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Original Research Paper

Development and In-Vitro Evaluation of a Biodegradable Biliary Scaffold System for the Treatment of Bile Duct Strictures

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ABSTRACT:
The main objective of this research is to create a biodegradable bile duct stent system that will aid in the restoration and maintenance of bile ducts that are diseased or damaged. The purpose of the scaffold is to offer a transient framework that will aid in tissue regeneration and repair, ultimately leading to the achievement of full biliary function. Bile duct strictures and infections often require surgery or transplantation to restore fluid and function. Conventional treatments, including synthetic stents and stents, have limitations which includes biocompatibility issues, lack of integration, and potential long-term complications. Biodegradable scaffolds offer a promising alternative by providing a temporary support structure that gradually integrates into tissue while preventing long-term retention of foreign bodies. The development process includes designing and fabricating scaffolds using biocompatible and biodegradable materials that can be Polylactic acid (PLA), polycaprolactone (PCL), polydioxanone suture (PDS) or other bioabsorbable polymers which have reasonable degradation rates and properties. The development of the biodegradable biliary scaffold system with PDS has shown promising results as an alternative to conventional stents for the treatment of biliary strictures. This study successfully designed and evaluated a self-expanding biliary scaffold system that would provide temporary structural support, is biocompatible, and degrades gradually over time, facilitating tissue regeneration without the risks associated with permanent implants.

Keywords: Bio-degradable scaffold, biliary strictures, tissue regeneration, Polydioxanone Suture, polylactic acid, polycaprolactone and regenerative medicine.

INTRODUCTION:

Biliary stricture, also referred to as bile duct stricture, occurs when the bile duct gets smaller or narrower. The bile duct is the tube that takes bile from the liver to the small intestine. When the duct becomes narrow, it makes it difficult for food to digest. Bile is a substance that helps in digestion of fats. Self expanding Biliary Scaffold System is a degradable implantable device which is a braided, flexible, fine mesh tubular prosthesis composed of Poly dioxanone suture (PDS). The implant is designed for placement in bile duct with biliary strictures. The biliary scaffold system is important in digestion. It regulates bile production, transport and storage. If there is an injury to the lymph nodes or a health condition such as stenosis or obstruction, major medical issues can arise (2014, V. Mahadevan). Traditional treatments usually include surgery, prosthetics or stents. However, these methods have limitations. They struggle with coherence, structural integrity and sustainability over time. Thus, finding alternative solutions is of crucial necessities.

Recent advances in tissue engineering and chemical engineering focus on biodegradable scaffold. These scaffolds facilitate tissue damage repair and regeneration (2016, Y.Cheng, etal). They act as a temporary structure, encouraging cell invasion and tissue growth. The result is the functional comfort. The use of biodegradable materials means that stents are absorbed by the body over time. This reduces long-term risks associated with foreign companies and issues with permanent implants (2006, B.Meng, etal.)

For biliary stenosis, biodegradable stents are emerging as a promising alternative. These alternatives provide supportive matrices for biliary tissue regeneration. This

can exacerbate outcomes for patients suffering from water injuries or illnesses (2019, IglesiasJF, MullerO). The ideal scaffold should have key characteristics: biocompatibility, strong structural integrity, controlled degradation rate, and ability to support cell growth and tissue proliferation (2020, WongMYW, SaxenaP). This research article examines the design of biodegradable biliary stent systems. It emphasizes the design and fabrication of stents using biocompatible and absorbable materials (2017, IwasakiH, MizushimaT).

Moreover, it provides a comprehensive overview of the complications of cholecystitis. The advantages of using a biodegradable stent to address these issues have also been discussed (2018, GreenbergJA, SugrueR). The introduction reviews the latest research and developments in stent technology, allowing for an in-depth discussion of the mechanisms and implications for effective and efficient biliary stents.

The inclusion of biodegradable scaffolds in biliary therapy represents a significant advancements in regenerative medicine. This can reduce complications and enhance patient outcomes. This research study aims to integrate traditional medical techniques with alternative strategies, seeking to develop improved solutions for conditions associated with biliary disease.

The use of biodegradable scaffolds in regenerative medicine has proven beneficial due to their ability to improve tissue regeneration and regeneration while reducing long-term complications associated with permanent implants. In the context of biliary strictures, where conventional therapy is often ineffective, the development of an aforementioned biodegradable biliary stent system is a good approach. This research study is based on the biodegradable stents development, their use in the biliary therapy, and the materials and technologies used in stent development process.

MATERIALS AND METHODS:

The functionality and effective operation of the stent depend heavily on the materials chosen for its construction. This structural material must be biocompatible, have sufficient properties to be compressed for loading into the tubular delivery system, and be able to afflict sufficient radial force upon expansion to re-establish the patency of the vessel.

Polydioxanone sutures (PDS) are absorbable sutures used in surgery for several years. It is reabsorbed in 4 to 6 months by fibroblast activity which in turn lays down collagen. It has been proposed that placing the PDO threads in multiple crisscross patterns produces more fibrogenesis and could improve the longevity of results.

Scaffold flexibility, migration resistance, and accuracy are highly dependent on the device's construction method and design architecture. The scaffold manufacturing process has multiple steps like braiding, primary shape setting, back braiding, secondary shape setting, marker attachment, delivery system assembly, primary packaging, ETO sterilization, and final packaging. The process description has been illustrated below.

Braiding machines vary in complexity and can range from simple hand-operated devices to highly automated systems. These machines have multiple carriers (also known as bobbins or spools) that hold the wires and control their tension and position during braiding. During braiding, the carriers move in a controlled pattern around a central core (mandrel), interlacing the wires in a specific geometric configuration. This creates a tubular structure with a reinforced wall that exhibits both axial strength and radial flexibility. The braiding process is done on 24 carriers' wire braiding machines with the help of SS316 Mandrel. This process includes 6-12 PDO sutures which are woven with each other from one side of the mandrel. Then it is transferred for the shape-setting process.

The Braided wire PDO mesh is fixed on a solid surface or object and then heated in vacuum oven up to the 80-90 °C temperature for 14 to 16 hours. PDO is an alloy that you can train to remember a shape, this means you can stretch, bend, or wind this alloy, and it will spring back to its original state after Shape Setting. Then it is transferred for the back braiding process. Back braiding process also includes 6-12 PDO wires which are woven with each other from the other side of the mandrel manually and then transferred again for shape setting. The Back Braided wire PDO mesh is fixed on a solid surface or object and then heated in vacuum oven up to the 80-90 °C temperature for 14 to 16 hours. PDO is an alloy that you can train to remember a shape, this means you can stretch, bend, or wind this alloy, and it will spring back to its original state after Shape Setting. After that marker attachment process is used to join the marker on Bioresorbable Biliary Scaffold System.

Delivery System Assembly is the process of joining the Catheter and Inner catheter with each other. This may involve the use of glue, epoxy, or one of a wide range of plastic agents that bond either through the evaporation of a solvent or curing via heat, time, or pressure.

The Bioresorbable Biliary Scaffold System and Delivery System are placed in a tray and then sealed pouch. The sealed pouch is inspected for sealing integrity, dent, holes, or any damage by visual inspection and a product information label is applied to it. Further, it is transferred for the sterilization process.

The primary packed Bioresorbable Biliary Scaffold System is sterilized using ETO sterilization and achieve

desired sterility assurance level of 10^{-6}. Then the sterile product is tested for in-house tests including microbiological, analytical, and performance tests. Then it is transferred to quarantine for some testing purposes.
The sterilized product is placed into the product's outer box along with instructions for use and a silica gel pouch. The finished product label is affixed on the product's outer box. The product box is placed in a polypropylene bag which is then sealed and further stored in the finished product store. The product image and size matrix is sown in figure 1 and table 1 respectively.

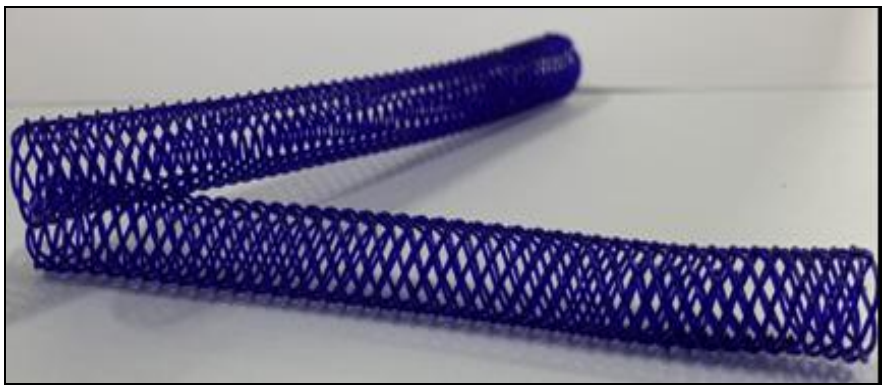

Figure 01 Bio-degradable Biliary Scaffold System

Table 01. Size matrix for a Developed Bioresorbable Biliary Scaffold System

Available Scaffold Diameter (mm)	Available Scaffold Lengths (mm)
8	40,60,80,100
10	40,60,80,100

<u>Assembly of Delivery System and Process for Scaffold Deployment</u>:
Assembled delivery systems Outer Sheath (Tube), Inner Sheath, Inner Lumen, Handle (Hub), Pusher (metal shaft), Bumper, Soft Tip, Marker (shown in figure 02) will be used to accurately and safely deploy biodegradable biliary scaffolds. The device system is made up of the catheter, the sheath, and the deployment mechanism so that scaffold can be released in a controlled manner. The assemblies are designed to move across biliary strictures and place the scaffold in the preselected target site for therapeutic purposes.

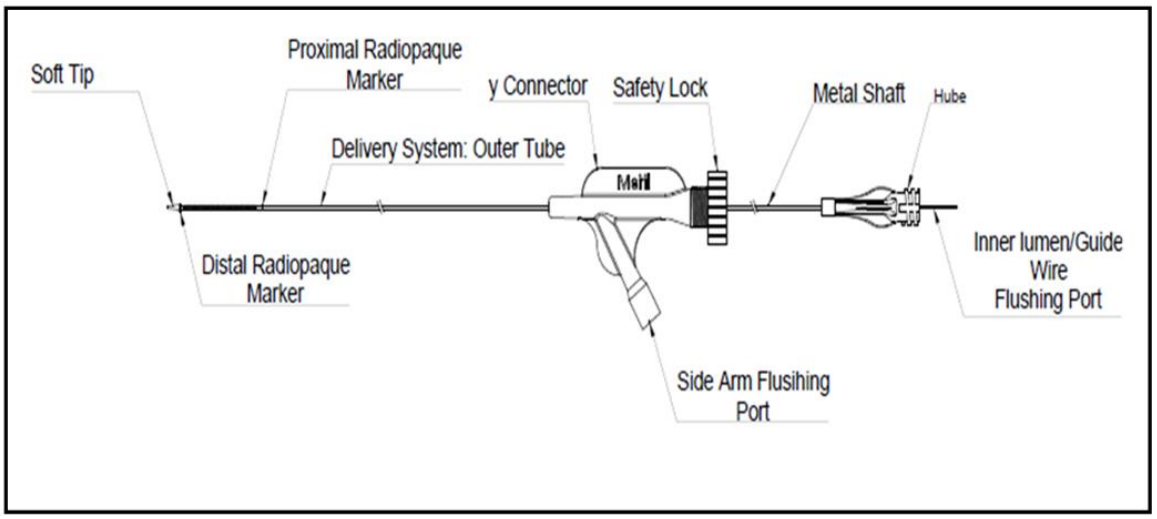

Figure 02 Bio-degradable Biliary Scaffold Delivery System

Loading of stent by hand:
Once the scaffold preparation process is completed, stent (scaffold) is loaded into the delivery system (8Fr- 14Fr). The scaffold will be in the right position inside the mechanism for deployment through careful hand manipulation without any risks for insertion or release.

Deployment Process:
The delivery system is assembled with the scaffold, then inserted into the patient, and advanced under fluoroscopic guidance into the biliary stricture. Fluoroscopy ensures continuous visualization of the system's position, providing guided access through the biliary tract.

Scaffold Deployment:
Once the delivery system reaches the appropriate site of the biliary stricture, the scaffold is released by the activation of the release mechanism. The biodegradable scaffold expands and sets in place in the target region.

Fluoroscopic Monitoring:
During the deployment of the scaffold, fluoroscopic imaging is used for monitoring the placement of the scaffold and for ensuring its proper deployment. This would ensure weather the scaffold is in the right place during the biliary stricture for a good therapeutic effect or not.

Post-Deployment Verification:
After deployment, further fluoroscopic verification is made in order to determine that the scaffold remains in the intended position following no migration or displacement.
The process and assembly conceive to ensure precision and safety along with successful placement of the scaffold within biliary strictures.

RESULT AND DISCUSSION:

The Self-expanding BioResorbable Biliary Scaffold System showed the most promising results when implanted in vitro in a simulated vasculature model. Such a model was chosen with great cautiousness since it can mimic the conditions that exist within the human body (in vivo) for real testing.

The catheter containing the stent was loaded into the delivery system during the experiment. Surprisingly, the delivery system was user friendly and efficient in the deployment of the stent at the desired location. The implantation procedure generally consisted of placement of the catheter in the model followed by the deployment of the scaffold using the retraction of the sheath. Then, the scaffold snapped back to its original form when deployed. This self-expanding property ensured that this scaffold was located appropriately within the biliary strictures, so precise positioning at the target site was possible. The Figure 03 (03A, 03B, and 03C) show the deployment procedure and deployment of BioResorbable Biliary Scaffold System in in-vitro model for evaluating the Scaffold's strength, flexibility, and ability to maintain patency by examine this we can predict how will the scaffold perform or behave during in vivo trail.

The delivery system design was more flexible and lubricated, which made it easier to navigate the simulated vasculature. As a result, the delivery friction and retraction friction were significantly reduced compared to other conventional systems. Lower friction made the process easier, along with a reduction in trauma possibilities around the tissue. Additionally, the setup time required for the delivery system was very minimal and underlines its feasibility to use clinically.

Because the PDS material it is made of, the stent possesses self-expanding characteristics that allowed it to expand without any hitch from the delivery configuration to the deployed configuration after being implanted. The soft catheter tip was very vital during the deployment procedure; it ensured there was no damage to the lumen, especially in compromised arteries or veins. It is a feature crucial for delicate structures, and therefore, the scaffold is even more appropriate for biliary applications.

The loading of the scaffold into the delivery system was intuitive, making the overall procedure easy and less prone to some form of damage to the implant. Ease of use accompanied by the scaffold's capability for deployability has really shown promising applications as a simple yet reliable intervention for biliary interventions.

Overall, it can be concluded that the Self-expanding BioResorbable Biliary Scaffold is quite effective within the simulated controlled environment. The scaffold was designed in such a way that it is user-friendly and minimizes complications that may occur during implantation procedures for biliary strictures. It would support for the regeneration of tissue, predictable degradation, and biocompatibility characterize PDS material used for making the scaffold.

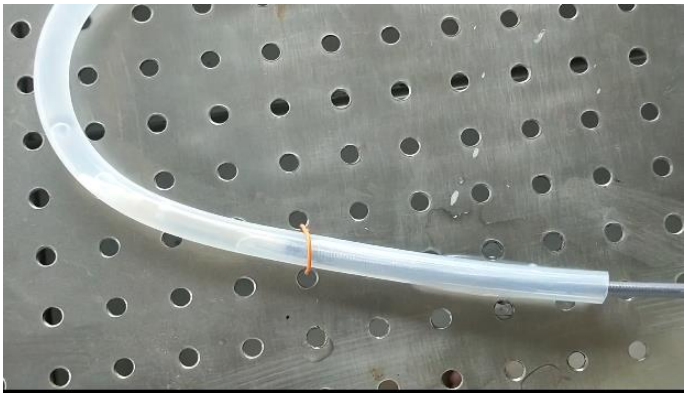

Figure 03 (A) Simulation Vasculature Model

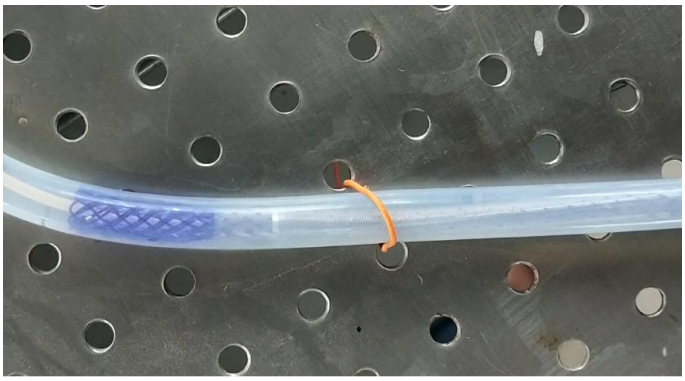

Figure 03 (B) Partially Deployment of a Biliary Scaffold System

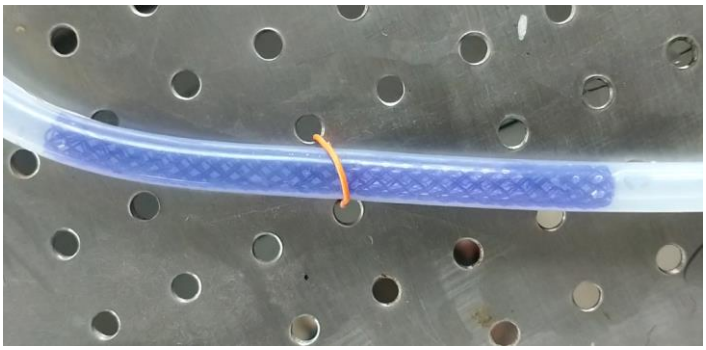

Figure 03 (C) Fully Deployed Scaffold

Figure 03 In-Vitro Deployment of a Self-Expanding Bio-Degradable Biliary Scaffold System

CONCLUSION:

The development of the Self-expanding BioResorbable Biliary Scaffold System represents a significant advancement in the treatment of biliary strictures. This study successfully demonstrated that the biodegradable scaffold, composed of Polydioxanone Sutures (PDS), provides temporary structural support while promoting tissue regeneration. The scaffold's biocompatibility and controlled degradation address many of the limitations seen in conventional treatments such as synthetic stents, which often suffer from biocompatibility issues, long-term retention, and lack of integration with tissue. The results from the in vitro testing in a simulated vasculature model indicate that the scaffold can be effectively deployed with minimal complications. The design of the delivery system was user-friendly, allowing for accurate placement with reduced friction and trauma, while the scaffold's self-expanding nature ensured proper positioning within biliary strictures. Moreover, the flexibility and lubricity of the delivery system further enhanced its operability, making the procedure safer and more efficient. Overall, the PDS-based biliary scaffold demonstrates strong potential as a viable alternative to traditional stents for biliary therapy. Its ability to provide

temporary support, degrade predictably, and facilitate tissue healing makes it a promising solution in regenerative medicine. While the in-vitro tests have demonstrated the mechanical efficiency of the device under simulated conditions, in-vivo testing is still necessary. Factors such as the body's inflammatory response and circulatory behavior must be assessed during pre-clinical evaluations. Once these are confirmed, we can make informed decisions regarding clinical trials.

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