Underfilled Balloon-Expandable Transcatheter Aortic Valve Implantation With Ad Hoc Post-Dilation — Pulsatile Flow Simulation Using a Patient-Specific Three-Dimensional Printing Model —

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Background: Underfilled transcatheter aortic-valve implantation with ad hoc post-dilation is a therapeutic option for patients with borderline annuli to avoid acute complication. The effects of this technique on valve leaflet behavior, hydrodynamic performances, and paravalvular leakage (PVL) using patient-specific three-dimensional (3D) aortic-valve models were investigated.

Methods and Results: A female octogenarian patient was treated with this technique by using a 23-mm Sapien-XT. Patient-specific models were constructed from pre-procedure computed tomography (CT) data. Change in aortic annulus areas during systolic/diastolic phases and post-procedure stent areas were adjusted to those of the patient. The following was performed: (1) −3 cc initial and −2 cc underfilled post-dilation to the scale-down model by adjusting percent oversizing; and (2) −1 cc initial underfilling, nominal volume, and repeat nominal volume post-dilation using the patient-specific model. Underfilling was associated with higher %PVL. Observation using a high-speed camera revealed distorted leaflets after underfilled implantation, with a longer valve-closing time and smaller effective orifice areas, especially in the −3 cc underfilled implantation. Micro-CT analysis revealed that the transcatheter valves shifted to the opposite side of the large annulus calcification after post-dilation and reduced the malapposition there.

Conclusions: Excessive underfilled implantation showed unacceptable acute hemodynamics. Abnormal leaflet motions after underfilled implantation raised concerns about durability. Flow simulations using patient-oriented 3D models could help to investigate hemodynamics, leaflet motions, and the PVL mechanism.

Key Words: Ad hoc post-dilation; Paravalvular leakage; Pulsatile flow simulation; Transcatheter aortic valve implantation; Underfilled implantation

Transcatheter aortic valve implantation (TAVI) has emerged as an effective treatment for patients with severe aortic stenosis (AS) who are at intermediate or greater surgical risk. Despite the advancements in balloon-expandable TAVI with an excellent mid-term outcome, inadequate undersizing could lead to paravalvular leakage (PVL), whereas excessive oversizing may result in coronary obstruction, periaortic hematoma, mitral valve injury, and annulus rupture. Multidetector computed tomography (MDCT) imaging could help to optimize size selection and reduce PVL and annulus rupture. However, balloon-expandable TAVI for smaller, borderline, and calcified annuli has a potential risk for complications due to limited size variations, even with the current devices. Therefore, determining the appropriate valve sizing for these particular anatomies is crucial and warrants further investigation.

Furthermore, Asian patients have adverse aortic root features with smaller body size and annulus area (AA) and shallow sinus of Valsalva, and have a higher rate of females who have TAVI than European patients. For extremely small annuli, a 20-mm balloon-expandable valve was made available after March 2013 in Japan; however, moderate prosthesis-patient mismatch (PPM) was more prevalent in the 20-mm valve than in the 23-mm valve. Moreover, in a Japanese patient cohort that had a small body size, the

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implantation and post-dilation and survived at 30 days; (2) whose AA was equivalent to the Japanese patient average (i.e., 376 mm$^2$), as previously reported by Watanabe et al.\(^7\); (3) with adverse aortic root features defined by Barbanti et al; extreme age, female, left ventricular outflow tract (LVOT) calcification, shallow sinus of Valsalva, and relatively small body size who was treated with >10% area oversizing;\(^8\) and (4) with MDCT imaging quality sufficient for model construction. During the study period, Sapien-XT (Edwards Lifesciences, CA, USA) was the only available TAVI device in Japan. Of 53 severe patients with AS treated with balloon-expandable TAV, an 86-year-old female met the criteria.

This study was approved by two local institutional review boards (SYEH and Waseda University), and the patient provided written informed consent. Pre-procedure MDCT revealed that the systolic maximum AA was 367 mm$^2$ (Figure 1A). We performed a −1 cc underfilled implantation using a 23-mm Sapien-XT (Figure 1E) because of adverse aortic root features, with 13% area oversizing and with LVOT calcification (Figure 1A, B), mitral annulus calcification (Figure 1C), shallow sinus of Valsalva, high age, female, and small body size. A color Doppler transesophageal echocardiography showed moderate paravalvular leakage (PVL; circumferential extent <10%, red arrow) that originated from the non-coronary cusp where large calcification was located in the pre-procedure MDCT (A, B).

Figure 1. (A) Pre-procedure maximum annulus area (AA; 367 mm$^2$) in the systolic phase on multidetector computed tomography (MDCT). (B) Pre-procedure minimum AA (348 mm$^2$) in the diastolic phase on MDCT. (C, D) Perpendicular view before implantation. Red triangles indicate aortic valve calcification, and yellow triangles display mitral annulus calcification. The yellow line demonstrates a perpendicular line. (E) Initial −1cc underfilled implantation of 23-mm Sapien-XT. (F) Post-dilation with nominal-volume inflation. (G) Aortography after deployment. Implantation height was 70%, which was calculated as follows: 100×(stent height to aorta/stent height). (H) Immediately after post-dilation, transesophageal echocardiography showed mild paravalvular leakage (PVL; circumferential extent <10%, red arrow) that originated from the non-coronary cusp where large calcification was located in the pre-procedure MDCT (A, B).

We developed aortic valve models with patient-specific anatomy using MDCT data of a patient. This study aims to investigate the effects of underfilled implantation and post-dilation techniques on stent-flame apposition to the aortic valve annuli, leaflet behavior during pulsatile circulations and hemodynamic alteration, is scarce. Inadequate valve leaflet motion may be induced by an underfilled implantation, which is a concern for long-term durability.

We developed aortic valve models with patient-specific anatomy using MDCT data of a patient. This study aims to investigate the effects of underfilled implantation and post-dilation techniques on stent-flame apposition to the aortic valve annuli, leaflet behavior, and hemodynamics using a pulsatile flow simulator, and to gain an understanding of the features of the underfilled implantation techniques in slightly built patients with small AA and annulus calcification.

### Methods

#### Patient Selection

To duplicate patient-specific models, we retrospectively selected a patient from the TAVI database of Saiseikai Yokohama City Eastern Hospital (SYEH) between February 2014 and September 2015. The criteria for patient selection were as follows: a patient (1) treated with underfilled implantation and post-dilation and survived at 30 days; (2) whose AA was equivalent to the Japanese patient average (i.e., 376 mm$^2$), as previously reported by Watanabe et al.\(^7\); (3) with adverse aortic root features defined by Barbanti et al; extreme age, female, left ventricular outflow tract (LVOT) calcification, shallow sinus of Valsalva, and relatively small body size who was treated with >10% area oversizing;\(^8\) and (4) with MDCT imaging quality sufficient for model construction. During the study period, Sapien-XT (Edwards Lifesciences, CA, USA) was the only available TAVI device in Japan. Of 53 severe patients with AS treated with balloon-expandable TAV, an 86-year-old female met the criteria.

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#### Patient-Specific Model

A patient-specific model was constructed using our recently reported methodology.\(^9\) Briefly, aortic valve models were duplicated based on 320 slice MDCT data with minimal AA (348 mm$^2$) at end-diastole (Figure 2A) because valve
AA changes during a cardiac cycle by pulsatile pressure and becomes smaller at end-diastole. Digital Imaging and COmmunications in Medicine (DICOM) images were imported into a segmentation software (Mimics, Materialise, Leuven, Belgium), and the patient’s anatomy was reconstructed (Figure 2B). First, calcified valve leaflets were manually excluded from the constructed MDCT data because the resolution of clinical MDCT is insufficient to detect valve leaflet geometry. The luminal models of aortic valve, excluding the calcified region, were duplicated using a stereolithograph (Objet 500; Connex Printer, Stratasys, Valencia, CA, USA), with a high-resolution layer slice of 15µm. The outer mold of the calcified region was also constructed (Figure 2C). The calcified regions between the two molds were constructed using silicone (KE-1603; Shin-Etsu Chemical, Tokyo, Japan). Elasticity of the calcified region was adjusted to that of the calcified human artery (12.6±0.1 MPa) by optimizing manufacturing parameters. Subsequently, a 2-mm-thick aortic wall was manufactured using a similar procedure (Figure 2D). The post-procedure stent-frame area on MDCT (367 mm²) in the patient was simulated in the model (370 mm², Figure 2F).
Hydrodynamic Performance Tests Using a Pulsatile Flow System

We sought to simulate the diastolic minimum AA (348 mm$^2$) and the systolic maximum AA (367 mm$^2$) of the patient in pre-procedure MDCT in the model during a pulsatile circulation. Patient-specific valve models were installed in a chamber whereby the inlet and outlet were connected to the circulation system (Figure 4A). By regulating pressure outside the valve models in the chamber, AAs in end-systole and end-diastole were reproduced in the pulsatile circulation (Figure 4B). The pulsatile circulation system was composed of the patient-specific valve model installed in a chamber to regulate pressure outside the valve model, a left ventricular model driven by a pneumatic console, a pre-load tank, an aortic compliant tube, and a vascular resistance unit (Figure 4A). Clinical echocardiogram data of blood pressure (123/60 mmHg), heart rate (61 beats/min), and forward flow (3.3 L/min) after TAVI were duplicated in the pulsatile circulation system. For the down-sized model, blood pressure and heart rate were adjusted to those of the patient-specific model. The forward flow for the down-sized model was 2.9 L/min, considering the ratio of its AA to that of the patient’s specific model. Pressures and flows were measured using a pressure transducer (UK-801; Baxter, CA, USA) and an electromagnetic flow sensor (FF-180; Nihon Kohden, Tokyo, Japan). Closing volume (CV), PVL volume (PVLV), and stroke volume (SV) were calculated using flow data.
Simulation of Underfilled TAVI and Post-Dilation

In the patient-specific model, the valve was deployed initially by −1 cc underfilled inflation, nominal post-dilation, and repeat nominal post-dilation. The height of the valves implanted, defined as the percentage of the stent downside from the AA, was matched between the model and patient at 70% (Figure 1G). The positional relationships of the native aortic valve commissure, TAV’s commissure, and the largest LVOT calcification were considered, which

(Figure 4C). The %CV (CV/SV) and %PVLV (PVLV/SV) were compared among the valve inflation conditions.

Valve Deployment Procedures

Valve deployment procedures are shown in Figure 3. In this study, 23-mm Sapien-XTs were used. In the down-sized model, the valve was deployed initially by −3 cc underfilled inflation and subsequently by −2 cc underfilled post-dilation.

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were technically uncontrollable in the clinical settings. The following three angle patterns were tested, and the average data were compared (Figure 5):

Angle-A: TAV commissure was on the native aortic valve commissure.
Angle-B: TAV commissure was on the largest LVOT calcification.
Angle-C: TAV commissure was on neither the native aortic valve commissure nor the largest LVOT calcification.

**Micro-Computed Tomography Analysis**
Stent-frame areas were measured at the top, middle, and bottom of the TAV. To understand the mechanism of PVL reduction after post-dilation, we calculated the percent reduction of malapposed areas and compared the results between the opposite side and the ipsilateral side of the largest LVOT calcification. In the patient-specific model, the malapposed areas were measured at 3 cross-sections: annulus level (0mm) and 1 and 2mm distal from the annulus level. In the down-sized model, malapposed areas were measured at the cross-section of the annulus level (0mm) and 0.933 and 1.867mm distal form the annulus level, taking the down-size ratio into consideration. Percent reduction of malapposition was calculated using the following formula: (malapposed areas after post-dilation−malapposed areas after initial underfilled implantation) / (malapposed area after initial underfilled implantation) ×100 (%).

**Dynamic Valve Leaflet Behaviors**
Dynamic valve leaflet behaviors were recorded using a high-speed microscope (VW-9000; Keyence, Osaka, Japan) at 1,000 frames/s. Leaflet coaptation at valve closure, percentage (%) of effective orifice area (%EOA), defined as EOA/AA×100 (%); and valve closing time were compared.

**Statistical Analysis**
Continuous variables were presented as mean±standard deviation. Three valves were used for each patient-specific model and down-sized model; thus, statistical analysis was not performed.
The valve leaflets after underfilled implantations were distorted compared with those after nominal-volume inflation (Figure 7A). Leaflet distortion was distinct in the −3 cc underfilled implantation. The leaflets of the underfilled valves did not have contact with the valve frame. %EOA and valve closing time are shown in Figure 7B and C. The %EOA after the initial −3 cc underfilled implantation was the lowest (42.2±0.6%). %EOA increased after post-dilation using −2 cc underfilling in the down-sized model (45.9±1.0%) and nominal inflation in the patient-specific model (46.8±0.7%). Valve closing time after the initial −3 cc underfilled implantation was the longest (61.6±1.02 ms). The post-dilations with −2 cc underfilling in the down-sized model and nominal inflation in the patient-specific model shortened the valve closing time (57.1±0.79 and 55.6±0.67 ms respectively). The repeated nominal post-dilation did not increase the %EOA and shorten valve closing time. Valve closing time was negatively correlated with TAV areas (r=−0.0932, R²=0.7487). Cardiac output was positively correlated with EOA (r=0.0071, R²=0.6644).

Leaflet Behavior
Observation using the high-speed microscope showed that the valve leaflets after underfilled implantations were distorted compared with those after nominal-volume inflation (Figure 7A). Leaflet distortion was distinct in the −3 cc underfilled implantation. The leaflets of the underfilled valves did not have contact with the valve frame. %EOA and valve closing time are shown in Figure 7B and C. The %EOA after the initial −3 cc underfilled implantation was the lowest (42.2±0.6%). %EOA increased after post-dilation using −2 cc underfilling in the down-sized model (45.9±1.0%) and nominal inflation in the patient-specific model (46.8±0.7%). Valve closing time after the initial −3 cc underfilled implantation was the longest (61.6±1.02 ms). The post-dilations with −2 cc underfilling in the down-sized model and nominal inflation in the patient-specific model shortened the valve closing time (57.1±0.79 and 55.6±0.67 ms respectively). The repeated nominal post-dilation did not increase the %EOA and shorten valve closing time. Valve closing time was negatively correlated with TAV areas (r=−0.0932, R²=0.7487). Cardiac output was positively correlated with EOA (r=0.0071, R²=0.6644).

**Results**

**Hydrodynamic Performances**
Hydrodynamic performances are shown in Figure 6. The initial underfilled implantation was associated with higher %PVLs (−3 cc underfilling: 18.5±4.5% in the down-sized model; −1 cc underfilling: 22.9±3.9% in the patient-specific model), which were reduced by post-dilation (−2 cc underfilling: 16.3±3.0% in the down-sized model; nominal filling: 20.7±3.5% in the patient-specific model) (Figure 6A). A slight reduction tendency of %PVL was observed after the repeated nominal post-dilation in the patient-specific model (19.8±3.7%). Percent CV was almost comparable among all procedures in both models (Figure 6B). However, cardiac output was distinctly low in the case of the initial −3 cc underfilled inflation in the down-sized model. In the other conditions, cardiac outputs were comparable (Figure 6C).
Stent-Frame Expansion and Change in TAV Malapposition After Post-Dilation

TAV frame areas in the initial −3cc underfilled implantation in the down-sized model were the lowest (Figure 8A). TAV frame areas of the initially underfilled implantation −3cc in the down-sized model and −1cc in the patient-specific model) increased after post-dilations using −2cc underfilling and nominal filling respectively. In the patient-specific model, the repeat nominal post-dilation increased the TAV frame area. Moreover, we compared the percent reduction of malapposition between the opposite side and the ipsilateral side of the largest LVOT calcification (Figure 8B). Representative cross-sectional micro-CT images are shown in Figure 8C. After post-dilation, percent reduction of malapposition at the opposite side decreased compared with that at the ipsilateral side in the down-sized (−60.6±30.4 vs. −15.6±8.3%) and patient-specific (−36.7±45.4 vs. 1.5±15.2%) models (Figure 8B). The repeat nominal post-dilation slightly reduced the malapposition at the ipsilateral side (nominal vs. repeat nominal; 1.5±15.2 vs. −9.0±7.9%; however, it did not contribute to the percent reduction of malapposition at the opposite side (−36.7±45.4 vs. −38.5±44.6%). Micro-CT analysis revealed that the TAV shifted to the opposite side of the large annulus calcification after post-dilation and reduced the malapposition there (Figure 8C).

Discussion

The main findings of this study are as follows: (1) underfilled 23-mm Sapien-XT exhibited acceptable acute hydrodynamic results, except for −3cc under-expansion; (2) TAV leaflets after underfilled implantation were distorted with longer valve closing time and lower EOA, which was distinct after −3cc under-expansion; (3) ad hoc post-dilation facilitated stent-frame expansion and contributed to PVL reduction even after repeat nominal inflation; (4) after post-dilation, TAV shifted to the opposite side of the largest LVOT calcification and reduced the malapposition there, but did not contribute to the reduction of malapposition adjacent to the largest LVOT calcification.

Advanced 3D-Printing Model for TAVI Simulation

Maragiannis et al demonstrated that a patient-specific 3D-printing model could replicate both the anatomic and functional properties of severe degenerative AS.15 For the treatment of severe AS, ex vivo simulation using a 3D-printing model before a procedure may be valuable to predict PVL and pacemaker implant (PMI) after TAVI.12 However, previous studies using 3D-printed models failed to simulate the stiffness of aortic annuli. Simple 3D aortic valve models by a 3D printer using polymers have a different elastic modulus from that of the human annuli. In this study, we simulated: (1) the post-procedure TAV frame area by separately regulating the elastic modulus of silicone both at the region of calcification and aortic annulus; (2) the diastolic AA by applying pressure from the outside the valve models in the pulsatile circulation system because the 3D structure constructed based on the CT data at end-diastole is pressurized with the end-diastolic pressure; and (3) diastolic and systolic alternations of AAs by applying the patient-specific pulsatile pressures. We believe that duplication of aortic annulus expansion properties under patient-specific hemodynamic conditions is indispensable for a precise assessment of stent flame, malapposition, and leaflet motion after implantation. Furthermore, the development of a down-sized model enabled the comparison of hemodynamics, leaflet motions, and malapposition between 2 percent oversizing (approximately 7%: initial implantation; 13–14%: post-dilation) among different underfilled implantation.

Underfilled Implantation of Balloon-Expandable TAV

The influence of underfilled implantation on the adverse event rate has not been well understood. A previous Western registry enrolled only 7 patients with underfilled 23-mm TAV because a Western cohort with a relatively large body size usually required no underfilling of 23-mm TAV.18 Barbanti et al reported clinical data on underfilled implantation, with approximately 10% contrast reduction (approximately −1cc underfilling in 23-mm TAV). However, in previous studies, no clinical data on excessive underfilled implantation have been reported. Hence, our study could help better understand valve performances under excessive underfilling.

In this study, −3cc underfilled 23-mm Sapien-XT resulted in a distinctly small TAV flame area, decreased EOA, and lower cardiac output compared with other inflation conditions. Although underfilled −2 and −1cc implantation showed lower EOA and longer valve closing time than nominal implantation, cardiac output was maintained. Our data suggested that underfilled −2 and −1cc TAVI as necessary for selected patients with an adverse root feature and may be acceptable as an initial implantable technique to reduce annulus rupture.

However, with regard to valve leaflet behavior, distorted leaflet motion was observed even after −1cc underfilling, which in turn resulted in concern regarding the long-term durability of underfilled TAV. Moreover, in previous reports, valve deterioration more likely occurred in younger patients with surgical prosthesis valve.13 Therefore, underfilled balloon-expandable TAVI should be avoided for patients with a longer life expectancy. A self-expandable valve with a merit of larger EOA due to supra-annulus leaflet position may be a viable alternative. Nevertheless, further study is needed for investigating leaflet durability of transcatheter valves.

Borderline Annulus Treatment by Balloon-Expandable Valve

Valve selection for borderline annuli has been extremely challenging. Although after the launch of Sapien-3, PVL and annulus rupture incidents have notably decreased, further treatment advancements remain necessary.14 Shivaraju et al showed that overexpansion (i.e., approximately +2cc volume addition to the 23-mm Sapien-3) is feasible.14 However, recently, Midha et al reported that overexpansion is related to leaflet thrombosis.15 They speculated that under-expansion may yield higher jet velocity, smaller space of neo-sinus with reduced tension in the leaflet, and subsequently a flush of blood (wash-out effect) in neo-sinus.15 Underfilling of a relatively large valve is associated with risks of annulus rupture, PPM, and poor durability, whereas overfilling of a relatively small valve is associated with risk of unfixed PVL, central leakage, and leaflet thrombus. Further study is needed to determine which strategy is better for borderline aortic annuli, while considering the current and next-generation balloon-expandable TAVs.
Mechanism of Paravalvular Leak and its Reduction by Ad Hoc Post-Dilation

Quantitative and semi-quantitative parameters and criteria to assess PVL following TAVI have been previously proposed. However, the exact PVL volume is usually unknown in clinical practice. In our study, we directly measured PVL volume using an electromagnetic flow sensor after underfilled inflation and ad hoc post-dilation. Furthermore, we measured TAV frame areas and malapposed areas using micro-CT and elucidated the efficacy and mechanism of post-dilation for PVL. Recently, we reported that the minimal gap area demonstrated by the micro-CT analysis of the patient-specific 3D-printing models has a significantly positive correlation with PVL volume.

Microporous areas using micro-CT and elucidated the efficacy and mechanism of post-dilation for PVL. Recently, we reported that the minimal gap area demonstrated by the micro-CT analysis of the patient-specific 3D-printing models has a significantly positive correlation with PVL volume. For our patient, post-procedure transesophageal echocardiography showed mild PVL that originated from a non-coronary cusp (Figure 1H) where large calcification was observed in pre-procedure MDCT (Figure 1A, B), and unfixed malapposition was located adjacent to the LVOT calcification in the patient-specific model (Figure 8C).

Observation using micro-CT revealed that even repeated nominal post-dilation contributed to stent-frame expansion and PVL reduction. A recent study on coronary intervention reported that repeat post-dilation with a consistent pressure is associated with increased stent area. Therefore, repeat nominal post-dilation of TAV could be an option, especially if additional 1cc post-dilation results in anulus rupture risk. Moreover, our result suggested the importance of the assessment of pre-procedure LVOT calcium distribution on MDCT. Protruded calcification and the presence of calcification at the counter part (both sides at 180°) may be refractory in PVL reduction by post-dilation.

Clinical Implication of the Patient-Specific Aortic Valve Model Using a Biomedical Engineering Technique

Our preliminary simulation of TAVI using patient-specific models has several clinical implications. The sizes of aortic valve models could be changed using 3D-printers, which in turn enables simulation of various aortic valve sizes (i.e., borderline, extremely small, or large valve size). Furthermore, accumulated patient data of an imaging modality (i.e., 3D transesophageal echocardiography, 4D CT, magnetic resonance imaging) may contribute to the development of an accurate model to simulate both configuration and stiffness of not only an anulus but also leaflet and LVOT. This simulation model may be useful to test the safety and efficacy of new TAV before first-in-man study and reduce the number of patients enrolled into a pre-approval randomized trial. Furthermore, this simulation model may be used in the education and training for TAVI, in the optimization of TAVI and device selection (balloon or self-expandable) for unusual anatomy (e.g., bicuspid valve and septal hypertrophy), in order-made therapy (personalized TAVI) for better outcomes, and in the feasibility test of challenging techniques (e.g., −3cc underfilling in our study).

Study Limitation

This preliminary study has some limitations. First, pre-/post-MDCT of the patient was retrospectively obtained. Although imaging quality was adequate, an additional imaging modality may have provided more detailed information for the model construction. Second, TAV leaflet was not duplicated in this study, because a non-calcified part in the native leaflet was not clearly detected using our clinical MDCT. Third, only one anulus slice in one patient was used for the construction of anulus stiffness. Effects of the stiffness of the LVOT and leaflet on TAV expansion could not be included. This serves as a challenging issue to be solved in future TAVI bench studies. Finally, this study used the previous generation Sapien-XT. Influences of leaflet distortion due to underfilled implantation on long-term durability should be addressed by future clinical study. Nevertheless, the pulsatile circulation system with patient-specific models may provide valuable insights for the selection of valve type and optimal size of new-generation TAV based on aortic root anatomy.

Conclusions

Our study indicated that underfilled 23-mm Sapien-XT implantation, except for excessive −3cc underfilling, showed acceptable acute hemodynamics. However, our data revealed abnormal leaflet behaviors after using this technique, which was a concern for long-term durability. Flow simulation using patient-oriented 3D models considering anulus stiffness enabled a detailed investigation of hemodynamics, leaflet motion, and the mechanism of PVL reduction by post-dilation.

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References


