Journal of Biomechanics 47 (2014) 973–980

Contents lists available at ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

In vitro assessment of a combined radiofrequency ablation and cryo-anchoring catheter for treatment of mitral valve prolapse

Steven M. Boronyak, W. David Merryman *

Department of Biomedical Engineering, Vanderbilt University, Nashville, TN, USA

ARTICLE INFO

Article history:
Accepted 14 January 2014

Keywords:
Mitral valve repair
Cardiac catheterization/intervention
Ablative therapy
In vitro studies

ABSTRACT

Percutaneous approaches to mitral valve repair are an attractive alternative to surgical repair or replacement. Radiofrequency ablation has the potential to approximate surgical leaflet resection by using resistive heating to reduce leaflet size, and cryogenic temperatures on a percutaneous catheter can potentially be used to reversibly adhere to moving mitral valve leaflets for reliable application of radiofrequency energy. We tested a combined cryo-anchoring and radiofrequency ablation catheter using excised porcine mitral valves placed in a left heart flow loop capable of reproducing physiologic pressure and flow waveforms. Transmitral flow and pressure were monitored during the cryo-anchoring procedure and compared to baseline flow conditions, and the extent of radiofrequency energy delivery to the mitral valve was assessed post-treatment. Long term durability of radiofrequency ablation treatment was assessed using statically treated leaflets placed in a stretch bioreactor for four weeks. Transmitral flow and pressure waveforms were largely unaltered during cryo-anchoring. Parameter fitting to mechanical data from leaflets treated with radiofrequency ablation and cryo-anchoring revealed significant mechanical differences from untreated leaflets, demonstrating successful ablation of mitral valves in a hemodynamic environment. Picrosirius red staining showed clear differences in morphology and collagen birefringence between treated and untreated leaflets. The durability study indicated that statically treated leaflets did not significantly change size or mechanics over four weeks. A cryo-anchoring and radiofrequency ablation catheter can adhere to and ablate mitral valve leaflets in a physiologic hemodynamic environment, providing a possible percutaneous alternative to surgical leaflet resection of mitral valve tissue.

1. Introduction

Depending on the lesions present, current MV repairs may include annuloplasty, leaflet resection, or chordal transfer or replacement. While there are several percutaneous annuloplasty and chordal repair devices in development (Boronyak and Merryman, 2012b; Chiam and Ruiz, 2011), there are currently no percutaneous techniques to perform leaflet resection, used in 70–80% of all surgical MV repairs (David, 2007; Flameng et al., 2008). Therefore, we believe there is a need for a percutaneous leaflet resection technique in the expanding MV repair armamentarium.

We have previously reported on the feasibility of using radiofrequency (RF) ablation as a percutaneous option for leaflet resection to reduce MV leaflet size (Price et al., 2010). Briefly, RF ablation induces resistive heating in tissues in direct contact with an ablation electrode. As collagen, the primary load-bearing component of MV leaflets, is heated to temperatures greater than 65 °C, it denatures and contracts. Thus, our technique uses RF ablation to reduce the size of enlarged, myxomatous MV leaflets.

While RF ablation has been shown to effectively reduce MV leaflet size, it is difficult to apply safely and reliably in the dynamic setting of the heart. When applied statically to the leaflets under open-chest surgery in a canine model, RF ablation reduced mitral regurgitation (MR) between 44% and 60%. However, when performed percutaneously, difficulty in maintaining adequate contact between the RF electrode and the MV leaflet surface resulted in off-target ablations (Williams et al., 2008). To address this problem, we have developed cryogenic anchoring (cryo-anchoring) (Boronyak and Merryman, 2012a), a technique similar to cryoablation that has been used to treat cardiac arrhythmias since 1999 and uses pressurized nitrous oxide to cool a catheter tip to temperatures as low as −80 °C (Boronyak and Merryman, 2012a; Khairy et al., 1999). The sub-freezing temperatures provide adhesion to the MV apparatus, allowing stable and reversible attachment of a catheter tip to a moving MV leaflet.

We have previously shown that when RF energy is applied to MV leaflets in a static environment with cryo-anchoring, leaflet

* Correspondence to: Room 9445D MRB IV-Langford, 2213 Garland Avenue, Nashville, TN 37232-0493, USA. Tel.: +1 615 322 7219 (office), +1 615 343 0009 (lab); fax: +1 615 322 6541.
E-mail address: david.merryman@vanderbilt.edu (W.D. Merryman).

0021-9290/$ - see front matter
http://dx.doi.org/10.1016/j.jbiomech.2014.01.021

size becomes significantly reduced, and infrared thermal imaging revealed that the cryo-anchor can be placed in close proximity to the RF electrode (Boronyak and Merryman, 2012a). However, the effectiveness of this combined RF ablation and cryo-anchoring approach has yet to be tested in a physiologic flow environment. In particular, it is unknown whether a cryo-anchor can adhere to a moving MV leaflet and if this process negatively affects the flow and pressure across the MV.

The purpose of this study was to develop and evaluate a combined RF ablation and cryo-anchoring catheter in a left heart flow simulation environment in order to optimize catheter performance and to determine procedure feasibility. We hypothesized that our combined RF ablation and cryo-anchoring catheter would adhere to moving porcine MV leaflets in a dynamic flow environment and effectively ablate the leaflet tissue with RF energy, mimicking surgical leaflet resection. To test this hypothesis, we constructed a left heart flow loop, similar to others (Hildebrand et al., 2004; Jimenez et al., 2007), in order to simulate the flow and pressure across healthy, excised porcine MVs. The data that follow support our hypothesis that the combined catheter prototype effectively adheres to and ablates MV leaflets in a physiologic flow environment without negatively altering flow or pressure during the procedure, and that the changes induced by RF ablation remain durable over four weeks.

2. Materials and methods

2.1. Left heart flow loop

A left heart flow loop was developed in order to reproduce physiologic pressure and flow waveforms (Fig. 1A). Others have used similar flow simulators in an effort to study MV disease states and the effects of various repair strategies on MV mechanics (Croft et al., 2007; Padala et al., 2009). MVs were obtained from healthy pigs from a local abattoir (Hampton Meats, Hopkinsville, KY), and the entire MV apparatus was excised and kept intact. The MV annulus was sewn onto a silicone membrane, and the papillary muscles were sewn onto adjustable papillary muscle holders (Fig. 1B). LabView software (National Instruments, Austin, TX) was used to control the output pressure to a pump connected to the left ventricle, and an adjustable flow resistor and vessel compliance chamber were used to independently control the flow rate. Transmitral pressure and flow waveforms (Transonic Systems Inc., Ithaca, NY) were captured to assess the effect of catheter placement and cryo-anchoring on hemodynamics.

2.2. RF ablation and cryo-anchoring catheter

A steerable catheter prototype was constructed utilizing components from a Freezer MAX Cardiac Cryoablation catheter (Medtronic, Minneapolis, MN). A RF electrode was placed in between two cryo-anchors on the tip of the catheter and was electrically insulated from the cryo-anchors (Fig. 1C). Liquid nitrous oxide delivery to the inside of the catheter tip, which is kept under vacuum, provides the cooling power for the cryo-anchor. A deflection wire was attached to a custom steering device to allow the catheter tip to be maneuvered. A viewing window on the left heart flow loop allowed for precise spatial localization of the catheter tip to the desired areas of the MV. The cryo-anchor temperature was controlled automatically by monitoring the temperature of the cryo-anchor and varying the duty cycle of a cryogenic solenoid.

2.3. Flow loop treatments

Two different treatments were tested on MVs placed in the left heart flow loop while under physiologic flow conditions. To determine the hemodynamic changes induced by cryo-anchoring, the cryo-anchoring procedure was performed without RF ablation on several locations of each MV leaflet for a total of 15 applications for 90 s each at a temperature of approximately −30 to–35 °C. The cryo-anchoring procedure targeted the central portion of the anterior and posterior leaflets, as demonstrated in Fig. 1B. In order to assess the ability to ablate the MV leaflets, RF ablation was performed during cryo-anchoring, also in the central portion of the anterior and posterior leaflets. RF ablation was applied while cryo-anchored to the MV at a power of 50 W for 90 s, with 15 applications.

2.4. Parameter fitting

Strain energy density was used to provide a quantitative measure of the extent of RF ablation, which allows post-treatment mechanical assessment of leaflets without any pre-treatment information. The strain energy density was determined by fitting post-treatment mechanical data to a three-parameter strain energy model using non-linear regression (Fung, 1993). After treatment in the left heart flow loop, MV anterior leaflets were excised, tracking markers were placed on the surface of the leaflet for strain tracking, and samples were placed into a biaxial mechanical test device and loaded to 90 N/m of membrane tension in each direction. For more details, see (Boronyak and Merryman, 2012a; Price et al., 2010).

Following mechanical testing, the strain energy density was determined by fitting the membrane tension and strain data to a three-parameter strain energy model (Yin et al., 1987), in order to determine the strain energy density (W):

$$T_{ij} = \frac{\partial W}{\partial E_{ij}}$$

$$W = c[e^{Q} - 1]$$

where

$$Q = A_1 E_{11}^2 - A_2 E_{22}^2$$

In which c, A_1, and A_2, are the parameters to be fit, E_{ij} is the Green–Lagrange strain tensor, W is a strain energy density function, and T_{ij} is a membrane tension representation of the 2nd Piola–Kirchhoff stress tensor. T_{ij} is a relation of membrane tension in the reference configuration to areas in the reference configuration and is defined as

$$T_{11} = \frac{P_1}{L_2 \lambda_{11}}$$

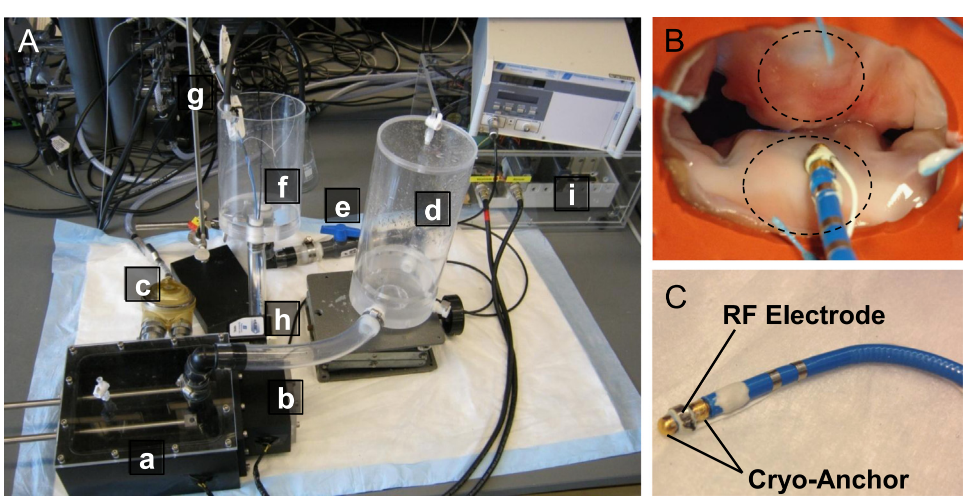

Fig. 1. Left heart flow loop (A) used to test catheter performance consisting of, a: ventricle, b: atrium, c: Thoratec VAD bladder pump, d: compliance chamber, e: flow resistor, f: media reservoir for catheter access, g: catheter prototype, h: Transonic flow probe, and i: LabView input/output controller. (B) A healthy MV mounted in the left heart flow loop with the catheter prototype placed on the anterior leaflet. Dotted lines represent regions targeted for cryo-anchoring and RF ablation. (C) Catheter prototype with cryo-anchoring elements and RF electrode.