proven efficacy in-vitro tests make it a promising tool in the hands of cardiologists at large. The device would go a long way in improving the accuracy and safety of balloon valvuloplasty procedures when performed in-vivo and make a lasting impact on patient outcomes, offering new hope to those suffering from the debilitating effect of aortic stenosis.

References:-

1. Baumgartner, H., Falk, V., Bax, J. J., et al. (2017). 2017 ESC/EACTS Guidelines for the Management of Valvular Heart Disease. **European Heart Journal**, 38(36), 2739-2791. https://doi.org/10.1093/eurheartj/ehx391
2. Nishimura, Rick A., et al. "2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines." Circulation 135.25 (2017): e1159-e1195.
3. Cribier, Alain, et al. "Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description." Circulation 106.24 (2002): 3006-3008.
4. Akahori, Hirokuni, et al. "Mechanisms of aortic stenosis." Journal of cardiology 71.3 (2018): 215-220.
5. Chambers, John B. "Aortic stenosis." European Journal of Echocardiography 10.1 (2009): i11-i19.
6. Luo, Xiao, Dan Zou, and Li Li. "Cardiovascular Therapeutic Devices: Material and Fabrication Progress." Biomaterials and Materials for Medicine. CRC Press, 2021. 1-34.
7. Rao, P. Syamasundar. "Percutaneous balloon pulmonary valvuloplasty: state of the art." Catheterization and Cardiovascular Interventions 69.5 (2007): 747-763.
8. Park, Kenneth Stuart. "Stents for transcatheter aortic valve replacement." (2017).
9. Vahanian, Alec. "Balloon valvuloplasty." Heart 85.2 (2001): 223-228.
10. Ewert, P., et al. "Balloon valvuloplasty in the treatment of congenital aortic valve stenosis—a retrospective multicenter survey of more than 1000 patients." International journal of cardiology 149.2 (2011): 182-185.
11. Wang, Andrew, J. Kevin Harrison, and Thomas M. Bashore. "Balloon aortic valvuloplasty." Progress in cardiovascular diseases 40.1 (1997): 27-36.
12. Grimard, Brian H., Robert E. Safford, and Elizabeth L. Burns. "Aortic stenosis: diagnosis and treatment." American family physician 93.5 (2016): 371-378.