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Novel *In Vitro* Test Systems and Insights for Transcatheter Mitral Valve Design, Part II: Radial Expansion Forces

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Abstract

Transcatheter mitral valve (TMV) replacement technology has great clinical potential for surgically inoperable patients suffering from mitral regurgitation. An important goal for robust TMV design is maximizing the likelihood of achieving a geometry post-implant that facilitates optimal performance. To support this goal, improved understanding of the annular forces that oppose TMV radial expansion is necessary. In Part II of this study, novel circular and D-shaped Radial Expansion Force Transducers (C-REFT and D-REFT) were developed and employed in porcine hearts ($N=12$), to detect the forces required to radially expand the mitral annulus to discrete oversizing levels. Forces on both the septal-lateral and inter-commissural axes (F_{SL} and F_{IC}) scaled with device size. The D-REFT experienced lower F_{SL} than the C-REFT (19.8 ± 7.4 vs. 17.4 ± 10.8 N, $p=0.002$) and greater F_{IC} (31.5 ± 14.0 vs. 36.9 ± 16.2 N; $p=0.002$), and was more sensitive to degree of oversizing. Across all tests, F_{IC}/F_{SL} was 2.21 ± 1.33 , likely reflecting low resistance to radial expansion at the aorto-mitral curtain. In conclusion, the annular forces opposing TMV radial expansion are non-uniform, and depend on final TMV shape and size. Based on this two-part study, we propose that radial force applied at the *commissural* aspect of the annulus has the most potent effect on paravalvular sealing.

Keywords

Transcatheter mitral valve replacement; transcatheter mitral valve implantation; transcatheter; mitral valve; in vitro; forces; sensor; transducer; device-tissue interaction; medical device

Introduction

A wave of transcatheter mitral valve replacement (TMVR) devices are currently in development, aiming to address the nearly 50% of severe, symptomatic mitral regurgitation patients denied for surgery due to increased operative risk.⁸ To date, at least 10 transcatheter mitral valves (TMVs) have reached clinical trials, and at least 20 others are in preclinical testing.¹ While no TMV has yet achieved regulatory approval, the wide diversity of devices currently under development reflects a lack of consensus regarding optimal design

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approaches. In pursuit of such consensus, increased engineering research and benchtop testing capabilities are necessary to characterize fundamental relationships between TMV design and performance.

In Part I of this two-part study, a test system was developed for the quantification of paravalvular leakage (PVL) following deployment of a TMV or TMV-like device in pressurized, explanted hearts.¹⁰ The system was successfully implemented to detect key differences in PVL rates according to trans-mitral pressure gradient, TMV shape (circular vs. D-shape), and TMV-annular oversizing, using a series of “mock TMV plug” devices. These findings may support the development and/or usage of next-generation TMV designs. However, while avoidance of PVL is one critical objective for safe and effective TMVR, many other related objectives exist simultaneously. Modifying TMV stent shape and size post-implant may affect TMV function, as well as the likelihood of left ventricular outflow tract obstruction, conduction defects, and/or elevated leaflet stresses.² Some of these are now becoming focal areas of new research.¹⁵ Long term, to reconcile these potentially competing objectives, any TMV designer will need to identify an optimal operating range for the device, in terms of the final stent profile post-implant.

Our current knowledge of the mitral annulus’ material properties is inadequate to predict how it will respond to a TMV being deployed with a given radial expansion force. One approach to this end may include the rigorous characterization of the annulus’ intrinsic material properties.⁴ Another more direct approach is the empiric determination of the annular resistive forces that the expanding TMV must overcome to establish a target shape/size post-deployment. In Part II of this study, a novel force transducer system was developed and employed in porcine hearts. This system detected the forces necessary to radially expand the mitral annulus to the same shapes and oversizing levels investigated in Part I.

Materials and Methods

Test Specimens

All testing was conducted on fresh porcine hearts (N=12) in a state of rigor mortis, which were sourced and selected as described in Part I.¹⁰ These hearts provided a model of the systolic state; contracture during rigor mortis has been reported to generate 60-100% of the tension as in normal systolic contracture.^{5, 14} As in Part I, only annuli having inter-trigonal distance 30mm, and perimeter as close as possible to 108.4mm, were selected. To prepare each heart for testing, all great vessels were removed, with the exception of the aorta, which was transected proximal to the brachiocephalic artery. Both atria were removed, taking care to leave approximately 15mm tissue intact superior to the mitral annulus. In preparation for device installation, a planar cut through the left ventricle (LV) was made, inferior to the papillary muscles and parallel to the annulus mid-plane.

Radial Expansion Force Transducers – Concept, Fabrication, and Operation

TMV radial expansion forces were measured using a pair of custom measurement systems termed the Radial Expansion Force Transducers (REFTs; Figure 1). The REFTs were designed using SolidWorks (Dassault Systemes, Waltham, MA). Their fundamental concept

was for a set of four arms, housed within a central hub, to be positioned within the mitral annulus of an explanted porcine heart, then driven radially outward by a central piston. The radial inward force with which the tissue opposed this expansion was measured along the septal-lateral (SL) and inter-commissural (IC) axes via strain gage circuitry on each arm. Two variants were the circular REFT (C-REFT) and D-shaped REFT (D-REFT).

The piston was comprised of a steel rod bonded to a plastic wedge. A single operator depressed the piston toward the LV apex, sliding the wedge between the arms and driving them radially outward. An aluminum threaded rod was bonded to the hub. As further explained below, the threaded rod and tapered region of the hub were passed through the mitral annulus, and a base plate was screwed onto the threaded rod until flush with the LV's cut surface. A pin could be passed through the cap (which was fixed to the hub) and any of four holes in the rod to set the C-REFT or D-REFT to any of four sizes. Shapes and sizes matched those of the mock TMV plugs used in Part I.¹⁰ Sizes were +0 (retracted), +2, +4, and +6; this referred to millimeters of oversizing relative to the native annulus, in terms of inter-trigonal distance. Although the degree of TMVR oversizing in eventual clinical practice remains unknown, we note that the +6 device constituted 21.4% oversizing by perimeter, while the largest Sapien 3 TAVR device (29mm; Edwards Lifesciences, Irvine, CA) is recommended to oversize a native annulus by no more than 10.7%, per the device Instructions For Use.

The annulus-contacting pad of each arm was 20mm in height and 23.7mm in length. Each successive step in oversizing using the C-REFT led to a 2.5mm increase along either axis. Each successive step in oversizing using the D-REFT led to a 2.0mm increase along the SL axis and a 2.7mm increase along the IC axis.

Plastic components were 3D printed from FormLabs Clear Resin at 25 μ m resolution (FormLabs, Somerville, MA). Metal components were machined in-house. Four strain gages were bonded to each arm in a full Wheatstone Bridge circuit (two each on the top and bottom faces). These were configured to detect only in-line strain (i.e., bending strain was mathematically eliminated). All strain gage materials and installation protocols were from Micro-Measurements (Wendell, NC). All data was recorded using hardware (cDAQ-9174 and accessories) and software (LabVIEW) from National Instruments (Austin, TX).

Note, while all four arms were identical for the C-REFT, the asymmetry in the D-REFT profile led it to possess four unique arms. Also, because the 23.7mm pad perimeter was held constant for all arms, the 3 and 9 o'clock arm shafts of the D-REFT were each rotated 13° posteriorly from the IC axis. The 13° rotation implied a 2.6% differential between measured forces at 3 or 9 o'clock and their components in the IC direction. This is an acknowledged design limitation, which is considered negligible in light of the small differential, and the likely similar resistive force facing the chosen arm design and a theoretical, alternate design in which the 3 and 9 o'clock arms were aligned on the true IC axis.

Radial Expansion Force Transducers - Calibration

Transducers were calibrated before and after use (with the average calibration factors used for data processing). To calibrate each REFT, a dedicated apparatus was constructed in-

house (Figure 2). Each apparatus had the ability to impose SL and IC forces, either independently or in tandem, on the expanded REFT arms. Mechanical loading was accomplished through a screw-piston-precision spring-pusher assembly (Figure 2C), whereby each full turn of the #6-40 screw applied a known compressive force along that REFT arm's major axis. All spring constants were measured before use with a validated load cell (coefficient of variation among all springs: 1.0%).

With the C-REFT or D-REFT expanded, both arms along a given axis were calibrated simultaneously, by applying increasing loads ranging from 0-62.2N. This process was repeated four times per axis. Calibration was performed with the entire setup submerged in a water tank, which was maintained at $37\pm 2^{\circ}\text{C}$.

Experimental Protocol

Either the C-REFT or D-REFT was passed through the mitral valve orifice and out the LV cut plane (each REFT was used in 6 hearts). The acrylic base plate was screwed onto the hub and tightened until the LV was supported at optimal REFT positioning (Figure 3A). Optimal REFT positioning was defined as having the mid-plane of the arms coincident with that of the annulus, and with the 12 o'clock arm centered between the left and right trigones.

The heart and chosen REFT were submerged in a water bath maintained at $37\pm 2^{\circ}\text{C}$ throughout all testing (Figure 3B–C). Tubing was installed in the aorta, connecting it to a steady flow pump also submerged within the bath (12U596, Dayton Electric Manufacturing, Co., Lake Forest, IL). A bypass, a pair of ball valves, and a pressure probe (6199, Utah Medical Products, Midvale, UT) were included; this simple flow loop enabled maintenance of aortic pressure at 120mmHg throughout all testing. This feature was included because, *in vivo*, TMVs must expand against the pressurized aortic root along the anterior annulus.

Several aspects of this setup were unique as compared to Part I.¹⁰ The LV was cut open, meaning there was no LV pressure and no trans-mitral flow. In the case of a TMV product, any LV pressure contacting the outer stent would act equally on its inner and outer surfaces, and so would likely not contribute to the radial forces under investigation here. With this in mind, the LV apex was removed to facilitate REFT positioning. Meanwhile, we considered aortic pressure a potentially important factor for TMV radial forces, because it could directly oppose device expansion into the anterior mitral annulus. Unlike in Part I, the steady flow pump used in Part II was *only* incorporated as a convenient means to pressurize the aorta. The flow into the aorta was relatively low; because the aortic valve was competent, this flow passed into the coronary circulation and out the many vessels that had been exposed along the heart's cut surfaces.

Each acquisition began with the chosen REFT set to the +0 size. After a five second recording, the pin was removed and the piston depressed to establish either the +2, +4, or +6 size. The pin was inserted and held in place for five seconds. The pin was removed and the piston retracted to re-establish the +0 size. The pin was inserted and held in place for five seconds. 24 acquisitions were collected per heart: eight with expansion to +2, followed by eight with expansion to +4, followed by eight with expansion to +6.

Data Processing and Statistical Analysis

Recorded data were processed and statistically analyzed using MATLAB (MathWorks, Natick MA). Any acquisitions in which aortic pressure unintentionally deviated by more than 10 mmHg were noted during data processing and discarded (8.3% of total). Force signals on each arm were computed as the differential between the expanded force (averaged over a 1.5 second window) and the *average* of the retracted forces from before and after expansion (each averaged over a 1.5 second window). Then, SL force (F_{SL}) was obtained by averaging the force signals at 12 and 6 o'clock; inter-commissural force (F_{IC}) was obtained by averaging the force signals at 3 and 9 o'clock. Note, F_{SL} and F_{IC} represent the forces necessary to expand *from +0 to any given oversizing level*. Effects on either F_{SL} or F_{IC} due to expansion shape and/or size were assessed via two-way ANOVA followed by Tukey's Honestly Significant Difference test. The ANOVA was run first without interaction terms to assess main effects, then accounting for shape-size interactions.

Micro-Computed Tomography

Following all C-REFT and D-REFT experiments, one additional porcine heart was subjected to micro-computed tomography (μ CT) to generate a clear depiction of the anatomical features that may underlie the observed force dynamics. Both atria were removed, and a ring of small sand markers was glued to the annular hinge line to delineate it clearly post-segmentation (these markers and their usage have been previously described⁹). Imaging used a Siemens Inveon scanner and Inveon Acquisition Workplace software (Siemens Medical Solutions USA, Inc., Malvern, PA), with settings optimized for soft tissue visualization (80kV, 500mA, 550ms integration time). Volumes were composed of 43.29 μ m isotropic voxels. Following data acquisition, images were analyzed using Inveon Research Workplace.

Results

REFT Performance

The C-REFT and D-REFT systems were qualified according to the following attributes:

Linearity of signal response—In each of the 8 REFT arms, the voltage response to applied force was linear throughout the full force range applied during calibration (R^2 : 0.976-0.999).

Validation of REFT force measurements—Following calibration, 16 loads from across the calibration range were re-applied to the four REFT arms. Mean relative error between true and measured forces was 4.3%.

Sensitivity—Force increments as small as 0.1N could be clearly detected.

Drift—Each data acquisition was performed over approximately 30 seconds. Signals drift over this duration was 0.05-0.1N. To remove the influence of drift, the baseline force signal was taken as the average signal before and after REFT expansion (as described above).

Cross-talk between measurement arms—The REFTs featured orthogonal or near-orthogonal arm orientations, plus a central hub that dampened force transfer between arms. Both of these attributes were intended to minimize “cross-talk” between septal-lateral (SL) and inter-commissural (IC) signals. Nevertheless, it was observed that at peak loading (62.1N), mean relative error between the true force applied on one axis and the force measured on the perpendicular axis was 1.1%.

Uncertainty estimation—The above noted 4.3% and 1.1% mean relative errors between true and measured forces propagate to a theoretical worst-case uncertainty of 5.4%.

Test Specimens

Testing of each heart commenced 5-11 hours post-mortem. Annular dimensions from the selected hearts are given in **Error! Reference source not found.**. Note, no differences were detected between the pre-procedural dimensions of these hearts and those tested in Part I,¹⁰ nor between the hearts assigned to receive either REFT. The experimental protocol caused the mitral annulus to stretch plastically. On average, experimentation caused 12.9% increase in valve perimeter, 28.7% increase in valve area, 15.9% increase in SL diameter (D_{SL}), and 14.0% increase in IC diameter (D_{IC}).

Radial Expansion Forces

The F- and p-values from the ANOVA are given in Table 2. Based on the representative data given in Figure 4, forces exhibited negligible drift during both the retracted (true-sized to the annulus) and expanded (over-sized) states. These data reflect the forces *preliminarily* measured on each arm. Hereafter, all forces are analyzed as F_{SL} (averaged from measurements at 12 and 6 o'clock) and F_{IC} (averaged from measurements at 3 and 9 o'clock).

The global mean $\pm$ SD for F_{SL} was 18.6 $\pm$ 9.4N. F_{SL} data are given in Figure 5. Averaged across all sizes, 13.9% more F_{SL} was required to expand the C-REFT versus the D-REFT (19.8 $\pm$ 7.4 vs. 17.4 $\pm$ 10.8N, respectively; $p=0.002$). Averaged across shapes, increasing oversizing from +2 to +4, or from +4 to +6, required a 51.3% or 22.1% increase in F_{SL} , respectively (+2 vs. +4 vs. +6: 12.7 $\pm$ 6.0 vs. 19.3 $\pm$ 7.8 vs. 23.5 $\pm$ 10.4N, respectively; each pair $p<0.001$). The effects of sizing on F_{SL} were driven mostly by the D-REFT: whereas the C-REFT required 44.7% more F_{SL} to expand to +6 versus +2, the D-REFT required 166.6% more F_{SL} to do the same. Whereas every pair of sizes within the D-REFT differed significantly in required F_{SL} (each $p<0.001$), no significant difference was detected between C+4 and C+6 (21.4 $\pm$ 6.6 vs. 22.8 $\pm$ 8.7N, respectively; $p=0.964$). Also of note, significantly more F_{SL} was required to establish the C+2 geometry than D+2 (15.8 $\pm$ 4.7 vs. 9.0 $\pm$ 5.4N, $p=0.002$).

The global mean $\pm$ SD for F_{IC} was 34.3 $\pm$ 14.0N. F_{IC} data are given in Figure 6. Averaged across all sizes, 14.6% less F_{IC} was required to expand the C-REFT versus the D-REFT (31.5 $\pm$ 14.0 vs. 36.9 $\pm$ 16.2N, respectively; $p=0.002$). Increasing oversizing from +2 to +4, or from +4 to +6, required a 51.8% or 31.3% increase in F_{IC} , respectively (+2 vs. +4 vs. +6: 22.7 $\pm$ 8.0 vs. 34.5 $\pm$ 10.6 vs. 45.2 $\pm$ 12.7N, respectively; each pair $p<0.001$). Similarly to F_{SL} ,

the effects of sizing on F_{IC} were driven mostly by the D-REFT: whereas the C-REFT required 56.8% more F_{IC} to expand to +6 versus +2, the D-REFT required 140.6% more F_{IC} to do the same. Whereas every pair of sizes within the D-REFT differed significantly in required F_{IC} (each $p < 0.001$), no significant difference was detected between C+4 and C+6 (35.2 ± 10.5 vs. 36.9 ± 6.2 N, respectively; $p = 0.969$). Also of note, significantly less F_{IC} was required to establish the C+6 geometry than D+6 (36.9 ± 6.2 vs. 52.2 ± 12.6 N, $p < 0.001$).

Although most trends within F_{IC} paralleled those of F_{SL} , F_{IC} consistently exceeded F_{SL} . The global mean $\pm$ SD for F_{IC}/F_{SL} was 2.21 ± 1.33 ($p < 0.001$ vs. hypothetical mean of 1, by one-sample t-test). μ CT imaging of a porcine heart (Figure 7) revealed that the amount of tissue opposing a radially expanding TMVR varied circumferentially, providing a likely explanation for this eccentricity. Along the annulus mid-plane, the wall thicknesses at 3, 6, or 9 o'clock (13.5 mm or more) were each at least five-fold greater than that at 12 o'clock (2.7 mm). Finally, we note that F_{IC}/F_{SL} was 35.3% lower using the C-REFT versus the D-REFT (1.73 ± 0.74 vs. 2.67 ± 1.59 , respectively; $p < 0.001$ by two-sample t-test).

Discussion

For any given TMV design, there exists some range of operating conditions that favor optimal performance. Two such considerations are its final shape and degree of oversizing (relative to the native annulus). Thus, a TMV stent's design can be meaningfully informed by first understanding the annular resistive forces it must overcome to achieve a target shape/size post-deployment. The circular and D-shaped Radial Expansion Force Transducers (C-REFT and D-REFT) were developed to quantify the resistive forces imparted by the porcine mitral annulus as their arms extended radially along pre-set paths.

Each device was designed, manufactured, and calibrated successfully. Forces were quantified simultaneously along the SL and IC axes, over a range of oversizing levels, for either circular or D-shaped TMV profiles. REFTs were employed in rigorously hearts, to mimic the geometry and material properties of the systolic, contracted state,^{5, 14} and thus to model the *peak* annular forces a TMV will encounter in the beating heart in a simple and cost-effective manner.

To our knowledge, this is the first study to measure the radial forces necessary to expand a TMV or TMV-like device into the mitral annulus. The closest parallel comes from Siefert et al,¹³ who investigated *in vivo* the septal-lateral and inter-commissural forces associated with cardiac contraction. A rigid transducer was surgically affixed to the mitral annulus, in normal ovine subjects (implanted in the flaccid, cardioplegic heart). For the sake of comparison, it may be approximately considered to have oversized the systolic annulus to diastolic dimensions. Siefert et al reported a peak cyclic contractile force of 9.2 N (septal-lateral). Using the REFTs, the mean recorded expansion force across all samples was 24.4 N, and the highest mean within any one configuration was 52.2 N (F_{IC} , using D+6). The higher forces observed here, versus in the study from Siefert et al, likely derived from displacing a taller section of annular tissue (20 mm vs. <3 mm pad height), having greater wall thickness (porcine vs. ovine), by a greater distance (47% area increase from the +0 to +6 profile, versus an approximate 12% change in area from diastole to systole during normal cardiac

function¹²). The presently studied radial expansion forces may also differ in the clinical setting. Relevant considerations may include, but would not be limited to: degree of annular dilation, degree of systolic dysfunction, degree of cardiac hypertrophy, degree of annular calcification, and patient age.

The finding that both F_{SL} and F_{IC} scaled positively with degree of oversizing agrees with intuition. Similarly, the finding that the C-REFT required greater mean F_{SL} and less F_{IC} than the D-REFT, was expected. This is because, whereas with each oversizing step the circular profile expanded 2.46 mm along either axis, the D-shaped profile expanded 2.05 mm in the septal-lateral direction and 2.68 mm in the inter-commissural direction.

Other findings were not expected. Across all shapes and sizes, the force eccentricity, F_{IC}/F_{SL} , was 2.21 ± 1.33 . This differs from other aspects of mitral valve annular mechanics. For example, Siefert et al's *in vivo* transducer detected lower contractile forces on IC axis.¹³ Gunning et al reported the anterior quadrant of the annulus (which sits along the SL axis) to possess the greatest circumferential stiffness.⁴ We previously reported that the anterior annulus exerts the greatest forces on annuloplasty ring sutures *in vivo*, and also possesses the greatest suture holding strength.¹¹ The present findings likely owe to the unique geometry under investigation. Siefert et al investigated phenomena within a few millimeters in height from the leaflet hinge line. The REFTs, meanwhile, applied force against a 20 mm tall ring of tissue, centered along the leaflet hinge line, and radially displaced the full thickness of the tissue emanating outward from its contact surface.

In the annular plane of a representative porcine heart, the tissue's radial thickness was at least five-fold greater at 3, 6, or 9 o'clock than at 12 o'clock (Figure 7). Additionally, sub-annularly, only the anterior leaflet is present at 12 o'clock. We therefore conclude that the REFTs' SL arms encountered far less resistance to expansion than did their IC arms. Any TMV stent having a sub-annular portion may encounter similar dynamics (less resistance to expansion along its septal-lateral axis). This includes many of the leading TMVs currently in clinical trials, such as Intrepid (Medtronic, Dublin, Ireland), Tendyne (Abbott Laboratories, Chicago, IL) and Tiara (Neovasc, Richmond, Canada), as well as various earlier-stage stent concepts.^{7,16} Effective stent design to achieve targeted levels of annular oversizing likely must account for the observed dynamics of this broader tissue region.

The ratio, F_{IC}/F_{SL} , was significantly further from 1.0 with use of the D-REFT. The opposite was anticipated, due to the D-shape conforming more closely to the native annular profile. This finding resulted from two of the aforementioned phenomena. As expected, the D-shape elevated F_{IC} and reduced F_{SL} relative to the circular shape. However, whereas this was expected to bring F_{IC} and F_{SL} closer together in magnitude, because F_{IC} unexpectedly exceeded F_{SL} with the circular shape, it instead drove them further apart. In other words, at each level of oversizing, the D-shaped device expanded more along the seemingly less compliant IC axis than the circular device (2.7 vs 2.5 mm, respectively), and less along the seemingly more compliant SL axis (2.0 vs. 2.5 mm).

Part I of this study demonstrated that the D-shaped TMV profile improved paravalvular sealing compared to the circular profile.¹⁰ However, the mechanism behind this observation

remained unclear. Was this because the D-shaped device applied force more uniformly along the annular circumference? Or, is it possible that TMV sealing derives not only from contact with the annulus but also with the *leaflets*, and thus the D-shape gains advantage by merely applying more *targeted* radial force at the commissural aspects of the annulus, where very little leaflet tissue exists? Part II of this study detected that radial expansion forces were significantly *less* uniform with the D-shaped profile than the circular profile. Further, it is notable that, whereas radial forces were much more greatly influenced by size than shape, PVL depended slightly more on shape.

These facts suggest that, for TMVs whose sealing is generated by contact between the native tissue and a straight tubular section, radial force is not the primary determinant of sealing. In turn, the D-shape's sealing must indeed derive from its ability to better reach the commissural aspects of the annulus. The notion that leaflet tissue plays a major role in TMV sealing supports the use of fabric covering the entire region of potential stent-leaflet contact. This is the case in most reported TMV designs,¹ but *not* in Edwards Lifesciences' Sapien, whose off-label use at the mitral position is of growing interest.³ The notion that expanding with more circumferentially uniform force against the annulus is less effective to improve sealing than merely expanding in the optimal positions (i.e., the commissures) is profound and potentially impactful. This may implicate stent flexibility as a critical variable to this end, as a more flexible stent can more fully conform to the annulus to engage its commissural regions. Although specific stiffness data for leading TMV stent designs is not publicly available, some designs, such as Medtronic's Intrepid, have emphasized optimized stiffness to improve anchoring and sealing.⁶

The following limitations of this study are noteworthy. The implications of the plastic stretch of the mitral annulus as a result of the experimental procedure (Table 1), the use of water rather than saline, and the use of normal porcine hearts are discussed in Part I of this study.¹⁰ Specific to Part II, we also note that the REFTs' four annulus-contacting pads were shaped to match the +0 profile, with 3.4 mm gaps between pads. Inevitably, when oversizing, these gaps grew larger, and the path described by the contact pads deviated from a true circle or a true D-shape at larger sizes. This deviation was likely negligible in terms of its impact on radial expansion force at each position.

Finally, we note that aortic pressure was held to approximately 120 mmHg in this study. Aortic pressure was likely a small contributor to the measured forces. Assuming the 12 o'clock annulus-contacting pad was 50% in contact with the aorto-mitral curtain (with the other 50% residing in the ventricle), the 120 mmHg aortic pressure would have acted over a 240 mm² area of the pad, and would therefore only impart a theoretical 3.6 N to F_{SL}. Meanwhile, mean F_{SL} was 18.6 N. Nevertheless, the effects of hypotensive or hypertensive aortic pressures may be worthy of future investigation.

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List of Abbreviations

C	Circular
D	D-shaped
IC	inter-commissural
LV	left ventricle
μCT	micro-computed tomography
MV	mitral valve
PVL	paravalvular leakage
REFT	Radial Expansion Force Transducer
SL	septal-lateral
TMV	transcatheter mitral valve
TMVR	transcatheter mitral valve replacement

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Figure 1.

Circular and D-shaped Radial Expansion Force Transducer (C-REFT and D-REFT) design. (A-H) C-REFT and D-REFT renderings. Wedge shown in orange. (A, B) Fully expanded, oblique view. (C, D) Fully expanded, section view. (E, F) Arms only, fully retracted. Blue circle: fully expanded profile. (G) Close-up of a single arm, highlighting strain gage locations and key dimensions. (H,I) C-REFT and D-REFT as manufactured, top view, cap and piston removed. (J, K) C-REFT as manufactured, fully retracted and fully expanded.

Figure 2.

Calibration system for REFTs. (A, B) Renderings of C-REFT and D-REFT calibration systems, (a) Septal-lateral loading mechanisms; (b) inter-commissural loading mechanisms; (c) base plate. (C) Close-up rendering of loading mechanism, (d) Screw; (e) piston; (f) precision spring; (g) pusher that contacts the REFT arm; (h) housing; (i) REFT arm. (D) D-REFT calibration system as manufactured, (j) screws securing REFT to base plate. (E) Representative calibration curve for one arm. Strains were computed by the LabVIEW software and are directly proportional to the strain gage circuit's voltage response.

Figure 3. REFT experimental setup. (A) After placing either the C-REFT or D-REFT in the heart, the base plate was screwed onto the REFT, supporting the heart at optimal REFT positioning. (B) Schematic of full setup for either REFT, including flow system to pressurize aorta. R1, R2: ball valves; P: probe. (C) D-REFT in fully-prepared heart.

Figure 4.

Representative raw data from a single REFT acquisition. (a) Force signals were zeroed at +0 size; (b) piston was depressed until pin can be inserted to set target expansion; (c) expansion was maintained for five seconds; (d) +0 size was re-established; (e) +0 size was maintained for five seconds.

Figure 5.

F_{SL} ANOVA results (means and 95% confidence intervals). From left to right, graphs show: forces for each REFT shape, averaged across sizes; forces for each REFT size, averaged across shapes; forces for each unique shape/size combination. Within each plot, pairs whose 95% confidence intervals do not overlap differ significantly ($p < 0.05$).

Figure 6.

F_{IC} ANOVA results (means and 95% confidence intervals). From left to right, graphs show: forces for each REFT shape, averaged across sizes; forces for each REFT size, averaged across shapes; forces for each unique shape/size combination. Within each plot, pairs whose 95% confidence intervals do not overlap differ significantly ($p < 0.05$).

Figure 7. Investigation of tissue thickness in the vicinity of the porcine mitral annulus. Left: photograph of heart. Others: multi-planar reconstruction of heart, obtained by μ CT. Blue border: mitral annular plane. Green border: septal-lateral plane. Red border: inter-commissural plane. LVOT: left ventricular outflow tract.

Table 1

Geometric descriptors for the 12 tested hearts (all p-values by t-test).

Pre-procedure			
	C-REFT	D-REFT	p (C vs. D)
Inter-trigonal distance (mm)	30.0 ± 0	30.0 ± 0	-
Perimeter (mm)	109.1 ± 4.0	108.7 ± 5.4	0.879
Area (cm ²)	8.5 ± 0.5	8.2 ± 0.9	0.513
D _{SL} (mm)	26.2 ± 2.4	25.1 ± 3.1	0.507
D _{IC} (mm)	35.1 ± 4.1	34.4 ± 4.3	0.784
D _{IC} /D _{SL}	1.35 ± 0.24	1.40 ± 0.30	0.783
Post-procedure			
	C-REFT	D-REFT	p (C vs. D)
Inter-trigonal distance (mm)	30.0 ± 0	30.0 ± 0	-
Perimeter (mm)	121.8 ± 4.2	124.1 ± 9.0	0.575
Area (cm ²)	10.6 ± 0.8	10.9 ± 1.7	0.647
D _{SL} (mm)	29.2 ± 1.8	30.0 ± 4.4	0.693
D _{IC} (mm)	38.9 ± 3.7	40.3 ± 3.6	0.538
D _{IC} /D _{SL}	1.34 ± 0.14	1.37 ± 0.25	0.800

Table 2

Omnibus results of ANOVA model.

		Factor	F	p
		Shape	9.55	0.002
		Size	39.75	<0.001
	Main effects			
F_{SL}	Interactions	Shape:Size	5.45	0.0048
		Shape	9.72	0.002
		Size	95.67	<0.001
	Main effects			
F_{IC}	Interactions	Shape:Size	21.95	<0.001