International Journal of Clinical Science and Medical Research

ISSN(print): 2770-5803, ISSN(online): 2770-582X

Volume 04 Issue 12 December 2024

DOI: https://doi.org/10.55677/IJCSMR/V4I12-03/2024, Impact Factor: 7.606

Page No : 429-443

Ensuring Non-Leakage Performance in Thoracic Aortic Repair in Preclinical Performance of a Minimally Invasive Thoracic Stent Graft: Results from a Porcine Model Study

Minocha Dr. PramodKumar[1], Kothwala Dr. Deveshkumar[2], Pandya Kamna[3], Bhandari Shreya[4], Durani Ovesh[5], Mishra Devdatt[6]

[1-6]Meril Medical Innovations Private Limited, Bilakhia House, Survey no.879, Muktanand marg, Chala, Vapi, Dist-Valsad, Gujarat, 396191, India.

ABSTRACT

The MeriGraft™ Thoracic Endovascular Stent Graft System was evaluated for its performance and safety in a controlled, one-day acute study using two large female porcine. Designed for minimally invasive repair of thoracic aortic aneurysms, the device was delivered via a 22-25F catheter introduced through the right femoral artery in the animal model. To evaluate the performance and safety of the MeriGraft™ Thoracic Endovascular Stent Graft System, an acute porcine model study was conducted. This one-day study aimed to assess stent leakage and overall feasibility of the device. The focus was on identifying any potential issues with fabric leakage, which could lead to Type 2 endoleaks. The study concluded that to prevent such leaks, the stent graft must be manufactured with high-quality fabric, as demonstrated by the animal study data. The Present study has an object to study that MeriGraft™ Thoracic Endovascular Stent Graft System is functionally suitable for its applications of assuring no leakage. While selecting the large animals we found the femoral artery is not suitable for its delivery system as in MeriGraft™ Thoracic Endovascular Stent Graft System it is fairly wider than available diameter of femoral artery. Yet the objective of suitability of MeriGraft™ Thoracic Endovascular Stent Graft System can be established if no blood leakage is found as per expectations from this under fluoroscopic guidance. Angiography was used to determine the appropriate stent graft sizes: 24x167 mm for P1 and 28x167 mm for P2. Both stents were successfully deployed in the descending aorta, expanding self-expansionally without procedural complications or mortality. Throughout the procedure, clinical monitoring showed no abnormal signs, and pre- and post-deployment blood tests revealed no significant changes, indicating stable hematological and biochemical profiles. The device's handling, visualization, hemostasis, and deployment were all found to be effective. Angiographic assessment confirmed proper endovascular flow and accurate stent graft positioning with no migration. X-ray imaging showed no structural or material disintegration. Histopathological analysis of the explanted aortas revealed no signs of inflammation, vascular injury, smooth muscle cell loss, or endothelial damage. Additionally, histomorphometric analysis demonstrated a beneficial increase in the internal luminal diameter with minimal changes in neointimal tissue. The device successfully sealed the aneurysm site, and no safety concerns were observed under acute testing conditions. These results affirm that the MeriGraft™ Thoracic Endovascular Stent Graft System system is effective and safe, offering a promising minimally invasive approach to treating thoracic aortic aneurysms.

Published Online : December 18, 2024

KEYWORDS:

MeriGraft™ Thoracic Endovascular Stent Graft System, Porcine Model, Safety Evaluation, Fluoroscopic Evaluation, Histopathological Findings.

Corresponding Author: Bhandari Shreya

***Cite this Article:** Minocha Dr. PramodKumar, Kothwala Dr. Deveshkumar, Pandya Kamna, Bhandari Shreya, Durani Ovesh, Mishra Devdatt (2024). Ensuring Non-Leakage Performance in Thoracic Aortic Repair in Preclinical Performance of a Minimally Invasive Thoracic Stent Graft: Results from a Porcine Model Study. International Journal of Clinical Science and Medical Research, 4(12), 429-443*

INTRODUCTION

A thoracic aortic aneurysm is a serious vascular condition characterized by the abnormal enlargement of the aorta, the primary artery responsible for delivering blood from the heart to the rest of the body. This dilation poses a significant risk

of rupture, which can lead to severe, life-threatening consequences. Traditionally, repairing a thoracic aortic aneurysm required invasive open surgery, a method fraught with considerable risks, extended recovery times, and substantial surgical trauma. The Present study has an object to study that MeriGraft™ Thoracic Endovascular Stent Graft System is functionally suitable for its applications of assuring no leakage. While selecting the large animals we found the femoral artery is not suitable for its delivery system as in MeriGraft™ Thoracic Endovascular Stent Graft System it is fairly wider than available diameter of femoral artery. Yet the objective of suitability of MeriGraft™ Thoracic Endovascular Stent Graft System can be established if no blood leakage is found as per expectations from this.

However, recent advancements in medical technology have introduced less invasive alternatives, such as the MeriGraft™ Thoracic Endovascular Stent Graft System, which offers a safer and more efficient approach. The MeriGraft™ Thoracic Endovascular Stent Graft System represents a modern solution for MeriGraft™ Thoracic Endovascular Stent Graft System. This technique involves the insertion of a stent graft via a catheter, which is guided to the aneurysm site within the aorta. Once positioned, the stent graft is deployed to reinforce the weakened section of the aorta, restoring normal blood flow and minimizing the risk of rupture without the need for traditional open surgery. Considering the available animal's femoral artery, the present study eventually has an objective to find the suitability of MeriGraft™ Thoracic Endovascular Stent Graft System and not the survival of the animal due to limited artery conditions.

To evaluate the performance and safety of the MeriGraft™ Thoracic Endovascular Stent Graft System, an acute porcine model study was conducted. This one-day study aimed to assess stent leakage and overall feasibility of the device. The focus was on identifying any potential issues with fabric leakage, which could lead to Type 2 endoleaks. The study concluded that to prevent such leaks, the stent graft must be manufactured with high-quality fabric, as demonstrated by the animal study data.

In this specific study, the MeriGraft™ Thoracic Endovascular Stent Graft System, sized 24x167 mm and 28x167 mm, were deployed in the descending thoracic aorta of two large female porcine (weighing 84.6 kg and 139.1 kg). The deployment was carefully monitored using fluoroscopy and angiography to ensure precise placement and to assess device handling, accuracy, and aneurysm repair effectiveness.

The results indicated that the stent graft system performed effectively, with no significant adverse clinical signs observed. Histopathological analysis of the aorta revealed no inflammation or substantial damage, confirming that the stent graft system is a safe and effective minimally invasive option for repair, successfully closing the aneurysm while maintaining a favorable safety profile under controlled conditions.

However the final objective is to use for human beings can be established by additional study than Femoral Artery where using 22- 25 French delivery system becomes is fairly risky. We are considering to carryout additional large animal study where artery is suitable and functional for this delivery system which is safer for 22- 25 French.
However for human applications, it is possible to use iliac artery which is fairly wider than femoral artery. This is actual diagram for Human femoral and iliac artery.

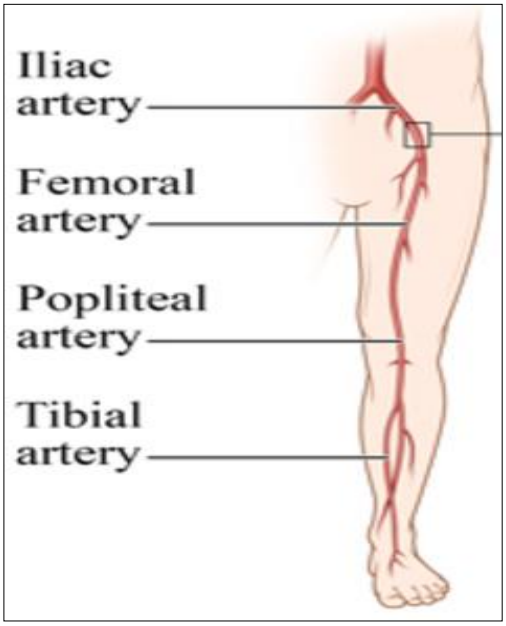

Figure1: Actual diagram for Human femoral and iliac artery.

Further animal study is being considered for additional safety aspects within available options in large animals prior to undertake its clinical trials.

MATERIALS AND METHODS

Medication Details

This section delineates the drugs administered to the animals prior to, during, and following surgery, as shown as Table No. 1 with the clinical signs illustrated in the table 2.

Table 1: Details of medications used in the study

Drug name	Manufactured by	Batch/Lot No.
Ketamine	Troikaa pharmaceuticals Ltd	K50514
Xylazine	IIL India	FHK 1003
Propofol	Celon labs	PF121906BCY
Isoflurane	Neon Lab	KPNP700013

Thiopentone Sodium	Neon Lab	173274
Heparin	Gland pharma Ltd	101109
Aspirin	USV Ltd	52001055
Clopidogrel	Cipla Ltd	SN91823
Tramadol	Maxon biotech Ltd	NC20025B
Atropine	Pentagon Labs Ltd	19GAS002
Omnipaque	GE Health care	163525468

Table 2: Animal P1 and P2 Clinical signs

Animal Number	**Acclimatization phase**	**Experiment phase**
	04211 & 04209	**P1 & P2**
Sex	**Female**	**Female**
Day of observations	Clinical sign / Incidences	Clinical sign / Incidences
Acclimatization phase (Day1 to 3)	0/2	--
Experiment phase (Day 0)	--	0/2

DEVICE DESCRIPTION

The MeriGraft™ Thoracic Endovascular Stent Graft System is designed to treat thoracic aortic aneurysms through minimally invasive endovascular techniques. The woven polyester graft provides a durable and flexible conduit for blood flow, while the nitinol stent locks the graft in place within the aorta, ensuring secure fixation. The nitinol wireframes reinforce the stent, enhancing its radial force and improving its ability to expand and conform to the aortic wall. The system is deployed using the delivery system, which ensures accurate and stable positioning of the stent graft, minimizing the risk of migration or complications during the procedure. The system is designed to be highly precise and minimally invasive, offering a safer alternative to traditional open surgical repair for thoracic aortic aneurysms.

DEVICE DESIGN: The MeriGraft™ Thoracic Endovascular Stent Graft System, depicted in Figure 2, is a self-expanding device designed for repairing thoracic aortic aneurysms. It comprises a woven polyester yarn graft (as shown in Figures 4 and 5) and a nitinol stent for secure placement, reinforced by nitinol wireframes to enhance radial force (as shown Figure 3). The delivery system includes an catheter with diameters ranging from 22Fr to 25Fr, an inner tube with a diameter of 1 to 1.5 mm, and an innermost tube measuring 0.9 to 1.6 mm. Additionally, the system features a Pebax tip to secure the graft within the sheath and a 0.89 mm delivery wire for precise deployment, ensuring accurate and stable positioning of the stent graft within the aorta.

PRODUCT IMAGE:

Figure 2: MeriGraft™ Thoracic Endovascular Stent Graft System

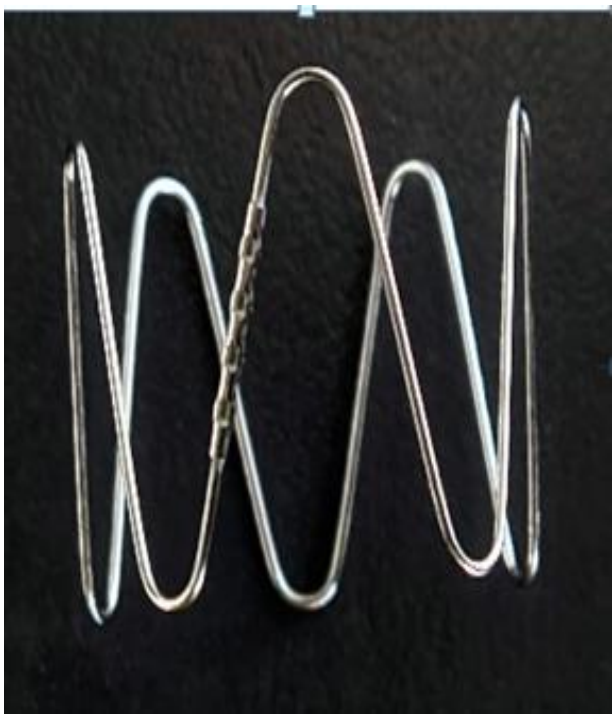

Figure 3: Frame for central structure

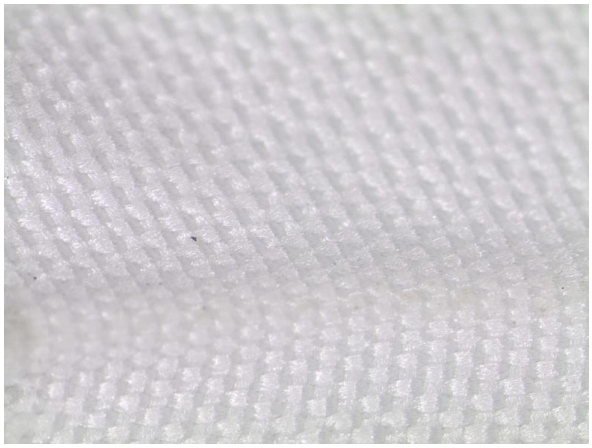

Figure 4: Polyester woven yarn to manufacture the graft, since it has high porosity and can withstand greater radial force.

Figure 5: Polyester woven yarn to manufacture the graft, since it has high porosity and can withstand greater radial force.

EXPERIMENTAL PROCEDURES

Fasting:

Feed and water were withheld overnight before the procedure.

Animal Preparation included:

The study animal was first weighed shown in table no 3, And pre-anesthetized with 0.05 mg/kg atropine. Anaesthesia induction involved 15 mg/kg Ketamine and 2.5 mg/kg Xylazine administered intramuscularly, followed by 1-3% Isoflurane delivered via face mask. To expedite induction, a 0.5 mg/kg bolus of Propofol was given intravenously. Hair was clipped from the neck, chest, and thigh to prepare for arterial access and ECG lead placement. Once the absence of glottis reflexes was confirmed, intubation with an appropriately sized intratracheal tube was performed. The animal was maintained under 1-3% Isoflurane anaesthesia, and all procedures were documented in the surgical record.

Table 3: Animal P1 and P2 body weights (Day 0)

Animal Number	Sex	Day 0
P1	Female	84.6 Kg
P2	Female	139.1 Kg

EXPERIMENTAL DESIGN OR ANIMAL TRIAL:

Day when procedure is performed can be said as 0 day:

Both the right and left groins of the animals were shaved, and an incision was made in the groin to expose the femoral artery. A 9-11Fr sheath was then inserted. To monitor anticoagulation, Activated Clotting Time (ACT) measurements were taken before and after administering heparin shown in Table No 4. Heparin was administered to maintain ACT values between 250 and 550 seconds, starting with an initial bolus dose of 100 IU/kg IV/IA, followed by additional doses adjusted according to ACT readings.

A stiff 150 - 300 cm, 0.035″ guide wire was inserted alongside a 6Fr pigtail catheter to stabilize the thoracic descending aorta. Angiography of the descending aorta was performed using the pigtail catheter to determine the optimal site for stent graft implantation. Baseline angiography, along with length and diameter measurements of the aorta, was conducted to select the appropriate implantation region. Based on these measurements and the Reference Vessel Diameter (RVD), a 24x167 mm thoracic endovascular stent graft system was chosen for the first animal (P1) and a 28x167 mm thoracic endovascular stent graft system for the second animal (P2). Both stent grafts were preloaded into a 22-25Fr delivery device. The catheter was withdrawn, leaving the guide wire with radio-opaque markers in place at the target site. The 9-11Fr sheath was replaced with a 22-25Fr thoracic endovascular stent graft system delivery long sheath, and the dilator. The thoracic endovascular stent graft system delivery as removed while keeping the guide wire in position device was advanced through the sheath over the guide wire. The thoracic endovascular stent graft system was deployed at the target site in the thoracic aorta by removing the sheath. Post-deployment, angiography, fluoroscopy, and aorta measurements were performed 30 minutes later to evaluate blood flow through the stent-implanted region.

Following the procedure, both animals (P1 and P2) were humanely euthanized on the same day for the immediate collection of the stented aorta. The harvested tissue was then used for photography, gross examination, and histopathological evaluation.

Table 4: Animal P1 and P2 ACT values (Day 0)

Sr. No.	Animal Number	Baseline ACT value	Post Heparin dose ACT Value
1	P1	89	304
2	P2	95	298

Monitoring during the procedure:
Electrocardiogram (ECG), respiration rate, heart rate, and oxygen saturation were monitored continuously and monitored throughout the procedure.

MEDICATIONS

Details of the drugs used for pre-operative in this study are given below in Table No 5.

Table 5: Drugs for Swine during pre, intra-operative

Purpose	Drug Name	Conc.	Dose	Route	Frequency
Anti coagulation	Heparin	5000 IU/mL	100 IU/kg	IV	Day 0, before the device implantation (every hour on discretion of interventionist)
Pre-anesthetic	Atropine	0.6 mg/mL	0.05 mg/kg	IM	Once before induction anaesthesia
Induction of Anesthesia	Ketamine	50 mg/mL	15 mg/Kg.	IM	Once to sedate animal
	Xylazine	23.32 mg/ml.	2.5 mg/kg	IM	Once to sedate animal
	Isoflurane	NA	1 %	Face mask	Induction
Maintenance of Anesthesia	Isoflurane	NA	2.5	Inhalation	For maintenance
Analgesic	Tramadol	50 mg/mL	2 to 4 mg/Kg	IM	Once before procedure
Euthanasia	Thiopental sodium	300 mg/mL	100 mg/Kg	IV	Once at the termination of procedure

Key: Conc - Concentration; mL- Millilitre; Kg - Kilogram; IM - Intramuscular; IV - Intravenous; % - Percentage; IU- Internation Unit; ; mg- Milligram; NA - Not applicable

OBSERVATION

Day when procedure is performed can be said as 0 day, the body weights of Animal P1 were recorded as 84.6 kg and Animal P2 as 139.1 kg, with no significant change. Mortality and morbidity were monitored throughout the study for Animals P1 and P2. Blood samples were collected on day 0 before the procedure and before euthanasia, and analyzed for hematology (complete blood count, differential count, reticulocytes count) and clinical biochemistry (LDH, AST, creatinine, creatine kinase, BUN, sodium, potassium, chloride, calcium). Test article performance was evaluated based on trackability, handling, visualization, hemostasis, deployment profile, leakage control, and ease of deployment and withdrawal. Angiographic patency was assessed to ensure proper blood flow through the stent-implanted region. Stent position, structural integrity, and functionality were verified using X-ray and histopathological analysis, focusing on endothelialization, inflammation, thrombus formation, Restenosis, and medial calcification. Adverse events were documented. Harvested stented arteries were processed, stained with Haematoxylin and Eosin (H & E), and examined for histopathological lesions.

RADIOGRAPHY AND ANGIOGRAPHIC FINDINGS

During the radiographic analysis, pre-implantation angiograms were used to measure the base line length and diameter of the blood vessels, providing reference values for stent implantation. After implanting the stent, measurements were taken 30 minutes later to calculate key metrics such as the stent-to-artery ratio, minimal lesion diameter, stenosis diameter, and early lumen loss (ELL). The percentage of vessel narrowing was assessed using specialized software to determine the degree of narrowing. All vessel and device measurements were recorded in the study-specific raw data for comprehensive analysis and evaluation of stent performance, as detailed in Table 6. Necropsy and histopathology findings after euthanasia on day 0. Radiography images illustrating the device and surrounding structures are shown in Figures 5 to 14 for animal P1 and Figures 15 to 24 for animal P2

Table 6: Radiographic Analysis

Sr. No	Stent size	Target vessel (Animal ID)	Baseline Diameters (mm)	Average (mm)	Stent Diameter (mm)	Stent To Artery ratio	Post Implantation D A diameter ELL(mm)	Average (mm)	Baseline A diameter ELL(mm)	% Angiographic stenosis
1	24x167mm Thoracic Endovascular Stent Graft system	Descending Aorta (04211-p1)	Proximal 19.0 mm Mid 19.3mm Distal 18.0mm Very distal 18.6mm	18.6	24	1.2	Proximal 17.4mm Mid 15.7mm Distal 13.6mm Very distal 18.1 mm	15.4	3.2	17.2%
2	28x167mm Thoracic Endovascular Stent Graft system	Descending Aorta (04209-P2)	Proximal 22.0 mm Mid 21.0 mm Distal 19.0 mm Very distal 18.3 mm	20.0	28	1.4	Proximal 20.9mm Mid 20.3mm Distal 19.5mm Very distal 18.1mm	19.7	0.3	1.5%

.Key: D A- Descending aorta; mm – Millimeter; % - percentage; ELL – Early lumen loss.

PATHOLOGY

Animals were euthanized with Thiopental Sodium (100 mg/kg IV), confirmed via chest auscultation, ECG, and oxygen saturation monitoring. Necropsy revealed no abnormalities in standard organs. Stented thoracic aortas were collected 2-5 cm above and below the stent, flushed with normal saline, fixed in 10% formalin-buffered saline, and processed for resin embedding. Sections were stained with Hematoxylin and Eosin (H&E) and analyzed microscopically. Histopathological scoring evaluated inflammation, vascular injury, smooth muscle cell loss, and fibrin deposition, while histomorphometric analysis measured luminal area, internal elastic lamina (IEL), and external elastic lamina (EEL). Percent area stenosis was calculated as Percent Area Stenosis = (1-Lumen area / IEL area) × 100% .Standard hematology and clinical chemistry tests conducted pre- and post-implantation showed no significant differences or abnormalities as shown in Table No 7 and 8.

Table 7: Clinical chemistry data on Day 0 (pre-procedure)

Parameters	P1	P2	Mean	SD
AST(U/L)	79	14	46.5	45.96
Ca(mmol/L)	2.56	2.42	2.49	0.10
CK(U/L)	2405	592	1498.5	1281.98
Creat(µmol/L)	126	97	111.5	20.51
LDH(U/L)	624	319	471.5	215.67
BUN(mmol/L)	3.85	1.67	2.76	1.54
Na(mm0ol/L)	142.0	141.6	141.8	0.28
K(mmol/L)	4.09	3.42	3.755	0.47
Cl(mmol/L)	104.9	104.4	104.65	0.35

Table 8: Clinical chemistry data on Day 0 (post-procedure)

Parameters	P1	P2	Mean	SD
AST(U/L)	100	10	55	45.0
Ca(mmol/L)	2.84	2.72	2.78	0.1
CK(U/L)	8099	533	4316	3783.0
Creat(µmol/L)	144	185	164.5	20.5
LDH(U/L)	588	376	482	106.0
BUN(mmol/L)	8.07	3.40	5.735	2.3
Na(mm0ol/L)	145.6	146.3	145.95	0.4
K(mmol/L)	4.25	4.07	4.16	0.1
Cl(mmol/L)	103.8	107.0	105.4	1.6

Key: AST- Aspartate amino transferase, Ca- calcium, CK – Creatine Kinase , Creat – Creatini

RADIOGRAPHY IMAGE

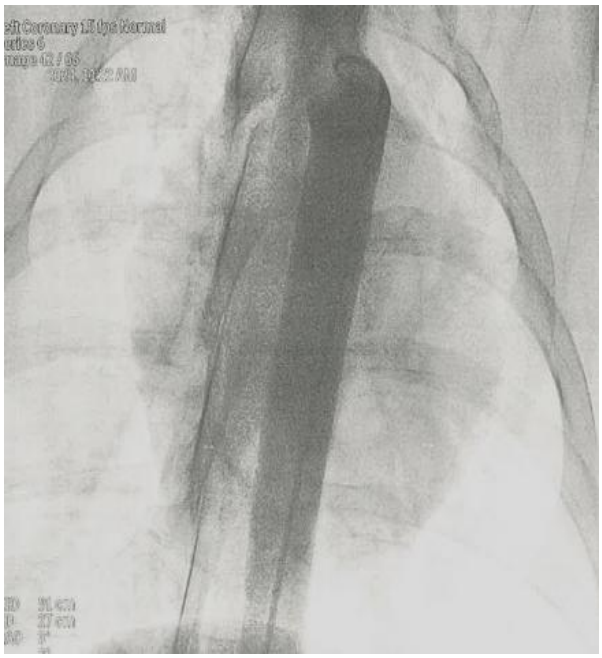

Figure 6: Animal P1 on day 0, baseline angiography of Descending aorta

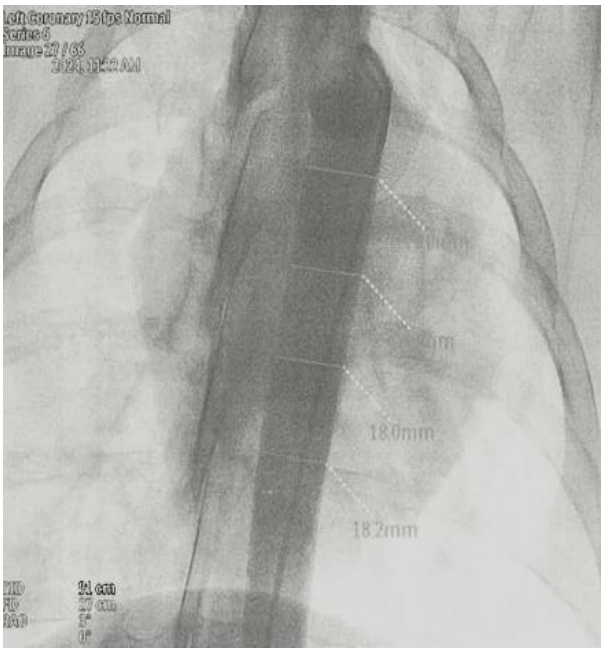

Figure 7: Animal P1 on day 0, baseline angiography measurements of descending aorta.

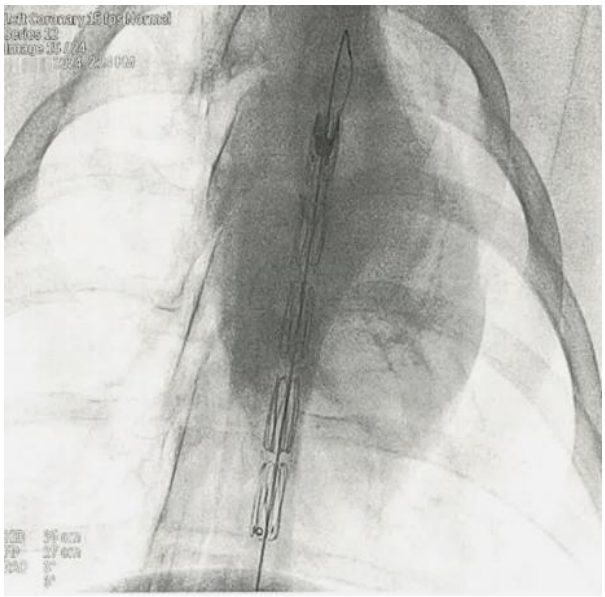

Figure 8: Animal P1 on day 0, Thoracic endovascular stent graft system was positioned in descending aorta.

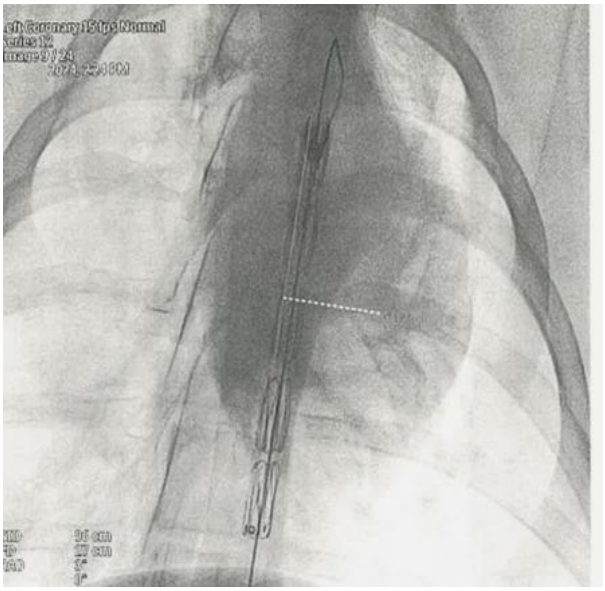

Figure 9: Animal P1 on day 0, Thoracic endovascular stent graft system crimp length was 102mm

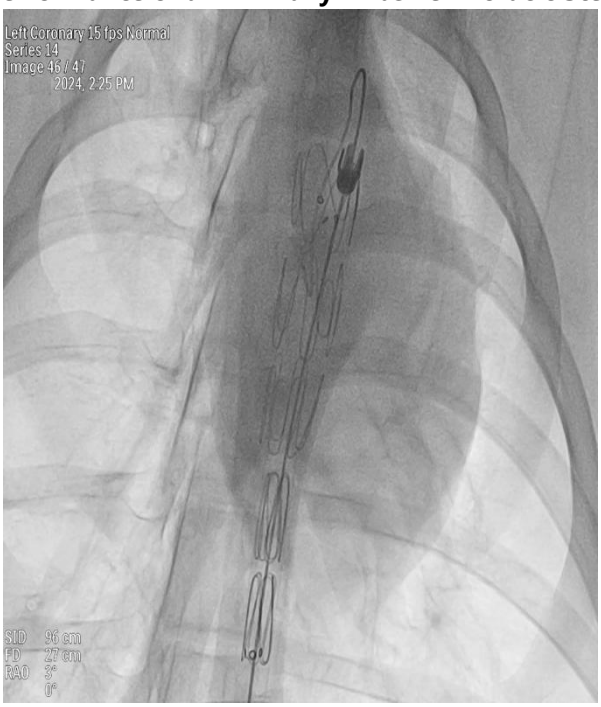

Figure 10: Animal P1 on day 0, Thoracic endovascular stent graft mid portion was opening in the descending aorta

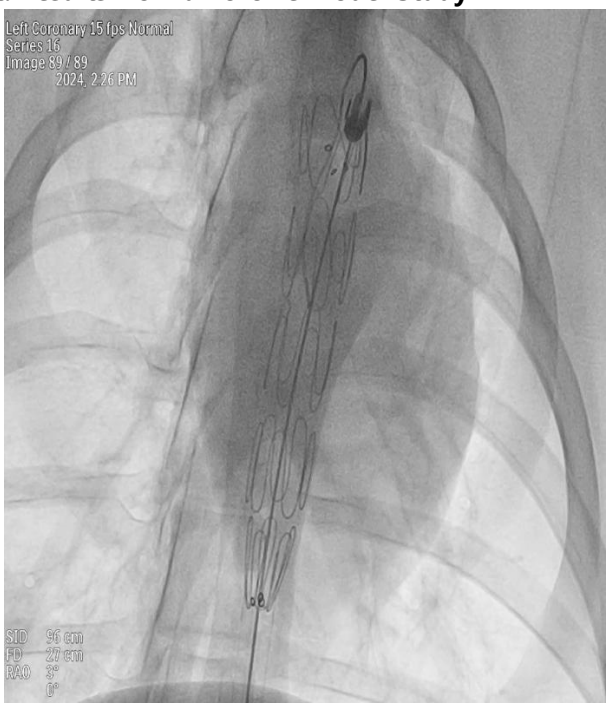

Figure 11: Animal P1 on day 0, Thoracic endovascular stent graft system distal portion was opening in the descending aorta.

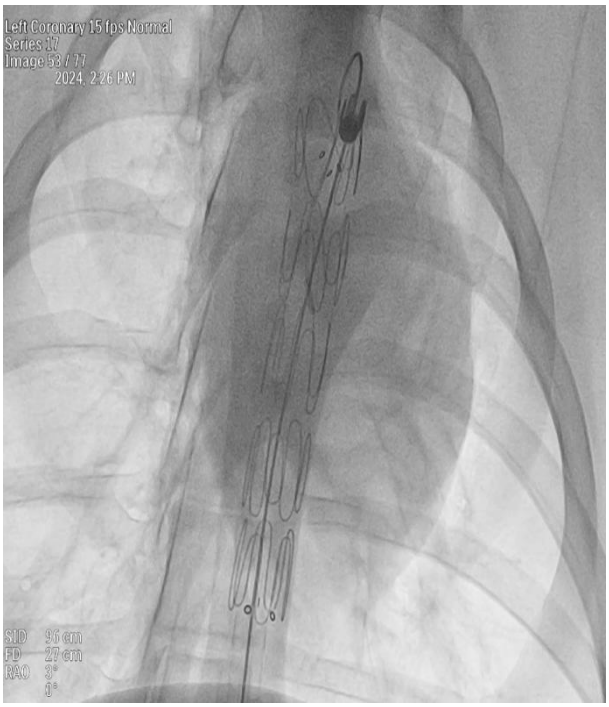

Figure 12: Animal P1 on day 0, Thoracic endovascular stent graft was completely opened in the descending aorta.

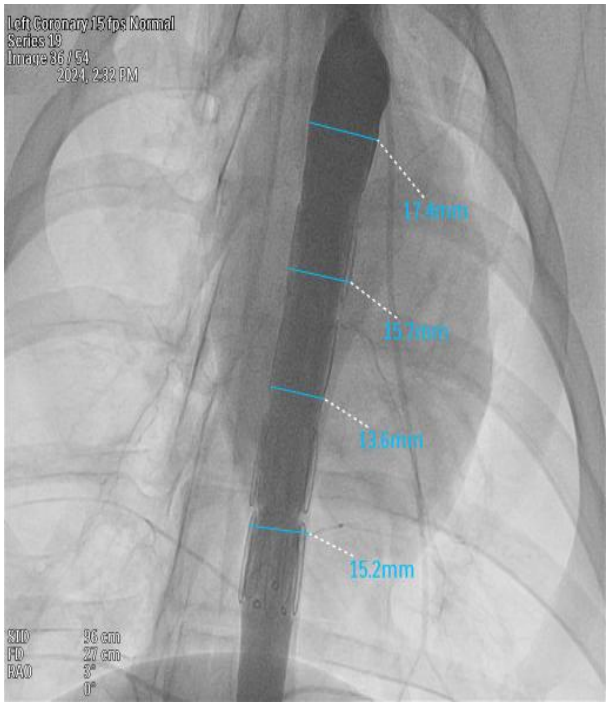

Figure 13: Animal P1 on day 0, post fluoroscopy of diameter measurements was thoracic endovascular stent graft system

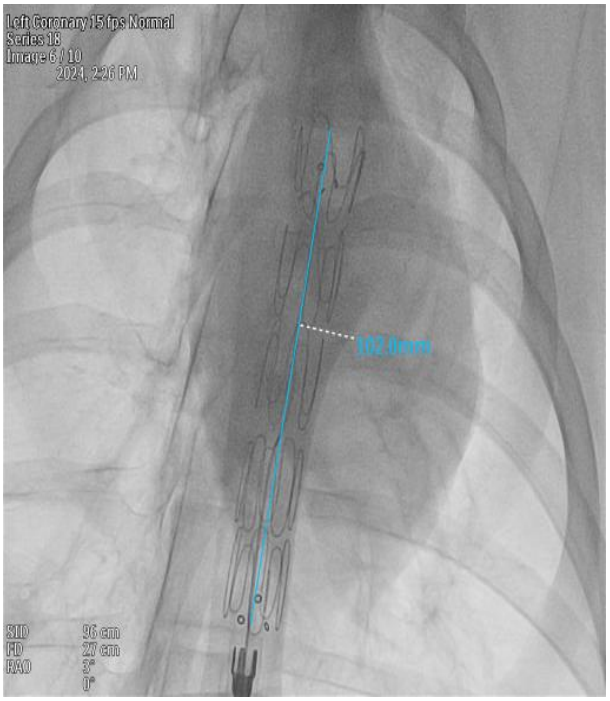

Figure 14: Animal P1 on day 0, post fluoroscopy of length measurement was thoracic endovascular stent graft system.

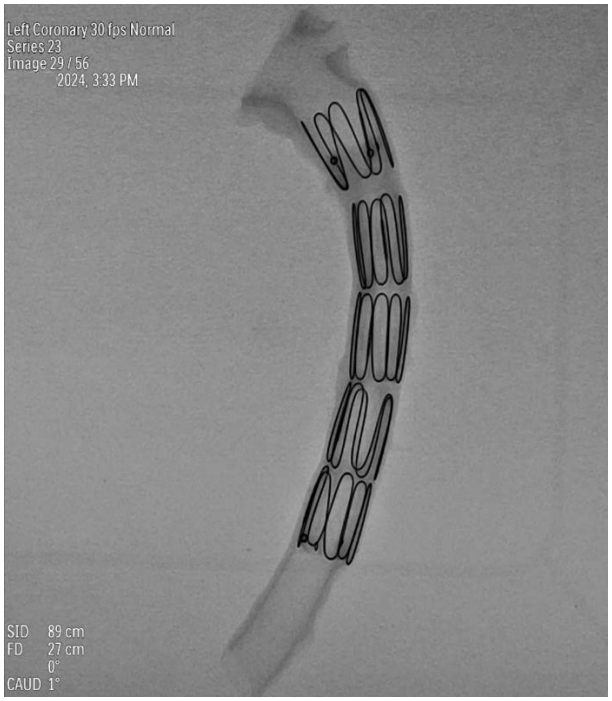

Figure 15: Animal P1 on day 0, collection of descending aorta with thoracic endovascular stent graft system was in fluoroscopy.

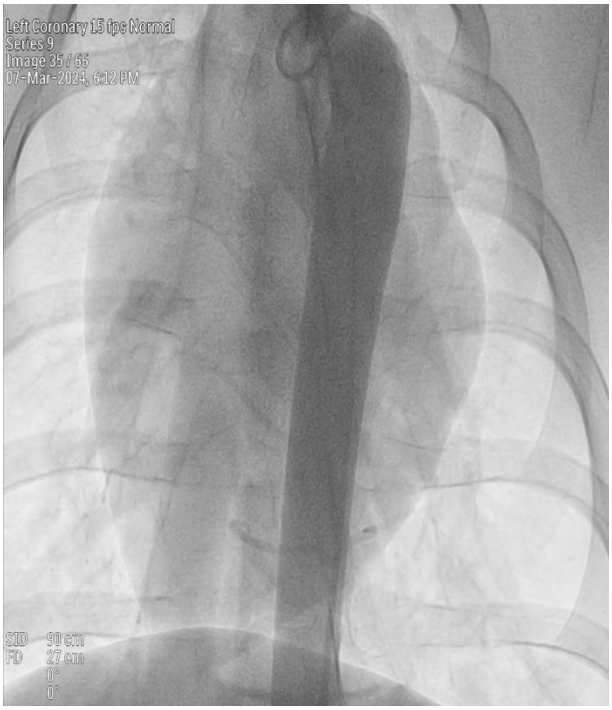

Figure 16: Animal P2 on day 0, baseline angiography of descending aorta

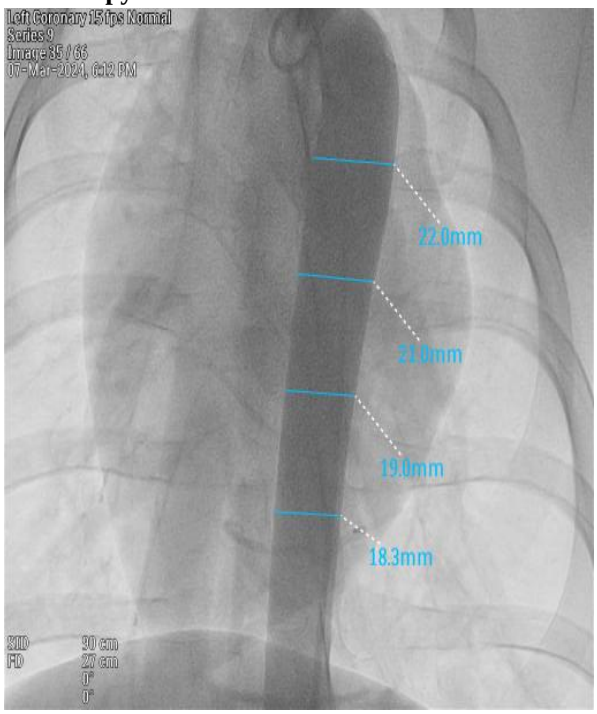

Figure 17: Animal P2 on day 0, baseline angiography measurements of descending aorta

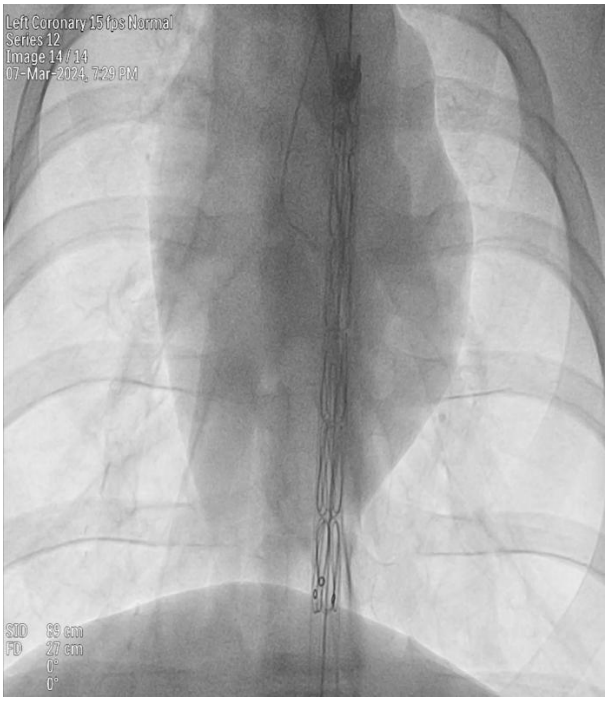

Figure 18: Animal P2 on day 0, Thoracic endovascular stent graft system was positioning in descending aorta.

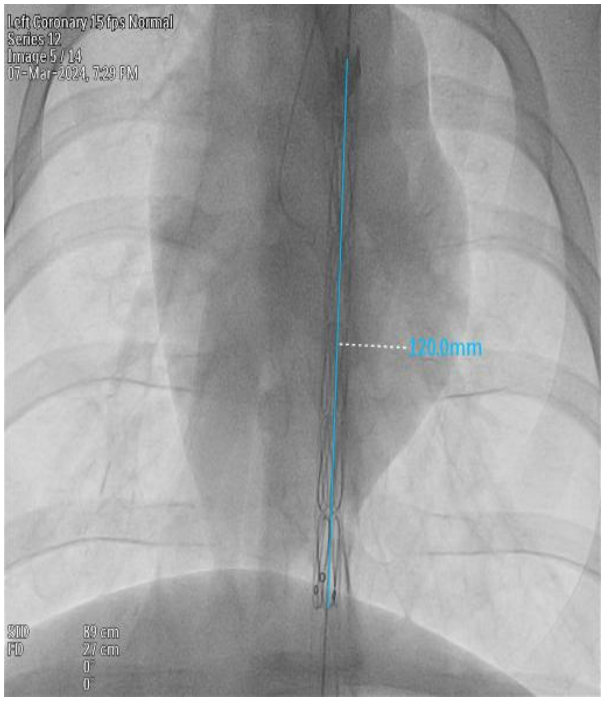

Figure 19: Animal P2 on day 0, Thoracic endovascular stent graft system proximal portion was opening in the descending aorta.

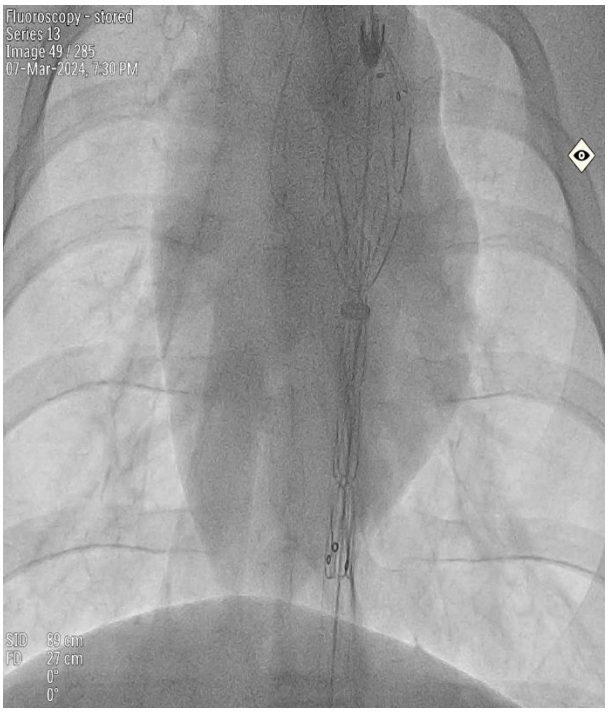

Figure 20: Animal P2 on day 0, Thoracic endovascular stent graft system proximal portion was opening in the descending aorta.

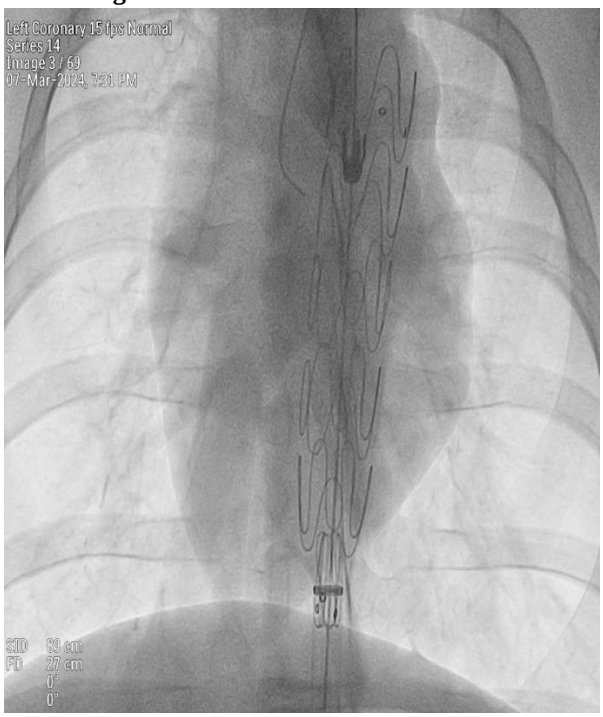

Figure 21: Animal P2 on day 0 thoracic endovascular stent graft system distal portion was opening in the descending aorta.

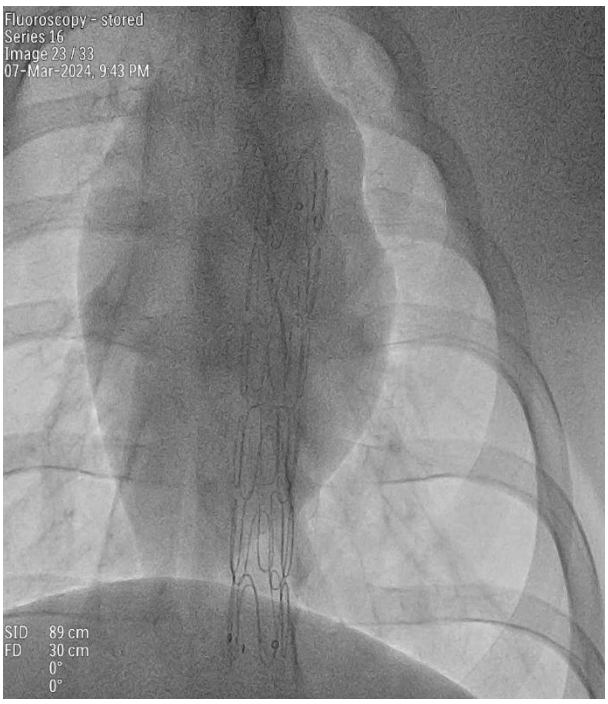

Figure 22: Animal P2 on day 0, stent was totally opening in thoracic endovascular stent graft in descending aorta

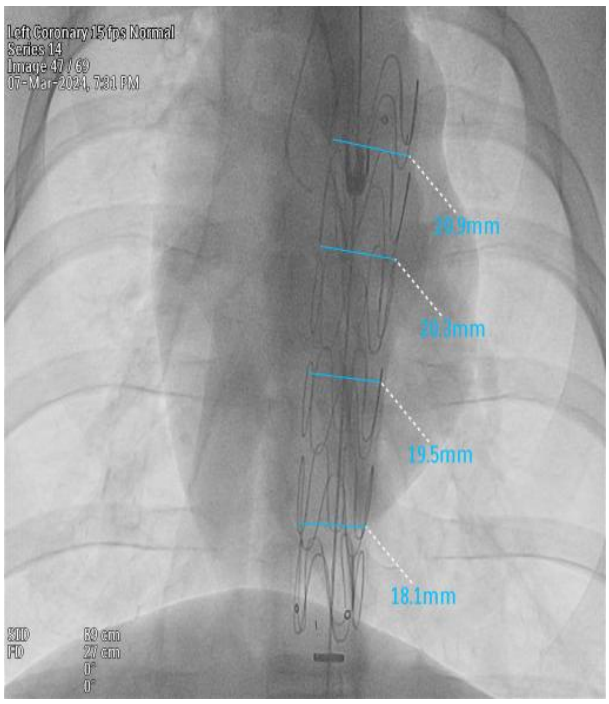

Figure 23: Animal P2 on day 0, post fluoroscopy of diameter measurements was thoracic endovascular stent graft system

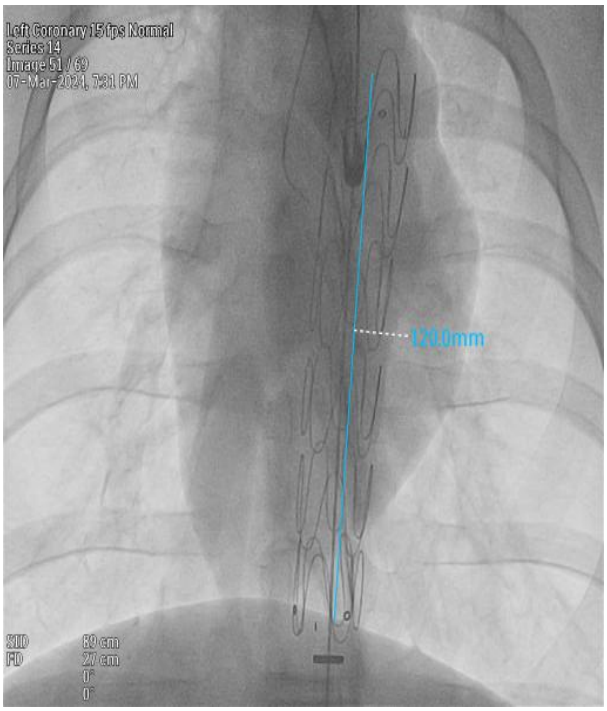

Figure 24: Animal P2 on day 0, post fluoroscopy of length measurements was thoracic endovascular stent graft system.

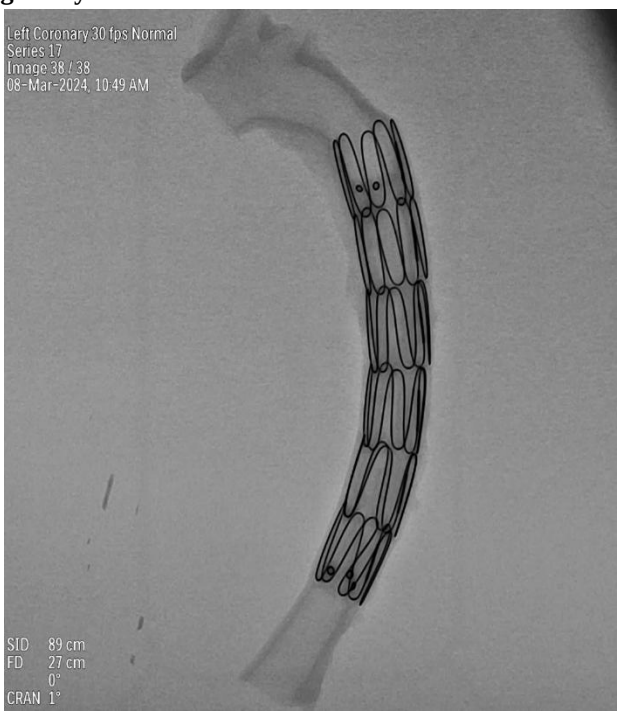

Figure 25: Animal P2 on day 0, collection of descending aorta with Thoracic endovascular stent graft was in fluoroscopy.

NECROPSY

On the freshly necropsied animals, initial photography of the implanted device (For animal P1 Figure No 25, 26, 27 and for animal P2 Figure No 28, 29, 30) situ was performed. Subsequently, the device was explanted to assess and document any regional lesions in contact with the device. On Day when procedure is performed can be said as 0 day, animals P1 and P2 were euthanized with an overdose of thiopental sodium (100 mg/kg, IV). A pathologist conducted a thorough examination of both external and internal gross pathological changes. The stented thoracic aorta was collected and preserved in 10% neutral buffered formalin. The target vessel with the stent from each animal was processed for resin embedding, sectioned to approximately

200 microns using a Secotome cutting machine, and further refined to the desired thickness with a Bainpol VTD Polishing machine. Tissue sections were stained with hematoxylin and eosin (H & E) and examined under a light microscope by the study pathologist to evaluate histopathological lesions.

Animal P1:

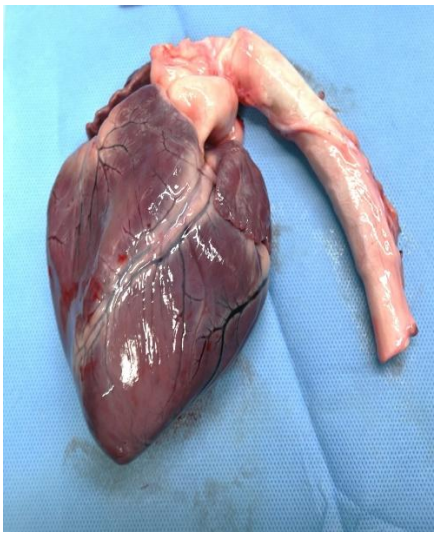

Figure 26: Heart with descending aorta in anterior view.

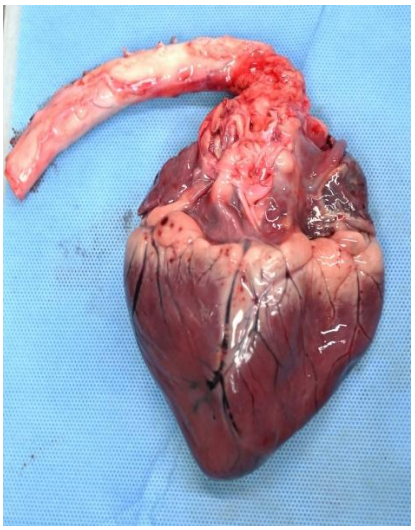

Figure 27: Heart with descending aorta in posterior view

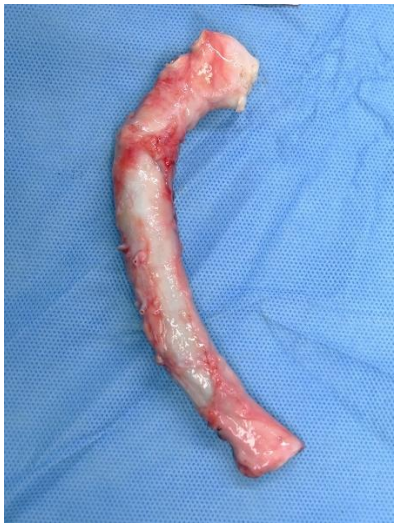

Figure 28: Image of the descending aorta

Animal P2:

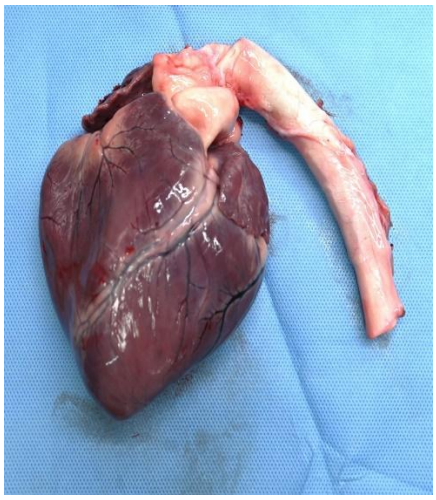

Figure 29: Heart with descending aorta in anterior view

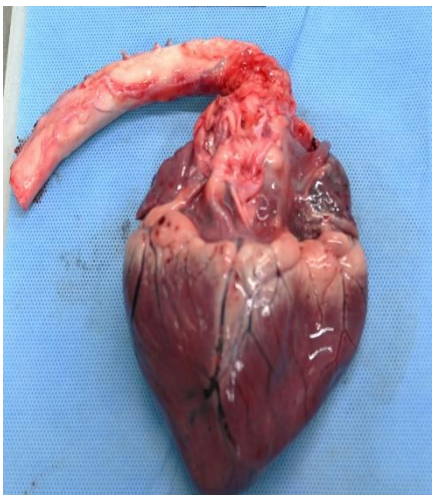

Figure 30: Heart with descending aorta in posterior view.

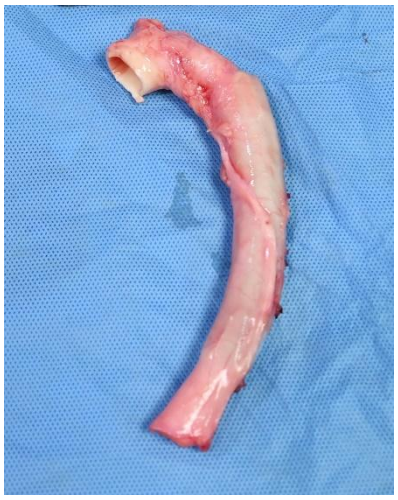

Figure 31: Image of the descending aorta

HISTOPATHOLOGY:

Porcine 1:

The examination of the artery with a stent showed no signs of inflammation, vascular injury, loss of smooth muscle cells, or loss of endothelial cells. Some mild fibrin buildup was observed in the proximal and middle sections, with minimal build-up in the distal section. The overall histopathology score was 1.67, likely due to the implantation procedure. Analysis also showed stable lumen diameter, internal elastic lamina (IEL) diameter, and external elastic lamina (EEL) diameter cross sections. The medial area remained consistent in the proximal (944.56 µm) and middle (1003.79 µm) sections, with a slight increase in the distal segment (1847.77 µm). Neointimal areas were similar: proximal (107.42 µm), middle (115.21 µm), and distal (123.48 µm). The average percent area stenosis was calculated to be 0.85%. (As shown in below Figure No 31, 32, 33, 34, 35, 36.)

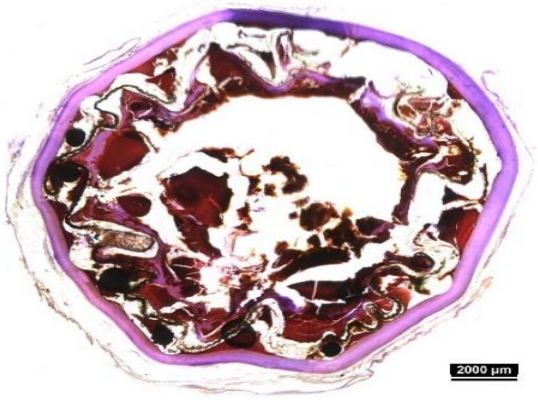

Figure 32: Distral, H&E 1.25X

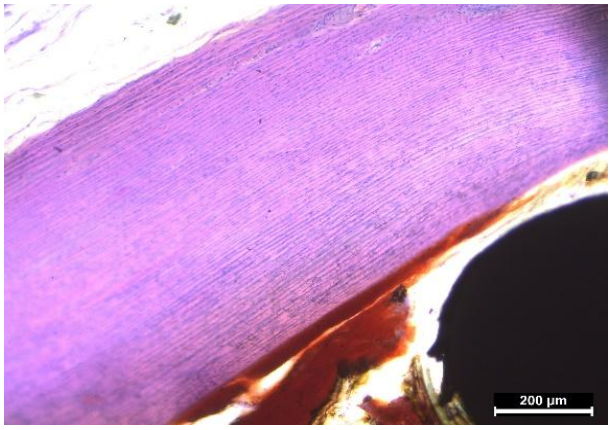

Figure 33: Mid, H&E 10X

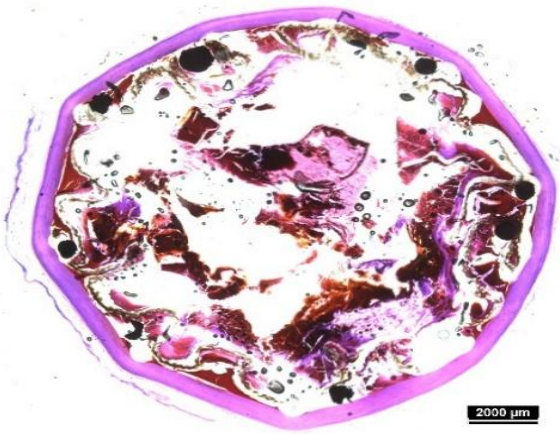

Figure 34: Proximal , H&E 1.25X

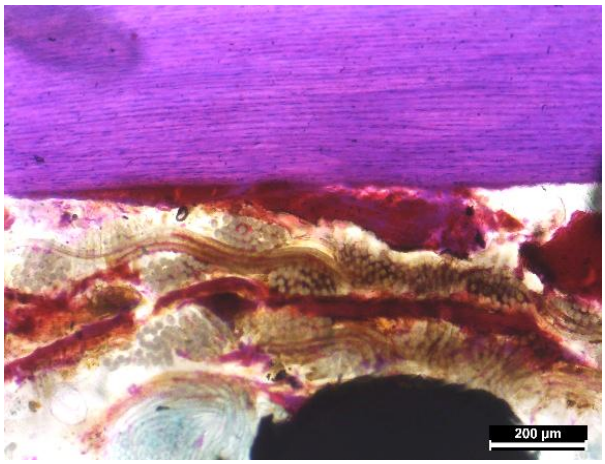

Figure 35: Proximal **, H&E 10X**

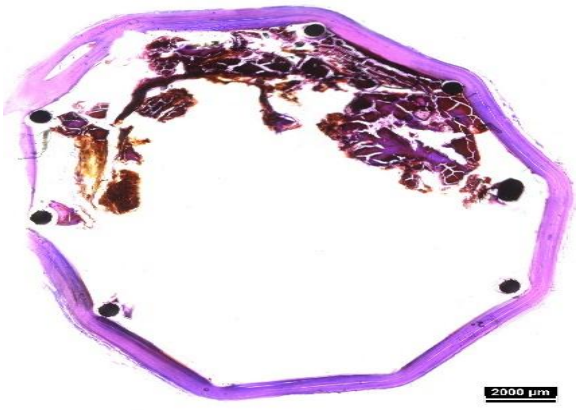

Figure 36: Distal , H&E 1.25X

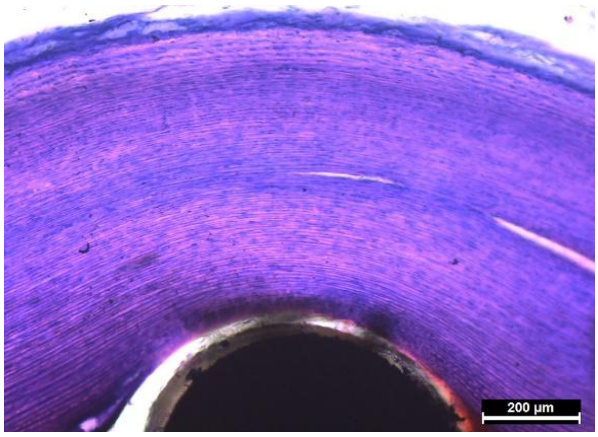

Figure 37: Distal ,H&E 10X

Porcine 2:

Histopathological evaluation revealed no inflammation, vascular injury, fibrin deposition, smooth muscle cell loss, or endothelial loss along the stent. The mean histopathology score was 0.00, reflecting no pathological changes. Histomorphometric analysis showed stable lumen diameter, internal elastic lamina (IEL) diameter, and external elastic lamina (EEL) diameter across all stent sections: proximal (1190.98 µm), middle (1825.82 µm), and distal (1401.52 µm). Neointimal areas remained consistent: proximal (90.80 µm), middle (120.47 µm), and distal (100.79 µm). The average percent area stenosis was 0.83%, with percentages of 0.72%, 0.96%, and 0.81% in the proximal, middle, and distal sections, respectively. (As shown in below Figure No 37, 38, 39, 40, 41, 42).

Figure 38: Mid, H&E 1.25X

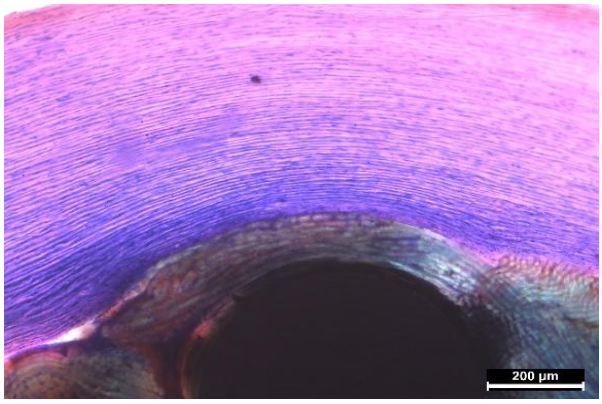

Figure 39: Mid ,H&E 10X

Figure 40: Proximal ,H&E 1.25X

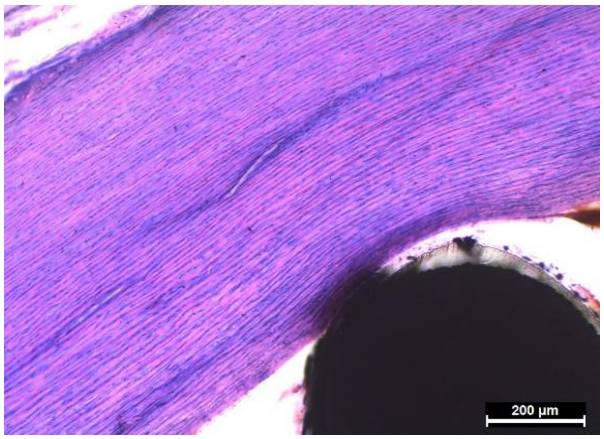

Figure 41: Proximal ,H&E 10X

Figure 42: Distal ,H&E 1.25X

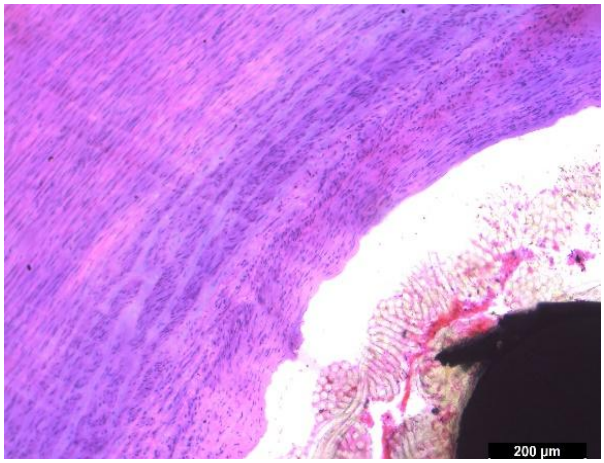

Figure 43: Distal ,H&E 10X

RESULT

On Day when procedure is performed can be said as 0 day, the body weights of the animals were recorded as 84.6 kg for P1 and 139.1 kg for P2. Throughout the study, there were no instances of morbidity or early elective events, and no abnormal clinical signs were observed before or during the experiment. Hematology and clinical chemistry tests conducted on blood samples collected before and after implantation showed no significant differences or abnormal values.

The test articles were evaluated based on several performance criteria. The trackability of the test item was assessed as good, as were the handling, visualization, and homeostasis of the delivery system. The deployment profile of the test item was considered good both qualitatively and quantitatively. No issues of leakage or homeostasis were observed with the delivery system, and the ease of deployment and withdrawal was rated as good. Angiographic patency was classified as TIMI (Thrombolysis in Myocardial Infarction) flow III, indicating successful placement. The test item was accurately

positioned in the descending aorta, fully expanded, and fit snugly, with no observed flow in the spinal arteries at the implantation site.

Following the procedure, the animals were humanely euthanized with a thiopentone injection (100 mg/kg) on On Day when procedure is performed can be said as 0 day. Death was confirmed through observation, ECG, and zero oxygen saturation. Necropsy revealed no significant external or internal pathological lesions. Histopathological evaluations showed no signs of inflammation, vascular injury, smooth muscle cell loss, or endothelial loss. porcine 1 exhibited mild fibrin deposition with a mean histopathology score of 1.67, while porcine 2 showed no significant findings, with a mean score of 0.00. Histomorphometric measurements indicated minimal changes in lumen diameter and stenosis in both animals.

DISCUSSION

The purpose of this study was to evaluate the safety and effectiveness of a stent designed for endovascular device insertion with minimal blood loss using a porcine model. The MeriGraft™ Thoracic Endovascular Stent Graft System was tested on two female porcine (P1 and P2). After catheterizing the femoral artery, a 6Fr pigtail catheter was placed in the thoracic descending aorta, and baseline angiography was performed to select the appropriate stent size. The stent was deployed using a 22-25Fr delivery catheter, and follow-up angiography conducted 30 minutes post-implantation confirmed that the stent was fully expanded and functioning properly, with normal perfusion indicated by TIMI (Thrombolytic in Myocardial Infarction) flow III.

The primary objective of this study was to assess the MeriGraft™ Thoracic Endovascular Stent Graft System's functional suitability for ensuring no leakage. During the selection of large animals for the study, it was found that the femoral artery was not suitable for the device's delivery system, as the diameter of the femoral artery was too small relative to the size of the stent graft, which is designed to be relatively wider. This observation suggests the need for alternative vascular access points in future applications.

Both porcine subjects were euthanized immediately after the procedure for further assessment. The stent's trackability, handling, and deployment were rated as good, achieving complete hemostasis with no observed leakage. Internal examinations revealed no pathological lesions, and histopathological analysis showed no signs of inflammation or significant tissue damage, although mild fibrin deposition was noted in P1. Histomorphometric analysis indicated minimal stenosis, with average values of 0.85% for P1 and 0.83% for P2, demonstrating the stent's effective performance with minimal adverse effects.

This one-day acute study provided strong evidence that the MeriGraft™ Thoracic Endovascular Stent Graft System is leakage-proof, underscoring its potential reliability and effectiveness in preventing fabric-related endoleaks. In summary, the results confirm that the stent is functionally suitable for its intended applications, demonstrating its capability to achieve effective aneurysm closure with minimal complications.

CONCLUSION

The acute preclinical study conducted with the MeriGraft™ Thoracic Endovascular Stent Graft System successfully demonstrated its suitability in achieving the primary objective of preventing blood leakage at the aneurysm site. The deployment of the stent graft was effective, with no procedural complications, adverse clinical signs, or structural/material failures observed during fluoroscopic and angiographic evaluations. The histopathological findings further validated the absence of inflammation, vascular damage, or other safety concerns, confirming the device's potential as a minimally invasive solution for thoracic aortic aneurysms. While the device performed well in this study, challenges related to the use of a 22–25 French delivery system in the porcine femoral artery were noted. Future studies involving larger animal models with anatomically suitable arterial systems are planned to further refine and validate the system's performance. These additional evaluations will support the transition to clinical applications, leveraging the iliac artery in humans as a more compatible access route for the device. The study underscores the importance of manufacturing with high-quality materials to ensure non-leakage performance, reaffirming the MeriGraft™ system's design philosophy aimed at delivering safety and efficacy.

REFERENCES

1. Minocha, P., Kothwala, D. M., & Durani, M. M. (2020). *Endovascular stent graft, delivery device and system therefor* (Patent No. 201921023537). Indian Patent.
2. Biological Evaluation of Medical Devices - Part 2: Animal welfare requirements. ISO 10993-2:2006(E).
3. Guidance Document on the Recognition, Assessment and Use of Clinical signs as humane endpoints for Experimental Animals used in Safety Evaluation. ENV/JM/MONO (2000)7. OECD, December 2000.
4. CPCSEA Guidelines for Laboratory Animal Facility. Indian Journal of Pharmacology. 2003; 35: 257-274.
5. Guide for the Care and Use of Laboratory Animals, Institute of Laboratory Animal Resources. Commission on Life Sciences. National Research Council. National Academy Press. Washington, D.C. 1996.
6. Cardiovascular Implants– Endovascular devices-: Vascular stents (ISO 25539-2:2020).