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A novel customizable stent graft that contains a stretchable ePTFE with a laser-welded nitinol stent

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Abstract

Customizable medical devices have recently attracted attentions both in dental and orthopedic device fields, which can tailor to the patients' anatomy to reduce the length of surgery time and to improve the clinical outcomes. However, development of the patient specific endovascular device still remains challenging due to the limitations in current 3D printing technology, specifically for the stent grafts. Therefore, our group has investigated the feasibility of a highly stretchable expanded-polytetrafluoroethylene (ePTFE) tube as a customizable graft material with the laser-welded nitinol backbone. In this study, a highly stretchable ePTFE tube was evaluated in terms of mechanical behaviors, *in vitro* biocompatibility of ePTFE with various stretchiness levels, and capability for the integration with the laser-welded customizable nitinol stent backbone. A prototype stent graft for the swine's venous size was successfully constructed and tested in the porcine model. This study demonstrates the ability of ePTFE tube to customize the stent graft without any significant issue, for example, sweating through the stretched pores in the ePTFE tube, as well as *in vivo* feasibility of the device for bleeding control. This novel customizable stent graft would offer possibilities for a wide range of both current and next-generation endovascular applications for the treatment in vascular injuries or diseases.

Keywords

stent graft; nitinol; highly stretchable ePTFE; endovascular device; finite element analysis

INTRODUCTION

As part of a growing trend in personalized medicine, patient specific instrumentation (PSI) was introduced in the last several years to obtain a customized implant fit for patients with greater accuracy and shorter rehabilitation.¹ For example, PSI has emerged as a new technology in total knee arthroplasty (TKA) as a replacement for the traditional instrumentation.² The medical implants—manufactured from magnetic resonance imaging (MRI), computed tomography (CT) imagery, or a combination—are specifically designed for the patient and intended to offer a faster, more accurate, and cost-effective surgery.

Recent advances in 3D printing have provided a new option to manufacture these patient-specific medical devices such as dental, spinal, and hip implants.^{3–5} Without the need for the surgeons to modify the implants into a desired shape, size, and fit for the patient, implants, and prostheses can be quickly produced and customized through the translation of X-ray, MRI, and CT scans into digital print files. It has been suggested that the 3D printed customized implants can reduce the length of surgery, lower the risks of complications such as infections, and improve clinical outcomes.⁶ While the future of 3D printing in medical implant applications is promising, for endovascular devices, which typically consist of ultra-thin metallic structures and polymeric membranes, there remain significant logistical issues for 3D printing. Typical endovascular devices need to be collapsed into a low-profile catheter with the diameter of a few millimeters for delivery and then deployed in the targeted vascular system up to 3 cm. It requires flexibility to accommodate dramatic device diameter reduction and expansion, sufficient structural mechanical strength (e.g., radial force) to prevent device migration inside the vessels, and a smooth surface contact with the tissues. These requirements cannot yet be fulfilled by current 3D printing technologies.⁷

Some endovascular devices require ultra-thin polymeric membrane, commonly (expanded) polytetrafluoroethylene (ePTFE),^{8,9} to cover the metallic-framed backbone because it has relatively high tensile strength, controlled porosity, low surface energy, and superior hemocompatibility. This is often done by fabricating the membrane separately and then integrating it with the metallic frames. As the conventional polymeric membranes have already been set with predefined geometry and dimensions, modifications often need to be performed by the surgeons to tailor to the specific patient needs. It significantly lengthens the operation time and might increase the complications as well. Therefore, an approach to customize existing PTFE tubing would be beneficial to manufacture patient-specific endovascular devices within a clinically relevant timeframe. Aside from clinical use, rapidly customizable PTFE sleeves are virtually indispensable for research on custom endovascular devices. By this approach, our group was able to quickly adapt PTFE to evolving needs and complicated sizing configurations, where other custom approaches would have introduced both significant delay and cost.

In this study, a rapidly customized expanded polytetrafluoroethylene (ePTFE) tube was investigated after combination with a laser-welded nitinol frame to create a stent graft, which first attempted for the endovascular devices. This device, for example, is intended for military or civilian vascular trauma, to be introduced and deployed endovascularly to rapidly control bleeding.^{10,11} A novel customized stent graft would provide an important treatment

option with the use of anatomically relevant endovascular devices for traumatic situations. Various crucial analyses on both materials, superelastic nitinol and ePTFE membrane, were conducted for validating the use of these two materials in new stent grafts. Next, prototypes were fabricated and utilized for *in vivo* swine studies to demonstrate the functionality of the devices.

MATERIALS AND METHODS

Materials

Two materials were primarily used to fabricate the customizable stent graft for the vascular injury management. The device uses (1) highly stretchable expanded polytetrafluoroethylene (ePTFE) for the covering membrane and (2) superelastic thin nitinol wire for the metallic backbone. An extruded ePTFE tube (ZEUS, inc., Orangeburg, SC) with an internal diameter of $0.394'' \pm 0.030''$ and a wall thickness of $0.005'' \pm 0.004''$ was used in covering the nitinol stent backbone for the study. The cold-drawn superelastic nitinol wire (Confluent, Fremont, CA) with 0.0155'' diameter was used for the stent backbone fabrication.

***In vitro* and *in vivo* tests for evaluating device's functionality, feasibility, and biocompatibility** **Stretchiness characterization of ePTFE membrane.**—The stress–strain behavior of the ePTFE membrane was measured using a mechanical testing system (FMS500, Starrett, MA). The 0.005'' thick (thickness T) ePTFE samples were cut into 25×25 mm (length $L \times$ width W) size and affixed to the two film test grips (G1008, Mark-10 Co., NY), one movable on the top and while another fixed on the bottom [Figure 1(a)]. The two grips were aligned carefully and the distance between two grips (D) was measured to calculate the strain. The grips on the top were connected to a load cell with the capacity of 500 N (FLC-500E, Starrett, MA) to measure the corresponding tensile force (F). The total travel displacement (ΔD) of the top grips was set as 40 mm with the traveling velocity of 4 mm/min and 10 mm with the velocity of 1 mm/min for radial direction and longitudinal direction, respectively. The sampling rate in load cell was set as 100 Hz and a tablet connected to the mechanical testing system recorded the travel distance (ΔD) and load force (F) in real time. All the parameters mentioned above can be set in the Starrett L3 series software. The stress (σ) and strain (ϵ) of the ePTFE membrane can be calculated from $\sigma_{\text{radial}} = \frac{F}{W \cdot T}$, $\sigma_{\text{longitudinal}} = \frac{F}{L \cdot T}$, $\epsilon = \frac{\Delta D}{D}$.

Porosity calculation with the applied strain.—The ePTFE membrane was stretched radially to 200%, 400%, and 550% (before fracture) using the methods described in Stretchiness characterization of ePTFE membrane section. Four samples including original (nonstretched), 200% stretched, 400% stretched, and 550% stretched ePTFE membranes were characterized by scanning electron microscopy (SEM-ZEISS Sigma500 VP, Carl Zeiss Microscopy, LLC, NY) after 45 s sputter deposition of thin Palladium layer. The SEM images with 1000x magnifications were imported into MATLAB R2014a as the matrices of greyscale values. The number of pixels on the ePTFE fiber region was counted in the matrices so the porosity of the ePTFE membrane with different stretchiness levels can be calculated from

$$\text{porosity} = 1 - \frac{\text{number of pixels on fiber regions}}{\text{total number of pixels}}$$

***In vitro* sweating test for evaluating potential leakage of ePTFE membrane.—**

Figure 1(b) shows the *in vitro* test setup for determining the ePTFE radial stretchiness with respect to the applied pressure induced by the incoming flow. The ePTFE tube was cut into 10 cm long with one end completely sealed using the biocompatible glue (LOCTITE 4061, Henkel Corporation, OH). Another end of ePTFE tube was connected to a pressure sensor (PRESS-S-000, Pendo-TECH, NJ) to measure the corresponding fluid pressure inside the ePTFE tube. The heparinized pig blood was applied with 50 mL/h flow rate. At the pressure levels of 30, 60, 90, and 120 mmHg, the corresponding ePTFE tube diameter and length were measured three times respectively and plotted against the pressure level changes. At the meantime, the ePTFE tube surface was monitored for evaluating any blood sweating during the tube expansion.

***In vitro* early thrombosis evaluation of Eptfe.—**Three sets of ePTFE samples (5 mm × 5 mm) were prepared with pre-stretchiness of 0%, 200%, and 400%, respectively, to be fixed on the glass substrate and placed in the petri dish. Each set of three samples were immersed into the fresh blood directly drawn from the living pig (i.e., non-heparinized blood) and heparinized pig blood for 1, 2.5, and 5 min to assess the early thrombotic response of the ePTFE. Then, the samples were gently rinsed with saline immediately and fixed. The samples were coated with palladium and subsequently characterized by SEM. SEM images were taken on a random location in each three samples under different pre-stretchiness levels and blood exposure times. Then, the corresponding number of cells were counted to quantify the thrombosis formations on ePTFE surface. Two-way analysis of variance (ANOVA) was performed to determine the statistical significance.

Finite element analysis of nitinol stent crimping process.—The stent crimping modeling was performed in Abaqus CAE 2016. Figure 3(a) shows the 3D model used in the finite element analysis (FEA). The stent model was simplified with a constant diameter cylindrical design and the crimping function was modeled with SFM3D4R elements (4-node quadrilateral surface element with reduced integration) and the stent backbone was modeled with 20,890 C3D8R elements (8-node linear brick element with reduced integration and hourglass control). The nitinol material property was defined as Young's modulus $E = 60$ GPa and Poisson's ratio $\nu = 0.3$.¹² The contact between the crimper and the stent backbone surface was defined as frictionless in the tangential direction and "hard" contact in normal direction so the stent will be crimped along with the crimper diameter reduction. A displacement loading normal to the crimper surface with magnitude up to 40% of the stent diameter was applied on the crimper's outer surface [Figure 2(a)] and the corresponding stress/strain distribution as well as reactional radial force was calculated from the software.

***In vitro* radial force measurement of nitinol backbone.—**A stent crimping experiment was conducted to quantify the radial force of the prototype nitinol stent backbone *in vitro* using the setup described in the published paper.¹³ Figure 2(b,c) show the

measurement configurations using the mechanical testing system. One end of the Dacron strap (Sailrite Enterprises, Inc., IN) was glued on the stainless steel rod at the bottom while the opposite end was clamped firmly by a grip connected to a load cell. The Dacron strap was wrapped around the stent backbone and exerted forces on the stent surface to crimp it approximately radially as the moving stage pulled the Dacron strap up with the displacement magnitude equal to 40% of the stent perimeter. Both the displacement and hoop force can be measured from the mechanical testing system. Then, the radial force can be calculated from the hoop force using the following equation¹³:

$$F_{\text{radial}} = 2 \cdot \pi \cdot F_{\text{hoop}}$$

The radial force with respect to stent diameter reduction (%) was plotted and compared with the FEA results. The results are presented in FEA results of crimping process of the nitinol backbone and *In vitro* measurement of the radial force sections. As the prototype stent has a tapered design (i.e., the diameter in the distal strut region is larger than the proximal strut region), we measured the radial force in these two regions separately.

***In vitro* force analysis and measurement to assess device migration.**—When the stent graft was deployed inside the vessels, the contact pressure can be calculated using the following equation with an elastic cylinder compressed into another cylinder model¹⁴:

$$P_c = \frac{\delta}{R \left[\frac{1}{E_o} \left(\frac{r_o^2 + R^2}{r_o^2 + R^2} + \nu_o \right) + \frac{1}{E_i} \left(\frac{R^2 + r_i^2}{R^2 + r_i^2} + \nu_i \right) \right]}$$

where δ is the overlap, R is the nominal radius, r_o and r_i is the inner radius of the outer cylinder (vessels) and inner cylinder (stent graft), respectively. And E_o , ν_o , E_i , ν_i is the Young's modulus and Poisson's ratio associated with outer cylinder and inner cylinder materials. Then, the pullout force of the stent graft inside the vessels to determine the stent migration can be calculated from¹⁴: $F = \mu(P_c \times A)$ where F is the pullout force, A is the contact surface area, and μ is the coefficient of friction.

The stent migration was experimentally assessed using an *in vitro* model [Figure 2(d)]. The prototype stent backbone was collapsed into silicone tubes with the inner diameter of 0.5" and 0.75", respectively, that is, the oversizing of the prototype stent backbone is about 51% and 27%, then, pulled out.

Stent graft fabrication process

A nitinol stent backbone was mainly fabricated using a precision microlaser-welding process with the mechanical bending process.^{10,15} The laser welding spots were created at every 2 cm location by aligning the two wires side by side. The intensity of laser is 1.4 kW, time for laser excitation is 1.2 ms, frequency is 3 Hz with step function waves, and spot size is 700 μm . Thermal shape setting was performed under 500°C for 40 min in the high temperature furnace (Lindberg/Blue M Moldatherm Box Furnace, Thermo Scientific, PA), and subsequently rapidly cool down in 25°C deionized water bath for 5 min. Once the nitinol

backbone is fabricated, the 5 mm diameter ePTFE tube was covered after the stretch using 20–26 mm diameter balloon catheters (Z-MED Balloon Dilatation Catheter, B. Braun Medical Inc., PA) [Figure 3(a)]. Since the short length of balloon (4 cm), the balloon inflation was conducted several times for stretch the entire length of the tube [Figure 3(b)]. The stretched ePTFE tube was covered on the nitinol backbone and fixed using a biocompatible polymer adhesive (Loctite 4011, Henkel, Germany).

***In vivo* test with swine model**

Yorkshire pigs ($n = 7$) were placed under general endotracheal anesthesia as part of a University of Pittsburgh approved IACUC protocol with inhaled isoflurane. Abdominal exposure was obtained by an abdominal incision with exposure of the infrarenal vena cava (large abdominal vein). The animals were heparinized with 100 units/kg of heparin to simulate post-traumatic coagulopathy and as required by the porcine model due to rapid clotting of this model at baseline. The prototype stent grafts were cleaned using saline before implantation. Following 18 G needle access of the infrarenal vena cava, the seldinger technique was used to injure the cava with a 22 French dilator, then a long 9 French sheath (Oscor, Palm Harbor, FL) was used to deploy the device under fluoroscopic guidance. A venous angiogram was then performed to document the vascular injury, stent control of the hemorrhage, and preserved flow beyond the stent. The stent graft was placed in the pig model for approximately 30 min. And in the final step, the stent graft was retrieved by advancement of the vascular sheath to collapse the stent graft. The vein tissue was fixed and characterized under SEM within 3 h after device retrieval.

RESULTS

Results on ePTFE's mechanical and biological behaviors

Stress–strain behavior of ePTFE membrane.—Figure 4(a,b) show the stress–strain behavior of ePTFE membranes under the tensile test using the test setup described in Stretchiness characterization of ePTFE membrane section. The ePTFE membrane was stretched in radial direction of the tube, reaching the fracture strain of approximately 550% and the corresponding stress of 0.7 MPa [Figure 4(a)]. This outcome demonstrates that the ePTFE membrane can be easily stretched up to 550% after the necking occurred during the tensile loading without mechanical failure. While there is no mechanical failure, there is changed structure of the fibers in ePTFE after the elongation. Detailed ePTFE structure analysis will be discussed in the next section (Porosity changes with applied strains in ePTFE). Figure 4(b) shows the stress–strain behavior when the ePTFE membrane was stretched in longitudinal direction of the tube. The fracture occurred approximately at 8% strain and the corresponding stress at fracture was as high as 23 MPa.

Porosity changes with applied strains in ePTFE.—Figure 5(a–d) show the SEM images of ePTFE membranes with 1000x magnifications under 0%, 200%, 400%, and 550% strains, respectively. Figure 5(e) show the calculated porosity from MATLAB with respect to the various applied strains. As can be seen, nonstretched ePTFE membrane exhibits an aligned dense microfiber structure with only 3% porosity that shows the adjacent fibers stay within a very small gap. With the increased strain in the radial direction of the tube, the gaps

between fibers tend to be enlarged exhibiting a higher porosity of 14.4% and 20.87% in average for samples with 200% and 400% strain, respectively. In addition, the multilayers of ePTFE fibers were stretched differently, therefore, wrinkled and relatively unorganized structures were found as shown in Figure 5(b,c). As the applied strain reached 550%, the gaps between fibers had the maximum of approximately 30 μm in length with 24.15% porosity in average, but the fiber networks were still connected and no fracture was observed under the fracture strain value. Both the qualitative and quantitative analysis on the SEM images have demonstrated that the structure porosity tends to increase along with the applied radial strain, but will reach plateau of 26% before the fracture occurs.

Sweating test results of ePTFE.—Figure 6(a) shows the ePTFE tube connected to the pump that is initially perfect cylindrical shape with the diameter of 5 mm without any stretch. While the blood is entering the tube by pump, the ePTFE tube slowly expands enlarging the pore sizes (see Porosity changes with applied strains in ePTFE section). Figure 6(c) shows the ePTFE tube diameter changes with the incoming blood from the syringe pump, which indicates the stretch levels of the ePTFE tube. The averaged diameter of the tube was significantly increased from 8.21 mm to 21.97 mm, 167% tube expansion as the fluid pressure elevated to 120 mmHg. No fracture or leakage was found at this level of pressure since the fracture strain of ePTFE polymer is higher than 500% in radial direction. Similarly, the ePTFE tube tends to be shortened during the expansion, and Figure 6(d) shows the length reduction with respect to the fluid pressure. At the pressure level of 120 mmHg, the ePTFE tube length decreased by about 8%, which is minimal compared to the significant diameter expansion. Hence, there is no sweating (or leakage) issue on the stretched ePTFE tube, which demonstrates that the tube can be used for the stent graft in the body where the applied pressure level is approximately 120 mmHg.

Assessment of the early thrombogenic response of ePTFE.—Figure 7(a) shows the SEM images of non-heparinized blood product adherence on the ePTFE surface with 0%, 200%, and 400% stretchiness for 1, 2.5, and 5 minutes, respectively. The number of blood cells (i.e., mostly red blood cells) adhered on the ePTFE surface increased significantly as the immersion time into the fresh pig blood increased from 1 min to 5 min (p -value < 0.0001). It confirms that more blood cells will grow onto the ePTFE surface if it has contact with the surface for a longer period of time. For medical device applications, these results suggest minimizing the device exposure to the blood to reduce the risks of thrombosis on the device surface. Figure 7(b) also demonstrates that there was no significant difference on blood cell attachment on ePTFE surface for different stretchiness levels (p -value = 0.9901). For the stent graft fabrication, the ePTFE membrane will be expanded before wrapping onto the stent backbone and *in vitro* results showed stretchiness level has no influence on the thrombosis formation.

While the blood products adherence study with non-heparinized blood is important to assess the hemocompatibility of the material used in the stent graft (i.e., ePTFE), identical study is needed with heparinized blood because anticoagulant solutions frequently injected to the blood stream during the endovascular procedure. Figure 8(a) shows the representative SEM images of blood cells adherence on ePTFE sample surface with heparinized blood. As the

blood are less prone to coagulate on ePTFE surface with heparin treatment, all the samples with 0%, 200%, and 400% stretchiness exhibit clean surface with minimal or no blood cells visible when the samples were immersed in heparinized blood for 1, 2.5, and 5 min, respectively. Figure 8(b) summarizes the count of blood cell attachment on the sample surface. It can be observed that the blood cells with the heparin treatment are less likely to be attached on the ePTFE sample compared with the blood cells from the one without heparin treatment. Again, this outcome demonstrates there is no significant influence of the stretchiness levels for the hemocompatibility.

Results on nitinol backbone's mechanical behaviors FEA results of crimping process of the nitinol backbone.

Figure 9(a,b) show the computationally modeled stress and maximum principal strain (MPS) field when the stent backbone was crimped by up to 40% considering the targeted vessel size. The maximal stress is 456 MPa and the maximal MPS is 0.6%, which is below the fracture strain of nitinol.¹⁶ Therefore, our nitinol backbone can be crimped down to 60% of the original size successfully without any mechanical failures. Also, as we can see from the calculated stress and strain fields in FEA results, the junctions of the struts exhibit both highest stress and strain values while the straight struts exhibit relatively negligible stress and strain values. Abaqus also calculated the corresponding radial force exerted by the stent backbone during the stent crimping process at the diameter reduction of 10%, 20%, 30%, and 40% and Figure 9(c) plots the radial force against stent diameter reduction (yellow line). It can be observed that the radial force increased from 0.60 N to 2.98 N when the stent diameter reduction increased from 10% to 40%.

In vitro measurement of the radial force.—Figure 9(c) (green and blue dots) show the measured radial force using the test setup described in in vitro radial force measurement of nitinol backbone section. As the nitinol backbone has a tapered design, we measured the radial force in large section as shown in blue dots (distal end) and small section as shown in green dots (proximal end) separately. The large section exhibits a higher radial force compared with the small section, as the large section experiences a higher strain deformation when the both sections are crimped into the same diameter size. As can be seen from the plots, the radial force increased from 0.75 N to 2.83 N for small section when the stent diameter reduction ramped from 10% to 40%. Similarly, the radial force value was from 0.94 N to 3.46 N for large section. The FEA results matched well with the experimental results.

In vitro force analysis and measurement to assess device migration.—The pullout force can be defined as the frictional force between the artery wall and the stent graft during the stent movement. Here, we used a silicone tube for the artery model. The measured pullout force of the stent backbone inside a silicone tube with ID of 0.5" (green line) and 0.75" (blue line) was plotted in Figure 9(d). From the plot, we can see that the pullout force in a silicone tube with ID of 0.5" (51% oversizing) is about 2.65 N, which is much higher than the one in a 0.75" (27% oversizing) tube (0.79 N). The pullout force is related to the contact pressure between the collapsed stent and the tubes and a higher pullout force inside the tube presents lower risks of stent migration inside the targeted vessels during

the treatment. Conversely, the higher contact pressure also presents high risks of damage to the vessel walls.

Prototype of stent grafts

Nitinol stent backbone was fabricated using a precise microlaser-welding process and subsequently Td radiopaque makers were attached on both distal and proximal ends as shown in Figure 10(a). The microlaser-welding technology for the nitinol wire enables the stent backbone fully customizable since both the spot welding in narrow regions and thermal shape setting process can easily tailor the geometry customizing the backbone structure. For the *in vivo* studies, two prototypes have been successfully fabricated, which were smoothly collapsed and inserted in 8–9 Fr delivery sheaths [Figure 10(b)]. Two types of prototype devices are shown in Figure 10(c–f). Figure 10(c,d) show the nitinol backbone covered by ePTFE from outside and Figure 10(e,f) show the nitinol backbone covered by ePTFE inside, respectively.

Results in a swine model

Angiography evaluation of device deployment in a swine model.—The fabricated stent graft was examined for control of bleeding in a porcine model that simulates traumatic injury of the vena cava, the large primary vein that carries blood back to the heart. The retrievable venous stent graft was deployed easily with simple sheath withdrawal and rapidly achieved control of the venous bleeding. As shown in Figure 11(a), a venogram demonstrates contrast (black) leaking from the vessel injury, whereas after deployment of the stent graft Figure 11(b), the contrast stays within the vessel.

Gross look of the device and SEM image analysis.—Figure 12a,b show the gross look of the harvested stent graft used in vein of the swine. As one can see in the images, there are some locations where partially detached ePTFE membrane from the nitinol backbone observed after the device deployment and retrieval. The device's surface looks mostly pristine except a few locations where the thrombosis was formed. This issue has been resolved by adding a few tiny suturing locations in the recent devices (not shown here). More importantly, the surface of ePTFE was investigated via SEM image analysis. Figure 12(c) shows a global view of the SEM image of the ePTFE outside. There are thrombosis covered on some areas and ePTFE structure is shown beneath the thrombosis. Figure 12(d) shows highly magnified SEM image, which explains individual blood products adhered on the surface of ePTFE membrane. Aggregated platelets, fibrin networks, and accumulated red blood cells were found in the thrombosis.

DISCUSSIONS

Various studies have been conducted for demonstrating the design, manufacturing and testings. The parameters in the experimental studies are selected based on the criteria typically used in endovascular devices and close to the human physiological conditions. Both *in vitro* and *in vivo* tests have been conducted to demonstrate the feasibility of the highly stretchable ePTFE tube as a graft material along with the laser-welded nitinol stent backbone. Stress–strain curve of ePTFE membranes in Figure 4 confirms that the ePTFE

membrane is less prone to be stretched in longitudinal direction compared with the stretchability in radial direction, that is, ePTFE membrane exhibits anisotropic mechanical behaviors in terms of tensile loading. This behavior can be explained from the microstructure of the ePTFE fibers observed under SEM. As the ePTFE fiber networks show the two types of fibers, the thick fiber struts [shown in blue circle in Figure 5(d)] and thin fibers connecting the fiber struts [shown in red circle in Figure 5(d)]. The ePTFE membrane is easier to be stretched along the thin fiber directions and the fracture happens once the thin fibers are disconnected from the thick fiber struts. Because of this unique stretch behavior in different directions, the ePTFE tube shows anisotropic stress–strain behaviors under tensile loading. This unique behavior of ePTFE membrane is beneficial for the customizable stent graft fabrication if the device requires various diameters in one stent graft for the patients' anatomy. Although the porosity increases to around 14.40% under the applied strain of 200%, no blood leakage was observed during the sweating test under 120 mmHg fluid pressure. The possible reason is that the thin fibers in ePTFE membrane tend to overlap each other during the elongation and thus reducing the pore size and creating the barriers for the blood flow to pass through. The anisotropic mechanical behavior and no blood leakage property of the stretchable ePTFE tube would exploit the benefits for the customizable stent graft construction. First, radially customizable ePTFE tube is suitable for the tapered vascularature in the torso area. Aortic regions close to heart typically have bigger diameter and narrowed when the artery approached to the iliac bifurcation. The ePTFE tube could be customized based on the dimensions obtained from the medical imaging techniques, such as MRI, CT scan, or angiographic images. As we demonstrated in this study, the blood leakage was not observed with the increased porosity when stretched. Therefore, this customizable approach for the stent grafts could be widely used in other vascular devices if the customization is needed.

For the mechanical behaviors of the nitinol backbone structure, there is a small discrepancy between the FEA results and experimental results in terms of radial force, which can be attributed to the material property defined in FEA calculations and a simplified 3D model of stent backbone during the stent crimping modeling. In the *in vitro* pullout force measurement, it is only an approximation to the stent migration inside the vessels as the interactions between ePTFE grafts and vessel tissues were not taken into account. Also, the blood vessel tissue is more flexible compared to the silicone tubing used in the testing and the deployed stent will conform to the vessel geometries. In the radial force analysis and measurement *in vitro*, the integration of ePTFE graft with the nitinol backbone also needs to be considered to account for the effects of expansion in ePTFE graft. In the stent migration evaluations, the stent needs to be deployed in a more realistic tissue model to mimic the more flexible blood vessel tissues. Both computational modeling and experimental test results have demonstrated that (1) the nitinol backbone exhibits superelastic behavior for the self-expanding stent grafts, (2) there is no material integration issues or defects observed during *in vitro* mechanical testing of ePTFE covered nitinol stent graft, and (3) both radial and pullout forces in the stent graft are in the range of smooth delivery and retrieval process of the device.

Based on the design and test results for both ePTFE tube and nitinol, two prototype devices were constructed using a microlaser welding and subsequent thermal shape setting

processes. Additionally, an integration of ePTFE and nitinol was conducted for completing the device construction. *In vivo* swine test results have demonstrated the prototype's feasibility and safety for the management of bleeding in vascular system. Gross look and SEM analyses showed the pristine surface of the device surface except a few locations with local moderate thrombosis. The number of swine models in this study is limited and we will evaluate our prototype performance in more swine models in future.

CONCLUSIONS

A novel customizable stent graft was manufactured from a highly stretchable ePTFE tube and laser-welded nitinol backbone. Various *in vitro* study results have successfully demonstrated the material's functionality and biocompatibility for the stent graft by evaluating mechanical behaviors, porosity, sweating, and hemocompatibility. Based on the highly stretchable ePTFE tube's performance and nitinol laser-welding technique a functional prototype has been fabricated and used for *in vivo* swine tests. Angiography results, gross look analysis of the device, and SEM analysis of the ePTFE's surface demonstrated the feasibility and safety of the materials as well as the stent graft. The current study suggests that a highly stretchable ePTFE tube is an excellent candidate material for the next-generation customizable stent graft improving the clinical outcomes as well as reducing the cost in device manufacturing.

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FIGURE 1.

(a) Test setup for the mechanical stretching of the ePTFE membrane to measure the stress–strain behaviors; (b) test setup for the ePTFE sweating test *in vitro*.

FIGURE 2.

(a) 3D model of stent backbone and boundary conditions for stent crimping in Abaqus, (b, c) experimental setup to measure the radial force of the stent backbone, (d) experimental setup for stent pullout force in a silicone tube.

FIGURE 3.
ePTFE covering process: (a) preparation of nitinol backbone and unexpanded ePTFE tube and (b) expanded ePTFE tube based on the anatomy of the animal model after three-step expansion

FIGURE 4.

Stress-strain behavior of ePTFE membranes in tensile loading; (a) stress-strain curve in radial direction of the ePTFE tube; (b) stress-strain curve in longitudinal direction of the ePTFE tube

FIGURE 5.

SEM images of ePTFE membranes with applied strain of 0% (a), 200% (b), 400% (c), and 550% (d) in radial direction under 1000x magnification. (e, f) the calculated porosity changes with respect to applied strain.

FIGURE 6.

(a) ePTFE tube before the sweat test; (b) expanded ePTFE tube after the test; (c) ePTFE tube diameter changes with respect to fluid pressure; (d) ePTFE tube length reduction (%) with respect to fluid pressure.

FIGURE 7.

(a) Representative SEM images of early thrombosis on three sets of ePTFE samples after 1, 2.5, and 5 min *in vitro* under 5000x magnifications using fresh non-heparinized pig blood.

(b) Number of cell counts on ePTFE samples after 1, 2.5, and 5 min.

FIGURE 8.

(a) Representative SEM images of early thrombosis on three sets of ePTFE samples after 1, 2.5, and 5 min *in vitro* under 5000x magnifications using heparinized fresh pig blood. (b) Number of cell counts on ePTFE samples after 1, 2.5, and 5 min.

FIGURE 9.

(a, b) Computed stress and strain distributions during stent crimping analysis in Abaqus. Unit of stress: MPa. (c) Calculated radial force from FEA and *in vitro* measurement. (d) Measured pullout force in two silicone tubes with ID of 0.5" and 0.75".

FIGURE 10.

Prototype devices; (a) nitinol backbone with Td radiopaque makers, (b) collapsed device in 8–9 Fr sheath, (c) side view of the device (outside covered), (d) front view of the device (outside covered), (e) side view of the device (inside covered), and (f) front view of the device (inside covered)

FIGURE 11.

In vivo comparison angiographic images; (a) vessel injury with bleeding and (b) treatment of the injured vessel with a stent

FIGURE 12.

(a, b) Gross look of the harvested device after the *in vivo* tests and (c, d) SEM image analysis of the thrombosis formed on ePTFE membrane.