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Original Research Paper

Evaluation of the Promesa™ JOY Self-Expanding Nitinol Peripheral Stent System's Safety and Performance in a Swine Model

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ABSTRACT:
The Peripheral Stent System is engineered for the treatment of peripheral artery disease (PAD), particularly in cases involving the superficial femoral artery and proximal popliteal artery. PAD leads to the narrowing or blockage of arteries, primarily affecting the lower extremities, which can result in severe complications like limb ischemia. This stent system, composed of a self-expanding nitinol stent paired with an over-the-wire (OTW) delivery system, is designed to reopen and maintain the patency of affected arteries, thereby restoring adequate blood flow. It adheres to rigorous standards as a class C implantable medical device, with its regulatory status authenticated by notification S.O. 1468 dated October 6, 2005. To assess its performance, the stent system was tested in a porcine model, specifically in the superficial femoral artery of three female pigs, chosen for their physiological similarities to human circulatory systems. The study included evaluations at six- and nine-months post-implantation, focusing on the deployment, patency, and vascular response of the stent. The results indicated that all animals remained healthy throughout the study, with no signs of morbidity or mortality. The stent system was deployed successfully in all cases, showing complete hemostasis and no blood leakage. Initial angiographic assessments revealed no early lumen loss; however, over time, some stenosis was observed 15% in one animal after six months and 10-12% in others after nine months. Histopathological analysis revealed moderate inflammation, mild to moderate vascular injury, and varying degrees of endothelial loss, with minimal to moderate fibrin deposition. Despite these findings, the stent system generally maintained vessel patency and blood flow, demonstrating its potential for clinical use in peripheral artery procedures. The study concluded that the Peripheral Stent System is safe and effective in this animal model, supporting its potential application for treating PAD in humans.

Keywords: Peripheral Stent System, Superficial femoral artery, Proximal popliteal artery, Nitinol stent, Porcine model, Deployment.

INTRODUCTION:

The Peripheral Stent System, classified as a class C implantable medical device, is specifically engineered for treating peripheral artery disease (PAD). PAD involves the narrowing or blockage of arteries, primarily in the lower extremities, resulting in reduced blood flow and potentially severe complications like limb ischemia. This stent system aims to combat these issues by reopening and maintaining the patency of the affected arteries, thereby restoring adequate blood flow.

The system consists of a self-expanding, braided nitinol (nickel-titanium alloy) stent paired with an over-the-wire (OTW) delivery system. The nitinol material ensures biocompatibility and flexibility, which are essential for the long-term success of the stent. It comes pre-mounted on a 6F to 8F OTW delivery system, compatible with 0.014" to 0.018" guide wires, and is available in lengths ranging from 80cm to 120cm. The comprehensive delivery system includes components such as an outer sheath, outer sheath flush port, guide wire flush port, handle, thumb slide, system lock, deployment lock, stent driver, stent length marker, distal sheath marker, and a catheter with a soft tip.

Indicated for patients with symptomatic de novo or restenotic native lesions, or occlusions of the superficial femoral artery and/or proximal popliteal artery, the Peripheral Stent System is also intended for peripheral vascular use following failed percutaneous transluminal

angioplasty (PTA). As a class C device, it adheres to rigorous standards to ensure safety and efficacy in clinical use.

To evaluate the deployment and vascular response of the stent system, studies were conducted on the superficial femoral artery of swine, chosen for their physiological similarities to human circulatory systems. In this research, the stent was implanted in three female pigs, with evaluations carried out at six- and nine-months post-implantation. These studies provided valuable insights into the stent's performance, including ease of deployment, patency rates, and histopathological outcomes.

MATERIALS AND METHODS:

Medication Details:

This section delineates the drugs administered to the animals prior to, during, and following surgery, specified in table no.1.

Table 1: Details of medications used in the study

Drug name	Manufactured by	Batch / Lot No.	Expiry date
Ketamine	Bharat Parenterals Ltd	PO293	April 2023
Xylazine	HL India	FHK0005	Jan 2023
Isoflurane	Neon Lab	KPNP700012	Feb 2023
Tramadol	Neon Lab	BN949265	Nov 2024
Enrofloxacin	VETINDIA	ES1924	Oct 2023
Thiopentone sodium	Neon Lab	172468	Feb 2023
Heparin 25000unis	Fusion	L11822105B	Mar 2024
Aspirin 75mg	USV private limited	04008665	Jun 2024
Clopidogrel 75 mg	Lupin	B2003651	Dec 2024

MATERIALS REQUIRED:

- Clippers (for hair removal)
- 18G puncture needle
- 8F sheath
- Guide wire (260 cm, 0.018-inch, Terumo)
- Guide catheter
- Angiography diagnostic catheter
- Stent delivery system (Peripheral Stent Systems)
- Outer sheath
- Outer sheath flush port
- Guide wire flush port
- Handle
- Stent driver
- Catheter with a soft tip

DEVICE DESIGN:

The Promesa™ JOY Peripheral Stent System is a Class C implantable medical device designed for peripheral vascular use, specifically indicated for treating patients with symptomatic de novo or restenotic native lesions or occlusions in the superficial femoral and or proximal popliteal arteries [1]. It is particularly suitable for patients who have not responded to percutaneous transluminal angioplasty (PTA). This system includes a self-expanding, braided stent made from biocompatible nitinol, a nickel-titanium alloy known for its flexibility and strength. The stent is pre-mounted on an over-the-wire (OTW) delivery system, available in 6F to 9F sizes, which is compatible with 0.014" to 0.018" guide wires and comes in 80 cm and 120 cm lengths. The OTW delivery system is equipped with an outer sheath, flush ports for both the sheath and guide wire, a handle, thumb slide, system and deployment locks, a stent driver, length and distal sheath markers, and a catheter with a soft tip for smooth navigation. The device is engineered to meet the challenges of peripheral vascular procedures by ensuring reliable delivery and deployment in complex vascular anatomy.

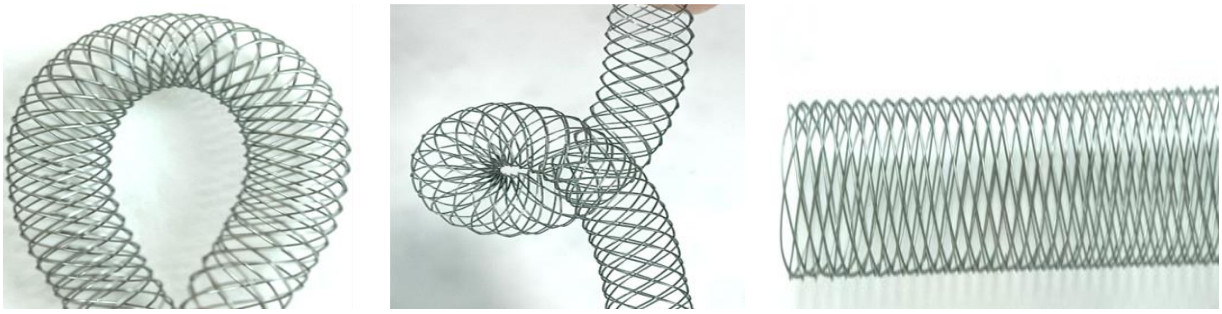
SIZE MATRIX:

Table 2: Size matrix of Stent and sheath

Stent Diameter (mm)	Stent Length (mm)	Sheath Compatibility ; F
4.00	20,30,40,60,80,100,120,150	6
5.00	20,30,40,60,80,100,120,150	

6.00	20,30,40,60,80,100,120,150	
7.00	20,30,40,60,80,100	7
8.00	20,30,40,60,80,100	

PRODUCT IMAGE:



(A) Front view (B) Flexibility (C) Side view

Figure 1: Braided Peripheral stent

DEVICE COMPONENT DESCRIPTION:

Table 3: Device components

Stent material	Nitinol wire
Wire thickness	150 / 200µm
Delivery system usable length	80cm to 120cm
Sheath compatibility	6F to 8F
Guidewire compatibility	0.014″ to 0.018″

EXPERIMENTAL PROCEDURES:

Fasting:

The animals were fasted, and water was withheld overnight before the procedure. Animals were kept NBM (Nothing by mouth) for 6 hours post-recovery from the procedure.

Animal Preparation included:

Before the surgical procedure, each animal was administered anticoagulant treatment, including Aspirin at 300 mg per animal and clopidogrel at 75 mg per animal, orally for at least 3 days. The anticoagulant treatment was continued from day 1 until the animals were sacrificed, with the doses being reduced to Tab. Aspirin 100 mg and Tab. Clopidogrel 75 mg per animal. Each animal was then anesthetized, instrumented, and monitored using Ketamine at a dosage of 15 mg/kg via intramuscular injection, Xylazine at a dosage of 2.5 mg/kg via intramuscular injection, and Propofol at a dosage of 0.5 mg/kg via intravenous bolus, followed by inhalation anesthesia ranging from 1-3% through a facemask. The animal's neck area was prepared by clipping it free of hair for the carotid artery approach and ECG leads application, and it was given atropine at a dosage of 0.05 mg/kg via intramuscular injection to control discharges from the respiratory tract that could obstruct the endotracheal tube placed for inhalation anesthesia. The animal was then prepared and draped aseptically for the surgical procedure with the appropriate medications, as specified in Table 1, and all relevant information regarding the surgical preparation and anesthesia for the study animals was recorded. Body weight of the animal at each time interval was specified in table no. 4.

Table 4: Animal P1, P2, P3 body weights (Day 0, 6 months, 9 months)

Animal Number	Day 0	6 months	9 months
P1	57.9 kg	83.8 kg	-
P2	54.2 kg		78.8 kg

P3	56.4 kg	-	85.2 kg

EXPERIMENTAL DESIGN OR ANIMAL TRIAL:

On Day 0, the procedure started with a cut-down at the neck to expose the carotid artery. An 18G puncture needle was used to insert a 6F to 8F sheath. Activated clotting time (ACT) was measured before and after heparin administration to ensure proper anticoagulation, aiming for ACT values between 250-550 seconds. An initial dose of 100 IU/kg IV heparin was given, with subsequent doses adjusted based on ACT values. A 260 cm, 0.018-inch guide wire (Terumo) and guide catheter were used to anchor the olio-femoral arteries. Angiography was performed on both olio-femoral arteries using a diagnostic catheter to select the implantation site. Baseline angiography and quantitative vascular angiography (QVA) were used to identify the target region based on Reference Vessel Diameter (RVD). Stents of appropriate size were selected according to QVA and RVD. The catheter was withdrawn, keeping the Guidewire with radio-opaque markers at the target site, and the stent delivery system was inserted using the Guidewire. Self-expandable peripheral artery stents were implanted following the instructions for use (IFU). The implantation matrix from the study plan served as a random guide, with stents deployed based on reference vessel diameter and target region length, and the actual stent used for each site recorded. Immediate follow-up angiography and QVA were performed 60 minutes post-implantation to assess and record antegrade flow through the stented region, after which the animals were allowed to recover.

On Day 1, the monitoring phase began, and the study duration depended on the stent performance. One animal was observed for 6 months, and two animals for 9 months, with anticoagulant treatment continuing until the 9-month terminal day. Health monitoring included cage-side observations and daily health status checks. At the 6-month follow-up, angiography and QVA were performed to assess antegrade flow, and the animals were euthanized for harvesting of the stented arteries for photography, gross, and histopathological evaluation. At the 9-month follow-up, the same procedures were repeated for the remaining animals. Final evaluations included gross necropsy and photography of all stented arteries to document findings. ACT values of the animals throughout the study was mentioned in table no.5.

Table 5: Animal Pl, P2, P3 ACT Values (Day 0 to Termination Day)

S. No	Animal Number	Day 0		6 Months		9 Months	
		Baseline (sec)	Post heparin	Baseline	Post heparin	Baseline	Post heparin
1	P1	82	281	94	298	-	
2	P2	92	290			91	284
3	P3	81	287	-	-	102	306

Monitoring During Procedure: Day 0 to 9 months:

The animals were continuously monitored throughout the procedure from Day 0 to 9 months. Their electrocardiogram (ECG), respiration rate, heart rate, and oxygen saturation were continuously recorded. Detailed records were kept for the drugs used, dosages, and methods of administration.

During the pre-operative, intra-operative, and post-operative phases, the following procedures were followed:

Tramadol was administered at a dosage of 4 mg/kg intramuscularly for analgesia before anesthesia induction. Atropine was given at a dose of 0.05 mg/kg intramuscularly as a pre-anesthetic. The animals were then sedated with Ketamine at 15 mg/kg intramuscularly, Xylazine at 2.5 mg/kg intramuscularly, and Propofol at 0.5 mg/kg intravenously, followed by inhalation of Isoflurane (1-3%) through a face mask. During the intra-operative and post-operative phases, anesthesia was sustained with 1-3% Isoflurane administered via endotracheal intubation. All medications given to each animal during the procedure were carefully documented, including details of the induction anesthesia drug, dosage, and route of administration, which were recorded in the surgical record.

Quantitative Vessel Analysis (QVA):

A pre-implant angiogram was conducted to establish the baseline mean vessel diameters for the test item implantation. Subsequently, quantitative vascular analysis (QVA) was performed on the post-implant and follow-up angiograms at 6 and 9 months. The following measurements were recorded:

1. Mean vessel diameter of the artery before implantation, compared to post-implant and follow-up diameters of the stented region.
2. Stent to artery ratio: calculated as the stent diameter (post-implant) divided by the mean vessel diameter (baseline).
3. Minimal Lesion Diameter (MLD) of the stented region post-implant.
4. Early Lumen Loss (ELL): calculated as the difference between MLD post-implantation and MLD at 60 minutes.
5. Late Lumen Loss (LLL): calculated as the difference between MLD post-implantation and MLD at follow-up.
6. Percent stenosis diameter, calculated using dedicated software. All results, vessels, and devices used were documented for each animal

OBSERVATION:

From Day 0 to 9 months, the following parameters were continuously monitored during the procedure: ECG, respiration rate, heart rate, and oxygen saturation. To manage pain, Tramadol (4 mg/kg IM) was given before the operation, while Atropine (0.05 mg/kg IM) was administered as a pre-anesthetic. Sedation was induced using Ketamine (15 mg/kg IM), Xylazine (2.5 mg/kg IM), and Propofol (0.5 mg/kg IV), followed by inhalation of Isoflurane (1-3%) using a face mask. Anesthesia was maintained through endotracheal intubation with 1-3% Isoflurane. Medications used during the procedure were documented, and standard parameters such as body weights, fluoroscopy, clinical pathology, necropsy, and histopathology were monitored. Body weights were recorded on the acclimatization start day, the day of the procedure, and the day of euthanasia. Throughout the day, observations were made for any signs of illness or distress, including the monitoring of pain, rebleeding, and cardiopulmonary patterns. After the procedure, observations continued to be made for any health deviations. The evaluation of the test items included assessing the delivery system's ability to access the target site, ease of movement and handling, visualization, functional hemostasis, deployment accuracy and efficacy, stent migration, withdrawal of the delivery system, leakage or hemostasis, self-expansion speed, ease of deployment and withdrawal, and angiographic patency. All deployed stents demonstrated patency and good flow, with no observed morbidity or mortality.

RADIOGRAPHY AND ANGIOGRAPHIC FINDINGS:

In this study, three test items of the peripheral self-expanded stents were examined. The test results showed the following findings:

P1 - 6.0X60 mm in SFA (Superficial Femoral Artery):

The trackability, handling, visualization, and haemostasis scores were all 9 out of 10. The stent expanded uniformly without jumping. After deployment, the stent length was 103.90 mm with no leakage, and it deployed very quickly. The delivery system was easily and swiftly withdrawn. Normal antegrade flow was observed with distal filling of all branches.

There was no immediate lumen loss after deployment, but the late lumen loss was 1.72 mm from a post-stent diameter of 5.71 mm. The Stent Area Ratio (SAR) was 1.21. At the 6-month follow-up, the stenosis percentage was 15.50%.

Table 6: Evaluated on qualitative deployment profile of the test items profile measurements criteria.

Sr No.	Stent Particulars	Reference Vessel Diameter	Stent length after deployment 60 min	Stent diameter after deployment 60 min	Crimped length
1	6X60mm Animal_P1_01538_SFA	4.63 4.31 3.82	103.90 mm	5.71 mm	145.7 mm
2	6X60mm Animal_P2_01528_SFA	5.49 4.93 4.40	95.40 mm	6.43 mm	145.6 mm
3	6X60mm Animal_P3_970418_SFA	6.59 4.93 4.52	82.20 mm	6.87 mm	154.0 mm

P2 - 6.0X60 mm in (Superficial Femoral Artery):

Higher scores indicate better performance. The trackability, handling, visualization, and hemostasis scores were all 9 out of 10. The stent expanded uniformly without jumping. After deployment, the stent length was 95.40 mm with no leakage, and it deployed very quickly. The delivery system was easily and swiftly withdrawn, and normal antegrade flow was observed with distal filling of all branches.

Angiographical measurement revealed no early lumen loss. The late lumen loss was 1.15 mm from a post-stent diameter of 6.43 mm. The Stent Area Ratio (SAR) was 1.14. At the 9-month follow-up, the stenosis percentage was 12.30%.

P3 - 6.0X60 mm in SFA (Superficial Femoral Artery):

Higher scores indicate better performance. The trackability, handling, visualization, and hemostasis scores were all 9 out of 10. The stent expanded uniformly without issues. After deployment, the stent length was 82.20 mm with no leakage, and it deployed very quickly. The delivery system was easily and swiftly withdrawn, and normal forward flow was observed with all smaller blood vessels filling properly.

Angiographical measurements revealed an early lumen loss of 0.75 mm from a post-stent diameter of 6.87 mm and a late lumen loss of 0.95 mm. The Stent Area Ratio (SAR) was 1.21. At the 9-month follow-up, the stenosis percentage was 10.50%.

Table 7: Angiographic quantitative vessel analysis and stenosis evaluation of test items.

S. No.	Stent	Target Vessel Animal ID	Baseline diameter(mm)	Stent Diameter (mm)	Stent to artery ratio	MLD (PI) (mm)	MLD 60 min (mm)	ELL (mm)	MLD follow up (mm)	MLD PI - MLD Follow up (mm)	LLL (mm)	% Angiographic stenosis
1	6.0X60 mm	SFA (9704I8-P3)	4.31	6.0	1.2170385	5.68	5.31	0.37	3.96	5.68-3.96	1.72	15.50%
2	6.0X60 mm	SFA (970418-P3)	5.24	6.0	1.1450381	5.32	5.74	- 0.42	4.17	5.32-4.17	1.15	12.30%
3	6.0X60 mm	SFA (01528-P2)	4.93	6.0	1.2170385	5.15	4.40	0.75	2.57	5.15-2.57	0.95	10.50%

Note- Note: LLD- Minimal Lesion Diameter; ELL- Early Lumen Loss; LLL- Late Lumen Loss; PI- Post implantation; SAR - Stent Artery ratio

PATHOLOGY:

Clinical Evaluation:

Blood samples were taken before the procedure on day 0 and again on the day of euthanasia. Hematology tests, including a complete blood count, differential count, and reticulocyte count, were performed. Biochemical parameters such as LDH, AST, creatinine, creatine kinase, urea, BUN, sodium, potassium, chloride, and calcium were also assessed before and after the procedure and the same was mentioned in table no.8 and table no.9.

Table 8 : Individual and summary data of clinical chemistry (Day 0)

Animal No.	Pl	P2	P3	Mean	SD
Aspartate amino transferase (U/L)	55	45	24	41.3	15.8
Calcium (mmol/L)	2.58	2.33	2.42	2.4	0.1
Creatine Kinase (U/L)	4400	1597	1730	2575.7	1581.3
Creatinine (Mmol/L)	139	174	125	146.0	25.2
Lactate dehydrogenase (U/L)	605	1047	467	706.3	303.0
Blood Urea Nitrogen (mmol/L)	3.08	2.94	2.94	3.0	0.1
Sodium (mmol/L)	142.1	140.1	141.7	141.3	1.1
potassium (mmol/L)	3.78	2.64	3.84	3.4	0.7
Chloride (mmol/L)	96.4	103.2	101.3	100.3	3.5

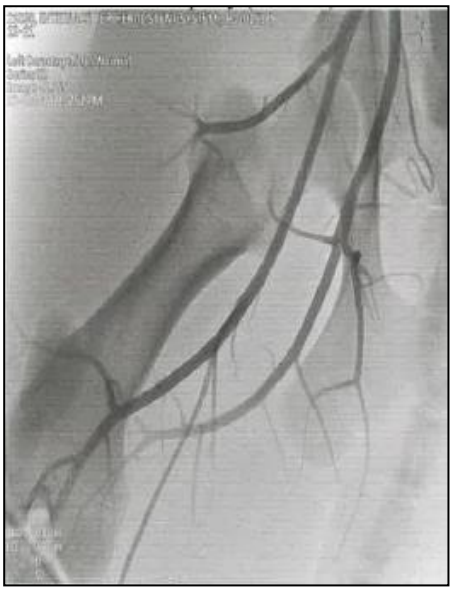
Table 9: Individual and summary data of clinical chemistry (terminal)

Animal No.	P1 (6 Months)	P2 (9 Months)	P3 (9 Months)
Aspartate amino transferase (U/L)	30	21	22
Calcium (mmol/L)	2.59	2.11	2.3
Creatine Kinase (U/L)	1653	609	1397
Creatinine (pmol/L)	188	126	177
Lactate dehydrogenase (U/L)	606	458	495
Blood Urea Nitrogen (mmol/L)	3.42	4.46	4.59
Sodium (mmol/L)	147	125.6	143.4
potassium (mmol/L)	3.7	4.08	3.44

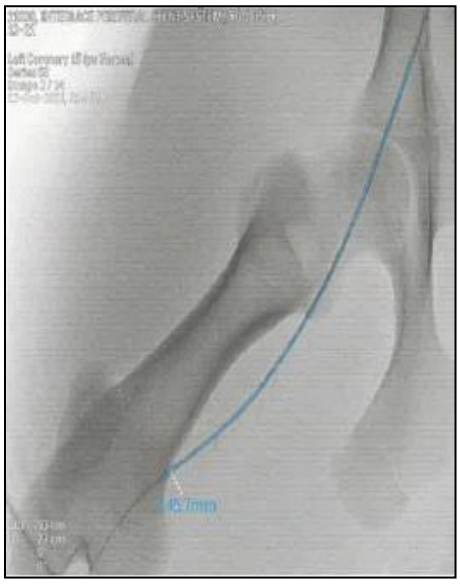
Chloride (mmol/L)	107.3	85.5	101.6

Euthanasia:
The animals were euthanized using intravenous thiopental sodium at a dose of 100 mg/kg. Death was confirmed by observing and listening to the heart and lungs, recording a systolic ECG, and noting zero oxygen saturation.

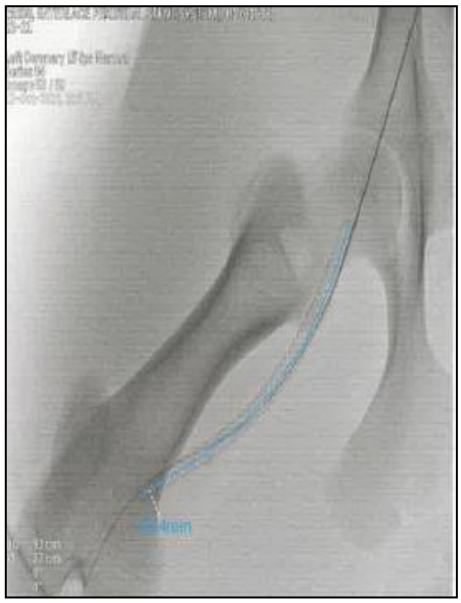
ANGIOGRAPHY IMAGE:



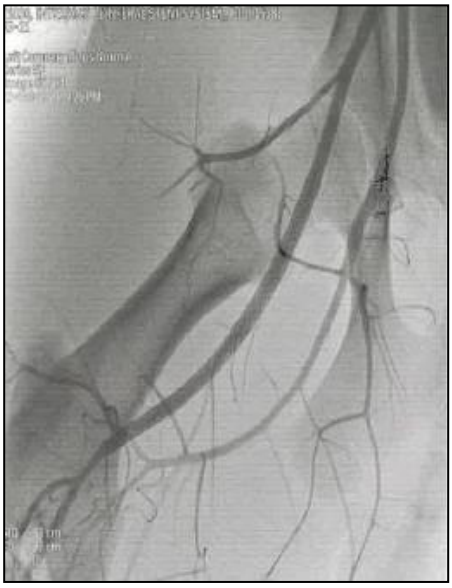
P1 SFA 6X60mm Base line angio on 0 day



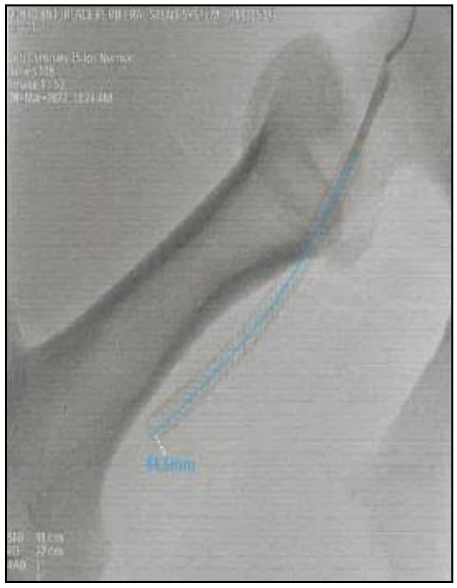
P1 SFA 6X60mm crimp length on 0 day



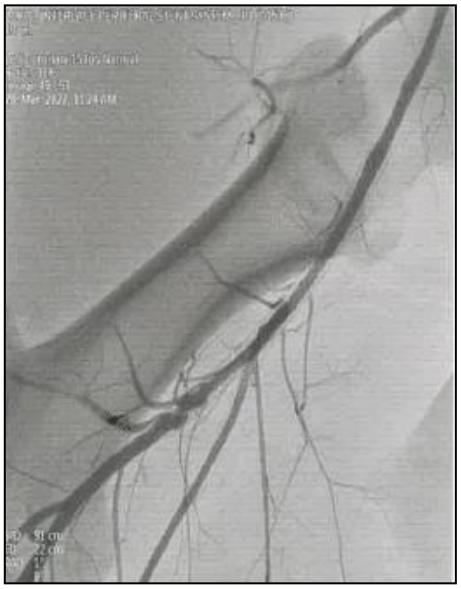
P1 SFA 6X60mm stent length on 0 day



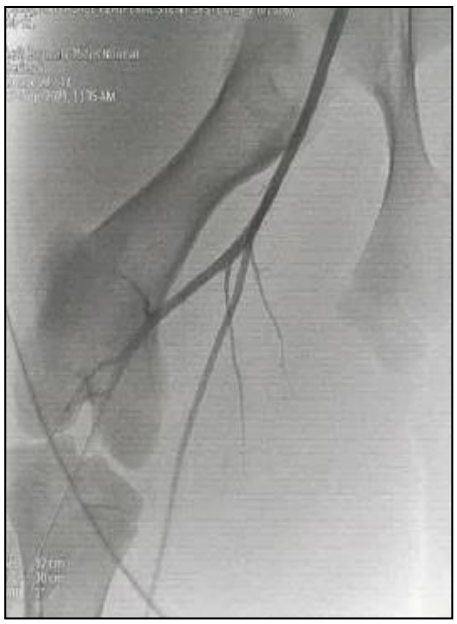
P1 SFA 6X60mm post stent angio on 0 day



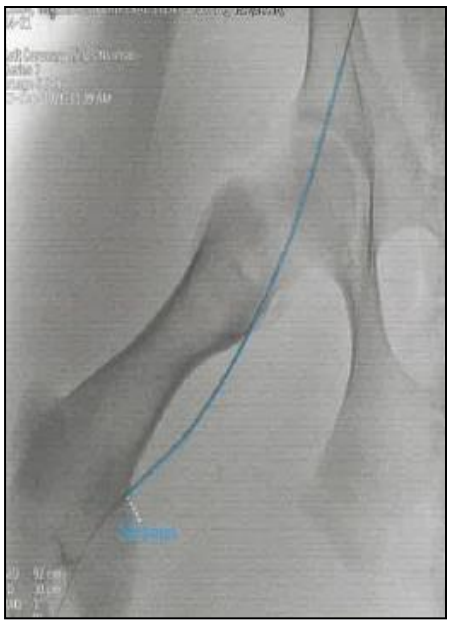
P1 SFA 6X60mm stent length on follow up day (6 month)



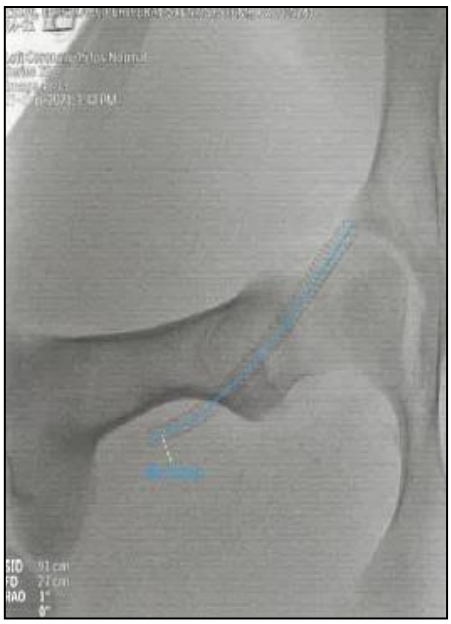
P1 SFA 6X60mm angio on follow up day (6 month)



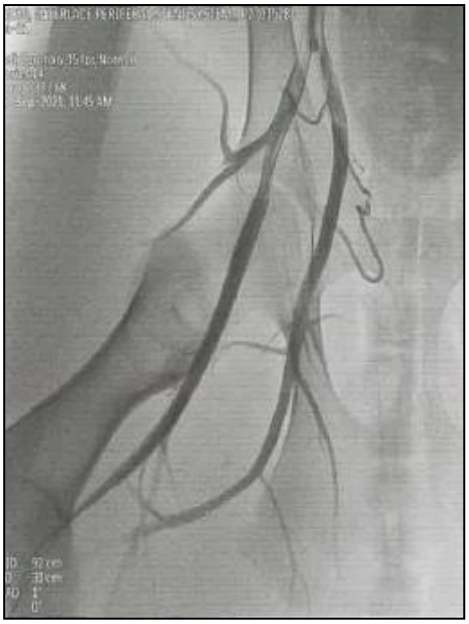
P2 SFA 6X60mm base line angio on 0 day



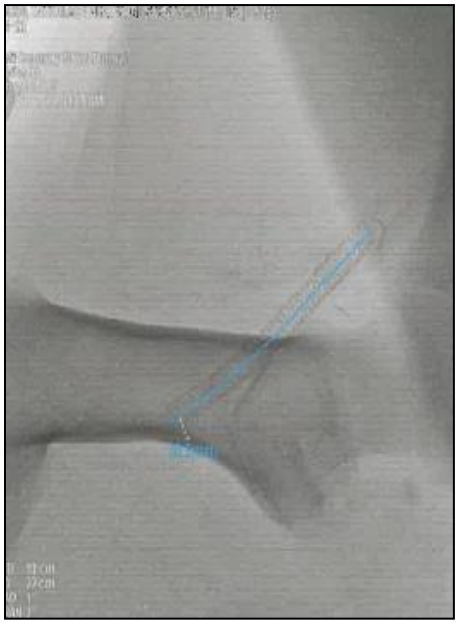
P2 SFA 6X60mm crimp length on 0 day



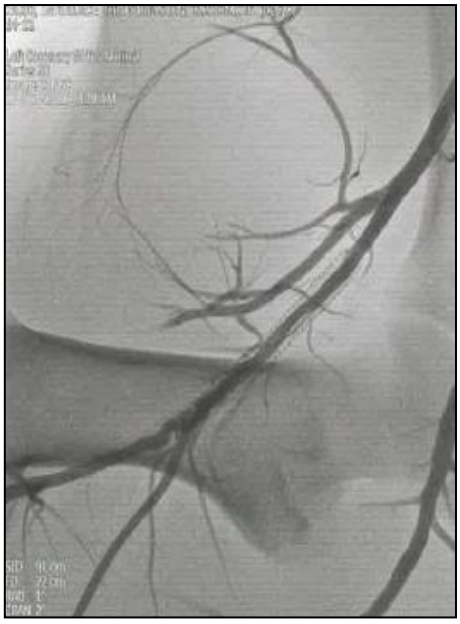
P2 SFA 6X60mm stent length on 0 day



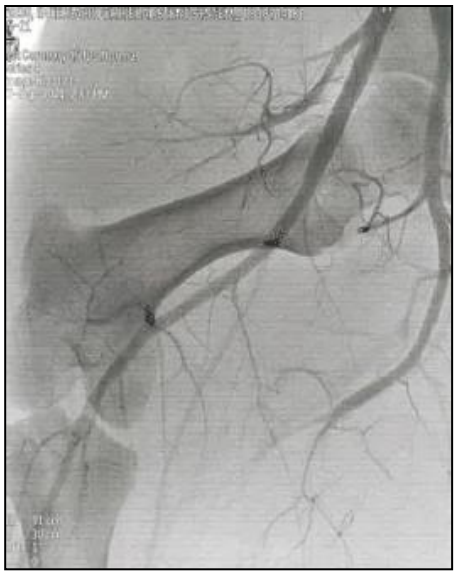
P2 SFA 6X60mm post angio 0 day



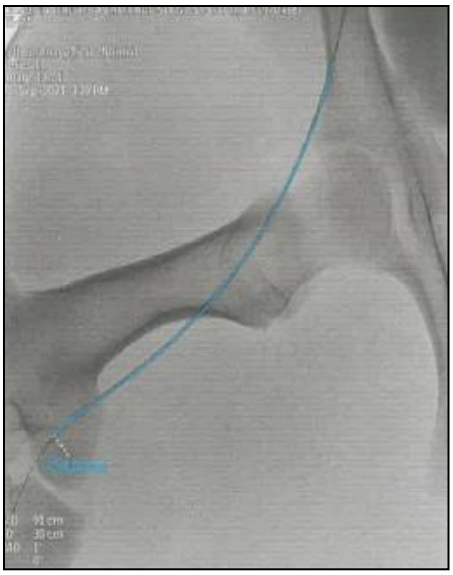
P2 SFA 6X60mm stent length on follow up day (9 month)



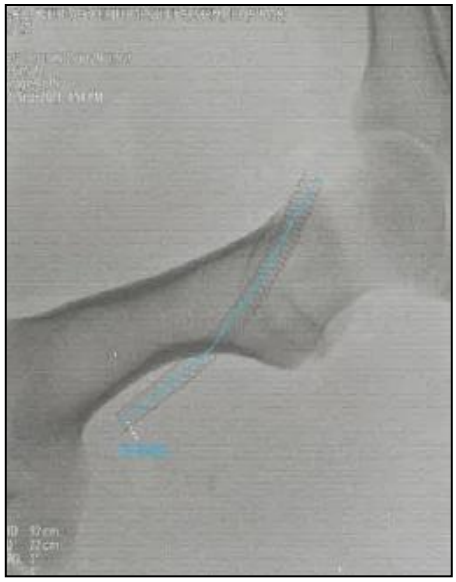
P2 SFA 6X60mm angio on follow up day (9 month)



P3 SFA 6X60mm base line angio on 0 day



P3 SFA 6X60mm crimp length on 0 day



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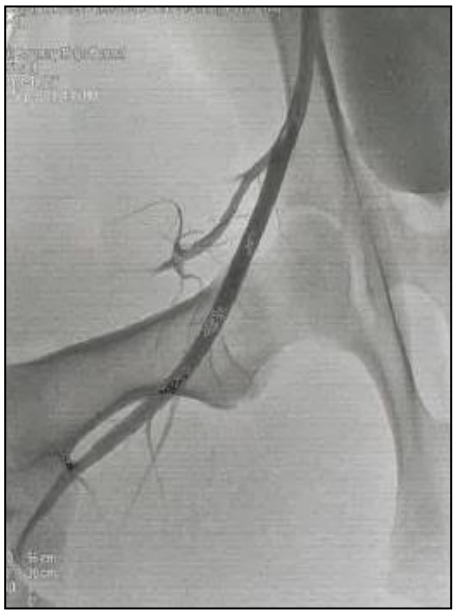
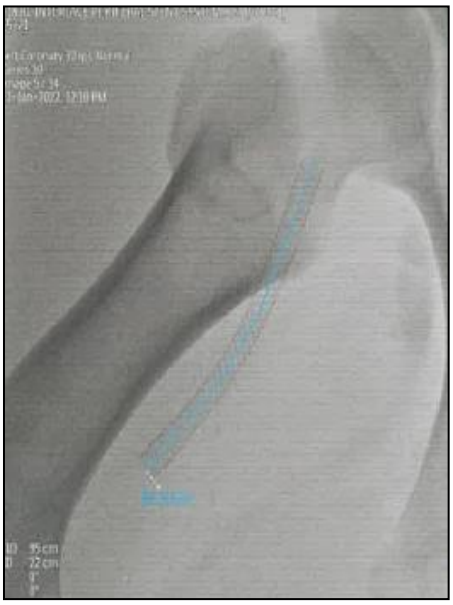
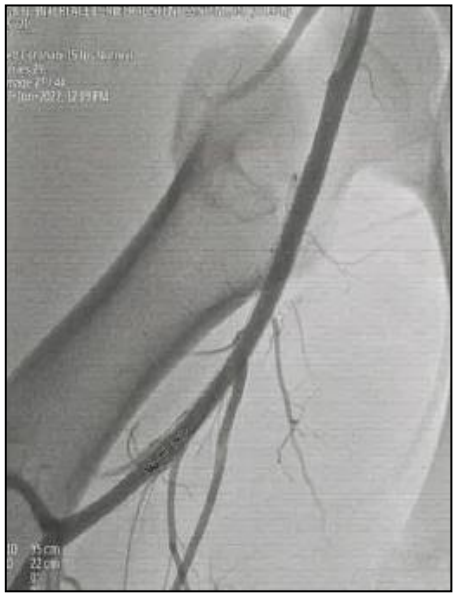


P3 SFA 6X60mm post stent angio 0 day



P3 SFA 6X60mm stent length on follow up day (9 month)



P3 SFA 6X60mm angio on follow up day (9 month)

Figure 2: Angiography Images of animal P1, P2 and P3

Table 10: Angiographic quantitative vessel analysis and stenosis of test items.

S. No.	Stent	Target Vessel Animal ID	Baseline diameter(mm)	Stent Diameter (mm)	Stent to artery ratio	MLD (PI) (mm)	MLD 60 min (mm)	ELL (mm)	MLD follow up (mm)	MLD PI - MLD Follow up (mm)	LLL (mm)	% Angiographic stenosis
1	6.0X60 mm	SFA (9704I8-P3)	4.31	6.0	1.2170385	5.68	5.31	0.37	3.96	5.68-3.96	1.72	15.50%
2	6.0X60 mm	SFA (970418-P3)	5.24	6.0	1.1450381	5.32	5.74	- 0.42	4.17	5.32-4.17	1.15	12.30%
3	6.0X60 mm	SFA (01528-P2)	4.93	6.0	1.2170385	5.15	4.40	0.75	2.57	5.15-2.57	0.95	10.50%

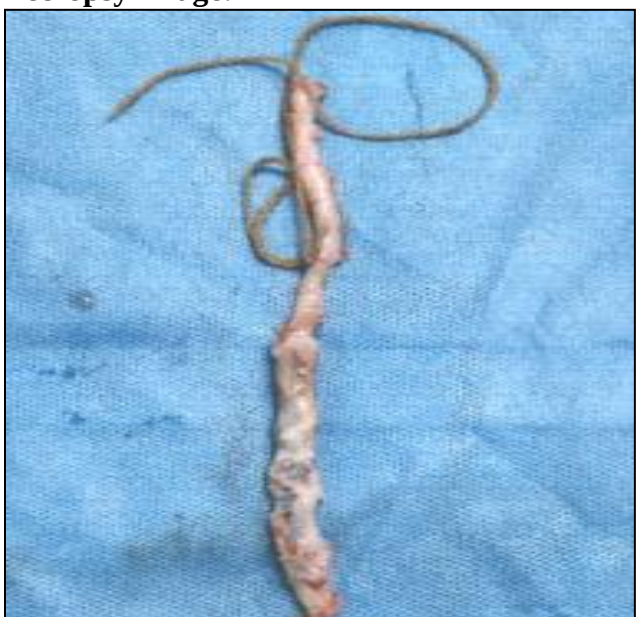
Note: LLD- Minimal Lesion Diameter; ELL- Early Lumen Loss; LLL- Late Lumen Loss;
PI- Post implantation; SAR — Stent Artery ratio

NECROPSY:

At scheduled sacrifice dates (PI at 6 months, P2 and P3 at 9 months), animals were euthanized by an overdose of thiopental sodium. External and internal examinations by pathologists revealed no lesions of pathological significance in any of the animals (PI to P3). The peripheral femoral arteries with stents were collected, flushed with normal saline to assess patency, and all stinted arteries were found to be patent, except for the superficial femoral artery (SFA) in animal P2, which was occluded.

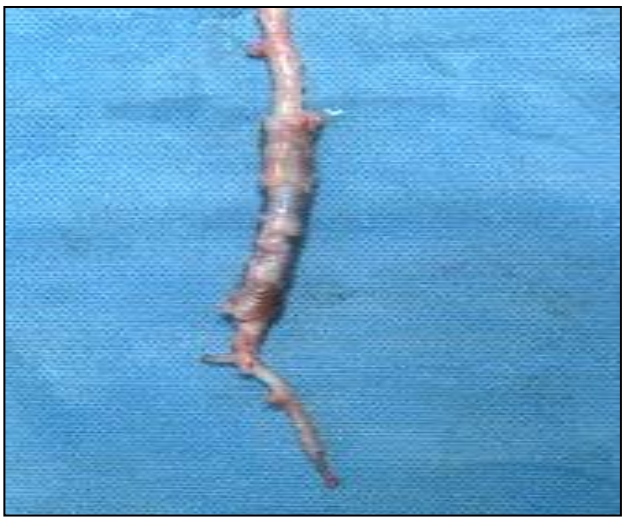
Gross necropsy was performed on the following organs: adrenals, aorta, bone marrow (femur/ribs/sternum), brain (including cerebrum, cerebellum, and pons), caecum, colon, duodenum, esophagus, eyes, gall bladder, heart, ileum, jejunum, kidneys, liver, lungs and bronchi, lymph nodes, mammary gland, skeletal muscle, sciatic or tibial nerve, ovaries, pancreas, parathyroid, pituitary, rectum, salivary glands, skin, spinal cord, spleen, stomach, thymus, thyroid, trachea, urinary bladder, uterus, and vagina. All organs were weighed, processed, and no abnormal findings were observed in any of them.

Necropsy Image:



Animal P1 superficial femoral artery

Animal P2 superficial femoral artery



Animal P3 superficial femoral artery (6X60 mm)

Figure 3: Necropsy Images of animal P1, P2 and P3

HISTOPATHOLOGY:

The histopathology report for animals from P1 to P3 indicates the following findings

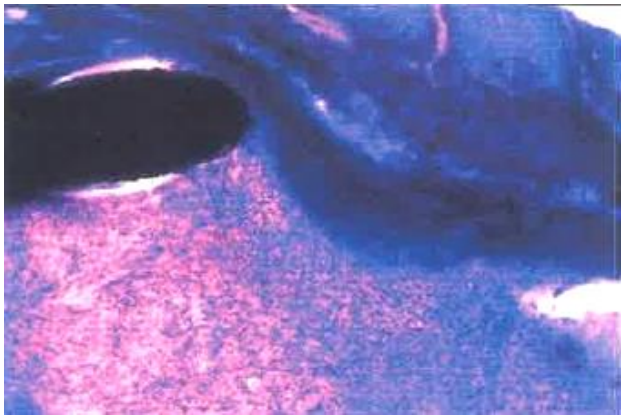
Animal 1:

During the gross necropsy of Animal 1, the heart, lungs, liver, and kidneys were thoroughly examined. The stented arteries were collected with the proximal section taken 2 cm above the stent and the distal section 5 cm below the stent.

Histological evaluation revealed an inflammation score of 2, indicating many inflammatory cells present around the strut, though they did not affect the surrounding tissue. Vascular injury was minimal, with a score of 1, reflecting a break in the internal elastic lamina. There was no smooth muscle cell loss observed (score 0). Fibrin deposition was mild and multifocal, receiving a score of 2 (Figure 4)

Morphometric measurements were recorded, including the luminal area, internal elastic lamina (IEL) area, and external elastic lamina (EEL) area, with percent area stenosis calculated accordingly. [Value] mm^2 represents the specific measurements obtained.

Histopathological images:

	
P1 proximal, superficial femoral artery,	**P1 proximal, superficial femoral artery,**

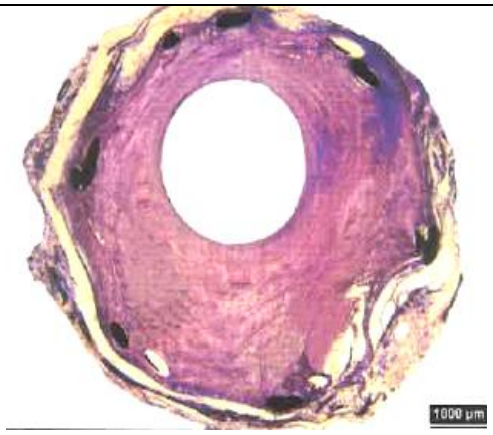
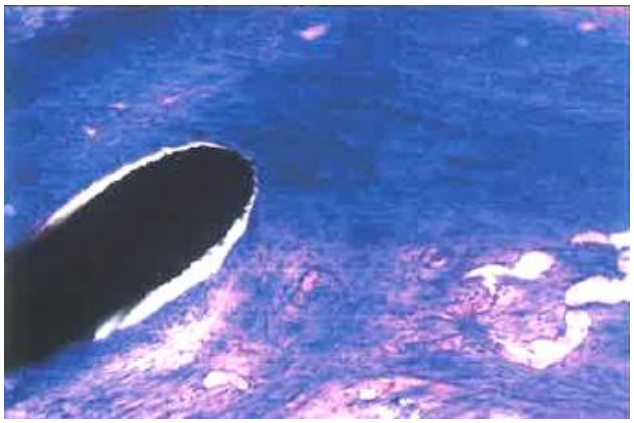
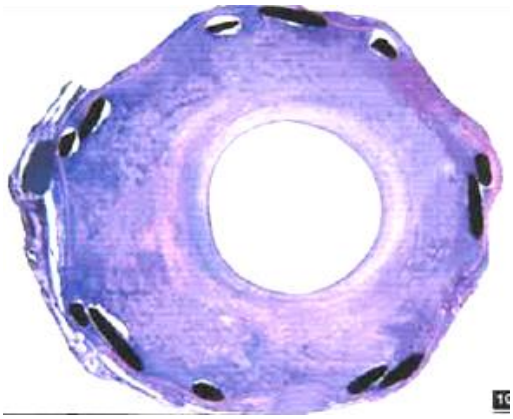
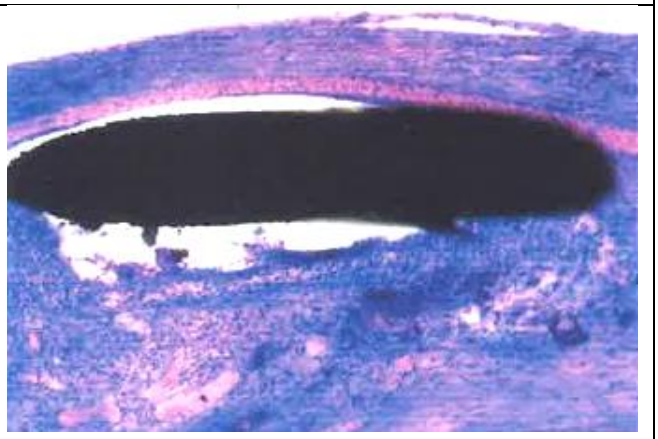
H&E 1.25X	H&E 10X
	
P1 mid, superficial femoral artery, H&E 1.25X	**P1 mid, superficial femoral artery, H&E 10X**
	
P1 distal, superficial femoral artery, H&E 1.25X	**P1 distal, superficial femoral artery, H&E 10X**

Figure 4: Histopathological images of animal P1

Animal 2:

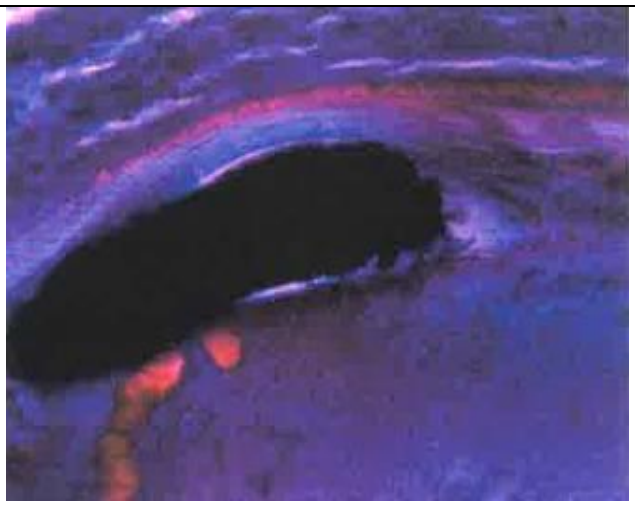
In the gross necropsy of Animal 2, the heart, lungs, liver, and spleen were examined. The stented arteries were collected with the proximal section located 3 cm above the stent and the distal section 4 cm below the stent.

Histological evaluation showed significant inflammation, with a score of 3, indicating many inflammatory cells that were effacing the surrounding tissue. Vascular injury was more pronounced, scoring 2 due to the perforation of the media. Smooth muscle cell loss was minimal, scoring 1, with less than 12% of the area affected. Fibrin deposition was moderate and regionally diffuse, earning a score of 3. (Figure 5)

Morphometric measurements were recorded for the luminal area, internal elastic lamina (IEL) area, and external elastic lamina (EEL) area, with the percent area stenosis calculated based on these values. The specific measurements are represented as [Value] mm^2.

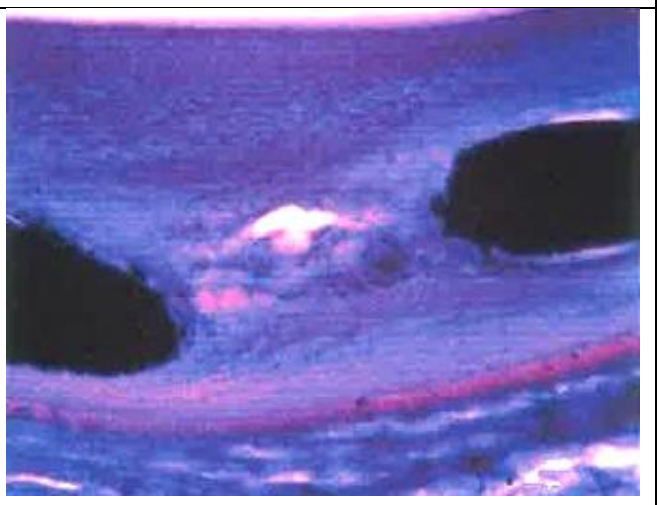
Histopathological images:

P2 proximal, superficial femoral artery, H&E 1.25X



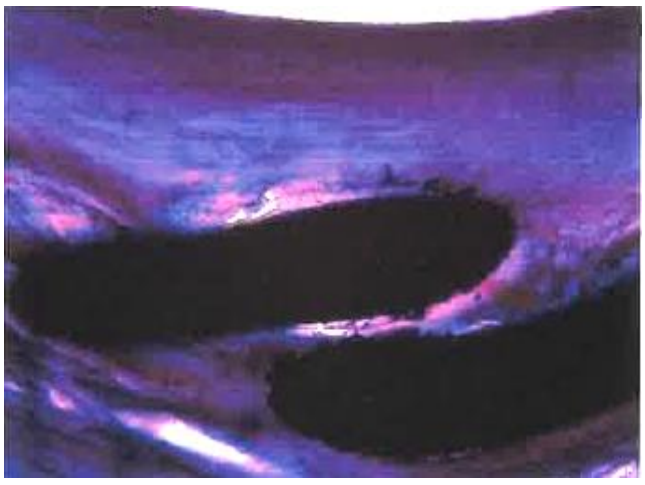
P2 proximal, superficial femoral artery, H&E 10X

P2 mid, superficial femoral artery, H&E 1.25X



P2 mid, superficial femoral artery, H&E 10X

P2 distal, superficial femoral artery, H&E 1.25X



P2 distal, superficial femoral artery, H&E 10X

Figure 5: Histopathological images of animal P2

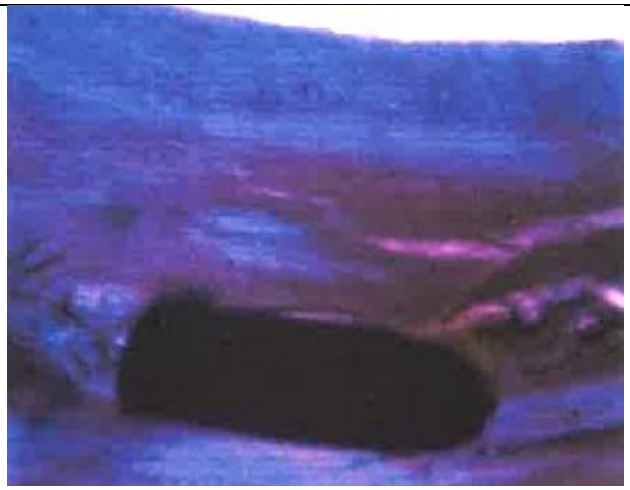
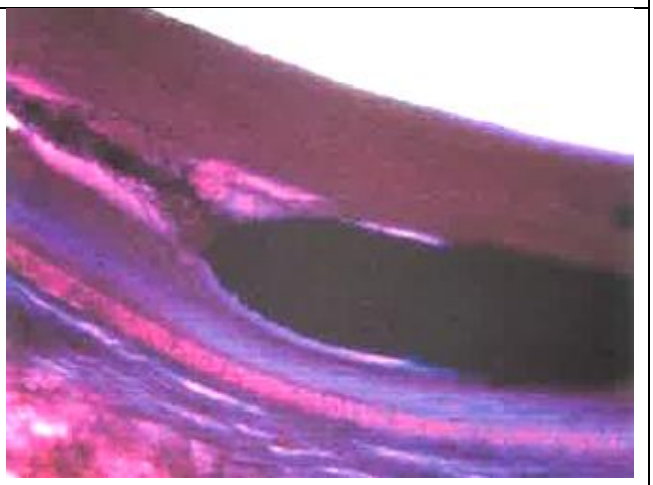
Animal 3:

In the gross necropsy of Animal 3, the heart, lungs, liver, and kidneys were examined. The stented arteries were collected with the proximal section 4 cm above the stent and the distal section 2 cm below the stent.

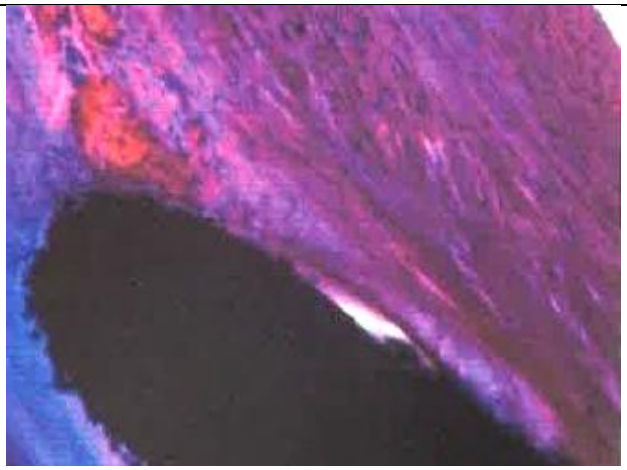
Histological evaluation revealed minimal inflammation, with a score of 1, indicating few inflammatory cells around the strut. Vascular injury was also minimal, with a score of 1 due to a break in the internal elastic lamina. No smooth muscle cell loss was observed (score 0). Fibrin deposition was minimal and focal, scoring 1. There was no endothelial loss detected, earning a score of 0. (Figure 6)

Morphometric measurements were taken for the luminal area, internal elastic lamina (IEL) area, and external elastic lamina (EEL) area, with percent area stenosis calculated from these values. The specific measurements are represented as [Value] mm^2.

Histopathological images:

<table>
<tr><td>  </td><td>  </td></tr>
<tr><td>P3 proximal, superficial femoral artery, H&E 1.25X</td><td>P3 proximal, superficial femoral artery, H&E 10X</td></tr>
<tr><td>  </td><td>  </td></tr>
<tr><td>P3 mid, superficial femoral artery, H&E 1.25X</td><td>P3 mid, superficial femoral artery, H&E 10X</td></tr>
</table>

P3 distal, superficial femoral artery, H&E 1.25X



P3 distal, superficial femoral artery, H&E 10X

Figure 6: Histopathological images of animal P3

RESULT:

Animal Health and Behavior: All animals remained bright, alert, and responsive throughout the study, with no signs of illness. They maintained normal eating, drinking, defecating, and urinating behaviors. The minimally invasive procedure caused minimal pain, managed effectively with analgesics.

Body Weights:

All animals exhibited an average weight gain of 20-30 kg from the procedure day to the termination day, indicating no adverse effects on their overall health.

Morbidity and Mortality: There were no instances of morbidity or mortality in any of the animals throughout the study.

Deployment and Handling:

The Peripheral Stent System was deployed quickly and easily, with no issues in reaching the target site or withdrawing the delivery system. The stents expanded uniformly and showed complete haemostasis with no blood leakage.

Angiographic and Radiographic Findings:

Initial evaluations showed no early lumen loss post-implantation. Over time, some stenosis was observed: 15% in one animal after six months and 10-12% in others after nine months

Clinical Chemistry and Hematology:

While some variations in clinical chemistry and hematology parameters were observed, none were deemed clinically significant.

Histopathology:

Inflammation and Injury: Moderate inflammation, mild to moderate vascular injury, and varying degrees of endothelial loss were noted. Fibrin deposition was minimal to moderate, with some arteries showing total occlusion due to spasmodic effects in narrower sections.

Histomorphometry:

Stenosis area measurements were consistent with angiographic evaluations, indicating lumen loss in some cases.

DISCUSSION:

Throughout the study, animals remained healthy with no significant health deviations or body weight loss, demonstrating the procedure's minimal impact on overall well-being. The test item, the Peripheral Stent System, showed ease of deployment and withdrawal, with no early lumen loss immediately after implantation. The delivery system performed well, with complete haemostasis and no blood leakage observed.

Angiographic assessments indicated some stenosis, with one case showing 15% stenosis after six months and other arteries displaying 10% to 12% stenosis after nine months. Histopathological evaluations revealed varying degrees of endothelialization, inflammation, and vascular injury, with moderate inflammation and fibrin deposition after six and nine months.

CONCLUSION:

The study assessed the safety and performance of the Peripheral Stent System in a swine model over a period of 6 and 9 months. Three female pigs were implanted with the stent and monitored for any adverse effects. The stent was found to be easy to deploy and withdraw, with no immediate post-implantation stenosis or lumen loss. However, angiographic evaluations revealed varying degrees of stenosis: one animal showed 15% stenosis after 6 months, while others had 10-12% stenosis after 9

months. Histopathological analysis showed moderate inflammation, mild to moderate vascular injury, and varying degrees of endothelialization, with some fibrin deposition. Despite these findings, the stents generally maintained blood flow, and no animals showed signs of clinical concern during the study. Overall, the Peripheral Stent System demonstrated safety and efficacy in maintaining vessel patency, supporting its potential for clinical use in peripheral artery disease treatment.

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