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Novel Self-Expandable Laser-Cut Device for Effective Thrombus Retrieval: Overcoming Limitations in Thrombectomy for Deep Vein Thrombosis, Peripheral Artery Disease and Pulmonary Embolism

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Abstract:- Pulmonary embolism (PE) is a serious complication of deep vein thrombosis (DVT) and peripheral artery disease, often leading to fatal outcomes. The first line of treatment for DVT and PAD is anticoagulation: preventing the thrombus, occlusion of blood vessels, and propagation of PE especially in the case of DVT where limb or life-threatening complications are at risk. Clots retrieved from vessels include mechanical and manual interventions such as catheter-directed thrombolysis and thrombectomy. Yet the risks involved with thrombotic and embolic vascular occlusions are high because they cause occlusion of blood flow in crucial vessels; this may lead to tissue damage, organ failure, and death. Most of the existing thrombectomy devices do not remove the organized thrombus completely while prevention of clot fragmentation is also lacking. The study presents a new, self-expanding laser-cut clot retrieval device specifically designed to remove both hard and soft thrombi with no trauma at all to the vessel wall. This is one of the promising advancements in thrombectomy that overcomes the disadvantages of other existing technologies and offers a stronger approach for the removal of occlusions in the vascular system associated with DVT, PAD, and PE. The simulation test in vitro and a trackability test have been conducted with the developed device together with its delivery system for validation. These tests were envisaged to demonstrate how the device can operate, for example, navigate through the vasculature, and retrieve thrombi safely and accurately.

Keywords:- *Pulmonary Embolization, Ischemic Stroke, Deep Vein Thrombolysis (DVT), Peripheral Artery Disease (PAD), Catheter-Directed Thrombolysis (CDT), Mechanical Thrombectomy Device (MTD), Post-Thrombotic Syndrome (PTS), Biocompatibility.*

I. INTRODUCTION

Existing thrombectomy devices and thrombolytic drugs often struggle to effectively remove large or hard blood clots, and can be associated with significant adverse outcomes Pharmacologic thrombolysis typically results in longer procedure times and often necessitates prolonged observation in an intensive care unit, leading to increased procedure-related costs. (WL, 2011) Therefore, a simple mechanical device that can safely and efficiently remove intact complex acute, subacute, and chronic thrombi from any vasculartur er. By using the catheter-based mechanical retriever demonstrated in prior benchtop in vitro tests to be capable of mechanically retracting both acute soft and hard chronic, organized thrombi. This mechanical thrombectomy device (MTD) is designed for easier access into anatomically challenge from the blood vessel. (R, 2022)

Venous thromboembolism is a major cause of preventable morbidity and mortality. Blood clot mostly found in DVT usually the lower part of the limb in deep veins of legs.(Hung,2021) while distal DVT continues into the thighs via the popliteal and femoral vein or pelvis via the iliac vein. Catheter-directed thrombolysis (CDT), and mechanical thrombectomy, are critical interventional treatments for severe or life-threatening cases of DVT, particularly when standard anticoagulation is insufficient to prevent complications such as limb ischemia, gangrene, or post-thrombotic syndrome (PTS). (Luraghi , 2021) Each method has specific indications and risks, and the choice of treatment depends on the severity of the DVT, patient risk factors, and available resources. These interventions help reduce the clot burden, alleviate symptoms rapidly, and prevent long-term complications in high-risk patients. (Mathews, 2023)

The subsequent in-vitro investigation is conducted in this study to provide a detailed analysis of the effectiveness and versatility of our innovative approach across various pre-clinical and clinical scenarios. This thorough examination will encompass a range of experimental conditions to ensure comprehensive evaluation and

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validation of our methodology's potential applications and benefits. (Monsky,2011)

II. MATERIALS AND METHODS

Our revolutionary approach to retrieval device design minimizes material usage while ensuring structural strength and durability. By employing a laser cut configuration and a unique welding process, we offer a retrieval that reduces the risk of thrombosis, ischemic stroke, pulmonary embolization, and long-term heart disease.

- *Laser Cut Process:*

The development of peripheral clot retrieval devices through advanced laser cut techniques represents a significant advancement in medical device manufacturing. Utilizing a commercial laser machine to continuously cut the nitinol tube, we have developed a retrieval device with an intricate and precise structure. To ensure precision during the laser cut process which has the strut thickness of the nitinol tube is 170µm-190µm, the width is 130µm– 170µm, the frequency is 9000Hz – 10000Hz, and the pulse energy is 0.024mm - 0.026mm.

The dimensions of the peripheral clot retrieval device, range from 6mm - 16mm in diameter and 10mm - 40mm in length. The delivery system is compatible with 9 French (9F) - 12 French (12F) catheters. In the in-vitro deployment simulation model, a 16mm diameter was selected, with a retrieval device length of 40mm.The peripheral vein/Artery in which the product is intended to be implanted during pre-clinical or clinical studies typically ranges in size, accommodating the retrieval device's various diameters, from 6mm to 16mm vessel.

- *Shape Setting Technique Process:*

The shape-setting procedure involves the attachment of the laser-cut peripheral retrieval stent to a specialized mandrel with the diameter ranging 4mm - 18mm. The heat treatment process for shape setting is a critical phase in the development of the braided pulmonary retrieval device. By subjecting the retrieval device to controlled temperatures ranging from 504ºC to 506ºC, the process established the desired shape and size of the device while optimizing the transformative and mechanical properties of nitinol. This ensures that the retrieval device can effectively support peripheral vessels, retain its shape after deployment, and provide long-term reliability and performance.

- *Sandblasting Process:*

Sandblasting is the process used to form a smooth surface on an implant. Microscopic burs are on the implant which is been removed by a micro-abrasive sandblasting process (at air pressure of 2.99 – 3.01 Bar. The sandblasting method is a general term used to describe the act of propelling very fine bits of material at high velocity to clean or etch the burrs. In general, the material of the bits can be sand, micro-abrasives etc.

- *Electropolishing Process:*

The aforementioned device is immersed in a temperature-controlled bath of electrolyte and serves as the anode, it is connected to the positive terminal of a DC power supply, the negative terminal being attached to the cathode. A current passes from the anode, where metal on the surface is oxidized and dissolved in the electrolyte, to the cathode. At the cathode, a reduction reaction occurs, which normally produces hydrogen. This process, referred to as anodic leveling, can be subject to incorrect analysis when measuring the surface topography. Anodic dissolution under electro-polishing conditions deburrs metal objects due to increased current density on corners and burrs. Electrolytes used for electro-polishing are most often concentrated acid solutions having a high viscosity, such as mixtures of sulphuric acid and phosphoric acid. Other electro-polishing electrolytes reported in the literature include mixtures of per chlorates with acetic anhydride and methanolic solutions of sulfuric acid which contain the acitic acid (CH_3COOH) 76% - 80% and Perchloric Acid ($HCLO_4$) 20% - 24%.

- *Mounting the Peripheral Retrieval Device over the Inner Lumen:*

The mounting of the laser-cut peripheral retrieval device over the inner lumen of the delivery catheter is a crucial step in the deployment process and jacketing process. It enables controlled and precise placement of the device within the vascular system, ensuring stability and efficiency during medical procedures.

- *Jacket Mounting over the Laser Cut Peripheral Retrieval Device by Laser Welding Process:*

Laser welding is a critical process in the assembly of laser cut retrieval devices, particularly for mounting the jacket's proximal end and distal end. This process begins with the careful preparation of retrieved device components, ensuring cleanliness and proper alignment. By carefully preparing the stent components and selecting precise laser parameters, the wavelength of 0.19mm - 0.21mm, power of 229V - 231V, pulse duration of 0.5ms – 0.7ms, and frequency of 0.5Hz – 0.7Hz this technique ensures strong, precise, and durable welds.

The laser cut retrieval device was examined under a stereo optical microscope, with specific attention given to analyzing the braid angle and pattern. Following this inspection, the laser-cut peripheral retrieval device underwent a sealing process within an aluminum pouch. Subsequently, it was transferred for loading into the delivery system after the pre-cleaning process, marking the progression of this stage in the comprehensive development process. The mounting of an aforementioned device onto the delivery system has been depicted in the figure 01.

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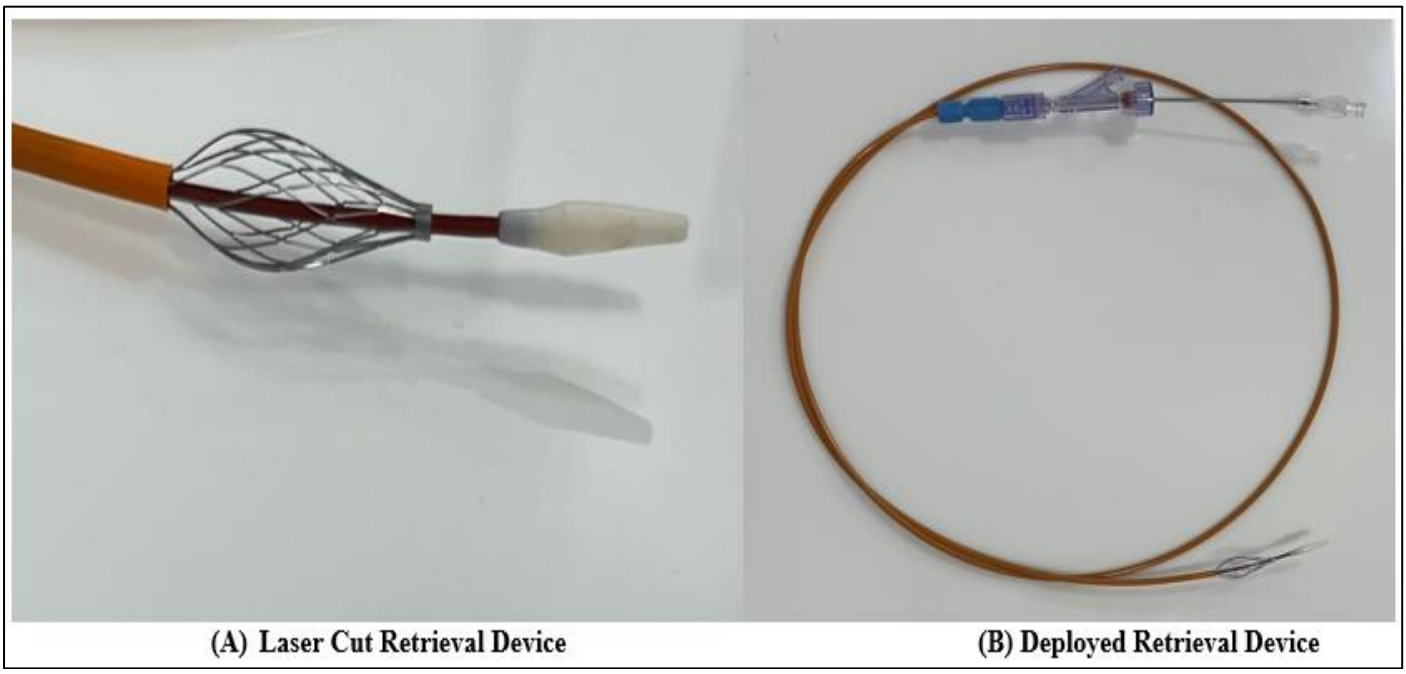

Fig 1 Depiction of a Laser Cut Peripheral Retrieval Device

➢ *Pre-Cleaning Process:*

The clot retrieval device is pre-cleaned by isopropyl accohol (IPA) which play important role to eliminates the contamination and residual from the clot retrieval device which ensure the contamination free in medical use. Initially, the clot retrieval device are deeped and washed with 80%-90% in Isopropyl alcohol solution and 30%-40% distilled water functioning as solvent to dissolved in solution to remove the contamination from the surface. The immersed device with gentle agitation which provides the cleanliness form the wall of the surface.

Subsequently, a designated soaking period allows the IPA to penetrate and dissolve contaminants effectively, varying in duration based on contamination levels and protocol specifications. Following soaking, the components undergo rinsing with purified water to flush out residual IPA and debris, enhancing cleanliness. A drying process, utilizing nitrogen gas to expedite and ensure complete moisture removal, follows to prevent water-related residues. A meticulous visual inspection, conducted under a stereo optical microscope by trained personnel, identifies any remaining contaminants for further cleaning if necessary, upholding stringent cleanliness standards. This comprehensive pre-cleaning process ensures the safety and performance of the stent components, safeguarding patient health throughout medical procedures.

III. THE DELIVERY SYSTEM

➢ *Loading of Laser Cut Peripheral Retrieval Device into a Catheter for Optimal Deployment:*

The preparation and assembly of a laser-cut peripheral retrieval device involve a series of steps to ensure the safe and effective deployment of the device In this process, the careful preparation of the catheter with a mounted retrieval clot over the inner lumen, which provide deliver mechanism for the retrieval device. The first step is preparing the catheter with mounted retrieval device remove any particles from the catheter's surface. This ensures that the catheter is clean and free of debris, minimizing the risk of contamination during the assembly process.

Once the catheter is prepared, the retrieval device (mounted retrieval device over inner lumen) is carefully positioned onto the distal end of the catheter, aligning it with the deployment mechanism. The retrieval device must be carefully handled and load the retrieval device carefully to avoid damage to its structure, which could compromise its performance during deployment. The retrieval device is securely placed and properly aligned into the catheter. To affix the retrieval device inside the catheter, crimp the retrieval device manually and employed to compress the retrieval device into the catheter. This process requires finesse to achieve a secure fit while preserving the structural integrity of the retrieval. Special attention must be paid to avoid exerting excessive force, which could deform or damage the device during crimping.

Once the retrieval device is securely loaded into the catheter, the assembly undergoes a thorough inspection to confirm proper alignment and integrity. Visual examination and tactile inspection are performed to ensure that the retrieval device is securely attached and positioned correctly for deployment.

At the proximal end of the catheter, a handle (Pusher Tube) is engaged to control the deployment process. This handle provides the physician with the ability to manipulate the catheter and precisely deploy the retrieval device at the target location within the patient's vasculature. The handle allows for smooth and controlled movement of the catheter; enabling it to retrieve the clot from the vessel by retrieval device with minimal trauma to the surrounding tissues.

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The flexibility and tractability of our retrieval device system facilitate precise delivery to the target thrombosis region, even in challenging anatomies. This ease of deployment enhances procedural success rates and minimizes the risk of complications associated with improper retrieve device placement. Proper loading and handling of the retrieval device and catheter assembly are essential to ensure the successful delivery and deployment of the laser cut peripheral retrieval device.

The delivery system comprises several components, including the outer sheath, outer sheath flush port, guide wire flush port, handle, catheter, haemostatic valve, and soft tip. Each component plays a crucial role in facilitating the delivery and deployment of the peripheral stent. The assembly of these components is depicted in Figure 02, providing a visual reference for clinicians and operators involved in the procedure.

➢ *The Delivery System Component*

- *Retrieval Device:*

A laser-cut peripheral retrieval device system consists of a nitinol metal tube forming a flexible mesh structure. In an in-vitro test, it undergoes evaluation for trackability, flexibility, and radial force within simulated vascular models to ensure its suitability for navigating and supporting blood vessels effectively during interventional procedures which consist of four sizes 06-16 mm diameter and in length sizes is 10mm – 40mm.

- *Handle:*

The handle (Pusher Tube) of the laser cut peripheral retrieval device system enhances control and maneuverability during in-vitro testing, facilitating precise navigation through simulated vascular pathways. This design enables healthcare providers to assess the retrieved device's trackability within laboratory conditions effectively and sizes are 3.95Fr- 4.95Fr.

It's simple design offers enhanced maneuverability and control during deployment, particularly beneficial in complex peripheral interventions, interventional cardiology, and vascular surgery. This ensures precise navigation through intricate vascular anatomy, improving procedural outcomes.

- *Catheter:*

The catheter of a delivery system for a laser-cut peripheral retrieval device system consists of a flexible catheter designed to navigate through blood vessels. It facilitates precise device deployment by allowing controlled advancement and positioning within in-vitro vascular models, essential for evaluating the device's trackability and performance along with the size of the catheter 11 Fr.-12 Fr.

- *Inner Lumen:*

The inner lumen provides the support to retrieval device and helps to navigate distally and proximally inside the catheter for the movement of deployment and retrieval of the stent from vessel 1.43mm - 2.43mm.

- *Soft Tip:*

The soft tip of a laser-cut peripheral retrieval device system enhances navigational capability by providing flexibility and reduced trauma during advancement through vessels. In-vitro tests evaluate its ability to smoothly traverse vascular models, simulating real-world conditions for safe and precise deployment in clinical settings and sizes of 3.1mm - 4.1mm.

- *Haemostatic Valve:*

The haemostatic valve of a laser-cut peripheral retrieval device system for in-vitro testing facilitates controlled access to the vascular phantom while maintaining homeostasis. It allows for the introduction and withdrawal of catheters or delivery systems during experiments, minimizing fluid leakage and maintaining a stable vascular environment for accurate assessment and sizes are 11Fr.-12Fr.

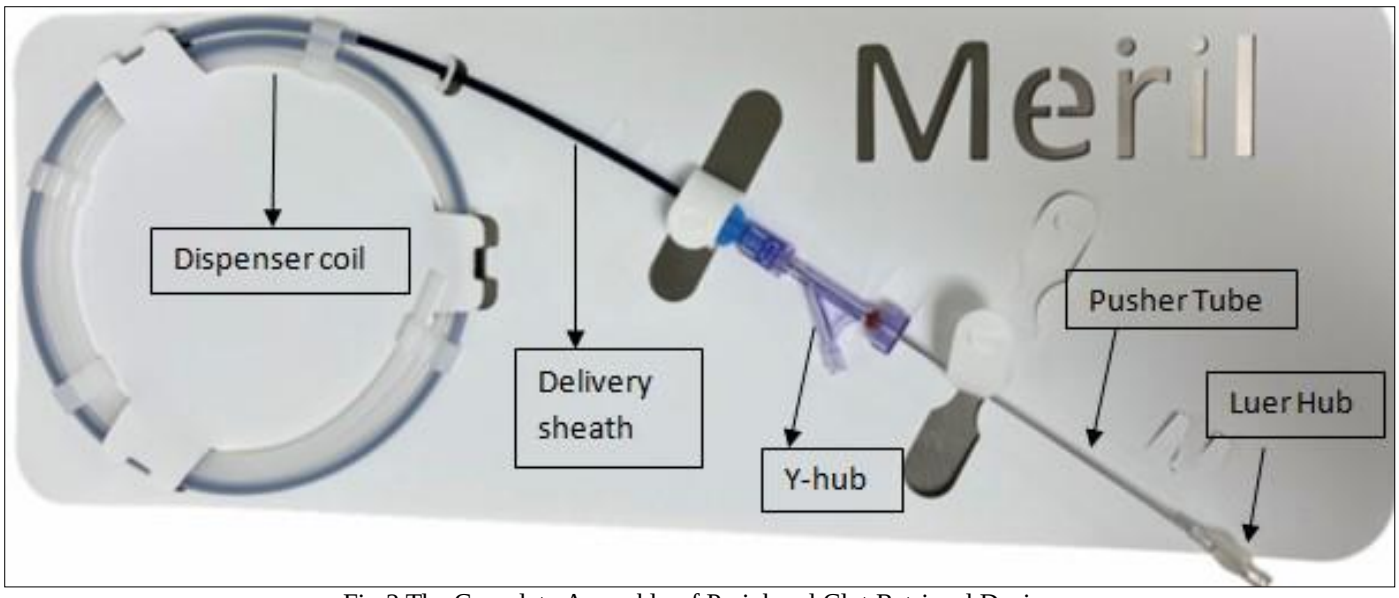

Fig 2 The Complete Assembly of Peripheral Clot Retrieval Device

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IV. RESULTS AND DISCUSSION

- *Trackability Test Assessment of a Developed Laser Cut Peripheral Retrieval Device:*

The trackability test of a laser cut peripheral retrieval device system is very important to evaluate and the device is conducted to assess the device's ability to navigate through tortuous vascular pathways with easy deployment and retrieval. In the realm of interventional peripheral, interventional cardiology, and vascular surgery, trackability refers to the retrieval device's capability to smoothly advance through vessels, ensuring accurate deployment and optimal positioning. This test is typically performed under laboratory conditions using in-vitro silicon models simulating the vascular environment.

In a trackability test, researchers utilized vascular silicon models that mimic the anatomical and physiological characteristics of human blood vessels. These models are often constructed using materials such as silicone rubber or polyurethane, which closely resemble vascular tissue in terms of mechanical properties and geometry.

During the test, the developed laser cut peripheral retrieval device system is introduced into the vascular phantom using the above-mentioned catheter or delivery system. The retrieval device's performance is then evaluated as it traverses through various simulated vascular pathways, including straight segments, bends, and narrow constrictions. A comprehensive trackability report of a laser cut retrieval device system typically includes detailed observations and quantitative measurements regarding the device's performance across different parameters. This report provides valuable insights into the stent's navigational capabilities and its suitability for pre-clinical use.

Overall, the trackability test and subsequent report play a crucial role in the evaluation and optimization of laser cut peripheral retrieval device systems, ensuring their safe and effective deployment in in-vivo practice. The setup of trackability test is depicted in Figure 03 however table 01 shows the test parameters of trackability test.

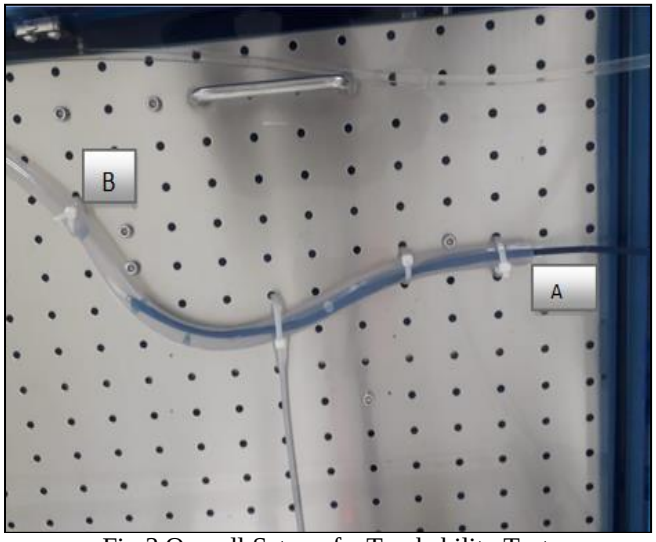

Fig 3 Overall Setup of a Trackability Test

Table 1 Test Parameters for Trackability Test

Sr no.	Parameter	Range
1	Guide wire	0.035"
2	Insertion rate	30-40 cm/min
3	Fluid Test Medium	Purified Water
4	Temperature	37 ºC ± 2 ºC
5	Sheath	3.67 – 4.0 MM OD

The distal end of the laser cut peripheral retrieval device system was advanced along the guide wire from point "A" to "B," while the proximal end of the system remained secured by a gripping mechanism, indicating the track length. During this process, the force necessary to maneuver the stent system along the "Simulated Peripheral Vascular Model" was carefully measured.

By calculating the average force, researchers can obtain a representative value that reflects the typical force required to navigate the laser-cut peripheral retrieval device system along the designated path within the simulated vascular model. This average force measurement obtained provided valuable insights into the system's trackability and navigational characteristics, aiding in the assessment of its performance and usability in pre-clinical settings. The results of the trackability test are depicted in Table 02. The push force test parameter is 50mm/Sec. of push speed and the push distance is 250mm in size of 06X16mm device.

Table 2 Result of Trackability Test

Number	Direction	Near Max (N)	Near Avg (N)	Standard Value
1	Push	1.04	0.50	3 N
2	Push	1.01	0.49	3 N
3	Push	1.02	0.50	3 N

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➢ *An in-Vitro Test Assessment for the Deployment of a Developed Laser Cut Peripheral Retrieval Device:*

The deployment and delivery process of the nitinol-based self-expanding laser cut peripheral retrieve device were executed to assess their efficacy and precision within the peripheral simulation test model shown in Figure 04. The procedural steps outlined for stent deployment were systematically followed, ensuring the controlled and secure placement of the device.

The retrieval device was advanced across the site of the thrombosis, positioning the distal marker band beyond the distal boundary of the dilated segment. The catheter was advanced until the distal marker band and proximal marker band encompassed the target thrombosis. To initiate deployment of retrieve device to retrieve the clot, the delivery system included a reciprocating mechanism that incrementally moved the retrieve device distally.

The retrieve device position was assessed, and repositioning was done if desired. Repositioning could only be performed when the retrieve device was slightly deployed from the outer sheath and not touching the vessel walls. During this time, the delivery system could be moved either proximally or distally, and the deployment process could be restarted.

The retrieve device position results were reconfirmed to assess the clot or thrombosis area. If some thrombosis is still into vessel and ensuring that the thrombosis are still into blood vessel than again initiate the procedure for remove the clot form vessel by laser cut retrieve device. The deployment procedure outlined was followed in a systematic manner:

➢ *Preparation:*

All necessary equipment was ensured to be ready, and the environment was sterile. The System was turned to the unlocked position for unlocking. Retrieval device deployment was initiated by advancing the pusher tube while allowing the outer sheath to retract proximally. The pusher tube was continuously and slowly moved forth. Shorter advancements may provide better control.

The process was repeated until the retrieved stent was no longer deployed by advancing the pushing by thumb. The pusher tube was fully advanced to completely release and retrieves the device. It was verified that the entire retrieved device was successfully released and finally the clot from the vessel.

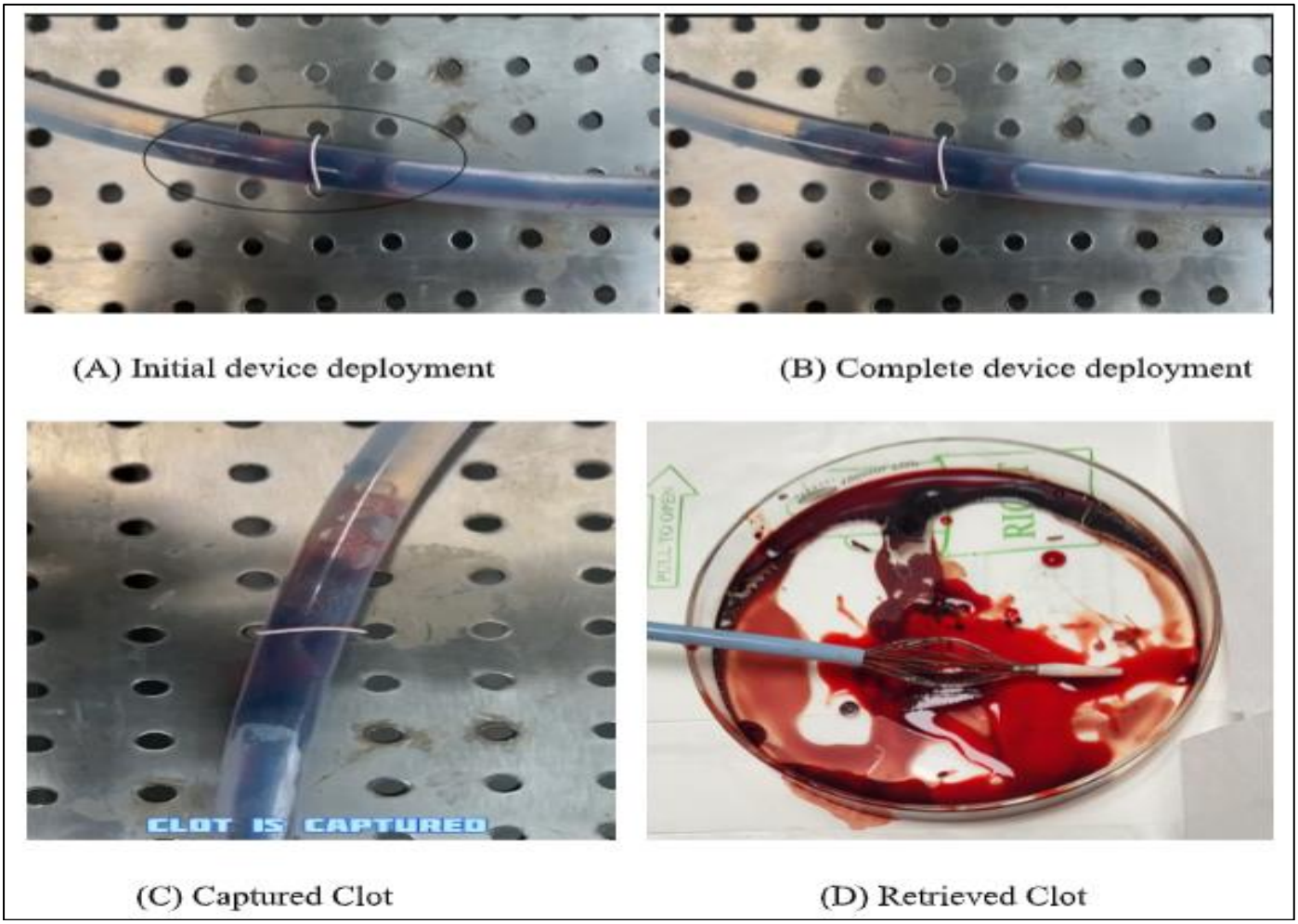

Fig 4 Overall Setup of an in-Vitro Peripheral Simulation Model for Retrieval of Clot and Remove by Peripheral Retrieval Device System

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V. CONCLUSION

In conclusion, in-vitro testing of the laser cut peripheral retrieval stent system has shown promising results, indicating its potential effectiveness in addressing Ischemic Stroke, & Pulmonary Embolization. The system demonstrated precise placement and controlled delivery within the target vessel during simulation, highlighting its capability to navigate vascular anatomy complexities. Additionally, positive outcomes from the trackability and pushability test emphasize the system's proficiency in negotiating challenging vessels and thrombosis, crucial for secure stent fixation and minimizing complications such as retrieval device migration. The successful replication of real-world navigational challenges underscores the retrieve device's ability to maneuver safely and effectively in pre-clinical settings, enhancing procedural outcomes and patient safety. These in-vitro test results complements existing evidence, emphasizing the braided pulmonary retrieval stent system's potential to address unmet needs in thrombosis treatment while ensuring optimal patient care and outcomes. Our upcoming article will focus on validating these promising results through pre-clinical evaluation, including randomized controlled trials and real-world observational studies, to further confirm its clinical efficacy and safety.

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