Published in final edited form as:

J Biomech. 2013 September 27; 46(14): 2550–2553. doi:10.1016/j.jbiomech.2013.07.013.

In-Vivo Mitral Annuloplasty Ring Transducer: Implications for Implantation and Annular Downsizing

Andrew W. Siefert, M.S.¹, Steven A. Touchton Jr¹, Jeremy R. McGarvey, M.D.², Satoshi Takebayashi², Jean Pierre M. Rabbah¹, Jorge H. Jimenez¹, Neelakantan Saikrishnan¹, Robert C. Gorman, M.D.², Joseph H. Gorman III, M.D.², and Ajit P. Yoganathan, Ph.D.¹

¹The Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, Georgia

²Gorman Cardiovascular Research Group, University of Pennsylvania, Philadelphia, Pennsylvania

Abstract

Mitral annuloplasty has been a keystone to the success of mitral valve repair in functional mitral regurgitation. Understanding the complex interplay between annular-ring stresses and left ventricular function has significant implications for patient-ring selection, repair failure, and patient safety. A step towards assessing these challenges is developing a transducer that can be implanted in the exact method as commercially available rings and can quantify multidirectional ring loading. An annuloplasty ring transducer was developed to measure stresses at eight locations on both the in-plane and out-of-plane surfaces of an annuloplasty ring's titanium core. The transducer was implanted in an ovine subject using 10 sutures at near symmetric locations. At implantation, the ring was observed to undersize the mitral annulus. The flaccid annulus exerted both compressive (–) and tensile stresses (+) on the ring ranging from –3.17 to 5.34 MPa. At baseline hemodynamics, stresses cyclically changed and peaked near midsystole. Mean changes in cyclic stress from ventricular diastole to mid-systole ranged from –0.61 to 0.46 MPa (in-plane direction) and from –0.49 to 1.13 MPa (out-of-plane direction). Results demonstrate the variability in ring stresses that can be introduced during implantation and the cyclic contraction of the mitral annulus. Ring stresses at implantation were approximately 4 magnitudes larger than the cyclic changes in stress throughout the cardiac cycle. These methods will be extended to ring transducers of differing size and geometry. Upon additional investigation, these data will contribute to improved knowledge of annulus-ring stresses, LV function, and the safer development of mitral repair techniques.

Keywords

Mitral Valve; Mitral Annuloplasty; Transducer; Strain Gage; Mitral Valve Repair

© 2013 Elsevier Ltd. All rights reserved.

Corresponding Author: Ajit P. Yoganathan, 313 Ferst Dr., Atlanta, GA 30332, Ph. (404) 894-2849, Fax. (404) 894-4243, ajit.yoganathan@bme.gatech.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of Interest Statement

None.

Introduction

Functional mitral regurgitation (FMR) occurs when the heart's mitral valve (MV) is rendered incompetent by left ventricular (LV) remodeling and gross three-dimensional distortions in MV geometry (Braunwald, 1999; Gorman et al., 2003). FMR affects approximately 3 million people in the United States and over 50% of patients with reduced LV ejection fraction undergoing coronary artery bypass grafting (Borger et al., 2006; Trichon et al., 2003). The surgical repair of this disease has relied on reducing the shape and size of the mitral annulus by implanting an undersized, complete rigid annuloplasty ring (Bolling et al., 1998). While effective in many patients, undersized annuloplasty has been demonstrated to result in poor survival, low rates of reverse LV remodeling, and recurrent severe mitral regurgitation in 10–15% of FMR patients who preoperatively exhibit a severely distended LV (McGee et al., 2004; Kuwahara et al., 2006).

Repair failure after undersized annuloplasty results from progressive leaflet tethering and LV dysfunction, implicating a mal-distribution of annular and subvalvular stresses as a probable mechanism (McGee et al., 2004; Kuwahara et al., 2006). While an array of annuloplasty rings are commercially available, no consensus exists for which rings may be best for a severely distended LV (Bruan et al. 2012). Moreover, only limited knowledge exists for how annuloplasty rings may reduce annular-ring stresses in hopes of improving postoperative LV function and patient outcomes (Jensen et al. 2008)

Understanding the complex interplay between annular-ring stresses and left ventricular function has significant implications for patient-ring selection, repair failure, and patient safety (Aguel et al., 2011; Bruan et al. 2012; Draft Guidance for Industry and FDA Staff, 2010). A step towards assessing these challenges is developing a transducer that can be implanted in the exact method as commercially available rings and can quantify stresses on the in-plane and out-of-plane annuloplasty ring surfaces. Developing these transducers will provide the ability to test the effect of ring size, shape, and implantation method on regional ring loading. These data will improve clinical knowledge by providing mechanistic understanding of how ring selection and stress may contribute to LV function. To this end, the aim of this study is to assess the feasibility of developing and implanting a strain-gage based transducer to quantify the stresses imparted on a flat mitral annuloplasty ring due to implantation and cyclic annular contraction.

Methods

Instrumented Annuloplasty Ring

A novel transducer was developed to measure in- and out-of-plane bending stresses endured by an annuloplasty ring from implantation and cyclic contraction of the mitral annulus. Similar to the shape of the native annulus, the ring's core possessed a kidney-shaped profile and was fabricated from 6-AL 4V titanium. This lower modulus alloy provided potential long-term biocompatibility and an excellent linear-elastic element for strain gage measurements. The ring's outer dimensions were based on mitral annular sizes measured in a healthy ovine model (Gorman et al., 2003), while the ring's thickness was constrained to the dimensions of the miniature strain gages to be adhered to the ring's surface (EA-031DE-350, Vishay Micro-Measurements, Malvern, PA) (Fig. 1). These gages have a measurable range of $\pm 3\%$ strain and minimum measurable value of approximately 0.1 microstrain (Window, 1989).

Strain gages were bonded to the titanium ring in a half-bridge configuration on the in-plane (posterior-anterior and septal-lateral) and out-of-plane (apical-basal) surfaces at the septal, lateral, and commissural segments (Fig. 1) (Window, 1989). Strain gages and lead-wire

terminals were bonded to the ring using M-Bond 43-B to provide thin, hard, and void-free bondlines (Vishay Micro-Measurements, Malvern, PA). Terminal strips were utilized to prevent damaging forces being transferred to the strain gages from the lead wires (0.18 mm diameter silver-plated copper wire, Vishay Micro-Measurements, Malvern, PA).

After installation, each bridge was thinly coated (<0.1 mm thick) with Loctite® M-31CL™ Hysol® Medical Device Epoxy (Ellsworth Adhesives, Germantown, WI) for mechanical protection. The ring was then coated with synthetic rubber to provide a secondary moisture barrier and an anchoring material for the suture cuff (Plasti Dip, Performix, Blaine, MN). To complete the suture cuff, cardiovascular polyester fabric (thickness 0.61 ± 0.10 mm) (611 Double Velour Fabric, C.R. Bard, Murray Hill, NJ) was tightly sewn around the ring to allow for implantation similar to commercial annuloplasty rings (Fig. 2). After fabrication, the ring exhibited a 6.9 cm² outer area, 2.6 cm septal-lateral dimension, 3.3 cm transverse diameter, and thickness of 0.7 cm. While the outer dimensions of the ring were comparable to a size 32 mm Carpentier-Edwards Physio ring, the inner orifice area was 1.6 cm².

Experimental Protocol

The animal used in this work received care in compliance with the protocols approved by the Institutional Animal Care and Use Committee at the University of Pennsylvania in accordance with the guidelines for humane care (National Institutes of Health Publication 85-23, revised 1996).

One Dorsett Hybrid sheep (45 kg) was intubated, anesthetized, and ventilated with isoflurane (1.5% to 2%) and oxygen. Surface electrocardiogram and arterial blood pressure was monitored. After establishment of cardiopulmonary bypass, a left atriotomy was performed. Ten 2-0 Ethibond Exel Polyester sutures (Ethicon, Piscataway, NJ) were placed in the subjects mitral annulus and through the cuff of the instrumented annuloplasty ring (Fig. 2A). Prior to lowering and securing the ring into the mitral annulus, each of the ring's strain gage bridges was zeroed. The annular sutures were secured to the ring in the following order: left fibrous trigone, right fibrous trigone, then each remaining suture proceeding clockwise from the left fibrous trigone (Fig. 2B). After implantation, the strains imparted on the ring by the flaccid mitral annulus were recorded.

Following atrial closure, degassing, and separation from cardiopulmonary bypass; continuous wave Doppler echocardiography was completed (Phillips ie33, Phillips, Amsterdam, Netherlands). A high-fidelity pressure transducer (SPR-3505; Millar Instruments, Houston, TX) was passed percutaneously into the LV through the femoral artery for continuous measurement of LV Pressure (LVP). Surface electrocardiogram (EKG), LVP, and arterial pressure (Hewlett-Packard 78534C monitor; Hewlett-Packard Inc, Santa Clara, CA) were monitored. Upon establishing baseline hemodynamics (90 mmHg peak LVP, 4.0 L/min cardiac output), cyclic ring strains were measured within the post-cardioplegic heart. After successful measurement of all endpoints, the subject was euthanized with 1 g thiopental and 80 mEq KCl. The heart was removed and opened to verify placement and firm anchoring of the device to the mitral annulus (Fig. 3).

Data Acquisition and Analysis

Annuloplasty ring strains and LVP were continuously acquired using a compact Data Acquisition System (cDAQ 9174), strain gage bridge module (NI 9237), and analog voltage module (NI 9215) (National Instruments, Austin, TX) at 1613 Hz. Ring strains, LVP, and EKG were monitored and recorded using a custom-built program within the LabVIEW software program (National Instruments, Austin, TX). Recorded data were processed offline using a custom MATLAB program (Mathworks, Natick, MA). Within this program,

measured strains were converted to stress using the elastic modulus of ring's titanium core (114 GPa). Ring stresses and LVP were averaged over 10 consecutive cardiac cycles and reported as a mean $\pm$ 1 standard deviation.

Results

Prior to cardiopulmonary bypass, echocardiography revealed the subject to exhibit an end-diastolic mitral annular area of 7.14 cm² with septal-lateral and transverse dimensions of 2.45 cm and 3.37 cm, respectively. Negligible MR (grade 1+) was observed. During cardiopulmonary bypass and ring implantation, the transducer was found to slightly undersize the mitral annulus. At implantation, a suture passed through the ring cuff inadvertently damaged the strain bridge measuring in-plane stresses on the septal portion of the ring. As a result, the study proceeded with 7 of 8 ring measurement locations.

Following successful implantation; the stresses imparted on the ring by the flaccid annulus were measured. The distribution of stresses on the ring surface was heterogeneous with a combination of compressive (–) and tensile (+) stresses. On both the in- and out-of-plane surfaces, these stresses ranged from –3.17 to 5.34 MPa (Fig. 3). The largest stress was observed on the apical-basal surface at the septal portion of the ring. While sutures were attempted to be placed at near symmetric locations around the ring's circumference, the order of suture anchoring was hypothesized to play a significant role in the heterogeneous sign and magnitude of the observed stresses.

After weaning from cardiopulmonary bypass and establishing baseline hemodynamics, local cyclic stresses in the ring were successfully measured. Two consecutive representative cardiac cycles of the ring stresses with LVP and EKG are plotted in Fig. 4. Throughout each cycle, ring stresses were seen to increase from ventricular diastole and peak near mid-systole (Fig. 4). Exceptions to this observation included the lateral ring area (in the apical-basal direction) and the posterior commissural area (in the anterior-posterior direction) whose stresses became more negative during isovolumetric contraction indicating local tensile loading. The mean peak change in ring stresses for 10 consecutive cardiac cycles is shown in Table 1.

Acquired 3D echocardiography images demonstrated the transducer to remain fixed in the annular plane throughout the experimental protocol. Using Doppler echocardiography, the implanted ring increased the mean transmitral pressure gradient from 1 mmHg (pre-implantation) to 8 mmHg at 126 beats/min. Combined with the inner orifice area of the ring transducer (1.6 cm²), ring implantation resulted in moderate MV stenosis. Upon the study's completion, the heart was explanted and transducer found to remain firmly secured to the mitral annulus with no thrombus formation (Fig. 2C).

Discussion

The stresses imparted on the ring at implantation were approximately 4-fold larger than the cyclic changes in stress throughout the cardiac cycle. From these initial stress results, mitral annular reconstruction with the rigid ring transducer restricted the ability of the surrounding myocardium to systolically shorten. These results compare favorably to previously observed reductions in annular dynamics from ring implantation (Rausch et al., 2012).

Understanding annuloplasty ring stresses can aid in the improvement of ring design and develop a greater understanding for the mechanistic relationship between ring implantation and LV function. Evaluating the relationship between mitral annular geometry and ring stress may lead to improvements for optimizing complete rigid ring geometry and materials. Measured in-plane and out-of-plane stresses that are specific to differing ring designs can

aid in identifying areas of high stress and develop methods or techniques to reduce them. Moreover, these transducers can aid in understanding how increasing the number of ring-annulus sutures may impact regional ring stresses and basal LV function.

While it was desired to isolate the magnitude and direction of forces acting on the annuloplasty ring, it was not possible to isolate directional forces through the use of a calibration apparatus. Since annuloplasty transducers are complete rings, a force applied to a given ring location will affect the material deformation at other ring locations. A ring deformation that is measured by a strain gage therefore can be the result of an infinite combination of directional forces acting at locations other than the intended calibrated location and direction. As a result, this study focused on quantifying the ring stresses that result from the multi-directional loading for which annuloplasty rings endure.

Several limitations exist in this study. In comparison to commercially available annuloplasty rings, the developed transducer is larger due to limitations in strain gage size. Measured ring stresses were likely affected by suture location and securing order. Increasing the number of implantation sutures may reduce ring stresses, but an optimal ratio of sutures to ring-annulus geometry is currently unknown. The physiological benefit of adding more sutures to reduce ring stress for a given ring-annulus geometry is also unknown and will be a subject of further investigation. Carefully controlling ring transducer manufacturing, methods of surgical implantation and number of annular-ring sutures will be critical for the success of future studies.

This study was successful in assessing the feasibility of developing a transducer to quantify the regional stresses imparted on a flat mitral annuloplasty ring due to implantation and cyclic annular contraction. Future studies will evaluate the effect of differing annuloplasty ring sizes, geometries, and implantation methods. The determination of these endpoints will significantly contribute to improved knowledge for the annulus-ring stresses, their relationship with LV function, and the safer development of surgical techniques and devices for MV repair.

Acknowledgments

We would like to acknowledge grants awarded from the National Heart, Lung, and Blood Institute (HL73021, HL63954 and HL090661). The authors would like to additionally thank James "Jim" McEntree for fabricating the titanium annuloplasty ring core and dedicate this manuscript in his memory.

References

- Aguel F, Hillebrenner M. U.S. Regulatory Considerations for Heart Valves Implantation by Minimally Invasive Surgery. *Cardiovascular Engineering and Technology*. 2011; 2:62–65.
- Bolling SF, Pagani FD, Deeb GM, Bach DS. Intermediate-term outcome of mitral reconstruction in cardiomyopathy. *The Journal of Thoracic and Cardiovascular Surgery*. 2003; 115:381–388. [PubMed: 9475533]
- Borger MA, Alam A, Murphy PM, Doenst T, David TE. Chronic ischemic mitral regurgitation: repair, replace or rethink? *The Annals of Thoracic Surgery*. 2006; 81:1153–1161. [PubMed: 16488757]
- Braun J, Klautz RJM. Mitral valve surgery in low ejection fraction, severe ischemic mitral regurgitation patients: should we repair them all? *Current Opinions in Cardiology*. 2012; 27:111–117.
- Braunwald, E. Valvular Heart diseases, in *Heart Disease: A Textbook of Cardiovascular Medicine*. Braunwald, E., editor. W. B. Saunders Co.; 1999. p. 1643
- Draft Guidance for Industry and FDA Staff. Heart valves-investigational device exemption (ide) and premarket approval (pma) applications. 2010 submitted for comment, January 20, 2010.

- McGee EC, Gillinov AM, Blackstone EH, Rajeswaran J, Cohen G, Najam F, et al. Recurrent mitral regurgitation after annuloplasty for functional ischemic mitral regurgitation. *Journal of Thoracic and Cardiovascular Surgery*. 2004; 128:916–924. [PubMed: 15573077]
- Gorman JH III, Gorman RC. Annuloplasty ring selection for chronic ischemic mitral regurgitation: lessons from the ovine model. *Annals of Thoracic Surgery*. 2003; 76:1556–1563. [PubMed: 14602285]
- Gorman, RC.; Gorman, JH., III; Edmunds, Jr; and, LH. Ischemic Mitral Regurgitation, in *Cardiac surgery in the adult*. Cohn, LH.; Edmunds, Henry JL., editors. New York, NY: McGraw-Hill; 2003. p. 751-769.
- Jensen MO, Jensen H. Saddle-Shaped Mitral Valve Annuloplasty Rings Experience Lower Forces Compared With Flat Rings. *Circulation*. 2008; 118:S250–S255. [PubMed: 18824763]
- Kuwahara E, Otsuji Y, Iguro Y, Ueno T, Zhu F, Mizukami N, et al. Mechanism of Recurrent/Persistent Ischemic/Functional Mitral Regurgitation in the Chronic Phase After Surgical Annuloplasty. *Circulation*. 2006; 114:I-229–I-534.
- Rausch MK, Bothe W. A quantitative clinical and mechanical comparison of different annuloplasty devices. *Annals of Biomedical Engineering*. 2012; 40:750–761. [PubMed: 22037916]
- Trichon BH, Felker GM, Shaw LK, Cabell CH, O'Connor CM. Relation of frequency and severity of mitral regurgitation to survival among patients with left ventricular systolic dysfunction and heart failure. *American Journal of Cardiology*. 2003; 91:538–543. [PubMed: 12615256]
- Window, AL. *Strain Gage Technology*. 2nd Ed. England: Springer; 1989. p. 48-239.

Fig 1. (A) Anatomical directions, (B) Annuloplasty ring core with dimensions, (C) Image of the titanium annuloplasty ring core with bonded strain gages and lead wire terminals, and (D) Planar orientation of the mounted strain gages with labels indicating their measurement direction.

Fig 2.

A. Ten 2-0 sutures are placed through the suture cuff of the annuloplasty ring transducer for implantation, B. While on cardiopulmonary bypass the transducer is implanted to the mitral annulus, C. Post-experimentation, the left atrium is removed and the transducer was inspected for firm anchoring to the mitral annulus.

Fig 3. Annuloplasty ring stresses measured after implanting the ring to the mitral annulus in the flaccid cardioplegic heart (all stresses are expressed in MPa) with arrows indicating compression (arrows pointing towards the ring) or tension (arrows pointing away from the ring) at each measurement location.

Fig 4.

Left: Two consecutive representative cardiac cycles of the apical-basal and planar ring stresses plotted with left ventricular pressure and electrocardiography; Right: pictorial representations of the ring with arrows indicating compressive stresses (arrows pointing towards the ring) or tensile stresses (arrows pointing away from the ring) at each measurement location at peak left ventricular pressure.

Table 1

10-cycle ensemble averaged stresses at each annuloplasty ring location and direction expressed as a mean $\pm$ 1 standard deviation in MPa (positive values indicate tension while negative values indicate compression at peak left ventricular pressure)

	Location on the Annuloplasty Ring			
Ring Direction	Septal	Lateral	Anterior Commissure	Posterior Commissure
Apical –Basal	0.63 $\pm$ 0.02	–0.49 $\pm$ 0.01	0.54 $\pm$ 0.02	1.13 $\pm$ 0.01
Planar	n/a	–0.31 $\pm$ 0.04	0.46 $\pm$ 0.01	–0.61 $\pm$ 0.01