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In-vitro Testing and Trackability Assessment of Developed Braided Peripheral Stent System for Treating Peripheral Arterial Disease

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Abstract

Peripheral arterial disease (PAD) imposes a significant global health burden, often requiring endovascular interventions for symptom relief and blood flow restoration. Self-expanding braided peripheral stents offer promise, characterized by their unique design and advantageous mechanical properties. Crafted through intricate wire interlacing, these stents exhibit exceptional flexibility, conformability, and radial strength, facilitating adaptation to complex anatomies and resistance against deformation. Manufacturing involves sophisticated techniques with minimal material to ensure consistent performance, biocompatibility and cost-effectivity leading to improved procedural outcomes and patient comfort. Deployment via minimally invasive endovascular approaches delivers the stent to the lesion site, where it expands to reinstate vessel patency and prevent restenosis. Successful in-vitro implantation studies and trackability testing support the potential of aforementioned braided peripheral stents for PAD treatment, highlighting the need for ongoing research and validation for pre-clinical & clinical efficacy as well as safety.

Keywords: Peripheral arterial disease (PAD), self-expanding braided peripheral stents, minimal material, biocompatibility, cost-effectivity, in-vitro implantation and trackability.

Introduction

Peripheral artery disease (PAD) is a significant global health concern, affecting millions worldwide and necessitating effective interventions for symptom alleviation and restoration of blood flow. According to the Global Burden of Disease Study (GBD) 2017, an estimated 236.62 million (5.56%) individuals aged 25 years or older were afflicted with PAD, with nearly 70% residing in low- and middle-income countries, indicating a notable shift in the epidemiological landscape. This underscores the pressing need for advanced treatment modalities to address the evolving burden of PAD and its associated morbidity and mortality risks.

Among the array of vascular stents available, the peripheral self-expanding braided nitinol stent has emerged as a promising solution, distinguished by its design and favorable mechanical properties. PAD profoundly impacts the quality of life of affected individuals and poses substantial health risks, underscoring the urgency for effective interventions. Fabricated through the weaving of nitinol wires, the aforementioned stent provides unparalleled flexibility, conformability, and radial strength. These characteristics facilitate seamless adaptation to complex anatomical configurations and offer robust support against deformation under physiological stresses.

The manufacturing process entails intricate braiding techniques, shape-setting methods, and rigorous quality control measures to ensure consistent performance and biocompatibility. Deployment of the peripheral self-expanding braided nitinol stent entails minimally invasive endovascular procedures, where it is delivered to the target lesion site via catheter-based systems. Utilizing mechanical or self-expanding mechanisms, the stent expands, restoring vessel patency and providing structural reinforcement to mitigate restenosis. Notable advantages include enhanced flexibility, reduced fracture risk, and superior conformability compared to traditional stents, resulting in improved procedural outcomes and heightened patient comfort.

Furthermore, successful in-vitro implantation studies and trackability studies have demonstrated the feasibility and efficacy of the peripheral self-expanding braided nitinol stent, further supporting its potential as a promising solution for PAD treatment. These findings underscore the importance of continued research and further validation to establish the safety and effectiveness of this developed stent technology in improving outcomes for patients with PAD.

Our stent system is engineered with cost-effectiveness in mind, offering healthcare providers a solution that delivers superior performance at a fraction of the cost. By leveraging distinguishing manufacturing processes and materials, we have optimized production efficiency without compromising on quality or efficacy. This translates to significant savings for healthcare facilities and patients alike, making advanced vascular care more accessible and affordable.

Incorporating the latest advancements in materials and technology, our braided peripheral stent system represents a paradigm shift in the treatment of peripheral artery disease. Its unique design and cost-effective approach not only improve patient outcomes but also address the economic challenges facing healthcare systems worldwide. With our product, healthcare providers can confidently deliver superior care while maximizing value for their patients and institutions.

Materials and Methods

The entire process for the development of a braided peripheral stent was executed under strict sterile conditions and in accordance with the guidelines of ISO 13485.

We've pioneered a revolutionary approach to stent design, minimizing material usage without compromising structural strength. By employing a braided configuration, our stent system not only reduces the risk of vascular injury and thrombosis but also fosters improved endothelialization and long-term vascular healing.

What sets us apart is our crucial welding process, a departure from conventional sleeve-based methods. This technique ensures unparalleled durability and reliability, all while preserving the stent's minimal material footprint.

Choosing Braided Stents: Overcoming the Drawbacks of Laser-Cut Stents

Laser-cut stents, while precise and customizable, have several disadvantages compared to braided stents. They tend to be less flexible, making them harder to navigate through tortuous vessels and more prone to kinking. The rigid structure can also lead to increased trauma to vessel walls during deployment. Additionally, laser-cut stents may exhibit less radial force uniformity and reduced conformability to vessel shape, which can impact their long-term stability and effectiveness. Braided stents, with their interwoven structure, generally offer superior flexibility and adaptability, providing smoother deployment and better conformability to varying vessel anatomies.

Development strategy for crafting nitinol based self-expanding braided peripheral stent for addressing peripheral arterial diseases (PAD):

Delving into the development process using braiding technique:

The development of our peripheral stent involved utilizing advanced braiding techniques with a commercial braiding machine. This machine worked continuously, weaving nitinol wires to form the intricate structure of the stent. Nitinol bobbin carriers were loaded onto the machine according to the specified diameter requirements of the stent, ensuring precision during the braiding process. The range of the braiding angle was between 80 - 250 degrees.

To ensure the quality and accuracy of the braided Peripheral Stent, a detailed examination of its properties was carried out. A thorough analysis of the braid angle and pattern was conducted to confirm alignment with the intended specifications.

After the inspection, the braided peripheral stent progressed to the next phase of the process. It was carefully encased in an aluminum pouch to maintain a controlled environment, crucial for preserving the integrity of the braided structure and preparing the stent for subsequent developmental stages.

Our peripheral stent system boasts exceptional radial strength, ensuring effective support for blood vessels in the peripheral vascular system. Engineered with precision and utilizing advanced materials, our stent provides robust reinforcement, promoting optimal blood flow and long-term patient well-being.

Our Stent dimensions range from 4mm to 8mm in diameter and 20mm to 200mm in length. The delivery system is compatible with 6 French (6F) to 7 French (7F) catheters. In the in-vitro deployment simulation model, a 5.5mm diameter was selected, with a stent diameter of 6mm and length of 60mm. The peripheral artery in which the product is intend to be implant during pre-clinical or clinical studies typically ranges in size, accommodating the stent's various diameters, from 4mm to 8mm.

Shape setting technique to execute the braided peripheral stent for optimal functionality:

The subsequent stage in the development process entailed shaping the braided structure to its intended form and dimensions. This was achieved by subjecting the braided peripheral stent to a heat treatment process for shape setting. The temperature scale **ranges from 450 ºC to 575 ºC.** This critical phase is vital for establishing the desired shape and size of the stent and optimizing the transformative and mechanical properties of nitinol for its shape memory characteristics.

During this specific shape-setting procedure, the braided Peripheral stent was securely attached to a specialized mandrel. Subsequently, both the mandrel and the peripheral stent were introduced into a furnace for precise heat treatment. This thermal process facilitated the transformation of the nitinol alloy, enabling the Peripheral stent to assume and maintain the required shape essential for its functionality.

Quality assessment remained paramount throughout the development process. The characteristics of the braided peripheral stent were examined using an optical microscope, focusing on aspects such as the braid angle and pattern. Following this thorough inspection, the braided peripheral stent was securely sealed, marking the conclusion of this phase, and it proceeded to the subsequent stage in the overall development process.

Manual reverse braiding and cutting technique to execute the braided peripheral stent for optimal functionality:

The stent required additional reinforcement or modification. Thin wire material compatible with the stent's composition and braiding pattern was selected. Using specialized hand tools such as fine needles or micro-hooks, the additional strands were manually woven into the desired areas of the stent preform. Precision and care were employed to maintain consistency in the braiding pattern and avoid distortion of the stent structure. It was ensured that the reverse braiding enhanced the stent's mechanical properties and overall performance. The desired length of the braided peripheral stent was determined based on anatomical considerations and procedural requirements. Precise cutting tools such as cutters or microtome blades were utilized to carefully sever the preform at the marked locations. Uniformity in the cutting process was maintained to ensure consistent stent dimensions and optimal functionality. Quality control measures were implemented to inspect the cut edges for smoothness and integrity, addressing any irregularities as needed. A thorough visual and tactile inspection of the cut stent segments was conducted to confirm dimensional accuracy and structural integrity.

Precision and efficiency in braided peripheral stent assembly: The role of laser welding technology:

Laser welding is a highly precise and efficient technique utilized in the assembly of braided peripheral stents to close the stent loop. This process begins with the careful preparation of stent components, ensuring cleanliness and proper alignment. Laser parameters, including wavelength, power, and pulse duration, are selected based on the material composition and thickness of the components. The parameters, encompassing wavelength, power, and pulse duration, frequency provide the following specifications: wavelength of 0.10-0.100 mm,

power of 220-240 V, and pulse duration of 0.1-0.50 ms frequency 1.0 to 50 Hz. The components are then securely aligned and fixture to maintain precise positioning during welding.

During the welding process, a focused laser beam is directed onto the interface between the meeting surfaces of the stent components. The laser generates localized heat, causing the material to melt and form a fusion bond at the weld joint. Control of the laser beams movement and intensity ensures uniform heating and penetration across the weld area.

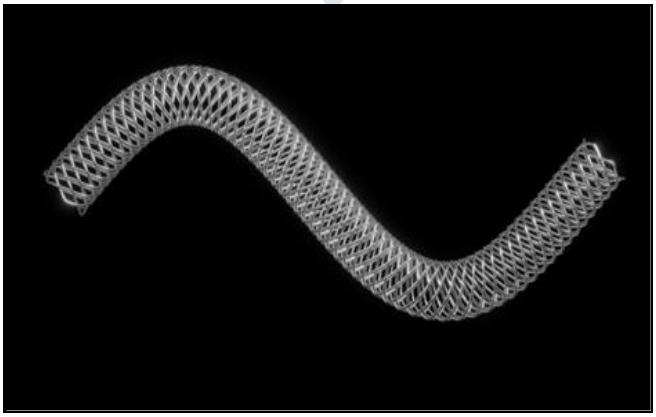
Post-weld inspection involves allowing the welded components to cool gradually to room temperature to avoid thermal stress and distortion. Visual and non-destructive inspection techniques used stereo optical conducted to assess weld quality. Overall, laser welding technology used for braided peripheral stents, enabling seamless closure of the stent loop and ensuring optimal performance and reliability in clinical applications.

Corrosion protection and nickel elimination: safeguarding nitinol in development:

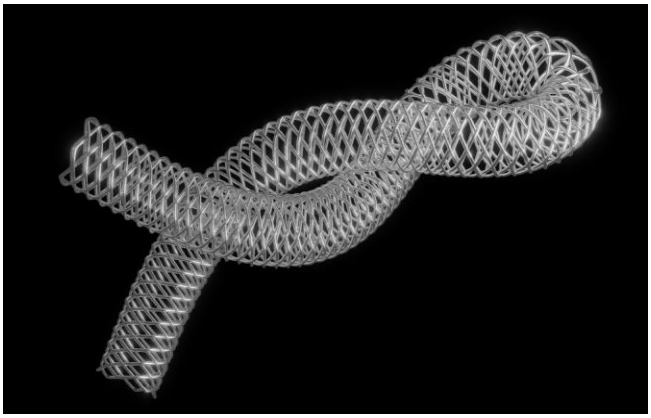
The prevention of corrosion and the elimination of nickel atoms from the surface of nitinol were important steps in its development process. An oxide layer was intentionally created in nitinol to serve as a protective barrier against corrosion and to remove nickel, which could be harmful if introduced into the body. The removal of nickel was particularly important due to its potential health risks.

Traditionally, the passivation of alloys involved employing heat and acids to eliminate iron or nickel from the material's surface. In the case of nitinol, a mild oxidant in combination with nitric acid was frequently used to create a thin oxide film. This film played a key role in shielding the material from corrosion and ensuring the safety of its use in medical applications.

The characteristics of the braided peripheral stent depicted in figure 01 were examined under a stereo optical microscope, with specific attention given to analyzing the braid angle and pattern. Following this inspection, the braided peripheral stent 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.



(A) Braided peripheral stent



(B) Flexibility characteristics

Figure 01 Depiction of a braided peripheral stent from diverse perspectives

Pre-cleaning process:

The pre-cleaning process of a peripheral stent system with isopropyl alcohol (IPA) is a crucial and meticulous procedure aimed at eliminating contaminants and residues from the stent components to ensure their cleanliness and integrity for medical use. Initially, the stent components are immersed in an IPA solution, functioning as a solvent to dissolve and dislodge surface contaminants. This immersion phase, coupled with gentle agitation, facilitates the thorough cleaning of intricate features and crevices. 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.

The Delivery System

Loading of peripheral stent into catheter for optimal deployment:

The preparation and assembly of a peripheral stent system involve a series of steps to ensure the safe and effective deployment of the stent. This process begins with the careful preparation of the catheter, which serves as the delivery mechanism for the stent. The first step in preparing the catheter involves removing any protective covers to expose the catheter's surface. This ensures that the catheter is clean and free of debris, minimizing the risk of contamination during the assembly process. Any residual debris or contaminants must be removed to maintain the sterility and integrity of the catheter.

Once the catheter is prepared, the stent is carefully positioned onto the distal end of the catheter, aligning it with the deployment mechanism. The stent must be handled with care to avoid damage to its structure, which

could compromise its performance during deployment. Precision is crucial in ensuring that the stent is securely placed and properly aligned on the catheter. To affix the stent onto the catheter, a crimping tool is employed to compress the stent onto the catheter's surface. This process requires finesse to achieve a secure fit while preserving the structural integrity of the stent. Special attention must be paid to avoid exerting excessive force, which could deform or damage the stent during crimping.

Once the stent is securely loaded onto 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 stent is securely attached and positioned correctly for deployment. Any discrepancies or irregularities must be addressed before proceeding with the deployment process.

At the proximal end of the catheter, a handle is engaged to control the deployment process. This handle provides the physician with the ability to manipulate the catheter and precisely deploy the stent at the target location within the patient's vasculature. The handle allows for smooth and controlled movement of the catheter, enabling accurate placement of the stent with minimal trauma to the surrounding tissues.

The delivery system comprises several components, including the outer sheath, outer sheath flush port, guide wire flush port, handle, catheter, hemostatic 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 flexibility and tractability of our stent system facilitate precise delivery to the target lesion, even in challenging anatomies. This ease of deployment enhances procedural success rates and minimizes the risk of complications associated with improper stent placement.

Proper loading and handling of the stent and catheter assembly are essential to ensure the successful delivery and deployment of the peripheral stent. Through careful preparation, precise alignment, and inspection, clinicians can achieve optimal outcomes while minimizing the risk of complications during the intervention.

The delivery system component:

Stent: A braided peripheral stent system consists of intertwined metal wires 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.

Handle: The handle of our braided peripheral stent system enhances control and maneuverability during in-vitro testing, facilitating precise navigation through simulated vascular pathways. This design enables healthcare providers to assess the stent's trackability within laboratory conditions effectively.

Its ergonomic design offers enhanced maneuverability and control during deployment, particularly beneficial in complex peripheral interventions. This ensures precise navigation through intricate vascular anatomy, improving procedural outcomes.

Catheter: The catheter of delivery system for a braided peripheral stent system consists of a flexible catheter designed to navigate through blood vessels. It facilitates precise stent deployment by allowing controlled advancement and positioning within in-vitro vascular models, essential for evaluating the stent's trackability and performance.

Soft Tip: The soft tip of a braided peripheral stent 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.

Haemostatic valve: The haemostatic valve of a braided peripheral stent 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.

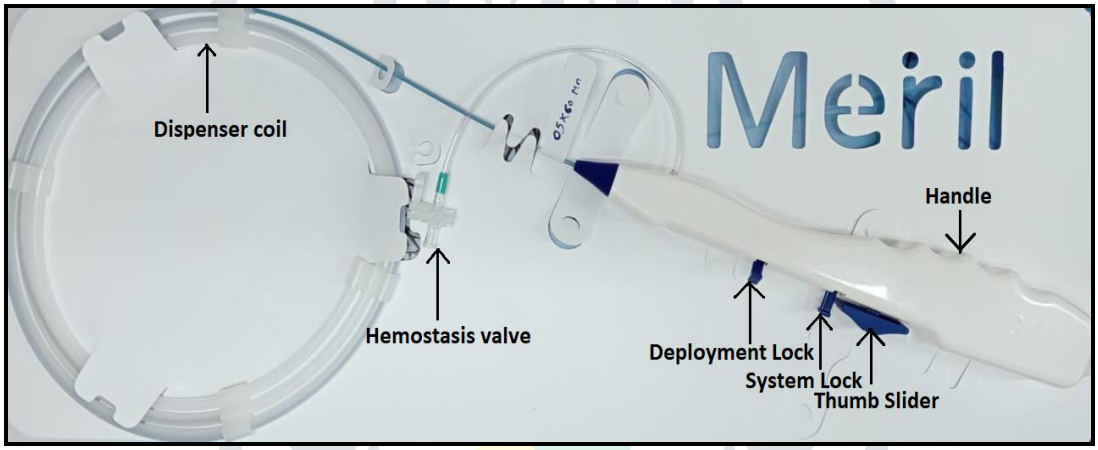


Figure 02:The complete assembly of delivery system

Results and Discussion

Trackability test assessment of a developed braided peripheral stent:

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

In a trackability test, researchers utilized vascular phantoms or 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 peripheral stent system is introduced into the vascular phantom using an above mentioned catheter or delivery system. The stent'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 peripheral stent system typically includes detailed observations and quantitative measurements regarding the stent's performance across different parameters. This report provides valuable insights into the stent's navigational capabilities and its suitability for clinical use.

Overall, the trackability test and subsequent report play a crucial role in the evaluation and optimization of peripheral stent systems, ensuring their safe and effective deployment in clinical practice. The setup of trackability test is depicted in Figure 03 however, table 01 is showing the test parameters of trackability test.

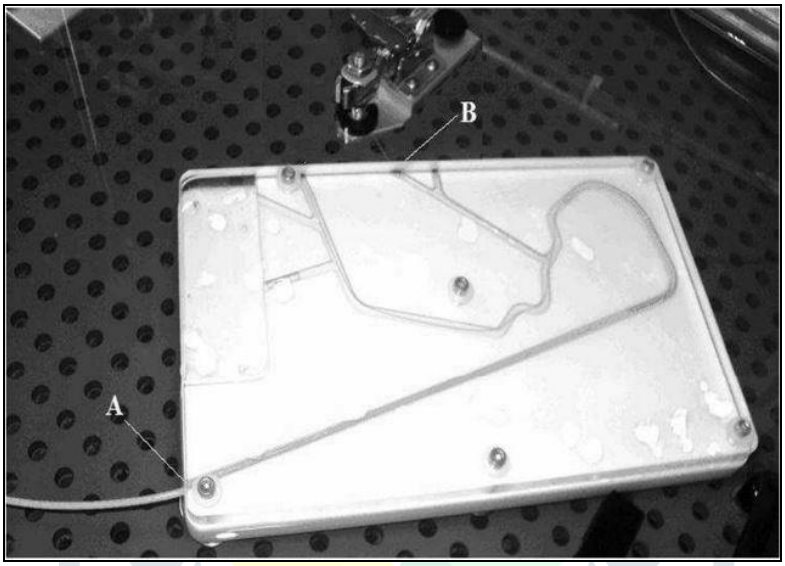


Figure 03 Overall setup of a trackability test.

Table 01 Test parameters for trackability test peripheral stent system

Sr no.	Parameter	Range
1	Guide wire	0.014" - 0.018"
2	Insertion rate	30-40 cm/min
3	Fluid Test Medium	Purified Water
4	Temperature	37 ºC ± 2 ºC
5	Guide Catheter	1.75 - 2.2 MM OD

The distal end of the peripheral stent 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.

Formula for force:

Average Force = sum of Individual force ÷ Number of Measurements

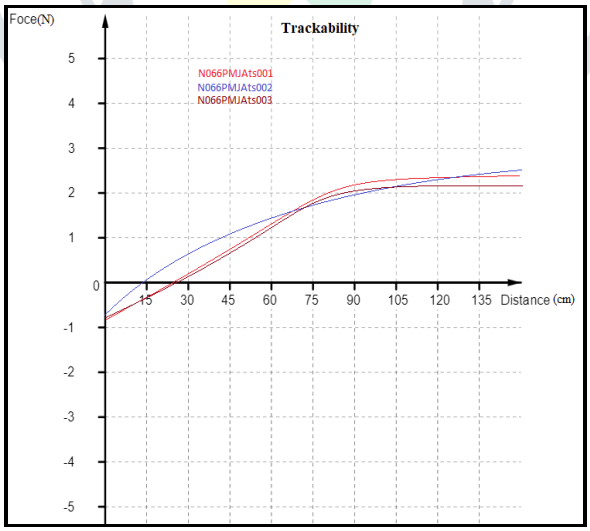
The "Sum of Individual Forces" represents the total force exerted during multiple measurements of tracking the stent system from point "A" to "B."

The "Number of Measurements" refers to the total number of tracking attempts performed during the test.

By calculating the average force, researchers can obtain a representative value that reflects the typical force required to navigate the peripheral stent 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 clinical settings. The results of trackability test is depicted in Table 02 and the graph of the Force vs. Distance Curve has also been illustrated.

Table 02 Result of trackability test of a peripheral stent system

Sample No.	Stent Size	Stent Sr no.	Maximum Force(n)
1	06 X 60 mm	N0660PMJAts001	2.11
2	06 X 60 mm	N0660PMJAts002	2.33
3	06 X 60 mm	N0660PMJAts003	2.05
Average			2.16
Standard Deviation			1.5



Graph 01 Force vs. Distance curve

An in-vitro test assessment for the deployment of a developed braided peripheral stent:

The deployment and delivery process of the nitinol-based self-expanding braided peripheral stent 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.

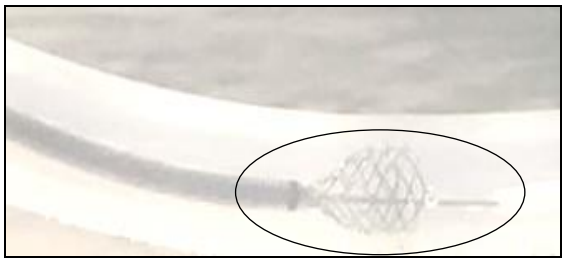
The stent was advanced across the site of the lesion, positioning the distal marker band beyond the distal boundary of the dilated segment. The catheter was advanced until the distal marker band and proximal marker band encompassed the target lesion. To initiate stent deployment, the delivery system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

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

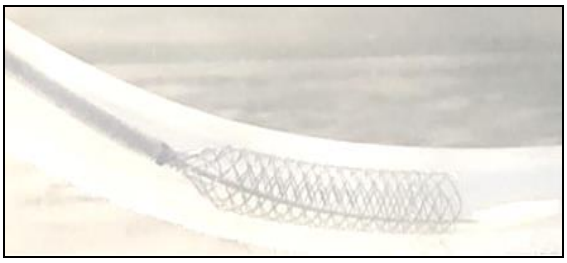
The stent position results were reconfirmed to assess the Implant area. If post-dilatation was necessary, ensuring that the final stent diameter matched the reference vessel diameter was crucial. It was assured that the stent wall was in contact with the simulated artery wall and that the stent was not left under expanded. This step ensured stability and control during the subsequent deployment process.

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 Lock was turned to the unlocked position for unlocking. Stent deployment was initiated by advancing the thumb slide while allowing the outer sheath to retract proximally. The thumb slide was continuously and slowly moved back and forth. Shorter advancements may provide better control. The process was repeated until the stent was no longer deployed by advancing the thumb slide. The Deployment Lock was turned to the unlocked position. The thumb slide was fully advanced to completely release the stent. It was verified that the entire stent was successfully released.

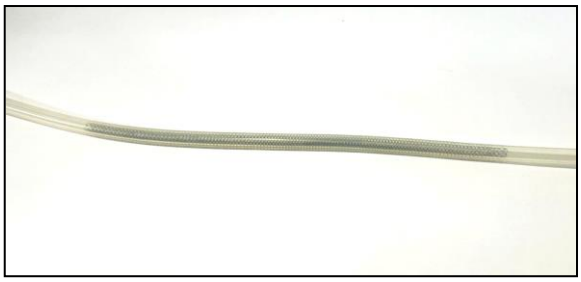


(A) Initial stent deployment



(B) Partial stent deployment

(C) Full stent deployment



(C) Post stent deployment

Figure 04 Overall setup of an in-vitro peripheral simulation model for deployment of peripheral stent system

Conclusion

In conclusion, in-vitro testing of the peripheral stent system has shown promising results, indicating its potential effectiveness in addressing Peripheral Arterial Disease (PAD). 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 test emphasize the system's proficiency in negotiating challenging vessels and lesions, crucial for secure stent fixation and minimizing complications such as stent migration. The successful replication of real-world navigational challenges underscores the stent's ability to maneuver safely and effectively in clinical settings, enhancing procedural outcomes and patient safety. These in-vitro test results complement existing evidence, emphasizing the peripheral stent system's potential to address unmet needs in PAD 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.

References

1. *"Global disease burden and its attributable risk factors of peripheral arterial disease":* [https://www.nature.com/articles/s41598-023-47028-5]

2."*Peripheral Artery Disease (PAD)."* American Heart Association. [https://www.heart.org/en/health-topics/peripheral-artery-disease]

3."*Treatment of Peripheral Arterial Disease.*" Circulation. [https://www.ahajournals.org/doi/full/10.1161/circulationaha.117.030729]

4."*Endovascular Treatment for Peripheral Artery Disease*." American College of Cardiology. [https://www.acc.org/latest-in-cardiology/articles/2019/05/16/12/42/endovascular-treatment-for-peripheral-artery-disease]

5."*Peripheral Artery Disease: Diagnosis and Treatment*." Mayo Clinic. [https://www.mayoclinic.org/diseases-conditions/peripheral-artery-disease/diagnosis-treatment/drc-20350579]

6."*Peripheral Artery Disease: Pathophysiology, Risk Factors, and Clinical Management*." Journal of Nursing Research.[https://journals.lww.com/jnrtwna/Fulltext/2019/12000/Peripheral_Artery_Disease__Pathophysiology,_Risk.2.aspx]

7."*Role of Stents in Peripheral Arterial Disease."* Endovascular Today. [https://evtoday.com/2016/09/role-of-stents-in-peripheral-arterial-disease]

8. *"Mechanical Testing of Vascular Stents":*
[https://www.researchgate.net/publication/341407683_Mechanical_Testing_of_Vascular_Stents**]**

9."*Peripheral Arterial Disease: Endovascular and Surgical Management*." Vascular Health and Risk Management. [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3194082/]

10."*Endovascular Treatment Options for Peripheral Artery Disease."* Radiology Society of North America. [https://pubs.rsna.org/doi/10.1148/rg.2016150070]

11."*Stent Placement in the Treatment of Peripheral Artery Disease*." American Family Physician. [https://www.aafp.org/afp/2017/1115/p661.html]

12."*Peripheral Artery Disease Treatment Overview*." Society for Vascular Surgery. [https://vascular.org/patient-resources/vascular-conditions/peripheral-arterial-disease-pad/treatment-overview]

13."*Current and Emerging Treatment Strategies for Peripheral Artery Disease*." British Journal of Cardiology. [https://bjcardio.co.uk/2018/05/current-and-emerging-treatment-strategies-for-peripheral-artery-disease/]