

Research Article,

A Biodegradable Mesh-Covered Drug Eluting Coronary Embolic Protection Stent: A Promising Solution for Embolization Treatment for Coronary Arteries

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Abstract:

The newly developed "Mesh Covered Drug Eluting Coronary Embolic Protection Stent" is specifically designed to address the problem of distal embolization during percutaneous coronary intervention (PCI), a common procedure for treating myocardial infarction. This study aimed to evaluate the strength of the mesh component in patients with coronary artery disease. The stent system consists of a cobalt-chromium metal stent covered with a knitted mesh made of biodegradable PLGA polymer, which effectively prevents embolic events. The findings of the study demonstrated that the stent system exhibited high radial strength, withstanding significant levels of deformation before failure. This indicates that the mesh covered drug eluting coronary embolic protection stent has the potential to effectively mitigate distal embolization during PCI. The use of a biodegradable mesh in conjunction with the stent offers advantages over traditional stents by reducing the risk of restenosis, thrombosis, and inflammation, thereby improving long-term outcomes. Through bench-scale experiments, we have verified that the "Mesh Covered Drug Eluting Coronary Embolic Protection Stent" exhibits robust strength, validating its potential as an effective solution for addressing distal embolization during percutaneous coronary intervention.

Keywords: Mesh Covered Drug Eluting Coronary Embolic Protection Stent, distal embolization, percutaneous coronary intervention, strength evaluation, restenosis, bench-scale experiments.

Introduction:

Primary percutaneous coronary intervention (PCI) with stent placement is the recommended treatment for patients diagnosed with ST-segment-elevation myocardial infarction (STEMI) patient (*O'Gara et al., 2013*). STEMI is a severe form of heart attack characterized by a complete blockage of a coronary artery, resulting in an interruption of blood flow to a specific area of the heart muscle. PCI involves inserting a catheter into the blocked artery to open it up and restore blood flow, and stent placement refers to the placement of a small wire mesh tube (stent) to keep the artery open and prevent it from closing again. This treatment approach is considered the preferred and most effective method for managing STEMI cases, as it helps to promptly restore blood flow to the affected area of the heart, minimizing damage and improving patient outcomes.

During a STEMI, a blood clot or thrombus forms within a coronary artery, causing a complete or partial blockage. Thrombus aspiration is a technique used during PCI to remove or reduce the clot burden before stent insertion. While thrombus aspiration can be successful in removing a significant portion of the thrombus, there is still a possibility of distal embolization occurring during the subsequent steps of stent placement. Distal embolization refers to the dislodgement of thrombotic material or plaque debris from the site of the blockage, which then travels downstream and occludes smaller vessels in the coronary circulation.

This can lead to reduced blood flow and compromise the blood supply to the heart muscle, potentially causing further damage or complications. The process of stent insertion itself carries a risk of dislodging or pushing thrombotic material downstream, especially if the clot is unstable or fragile. Despite successful thrombus aspiration, small particles or fragments can still be present within the vessel and can be mobilized during stent deployment. Additionally, the expansion of the stent within the artery can cause disruption or fragmentation of existing plaque, which may also result in embolic material being released into the distal circulation. Therefore, even with successful thrombus aspiration, the risk of distal embolization during stent insertion remains a concern. Strategies such as using embolic protection devices, including the mesh-covered drug-eluting coronary embolic protection stent mentioned earlier, is being developed and utilized to minimize the risk of embolization and optimize patient outcomes during PCI procedures for STEMI.

Hence, this research study introduces a new type of stent called the "Mesh Covered Drug Eluting Coronary Embolic Protection Stent." It is designed to reduce the occurrence of distal embolization in blood clot-containing arteries. The stent has a thin and flexible biodegradable mesh covering, which helps to reduce the risks like restenosis (re-narrowing of the artery) and stent thrombosis (blood clot formation on the stent). The stent is coated with a drug called sirolimus, which works differently from other drugs by preventing the activation and growth of certain immune cells and the formation of antibodies. This drug mechanism makes it effective for preventing infection in the coronary arteries after stent implantation. Through bench-scale experiments, we have confirmed that the "Mesh Covered Drug Eluting Coronary Embolic Protection Stent" is strong and durable that has the potential to effectively address the issue of distal embolization during the procedure known as percutaneous coronary intervention.

Materials and Methods:

(a) Stent Design

The cobalt chromium L605 laser slotted hypo-tube plays a crucial role as a primary component in the production of a bare metal stent. This stent consists of multiple segments that enable controlled expansion and seamless integration with the pericardial cylinder. The stent's meticulous design ensures exceptional radial force and remarkable flexibility. The stent depicted in figure.01 is manufactured by (*Meril Life Sciences Private Limited*) and is further coated with the sirolimus drug. Its primary purpose is to offer flexibility and radial force while mitigating the risk of distal embolization to the coronary artery during percutaneous coronary intervention (PCI).



Figure.01 Sirolimus drug coated metal stent

(b) Knitted Mesh as a Covering Material

The coronary embolic protection stent incorporates a 28 micron Poly Lactic-co-Glycolic Acid (PLGA) polymer filament sleeve, manufactured by *Biogeneral-USA*, which acts as a protective barrier. This sleeve, depicted in figure.02, is a knitted mesh comprising micron-level fibers arranged in an optimal geometric configuration. The primary objective is to balance flexibility and strength characteristics of the fiber material to ensure optimal performance. The sleeve can be securely attached to various stent types and expands

seamlessly upon stent deployment, preserving the stent's structural integrity. Functioning as a defense against emboli, the knitted mesh serves as a reliable protective shield. The use of biodegradable materials eliminates the need for additional removal procedures, providing an advantageous feature. Overall, the embolic protection stent offers an effective solution for preventing emboli while remaining compatible with different stent types.

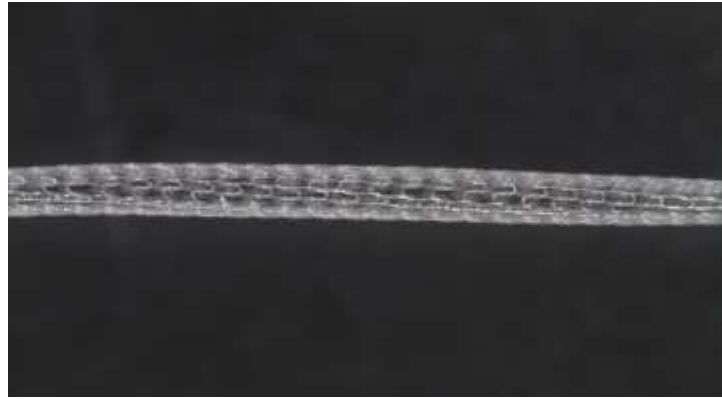


Figure.02 Biodegradable Poly (Lactic-co-Glycolic Acid) (PLGA) Knitted Mesh

A circular weft knitting machine (*Lamb-United States*) was used to create a knitted mesh tube with an average diameter of 1.4 mm. The machine's knitting head had a diameter of 3 mm, allowing for post-implantation over-expansion. The knitted mesh cylinder was positioned beneath the proximal and distal elements of the stent, covering its main body. The opposing bars on the ends of the proximal and distal elements were tucked under the knitted mesh cylinder. To secure the knitted mesh cylinder to the stent, the same filament and a predetermined knotting pattern were used. This arrangement ensured that the stent had single-layer coverage, avoiding folding or double layers that could increase its profile. It also maintained the stent's trackability and flexibility. Figure.03 depicts the knitting machine, while figure.04 illustrates the knitting head used in the process which consisted of mainly three components: Yarn guide assembly, sleeve alignment keys and sleeve.



Figure.03 Knitting Machine

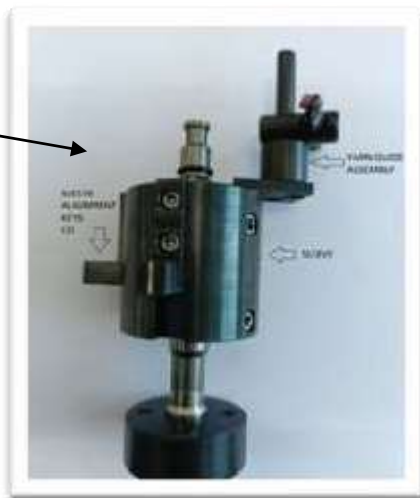


Figure.04 Knitting Head

(c) Covering of Biodegradable Polymeric Knitted Mesh on Stent

The procedure involved a meticulous process using forceps and a needle to precisely wrap a mesh around a cobalt-chromium metal stent, which had been coated with the drug sirolimus. The mesh was thoroughly cleaned using 70% isopropyl alcohol (*Sigma-Aldrich, USA*). A balloon catheter with a diameter of 3.5 mm was utilized to inflate and securely fasten the mesh around the stent. To secure the loose ends of the mesh's thread, a 28-micron monofilament made of PLGA was employed, and the knots were held in place using a supporting mandrel. The resulting assembly, as depicted in figure 05, consisting of the mesh-covered stent, underwent a comprehensive visual inspection to ensure that the surface, position, and knots met the specified requirements.

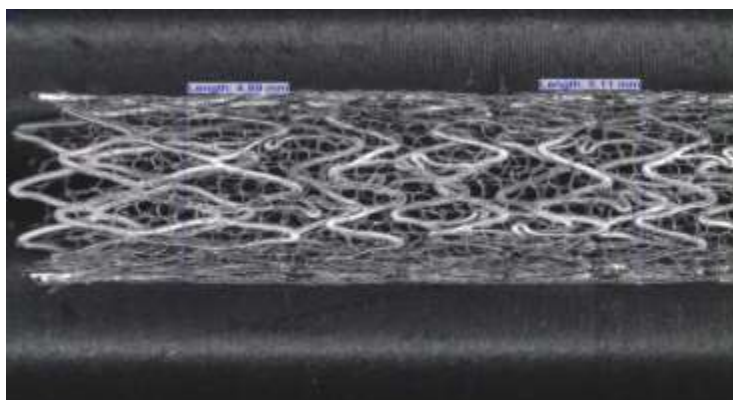


Fig.05 “Coronary Embolic Protection Stent” Covered with Biodegradable Polymeric Knitted Mesh

Hypothesis suggests that when knitted mesh is applied to a drug-coated stent, there is a high likelihood of unintentional drug loss. To address this issue and retrieve the lost drug, the mesh-covered stent was re-coated with sirolimus drug by spray coating gun as shown in the figure.06 to replenish the exact amount of drug that was inadvertently lost during the mesh application process.

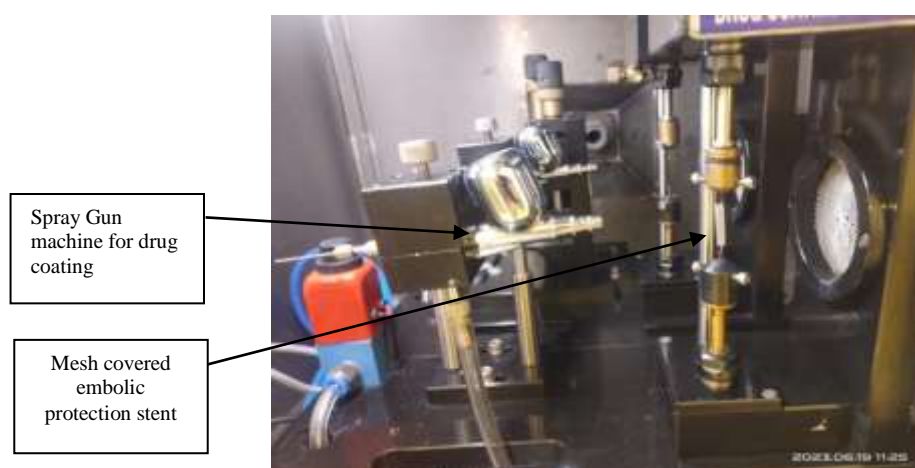


Figure.06 Drug Coating onto a Mesh-Covered Stent using a Spray Gun Machine

Once the inspection confirmed the desired specification, the embolic protection stent was released for crimping onto the delivery system. Furthermore, the stents were stored in airtight centrifuge tubes until they underwent the crimping process.

(d) Crimping of Mesh Covered Implant on Delivery System

The drug-coated embolic protection stent, equipped with a mesh covering, underwent a meticulous folding procedure onto the balloon catheter. This precise operation, illustrated in figure.07, took place within a controlled environment utilizing a crimping machine (*FabTech Technologies International Ltd*). The clean room facility strictly adheres to class-100 standards, guaranteeing a remarkably pure and meticulously filtered laminar airflow. The crimping process, carried out under class-10000 conditions, was executed in accordance with a thoroughly validated and approved method, ensuring unwavering consistency and superior quality.

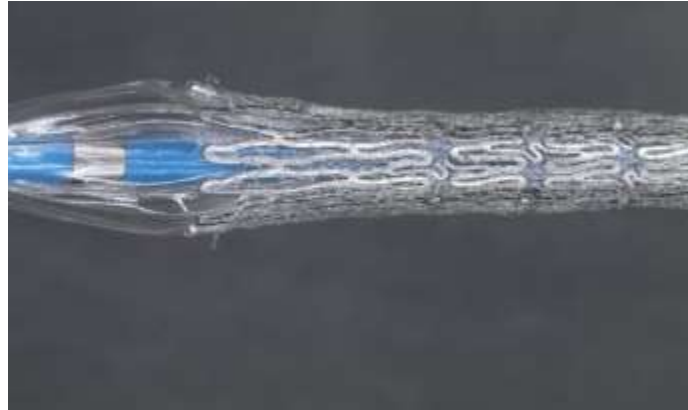


Fig.07 "The Mesh-Covered Drug-Coated Coronary Embolic Protection Stent System" is carefully crimped onto a balloon catheter

The percutaneous transluminal coronary angioplasty (PTCA) balloon catheter's hub was connected to a crimping machine's luer clamp, specifically the one manufactured by Machine Solutions Inc. USA. The opposite end of the PTCA balloon catheter was linked to an embolic protection stent, which was meticulously positioned on a V-shaped block and inserted into the crimping head. Within the crimping head, the stent was properly situated, sandwiched between two teflon films serving as a continuous barrier between the stent's mesh and the crimp head. After each cycle, the system automatically introduced new film from attached spools into the crimp head.

The crimping process for the embolic protection stent entailed several steps. A total of six phases or runs were performed, and the specific diameter, force, and dwell time required for crimping depended on the stent's size. Following the initial run, the stent was removed from the crimp head and positioned between two radio-opaque markers using a 10X eyeglass. If necessary, the stent system might have been repositioned within the crimp head to achieve the desired shape. Once the stent was successfully crimped, it was extracted from the crimp head and luer clamp, and the movement of the protective wire (stylet) was examined to ensure there was no resistance. The uniformity of the crimping and the final diameter of the crimped stent were assessed at three positions: proximal, middle, and distal. The position of the stent between the radio-opaque markers was verified using a stereoscopic microscope. An inflating device was utilized to detect any leakage in the stent system. If all the evaluations were satisfactory, the crimped embolic protection stent system, along with the delivery system (balloon catheter), was placed in a protective coil or hoop tray. Subsequently, it was inserted into a coated TYVEK pouch and sterilized using ethylene oxide gas.

Result and Discussion:

(a) Ensuring Compliance: Validating the Universal Radial Compression Property of a "Coronary Embolic Protection Stent"

"The Coronary Embolic Protection Stent" manufactured by (*Meril life sciences Pvt. Ltd*) underwent radial strength testing to verify its universal radial strength value according to the EN ISO 225392:2012 standard.

To assess the stent's strength, a radial strength testing procedure was conducted on a total of three sterile samples, each with different diameters. The testing was performed using a 15 mm master calibrated radial analyzer shown in the figure.07 manufactured by (*Blockwise Engineering in Germany*). This equipment is specifically designed for measuring radial strength in stents. The radial strength measured for the three sterile samples with different diameters, resulted in values of 34.46 N, 58.85 N, and 38.85 N. According to the EN ISO 225392:2012 standard, the minimum required universal radial strength for stents is 10 N. All three samples surpassed this minimum requirement, indicating that their radial strength exceeded the specified threshold. Based on these findings, it has been concluded that the tested stent samples are suitable for implantation in coronary arteries. This validation confirms that the stents possess the necessary strength which would withstand the forces exerted within the coronary arteries and would further maintain their structural integrity during implantation and subsequent use.

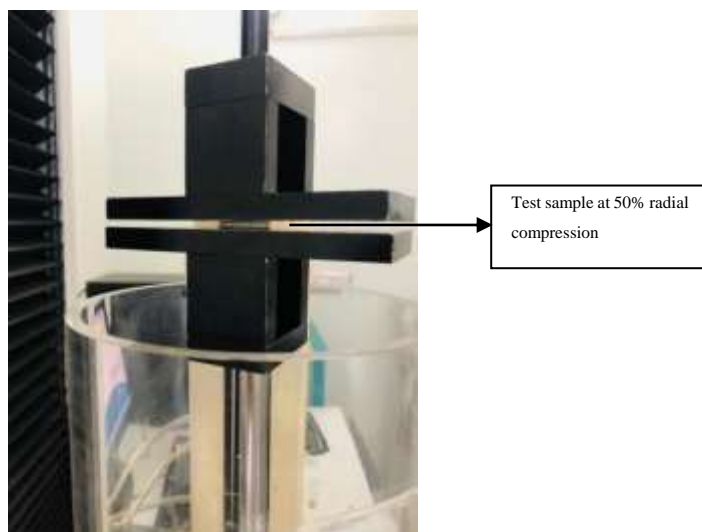


Fig.07 The Test Sample is subjected to a 50% Radial Compression using Universal Radial Strength Equipment

(b) Test Method to Assess the Tensile Strength Characteristics of the 28 micron PLGA Monofilament Utilized to Compose the Covered Mesh:

In order to ensure stability during deployment, the PLGA monofilament used to knit a mesh may experience repulsion from the inner surface of the catheter. To address this issue, it is crucial to secure the strength of the filament. Therefore, we conducted a tensile strength test to assess its performance under these circumstances.

The tensile strength of the monofilament was evaluated using the Win Test TM Analyzer, a Universal Testing Machine. Various parameters were measured during the test, including peak stress (psi), elongation (%), modulus (ksi), and break load (gf). The test outcomes, along with the corresponding readings are summarized in Table.01.

Table.01 Test outcomes of Monofilament Tensile Strength.

Specimen	Diameter (in)	Peak Stress (psi)	Elongation (%)	Modulus (Ksi)	Break Load (gf)
1	0.00109	90169	43	713	37.546
2	0.00108	92520	42	641	38.394
3	0.00109	97876	45.1	712	41.262
4	0.00111	103764	47.5	666	45.488
5	0.00109	103855	48	718	43.861
Mean	0.00109	97637	45.1	690	41.310
Minimum	0.00108	90169	42	641	41.262
Maximum	0.00111	103855	48	718	37.546

Table.01 presents the average tensile characteristics of the specimen, which are crucial for ensuring the required strength to withstand external forces that may impact the physical properties of the outer mesh. By reporting the mean values, the table offers a representative measure of the typical or average strength of these important parameters. This information is vital as it enables the evaluation of the outer mesh's capability to endure various external forces without experiencing adverse effects. The inclusion of mean values serves to highlight their significance as a benchmark or reference point for assessing the strength of the outer mesh. Consequently, significant deviations from these mean values in the actual specimen measurements may indicate potential weaknesses or vulnerabilities in the mesh's ability to withstand external forces. To summarize, the table presenting mean values of the specimen provides insights into the typical strength of the outer mesh and facilitates the assessment of its resilience against external forces that could potentially impact its physical properties.

Conclusion:

In conclusion, the experimental evaluation of the "Mesh Covered Drug Eluting Coronary Embolic Protection Stent" demonstrated strong evidence supporting its successful performance and compatibility. The stent's radial compression property and the monofilament tensile strength of the "28 micron PLGA monofilament" used in the construction of the covered mesh, emphasizes its durability and flexibility of the stent system. In-house bench-scale testing confirmed the stent's flexibility and durability, which are crucial factors for in-vivo implantation. Therefore, it ensures that if this "Mesh Covered Drug Eluting Coronary Embolic Protection Stents" were implanted in a patient, it would deploy smoothly, conform to the vessel anatomy, adapt to vessel movement, and provide patient comfort. We have commenced a pre-clinical study, and we anticipate unveiling the results in our forthcoming research article.

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