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In-Vitro Assessment of Atrial Septal Defect Occluder Deployment: A Crucial Step in Occluding Atrial Septal Defects and Restoring Cardiac Function

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Abstract:- This research article introduces an innovative Atrial Septal Defect (ASD) Occluder tailored for treating atrial septal defects. Crafted from nitinol wire, the occluder incorporates strategically placed PET fabric in its design, enhancing its thrombogenicity and occlusion efficacy. The primary objective of this occluder is to halt blood flow between the atria, thus correcting the defect's impact on cardiac function. Through rigorous in-vitro testing, the occluder's deployment via catheter and its performance and efficacy are comprehensively evaluated. The study focuses on assessing its ability to effectively obstruct blood flow across the defect site while minimizing the risk of adverse effects or complications. This research marks a significant advancement in interventional cardiology, offering a promising solution for managing atrial septal defects. By detailing the occluder's developmental trajectory and key design considerations, this study provides valuable insights for future research endeavors and clinical implementations in the field. Ultimately, this occluder holds the potential to improve patient outcomes and enhance the safety and efficacy of ASD closure procedures.

Keywords:- *Atrial Septal Defect Closure Device, Nitinol Alloy Construction, Cardiac Occlusion Efficacy, Transcatheter Intervention, Thromboresistance Properties.*

I. INTRODUCTION

Interventional cardiological procedures are pivotal in managing various septal defects, particularly atrial septal defects (ASDs) having sizes of 4mm to 36mm, where the use of occluders plays a crucial role in obstructing blood flow within the atrial chambers. With an escalating demand for precise and durable occlusion solutions for ASDs, there's a burgeoning interest in innovative designs and materials to enhance occluder performance. One such promising advancement is the introduction of Atrial Septal Defect Occluders, integrating strategically placed PET Non-Woven fabric to bolster thrombogenicity and occlusion effectiveness.

This research study aims to elucidate the development and in-vitro testing of an ASD Occluder tailored explicitly for ASD occlusion procedures. Constructed from nitinol wire, ensuring excellent visibility under fluoroscopy and facilitating accurate deployment within the targeted septal region, the occluder is engineered to optimize thrombogenicity with PET Fabric incorporated into its waist and left and right discs.

In-vitro testing of the ASD Occluder comprehensively assesses its deployment characteristics, performance, and efficacy in obstructing blood flow within simulated atrial septal models. Special attention is devoted to evaluating the occluder's ability to achieve complete and durable ASD occlusion while mitigating adverse effects such as migration, thus providing crucial insights into its safety profile and therapeutic efficacy.

Moreover, this research underscores a significant stride in interventional cardiology by introducing a next-generation ASD Occluder tailor-made for ASD procedures. By enhancing precision and durability in septal defect occlusion, these occluders hold promise in improving patient outcomes and reducing the risks associated with vascular interventions.

In essence, the development and evaluation of ASD Occluders mark a substantial leap forward in interventional cardiology. Through innovative design features and material integration, these occluders offer heightened performance and efficacy, addressing a critical need in managing atrial septal defects and advancing the field towards better patient care.

II. MATERIALS AND METHODS

The development and fabrication process of the Atrial Septal Defect Occluder involved several steps carried out under sterile conditions and in compliance with ISO 13485 guidelines. The detailed overview of the implant is provided in Figure 01, with its size matrix listed in Table 01.

- *Braiding:*

A braid (also referred to as a plait) is a complex structure or pattern formed by interlacing three or more strands of filaments or wire such as textile yarns, wire, or polymer filament. A braid is usually long and narrow, with each component strand functionally equivalent in zigzagging forward through the overlapping mass of the others.

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➢ *Primary Heat Setting:*

"Annealing" or "Shape setting" refers to the process used to form self expanding braided mesh of Nitinol. Annealing is the process of heat treatment of the nitinol wire at a closely controlled time of 3 - 7 min and temperature of 500°C - 510°C to achieve a desired shape in the material. After the material is removed from the annealing machine, the wire will "remember" its shape.

➢ *Cutting and Tube Mounting:*

Tube mounting process refers to the process used to attach a stainless steel tube or ring to the end part of braided mesh. The mounting method can be performed a manually or by fixture. The mounting process is done to secure the ends of filament cluster, also to keep them together or for attaching the same to the other part or components. After annealed process the filaments were cut as per desired size and a circular ring (tube) is placed over the filament cluster at the ends to keep the filaments together and in place.

➢ *Primary Welding:*

Welding is process of permanent joining or attaching two or more than two metals together by means of extreme heat. Laser spot welding is a non-contact process which uses a laser to create a single weld spot to weld metals together. Lasers welding machine delivering pulse at 0.20 - 0.60 mm of light with accurate repeatable energy at 2Hz frequency for duration of 0.5 - 1.8 millisecond. The diameter of the spot formed by laser welding can be varied for different purposes. Here, we used a micro level laser welding machine for welding a micro filament weld together.

➢ *Moulding and Secondary Heat Setting:*

Moulding constitutes the manufacturing process wherein raw materials are shaped through the utilization of a rigid framework known as a mold or matrix. It may have been made using a pattern or model of the final object. A mold is the counterpart to a cast. Secondary Heat setting is the process for heat treatment of the mould wire at a closely controlled time of 3 - 7 min and temperature of 500°C - 510°C to achieve a desired shape in the material.

➢ *Secondary Welding:*

Jacketing process refers to the process used to attach a stainless steel ring or jacket to the end part of tube. The jacketing method can be performed by Laser welding machine. The jacketing process is done to secure the secondary jacket with primary jacket. Lasers welding machine delivering pulse at 0.20 mm of light with accurate, repeatable energy at 2Hz frequency for duration of 0.60 milliseconds.

➢ *Pre Cleaning:*

Pre-cleaning operation is performed under laminar air flow unit (class 100) in class 10000 environment. The Occluder is cleaned with isopropyl alcohol and pressurized air.

➢ *Stitching:*

Sewing or Stitching is the craft of fastening or attaching objects using stitches made with a needle and thread, Suture or Yarn. Suture or thread is inserted in needle eye or hole then manually stitch on fabric to fabric or other material. There are numbers of stitching pattern for different application and different material like 1x1, 1x2 and 2x2 patterns.

In medical device stitching, a fabric or tissue is sewn using medical-grade suture or yarn with a semi-circular needle, all within an aseptic environment.

➢ *Primary Packaging and Sterilization Process:*

The Atrial Septal Defect Occluder is placed in 1073B coated tyvek pouch and sealed. The sealed pouch is inspected for sealing integrity, holes or any damage by visual inspection and product information label is applied to it.

Following the comprehensive packaging process, the sealed pouches are transferred to the sterilization section, where they undergo a rigorous sterilization procedure to ensure the complete eradication of any potentially harmful microorganisms.

Within the sterilization chamber, the pouches are strategically arranged to facilitate maximum penetration of the sterilizing agent and efficient removal during subsequent aeration processes. Chemical process indicators are affixed to each pouch to monitor the sterilization cycle, providing an additional layer of assurance regarding the efficacy of the process.

Furthermore, to guarantee the effectiveness of the sterilization process, biological indicators and process challenge devices are included in each sterilization load. These meticulous measures ensure that every Occluder undergoes thorough sterilization, meeting the stringent standards outlined in ISO 11135:2007.

The entire sterilization process is controlled through the utilization of a programmable logic controller (PLC) operated sterilizer, allowing for precise adjustment of temperature and aeration time parameters. Additionally, the process undergoes regular re-validation procedures to ensure ongoing compliance with industry standards and regulations, further underscoring the commitment to product quality and safety.

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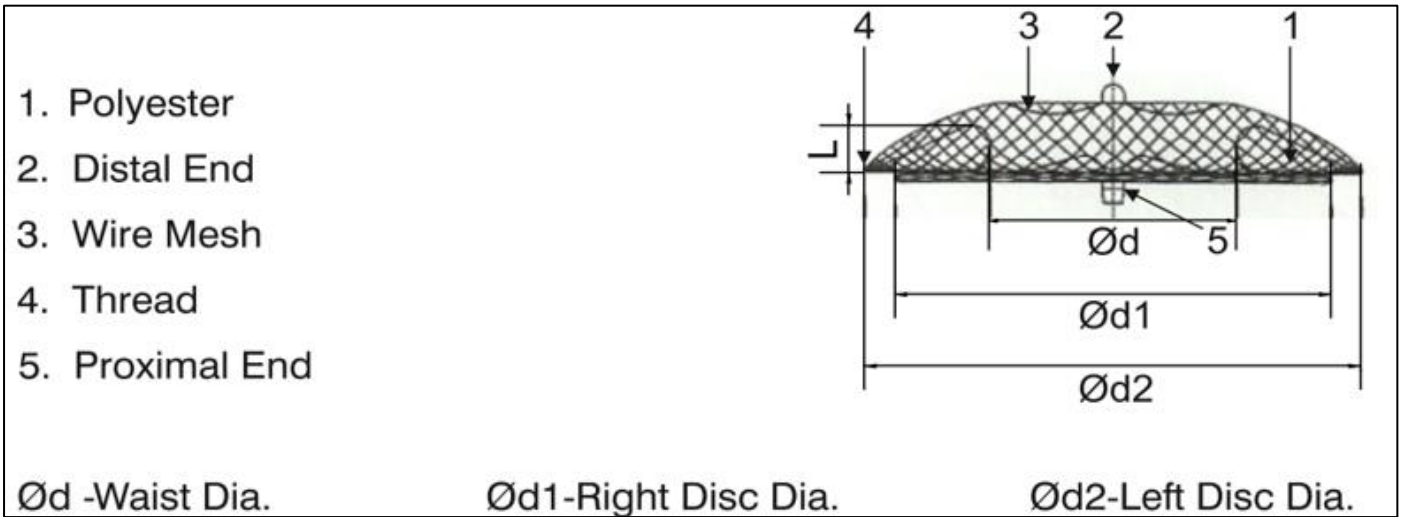

Fig 1 Implant's Detailed Overview

Table 1 Size Matrix of ASD Occluder

Reference No.	Diameter of Waist (ϕd)	Dia. of Right Disc (0d1)	Dia. of Left Disc (ϕd2)	Length (L)	Min. Sheath Recommended
FA06MM	6mm	14mm	18mm	3.5mm	7F
FA08MM	8mm	16mm	20mm	3.5mm	8F
FA10MM	10mm	18mm	22mm	3.5mm	8F
FA12MM	12mm	22mm	26mm	4.0mm	9F
FA14MM	14mm	24mm	28mm	4.0mm	10F
FA16MM	16mm	26mm	30mm	4.0mm	10F
FA18MM	18mm	28mm	32mm	4.0mm	10F
FA20MM	20mm	30mm	34mm	4.0mm	12F
FA22MM	22mm	32mm	36mm	4.0mm	12F
FA24MM	24mm	34mm	38mm	4.0mm	12F
FA26MM	26mm	36mm	40mm	4.5mm	12F
FA28MM	28mm	38mm	42mm	4.5mm	12F
FA30MM	30mm	40mm	44mm	4.5mm	14F
FA32MM	32mm	42mm	46mm	4.5mm	14F
FA34MM	34mm	44mm	50mm	4.5mm	14F
FA36MM	36mm	46mm	52mm	4.5mm	14F
FA38MM	38mm	48mm	54mm	4.5mm	14F
FA40MM	40mm	50mm	56mm	4.5mm	14F
FA42MM	42mm	52mm	58mm	4.5mm	14F

➢ *The Delivery System:*

- **Loader:** Used to introduce the occluder into the delivery sheath.
- **Delivery Sheath:** Provides a pathway for delivering the occluder.
- **Dilator:** Facilitates easy tissue penetration.
- **Delivery Cable:** The occluder is attached to the distal tip of the delivery cable, allowing for precise placement and, if necessary, retrieval of the device.

The detailed overview of the Delivery system is provided in Figure 02, with its size matrix listed in Table 02.

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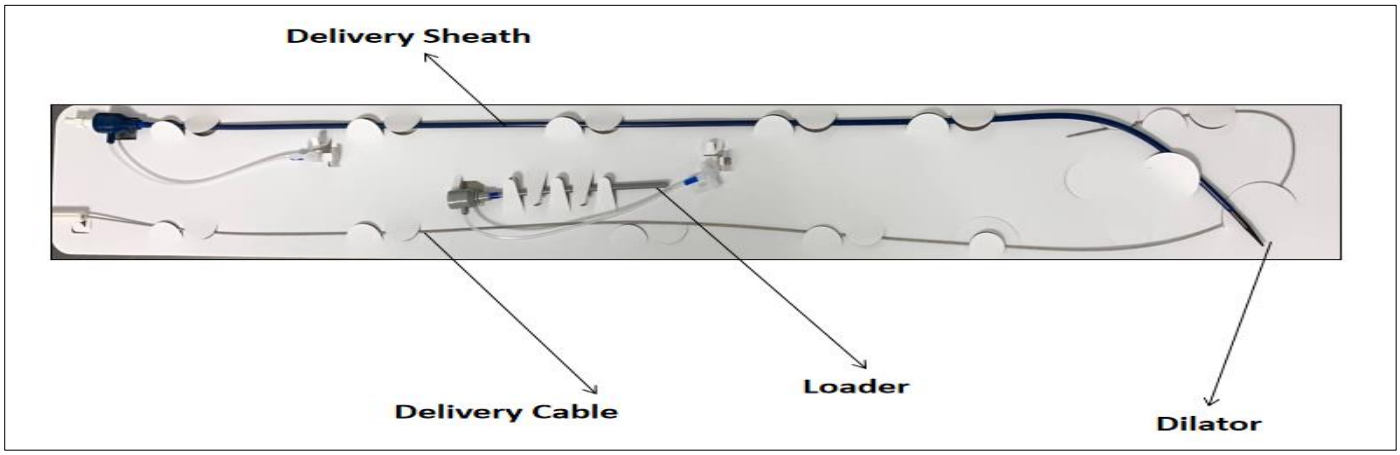


Fig 2 The Delivery System Assembly for Delivery & Deployment of a Developed ASD Occluder Device

Table 2 Size Matrix for Delivery System

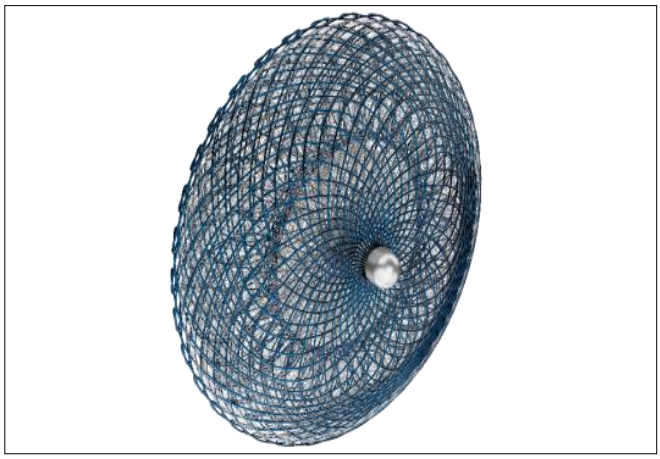
Delivery System Architecture			
Components	**Length (mm)**	**Inner Diameter (mm)**	**Outer Diameter (mm)**
Delivery Sheath	856	2.16 - 4.83	2.64 - 5.38
Dilator	930	1.1 - 3.46	2.06 - 4.7
Delivery Cable	1120	-	1.80
Loader Length	1350	2.05 - 4.7	2.76 - 5.5

III. RESULTS AND DISCUSSION

To perform the in-vitro study, the following procedure was planned and executed using an in-vitro simulation model, depicted in Figures 04 and 05, which mimics the conditions of a living heart.

Experiment: An artificial septal defect was created using 3D printing technology with PLA material, resulting in a realistic model for simulating a septal defect. To replicate the heart's environment, this 3D-printed defect was placed in a glass chamber filled with water maintained at 38°C. The implantation process began with the insertion of a guide wire through an introducer sheath to accurately position it at the defect site. The delivery sheath was then flushed with a dilator to ensure smooth passage before it was advanced over the guide wire and positioned through the septal defect.

The next step involved preparing for implantation: first, the loader was flushed, and the delivery cable was passed through it. The implant was then attached to the end of the delivery cable by screwing it in place, and the delivery cable was pulled to load the implant into the loader. Following this, the guide wire and dilator were removed from the setup. The loader was attached to the sheath, and the delivery cable was advanced through the sheath to deploy the left disc of the implant into the right atrium. The sheath's position was adjusted slightly to align it properly in the left atrium before deploying the implant. Finally, after successful deployment, the torque device was rotated counterclockwise to securely release the implant. This detailed procedure ensures that the implantation of the occluder (shown in Figures 03 (A) and (B)) is performed with precision, closely simulating the conditions of a living heart.


(A) Isomatric View of ASD Device

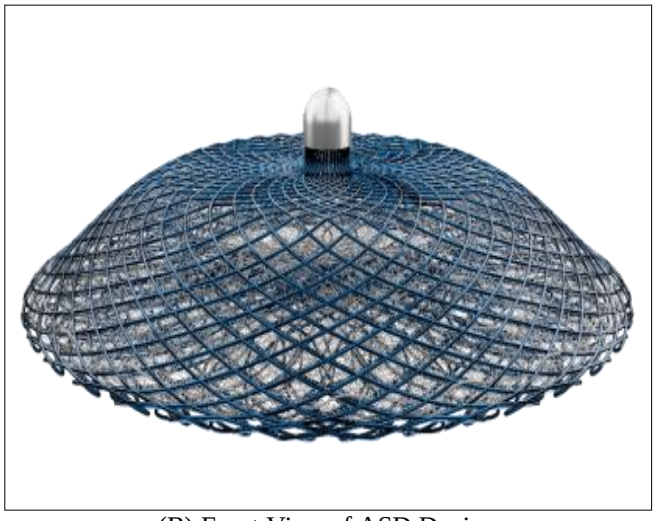

(B) Front View of ASD Device

Fig 3 Atrial Septal Defect Occluder Shown from Various Views

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The deployment and delivery process of the Atrial Septal Defect (ASD) Occluder are important in ensuring its efficacy in structural heart septal occlusion procedures. Our study focused on evaluating the performance and effectiveness of the deployment process of the ASD Occluder through in-vitro testing. This involved assessing its ability to obstruct blood flow effectively without inducing adverse effects or complications.

The ASD Occluder is constructed with nitinol wire, a material known for its shape memory properties, allowing for self-expanding deployment. Nitinol wire offers high radiopacity and excellent biocompatibility, crucial for clear visualization under fluoroscopy during deployment and minimizing the risk of adverse reactions or inflammatory responses in patients.

During the deployment process, the ASD Occluder is delivered through a delivery sheath to the target site within the femoral artery or vein. Precise positioning of the occluder is essential to ensure proper placement and maximum contact with the septal wall. Once positioned correctly, the occluder is gradually deployed, allowing it to expand and conform to the shape of the septal defect, thereby achieving effective occlusion.

By performing in-vitro tests, we evaluated the deployment process of the ASD Occluder using simulated septal defect models composed of Polycaprolactone (PCL) designed to mimic the characteristics of the atrial septal wall. Key parameters assessed included the ease of occluder delivery through the catheter, its ability to conform to the shape of the septal defect, and its stability post-deployment. Additionally, we examined the occluder's ability to achieve complete occlusion of the simulated septal defect and assessed any potential migration or displacement post-deployment.

Results from our study demonstrated that the ASD occluder was effectively delivered and positioned at the defect with minimal risk of displacement and migration. Based on these results, we can predict that in in-vivo practice, the device will effectively obstruct blood flow. The strategic incorporation of PET non-woven fabric at the waist and on the left and right discs of the occluder has been shown to augment thrombogenicity and enhance occlusion efficacy, thereby further optimizing its performance.

Overall, our findings suggest that the ASD Occluder offers a promising solution for surgical closure procedures, providing effective occlusion while minimizing the risk of complications. However, non-clinical and clinical findings are necessary to assess the long-term safety and efficacy of the occluder. This research study will serve as a valuable reference for future evaluations. Hence it would provide valuable insights into the real-world performance of the ASD Occluder and its potential impact on patient outcomes.

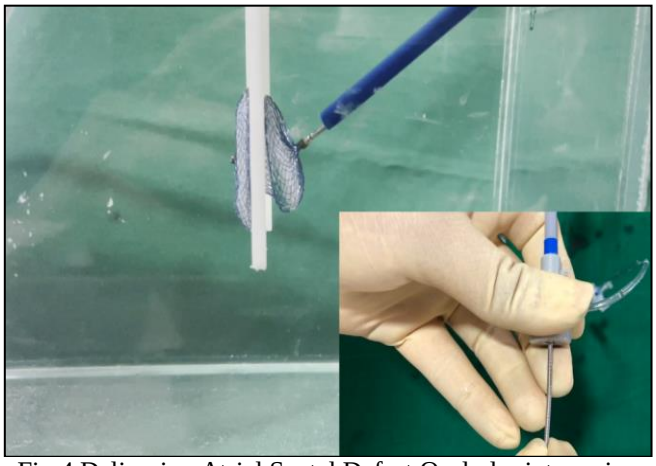

Fig 4 Delivering Atrial Septal Defect Occluder into an in-Vitro Simulation Model

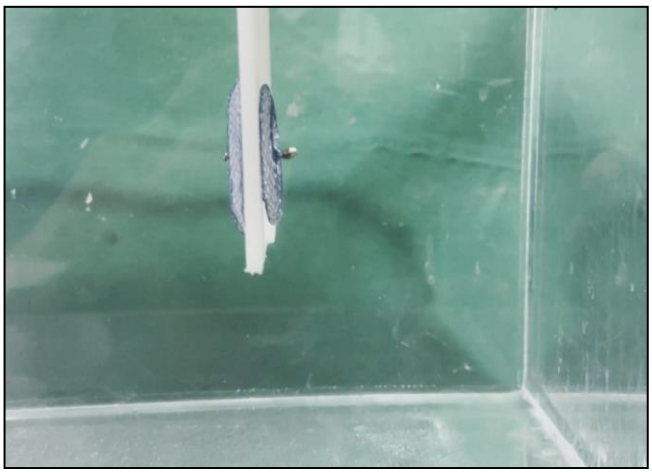

Fig 5 Successful Deployment of Atrial Septal Defect Occluder into an in-Vitro Simulation Model

IV. CONCLUSION

This study introduces a novel Atrial Septal Defect (ASD) Occluder designed to address atrial septal defects with enhanced efficacy and safety. Through comprehensive in-vitro testing, the occluder demonstrated its ability to effectively obstruct blood flow across the defect site while minimizing the risk of adverse effects such as migration or displacement. The key findings of this research underscore the occluder's potential to improve patient outcomes in ASD closure procedures, offering a significant advancement in interventional cardiology. The results of this study not only validate the occluder's design but also highlight its broader significance in the field. By providing a detailed analysis of the occluder's performance, this research emphasizes the importance of continued innovation in medical device development, particularly for complex cardiac interventions. The insights gained here lay the groundwork for future pre-clinical and clinical studies and potential applications in real-world settings, reinforcing the critical role of this occluder in advancing patient care.

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