A Comprehensive Study on the Development of a Self-Expanding Metallic Urethral Stent System for Canine Urethral Obstructions: A Bench Scale Evaluation

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Abstract- **The human body relies on a complex network of organs and systems to maintain its vital functions, and one of these crucial systems is the urinary tract. The urethra, a narrow tube connecting the urinary bladder to the urinary meatus, plays an important role in the elimination of waste products from the body, primarily in the form of urine. However, in the canine population, urethral obstructions can pose severe threats to health. These obstructions can be the result of various factors, including trauma, benign tumors, or urinary stones, and they impede the normal flow of urine. Urgent veterinary care is essential in such cases to alleviate pain, prevent potentially life-threatening complications like bladder rupture, and restore regular urinary function. In the field of urology, urinary drainage treatment often involves the use of urinary stenting, which has become a standard practice. These stents are typically used to support and protect the Urethra primarily as supplementary equipment in urology and endourology to regulate urine flow. This research article introduces an innovative approach to address benign urethral obstructions in canines. It presents a self-expanding metallic urethral stent system constructed from a nitinol alloy manufactured using laser-cut technology. The stent is designed with closed-cell segments and flares at both ends to prevent migration and features a radiopaque marker for enhanced placement accuracy. This approach aims to open or restore blocked urethras, ultimately improving the quality of life for affected canines. To ensure its safety and effectiveness in maintaining regular urine flow through the urethra, the radial strength of the stent was evaluated through bench-scale testing, specifically the three-point bend test. This research represents a significant advancement in veterinary medicine, offering a promising solution to a critical health issue in the canine population.**

Keywords: **Urinary tract, Urethral obstructions, Veterinary care, Urinary stenting and Nitinol urethral stent.**

INTRODUCTION

The urinary system's main function is to filter blood and generate urine as a byproduct in the course of this process. The urinary system comprises organs such as the kidneys, renal pelvis, ureters, bladder, and urethra. In the act of urination, the urethra serves as the conduit for transferring urine from the bladder to the external body. The urethra exhibits various notable species and gender specific variations, encompassing characteristics like length and diameter. Distinct anatomical relationships with reproductive systems contribute to significant differences in the properties of male and female urethras.

The urethra is a significant organ within the urinary system, and various conditions can impact it. Examples include hypospadias, benign urethral cancer, and chronic inflammation of the urethra. Urethral strictures, a condition where a segment of the urinary tract narrows, is another concern. This narrowing may arise from the development of scar tissue in the urinary tract, leading to symptoms such as reduced urine flow, increased frequency of urination, urinary tract infections, and bleeding. Urethral neoplasia refers to the formation of mass cells either within or on the exterior of the urinary tract in dogs. While this growth can be either benign or malignant, it commonly manifests as transitional cell carcinoma (TCC). In canines, this condition presents with prominent symptoms such as frequent urination, vomiting, abdominal pain, weakness, lethargy, loss of appetite, and reluctance to exercise, and weakness in the hind legs.

When there is suspicion based on symptoms, initial tests such as blood tests, urinalysis, and a biochemistry profile are conducted for confirmation. In addition to the biochemistry profile and urinalysis, the veterinarian may also perform cytology and histopathological examinations as part of laboratory findings. These tests help differentiate between benign and malignant tumors and provide specific information about the type of cancer to the veterinarian. Variations in parameters identified through these tests can impact treatment response and contribute valuable insights into the onset and progression of the disease.

In cases of benign urethral conditions, the use of urethral stents is a common practice, providing a straightforward treatment option for dogs with benign obstructions. This research introduces a newly developed Self-Expanding Urethral Metallic Stent, designed for minimally invasive insertion into the urethral tract, either temporarily or permanently, to facilitate its opening. The stent is manufactured from a nitinol alloy, chosen for its super-elastic and shape-retaining properties. The focus of this research article is on treating benign obstructions in canines by implanting the developed self-expanding urethral metallic stent in the urethral tract. The radial strength of the stent was evaluated using a three-point bend test at the bench scale to ensure both safety and efficacy in maintaining normal urine flow. This study presents a practical solution for a significant health concern in the canine population, representing a notable advancement in veterinary care.

Materials and Method

Development of a Self-Expanding Urethral Metallic Stent System

Laser Cutting Technology:

The self-expanding urethral stent system was developed utilizing nitinol, a specialized nickel-titanium alloy chosen for its unique properties. The design of the stent was implemented through the utilization of computer-aided design (CAD) software, ensuring that every dimension, pattern, and feature adhered to the specified requirements.

A laser cutting machine was employed, equipped with a laser source, precise focusing optics, a CNC (Computer Numerical Control) system, and a versatile worktable. The CAD design served as the guiding blueprint for the machine, which had been programmed to intricately cut the desired pattern into the nitinol material.

During the cutting process, the laser beam, emitted from the laser source, was focused onto the surface of the nitinol material. The CNC system, operating based on the programmed instructions, guided the laser beam along the specified path with utmost accuracy. The nitinol material, provided in the form of a thin tube or sheet, gone through precise cutting as the laser maintained its focus on the surface, intricately sculpting the stent's structure. The utilization of this technology ensured the creation of the self-expanding urethral stent system with precision and efficiency.

Grinding and Honing for Surface Precision of Self-Expanding Urethral Stent System:

Following laser cutting, the implant frequently displayed surface irregularities, such as burns and rough edges. To address these issues, a grinding and honing process was implemented. The important procedures like Grinding, utilizing abrasive materials, effectively eliminated unwanted material and were automated to ensure consistency. The honing process, employing abrasive tools, achieved a smooth and polished surface, thereby enhancing precision. Both automated procedures played a crucial role in guaranteeing the implant's biocompatibility, mitigating the risk of tissue irritation or damage during insertion, and bolstering overall performance and safety.

Shaping self-Expanding Urethral Stent System through Shape Setting Process:

After achieving surface precision, the urethral stent underwent a shaping procedure utilizing the shape-setting technique. A key component in this process involved using a mandrel, typically made from heat-resistant material, serving as a guiding template. Careful placement of the nitinol implant onto the mandrel or fixture ensured comprehensive contact with its surface.

Following precise placement, the assembly underwent a controlled heating process, crucial due to nitinol's unique property known as shape memory. This characteristic allows nitinol to memorize and maintain a specific shape when exposed to a particular temperature. Upon reaching the critical temperature, the inherent shape memory of nitinol was activated, facilitating the implant's return to the predetermined shape. The temperature range for shape setting process is 505-515 degree celcius. Importantly, this method incorporated a shape specific mandrel, which was intended to create a flared ends on the urethral stent, enhancing its functional design for preventing migration and overall effectiveness.

Addressing Surface Imperfections in Self-Expanding Urethral Stent System through Sandblasting:

Sandblasting is an essential post-processing technique in biomedical applications, specifically engineered to achieve a consistent and superior surface finish. Despite shaping procedures, implant surfaces may retain microscopic imperfections, irregularities, and contaminants such as minute burrs, residual material, or uneven textures. To address these issues, sandblasting utilizes abrasive particles like aluminum oxide to refine the implant's surface, aligning it with the stringent requirements of biomedical standards. The primary objectives of sandblasting include:

- Corrosion mitigation: Sandblasting enhances the implant's resistance to corrosion, a crucial factor in ensuring long-term biocompatibility and functionality.
- Bacterial adhesion reduction: By creating a smoother, more uniform surface, sandblasting minimizes bacterial adhesion and biofilm formation, thereby reducing the risk of implant-associated infections.

- Biocompatibility enhancement: Sandblasting promotes biocompatibility by modifying the implant's surface properties, facilitating tissue integration and reducing the likelihood of adverse reactions.
- Aesthetic improvement: Sandblasting can refine the implant's surface texture, enhancing its aesthetic appeal and contributing to patient satisfaction.

The strategic application of abrasive particles during sandblasting ensures the refinement of the implant's surface, ensuring that it meets the demanding requirements of biomedical standards.

Electro-Polishing: Refining the Surface of Self-Expanding Urethral Stent System:

The application of electro-polishing emerged as an important strategy to eradicate lingering imperfections and enhance the overall surface quality of the implant. This electro-chemical process involved the dissolution of surface material in an electrolyte solution, effectively eliminating contaminants, edges, and burrs. The implant underwent immersion in the electrolyte solution, and an electric current was applied. This orchestrated the dissolution of metal ions from the surface into the solution. The consequence was a refined, smoother, and uniformly treated surface for the urethral stent system. This process worked synergistically to level and eliminate any sharp or uneven features, ensuring that the final product shown in the figure 01 having size of 10mm X 60mm adhered to stringent standards of quality and functionality within biomedical applications.

Figure 01 Self-Expanding Metallic Urethral Stent System for Canine Urethral Obstructions

The Delivery System

Insertion of Self-Expanding Urethral Stent into the Delivery System:

The "Urethral stent system" employs a highly efficient push-pull mechanism designed for precise and accurate placement. The delivery system, illustrated in the figure 02, comprises several integral components. These include a 6Fr delivery catheter, a pusher tube, an inner tube *(Shanghai Eco Precision, Zhangjiang, China)* and a PT/IR marker *(Piertech in Jiangyin, China)*. The seamless collaboration of these components brought about to achieve a controlled positioning of the laser-cut stent. This elaborate system ensures not only the accuracy of placement but also the reliability and consistency required in medical procedures, emphasizing the sophisticated interplay of each component in the overall functionality of the urethral stent system.

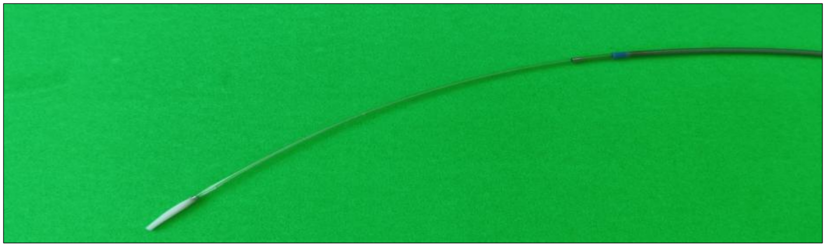


Figure 02 6 Fr Delivery System

During the urethral stent insertion procedure, the PEEK 450G Pusher Tube plays an important role in facilitating precise and controlled stent delivery. Its smooth and consistent pushing force ensures that the aforementioned laser-cut stent reaches the intended location within the urethra, enabling effective treatment.

To further enhance visualization and ensure accurate placement, the stent system incorporates platinum radio-opaque marker rings positioned at two strategic points: one on the braided tube and one on the inner tube. These markers, clearly visible during fluoroscopy procedures, serve as reliable radiographic guides, allowing medical professionals to closely monitor stent placement within the urethra. The markers' strategic positioning ensures that the stent is aligned precisely and placed correctly, maximizing its therapeutic efficacy.

The synergy between the PEEK 450G Pusher Tube and the radio-opaque markers exemplifies the meticulous design considerations that underpin the urethral stent system. This collaborative effort ensures that the stent reaches the intended location accurately, laying the foundation for successful treatment.

The Loading of Self-Expanding Urethral Stent into the Braided Tube:

The procedure begins with insertion of the urethral stent into the braided tube *(Shangai Eco Precesion China)*, with the help of a crimping machine *(MSI USA)* as shown in figure 03.

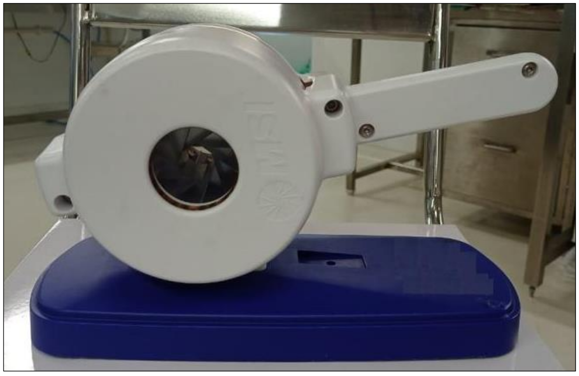
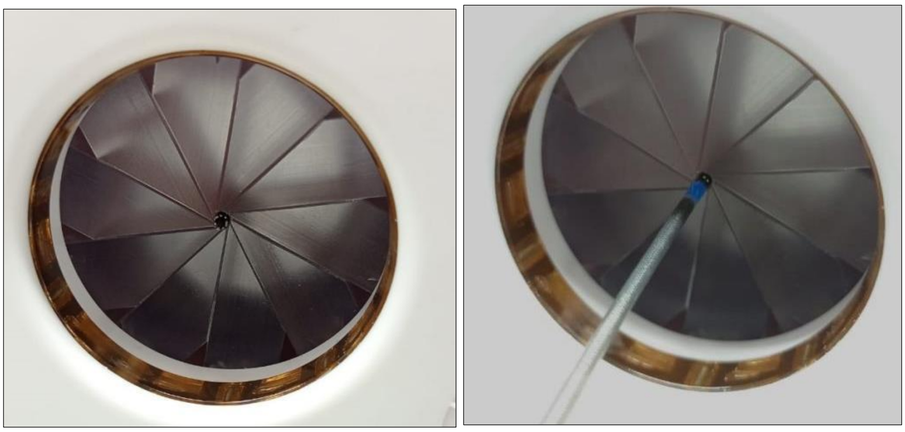


Figure 03 Crimping Machine

The stent insertion process begins with crimping one end of the urethral stent using a specialized crimping machine. The crimped stent is then carefully inserted into the braided tube from the opposite end of the crimping tool. This process is repeated incrementally, gradually advancing the stent into the braided tube until the entire stent is securely housed within the tube. This step-by-step approach ensures the precise alignment and secure placement of the stent within the braided tube, laying the successful urethral stent insertion.

The combined use of the crimping machine and the braided tube, shown in the figure 04 facilitates a controlled and efficient stent insertion process, minimizing the risk of complications and maximizing the likelihood of favorable treatment outcomes.



(A) **(B)**

Figure 04 Crimping the Urethral Stent through Crimping Machine for Inserting into the Braided Tube

Self-Expanding Urethral Stent Deployment and Access Point:

The complete delivery system assembly for deploying urethral stent into the urethra is depicted in the figure 05. To initiate the procedure, a guide wire is carefully inserted to the intended target site, serving both as a pathway and a reference point for the subsequent delivery of the aforementioned laser-cut urethral stent. The insertion of the guide wire is facilitated by fluoroscopy, an advanced real-time X-ray imaging technique that provides precise visualization of the guide wire's movement and positioning within the urethra.

Once the guide wire is precisely positioned, it is carefully advanced to the target location under fluoroscopic guidance, ensuring accurate placement within the urethra. Following this, the laser-cut stent system is delivered over the positioned guide wire. The unique design of the laser-cut stent enables it to self-expand upon deployment.

The next step involves maneuvering a catheter containing the laser-cut stent over the guide wire. The catheter is intricately manipulated until the laser-cut stent reaches its intended target site within the urethra.

In summary, this delivery process ensures the exact placement of the self-expanding urethral stent system through the utilization of a guide wire, guided by fluoroscopic imaging, and the inherent self-expanding nature of the stent. The ultimate result is the precise deployment of the stent to the specified location within the urethra, facilitated by the over-the-wire technique using a 6Fr delivery system. This comprehensive approach underscores the steps taken to achieve accurate and controlled placement of the urethral stent within the urethral anatomy

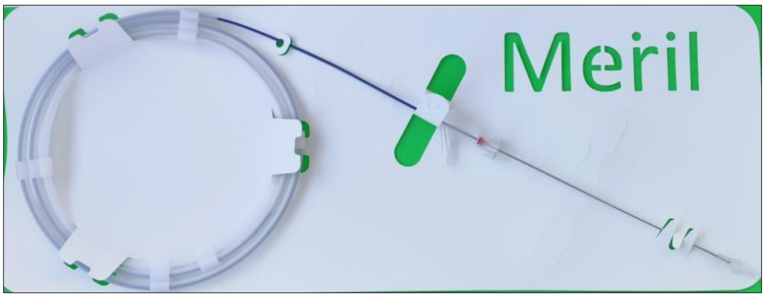


Figure 05 The Complete Assembly of a Delivery System for Delivering 'Urethral Stent System' into the Urethra.

Result and Discussion

Assessment of Three Point Bend Test: A Bench Scale Evaluation

The primary objective of this test was to assess the radial strength of the self-expanding urethral stent by determining its flexural strength and evaluating its ability to withstand external pressure or stress during bending failure.

Test Setup: The experimental setup utilized a Universal Testing Machine *(Instron, USA)*, as illustrated in Figure 06. This machine was specifically designed to measure the flexural strength of the self-expanding stents, simulating conditions akin to those experienced when the stent is implanted in the body.

Test Parameters: The Universal Testing Machine was programmed with the following parameters for the testing process:

Test Type: Three-point bend (Flexural)

Test Speed: 12 mm/min

Load Cell: 10 N

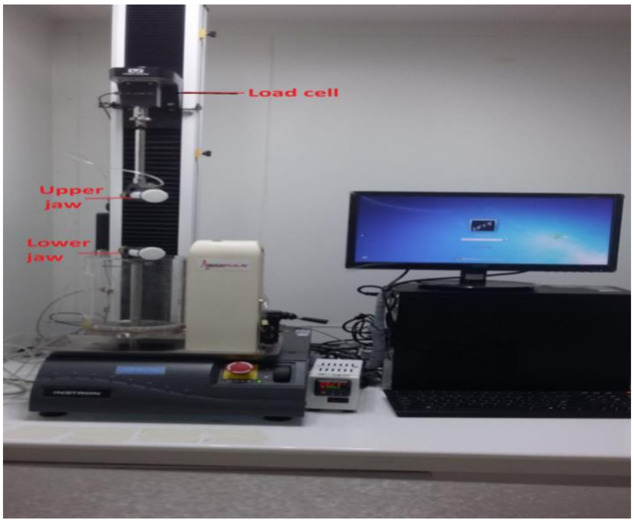


Figure 06 Universal Testing Machine

Testing Procedure and Data:

Initial State: The test began with the urethral stent sample in its original state, without any extension, compression, or stretching. At this point, the pressure applied to the test sample was recorded as 0.0 Newton (N), establishing a baseline for subsequent measurements.

Maximum and Minimum Forces: Throughout the testing process, the Universal Testing Machine recorded a maximum force of 0.456 N, representing the highest force experienced by the stent. Conversely, the minimum force recorded was 0.377 N, indicating the lowest force applied to the stent during the experiment.

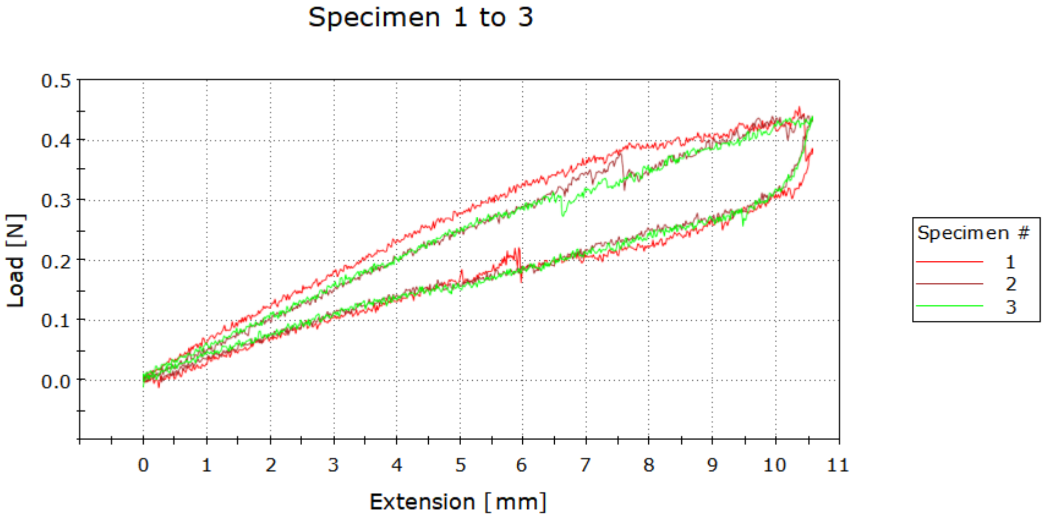
Results Findings: The overall results of the three-point bend test for the self-expanding metallic urethral stent are summarized in Table 01(Derived from the Universal testing machine) and visually represented in Graph 01. From a technical analysis perspective, the urethral stent demonstrated resilience, as it exhibited no permanent kink, crack, or break during the three-point bend test.

Based on the findings of this study, the self-expanding metallic urethral stent can be considered robust and resistant to permanent deformation, as evidenced by its performance in the three-point bend test. These results contribute valuable insights into the stent's mechanical properties and its potential suitability for clinical applications.

	Sr. No.	Force @ Peak[N]	Deflection @ Peak[mm]
1	01	0.456	10.371
2	02	0.377	7.544

3	03	0.438	10.581
Minimum		0.377	7.544
Mean		0.424	9.499
Maximum		0.456	10.581
Standard deviation		0.041	1.69611

Table 01 Results of Three Point Bend Test for **'**Self-Expanding Metallic Urethral Stent'



Graph 01 A Graphical Overview of the Three Point Bend Test for 'Self-Expanding Metallic Urethral Stent'

Conclusion

This research paper introduces a self-expanding urethral stent system as an innovative solution for treating benign urethral obstruction in canines. Employing a minimally invasive approach with an over-the-wire (OTW) delivery system enhances overall stability and optimizes performance. Beyond its immediate application, the study enhances our understanding of common features of benign urethral obstruction across species. Adapting a transformative technique from human medicine to the veterinary context underscores the interconnectedness of medical advances. Bench scale evaluation confirmed the mechanical strength of the stent system, affirming its suitability as a therapeutic agent. However, due to the preliminary nature of the development, further rigorous evaluation is essential. A forthcoming publication will demonstrate the feasibility of this stent in a Good Laboratory Practice (GLP) study. In conclusion, the introduction of this stent system signifies a significant advancement in veterinary medicine. It not only addresses an urgent medical issue in animals but also embodies the spirit of innovation and adaptation from human medical practices. Consequently, this stent system holds great promise for enhancing the quality of life for animals facing challenges from benign urethral obstruction.

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