◆ EXPERIMENTAL INVESTIGATION ◆

Fatigue and In Vivo Validation of a Peritoneum-Lined Self-Expanding Nitinol Stent-Graft

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Purpose: To assess the fatigue and in vivo performance of a new stent-graft incorporating bovine peritoneum lining that is designed for application in peripheral vascular occlusive disease.

Methods: Bovine peritoneum-lined stent-grafts were subjected to accelerated in vitro pulsatile fatigue and axial/torsional fatigue testing designed to simulate 10 years of physiological strain on the devices. At specified times the devices were evaluated for stent fracture, suture failure, or tissue tearing. Seven dogs underwent bilateral common iliac artery (CIA) balloon angioplasty injury with unilateral placement of the peritoneum-lined stent-graft. Angiography and intravascular ultrasound were performed prior to treatment, after treatment, and prior to sacrifice at 30 days. Vessels were perfusion fixed and histologically evaluated at 5 regions: above stent, proximal stent, mid stent, distal stent, and below stent.

Results: No evidence of stent, suture, or tissue failure was present during or after pulsatile and axial/torsional fatigue testing. At 30 ± 0.3 days after implantation, all vessels were patent. The average lumen area at explantation across stented vessels was 25.45 mm^2 . Lumen areas tended to be reduced above (23.57 mm^2) and below (24.17 mm^2) the stent. Lumen areas were consistent across stented regions at explantation (proximal stent 27.80 mm^2 , mid stent 25.88 mm^2 , and distal stent 25.81 mm^2). The mean neointimal area in peritoneum-lined stents was $2.02 \pm 1.52 \text{ mm}^2$, with a neointima:media ratio of 1.03 ± 0.50 . These values were significantly lower in the above and below stent areas than in the stented regions, but there was no difference in either measure within the proximal, mid, or distal stent.

Conclusion: The custom-designed peritoneum-lined stent-graft is promising for clinical peripheral applications due to its ability to resist relevant long-term physiological stresses and outstanding short-term patency rates in canine implantations.

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Percutaneous interventions for peripheral vascular occlusive disease (PVOD) continue to grow in popularity due to reduced invasiveness and greater patient preference for the procedure. Many percutaneous endoluminal devices have been applied with great success, such as aortic stent-grafts and iliac or coronary artery stents for atherosclerosis. Unfortunately, similar interventions for lower extremity PVOD have been plagued by suboptimal results. Superficial femoral artery (SFA) stents in particular have been shown to suffer from high premature failure and restenosis rates thought to be related to two central factors: neointimal hyperplasia and stent fatigue/stent fracture.^{1,2}

Several approaches to improving SFA stent design have attempted to reduce neointimal hyperplasia as a means of improving stent patency and failure rates, including new architecture, drug-coated stents, and expanded polytetrafluoroethylene (ePTFE) prosthetic-lined stent-grafts. Unfortunately, drug-coated stents have not been shown to have an advantage over bare metal stents for the treatment of PVOD in the SFA,³ and ePTFE-lined stent-graft results have been disappointing, in some cases performing even worse than bare metal stents.^{4,5}

Other approaches to improving failure and restenosis rates in SFA applications have targeted stent fracture/fatigue. Stent fracture was identified early on as an important cause of long-term stenosis and thrombosis in SFA stent-graft applications.² The anatomical course of the SFA results in significant axial and torsional fatigue, in addition to pulsatile fatigue inherent to the vascular system. In fact, walking >5000 steps per day was the strongest determinant of stent fracture, along with lesion length >100 mm, overlapping stents, and distal SFA implantation.⁶ Several studies have noted that available nitinol stent designs are poorly suited to resist mechanical fatigue and that revising strut alignment into helical

connecting bridges and reducing overall cell interconnections could dramatically improve stent flexibility and resistance to fracture.^{7,8} Thus, many second-generation SFA stents boast improved fracture resistance. Still, a recent study comparing mechanical strain test results of 7 second-generation SFA stents attributed differences in fracture resistance to stent design,⁹ suggesting that optimal designs remain to be identified.

Our group has had previous success in developing a new generation of stent-grafts in which commercially available, balloon-expandable nitinol stents were lined with bovine peritoneum. Our peritoneum-lined stents have been shown to resist neointimal hyperplasia and maintain superior patency rates vs. Dacron-lined stent-grafts in canine trial implantations.¹⁰ While these results were promising, the design of commercially available stents is not ideal for tissue attachment. Here, we seek to further develop our approach to reducing neointimal hyperplasia and stent fracture in SFA stent-graft applications by combining our bovine peritoneum lining with a new self-expanding nitinol stent design suited to the unique mechanical characteristics of the SFA while taking into account the demands for tissue attachment. Our goal was to examine the in vitro durability of this self-expanding stent-graft design through 10-year accelerated mechanical stress testing, as well as its short-term performance in vivo with canine models of iliac artery balloon angioplasty injury.

METHODS

Stent Design

A nested stent cell design was developed to accommodate both the need for tissue attachment sites and the unique mechanical environment of the SFA. Specifically, eyelets were incorporated along the length of the stent to allow suture attachment of the tissue via knots sewn through the eyelets (Fig. 1).

Figure 1 ♦ (A) Nitinol stent design. The proximal and distal ends of the stent are flared. (B) Face-on view looking down the lumen of the stent (protrusions correspond to the flared ends, which have a larger radius than the stent body). (C) Magnified view detailing struts, bridges, and eyelet designed to provide a location to suture tissue to the stent. (D) Complete stent-graft, with peritoneum attached to the luminal side of the stent, sewn with sutures through stent eyelets.

The body of the stent was designed to have variable stiffness progressing from the center to the ends. This was accomplished by varying the strut lengths and widths and allows the stent to better conform to the SFA during torsion of the vessel. In addition, an outward flare was incorporated on both the proximal and distal ends of the stent to facilitate changes in blood flow from the vessel to the stent.

Peritoneal Tissue Harvest

All animal studies were approved by the animal review committee and were conducted in accordance with institutional guidelines as well as the Guide for Care and Use of Laboratory Animals (NIH Publication No. 86-23). Studies were conducted at the Los Angeles Biomedical Research Institute, Harbor UCLA Medical Center (Torrance, CA, USA). Bovine peritoneum was harvested as previously described.¹¹ After harvest, specimens were transported to the laboratory in a container with 0.9% phosphate-buffered saline (PBS; pH 7.4) at 4°C. Tissue was then cut into segments and sutured onto polyethylene plates, which were placed in sterile jars and washed in 0.9% PBS for 1 hour to reach room

temperature. The tissue was then fixed with 2.5% glutaraldehyde solution (Fisher Scientific, Fairlawn, NJ, USA) in PBS for 24 hours in order to eliminate antigenicity. The tissue was then rinsed in PBS for 1 hour and sterilized with 50% ethanol for 24 hours. After another rinse in PBS for 1 hour, prion inactivation was performed in 1M NaOH for 2 hours and was followed by a final rinse in PBS before storage in a 0.625% glutaraldehyde solution.

Stent-Graft Preparation

Stent-grafts were prepared by suturing the peritoneum into the shape of a tube using a 7-mm dowel and 6-0 Prolene suture, with the mesothelial surface aligned toward the inner lumen. Peritoneum was then attached to the stents with 6-0 Prolene sutures, using the available suture attachment sites. The completed stent-graft was placed in a solution of 0.625% glutaraldehyde and stored at 4°C.

Axial and Torsional Fatigue Testing

Seven 7×100-mm prepared stent-grafts were subjected to accelerated in vitro axial and torsional fatigue testing on a Bose CLC

Figure 2 ♦ Axial/torsional combined loading fatigue test. Visual observation of stents at (A) 0.5M cycles, (B) 1M cycles, (C) 2M cycles, (D) 4M cycles, and (E) 10M cycles. After 10M cycles, stents were removed from test fixtures and closely examined. No abnormalities were present on any of the stents.

ElectroForce 3300 AT stent testing machine (Bose Corporation, Eden Prairie, MN, USA). This testing methodology was intended to provide empirical evidence of the continued integrity of the stent-grafts when subjected to mechanical torsional and axial fatigue and was designed to simulate a minimum of 10 years of physiological strain on the devices in vivo. Fatigue testing was performed on fully-assembled stent-graft constructs in order to most accurately represent the complete array of strains experienced by the device under physiological deformation, including the potential strain that physical attachment of the tissue may impose on the nitinol stent. This accelerated testing allows durability results to be obtained in a much shorter period of time than physiological rates would allow. Test conditions were designed to meet the requirements of in vitro mechanical fatigue testing stated in ASTM WK23330 (*Standard Guide for*

In Vitro Axial, Bending, and Torsional Durability Testing of Vascular Stents) and FDA Guidance 1545 (2010; *Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Devices and Associated Delivery Systems*).

Testing was conducted under simulated physiological conditions at $37^{\circ}\text{C} \pm 2^{\circ}\text{C}$ with distilled water. Test parameters were calculated based on a 0 mm starting point in order to obtain the appropriate axial tension strain level of 7% (3.29-mm displacement), compression strain level of 3% (−1.415-mm displacement), and torsional strain of 19° . Test frequency was 6 Hz, and the test duration was 10 million cycles. Cycle count, water temperature, rotation, and displacement peak/valley were monitored and recorded daily. Photographs and visual inspections for stent fracture, suture failure, or tissue tearing were obtained at 0.5, 1, 2, 4, and 10 million cycles (Fig 2).

Pulsatile Fatigue Testing

Eight 7-mm-diameter prepared stent-grafts of varying lengths (2 at 120 mm, 2 at 100 mm, 3 at 60 mm, and 1 at 40 mm) were subjected to accelerated in vitro pulsatile fatigue testing on a Bose EnduraTEC Model 9100 Stent/Graft Tester with Temperature Controller (Bose Corporation). This pulsatile fatigue test system is designed to accommodate stents of the same diameter, with results independent of stent length. The testing methodology was intended to provide empirical evidence of stent-graft durability over a minimum period of 10 years when subjected to hydrodynamic loading that simulates the changes in diameter that the device will experience in vivo. Test conditions were designed to meet the requirements of in vitro mechanical fatigue testing stated in ASTM F2477-07 (*Standard Test Methods for in vitro Pulsatile Durability Testing of Vascular Devices*) and FDA Guidance 1545 (2010).

All testing was conducted under simulated physiological conditions at $37^{\circ}\text{C} \pm 2^{\circ}\text{C}$ in PBS. The compliance of thin-walled silicone mock vessels was verified to be $4.5\% \pm 0.5\%$, designed to match the compliance of the SFA.¹² The stent-grafts were deployed into the mock vessels and were run under test conditions at 1.2 Hz (72 bpm) from 80 to 160 mmHg (± 5 mmHg). Device maximum and minimum outer diameters (ODs) were measured and used to determine physiological loading conditions. These conditions were then used to calculate equivalent maximum and minimum ODs of the stent in a thick-walled test vessel that is necessary to withstand the rapid cycling characteristic of accelerated testing. The process and calculations are described in detail in ASTM F2477-07.

Thick-walled test vessels were installed on the stent-graft tester, the stent-grafts were deployed, and the volumetric displacement of the system was adjusted to achieve physiological loading conditions. Testing proceeded under the aforementioned conditions for a total of 400 million cycles. Laser micrometer measurement of radial strain of the devices was performed daily at repeated positions along each stent to ensure that desired levels

of strain were met throughout the test duration. Devices were inspected for stent fracture, suture failure, or tissue tearing with a video endoscope at the completion of 50, 100, 200 and 400 million cycles (Fig. 3).

Stent-Graft Implantation

Seven female dogs weighing 25.8 ± 2.3 kg were quarantined for 14 days prior to the surgical procedure; food and water were withheld for 1 day prior to stent-graft implantation. Animals were administered oral aspirin (325 mg) 1 day prior to surgery. Preoperative anesthesia was achieved with an intramuscular injection of acepromazine (0.1–0.5 mg/kg) and atropine (0.04 mg/kg); ketamine (5 mg/kg) and diazepam (0.25 mg/kg) were administered intravenously. Animals were intubated and anesthesia maintained with isoflurane (0.5%–2.5%). Preoperatively, each dog received cefazolin (500 mg) intravenously. The neck was shaved, prepped with 70% alcohol and povidone iodine, and sterilely draped.

Seven dogs underwent bilateral common iliac artery (CIA) balloon angioplasty injury with unilateral placement of the peritoneum-lined stent-graft. Implantation was alternated between the left and right sides. Prior to implantation, the stent-graft was rinsed in PBS with heparin for 5 minutes to eliminate the glutaraldehyde. The right common carotid artery was surgically exposed and heparin (100–200 U/kg) was administered. Additional heparin was given to maintain an activated coagulation time >250 seconds. An access needle was placed in the artery and cannulated with a guidewire. The needle was removed and a 5-F introducer sheath (Boston Scientific, Natick, MA, USA) was placed in the artery. Using an appropriate catheter, a guidewire was passed into the descending thoracic aorta under fluoroscopic guidance (OEC 9800; GE Medical Systems, Salt Lake City, UT, USA). The 5-F sheath was removed, and a 55-cm, 9-F Flexor sheath (Cook Medical, Bloomington, IN, USA) was advanced into the distal abdominal aorta. An angiogram of the iliac bifurcation was obtained. A 0.018-inch guidewire was passed into one iliac artery. An intravascular ultrasound (IVUS) catheter was passed

Figure 3 ♦ Endoscopic images looking down into the lumen of the stent-graft at the mid stent region during pulsatile fatigue testing at (A) 50M cycles, (B) 100M cycles, (C) 200M cycles, and (D) 400M cycles.

over the guidewire, and the iliac artery diameters were measured in 2 perpendicular directions using a Visions PV 0.018 IVUS catheter (Volcano Corp., Rancho Cordova, CA, USA). Measurements were taken at the proximal, mid, and distal iliac artery.

Arterial injury was then induced by inflating a 7- or 8-mm angioplasty balloon (Ultra-thin; Boston Scientific) to $\sim 120\%$ of the measured IVUS diameter. The stent-graft was crimped onto the same balloon catheter and deployed into the CIA under fluoroscopic guidance. Following deployment, IVUS measurements were recorded at the proximal artery, proximal stent, mid stent, distal stent, and distal artery. The contralateral iliac artery underwent balloon dilation only, with no stent placement. In this vessel, pre- and post-treatment IVUS measurements were recorded at the proximal, mid, and distal iliac artery. Completion angiograms were taken to verify patency and position. The carotid artery was then ligated, and the incision was closed in standard fashion. The incision site was infiltrated subcutaneously with an-

algesic (bupivacaine), and the anesthesia was discontinued. The animal was recovered from anesthesia. Postoperative pain was managed with subcutaneous buprenorphine (0.005–0.01 mg/kg). Aspirin (81 mg/d) was administered for the duration of the study. Femoral pulses were palpated at procedure completion, daily for the first week, and weekly thereafter.

Angiography, IVUS, and Vessel Harvest

The 7 canines with a mean weight of 26.2 ± 2.6 kg were sacrificed at 30 ± 0.3 days after implantation. The animals were anesthetized as described above. Anesthesia was maintained with 0.5% to 2.5% isoflurane. The left common carotid artery was surgically exposed and heparin (100–200 U/kg) was administered. An access sheath was placed in the carotid artery and an appropriate guidewire and a catheter were positioned at the aortic bifurcation under fluoroscopic guidance. Angiograms of the aorta and iliac vessels were obtained in anteroposterior and

lateral views. A 0.018-inch guidewire was advanced into one iliac artery and IVUS was used to determine vessel diameters in 2 directions (minimum and maximum). In the stented arteries, measurements were taken at 5 regions of each vessel (AS: 1 cm above the stent, PS: proximal stent, MS: middle stent, DS: distal stent, and BS: 1 cm below the stent). For the unstented iliac arteries, IVUS measurements were taken at the proximal iliac, mid iliac, and distal iliac artery. Following IVUS, the aorta and iliac vessels were exposed through a midline abdominal incision. Aneurysm formation, inflammation, and adhesions were documented through gross observation. Vessels were perfusion fixed in situ with 10% buffered formaldehyde then harvested with 2 to 3 cm of native artery proximal and distal to each stent or treated section.¹³ Specimens were stored in 10% buffered formaldehyde until histology could be performed.

Histological Processing and Digital Morphometric Analysis

Vessel histology was performed at Mayo Clinic (Rochester, MN, USA). Formalin-fixed stented specimens were dehydrated through an ethanol gradient then embedded in epoxy resin. Embedded specimens were divided into 5 sections; AS: 1 cm above the stent, PS: proximal stent, MS: middle stent, DS: distal stent, and BS: 1 cm below the stent. Sections were mounted on plastic slides then ground and polished to a thickness of 30 to 40 μm . Specimens were stained using standard technique with Masson's trichrome to differentiate collagen and muscle tissue. Non-stented specimens were embedded in paraffin, cut into 5- μm -thick sections, and stained with Movat pentachrome to identify vascular layers. All samples were scanned into digital files using an Olympus VS120-S5 microscope for whole-slide scanning (Olympus, Center Valley, PA, USA) at 20 $\times$ magnification. Digital morphometric analysis to determine the luminal area, intimal area, and media area was performed using measurement tools in OlyVIA software (Olympus). Intimal area was defined as the area between the luminal

border and the luminal edge of the peritoneal tissue. Media area was defined as the muscle layer bordered by the internal and external elastic laminae. The neointima:media ratio was calculated from the 2 area measurements.

Statistical Analysis

Means and standard deviations were used to summarize the distribution of both IVUS and digital morphometry-derived area measurements. Two-sample comparisons were made using a 2-tailed 2-sample *t* test, and group comparisons were performed with ANOVA using a Tukey post-hoc test to detect differences between individual samples within the group. $P < 0.05$ was considered significant. Statistical analysis was performed using Minitab 16 software (Minitab Inc., State College, PA, USA).

RESULTS

Axial and Torsional Fatigue Testing

The 7 prepared 7 $\times$ 100-mm stent-grafts that underwent accelerated 10-year/10,000,000 cycle axial and torsional fatigue testing were visually inspected and photographed at 0.5, 1, 2, 4, and 10 million cycles. Data logs revealed that test conditions were maintained to meet protocol requirements. There were no gross visual defects detected during inspection at any point in the testing cycle (Fig. 2). There was no evidence of stent fracture, suture failure, or tissue tearing in any stent-graft at any point during or upon completion of testing.

Pulsatile Fatigue Testing

The 8 prepared 7-mm-diameter stent-grafts that underwent accelerated 10-year/400,000,000 cycle strain controlled cycles for pulsatile fatigue testing were visually inspected and photographed with a video endoscope at 50, 100, 200 and 400 million cycles. There was no evidence of stent fracture, suture failure, or tissue tearing in any of the stent-grafts for any of the inspection time points (Fig. 3).

Figure 4 ♦ Stent-graft explant. (A) Gross image of left (stented) and right iliac arteries prior to explantation. (B) Angiogram of the right and left iliac arteries at explant shows both sides patent. (C) Right iliac artery. (D) Left iliac artery, demonstrating the 5 analyzed regions of the stent: above stent (AS), proximal stent (PS), mid stent (MS), distal stent (DS), and below stent (BS). The location of the stent in relevant images is denoted by arrows at the proximal and distal ends. A color version is available online at www.jevt.org.

Canine Trial Implants

Angiograms revealed that all vessels were patent after 30 days of implantation (Fig. 4). Additionally, there was no loss of limb or observable gait changes in any animal during the trial period. IVUS demonstrated no gross abnormalities. In one animal, there was a rim of hyperplasia in the mid stent area causing mild luminal narrowing. In another device,

there was mild luminal narrowing in the distal stent area. Lumen area at the time of explant was determined from IVUS diameter measurements assuming a circular lumen. Overall, the average lumen area at explantation across all stented vessels was 25.45 mm² (Fig. 5). Lumen areas tended to be reduced above the stent and below the stent, with average areas of 23.57 and 24.17 mm², respectively. Lumen areas were relatively consistent across

Figure 5 ♦ Lumen area across the length of the stents at implantation and explantation, determined from IVUS diameter measurements. AS: above stent, PS: proximal stent, MS: mid stent, DS: distal stent, BS: below stent. Results are presented as mean $\pm$ standard deviation, $p < 0.05$.

all stent areas at explantat; averages for the proximal, mid, and distal stent were 27.80, 25.88 and 25.81 mm², respectively. Within each region, reduction in luminal area after 1 month of implantation caused by neointimal hyperplasia was significant only in the mid stent region, where there was no outward flare. There were no anatomical abnormalities of the vessels upon gross inspection during vessel harvest (Fig. 4). Following vessel harvest, there was no evidence of stent fracture in any explanted devices.

Histology and Digital Morphometric Analysis

Histological evaluation revealed all vessels were patent (Fig. 6). Morphometric analysis

Figure 6 ♦ Histological appearance along the length of the stent-grafts (A) above stent, (B) proximal stent, (C) mid stent, (D) distal stent, (E) below stent (Masson's trichrome, original magnification $\times 20$). (F) Contralateral non-stented artery (Movat pentachrome stain, original magnification $\times 20$). A color version is available online at www.jevt.org.

TABLE

Histological Morphometric Measurements Along the Peritoneum-Lined Stent-Graft and Adjacent Regions

	Across Full Stent	AS	PS	MS	DS	BS
Neointimal area, mm ²	2.02 $\pm$ 1.52	0.04 $\pm$ 0.06	1.90 $\pm$ 1.75	2.16 $\pm$ 2.06	1.99 $\pm$ 0.59	0.53 $\pm$ 0.44
Medial area, mm ²	1.83 $\pm$ 0.56	2.21 $\pm$ 0.62	1.74 $\pm$ 0.51	1.78 $\pm$ 0.61	1.96 $\pm$ 0.62	3.01 $\pm$ 0.82
Neointima:media ratio	1.03 $\pm$ 0.50	0.01 $\pm$ 0.02	1.01 $\pm$ 0.62	1.06 $\pm$ 0.65	1.02 $\pm$ 0.18	0.16 $\pm$ 0.13

Data are presented as the means $\pm$ standard deviation.

AS: above stent, PS: proximal stent, MS: mid stent, DS: distal stent, BS: below stent.

Figure 7 ♦ Digital morphometric analysis. (A) Neointima:media ratio across the length of the stent-grafts. (B) Area of the media across the length of the stent-grafts. Results are presented as mean $\pm$ standard deviation. Asterisks denote that AS and BS regions have significantly lower neointima:media ratios compared to the 3 stented regions, $p < 0.05$.

found a mean neointimal area in peritoneum-lined stents of $2.02 \pm 1.52 \text{ mm}^2$, a media area of $1.83 \pm 0.56 \text{ mm}^2$, and a neointima:media ratio of 1.03 ± 0.50 (Table). Neointimal area and neointima:media ratio were significantly lower in the above and below stent regions than in the stented regions, but there was no difference in either measure within the stent (Fig. 7A). Media area was not significantly different across the 5 vessel regions analyzed (Fig. 7B).

DISCUSSION

Stent design has received a great deal of attention in recent years, since stent fracture was identified as a major contributor to long-term stenosis and thrombosis in SFA stent applications.² This study sought to demon-

strate that a tissue-lined stent-graft designed specifically for SFA applications can mitigate long-term failure rates by improving resistance to mechanical stresses unique to the SFA. Additionally, this new stent-graft has the potential to address all of the issues leading to both early and late SFA stent-graft failures by resisting neointimal hyperplasia as well.

While stent fracture has been implicated in long-term stent failure, neointimal hyperplasia following SFA interventions has been identified as the leading cause of early failures. Various early stent-graft approaches targeting neointimal hyperplasia have been met with disappointing results. Prosthetic stent-grafts, mostly utilizing ePTFE, have been shown to have poor 1-year patency rates.^{4,5} Other designs employed saphenous vein as a lining, but patency rates were poor, and other logistical issues arose due to limited lumen diameter and concerns about tissue thickness.¹⁴ Drug-eluting SFA stents have also suffered from higher early stenosis rates than expected¹⁵ and have only just recently begun to show some promise.¹⁶ Previous studies with our first-generation, balloon-expandable, bovine peritoneum-lined stent-graft have shown promising results where these other approaches have failed. The peritoneum-lined stent-grafts were shown to reduce neointimal hyperplasia and enjoy higher patency rates and greater lumen diameters when compared to a Dacron stent-graft control.⁶ The current study builds upon that work by applying the same peritoneal lining strategy to a new self-expanding stent scaffold designed specifically to resist SFA mechanical stresses while accommodating tissue.

Indeed, the results of in vitro mechanical fatigue testing in this study were promising, as there were no stent failures in either the axial/torsional or pulsatile fatigue tests. These data indicate that our stent design is effective at resisting physiologically relevant stresses that would be present in the SFA. Mechanical stress testing was designed to simulate 10 years of stresses that these stents would endure in vivo. Tissue durability was a significant concern during long-term accelerated testing. Whereas the stent scaffold

fold was designed to resist these stresses, it was unclear how well the tissue would fare. However, observation of the stents after both axial/torsional and pulsatile fatigue testing showed that the integrity of the tissue remains intact, verifying the durability of the peritoneal lining as well as the connection of that lining to the stent itself. It is unclear how relevant peritoneal durability will actually be in vivo since the peritoneum is thought to act as a scaffold for rapid re-endothelialization, which will improve its durability and may also explain its propensity for reducing neointimalization.⁶ Nevertheless, these tests indicate that this stent-graft would be well suited to resist long-term stent fracture in the SFA.

Results for short-term canine implantations were similarly promising, with all stents remaining patent at 30 days. There was some initial concern moving from the balloon-expandable stent-graft we worked with previously to an unproven self-expanding stent-graft. The self-expanding design is critical for applications in the SFA, allowing the stent to resist permanent crush deformation caused by the tortuosity and movement of the vessel. The size of the canine vessels precluded using the SFA in our model, making the iliac arteries the most suitable choice. As a result, this model does not take into account the movement of the SFA during ambulation; however, the fatigue and durability testing do account for this. We performed a previous study using the same animal model in which a Dacron-lined stent (DLS) was investigated,⁶ and the peritoneum-lined stent in the present study shows significant reduction in neointimal area and neointima:media ratio compared to the DLS, suggesting efficacy of the peritoneal lining. In addition, the results of the present peritoneum-lined stent-graft study are comparable to the results in the previous study in terms of neointimal and media area as well as neointima:media ratio. Based on our previous investigation, we are confident that this new iteration of peritoneum-lined stent-graft is likely to enjoy the same improved resistance to neointimal hyperplasia and early stent failure over other stent-grafts. As with our previous

work, the tissue-lined stent-grafts displayed only a mild inflammatory response and smooth muscle proliferation. There was no histological evidence of calcium deposition, but one would not expect this in such a short time frame.

Conclusion

This custom designed SFA stent-graft is well suited to resist relevant long-term physiological stresses and shows outstanding short-term patency rates in canine trials, likely attributable to its resistance to neointimal proliferation shortly following implantation. This stent-graft addresses causes that have been identified for both short and long-term SFA stent failure and offers promise for future clinical peripheral stent applications. With the recent development of a simplified delivery system, the stent is now well suited to begin clinical investigation.

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