श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेंद्रम, तिरुवनन्तपुरम - 695 011, केरल, भारत
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PROJECT COMPLETION REPORT

1. **Project Number** : 8128

2. **Title of the Project** : Development of Annuloplasty ring for Mitral Valve Correction

3. **Funding Agency Name** : TRC DST

4. **Project Reference Number provided by the Funding Agency**: 8128

5. **Principal Investigator (Name & Address) :**

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DAIO,
BMT Wing,
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Poojappura,
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6. **Co-Investigators (Name & Address):**

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Precision Fabrication Facility
BMT Wing
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7. Implementing Institution **:**SCTIMST

8. Collaborating Institutions SITRA Coimbatore

9. Date of Commencement : 01/01/2018

10. Duration : 51 months

11. Date of Completion : 31/03/2022

12. Objectives as approved :
Development of an Annuloplasty ring for correction of Mitral regurgitation

13. Deviation made from original objectives if any, while implementing the project and reasons thereof : Nil

14. Field/Experimental work giving full details of summary of methods adopted, data collected supported by necessary tables, charts, diagrams and photographs :

A thorough review of the literature(product literature as well as scientific publications) was done. Risk analysis was done to identify known risks associated with predicate devices. Based on this a specification for the device was arrived upon. The next step was selection of materials and material characterization. This was followed by design concept evolution and detailed analysis of different candidate designs. Structural analysis(fea) of candidate designs was done and thus zeroing up on the best design. A prototype of the design was done using 3D printing and evaluated. This was followed by developing detailed design drawings and the prototype was fabricated in the Precision Fabrication Facility of the institute. This was followed by multiple stages of polishing(hand polishing, tumbling, buffing etc) to arrive at an acceptable surface finish. In vitro tests to evaluate the mechanical strength and fatigue life of the device was done. Pilot production of 3 sizes of the device (Nominal size-24,26,28) was done 3 numbers each. The device was then implanted in 3 animals(sheep). The animals were evaluated for a period of six months and were then sacrificed. All animals completed the evaluation period without any adverse events. After explants the vitals organs and the explanted device was send for detailed histopathological analysis

15. Detailed anaylsis of results :

16. Summary sheet of not more than 2 pages under following heads : (Title, Introduction, Rationale, Objectives, Methodology, Results, Translational Potential)

Introduction

The Annuloplasty ring is a rigid or flexible ring implanted around the mitral annulus for correction of mitral regurgitation. Mitral regurgitation(MR) or mitral insufficiency is the most common valvular disease. The surgical treatment options for MR are either valve replacement or valve repair. Of these two options valve repair has better outcomes in terms of patient motalility, morbidity, thromboembolic episodes, requirement for reoperation etc. Hence mitral valve repair using an Annuloplasty ring is the gold standard for treatment of mitral regurgitation.

There are different varieties of Annuloplasty ring in the market : rigid, flexible, complete, incomplete, adjustable etc. This product is a rigid annuloplasty ring with a 3D annular configuration to match the shape of the mitral annulus during the systolic phase of the cardiac cycle. The device consists of an inner metallic rigid core and a suture ring sewn around the core for affixing to the mitral annulus.

Rationale for development of Rigid complete ring

Alain Carpentier the pioneer in the field of Mitral Valve Repair classified Mitral Regurgitation functionally into 3 types :-

Type I: Valve dysfunction with normal leaflet motion.

In type I valve dysfunction, the course of the leaflets between systole and diastole has normal amplitude. The valve is regurgitant because of either leaflet perforation or lack of leaflet coaptation, a consequence of annular dilatation.

Type II: Valve dysfunction with excess leaflet motion (leaflet prolapse).

In type II dysfunction, the motion of one or more leaflets is increased and the free edge of one or several leaflets overrides the plane of the orifice during valve closure. The hemodynamic consequence is a regurgitation. A leaflet prolapse may be due either to chordae rupture or elongation or to papillary muscle rupture or elongation.

Type III: Valve dysfunction with restricted leaflet motion.

In type III dysfunction, the motion of one or more leaflets is limited, either during valve opening and closure (type IIIa), leading to various degrees of valve stenosis and regurgitation, or during valve closure (type IIIb), leading to valve regurgitation

The purpose of the rigid complete ring is to reduce the size of the annulus (restore it to its natural shape and size) in case of annular dilatation as in the case of Type I valvular dysfunction or to stabilize the annulus accompanied with concomitant correction procedures on the leaflet or connecting structures like the chordae in case of Type II or Type III valve dysfunction.

Objectives

To develop an annuloplasty ring for correction of mitral regurgitation with all accessories(sizers, holders for implantation)

Methodology

The mitral valve can be compared to an entrance gate or a French door: the leaflets are the doors; the mitral annulus is the frame. Any distortion or alteration of one or both of these components leads to dysfunction. To restore normal function, the geometry of each component must be reconstructed. If the frame is deformed, its reconstruction is guided by the size and the shape of the doors. If the doors are deformed, they should be repaired to fit the shape and the size of the frame. If both the frame and the doors are deformed they must be reconstructed so that their respective size and shape match perfectly. The same principles apply to the mitral valve. Prosthetic rings with optimal shape and size are used to restore the normal annular configuration, a condition for optimal leaflet coaptation

Restoring the shape implies restoring the normal systolic relationships between the transverse diameter and the antero-posterior diameter (Fig. 1). During systole, the shape of a normal annulus is ovoid with the transverse diameter, T, being greater than the antero-posterior diameter, A (T > A), with a 4 : 3 ratio (Fig. 1- a). In mitral valve regurgitation, this relationship is reversed, with A being greater than T (Fig. 1- b). This deformation involves predominantly the posterior annulus and, to a lesser extent, the anterior annulus.17 It may be symmetrical (Fig. 1- b) or asymmetrical (Fig. 1- c). Whatever the deformation, the implanted ring restores a normal shape to the annulus (Fig. 1- d).

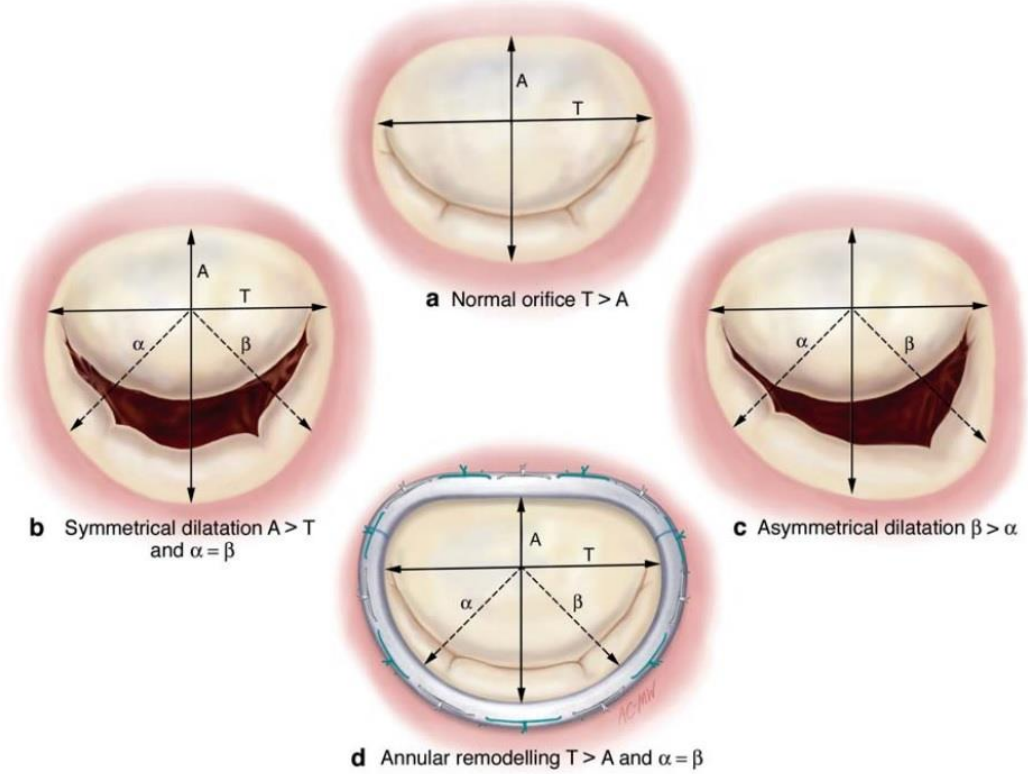


Fig.1 Annular remodelling

Restoring the size of the annulus implies restoration of an optimal relationship between the mitral orifice area and the surface area of the leaflets, a sine qua non condition for the leaflets to fully coapt during systole with a regular surface of coaptation. In mitral valve regurgitation, this relationship is modified because of either an orifice that is too large or a surface area of leaflet tissue that is too small, or both. Whatever the discrepancy, the ring corrects the anomalies in a durable fashion.

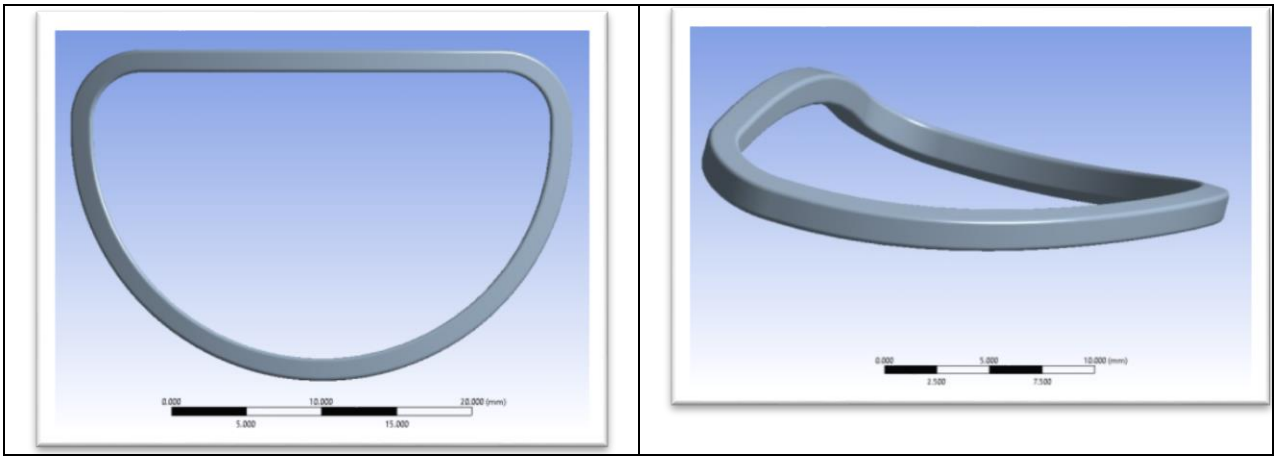
The remodeling ring restores the normal systolic shape and size of the annulus, a condition needed for optimal leaflet coaptation. It also prevents further deformation.

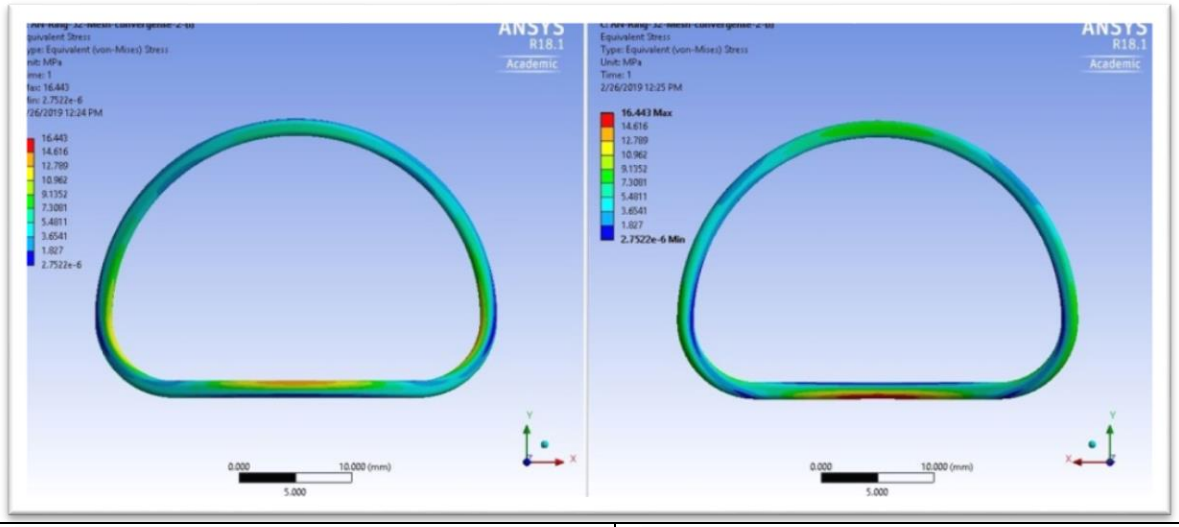
In India the most common cause of heart valve disease is of rheumatic origin. Valvular damage as a result of rheumatic fever is characterized by annular dilatation and chordal elongation leading to increased leaflet tip mobility of the mitral valve and associated with mild-moderate regurgitation1. As a result of rheumatic fever the annulus becomes highly fibrotic and loses its shape. In-order to prevent annular

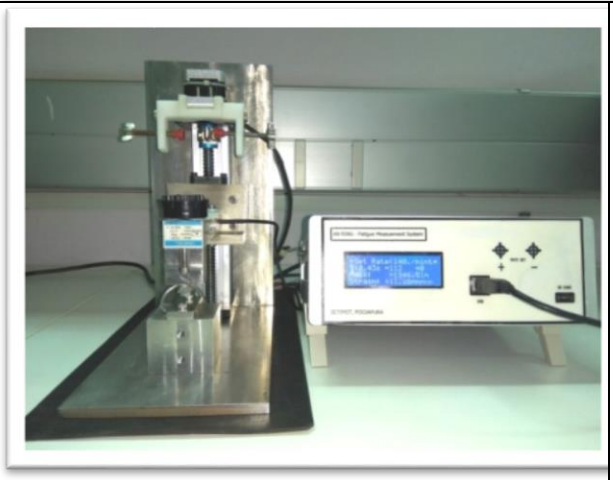
dilatation and restore the shape and stability of the annulus a rigid complete ring with a metallic core is recommended. The device maintains the characteristic 3:4 ratio between the anterio- posterior axis and the transverse axis. The device also has a 3D configuration with an annular height to commissural width ratio of 15%. The device 3D configuration is set to match the shape of a healthy mitral annulus during the systolic phase of the cardiac cycle. The device is covered by a suture ring made of knitted polyester fabric to attach the leaflet onto the annulus. The suture ring has markers in green color to show key anatomical positions: the two trigones and the base of the posterior annulus. These markers are an aid to the surgeon during the implantation procedure. The device also has a running line in green covering the length of the ring demarcating the rigid core portion from the periphery where the surgeon takes the byte. This is for ease of the surgeon while taking the bytes during surgery.

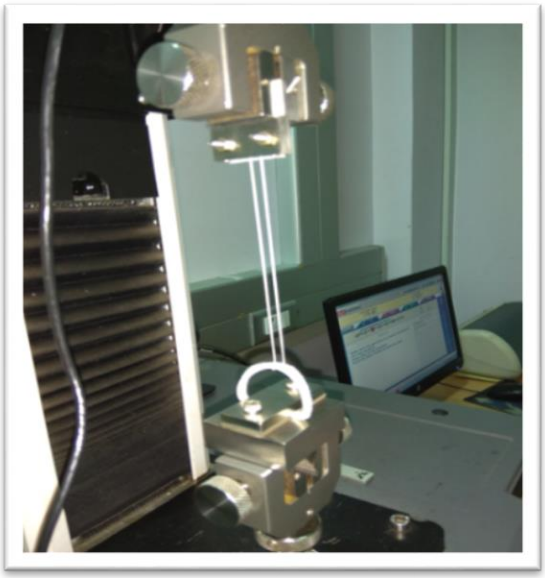
Results

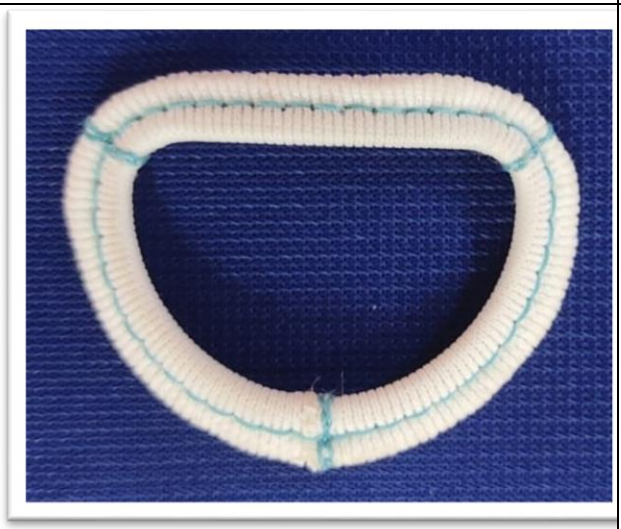
Based on a review of the scientific and product literature and as per inputs from the clinical investigator a specification for the device was arrived upon. The next step was selection of materials and material characterization.Commercially pure Titanium grade 2 was chosen as the material for the metallic inner core of the device. Warp knitted polyester fabric was chosen as the wrap covering for the inner core. The fabric cover functionality is to suture the ring on to the annulus and also aid in healing. This was followed by design concept evolution and detailed analysis of different candidate designs. The main consideration here was the geometric anatomy of the healthy native annulus. Structural analysis(fea) of candidate designs was done and to ensure safety. A modal analysis was performed to select the type of structural analysis (i.e Static or transient structural) needed to check the structural integrity of ring. A linear static structural analysis was done to find the peak stresses and displacements on the device under conditions as experienced in vivo and thus to ensure that the device is safe as regards the yield and fatigue criteria. A prototype of the design was done using 3D printing and evaluated. This was followed by developing detailed design drawings and the prototype was fabricated in the Precision Fabrication Facility of the institute. This was followed by multiple stages of polishing(hand polishing, tumbling, buffing etc) to arrive at an acceptable surface finish. Custom fixtures were developed for hand polishing. In vitro tests to evaluate the mechanical strength and fatigue life of the device was done. The fabric for the covering was cut to size using a laser cutter and was then went through an elaborate process of cleaning(IP extraction using the Soxhlet apparatus) and drying. A process was developed for suturing the fabric onto the inner core. Custom fixtures were developed for suturing the fabric. Pilot production of 3 sizes of the device (Nominal size-24,26,28) was done 3 numbers each. The device was then implanted in 3 animals(sheep). The animals were evaluated for a period of six months and were then sacrificed. All animals completed the evaluation period without any adverse events. After explants the vitals organs and the explanted device was send for detailed histopathological analysis











17. Contributions made towards increasing the state of knowledge in the subject :

As per our knowledge this is the first attempt to develop a mitral valve correction device in India. Knowledge gained regarding the mitral anatomy and physiology would help in future devices like mitral clip, transcatheter heart valve etc

18. Conclusions summarising the achievements and indication of scope for future work :

- ✓ A mitral annuloplasty ring has been developed and has undergone in-silico, in-vitro and in-vivo studies
- ✓ The device has been implanted in 3 animals all of which completed the stipulated evaluation period without adverse events
- ✓ Safety and efficacy of the device has been demonstrated
- ✓ Proof of concept of the device has been demonstrated and the device may be taken to pre-clinical evaluation

19. Science and Technology benefits accrued :

a. List of research publications with complete details :

Structural reliability assessment of a novel saddle shaped rigid annuloplasty ring Sunson Sunny, Ranjith G, Vivek V Pillai, Subhash NN, Ramesh Babu V, Subhash Kumar MS, Muraleedharan C V

Submitted to Journal of Cardiovascular Engineering and Technology

b. Manpower trained on the project :

i. Research Scientists or Research Fellows	**:**	Senior project engineer- 1 Project Assistant -1
ii. No. of PhD's produced	**:**	
iii. Other Technical Personnel trained	**:**	

c. Patents taken, if any **:** MITRAL ANNULOPLASTY RING
Ranjith Gopinathan,
Sunson Sunny,
Muraleedharan Chirathodi Vayalappil,
Ramesh Babu Venkatesan,
Subhash Kumar Mahadevan
Subhash Mandiram,Sarath Muraleedharan
Application No: 202041044910
Date of filing: 15/10/2020

d. Products developed, if any **:** Mitral annuloplasty ring

20. Abstract: (In 300 words for possible publication in ..... Bulletin)

a. Background: Mitral regurgitation(MR) or mitral insufficiency is the most common valvular disease. The surgical treatment options for MR are either valve replacement or valve repair. Of these two options valve repair has better outcomes in terms of patient motalility, morbidity, thromboembolic episodes, requirement for reoperation etc

b. Materials: A mitral annuloplasty ring has been developed and has undergone in-silico, in-vitro and in-vivo tests. The device was implanted in 3 animals. All 3 animals completed the required evaluation period(6 months) without any adverse events.

c. Results: The safety and efficacy of the device has been demonstrated through in-vitro and in-

vivo studies

d. Conclusion: Proof of concept of the device has been demonstrated and the device may be taken to the pre-clinical stage. We may also look for interested Industrial partners for possible collaborations.

21. Procurement/Usage of Equipment:

a. Details of Equipment: No new equipment purchased. Existing equipment were used

Sl. No.	Name of Equipment	Make/ Model	Cost (Rs.)	Date of Installation	Utilisation	Remarks regarding maintenance breakdown

b. Suggestions for disposal of equipment(s): Nil

29/11/2023

(Name and Signature of PIs with date)

Routing: *Signed copy of "Project completion Report" by PI → root@sctimst.ac.in, rpc@sctimst.ac.in*