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A novel trileaflet mechanical heart valve: first *in vitro* results

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Key question

What are the essential functions of the novel mechanical heart valve?

Key finding(s)

The novel mechanical heart valve has improved haemodynamics and thrombogenicity.

Take-home message

Placing hinges in the systolic flow helps to improve the haemodynamics and thrombogenicity of the heart valve prosthesis.

Abstract

OBJECTIVES: Heart valve prostheses are the therapy of choice for patients with severe heart valve diseases. Two types of prostheses that can be implanted in patients are available: biological and mechanical. Though mechanical heart valves have some disadvantages like necessity of life-long anticoagulation, biological heart valve prostheses often necessitate reinterventions due to limited durability. Therefore, a new trileaflet mechanical heart valve was developed, featuring hinges in the systolic flow with the aim of function and thrombogenicity.

METHODS: We first compared the new trileaflet mechanical heart valve to conventional bileaflet heart valves (St. Jude Medical and On-X valves) *in vitro*. Haemodynamic measurements were performed in a pulse duplicator system, and clot formation was examined with an implemented method using enzyme-activated milk as the test medium.

RESULTS: Haemodynamic measurements showed the largest effective orifice areas and smallest pressure gradients for the trileaflet prosthesis compared to the bileaflet valve. Opening and closing characteristics of the trileaflet valve and of the St. Jude Medical valve were comparable. Clotting tests depicted only minor isolated deposits for the new trileaflet valve whereas the bileaflet valves showed distinct clots in the area of the hinge in all experiments.

CONCLUSIONS: Haemodynamic and clotting tests showed improvements for the new trileaflet valve compared to common bileaflet valves. The off-wall systolic position of the hinges, which eluded adverse flow areas, was a major advantage of the new valve.

Keywords: Mechanical heart valve • Haemodynamic • Thrombogenicity

INTRODUCTION

The prevalence of heart valve diseases is increasing due to the ageing population, especially aortic valve stenosis in high-income countries [1, 2]. The therapy is either reconstruction or replacement of the valve. For the latter, 2 types of prostheses are available, biological and mechanical. The biological heart valve prostheses exhibit good haemodynamics and haemocompatibility. However, a disadvantage is their limited durability due to leaflet degeneration necessitating surgical reinterventions. Mechanical heart valves, on the other hand, provide excellent durability; however, life-long anticoagulation therapy is needed [3].

The goal of developing a new mechanical heart valve is to improve the flow conditions to overcome the need for life-long anticoagulation [4]. In contrast to the conventional bileaflet valves, the hinges of the novel trileaflet valve were placed in the central systolic flow, thereby eluding the adverse flow areas near the housing of the valve. In this study, haemodynamics and deposition behaviours of the novel trileaflet mechanical heart valve were tested *in vitro* and compared with results of 2 conventional bileaflet mechanical heart valves.

MATERIALS AND METHODS

The housing of the novel trileaflet mechanical heart valve was made of a titanium-aluminium-vanadium alloy (TiAl6V4), and the leaflets were made of poly-ether-ether-ketone (PEEK). The 3 leaflets are mounted on 6 hemispherical hinges in the systolic flow (Fig. 1). Two commercial bileaflet valves, the St. Jude Medical (SJM) Regent (Abbott, Chicago, IL, USA) and the On-X heart valve (CryoLife Inc., Kennesaw, GA, USA) were used as controls. All valves had a labelled size of 21 mm.

In the first part of the study, the haemodynamic behaviours of the 3 valve types ($n = 5$ each) were examined. The valves were mounted in a pulse duplicator that simulates the physiological system and was described elsewhere [5]. These measurements yielded leaflet movement and pressure and flow conditions in the ascending aorta and the resulting effective orifice area (EOA) of the valve [3, 6]. The system was filled with saline solution (0.9%), and the values obtained for a systemic pressure of 125/80 mmHg, a frequency of 64 bpm and different mean flow rates from 9.5 l/min to 15.8 l/min. Leaflet motion was recorded with a Motion Pro Y3 high-speed camera (Imaging Solutions GmbH, Eningen u. A., Germany), taking 500 pictures per second. Leaflet motions were analysed particularly in relation to the valve closing period, at which the starting point (when the respective leaflet starts to move towards closing) and the moment of final closure were detected. Values are given as mean and standard deviation.

To compare the pressure gradients and the EOAs, flow values were assigned to group 1 (range 9 l/min to <11 l/min), group 2 (range 11 l/min to <13 l/min) or group 3 (range >13 l/min). The values were tested for normal distribution, and *t*-tests were performed to detect differences between the valve types; *P*-values >0.05 were considered significant.

Clot formation was simulated using an *in vitro* test setup already described by Scharfschwerdt *et al.* [7]. This model allows the detection of potential clotting spots, and early stages of deposits can be observed. The test medium was fresh unpasteurized milk activated with microbiological rennet diluted with distilled water (1:2). The milk was warmed to 37°C, and tests were run with a pulsatile flow of 2 l/min at a heart rate of 70 cycles per min, to simulate conditions critical for clot formation. Five tests each were performed for 5 prototypes of the novel trileaflet valves. Results were analysed qualitatively and documented photographically as a general view and as a detailed view and indexed as followed: deposits below the struts, deposits at the hinges in a medial orifice orientation, deposits at the hinges in a medial leaflet orientation and deposits at the hinges in a lateral leaflet orientation (Fig. 2A). The numbers of deposits at the struts and hinges were counted. To compare the deposits of the SJM and On-X valves, the observations of the former study were used [7]; nevertheless, 1 test for each valve was also performed to confirm the validity of the method. The novel trileaflet valve and the SJM were tested for 25 min, and the On-X valve was tested for 22 min, because onset of initial clot formation differed for each valve [7].

RESULTS

Haemodynamics

The trileaflet mechanical heart valve showed the lowest gradients and largest EOAs in the applied range of flow rates as shown in Fig. 3. There was a significant difference for all groups of the On-X and trileaflet valves (pressure gradient $p_1 = 0.020$, $p_2 = 0.037$, $p_3 = 0.000$; EOA all $P < 0.01$). Pressure differences of the SJM and trileaflet valves were not significant except for the third group ($p_3 = 0.047$), whereas the EOAs of these 2 valves show significant differences for the first 2 groups ($p_1 = 0.008$, $p_2 = 0.001$).

Leaflets of the On-X valve started to close first, followed by the trileaflet and the SJM (Fig. 4). It took the On-X valve 38.8 ± 16.8 ms to close; however, the starting point of closing was difficult to detect because of the continuous movement of the leaflets during systole. Also, the leaflets did close simultaneously but sometimes 1 leaflet stayed open even if the other leaflet had already started to

Figure 1: Photographs of the novel trileaflet mechanical heart valve [4]. Left: closed aortic view. Right: opened ventricular view.

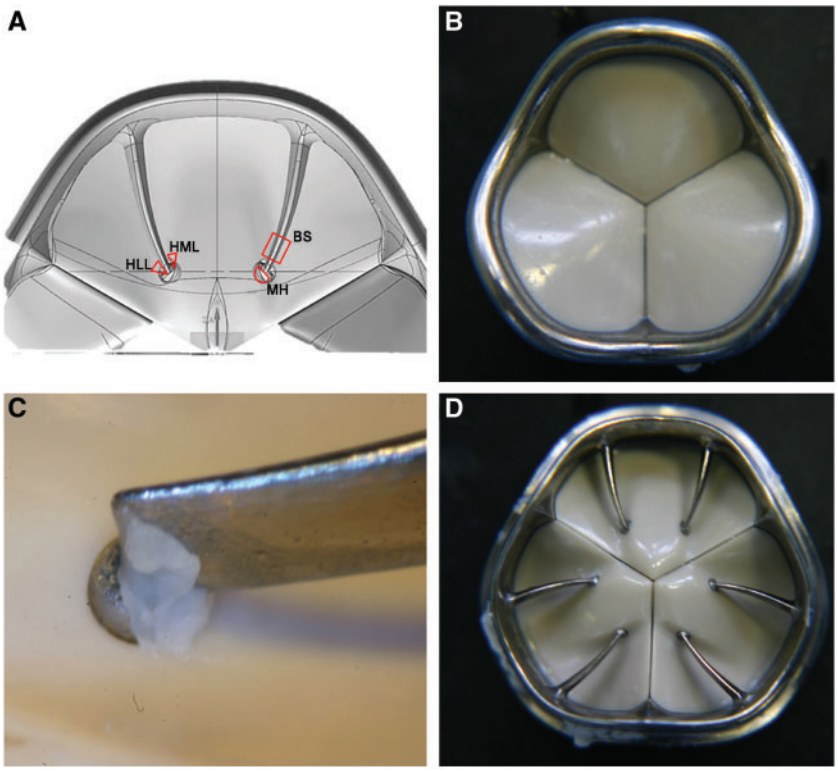

Figure 2: Results of the *in vitro* clotting test of the novel trileaflet valve. (**A**) Classification of deposit sites in the trileaflet valve; (**B**) view of a tested valve, downstream side; (**C**) example of a deposit at HLL (magnification ×32); (**D**) general view on the upstream side of a tested valve. BS: deposits below the struts; HLL: deposits at the hinges in lateral leaflet orientation; HML: deposits at the hinges in the medial leaflet orientation; MH: deposits at the hinges in medial orifice orientation.

close. The closing time of the trileaflet valve was 43.5 ± 16.4 ms and that of the SJM valve, 63.0 ± 49.8 ms. The velocity of the trileaflet valve and that of the SJM valve were comparable (78.4 ± 32.2 cm/s and 75.2 ± 23.6 cm/s, respectively). The closing velocity of the On-X valve was 84.7 ± 40.4 cm/s. The general leaflet motion patterns of the trileaflet valve and the SJM valve were comparable, but the leaflets of the SJM valve did not open completely for each cycle (opening angle 82–84°) whereas all leaflets of the trileaflet valve were always fully opened to 84°.

The least leakage volume was measured for the SJM valve, followed by the trileaflet and the On-X valve (Table 1).

Deposit behaviour

For the trileaflet valve some clots were detected around the hinges and below the struts. The most exposed region for clot formation was at the hinges in a lateral leaflet orientation followed by the deposits below the struts (Table 2). At this position, deposits were detected at the upstream portion of the leaflets (Fig. 2). On average, 3 of the 6 struts of a valve evinced deposits.

Visual examination of the results of the On-X valve showed deposits in the vicinity of the pivot. Further clots were detected at the leaflet edge (Fig. 5). The observations were similar to previous results.

Results of the SJM were comparable with results of the On-X. Clot formation was mainly located in the vicinity of the pivot. Some deposits could also be detected between the leaflet edge and the orifice ring (Fig. 5).

For both valves, deposits were observed at the downstream portion of the leaflets. Most of the deposits were solitary. After all tests, all indexed positions showed clot formations, although in different intensities.

DISCUSSION

We introduced a novel trileaflet mechanical heart valve that provides an innovative design characteristic whereby the pivots are placed in the main flow stream to avoid wake areas and thus to reduce the potential thrombogenicity. This study represents the first *in vitro* haemodynamic and clot formation results of the novel valve compared to the conventional bileaflet valves SJM and On-X.

Haemodynamics

Comparing the haemodynamic results of the 3 valves showed the lowest pressure gradient and largest EOA for the trileaflet valve [6]. The On-X valve had the highest gradient, similar to results reported by other groups [8]. The statistical results of the SJM and trileaflet valve were not always significant, possibly due to the small values in the low flow ranges.

The excellent results of the novel valve may be related to the valve design, especially the geometry of the leaflet, which is slightly curved, and thus flow streams can follow. The leaflets of the bileaflet valves are plain structures without any fitted geometrical parts. Consequently, the flow through the trileaflet valve may be more homogeneous with fewer vortices and wake areas for implemented anatomical inflow geometry compared to the bileaflet valves [9]. The geometry of the leaflets of the bileaflet valves leads to elevated shear stresses due to the 3-jet flow through the valve orifice and wake areas with shed vortices as observed by Bluestein *et al.* [10]. These observations also result in stronger jets in the orifice and consequently in larger differences in velocities between the jet and the valve edge. However, the

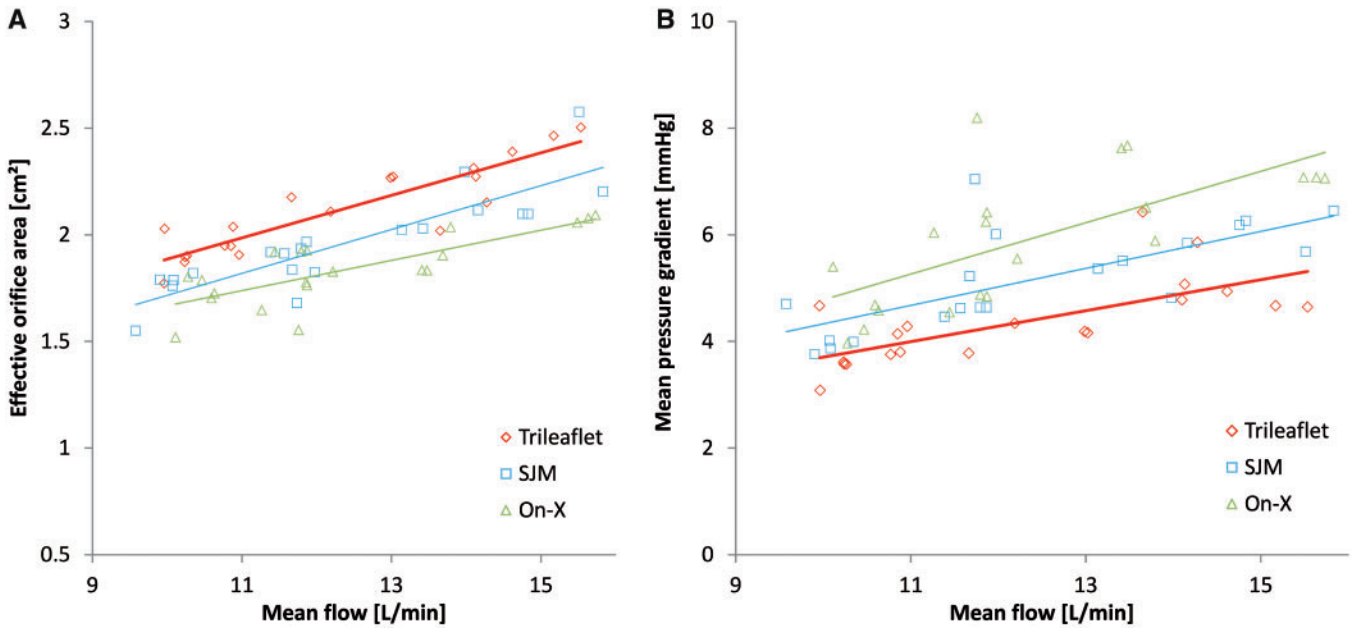

Figure 3: Effective orifice area (**A**) and mean pressure gradient (**B**) of the 3 tested valves. Lines show linear regressions of measured data for each valve type. SJM: St. Jude Medical.

flow analyses are not completed, comparisons have not yet been performed and final conclusions cannot be made pending further investigations, including computational fluid dynamics, particle image velocimetry and 4-dimensional flow magnetic resonance imaging.

Further, the hinges of the new valve are positioned in the central systolic flow, which also leads to an improved flow profile without wake areas and complete washing of the pivot area. In contrast to bileaflet valves, there is no diastolic flow through the hinges. The motion of the leaflets of all 3 valves showed the best valve performance for the trileaflet valve. All 3 leaflets were fully open during each cycle and started closing before regurgitation began (Fig. 4). Further, the 3 leaflets were completely closed at almost the same time. The On-X valve started to close slightly earlier, but the leaflets were moving during the systolic flow and did not consistently close at the same time. Sometimes 1 leaflet lagged behind. This asymmetrical leaflet closure has been observed for bileaflet valves in other studies [11]. It seems that the leaflets influence each other, depending on the effective flow profile through the valve.

Leaflet velocity during closure has an impact on the negative side effects of the valve, like cavitation and noise generation [12]. Slower velocity generates less cavitation and may also reduce noise generation. In this regard, the novel trileaflet valve and the SJM valve are comparable, and both provide slower leaflet closing velocities than the On-X valve [11]. The impact on cavitation and noise generation has to be examined further.

Deposit behaviour

Investigation of clot formation in the bileaflet valves showed deposits at the pivots on the downstream side and between the downstream leaflet edge and the orifice ring. These results were observed in a previous study and in patients with the bileaflet valves tested in this study [7, 13]. In this respect, it could be assumed that clot development in bileaflet valves was not only influenced by diastolic reverse hinge flow but also by adverse systolic forwards flow patterns. Even if there is no detailed flow analysis available, it might be assumed that stagnant flow and wake areas appear behind the leaflets and in the downstream vicinity of the leaflets [10]. Further, leaflets were in close contact with the outer ring of the valve, both during systole and diastole. At the outer edge of any flow orifice the velocity of the streaming medium is obviously low and disturbances are more likely, increasing the risk of clot formation. In bileaflet valves, hinges are charged in diastole; indeed, there is some kind of washout flow through the hinge gap. This leakage flow also creates high shear stresses and may promote haemolysis and thrombus formation [14, 15]. However, there are also approaches that assume platelet activation in both systole and diastole due to the combination of shear and deformation stress. Further, observed wake areas around the leaflets also result in platelet activation and increase the potential for thromboembolic activity [10].

The novel trileaflet valve showed only small and isolated deposits in the vicinity of the hinges (Fig. 2C). These deposits may be due to a yet not completely optimized systolic forwards flow pattern in this region and are the subject of further development. However, other parts of the valve were free of clot formation (Fig. 2B and D). The observed deposits at the hinges do not lead to dysfunction of the leaflets similar to that which occurs with the bileaflet valves. Positions of deposits vary slightly but in a confined area. These favourable results show that potential sources of haemolysis and clot formation can be reduced by placing the hinges in systolic flow. Regions of wake areas and stagnant flow might also be reduced compared to the bileaflet valves, as a consequence of the valve design. In this regard, a recent computational fluid

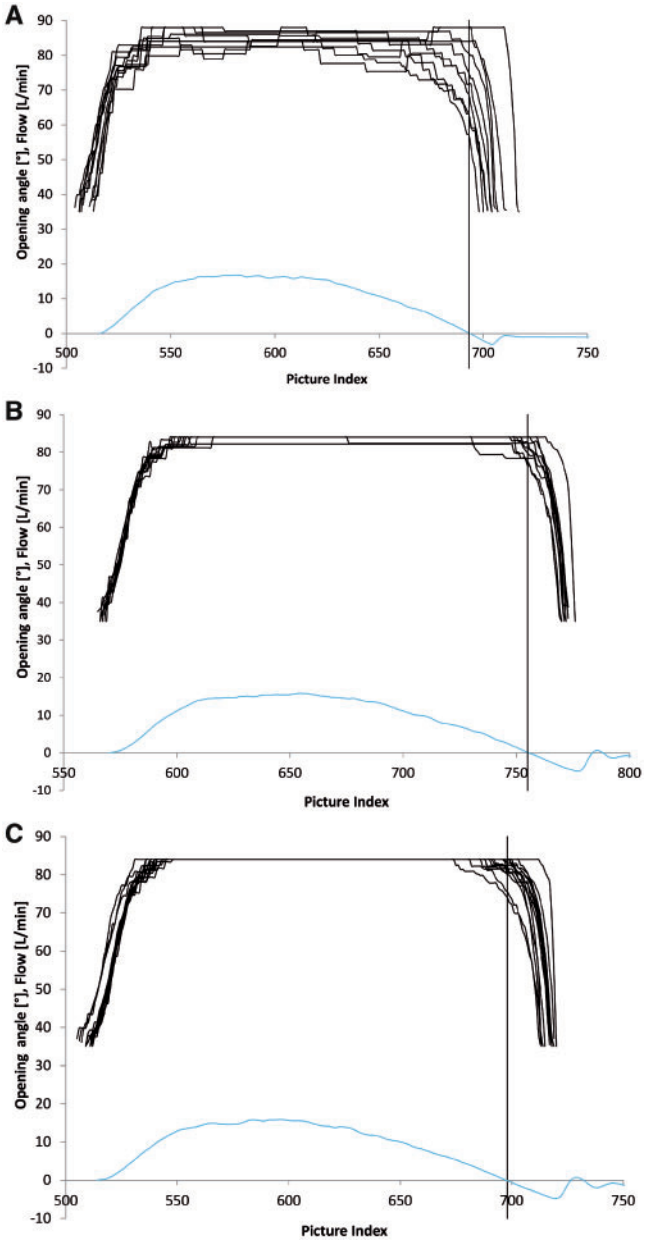

Figure 4: Leaflet motion of the 3 valves (upper lines), including flow profile (lower curve) and onset of regurgitation (vertical line). (**A**) On-X heart valve, (**B**) St. Jude Medical heart valve and (**C**) trileaflet heart valve. Note the sustained movements of the On-X valve leaflets during systole (1 picture index is equivalent to 2 ms.).

dynamics investigation of the trileaflet valve showed a relatively homogeneous flow profile in an anatomical inflow model [9].

Limitations

Some limitations of the study should be taken into account. The *in vitro* test setup might not completely resemble the native flow situation. Also, tests were run with saline water, which has a different viscosity than blood; thus, absolute values may be different. However, all tests were run under the same conditions, allowing for comparison. Only a small valve size was tested due to subsequent animal experiments. Results might differ for larger valve sizes.

The results of clot formation should be critically examined because this *in vitro* test might not represent real thrombus formation due to differing behaviours of the medium used and blood and is limited to flow-induced clot formation. In this respect, further *in vivo* experiments are required for more conclusive results. However, in previous studies, this method showed results similar to those observed in patients with bileaflet heart valve prostheses [7, 13].

Table 1: Values from leaflet motion and regurgitation analyses

	Trileaflet valve	On-X valve	SJM valve
Closing time of leaflets (ms)	43.5 ± 16.4	38.8 ± 16.8	63.0 ± 49.8
Leaflet velocity during closing (cm/s)	78.4 ± 32.2	84.7 ± 40.4	75.2 ± 23.6
Leakage volume (ml)	8.9 ± 1.1	9.2 ± 0.7	6.9 ± 0.6
Maximal flow (l/min)	15.6 ± 1.3	16.9 ± 0.4	16.2 ± 0.5

All values are expressed as mean ± SD; $n = 5$.
SJM: St. Jude Medical.

Table 2: Amount of deposits on the indexed locations

	Valve 1	Valve 2	Valve 3	Valve 4	Valve 5	Percentage
BS	4		3			29.2
HM	1		2			12.5
HML	1	1	3		1	25
HLL	1	1	3	2	1	33.3
Number of struts	4	1	6	2	2	50

BS: below the struts; HLL: at the hinges in the lateral leaflet orientation; HM: hinges in the medial orifice orientation; HML: hinges in the medial leaflet orientation.

CONCLUSION

The first *in vitro* test results of the haemodynamics and clot formation of the novel trileaflet valve showed promising results with a large EOA and minor deposits. However, the valve is still under development, and the design of the valve is optimized continuously. Further studies are in progress, and *in vivo* experiments will give results about the real performance of the novel design.

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Conflict of interest: Hans-Hinrich Sievers holds a patent for the novel mechanical heart valve described in this article.

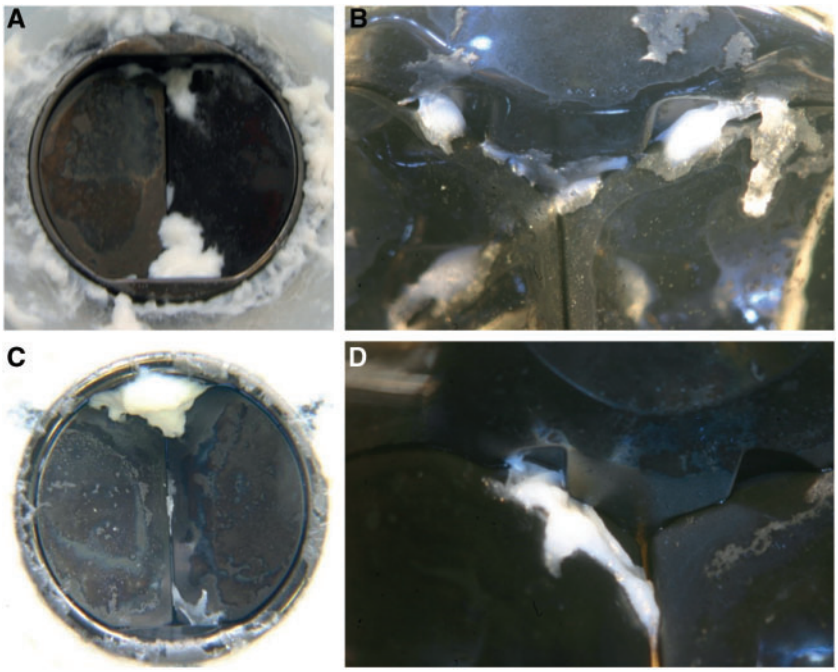

Figure 5: Results of the *in vitro* clotting test of the On-X valve showing (**A**) deposits at the downstream side; (**B**) deposits at the downstream side pivot; and of the St. Jude Medical valve showing (**C**) deposits at the downstream side and (**D**) deposits at the downstream side pivot.

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