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DEVELOPMENT OF NEUROVASCULAR FLOW DIVERTER FOR THE TREATMENT OF CEREBRAL ANEURYSM: AN IN-VITRO STUDY ANALYSIS

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ABSTRACT

An aneurysm is an abnormal bulging in the artery wall, typically arising from a weakened area. If left untreated, aneurysms have the potential to rupture, causing internal bleeding and resulting in lasting damage to the affected body part. Various approaches are employed to address this condition, including the implementation of flow diverters or alternative methods. Depending on the aneurysm's location, diverse types of flow diverters are utilized to ensure unimpeded blood flow. These diverters are developed from different materials or a combination of metal alloys. This research article provides a comprehensive overview of the development of a flow diverter composed of a nitinol alloy, specifically made for the treatment of cerebral aneurysms. The primary objective of this flow diverter is to be positioned within the parent blood vessel, spanning the neck of an intracranial aneurysm. By doing so through the implantation process, the flow diverter effectively redirects excessive blood flow away from the aneurysm, resisting its growth and reducing the risk of rupture. The systematic evolution of the flow diverter is elucidated in this research article, emphasizing key parameters that demand careful consideration during its development. Additionally, the article underscores the effectiveness of the flow diverter in addressing cerebral aneurysms in patients, supported by findings from in-vitro simulation studies.

KEYWORDS: Cerebral aneurysms, Flow diverter, Nitinol and In-vitro testing.

INTRODUCTION

Aneurysm identifies as weakening of the arterial wall, resulting in the formation of a bulge or distension in the artery. This condition can lead to the development of blood clots that obstruct the normal blood flow within the artery. The potential rupture or clotting of an aneurysm, depending on its location, poses a life-threatening risk. Aneurysms can manifest in various arteries throughout the body, including the heart, abdomen, brain, or legs. Examples of different types of aneurysms include Abdominal Aortic Aneurysm (AAA), Cerebral Aneurysms, Thoracic Aortic Aneurysm, Carotid Aneurysm, Mesenteric Artery Aneurysm, and Splenic Artery Aneurysm. Individuals with an aneurysm may experience various symptoms such as light-headedness, rapid heartbeat, sudden severe pain in the head, chest, abdomen, or back, and a sudden loss of consciousness following a severe headache.

Prompt treatment is imperative for all types of aneurysms, as prolonged instances can lead to rupture, resulting in a stroke. Untreated aneurysms can be fatal, but with immediate intervention, outcomes can vary. Ruptured brain aneurysms commonly occur in the space between the brain and its thin covering tissues, leading to a type of hemorrhagic stroke known as subarachnoid haemorrhage.

Diagnosis methods for aneurysms include CT scans, MRIs, and ultrasounds. Treatment options depend on the type, location, and size of the aneurysm and may involve medication or surgery. Specifically for Cerebral Aneurysms, Catheter embolization emerges as a favourable treatment option. The primary objective in treating brain aneurysms is to halt or diminish the blood flow into the aneurysm, a task efficiently achieved through the application of a nitinol-based braided flow diverter. This flow diverter undergoes rigorous manufacturing processes and adheres to stringent quality parameters, rendering it the optimal choice for addressing brain aneurysms.

This research article elucidates the imperative role of the nitinol flow diverter, delving into its necessity, the intricacies of its manufacturing, and an in-depth in-vitro analysis. These aspects collectively contribute to enhancing the treatment of patients with cerebral aneurysms by redirecting blood flow away from the aneurysm, thereby mitigating the risks of maturation and rupture associated with aneurysms.

MATERIALS AND METHODS

The entire process of the flow diverter was executed under strict sterile conditions and in accordance with the guidelines of ISO 13485.

Development strategy for crafting nitinol based flow diverter for addressing cerebral aneurysms

Delving into the development process using braiding technique

The development process of the flow diverter involved complex braiding techniques using a commercially available braiding machine. This machine was employed in conjunction with a suitably sized having flexibility and adequate strength DFT core wire to create the braided structure of the flow diverter. The operation of the machine was continuous, and nitinol bobbin carriers were loaded in accordance with the specified diameter requirements of the flow diverter.

To ensure the quality and precision of the braided flow diverter, an examination of its properties was conducted. A stereo optical microscope was employed for this purpose, allowing a detailed analysis of the braid angle and pattern. This served to verify the conformity of the braided structure to the intended specifications.

Following the thorough inspection, the braided flow diverter was gone through the next phase of the manufacturing process. It was carefully enclosed in an aluminium pouch, ensuring a controlled environment. This step was crucial in maintaining the integrity of the braided structure and preparing the flow diverter for subsequent stages in its development.

Shape setting technique to execute the braided flow diverter for optimal functionality

The next step in the development process involved shaping the braided structure to its intended form and dimensions. To achieve this, the braided flow diverter was carefully placed in an oven, where it gone through a heat treatment process to ensure the establishment of its desired shape and size. This critical phase is known as shape setting, and it plays an important role in configuring the transformative and mechanical characteristics of nitinol for its shape memory properties.

In this specific shape-setting process, the machine-braided flow diverter was securely affixed to a specialized mandrel. The mandrel, along with the flow diverter, was then introduced into a furnace for precise heat treatment. This thermal process facilitated the transformation of the

nitinol alloy, allowing the flow diverter to adopt and retain the desired shape necessary for its functionality.

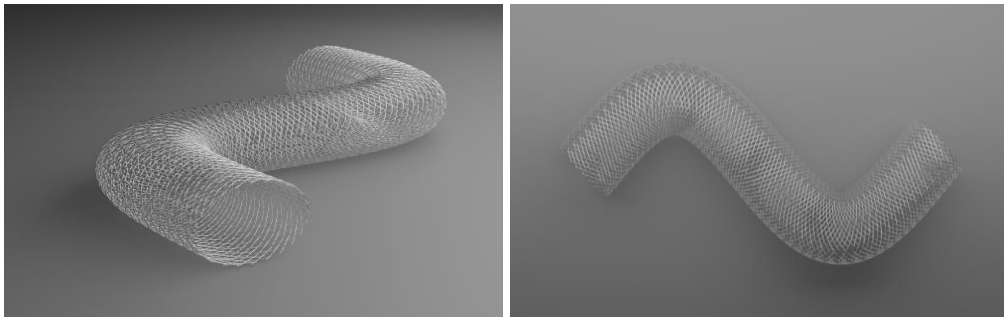
Quality assessment remained a key aspect of the development process. The characteristics of the braided flow diverter were thoroughly examined using a stereo optical microscope, with a focus on the braid angle and pattern. Following this inspection, the braided flow diverter was sealed securely, marking the conclusion of this particular phase, and it was then advanced to the subsequent stage in the overall development process.

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 flow diverter 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 flow diverter underwent a sealing process within an aluminium 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) **(B)**

Figure 01: Depiction of nitinol based flow diverter from diverse angles.

Pre-cleaning process

During the development process, the flow diverter was handled gently to prevent damage. The IPA was spilled out from the weighing bottle containing the flow diverter. Using a stylet, the flow diverter was removed from the weighing bottle. Each flow diverter was mounted on a needle, and IPA was dried by spraying nitrogen gas (N2). The flow diverter was washed with purified water using a bottle or spray gun. Purified water was then dried from the flow diverter by spraying nitrogen gas (N2). If foreign particles were observed under the microscope, an additional wash was performed.

Loading of flow diverter into Micro-catheter for optimal deployment

The loading process of the flow diverter into the micro-catheter demanded precise functioning. The aforementioned device, carefully constructed through prior development stages, was seamlessly integrated into a micro-catheter with a suitable diameter in the range of 0.5 to 0.7 mm.

This integration was executed using a specialized crimper. The crimper played an important role in compressing the flow diverter in a radial direction, employing a 1750-1900 mm long stainless still delivery wire. The outcome of this radial compression was a crimped configuration.

The crimped flow diverter, having undergone this careful compression, was then delicately inserted into the micro-catheter. Within the confined space of the micro-catheter, the flow diverter was allowed to expand, aligning appropriately with the dimensions and requirements of the micro-catheter itself.

This loading process was not merely a procedural step; it was a crucial determinant for the subsequent deployment and optimal functioning of the flow diverter within the micro-

catheter. Achieving the desired radial compression and subsequent controlled expansion required a high degree of precision, emphasizing the importance of handling during this phase.

The use of the crimper emerged as an instrumental element in this loading process, facilitating controlled compression and contributing significantly to the overall effectiveness of the device. This level of precision in loading ensures that the flow diverter is poised for its intended function within the micro-catheter, emphasizing the commitment to quality and efficacy in the device development.

RESULTS AND DISCUSSION

Deployment and Delivery process of the nitinol flow diverter: In-vitro test analysis

The deployment and delivery process of the nitinol flow diverter was executed to assess its efficacy and precision within the In-Vitro Neurovascular Simulation model shown in the figure 03. The procedural steps outlined for stent deployment were followed systematically, ensuring the controlled and secure placement of the device.

To initiate the deployment, the insertion of the guide wire marked the commencement of the procedure, with the micro catheter threaded over the guide wire. The micro catheter's tip was strategically positioned at least 10-20 mm beyond the distal edge of the simulated aneurysm. To reduce slack in the micro catheter, a gentle retraction was performed before proceeding further.

The introducer sheath was partially inserted into the hemostatic valve at the catheter hub and securely closed, effectively locking down the sheath. This step ensured stability and control during the subsequent deployment process. The introducer sheath was then secured tightly to the hub, further reinforcing the stability of the system.

With the preparatory steps complete, the delivery wire was pushed approximately 1000-1250 mm for the safe deployment of the flow diverter system inside the micro catheter. The introducer sheath was subsequently removed, allowing unobstructed access for the advancement of the flow diverter device into the micro catheter.

The actual delivery process commenced by aligning the tip of the delivery wire with the tip of the micro catheter. The flow diverter device was then unsheathed and simultaneously pushed forward. The distal end of the flow diverter successfully expanded, initiating the deployment

of the remaining device by continuing to push the delivery wire and/or unsheathing the flow diverter.

After the stent was fully deployed as shown in the figure 04, a calibrated measuring scale was employed to measure its length. The stent achieved complete deployment in the target location within the In-Vitro Neurovascular Simulation model, simulating a 4.2 mm intracranial artery. Verification of the deployed stent's size confirmed the accuracy and precision of the delivery process.

These results highlight the potential clinical applicability of the nitinol flow diverter in neurovascular interventions, showcasing its ability to navigate intricate anatomical structures with accuracy. The developed deployment protocol serves as a foundation for further investigations and underscores the importance of meticulous procedural steps in optimizing the performance of neurovascular devices.

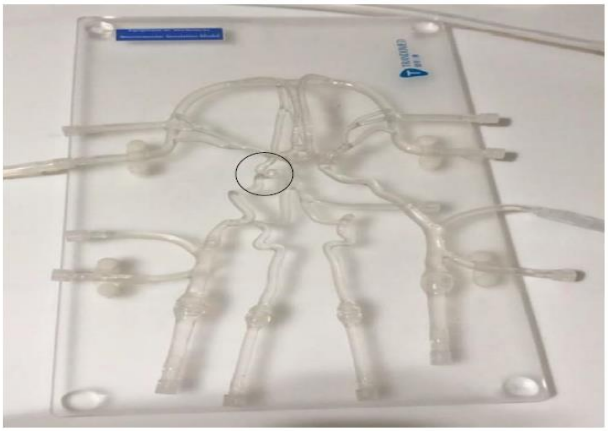


Figure 03: Overall Setup of In-Vitro Neurovascular Simulation Model with Aneurysm for Deployment of Nitinol Flow Diverter.

Figure 4: Successful Deployment of Nitinol Flow Diverter into an In-Vitro Neurovascular Simulation Model.

CONCLUSION

In conclusion, this research article delves into the complexities of addressing cerebral aneurysms, recognizing them as abnormal bulges in artery walls that, if left untreated, pose a significant risk of rupture and internal bleeding, leading to subarachnoid haemorrhage like damage. Throughout the article, we outlined the systematic evolution of the nitinol flow diverter, emphasizing crucial parameters that demand careful consideration during its development. The deployment process showcases the precision and accuracy achieved in deploying the stent within the In-Vitro Neurovascular Simulation model, simulating a 4.2 mm intracranial artery. The measured length of the fully deployed stent, verified using a calibrated measuring scale, attests to the accuracy and precision of the delivery process. These findings, supported by in-vitro simulation studies, underscore the effectiveness of the nitinol flow diverter in mitigating cerebral aneurysms. Furthermore, the demonstrated ability of the flow diverter to navigate intricate anatomical structures with precision highlights its potential clinical applicability in neurovascular interventions. The deployment protocol not only substantiates the success of the current study but also lays a search for future investigations. It accentuates the importance of procedural steps in optimizing the performance of neurovascular devices, promising advancements in the field of aneurysm treatment. Therefore, our forthcoming article will explore clinical studies that provide support for the implantation of Neurovascular Flow Diverter in human applications.

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