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TAVI-Mimic for testing of heart valve leaflet materials in physiological loading situations

Abstract: The loading situation of the aortic valve is complex, complicating the identification of innovative approaches for heart valve leaflet materials, e.g. for transcatheter aortic valve implantation (TAVI). Materials engineering experiments allow for screening of materials but especially for durability testing, the consideration of physiological loads is vital/critical for the suitability-assessment of innovative leaflet materials.

For this reason, a framework structure for the testing of leaflet materials in physiological loading (TAVI-Mimic) was developed. The exemplary use case for the TAVI-Mimic was a test for calcification propensity of pericardium during durability testing. The TAVI-Mimic was designed as a four-parted frame, based on previous work of our group. The leaflet material can be attached between inner and outer shells without sewing. In a second step, the TAVI-Mimic was optimized regarding radial load-deformation in comparison to a commercial TAVI by means of finite element analysis (FEA) and hydrodynamic characterization in a pulse duplicator system. Mechanical properties dependent on water uptake of different materials for 3D-printing of the TAVI-Mimic were investigated.

After optimization, TAVI-Mimics were equipped with glutaraldehyde-fixated pericardial tissue and prototypes were calcified by using a heart valve durability tester and a metastable calcification-liquid, developed in earlier studies. The development of the TAVI-Mimic using FEA and experiments was successful, leading to a radial load dependent deformation of 0.6 mm which correlates with commercial TAVI. Two methacrylic photopolymers were identified for

3D-printing of the TAVI-Mimic and prototypes attached with pericardial tissue were manufactured.

Pericardium TAVI-Mimics were calcified in vitro for one week and an average calciumphosphate precipitate of 0.34-0.54 mg/cm² was measured.

The optimization of the TAVR-Mimic led to an improved load-dependent behaviour compared to a commercial prosthesis while testing. The calcification method, combining the TAVI-Mimic, the metastable calcification solution and the durability tester enabled a successfully calcification of pericardial tissue, approaching the in vivo situation.

Keywords: finite element analysis, transcatheter aortic valve implantation, calcification tendency

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1 Introduction

Clinical studies like the PARTNER 2A and the Sapien 3 have confirmed that TAVI shows superior results compared to aortic valve surgery applied at patients who belonging to a medium risk or younger age group [1]. Therefore, newly developed the transcatheter aortic valve prostheses (TAVP), currently designed for a lifetime of at least ten years, have to last much longer than this period. The increased implantation time raises the probability of a restenosis of the TAVP mainly caused by calcification of the prosthesis leaflets. Previous investigations showed that the type and the velocity of the calcification process depend on material stress during the cyclic valve opening-closing processes [2, 3].

For this reason, when developing next generation TAVP with increased durability for a time period longer than ten years it is necessary to at least screen innovative leaflet materials concerning calcification tendency and in a next step develop anti-calcification-strategies to inhibit future valve restenosis. Material screening is an iterative process; hence it is not suitable to manufacture a TAVP at any time.

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Therefore, the aim of this work was to develop and optimize a framework structure for heart valve leaflet material testing under physiological loading situation, e.g. in a pulse duplicator system or heart valve durability tester. A four-parted framework structure called TAVI-Mimic was initially developed in previous works and was optimized in terms of radial load deformation compared to commercial TAVP and materials used for productization of the TAVI [4].

To show the potential of the TAVI-Mimic, the framework structure was used for the investigation of the calcification tendency of porcine pericardium during in a heart valve durability tester containing a meta-stable calcification solution also developed in earlier studies [5]. To analyze and quantify calcification scanning electron microscopy and a photometric assay was used.

2 Materials and Methods

2.1 Analysis of the existing TAVI-Mimic

For improving the TAVI-Mimic, four samples of the existing design were 3D-printed and the manufactured prototypes were tested in a HDTi-6000 pulse duplicator system (BDC Laboratories, Wheat Ridge, CO, USA) to measure the radial load dependent deformation. The test was carried out by a fluid temperature of 37 °C, a mean aortic pressure of 100 mmHg, a pressure difference of 40 mmHg, a cardiac output of 5 L/min and with 0.9 % saline testing solution.

Moreover, the prototypes were tested in the accelerated wear tester VDT 3600i (BDC Laboratories, Wheat Ridge, CO, USA) to measure the durability. The tests were carried out with a temperature of 37 °C, a testing time of one week, a stroke of 5 mm, a 0.9 % saline solution and a frequency of 15 Hz.

2.2 TAVI-Mimic optimization

2.2.1 Selection of a suitable material for rapid manufacturing of the TAVI-Mimic

The TAVI-Mimic was manufactured with the 3D-printer Form 3 (Formlabs, Somerville, MA, USA). To optimize the TAVI-Mimic, three 3D-printing materials (Rigid, HighTemp V2 and Tough, Formlabs, Somerville, MA, USA) were chosen and examined regarding mechanical properties and water uptake during long time usage. Firstly, specimens were printed from each material. To consider the influence of the typical layer-

by-layer manufacturing of the 3D-printing process, five samples of each material were printed horizontally, vertically and in an angle of 45 degrees to the building platform.

Then, uniaxial quasi-static tensile tests were performed. Elastic modulus was calculated from the tests and compared between the different specimens.

Additionally, the different materials were investigated regarding their water uptake in long time use. Therefore, samples of each material were printed and stored in distilled water for 24 hours. Water uptake was measured by means of weighting samples before and after storage in water. Afterwards, uniaxial quasi-static tensile tests were performed to determine the influence of water uptake on the mechanical properties of the 3D-printed samples.

2.2.2 Design improvement of the TAVI-Mimic

After choosing the right material, the TAVI-Mimic was redesigned to increase the radial load deformation. Therefore, various grooves and other design elements were added to the framework structure by means of computer aided design (CAD) (Creo 6, PTC Inc., Boston, MA, USA). The influence of the design features on the load dependent behaviour of the TAVI-Mimic was determined by means of finite-element-analysis (FEA) (Ansys 18.1, ANSYS inc. Canonsburg, PA, USA).

To validate the FEA a ring folding test was performed for each material. Therefore, rings with a wall thickness of 0.75 mm and 1.25 mm, a diameter of 24 mm and a length of 17.5 mm were 3D-printed. The rings were fixed radially in the tensile testing machine and loaded between two horizontal plates until failure. This ring folding test was re-simulated in FEA and the results were compared to each other.

For the FEA the measured elasticity modules of the materials and a poisson's ratio of 0.4 were used. To simplify the simulation the CAD-Model was divided into six parts and only one part was simulated. The toughening planes of the model were loaded with a friction coefficient of 0.4.

To simulate the physiological loading situation of the TAVI-Mimic a remote force in the center of the frame was imported. The force was calculated by equation 1 and appeared in negative flow direction.

$$F = \frac{p \cdot A}{6} \quad (1)$$

With a pressure p of 120 mmHg and an area A of 452.4 mm², the remote force was 1.21 N. Using this settings the radial load dependent deformation was calculated.

In the next step, TAVI-Mimic prototypes with porcine pericardium were manufactured and tested in the pulse dupli-

cator system to verify the calculated radial load dependent deformation of the FEA with the experimental result

2.2.3 Implementation of the TAVI-Mimic into accelerated calcification testing

As a final step and to show the potential of the TAVI, for future heart valve development or at least material screening, the TAVI-Mimic prototypes were equipped with glutaraldehyde-fixated pericardial tissue and implemented in an accelerated wear testing system (VDT 3600i, BDC Laboratories, Wheat Ridge, CO, USA) and calcified for one respectively two weeks by using a metastable calcification solution which was developed in preliminary works [5].

After the accelerated wear test, calcification tendency of the pericardium was investigated using scanning electron microscopy (SEM) to show morphology of the calcification on the fibrous structure of the pericardium. Additionally, a photometric assay was used to quantify calcium concentration and apatite mass.

3 Results and Discussion

3.1 Analysis of the existing TAVI-Mimic

The hydrodynamic testing of the existing TAVI-Mimic using a pulse duplicator system resulted in a value of 0.03 ± 0.05 mm for the radial load dependent deformation. These results did not correlate with commercial TAVP value of 0.8 mm. Furthermore, the accelerated wear test showed that the leaflet material failed on the cavities near the attachments of the prototypes.

3.2 TAVI-Mimic optimization

The results of the tensile testing of differently 3D-printed samples showed that the layer configuration had only a minor influence on the mechanical behaviour, see figure 1.

Table 1 shows the elastic modulus of the different materials with respect to water absorption. For the material Tough the modulus of elasticity changed by 88.0%. The material HighTemp V2 just showed a change by 6.4% and the material Rigid just showed a change by 18.6%. Furthermore, the material Tough has absorbed the most water in 24 hours.

Since, the accelerated calcification test should be performed in water for two weeks, the material Tough was not considered suitable. For this reason, the outer shells of the

TAVI-Mimic were made of HighTemp V2 and the inner shells were made of Rigid.

Figure 1: Stress-strain curves of 3D-printed samples with differential layer configuration (horizontal: left column, vertical: middle column, 45°: right column) and printed from different materials (Tough (a – c), HighTemp V2 (d – f) and Rigid (g – i))

After choosing the right material for the TAVI-Mimic the existing CAD-Model was optimized to increase the radial load dependent deformation and reduce the wear of the leaflet material along the cavities near the attachments of the prototype. Figure 2 shows the optimized CAD-Model of the outer and inner shell of the TAVI-Mimic.

Table 1: Summary of the results of the water absorption test of the chosen materials for the manufacturing of the TAVI-Mimic (E = modulus of elasticity)

Material	Water absorption [mg]	E (dry) [MPa]	E (wet) [MPa]
Tough	18.9	918 ± 106	110 ± 9
HighTemp V2	2.4	1963 ± 67	1837 ± 83
Rigid	7.9	2126 ± 284	1730 ± 57

Recesses were inserted on the outer and inner shells to increase the radial load dependent deformation. Furthermore, on the outer shells tongues and on the inner shell grooves were modelled, to improve the adhesion between the shells. Finally, the shoulders on the outer shells were downsized and provided with a rounding. The edges along the cavities of the inner shell were provided with a rounding too, to decrease the wear of the leaflet on the cavities near the attachments.

Then, the optimized CAD-Model was implemented in the FEA. The results of the ring folding test correlated with the simulated results. In the figure 3 a, the simulated defor-

mation of the TAVI-Mimic loaded with the remote force, is visualized. The maximum calculated radial load dependent deformation was 0.52 mm.

Figure 2: Schematic picture of the optimized CAD-Model of the outer (left) and inner shells (right) of the TAVI-Mimic

As a final step, TAVI-Mimics were 3D-printed and equipped with porcine pericardium (see figure 3b). The prototypes were implemented in the pulse duplicator system. The measured radial load dependent deformation was $0.6 \text{ mm} \pm 0.1 \text{ mm}$, correlating on the one hand with the calculated value and with commercial TAVP.

Figure 3: By the FE-Software created picture of the maximum deformation of the optimized TAVI-Mimic loaded with the remote force (a) and a macroscopic picture of the inner shell of the TAVI-Mimic with a sewn in porcine pericardium leaf (b)

Pericardium TAVI-Mimic prototypes were calcified accelerated by one respectively two weeks. To evaluate the calcification tendency SEM and photometric assays were used.

The SEM-analysis showed that the pericardium was successfully calcified; see figure 4a. Apatite crystals, which are the result of the calcification, can be seen on the surface of the pericardium in the form of clumps.

Figure 4: Macroscopic picture of a porcine pericardium calcified by two weeks in an magnification of x300 (a) and the calcium-concentration-and apatite mass-results from the photometric assay of prototypes calcified for one respectively two weeks (b)

Figure 4b shows the results of the photometric assay, which are visualized in bar graphs. Both the calcium concentration and the apatite mass increased from one to two weeks of calcification. This shows that not only the calcification mass but also the content of the calcification changes over a longer period of time.

4 Conclusion

In the extent of this work, a TAVI-Mimic framework for testing leaflet materials of heart valve prototypes could be optimized. With the applied optimization steps, the TAVI-Mimic became more elastic and the radial load dependent deformation was adapted to physiological loading conditions. Furthermore, the wear of the leaflet material at the critical edge along the cavities near the attachments could be decreased. Then, the TAVI-Mimic was implemented into a heart valve durability tester and accelerated calcification tests were performed successfully. Finally, the calcification tendency could be successfully analyzed by using SEM and photometric assay. The result of this study is that the optimized TAVI-mimic is a simple alternative instead of heart valve prostheses for the physiological characterization of the calcification tendency of innovative heart valve leaflet materials.

Author Statement

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