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Suture Dehiscence and Collagen Content in the Human Mitral and Tricuspid Annuli

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Abstract

Post-operative suture dehiscence is an important mode of short-term mitral and tricuspid valve (MV, TV) repair failure. We sought to evaluate suture pullout forces and collagen density in human atrioventricular valves for a better understanding of the comparative physiology between the valves and the underlying mechanobiological basis for suture retention. Mitral and tricuspid annuli were each excised from hearts from human donors age 60–79 with no history of heart disease (n=6). Anchor sutures were vertically pulled until tearing through the tissue. Suture pullout force (F_p) was measured as the maximum force at dehiscence. Subsequently, tissue samples from each tested suture position were evaluated for collagen content using a standard hydroxyproline assay. Among all mitral positions, no significant differences were detected among positions or regions with mean F_p values falling between 6.9 ± 2.6 N (posterior region) and 10.3 ± 4.7 N (anterior region). Among all tricuspid positions, the maximum and minimum F_p were 24.0 ± 9.2 N (trigonal region), and 4.5 ± 2.6 N (anterior region). Although for the MV, a given sample's collagen content had no correlation to its corresponding F_p , the same relationship was significant for the TV. Further, the TV exhibited comparable F_p to the MV overall, despite a nearly 40% reduction in collagen content. These findings suggest that sutures placed in the trigonal region of the TV have higher pullout force than those placed along other segments of the annuli. Furthermore, there are likely differences in collagen orientation between the mitral and tricuspid annuli, such that collagen content strongly impacts F_p in one, but not the other.

Keywords

suture dehiscence; collagen; mitral annulus; tricuspid annulus; functional mitral regurgitation; functional tricuspid regurgitation

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Conflict of Interest

The authors declare that they have no conflict of interest.

Introduction

The four heart valves, which separate the chambers of the heart and ensure the unidirectional flow of blood, fall into two categories: the atrioventricular (mitral and tricuspid valves, MV and TV, respectively) and semilunar valves (aortic and pulmonary). Regurgitation of the atrioventricular valves occurs from the inability of valve leaflets to properly coapt and results in a backflow of blood from ventricle to atrium. In the United States, mitral and tricuspid regurgitation (MR and TR) are highly prevalent, with 19% and 14.8–18.4% of the population suffering from at least mild forms of MR and TR respectively¹. Functional mitral and tricuspid regurgitation (FMR and FTR) are the most common forms of regurgitation of atrioventricular valves which occur due to dilation of the left and right ventricles respectively. Left uncorrected, these diseases result in decompensated heart failure, reduced cardiac output, and significant comorbidities and mortality.

The gold-standard surgical approach for repair of FMR and FTR is implantation of an undersized annuloplasty ring^{2,3}. In this technique, the ring is sutured to the valve annulus to enforce a reduced annular profile, thus correcting the enlarged orifice area that most commonly leads to MR and TR and reducing regurgitant volume. In the case of functional MR and TR, undersized rings are commonly utilized to correct the dilated annular profile^{4–6}. Suture dehiscence remains a primary mode of short-term device failure and re-operation^{7,8}; 13–42% of MV re-operations are directly attributable to suture dehiscence^{9–11}. Dehiscence has also been reported to occur in up to 10% of surgical TR patients, depending on ring type¹². Understanding the mechanical and structural environment of the mitral and tricuspid annuli is therefore invaluable for the implementation of devices and guidelines aimed at reducing the risk and incidence of ring dehiscence.

Prior studies have demonstrated, using ovine mitral and tricuspid valves, that the force required to pull out sutures from the annulus varies significantly with circumferential position around the annulus^{13,14}. These studies further demonstrated correlations between the suture force dynamics at a given annular position and that position's relative collagen density (as measured by colorimetric analysis of multi-photon excitation fluoroscopic images).

Expansion of these studies into human patients is beneficial for a better understanding of dehiscence risk because 1.) there are significant differences in mechanical and structural properties between animal and human dehiscence models^{15–18}, and 2.) aged human tissue microstructure plays a role in tissue strength. Additionally, as MR-repair devices expand to TR applications¹⁹, a comparative understanding of mitral and tricuspid annular mechanics is necessary in order to effectively adapt these devices. The study presented herein therefore provides a quantitative and comparative evaluation of the mechanical and structural environment of both the mitral and tricuspid annuli from the same human patients in order to better understand the factors governing the risk of device dehiscence in humans. Insights from this study could also inform next-generation repair device design.

Methods

Valve Selection and Preparation

Hearts from human donors with no history of heart disease (n=6) were acquired from Science Care, Inc. (Phoenix, AZ). Immediately upon receipt, mitral and tricuspid annular tissue were excised. Approximately 15 mm of annular tissue superior to the leaflet hinge line was retained, and the leaflets remained attached. Each specimen was cryopreserved using a 90% RPMI-1640 and 10% DMSO solution at -80°C ^{20,21}. Specimens were thawed through incremental dilution of DMSO with 0.9% saline solution over the course of 40 minutes.

Suture Pullout Force Testing

Immediately after thawing, each annulus was mounted to a test plate using inner and outer running suture rings with Ford interlocking stitch. The endocardial surface faced up (Fig 1B–C). 10 or 12 sutures (Y-31 2–0 TiCron, Medtronic, Dublin, Ireland) were placed around the mitral or tricuspid annulus, respectively, at positions depicted in Fig 1A. For mitral valves, ten suture positions were numbered thus: LT and RT (left and right trigones), 11 and 1 (anterior annulus), and 3–5, 7–9 (posterior annulus). For tricuspid valves, suture positions were numbered with respect to the anterior-posterior commissure in a clockwise fashion with one suture placed at each commissure and three placed along the annular segment corresponding to a leaflet. Sutures were placed 1 to 2 mm above the leaflet hinge, with bite width of 10 mm, per published recommendations for annuloplasty suture placement²².

Mounted specimens were submerged in a 0.9% saline solution at 37°C . Suture pullout tests were conducted with a TestResources 100Q Universal Testing Machine (Shakopee, MN). The axial force was measured using a 500 lbf load cell (TestResources SM-500–294) and recorded through a custom LabVIEW code. For each test, the suture was tied to the upper arm and vertically pulled (normal to the annulus) at 1 mm/s until tearing through the tissue. As previously described^{13,14}, the force direction (perpendicular to the test plate) corresponded to the direction of force on annuloplasty sutures *in vivo* in undersized ring annuloplasty (radially inward).

Collagen quantification testing

After all sutures from a valve were pulled out, tissue samples from each suture position were carefully excised. The excised section was a rectangular prism whose boundaries were approximately 1 mm beyond the suture path in all directions. Each sample was homogenized by grinding with exposure to liquid nitrogen.

To account for the influence of moisture content on the results of the hydroxyproline assay, both wet and dry sample weights were obtained. Dry weights of each homogenized sample were measured after desiccating the tissues for 18 hours at 37°C under vacuum pressure. Each sample was hydrolyzed at 120°C for 3 hours, using 200 μl 6 M HCl per 10 mg of the sample's initial wet weight. The hydrolysate was tested for mass of hydroxyproline per unit volume, via a commercial assay (MAK008, Sigma-Aldrich, St. Louis, MO). Hydroxyproline is a major component of collagen and is a standard indicator for collagen content. Using a series of 96-well plates, the assay was performed for each sample in duplicate, according to

the supplier's protocol. Absorbance readings for each sample, in addition to three sets of hydroxyproline standards per plate, were obtained at 560 nm.

Data Analysis

Suture pullout force (F_p) was defined as maximum recorded force during pullout (maximum force on the force-displacement curve). Absorbance readings from the hydroxyproline assay were converted to hydroxyproline mass fraction for wet and dry tissue (HYP_{wet} and HYP_{dry}). A standard curve ($R^2 > 0.98$) was computed and used to obtain HYP per well from absorbance readings. For analysis, the annular regions for the mitral valve were defined as: trigonal (LT, RT), anterior (11 and 1 o'clock), and posterior (3–9 o'clock). For the tricuspid valve, the annular regions were defined as: trigonal (7 and septal-anterior commissure, SAC), anterior (9–11 o'clock), and postero-septal (APC-6 o'clock; Fig 1A). All results are reported as mean $\pm$ standard deviation. All statistical analyses were performed with Minitab 17 (Minitab Inc., State College, PA). Nested one-way analyses of variance (ANOVA) were used to test for differences in both F_p and HYP according to suture position and/or region. Separate ANOVA models were used for MV and TV. Normality of the residuals of the ANOVA models was confirmed using the Shapiro Wilk test. Pearson's correlations were obtained to investigate the relationship between pullout forces and hydroxyproline content for both valve types. Although the ANOVA models exhibited normally distributed residuals, the F_p or HYP results themselves were not normally distributed. Therefore, F_p or HYP results were compared between valves via Mann-Whitney U-test. Further comparisons between valves were carried out after excluding the TV trigonal region. This is of interest because the atrioventricular node sits very close to this region, and surgeons often avoid placing sutures in this region to minimize risk of introducing cardiac rhythm defects. For all hypothesis testing, significance was concluded at $p < 0.05$.

Results

Key donor descriptors are shown in Table 1. 50% of donors were male.

Representative raw load displacement curves for each suture position in the MV and TV are shown in supplementary figure 1. Among all MV samples, pullout force was 7.8 ± 2.9 N and hydroxyproline mass fraction was 8.2 ± 2.5 mg/g wet weight or 35.6 ± 18.8 mg/g dry weight. Among all TV samples, pullout force was 8.2 ± 6.1 N, and hydroxyproline mass fraction was 5.0 ± 2.7 mg/g wet weight or 19.9 ± 11.9 mg/g dry weight.

MV Pullout Forces

Among all MV positions, the maximum F_p was recorded at 11 o'clock on the anterior annular segment (10.3 ± 4.7 N) and the minimum at 8 o'clock on the posterior segment (6.9 ± 2.6 N). No significant differences were found between anchor positions. Similarly, although the anterior annular segment showed a trend toward higher pullout force, no significant difference was found between the anterior and trigonal, and anterior and posterior segments of the mitral valve (9.6 ± 3.8 N vs 7.3 ± 2.7 N, 7.5 ± 2.5 N; $p = 0.201$, $p = 0.130$ respectively) (Fig. 2).

MV Collagen Mass Fraction

Among all MV positions, the maximum HYP by wet and dry weights was recorded at 1 o'clock on the anterior annular segment (13.6 ± 3.7 mg/g, 60.9 ± 18.1 mg/g) and the minimum at 3 o'clock on the posterior segment (5.6 ± 2.7 mg/g wet tissue, 19.7 ± 13.0 mg/g dry tissue; Fig 2). Trigonal and anterior annular segments showed a significant trend toward higher HYP compared to the posterior segment. Significant differences in wet weights were found between posterior and both the trigonal and anterior segments (7.0 ± 3.3 mg/g vs 10.2 ± 4.7 mg/g, 11.1 ± 4.0 mg/g; $p = 0.047$, $p = 0.006$). For dry weight measurements, the 1 o'clock position showed higher HYP than three other posterior positions. Furthermore, while anterior and posterior segments remained significantly different (53.4 ± 20.4 mg/g vs 28.6 ± 14.1 mg/g, $p < 0.001$), posterior and trigonal segments were not significantly different.

TV Pullout Forces

Among all tricuspid positions, the maximum F_P was at SAC, within the trigonal region (24.0 ± 9.2 N), and the minimum was at 10 o'clock, within the anterior region (4.5 ± 2.6 N; Fig 3). F_P at SAC was significantly higher than at all other positions ($p < 0.001$). When analyzing by region, the trigonal region had higher F_P than the postero-septal and anterior regions (17.4 ± 10.1 N vs 6.8 ± 2.0 N, 5.1 ± 1.8 N, $p < 0.001$).

TV Collagen Mass Fraction

When analyzing by individual positions, SAC exhibited greater HYP than all other positions except 7 o'clock by either wet or dry weight. By wet weight, 7 o'clock HYP was not higher than other positions, but by dry weight, it was higher than five other positions (Fig. 3).

When analyzing by region, the trigonal region exhibited greater HYP than each other region, whether by wet or dry weight. By wet weight, the postero-septal region showed a trend toward higher HYP than the anterior region ($p = 0.318$); by dry weight, this difference was significant.

Relationship between pullout force and collagen content

No relationship was found between F_P and HYP for the mitral valve using individual measurements ($r^2 = 0.004$, $p = 0.65$) or mean values for each annular position ($r^2 < 0.051$, $p = 0.53$; Fig 4). Conversely, for the tricuspid valve, a strong correlation was found between pullout force and HYP using both individual measurements ($r^2 = 0.557$, $p < 0.001$) and positional mean values for each annular position ($r^2 = 0.889$, $p = 0.001$).

Comparisons between valves and measured quantities

A summary of comparisons between atrioventricular valves for F_P and HYP is shown in Table 3. The tricuspid valve had lower HYP than the mitral valve using both wet and dry weights. The TV exhibited comparable pullout force to the MV overall (8.2 ± 6.1 vs 7.8 ± 2.9 N, $p = 0.639$), despite a nearly 40% reduction in HYP. However, when SAC and 7 o'clock F_P measurements were excluded, TV showed lower mean F_P (7.8 ± 2.9 vs 6.3 ± 2.1 N, $p = 0.021$).

Discussion

In this study, mitral and tricuspid annuli were tested for suture pullout force and hydroxyproline mass fraction (a direct measure of collagen). This work extends our recent studies into annular suture mechanics^{13,14} in three key ways. First, human tissue from 60–79-year-old donors was used in this study rather than ovine models, likely yielding a more accurate description of mechanical properties and collagen distribution in patients undergoing atrioventricular valve surgery. Second, the mitral and tricuspid valve pairs were excised from the same heart, and F_P and HYP were measured from the same samples. For the first time, this enabled an investigation of the relationship between F_P and HYP on a point-by-point basis. Third, collagen content was evaluated in absolute units of hydroxyproline, rather than in terms of relative differences in collagen content within annular positions from a given valve. Thus, for the first time, direct comparison of collagen content between MV and TV is possible; in the future, these data may be further compared against other valve types, disease states, or species.

Although the mitral pullout forces showed a similar trend to similar studies¹⁴ with higher F_P in the anterior region of the annulus, these differences were not significant. Furthermore, these regions of higher pullout force tend to have higher collagen content. This would suggest that the presence of more densely packed collagen fibers in the trigonal region plays a role in suture retention. However, in the MV, no direct correlation was found between retention force magnitude and collagen density.

In the setting of tricuspid valves, this study demonstrated that tricuspid annular sutures placed in the vicinity of the trigone have significantly higher pullout forces. This is likely explained by the higher collagen density in the SAC region as quantified in this study and corroborated by previous work with ovine tissue¹³. Furthermore, the higher strength of the TV trigonal region lends credence to the notion that the higher clinical prevalence of tricuspid dehiscence from the septal annulus¹² likely results from sub-optimal suture placement in that region (in an effort to avoid injury to the atrioventricular node). A strong positive correlation was confirmed between suture retention force and collagen content in the tricuspid valve, suggesting that although other structural factors may play important roles, collagen density is a strong predictor of suture pullout force. This trend is consistent with previous findings¹⁴.

In contrast to the tricuspid annulus, where a strong correlation was observed, for the mitral annulus, collagen and F_P showed no relationship. Although median TV F_P was within 11% of median MV F_P , median TV HYP was over 35% reduced versus median MV HYP. In other words, although tricuspid annular collagen was substantially reduced versus mitral annular collagen, this did not translate to an equal reduction in suture holding strength. Taken together, these two findings allude to fundamental structural dissimilarities between the atrioventricular valve annuli. There are likely differences in collagen orientation and/or sub-type between the mitral and tricuspid annuli, such that collagen content strongly impacts pullout force in one, but not the other. For example, collagen alignment parallel to the suture path (i.e. circumferentially aligned) could inhibit the suture's ability to engage the fibers' load-bearing capacity, even if they are more densely packed. Since collagen fiber alignment

and sub-type are known to influence tissue material properties^{23,24}, further studies are needed to elucidate these differences in atrioventricular valve annuli.

It was also observed that removing moisture content from tested annular segments prior to quantifying collagen content yielded slightly different trends compared to hydrated segments with one of the anterior sutures showing more significantly higher collagen density compared to the others. This suggests a potentially significant role of moisture content in suture retention and a possible point of interest for future studies. Nevertheless, the minor differences in results from wet and dry weight measurements did not influence the overall conclusions of this study and ostensibly may not be of vital importance.

The suture pullout forces reported here, while following the general trends reported in ovine models^{13,14} are higher as a whole. Although this *may* reflect that human annular tissue is indeed stronger than its ovine analog, the fact that these studies were conducted years apart, with different operators placing sutures and different test setups, diminishes the reliability of such absolute comparisons. Nevertheless, the *relative* F_p distributions may be reliably compared between studies. It is notable that for the TV, the *skewness* in F_p toward the trigone was far more pronounced in human tissue than ovine tissue. The strongest position on the ovine TV annulus was about 62% higher in pullout force than all others, whereas the strongest on the human TV annulus was about 257% higher than all other positions.

It has been observed that sutures placed in the septal annulus of the mitral valve have the highest margin of safety, despite experiencing greater loading *in vivo*²⁵. Hence, methods that reallocate suture forces toward the septum in the mitral valve may enhance anchoring stability. Despite higher pullout forces around the septal anterior commissure of the tricuspid annulus, evidence suggests *in-vivo* cyclic suture forces are too high in this region¹⁴. Dehiscence has been clinically reported primarily around the tricuspid septal annulus¹². Hence, in contrast to the mitral valve, methods that redistribute cyclic suture forces away from the septum are expected to enhance anchoring stability. Furthermore, in light of the linear relationship between suture anchor force and collagen content in the tricuspid valve, emerging technologies for tissue evaluation via CT imaging may be valuable in surgical planning for tricuspid valve repair in the future²⁶.

Two limitations of this study are acknowledged. First, in order to eliminate any confounding factors, only hearts from donors with no history of heart disease were selected for this study. Patients undergoing atrioventricular surgical intervention have typically been diagnosed with some form of valvular insufficiency or stenosis. The tissue tested presently did not reflect these pathological states. Second, the suture pullout direction used for force measurements best approximated undersized ring annuloplasty, with standard placement technique²², and may not be representative of all repair procedures.

In conclusion, sutures placed in the trigonal region of the TV have higher pullout force than those placed along other segments of the annulus. The mitral valve has an overall higher collagen density than the tricuspid valve. Collagen density was found to vary linearly with anchor force in the tricuspid valve, but not in the mitral. These findings, building on previous work, further elucidate the factors governing the risk of device dehiscence in

humans and could also inform next-generation repair device design. Future studies investigating the structural differences between atrioventricular annuli may shed light on the relationship between suture retention force and collagen density in the mitral annulus.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

Further analysis was carried out to further elucidate the dehiscence mechanism and differences between the atrioventricular annuli. Two additional metrics were computed: total energy required for tissue failure (TERTIF) and full width at half maximum (FWHM). TERTIF was defined as the integral of the force-displacement curve from 5 seconds prior to failure until failure (to ensure any slackness at initial loading did not influence the analysis). TERTIF was a measure of required loading for tissue failure. FWHM was defined as the duration during which greater than half the pullout force (FP) was applied before and after tissue failure. FWHM may shed light on uniformity of collagen crimp in MV and TV annuli; barring the influence of other factors e.g. alignment direction, homogeneously crimped collagen fibers should load/break more quickly (lower FWHM), and heterogeneously crimped fibers should load/break more slowly (higher FWHM).

No differences were found in TERTIF between MV and TV annuli (29.1 $\pm$ 13.6 vs 33.3 $\pm$ 28.6 Nmm, $p=0.280$). Although the MV annulus showed a trend of lower FWHM compared to the TV annulus, this difference was not significant (6.7 $\pm$ 1.8 vs 7.4 $\pm$ 2.7s, $p=0.086$). These results allude to a difference in homogeneity in collagen crimp between the two annuli. However, further studies with larger sample sizes are necessary to confirm this hypothesis.

Figure 5 shows a summary of correlation analyses carried out on FWHM and TERTIF. We found a strong positive linear correlation between FWHM and HYP for both wet and dry weights of the TV ($r^2=0.2634$, $p<0.001$; $r^2=0.2935$, $p<0.001$), whereas a weak negative relationship was found for the MV ($r^2=0.0787$, $p=0.037$; $r^2=0.0262$, $p=0.237$). This suggests that along the TV annulus, in areas with higher collagen content, barring differences in fiber alignment, collagen fibers tend to be less uniformly crimped. Along the MV annulus, this trend is non-existent and possibly reversed.

Similarly, a strong positive linear correlation was found between TERTIF and HYP for both wet and dry weights of the TV ($r^2=0.6083$, $p<0.001$; $r^2=0.5779$, $p<0.001$), a weak negative relationship was found for the MV ($r^2=0.082$, $p=0.034$; $r^2=0.0083$, $p=0.508$). This result indicates that along the TV annulus, positions with higher collagen content required higher

energy for tissue dehiscence, a finding consistent with our reported results for pullout force. Conversely, along the MV annulus, the linear relationship appears to be the reversed or nonexistent.

Taken together, the results of this additional analysis further underline structural differences between the two atrioventricular annuli. However, further studies dedicated towards identifying collagen alignment and crimp differences between the annuli are needed to confirm these hypotheses.

References

1. Singh JP, Evans JC, Levy D, et al. Prevalence and clinical determinants of mitral, tricuspid, and aortic regurgitation (The Framingham Heart Study). *Am J Cardiol.* 1999;83(6):897–902. doi: 10.1016/S0002-9149(98)01064-9. [PubMed: 10190406]
2. Adams DH, Filsoofi F, Byrne JG, Karavas a N, Aklog L. Mitral valve repair in redo cardiac surgery. *J Card Surg.* 2002;17(1):40–45. <http://www.ncbi.nlm.nih.gov/pubmed/12027126>. [PubMed: 12027126]
3. Siefert AW, Pierce EL, Lee M, et al. Suture forces in undersized mitral annuloplasty: Novel device and measurements. *Ann Thorac Surg.* 2014;98(1):305–309. doi:10.1016/j.athoracsur.2014.02.036. [PubMed: 24996707]
4. Ghoreishi M, Brown JM, Stauffer CE, et al. Undersized tricuspid annuloplasty rings optimally treat functional tricuspid regurgitation. *Ann Thorac Surg.* 2011;92(1):89–96. doi :10.1016/j.athoracsur.2011.03.024. [PubMed: 21718833]
5. Bolling SF, Deeb GM, Brunsting L a, Bach DS. Early outcome of mitral valve reconstruction in patients with end-stage cardiomyopathy. *J Thorac Cardiovasc Surg.* 1995;109(Lv):676–682-683. doi:10.1016/S0022-5223(95)70348-9.
6. Bax JJ, Braun J, Somer ST, et al. Restrictive annuloplasty and coronary revascularization in ischemic mitral regurgitation results in reverse left ventricular remodeling. *Circulation.* 2004; 110(11 SUPPL.). doi:10.1161/01.CIR.0000138196.06772.4e.
7. Machiraju VR, Schaff HV., Svensson LG. Redo Cardiac Surgery in Adults.; 2013. doi: 10.1007/978-1-4614-1326-4.
8. Levack MM, Vergnat M, Cheung AT, Acker MA, Gorman RC, Gorman JH. Annuloplasty Ring dehiscence in ischemic mitral regurgitation. *Ann Thorac Surg.* 2012;94(6):2132. doi:10.1016/j.athoracsur.2012.04.051. [PubMed: 23176936]
9. Cerfolio RJ, Orszulak TA, Pluth JR, Harmsen WS, Schaff H V. Reoperation after valve repair for mitral regurgitation: early and intermediate results. *J Thorac Cardiovasc Surg.* 1996.
10. Gillinov AM, Cosgrove DM, Lytle BW, et al. Reoperation for failure of mitral valve repair. *J Thorac Cardiovasc Surg.* 1997;113(3):467–475. doi:10.1016/S0022-5223(97)70359-3. [PubMed: 9081091]
11. Dumont E, Gillinov a M, Blackstone EH, et al. Reoperation after mitral valve repair for degenerative disease. *Ann Thorac Surg.* 2007;84:444–450; discussion 450. doi:10.1016/j.athoracsur.2007.03.078. [PubMed: 17643613]
12. Pfannmüller B, Doenst T, Eberhardt K, Seeburger J, Borger MA, Mohr FW. Increased risk of dehiscence after tricuspid valve repair with rigid annuloplasty rings. *J Thorac Cardiovasc Surg.* 2012;143(5):1050–1055. doi:10.1016/j.jtcvs.2011.06.019. [PubMed: 21798563]
13. Paul DM, Naran A, Pierce EL, Bloodworth CH, Bolling SF, Yoganathan AP. Suture Dehiscence in the Tricuspid Annulus: An Ex Vivo Analysis of Tissue Strength and Composition. *Ann Thorac Surg.* 2017;104(3):820–826. doi :10.1016/j.athoracsur.2017.02.040. [PubMed: 28527966]
14. Pierce EL, Siefert AW, Paul DM, et al. How Local Annular Force and Collagen Density Govern Mitral Annuloplasty Ring Dehiscence Risk. *Ann Thorac Surg.* 2016;102(2):518–526. doi:10.1016/j.athoracsur.2016.01.107. [PubMed: 27133454]

15. Zuo K, Pham T, Li K, Martin C, He Z, Sun W. Characterization of biomechanical properties of aged human and ovine mitral valve chordae tendineae. *J Mech Behav Biomed Mater*. 2016;62:607–618. doi:10.1016/j.jmbbm.2016.05.034.
16. Li K, Wang Q, Pham T, Sun W. Quantification of structural compliance of aged human and porcine aortic root tissues. *J Biomed Mater Res - Part A*. 2014;102(7):2365–2374. doi:10.1002/jbm.a.34884.
17. Martin C, Sun W. Biomechanical characterization of aortic valve tissue in humans and common animal models. *J Biomed Mater Res - Part A*. 2012;100 A(6):1591–1599. doi:10.1002/jbm.a.34099.
18. Martin C, Pham T, Sun W. Significant differences in the material properties between aged human and porcine aortic tissues. *Eur J Cardio-thoracic Surg*. 2011;40(1):28–34. doi:10.1016/j.ejcts.2010.08.056.
19. Taramasso M, Pozzoli A, Guidotti A, et al. Percutaneous tricuspid valve therapies: The new frontier. *Eur Heart J*. 2017;38(9):639–647. doi:10.1093/eurheartj/ehv766. [PubMed: 26802134]
20. Gerson CJ, Goldstein S, Heacock AE. Retained structural integrity of collagen and elastin within cryopreserved human heart valve tissue as detected by two-photon laser scanning confocal microscopy. *Cryobiology*. 2009;59(2):171–179. doi:10.1016/j.cryobiol.2009.06.012. [PubMed: 19591817]
21. Bia D, Pessana F, Armentano R, et al. Cryopreservation procedure does not modify human carotid homografts mechanical properties: An isobaric and dynamic analysis. *Cell Tissue Bank*. 2006;7(3):183–194. doi:10.1007/s10561-005-0655-0. [PubMed: 16933040]
22. Filsoufi F, Carpentier A. Principles of Reconstructive Surgery in Degenerative Mitral Valve Disease. *Semin Thorac Cardiovasc Surg*. 2007;19(2):103–110. doi:10.1053/j.semtcvs.2007.04.003. [PubMed: 17870003]
23. Kunzelman KS, Cochran RP. Stress/strain characteristics of porcine mitral valve tissue: Parallel versus perpendicular collagen orientation. In: *Journal of Cardiac Surgery*. Vol 7 ; 1992:71–78. doi: 10.1111/j.1540-8191.1992.tb00777.x. [PubMed: 1554980]
24. Lodish H, Berk A, Zipursky S. Collagen: The fibrous Proteins of the Matrix. In: *Molecular Cell Biology*. ; 2000:Section 22.3.
25. Pierce EL, Bloodworth CH, Siefert AW, et al. Mitral annuloplasty ring suture forces: Impact of surgeon, ring, and use conditions. *J Thorac Cardiovasc Surg*. 2017. doi:10.1016/j.jtcvs.2017.06.036.
26. Zachrisson H, Engström E, Engvall J, Wigström L, Smedby Ö, Persson A. Soft tissue discrimination ex vivo by dual energy computed tomography. *Eur J Radiol*. 2010;75(2). doi: 10.1016/j.ejrad.2010.02.001.

Fig. 1.

a. Naming scheme for mitral and tricuspid suture positions and position groups. Mitral regions: trigonal (orange), anterior (yellow), posterior (green). Tricuspid regions: trigonal (orange), anterior (yellow), postero-septal (green) **b-c.** Sample photos of mounted valves **b.** Mitral **c.** Tricuspid

Fig. 2. Comparison of **a.** pullout force and **b-c.** hydroxyproline content (HYP) across suture positions and annular regions of the mitral valve. Plots show mean and standard deviation. Bars represent significantly different pairs.

Fig. 3.

Comparison of **a.** pullout force and **b-c.** hydroxyproline content (HYP) across suture positions and annular regions of the tricuspid valve. Plots show mean and standard deviation. Bars represent significantly different pairs. *- significantly different from all; # - significantly different from all except 7 o'clock

Fig. 4. Correlation between suture pullout force and hydroxyproline content (HYP) for mitral and tricuspid valves. **a.** Individual measurements **b.** Mean values for each annular position across six hearts.

Fig. 5.
Correlation between **a-b.** FWHM and hydroxyproline content (HYP) **c-d.** TERTIF and HYP

Table 1

Patient population descriptors

	Min	Mean	Max
Age	60	71	79
Post-mortem interval (days)	3	5.7	8
BMI	16.7	22.5	28.6

Table 2

Comparison of means of pullout force and hydroxyproline content between mitral valve (MV) and tricuspid valve (TV).

	MV mean	TV mean	p value	TV mean (without trigonal positions)	p value
Pullout Force (N)	7.8	8.2	0.639	6.3	0.021
Hydroxyproline (mg/g wet tissue)	8.4	5.0	< 0.001	4.3	< 0.001
Hydroxyproline (mg/g dry tissue)	35.6	19.9	< 0.001	16.8	< 0.001