1. Introduction

Intracranial aneurysms are local dilations of the arterial vessels supplying the brain. When untreated, these dilations can rupture and cause subarachnoid hemorrhage with a lethal outcome in 35% of cases.[1] Aneurysms can be treated with minimally invasive endovascular therapy or by surgical interventions.[2] Current minimally invasive treatments include coiling[3] for relatively simple aneurysms and stent-assisted coiling[4] in complex aneurysm geometries. Further challenging aneurysm geometries motivated the current state-of-the-art treatments, using a stand-alone braided flow diverter (FD) stents. The majority of FD stents are made of TiNi shape-memory wires and reconstruct the vessel shape by disrupting the intra-aneurysmal flow.[5–7] Braided FDs have low porosity (70–80%)[8] compared to the stents used for stent-assisted coiling (>90%).[9] The low porous design promotes blood flow along the parent vessel, thus isolating the aneurysm sac and promoting endothelization at the aneurysm’s neck (ostium). The braided FDs are fabricated from 40–60 interwoven wires with a thickness of 20–40 µm. The shape-memory materials[10] allow the braided FDs to self-expand upon release from the catheter. Many similar products are currently available with slight design variations, such as the number of wires, braiding angles, and radiopaque markers.[11]
Though the braided FDs successfully treat aneurysms, the reported overall complication rate is 17%, considering all associated studies up to January 2016.[12] We want to address such complications in our work and propose a solution using thin-film FDs to address them.

**Torsional collapse:** The brain vessels are tortuous in nature, causing torsion to be built up in the catheter-based deployment system. This built-up torsion can cause a collapse of the braided FD during deployment.[13] After the stent has collapsed, reopening it is hardly achievable as seen experimentally.[13] Therefore, the only way to correct this is to remove the partially deployed, collapsed stent during the treatment procedure and repeat the treatment with a new FD stent.

**Variable porosity:** Clinically, the porosity of the braided FD devices has been shown to vary along the ostium during the deployment by compressing or expanding the stent, attributed to braided design. A previous computational fluid dynamic (CFD) study showed that the flow entering into the aneurysm depends on the FD’s compression along the ostium. Janiga et al. reported a flow reduction of 24.4% for non-compressed cases versus 33.4% for the optimally compressed case.[14] Porosity is referred to as an essential design variable that affects treatment outcomes.[15] Thus, success rates depend on the interventionalist’s experience in deploying the FD with optimal porosity. In some instances, a second or even more FDs (placed telescopically along with the first one) are required to get a better flow reduction.[16]

**Side branch occlusion:** The FDs reduce the blood flow not only into the aneurysm but also along the side branches, which in some cases causes branch occlusion.[17] In a review of over 3000 patients, a complication rate of 4.9% was reported for side branch occlusions.[12]

We believe that the absence of sudden torsional collapse, constant porosity along the ostium, and the ability to modify the design as per the patient’s vessel anatomy to avoid incident side branch occlusions will decrease the complication rate of the aneurysm treatments.

Previously, Chen et al. proposed a novel FD stent that consists of a TiNi thin-film glued to a commercially available highly porous Neuroform stent (Stryker).[18] In a different approach, Nakayama et al. tested a balloon-expandable high porous CoCr stent dip-coated with 20 µm thin polyurethane film, which was structured with honeycomb micropores for an adequate flow reduction into giant aneurysms.[19] However, mesh structures and the backbones are either glued or dip-coated, but neither is monolithically fabricated with the backbone, ensuring durability. To our knowledge, neither study reported their flow performance when compared with commercially established braided FDs.

We demonstrate that shape memory alloy thin-films with superior mechanical properties[20] can be used to produce such novel FDs. This planar wafer-based technique allows integrating multiple layers for additional functionality such as bio-sensing[21] and increased radiopacity.[22] Thin films fabricated using such techniques have a high design freedom and can be made of monolithic films with conventional fabrication methods.[23] Thin-film FDs are quite attractive for implant design as different layers (backbone and mesh) can be designed individually with different thicknesses for their specific functionality. 2.5 D thin-film stents offer patient-specific design solutions by controlling critical design parameters such as porosity, individual local FD diameter, and mesh density.

In this work, we demonstrate the feasibility of designing and fabricating a novel 2.5 D thin-film FD stent. The developed thin-film FD’s was characterized and compared to a state-of-the-art commercially available braided FD. The described workflow can serve as a blueprint for developing future patient-specific implants.

### 2. Results and Discussion

#### 2.1. Workflow to Fabricate Patient-Specific Thin-Film FDs

The routine for patient-specific stent design (Figure 1) summarizes the concept of this work. The workflow can be split into seven steps:

1) **Problem definition:** identifying the aneurysm geometry which is challenging to treat with braided FD.

2) **Solution design:** the thin-film FDs can overcome these limitations and meet the requirements by offering patient-specific solutions.

3) **Finite element analysis (FEM) crimping analysis:** the local stress contours on the backbone when crimped have been estimated. Crimping (to 1 mm diameter) is essential to deliver the stent via minimally invasive surgery.

4) **Virtual flow analysis:** the hemodynamic performance after placing the FD into the virtual aneurysm model has been estimated with CFD. The FD designs were compared for flow reduction into the ostium.

5) **Fabrication:** the thin-film FD prototypes have been produced based on the FD design resulting from steps 3 and 4.

6) **Experimental testing:** mechanical properties of the thin-film FDs (circumferential radial force, torsional force, and 3-point bending force) and flow performance (when...
placed in patient-specific 3D printed aneurysm models) have been characterized. The results have been compared for a similar testing with commercially available braided FD (Derivo, Acandis), referred to as “FD0”. 7) Outcome evaluation: results (step 6) have been interpreted, and the shortcomings have been evaluated for design reiteration. Optimally, the time required to build a patient-specific thin-film FD was in the range of 7–10 days.

**2.2. Design Development for Thin-Film Based FD Stents**

The proposed design consists of a thick (42 µm) backbone structure for stabilizing the FD in the artery and a thin (7 µm) mesh structure for reducing the aneurysmal flow (Figure 2). The backbone design consists of 8 single rings, partially connected at position 5 (Figure 2a, bottom left). Each stent ring consists of 4 cell units, called further as a “stent strut” (Figure 2a, bottom right). The length of the backbone is ≈ 43 mm (8 x L1, Table 1). The stent perimeter has been calculated by multiplying dimension (L2) * 4 = 14.16 mm, and from this, we can obtain the backbone diameter as ≈ 4.5 mm. The width of L4 is intentionally thicker than the rest of the strut to increase the radial force of the backbone. The mesh structures have a similar unit cell design (Figure 2b, red square) compared to the backbone but with a considerably smaller cell size (Table 1).

Three different mesh sizes were considered with varying cell-areas, 0.13, 0.21, and 0.47 mm² for Meshes 1–3, respectively (Table 1). The unit cell size of mesh design was chosen to have dimensions similar to those of braided FDs. The length of the unit cell for braided FDs was estimated ≈ 200 – 300 µm. The same unit cell dimensions for the mesh design were not feasible as the mesh unit cell consisted of varying dimensions.
(L1–L5, Table 1) which differ by over an order of magnitude. Thus, the smallest mesh unit cell that can be achieved was limited by the width of L3 (least dimension in the unit cell), which due to fabrication and handling reasons was limited to 10 µm. Thereby, the smallest scalable unit cell was considered for Mesh-1. The unit cell sizes for mesh-2 and mesh-3 were scaled from mesh-1 with a factor of 1.2 and 1.8, respectively. The pore density/cell density is defined as the number of cells per given area (1 mm²) and is calculated by dividing 1 over the area of an individual cell (Table 1). Though the cell-area is varied between meshes 1–3, the porosity was kept the same (~79%) and this value was in the range of porosity of braided FDs.[24]

The FD design Mesh-1 is a combination of a thick (42 µm) backbone strut and a thin (7 µm) mesh-1 structure between the stent struts, and the same for Mesh 2–3 (Figure 2b–d). The stent strut dimensions (L1–L5), cell-area, and thickness of the backbone and Mesh-1–3 are listed in Table 1.

In a first design approach, a generic stent design with straight struts was considered and characterized virtually.[25] The straight struts had a lower radial coverage, i.e., 5 stent struts were required for a stent ring of 4 mm diameter. The curved struts have a higher radial coverage in the current approach, with only four struts for a stent ring of 4.5 mm diameter. Such a design is also essential in reducing stress (Section 2.3) in the strut’s V-shape edges when crimped. By reducing the number of stent struts, the flow diverging meshes can be accommodated in between them.

### 2.3. Finite Element Modeling: Crimping Evaluation

#### 2.3.1. Virtual Design of the Stent Strut and Crimping Setup

Stent strut from the backbone alone (Figure 2a, bottom right) was considered for the crimping analysis. The backbone design was radially and longitudinally symmetric; such configuration reduces the computational effort. The 2D design of the stent strut (Figure 2a and Table 1) with a thickness of 50 µm was modeled and imported into the Abaqus 2018 (Dassault Systemes, France) as a 3D model (see Experimental Section). The crimping routine was realized in Abaqus as previously described.[24] The built-in superelastic material model was used for the crimping analysis. Previously reported material properties for the superelastic NiTi thin films validated using tensile test experiments by Velvaluri et al., were applied in the current work.[25] The crimping plates were placed around the stent forming a cylindrical shell when assembled (Figure 3a). The plates were then radially displaced (along r-axis, Figure 3a) so that the stent could be crimped from an initial diameter of 4.5 to 1 mm.

#### 2.3.2. Crimping Analysis of the Stent Strut

The von Mises stress contours (given in MPa) on the crimped stent strut at crimped position (1 mm diameter) are given in Figure 3b. The stent ring was generated by mirroring the stent strut radially (Figure 3c). The stent ring is shown at the initial (gray) and the crimped (color) positions, with a radial strain of about 77%. The maximum amount of stress generated is 1025 MPa, which is slightly above the martensite’s elastic limit for thin-film samples (~800 MPa).[26] Thereby, this design on crimping should not have significant plastic deformation and could recover the initial shape on unloading. A generic stent design was previously considered by Velvaluri et al., for the crimping routine and reported stresses, which are >2200 MPa on similar crimping (4 to 1 mm).[25] Thus, the maximum stress was reduced by half in the proposed curve design as compared to the generic design. The curved strut proposed in Section 2.1 also plays an essential role in reducing the stress along the strut’s V-edges.

The major shortcoming of the crimping routine is the built-in superelastic material model. Though the discussed material model was robust enough to realize complex 3D crimping behavior, it did not replicate the exact experimental material behavior, such as remanence strain on unloading, martensite reorientation, and plastic deformation. However, the described routine gives first-hand knowledge about the stress generated during crimping. Another shortcoming is the combined Mesh 1–3 designs were not crimped to analyze the stress contours. The assembly required very fine mesh to provide sufficient accuracy for varying thicknesses cases, which exponentially increased the computational effort. However, the unit cell (stent strut) of the mesh structures is similar to the backbone (with a variation in thickness); from the obtained result, we can hypothesize that the individual stress contours on crimping will be similar if not the same. More complex computations with appropriate material models are required to verify this.

### 2.4. Virtual Flow Analysis and Optimizing the Mesh Design

#### 2.4.1. Intracranial Aneurysm Model for Virtual Flow Assessment

A virtual model of a para-ophthalmic left internal carotid artery (ICA) aneurysm (max. dimension 14 mm) was segmented from clinical 3D rotational angiographic (3D-RA) images of a patient (see Experimental Section). Patient management during 3D-RA was conducted in compliance with institutional standards. The resulting virtual aneurysm model was modified as follows: 1) all branches that were less than 1 mm in inner diameter (ID) were removed, 2) proximal and distal branches were cut to the length of at least 10 x ID, and 3) all distal branches were connected.
to form one outlet (Figure S1, Supporting Information). Details can be found elsewhere.[27]

2.4.2. Virtual Stent Deployment

Since the production of patient-specific flow-diverting devices is cost-intensive, a virtual assessment of the hemodynamic efficacy was carried out for all stent configurations in advance. The virtual aneurysm model was used to deploy different pre-defined configurations (Table 1) for virtual testing. Here, the in-house stent deployment software package VISCA was used, resulting in a sufficient reproduction of a possible clinical treatment.[14] A representative deployment result is illustrated in Figure 4 from two perspectives. For further details regarding the fast-virtual-stenting procedure, refer to Berg et al.[28]

2.4.3. Hemodynamic Simulations

For the virtual assessment of the hemodynamic efficacy, blood flow simulations based on CFD were carried out. Since no
patient-specific boundary conditions were available, phase-contrast MRI measurements from a healthy volunteer were applied at the inlet of the model.\cite{29} The actual patient-flow profile might vary from one that was used for the simulations. However, as the goal was to estimate the flow diversion efficiency of the developed thin-film stents, the identical conditions between simulations for different stent configurations have a primary effect, not the flow curve. Therefore, the chosen flow profile cannot disrupt the commonality of obtained results. A constant pressure was defined for each outlet, and the vessel and stent wall were assumed to be rigid. Blood was treated as an incompressible ($\rho = 1055$ kg m$^{-3}$), Newtonian ($\eta = 0.004$ Pa s) fluid, and laminar flow conditions were considered. Three cardiac cycles were simulated for each configuration to obtain a periodic solution. For the qualitative and quantitative analysis, only the last cardiac cycle was included. Further details required to obtain realistic hemodynamic simulation results can be found in Berg et al.\cite{30}

To assess the flow reduction efficacy of individual device configurations, quantitative analysis was carried out (Figure 5a). This included measuring the neck inflow rate, a crucial metric assessing the amount of blood entering the aneurysm sac. As illustrated in Figure 5a, one can notice the apparent flow reduction after virtual treatment. For a quantitative comparison, the peak flow rate at $t \approx 0.2$ s was compared for different configurations. The no device configuration shows a peak flow rate of 9.34 mL s$^{-1}$; with the pure backbone structure, a minor decrease in flow rate to 8.68 mL s$^{-1}$ was observed. Notably, the addition of mesh elements (Meshes 1–3) considerably reduced the peak flow 7.16 – 7.73 mL s$^{-1}$ and outperformed even the conventional

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**Figure 5.** a) Flow curves were calculated at the aneurysm neck (violet plane) based on CFD simulations before and after treatment with all considered FD configurations. Notice that the neck inflow rate is considerably reduced by the Mesh 1–3, and a noticeable improvement is obtained compared to a conventional braided FD stent (similar to FD$_0$). b) Visualization of the time-averaged wall shear stress (AWSS) for the untreated configuration, the raw backbone structure, Mesh-2 configuration of the novel stent design, and a conventional braided flow-diverter (design similar to FD$_0$). Notice the apparent reduction of the AWSS in the presence of Mesh-2 (yellow arrow).
braided FD (similar to FD0) 780 mL s⁻¹. The best flow reduction was given by Mesh-2, with a 14% higher flow reduction than FD0 at the peak.

Furthermore, time-averaged wall shear stress (AWSS) was evaluated (Figure 5b) to understand the rupture risk. After implantation of Mesh-2, the AWSS was reduced from 6 to 3 Pa on the aneurysm’s left side (yellow arrow). Qualitatively, AWSS contours of the Mesh-2 and the FD0 were similar. Lower AWSS were observed because impingement of the flow jets was lower, thus reducing the rupture risk. As the Mesh-2 configuration showed the best flow reduction, it was selected for further fabrication.

2.5. Fabrication of Thin-Film Stents

The optimized thin-film FD stents were fabricated using thin-film technology, which uses a combination of microsystem processes such as UV lithography, magnetron sputtering, and wet chemical etching of sacrificial layers. The basic fabrication routine to obtain free-standing 2D NiTi thin films is discussed in detail elsewhere. However, the reported stents have the 2.5 D design with structures of two different thicknesses obtained by repeating the above processes in combination. The brief details of the monolithic thin-film fabrication process are discussed in the Experimental Section.

The fabrication was wafer-based and resulted in planar thin films. These films were then shape set into stents using fixtures such as tubes at high temperatures under vacuum. The current devices were shaped into a cylinder of 4.5 mm in diameter using rapid thermal annealing at 550 °C. The alloy composition was a slightly Ni-rich binary TiNi alloy (TiNi 51 ± 0.5 at%), thus exhibiting superelastic material properties (self-expansion) at body temperature (37 °C) (appropriate differential scanning calorimetry (DSC) scan in Figure S2, Supporting Information).

Figure 6a shows a successfully fabricated thin-film FD (Mesh-2) stent. Figure 6b shows the scanning electron microscope (SEM) side view of the stent; the marked yellow square was expanded and shown in Figure 6c. The difference in the thickness of the backbone (42 µm) and mesh structures (7 µm) can be seen in Figure 6d. The SEM image also reveals the feasibility of realizing thin-film FD structures without any defects. Figure 6e shows the ends of the rolled-up stent with holes, a feature to close the stent using wires/biocompatible glue if necessary.

The thin-film fabrication technique has advantages over the conventional stent manufacturing techniques (wire braiding and laser cutting), such as: high design freedom and the ability to combine different materials for increased radiopacity or even...
biosensing. Additionally, TiNi thin-films show very similar mechanical properties compared with traditional TiNi structures (tube, wire, and sheet), with a shorter transformation plateau[12] and better fatigue. The shorter transformation plateau is due to the absence of cold work during the fabrication route, but this does not affect the performance and can be taken care of by selecting the suitable geometry. The better fatigue resistance is reflected due to the absence of inclusion or carbides.[26]

Moreover, the backbone and meshes were structured individually during the fabrication. Therefore, the mesh cells can be modified between the struts as per the patient's requirement. In the current analysis, the mesh was kept constant between all the struts for simplicity. In principle, we can individualize the mesh between each strut from no mesh to a dense mesh, e.g., placing the denser mesh at the aneurysm ostium while keeping no mesh at the side branches. The individualization can be performed both in circumferential and longitudinal directions along the stent. In such a case, the denser mesh regions could be further made visible with a radiopaque marker to guide the interventionalist during the stent placement.

### 2.6. Experimental Testing

#### 2.6.1. Mechanical Characterization

The thin-film FD (Mesh-2) was characterized for circumferential radial force, torsional force, and 3-point bending force and was compared with the FD0. The tests were performed at body temperature (37 °C).

**Circumferential Radial Force:** The circumferential radial force is an important parameter that indicates how well the stent is anchored in its position when placed in the artery. If the stent migrates during the post-procedure period, this could lead to unwanted clinical outcomes. The braided FDs (FD0) are extensively used in vivo and show low complication rates (3.7%) for stent migration; therefore, we considered these force values as a benchmark.

The force was evaluated for the Mesh-2 by compressing the stent circumferentially using an iris-type setup built in-house.[24] The stent was placed into the apparatus during the analysis, compressed radially from 4.5 to 1 mm diameter, and back. Three measurements were done for each of the stents, and the corresponding mean, with the standard deviation, are shown in Figure 7a. It also shows the circumferential radial force curve for the FD0. As the FD0 measurement was only available during expansion from the diameter of 2.2 mm adapted from Velvaluri et al.,[24] we made a detailed comparison with the Mesh-2 in these diameters.

The radial force exhibited by FD0 consists of two major regimes, first, up to 2.6 mm diameter and second, from 2.6 mm to 4.5 mm diameter (Figure 7a). The first regime shows a pronounced variation between the FD0 and Mesh-2 force values. The second regime is of great interest because it is the recommended diameter range (so-called deployable diameters) by the manufacturer to place the FD0 in vivo. In the deployable diameters (second regime), the FD0 and Mesh-2 are very similar during expansion (Figure 7a). A linear fit (mean and standard deviation) yielded a slope of $-0.20 \pm 0.002$ N mm$^{-1}$ and $-0.185 \pm 0.002$ N mm$^{-1}$ for the FD0 and Mesh-2, respectively.

Thus, the radial force exhibited by Mesh-2 has a similar dependence on diameter as a widely available FD0. However, the detailed comparative evaluation of the slopes and a paired t-test (p-value = 0.07, see Supporting Information) for both the data sets suggest a slightly higher radial force for FD0 compared to Mesh-2. Such a difference in force can be compensated by increasing the backbone thickness for Mesh-2.

**Torsion:** Torsional characterization of the stents was performed where one end of the stent was fixed while the other end was rotated with respect to it. The force was measured when Mesh-2 was rotated from 0°–270° and back; details about the setup are discussed elsewhere.[23] Three repetitions were done, and the corresponding mean and standard deviation were reported.

Visually, on being subjected to torsional testing, the Mesh-2 did not collapse suddenly. Instead, we saw a gradual closing (twisting) when rotated, which also opens up gradually on release. The torsional force versus angle of rotation is shown in Figure 7b; we see no sharp changes in the force values during the forward (solid legend) and reverse (hollow legend) rotation.

Previously similar characterization was reported on the braided FD stents, which showed a sudden collapse at a

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**Figure 7.** a) Shows the circumferential radial force of Mesh-2 and FD0. The circumferential radial force was evaluated by radially compressing the stents from 5 to 1 mm (solid legend) and back (hollow legend); the blue arrows show the direction of measurement. The FD0 testing curve during expansion from 2.2 mm diameter was adapted from previous work.[24] Note that both FD0 and thin-film stent have similar forces in the deployment diameters, i.e., 2.6–4.5 mm. b) Torsional testing for the Mesh-2 is shown. The devices are rotated from 0°–270° (solid legend) and back (hollow legend), during which one end was fixed while the other end was rotated. The blue arrows show the direction of measurement. The obtained torsional force curves do not show sudden collapse on torsion. c) Shows the three-point bending force curves of Mesh-2. The force was recorded as the devices were bent to an arc of 16 mm radius of curvature (solid legend) and back (hollow legend); the blue arrows show the direction of measurement. The above measurements are done three times for each device, and the mean is plotted in the curves while the standard deviation is shown in error bars.
particular angle.\textsuperscript{[13]} The sudden collapse (seen visually) resulted in a sharp fall in the torsional force versus angle graph. Likely, the main reason for such a collapse is the design’s braided nature. Comparatively, no sharp collapse was seen visually and in the force graph for the Mesh-2 design (Figure S5, Supporting Information). Thus, thin-film FDs can potentially perform similar to the high porous stents fabricated using laser cutting devices (Neuroform, Stryker); previous clinical experiences report no torsional collapses on these devices.\textsuperscript{[34]}

\textbf{3-Point Bending Test:} Three-point bending tests of the stents are performed using special clamps (designed according to ASTM F2606-08) built in the tensile testing machine (Zwick-Roell, Z0.5, 100 N Load cell). The thin-film FDs are placed between the clamps, fixed at three points, two in the bottom and one at the top at a pre-load. The top clamp is displaced by 6 mm, i.e., to a radius of \( \approx 16 \) mm curvature. The resulting flexural curves during the loading and unloading for three consecutive measurements of Mesh-2 are shown in Figure 7c. The comparison to FD\(_0\) could not be shown in the image as the stents’ braided nature does not allow for identical testing. However, the force required to bend to the 14 mm radius curvature was evaluated previously\textsuperscript{[24]} and this is an order of magnitude higher (100–250 mN) than the currently reported values (15 mN) for the thin film-based flow diverter films, thus suggesting that thin-film FDs have higher longitudinal flexibility, which permits them to navigate tortuous brain vessels. Appropriate testing along with FD\(_0\) in flexible vasculature models has to be performed to confirm these findings.

\subsubsection*{2.6.2. Flow Characterization}

\textbf{Aneurysm Flow Model Production and Implantation of Flow Diverter Stents:} The digital model described in Section 2.3.1 was used for experimental flow analysis (Figure 8a). An outer layer was added to the vessel lumen to form a vessel wall. Then flow connectors (Fusion 360 2.0, Autodesk, USA) were integrated into the model outlets to plug the models into a flow loop. Next, the four identical aneurysm models were 3D printed: one control, one to place FD\(_0\), and two for thin-film FDs (backbone and Mesh-2). Due to the lack of the deployment system for the novel thin-film stents, the corresponding models were produced with two separate parts: the main aneurysm body and the part of the aneurysm dome (Figure 8b). The thin-film FDs (backbone and Mesh-2) were manually placed from the inlet and maneuvered to outlet 2 (see Experimental Section). The different pieces were glued together after printing. The FD\(_0\) was placed using a commercial deployment system by an experienced neuroradiologist, similar to FD placement into the patient (see Experimental Section).

\textbf{Flow Analysis:} The models were placed along a flow loop to mimic in vivo blood flow (see Experimental Section). The FDs’ efficiency was evaluated by the flow-sensitive MRI experiments (4D flow MRI, see Experimental Section). Visualization and quantitative analysis were performed with dedicated software (Gtflow, Version 3.1.12, Gyrotools, Switzerland).

Qualitatively, the intensive vortex flow with two flow jets located near the aneurysm wall was observed in the untreated model (Figure 9a). The vortex was observed in the presence of backbone structure too. However, only one jet remained in the aneurysm sac, and it was dislocated from the wall toward the center of the aneurysm. In the presence of Mesh-2, the vortex was faint, and it disappeared entirely when the FD\(_0\) was deployed.

The quantitative assessment includes calculating the net flow in the outlet 2–4 and intra-aneurysmal forward flow rate at position 5 (Figure 8a). The forward flow evaluation in an aneurysm was chosen since the flow is entering the aneurysm and then leaving it, resulting in zero net flow. Position 5 at the aneurysm sac was chosen as close as possible to the aneurysm neck but at the same time as far as needed to avoid the intersection with MRI signal voids caused by the stents’ presence (metal artifacts). The time-varying flow curves are shown in Figure 9b.

The placement of flow diverter stents into the parent aneurysm vessel is a successful technique to treat aneurysms.\textsuperscript{[15]} The treatment relies on the intra-aneurysmal flow reduction by
covering the aneurysm neck with a tight mesh of wires. Next, as a result of reduced flow, the aneurysm is occluded owing to coagulation and thrombus. Recently, an in vivo study showed an association between reducing flow velocity in the aneurysm sac after stent implantation, measured with MRI, and the rate of aneurysm occlusion. The flow reduction was observed in the current study after the placement of thin-film FDs. The aneurysmal flow rate at the peak time at position 5 ($t = 0.28$ s, red-dotted line Figure 9b) was evaluated, 11.6, 8.67, 2.43, and 0.28 mL s$^{-1}$ for no device, backbone, Mesh-2, and FD$_0$, respectively. The peak flow rate entering the aneurysm was reduced 79% when Mesh-2 was placed, while in the presence of FD$_0$, the flow was reduced 97% compared to the flow without a device. The flow reduction into the aneurysm with the Mesh-2 can be further improved with a denser mesh along the ostium in the next design iteration.

The denser mesh of FD$_0$ results in a better flow diversion. However, there is no clear consensus on how much the flow should be reduced to provide stable thrombus formation. Besides, the uniform, denser mesh of FD$_0$ can result in the

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**Figure 9.** a) Velocity visualization with instantaneous velocity streamlines in an untreated aneurysm flow model and models with deployed FDs: backbone, Mesh-2, and FD$_0$. b) The net flow rate in vascular branches: outlet 2–4, and forward intra-aneurysmal flow calculated in position 5 as indicated in Figure 8a. The quantitative analysis at the peak flow has been made at the peak time $t = 0.28$ s (red line) for the intra-aneurysmal flow and at outlet 3 to characterize the FD flow diversion performance. Note that Mesh-2 reduces the flow into the aneurysm while keeping blood flow along all the side branches.
occlusion not only of the aneurysm but also in the adjacent branches.[17,37] The substantial flow reduction in outlet 3 in the presence of FD0 was observed versus Mesh-2 (Figure 9b). The flow along the outlet 3 at the same peak time (t = 0.28 s, red-dotted line Figure 9b) is 1.11, 1.05, and 0.02 mL s⁻¹ for no device, Mesh-2, and FD0 configurations. With FD0 showing 98% flow reduction compared to no device case, such strong flow reduction could cause endothelization at the branch opening, leading to side branch occlusion.[37]

According to the preliminary flow diversion results evaluated with CFD, the thin-film FDs outperformed commercial FD0. However, the MRI results were different. We would like to point out that we did not intend to contrast the results of MRI and CFD. The methods have their pros and cons, as well as experimental and simulated flow conditions, which were different too.

Blood flow simulations using CFD and MRI both can provide complete hemodynamic information. However, CFD results depend on the boundary conditions applied, the quality of the virtual model, etc.[30] The virtual stent deployment is associated with high computational costs. Often, a detailed 3D description of the interaction between the stent struts, the vessel wall, and the flowing blood is required. Here, we used fast-virtual-stenting developed in-house,[31] which result in a fine reproduction of a possible clinical treatment.[18] However, this procedure was not tested for the newly developed thin-film stents.

In addition to that, in vitro experiments using physical flow models encounter challenges, too: lack of realistic vessel wall features, imperfections of blood-mimicking fluids, and physiological flow conditions. But, the deployment of the stent in physical flow models can mimic patient intervention settings. Therefore, we do not compare the results obtained with these different modalities. We have used a virtual approach, namely, to perform simulation studies at an earlier state of stent development, get a first impression on the stent flow diversion, modify stents, and reduce the number of labor-intensive in vitro MRI experiments.

The flow conditions were different too. CFD simulation was based on the MRI flow profile of a healthy volunteer, and the in vitro model was supplied with a flow of 4.2 mL s⁻¹ (250 mL min⁻¹), which is in accordance with the detected flow in vivo in internal carotid artery 257 ± 48 mL min⁻¹.[38]

2.7. Limitations and Evaluation

Our study has certain shortcomings: 1) We did not evaluate the FEM modeling behavior of the stent when the stent was subjected to complex bending, as seen in vivo. We saw that the backbone did not have a sufficient wall opposition in 3D printed model during deployment. Virtual evaluation using complex FEM models can help optimize the design. A dedicated FEM crimping routine for the assembly of backbone and meshes have to be evaluated. 2) Patient-specific boundary conditions were not considered for the CFD simulations; however, identical conditions were used to compare the stent designs. 3) The fast virtual stenting in the segmented intracranial aneurysm model was based on free-form deformations.[28] Hence, material and mechanical interactions between the stent and the surrounding surface model were not considered. However, due to the explicit representation of all individual stent struts, a precise investigation of the stent efficacy was feasible. 4) The stents were placed in the 3D printed models manually as there was no available deployment system; the possible uncertainties were not investigated; more test cases with n = 3 for both FD0 and thin-film FDs are required to comment on this.

3. Conclusion

We developed a thin-film based FD stent and presented a workflow for fabricating patient-specific devices. Despite the limitations, we successfully demonstrated the feasibility of manufacturing a FD stent prototype according to the proposed solution design. The developed thin-film FD has overcome a few complications known for braided FD stents. The thin-film FD reduced flow in the aneurysm while maintaining the flow to the side branches, no sudden collapse on torsion was observed, and constant porosity over ostium was achieved. The suggested workflow can serve as a blueprint to fabricate any patient-specific FD stents. The process is iterative and the design can be modified as required to fit the geometric needs in a specific patient geometry’s need. Therefore, we believe that FD devices from this novel technique are pivotal in treating patients with challenging aneurysm geometries and will help reduce complication rates.

4. Experimental Section

Design of the Stent Strut: The 2D design of the stent strut was carried out using AutoCAD 2018 (Autodesk Inc., California, USA) as per the given dimensions (Figure 2a and Table 1), which was then extruded to a thickness of 50 μm. The stent strut was exported to Creo Parametric 4.0 (PTC Inc., Massachusetts, USA), where it was bent using the “Toroidal bend” tool to a radius of 2.25 mm. Finally, it was imported into Abaqus as a 3D element for the crimping analysis.

FEM Analysis for Crimping: The interactions between the outer stent surface and the crimp plate were modeled using the penalty method with a frictional coefficient of 0.1. The stent strut elements were considered as 3D stress tetragonal elements (C3D10) with a cell size of 0.05 with 3528 total number of elements, and the rigid plates have a mesh size of 0.2. A displacement load was applied for the rigid plates to crimp the stent.

Patient-Specific Model Production and Spatial Discretization for CFD: The segmentation was performed with a threshold-based region-growing algorithm[39] that provided a scalar mask of the aneurysm sac and adjacent vessel lumen. Next, the mesh was generated based on the resulting scalar mask using a marching cube’s algorithm[40] (MevisLab 3.0.1, MeVis Medical solution, Germany). After successfully placing all stent configurations within the patient-specific aneurysm model, it was required, we needed to identify an appropriate simulation approach. Since the complete geometric properties were maintained, simplified numerical assessments were not needed to consider each single stent strut. To be able to carry out realistic blood flow simulations, an appropriate spatial discretization was needed. Here, polyhedral elements were generated using the finite volume fluid dynamics solver STAR-CCM+ 12.04 (Siemens Product Lifecycle Management Software Inc., Plato, TX, USA). This type of element was chosen for the considered vessel section since polyhedrals are highly flexible and represent a sufficient trade-off between computational costs and numerical stability. Nevertheless, due to the fine stent structure, many elements were needed to obtain mesh-independent solutions (ranging from 0.8 to 9.2 million depending on the configuration).

Fabrication of the Thin-Film FD Stents: The stents were completely fabricated in a cleanroom facility at “Kiel Nanolabor, Kiel, Germany.” The
fabrication for free-standing thin films is discussed briefly here and in detail by Miranda et al.[23] It is mainly based on UV lithography using a mask aligner (Karl Suss), magnetron DC sputtering (Von Ardenne, CS 730s), and wet chemical etching. Initially, a sacrificial layer of Cu was deposited on the Si wafer, and a thin NiTi seed layer was sputtered on top of the Cu. A photoresist (AZ1518) with a thickness of 2.3 μm was spin-coated on the top of the NiTi layer. The pattern was transferred to the photoresist and developed (AZ716 MIF) using a mask aligner. The pattern was transferred to the NiTi seed layer by wet etching with HF solution with an etch rate of 10 nm s⁻¹. Thereafter, the isotropic etching of Cu was carried out with a BASF Selectipur Chromium Etch (etch rate of 13.5 nm s⁻¹). Due to the undercut of Cu caused during the isotropic etching, inverted mushroom structures are obtained. The photoresist was stripped using Acetone, and the thick NiTi layer of desired thickness was sputtered on the wafer. Finally, the sacrificial Cu layer was wet-etched using the BASF Selectipur Chromium Etch, which resulted in free-standing NiTi thin-films.

The fabrication of the 2.5 D thin-films used a similar process in combination to obtain the two thickness films with varying structures. The target used for the sputtering was a binary NiTi alloy; the composition of the target was selected by keeping in mind the variation caused due to sputtering. In the current work, binary TiNi 46 at% target was used to obtain film composition of TiNi 51 ± 0.5% (EDX measurement error). The NiTi was DC sputtered at a power of 150 W, at a chamber pressure of 2.3 × 10⁻³ mbar with an Argon flow of 25 sccm and the Cu deposited at 400 W, with a chamber pressure of 6.0 × 10⁻³ mbar with an Argon flow of 30 sccm (all the parameters were optimized for the geometry of the sputtering system). The 2D free-standing amorphous thin-films were then heat-treated using rapid thermal annealing apparatus to crystallize and shape set the stent. The shape setting was achieved by placing the devices between two stainless steel tubes, vacuum-compatible, and heat-treated at 550 °C for 5 min.

**Mechanical Characterization:** The circumferential radial force was carried out in the machine built at our institution. The actual machine was slightly modified from an available patent from Motsenbocker et al.,[41] further details about the machine and the calibrations are discussed elsewhere.[24] The machine was equipped with a 100 N miniature load cell (Disynet GmbH, Brüggen, Germany). The details about the torsional setup are described elsewhere.[23] The actual setup image and the line diagrams of the circumferential radial force and torsional force measurements are discussed in Supporting Information (Section 4, Figures S3 and S4: Supporting Information). The clamps of the three-point bending apparatus are designed as per the ASTM standards F2606-08 with jaw modification required to fit tensile testing device Zwick Roell (Z0.5, 100 N Load cell). The stent was placed between the clamps, fixed at three points, two in the bottom and one at the top at a pre-load. The top clamp was displaced to 6 mm and back, during which the force was determined and plotted.

The diameter of the FD₀ taken from the literature for the circumferential radial force, three-point bending force, and torsional characterization reported was 4 mm.[13,24] Flow Loop: A glycerol-water mixture (40/60% by volume) with diluted contrast agent 0.3 mmol L⁻¹ Gadobutrol (Gadovist, Bayer Vital, Germany) was pumped through the aneurysm models using a pulsatile pump (PD-1100, BDC laboratories, USA) to mimic in vivo blood flow. The supplied flow rate of 4.2 mL s⁻¹ was controlled with an inline transonic flow sensor (ME6PXN325, Transonic System Inc., USA) at the pump’s outlet. However, the detected by MRI inflow profile was found to have slightly different flow rate shapes with an average inflow value of 4.3 ± 0.2 mL s⁻¹ (Figure S6, Supporting Information). All experiments were carried out at room temperature (21 °C).

**FD Placement:** The patient-specific model was 3D printed (Form 3, Formlabs, USA). To simplify the stent deployment, the connected distal branches were separated before printing. The difference between the inner lumen and the 3D printed model is illustrated in supporting materials (Figure S1, Supporting Information). As the thin-film lacked a proper deployment system, the 3D model was printed as two separate parts. Thus, the disconnected distal aneurysm part provided an opening to the proximal part of the aneurysm sac, aneurysm neck, and parent vessel.

Then, the thin-film FDs (backbone and Mesh-2) were placed via the inlet artery (Figure 8a,b) up to the aneurysm sac and then manually maneuvered to the outlet branch (outlet 2). Next, the distal part of the aneurysm was placed back and glued to seal the model. After the stent placement, the models were submerged into 3% agarose gel. For comparison, the FD₀ (Derivo, Acandis; diameter: 5.5 mm, length: 25 mm) was implanted under fluoroscopy (Allura Xper FD, Philips, The Netherlands) by an experienced neuroradiologist into the sealed model immersed in agarose gel. The commercial stent had different dimensions, bigger diameter, and shorter length than thin-film stents. According to the manufacturer (Acandis), the FD₀ needs to be oversized. So, the intended use for the Derivo 5.5 is the vessel diameters between 4.5 and 5.5, according to the manufacturer’s sizing support chart.[42] Besides, any braided stent design is changing its length depending on the vessel diameter deployed. So, the considered Derivo 5.5 with a length of 25 mm will have the length of 41 mm when deployed in a 4.5 mm vessel. With this in mind, the thin-film and the braided stent have quite similar dimensions.

**MR Imaging:** 4D flow MRI was performed in a 3T MRI system (Ingenia CX, R5 V6.1, Philips Healthcare, The Netherlands) using a 3D spoiled gradient Ti-weighted turbo gradient echo sequence with Cartesian sampling (TE/TR: 5/8.4 ms; FOV: 110 × 110 × 50 mm³, voxel size (0.75 mm)³). The sequence was 4.5-fold accelerated with a compressed-sensing technique implemented by the vendor (Philips). For velocity encoding, a non-symmetric 4-point phase-contrast encoding scheme (MPS) was used; the maximum velocity encoding parameter was set to 50–80 cm s⁻¹. An integrated artificial digital trigger was used for temporally resolved data acquisition, and 20 cardiac phases were obtained. The magnitude and phase difference images of 4D flow MRI were reconstructed on the MRI console.

Supporting Information
Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest
Author O. Jansen reports consultancy activities for: Acandis, Pforzheim, Germany. Cerus Endovascular, Fremont, USA. Cerenovus, Galway, Ireland outside the submitted work. F. Wodarg reports personal fees from consultant activity from: Microvention. Acandis, Germany. Cerus Endovascular, USA. Cerenovus, Ireland outside the submitted work. M. Pravdivtseva reports consultancy activities for Cerus Endovascular, USA outside the described work.

Data Availability Statement
The data that support the findings of this study are available from the corresponding author upon reasonable request.
Keywords

4D flow MRI, computational fluid dynamics, finite element modelling, novel flow diverter stents, thin-films

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[1] D. J. Nieuwkamp, L. E. Setz, A. Algra, F. H. Linn, N. K. de Rooij, G. J. Rinkel, *Lancet Neurol.* 2009, 8, 635.

[2] J. Zhao, H. Lin, R. Summers, M. Yang, B. G. Cousins, J. Tsui, *Angiology* 2018, 69, 17.

[3] J. M. Eskridge, J. K. Song, *J. Neurosurg.* 1998, 89, 81.

[4] L. Pierot, A. K. Wachtlo, *Stroke* 2013, 44, 2046.

[5] F. Briganti, G. Leone, M. Marseglia, D. Cicala, F. Caranci, F. Maiuri, *J. Neurointerv. Surg.* 2016, 8, 173.

[6] D. L. R. M. U. Yilmaz, H. K. G. F. M. Cattaneo, *Clin. Neuroradiol.* 2017, 27, 335.

[7] O. I. Tähtinen, H. I. Manninen, R. L. Vanninen, J. Seppänen, T. Niskakangas, J. Rinne, L. Keski-Nisula, *Neurosurgery* 2012, 70, 617.

[8] A. Makoyaeva, F. Bing, T. E. Darsaut, I. Salazkin, J. Raymond, *Am. J. Neuroradiol.* 2013, 34, 596.

[9] J. Ma, Z. You, J. Byrne, R. R. Rizkallah, *Ann. Biomed. Eng.* 2014, 42, 960.

[10] L. Petruni, F. Migliavacca, *J. Metall.* 2011, 13, 1.

[11] S. Dandapat, A. Mendez-Ruiz, M. Martínez-Galdámez, J. Macho, S. Derakhshani, G. Foa Torres, V. M. Pereira, A. Arat, A. K. Wachtlo, S. Ortega-Gutierrez, *J. Neurointerv. Surg.* 2021, 13, 54.

[12] G. Zhou, M. Su, Y. L. Yin, M. H. Li, *Neurosurg. Focus* 2017, 42, E17.

[13] P. Velvaluri, J. Hensler, F. Wodarg, O. Jansen, E. Quandt, *Clin. Neuroradiol.* 2021, https://doi.org/10.1007/s00062-020-00991-2.

[14] G. Janiga, L. Daróczy, P. Berg, D. Thévenin, M. Skalej, O. Beuing, *J. Biomech.* 2015, 48, 3846.

[15] L. Augsburger, M. Farhat, P. Reymond, E. Fonck, Z. Kulcsar, N. Stergiopoulos, D. A. Rufenacht, *Clin. Neuroradiol.* 2009, 19, 204.

[16] A. Wagner, M. Cortsen, J. Hauerberg, B. Romner, M. P. Wagner, *Neuroangiology* 2012, 54, 709.

[17] S. Hohenstatt, A. Arrichiello, G. Conte, G. Capraro, F. Caranci, A. Angileri, D. Levi, G. Carrafiello, A. Paolucci, *Acta Biomed.* 2020, 91, 2020003.

[18] Y. Chen, C. Howe, Y. Lee, S. Cheon, W. H. Yeo, Y. Chun, *Sci. Rep.* 2016, 6, 23698.

[19] Y. Nakayama, T. Satow, M. Funayama, T. Moriwaki, T. Tajikawa, M. Furukoshi, E. Hamano, D. Ishi, M. Hayashi, S. Sugata, H. Ishibashi-Ueda, J. C. Takahashi, *J. Artif. Organs* 2016, 19, 179.

[20] C. Chluba, G. Wenwei, R. Lima de Miranda, J. Strobel, L. Kienle, E. Quandt, M. Wuttig, *Science* 2015, 348, 1004.

[21] C. Chluba, K. Siemsen, C. Bechtold, C. Zamponi, C. Selhuber-Unkel, E. Quandt, R. Lima de Miranda, *Biosens. Bioelectron.* 2020, 153, 112034.

[22] C. Bechtold, R. Lima de Miranda, C. Chluba, C. Zamponi, E. Quandt, *Shape Mem. Superelasticity* 2016, 2, 391.

[23] C. Bechtold, R. Lima de Miranda, E. Quandt, *Shape Mem. Superelasticity* 2015, 1, 286.

[24] P. Velvaluri, M. S. Pravdivtseva, J. Hensler, F. Wodarg, O. Jansen, E. Quandt, J.-B. Hoevener, *Expert Rev. Med. Devices* 2021, 1, https://doi.org/10.17344/2021.1920923.

[25] P. Velvaluri, M. S. Pravdivtseva, R. Lima de Miranda, J. B. Hövener, O. Jansen, E. Quandt, *Shape Mem. Superelasticity* 2019, 5, 195.

[26] G. Siekmeyer, A. Schler, R. L. De Miranda, J. Hövener, *Med. Phys.* 2021, 48, 1469.

[27] P. Berg, L. Daróczy, G. Janiga, in *Computing and Visualization for Intravascular Imaging and Computer Assisted Stenting*, Elsevier Inc., New York 2017, pp. 371–471.

[28] P. Berg, D. Stucht, C. Janiga, O. Beuing, O. Speck, D. Thévenin, *J. Biomech. Eng.* 2014, 136, 041003.

[29] P. Berg, S. Saalfeld, S. Voß, O. Beuing, C. Janiga, *Neurosurg. Focus* 2019, 47, E15.

[30] P. Berg, S. Saalfeld, G. Janiga, O. Brina, N. M. Cancellieri, P. Machi, V. M. Pereira, *Int. J. Artif. Organs* 2018, 41, 698.

[31] R. Lima De Miranda, C. Zamponi, E. Quandt, *Adv. Eng. Mater.* 2013, 15, 66.

[32] W. McAuliffe, W. V. Yucoco, H. Rice, C. Phatouros, T. J. Singh, *J. Mater. Eng.* 2012, 33, 164.

[33] W. K. A. Peker, A. Arat, *Interv. Neuroradiol.* 2014, 28, 263.

[34] B. Kraus, L. Goertz, B. Turowski, J. Borggreve, M. Schlamm, F. Dorn, K. Klabasch, *J. Neurointerv. Surg.* 2014, 7, 1371.

[35] O. Brina, P. Bouillot, P. Reymond, A. S. Luthman, C. Santarosa, M. Fahrt, K. O. Lovblad, P. Machi, B. M. A. Delattre, V. M. Pereira, M. I. Vargas, *J. Neurointerv. Surg.* 2019, 40, 2117.

[36] P. Berg, C. J. Isifal, S. Ponsonnard, C. Yardin, G. Janiga, C. Mounayer, *J. Biomech.* 2016, 49, 4.

[37] L. Zarrinkoob, K. Ambarki, A. Wáhlin, R. Birgander, A. Eklund, J. Malm, *J. Cereb. Blood Flow Metab.* 2015, 35, 648.

[38] R. Adams, L. Bischof, *IEEE Trans. Pattern Anal. Mach. Intell.* 1994, 16, 641.

[39] W. E. Lorensen, H. E. Cline, in *Proc. 14th Annual Conf. on Computer Graphics Interactive Techniques SIGGRAPH 1987*, Association For Computing Machinery, Inc, New York, USA 1987, pp. 163–169.

[40] T. Moschenbocker, E. Coff, *Radial Expansion Force Measurement Technology*, US007069794B2.

[41] “SizingchartAcandis,” can be found under https://www.acandis.com/down/uploads/derivo-sizing-support-chart_410_1581409594.pdf (accessed: May 2021).