Abstract

Cardiac arrhythmia is a disease characterized by abnormal electrical conduction in the heart that results in ineffective pumping. Dysfunctional nodes in the conduction pathway or in the cardiac muscles lead to irregular heartbeat patterns that can potentially induce severe complications such as cardiac arrest. Radiofrequency ablation, the current gold-standard cardiac arrhythmia treatment procedure, has proven effectiveness but suffers from shortcomings due to instability between the RF tip and the target site. In this prototype anchor that incorporates RF ablation with a cryogenic adhesion system was shown to anchor to cardiac tissue with enough adhesion strength to maintain attachment during cardiac contractions. The thermal interference between heat generated by RF ablation and the cryogenic temperatures of cryogenic anchoring was not significant, demonstrating the feasibility of utilizing both technologies simultaneously. These results suggest that combining RF ablation and a cryogenic anchor into one catheter enables a physician to treat cardiac arrhythmia with improved stability and may be utilized for anchored tissue ablation of other organs where instability is an issue.

Background

Cardiac arrhythmia affects approximately 14.4 million people in the United States [1]. Arrhythmia, defined as irregular cardiac rhythmic patterns, is caused by abnormal initiation or propagation of electrical excitation signals within the heart and leads to cardiac arrest in more than 600,000 Americans each year [2]. Current treatments for cardiac arrhythmias include pacemakers, anti-arrhythmic drugs, and cardiac tissue ablation [3]. Ablation is a low-risk procedure compared to pacemakers, and is used when anti-arrhythmic drugs are ineffective [4].

Radiofrequency (RF) catheter ablation is a minimally invasive procedure that strategically removes dysfunctional tissue by using alternating electrical current at radiofrequency [5]. Joule or resistive heating to temperatures greater than 45 ºC permanently removes the tissue that causes arrhythmia [6][7]. It is the current “gold standard” in minimally invasive cardiac arrhythmia surgical treatment due to the following advantages: rapid ablation (1 min/site), high efficacy (98.4%), and low recurrence (4.4%) [8][9]. However, Hugh et al. conducted a survey of cardiologists that suggested RF ablation still possesses one major flaw: lack of control due to catheter instability [10]. Cardiac forces such as contraction and shear stress from concurrent blood flow often displaces the tip relative to the physician’s desired location, causing ablation of unintended sites [11]. The potential for severe surgical complications due to instability may further aggravate arrhythmia, especially around sensitive areas such as the atrioventricular node, leading to a need for permanent pacemaker or defibrillator implantation [12]. Another tissue ablation treatment is cryoablation, which possesses the advantage of tip stabilization through freezing of tissue at -80 ºC [13]. Cryoablation poses more significant drawbacks relative to RF ablation including increased treatment times, reduced efficacy, and increased arrhythmia recurrence [14].

Currently, no technology or method to stabilize the RF ablation tip is used clinically to prevent ablation of unintended sites [15]. Sklar et al. attempted to improve RF ablation stability by creating an anchor attached to the RF tip that physically pierced the cardiac tissue with sharp, trocar-like ends [15]. One issue they encountered with this approach is that the anchor caused significant collateral damage to the cardiac tissue, and no recent progress has been made with this technique for stabilizing RF ablation catheters [15]. Previously, Boronyak et al. studied the viability of simultaneous cryogenic anchoring and radiofrequency treatment of mitral valve prolapse [16]. The effectiveness of the catheter was demonstrated in-vitro by examining thermal distribution, and cryogenic anchor strength. The conclusion of the study was cryogenic anchoring may be a feasible technique for secure attachment of a catheter to a mitral valve leaflet. However, due the geometry of the cryogenic anchor, their catheter was only suitable for treating mitral valve prolapse and not for other purposes.

Catheter Design:

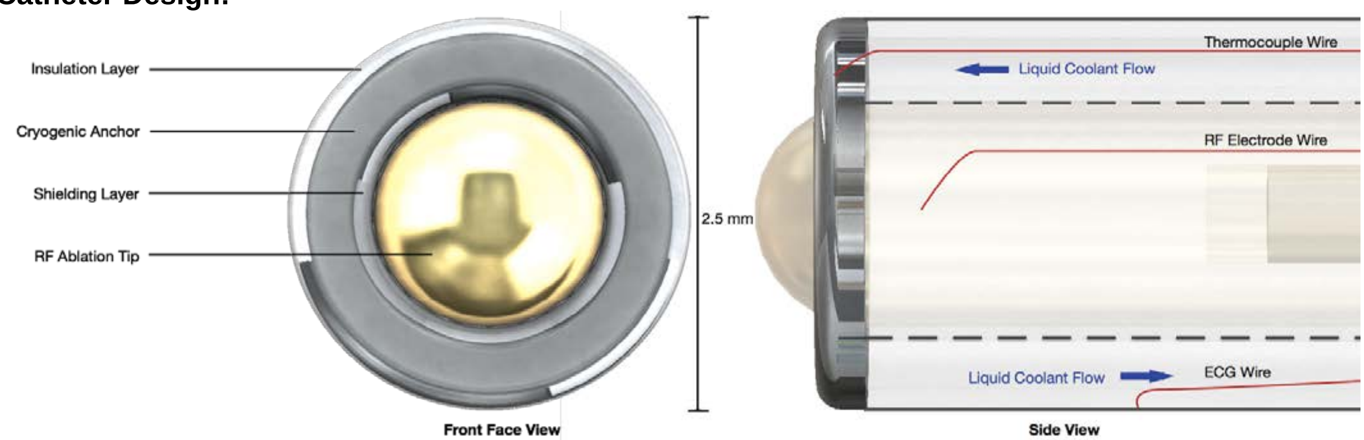


Figure 1. A 2 mm RF ablation catheter is encircled with an outer concentric cryogenic ring to serve as the cryogenic anchor. The RF ablation electrode tip is located in the center of the catheter due to the need for precise ablation (front face view). A shielding layer protects the RF ablation tip from the cryogenic anchor. A liquid coolant will be cycling through the cryogenic anchor (side view). The outermost insulation layer, made from silicone, is biologically inert and unreactive to bodily fluids. The catheter should not exceed 2.5 mm in diameter to remain viable for minimally-invasive procedures.

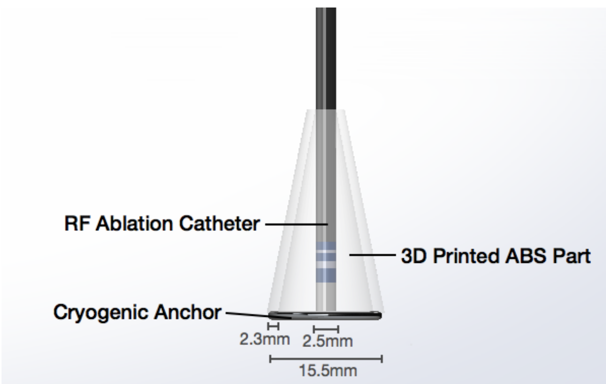
Our group attempted to resolve the instability issue associated with RF ablation by utilizing a cryogenic anchor. This design addresses the issue associated with the previously described stabilization approach (Sklar et al.) by avoiding collateral damage. Our catheter consists of a concentric cryogenic anchor positioned at the catheter tip such that the RF electrode is in contact with the arrhythmic source (Fig. 1). To achieve cryogenic anchoring, a cryogenic fluid was pumped through insulated tubing to reach the cryogenic anchor located at the catheter tip. At -20 ºC, the cryogenic anchor froze fluids adjacent to the cardiac surface and attached to it, creating an interface of adhesion strong enough to withstand the forces of cardiac contractions [16]. Because irreversible tissue damage only occurs at temperatures below -30 ºC, -20 ºC was the target temperature for operation of a cryogenic anchor [17]. Ablation was performed solely through the RF component while the cryogenic component provided an anchor for stability.

Another potential benefit of our cryogenic anchoring mechanism is cryomapping, a process that allows the physician to locate arrhythmic sites. At -10 ºC to -20 ºC, cardiac tissue becomes temporarily dysfunctionalized [4]. Altered electrical conduction visualized through electrocardiogram (ECG) patterns can consequently provide physicians information on the catheter tip position. If undesirable effects are observed on an ECG during cryomapping, RF ablation will not be performed at that site. Likewise, an improved ECG reading during cryomapping indicates the arrhythmic site has been located and RF ablation should be performed there. Cryogenic anchoring at the arrhythmic site can then proceed by lowering the temperature to -20 ºC. Therefore, this mechanism allows for immediate catheter tip attachment after an arrhythmic source is located [18].

Working Prototype:

The purpose of our experiments was to determine the feasibility of simultaneous use of a cryogenic anchor and RF ablation on the same catheter tip, and to quantify the thermodynamic effects of the system on porcine cardiac tissue. We hypothesized that a RF ablation catheter with simultaneous cryogenic anchoring will adhere to and ablate cardiac tissue to effectively treat the source of arrhythmia. A catheter prototype was developed containing both a cryogenic anchor for stability and a RF electrode for ablation. The effects of using cryogenic temperatures and resistive heating in close proximity were determined using finite element analysis to locate distinct thermal regions within the tissue. The results of the simulations were verified through thermocouple temperature measurements. Our group also quantified anchor strength of the cryogenic anchor both with and without RF ablation. The data supports the hypothesis that simultaneous cryogenic anchoring with RF ablation can provide necessary adhesion, and function effectively in close proximity on a single catheter tip. Therefore, combining RF ablation and cryogenic anchoring into one catheter enables a physician to treat cardiac arrhythmia with improved stability, and may be utilized for anchored tissue ablation of other organs where stability is an issue.

A



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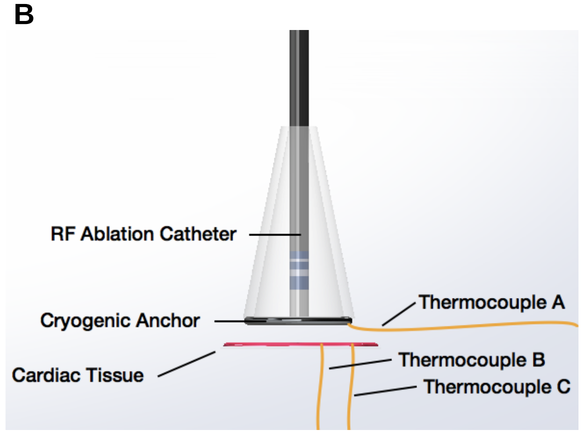

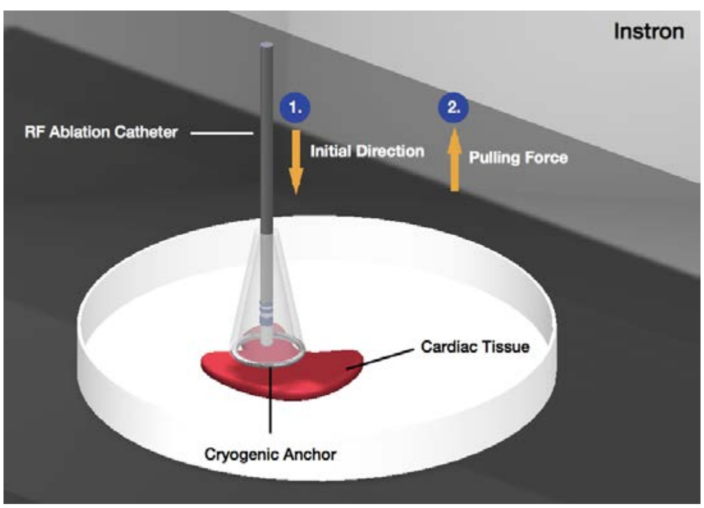

C

Figure 2. A. A side view of the catheter prototype used for experiments, indicating the dimensions of the cryogenic anchor and RF ablation catheter. **B.** Thermocouple A measured the temperature of the cryogenic anchor. Thermocouple B measured the temperature equidistant (r=7.75 mm) from the site of RF ablation and the cryogenic anchor on top of the cardiac tissue. Thermocouple C was positioned between the cryogenic anchor and cardiac tissue. **C.** Initial force was applied downward onto cardiac tissue by the Instron (Direction 1). After cryoadhesion was achieved, the Instron initiates upward force at an increasing rate (Direction 2). Force applied at the point of cryogenic anchoring and tissue detachment allows calculation of cryogenic adhesion force.

Modeled Temperature Distribution

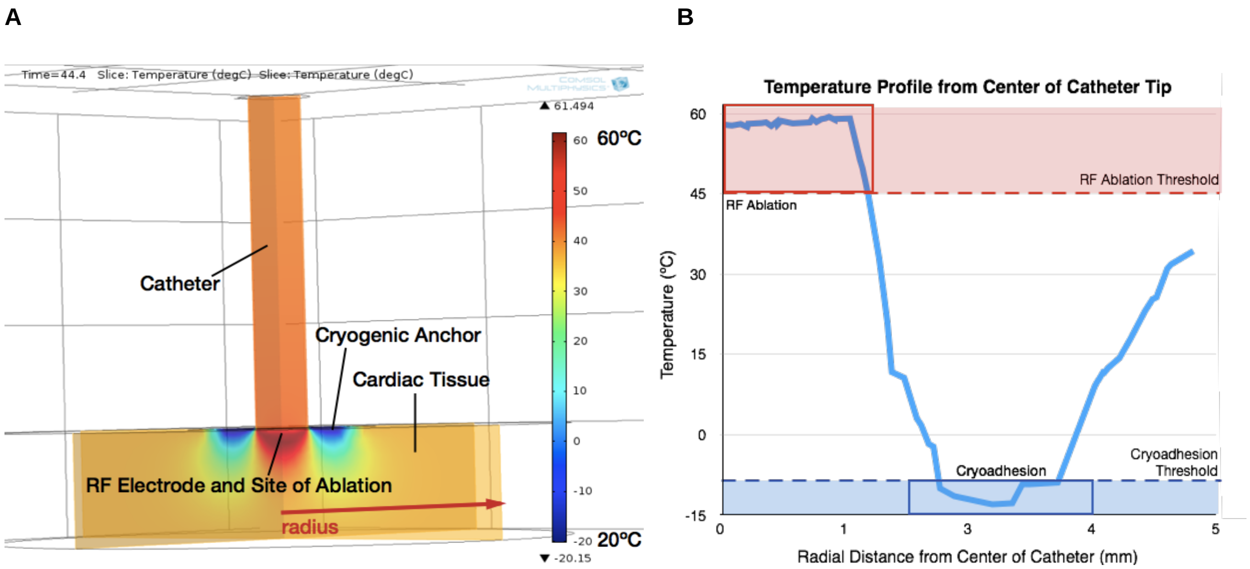

Figure 3. A. Simulated temperature distribution of minimally-invasive dimensions catheter. **B** Temperature measurements taken 1 mm below the cardiac surface.

The temperature map (Fig. 3a) showed distinct areas of cryogenic anchoring and RF ablation without interference or temperature gradient overlap. The highest temperature expected due to RF ablation was 70 ºC while the lowest temperature expected due to cryogenic anchoring was -20 ºC. When temperature was plotted as a function of radial distance from the origin or center of the catheter, temperature deviations from physiological 37 ºC due to RF ablation and cryoadhesion do not overlap (Fig 3b) [19]. At a radial distance of zero where the RF electrode was situated, the temperature was 70 ºC and surpasses 45 ºC, the conservative temperature threshold for permanent ablation [6][7]. At distances 7.75 mm from the center where the cryogenic anchor is located, the temperature was lower than physiological norm, reaching -20 ºC, which is sufficient for cryoadhesion [16]. The gradient for cryoadhesion is much broader than that of RF ablation, because the latter utilizes the Joule heating effect to heat tissue whereas the former utilizes bioheat transfer from contact with a cold, thermally conductive material [7]. Between 1 mm and 6 mm from the catheter center, temperature remained constant at physiological tissue temperature of 37 ºC [19]. Therefore, the thermal effects on these regions due to RF ablation and cryogenic anchoring were not significant.

Proof of Concept Catheter Prototype for Temperature and Adhesion Strength Experiments

A 2.7 mm (8 French) prototype was developed that contained a 15.5 mm diameter cryogenic cooled metal anchor ring to surround a RF ablation catheter (EZ Steer ThermoCool, Biosense Webster, Diamond Bar CA) (Fig. 2A). The hollow ring was connected to the catheter using an acrylonitrile butadiene styrene (ABS) 3D-printed clasp, which allowed the ring to be physically attached to the catheter as one device (Fig. 2A). The effective surface area of the ring was 79.7 mm^2 . RF ablation was performed at 70 ºC with a Stockert 70 Radiofrequency Generator (Biosense Webster, Diamond Bar CA) capable of delivering a 500 kHZ electrical signal at power up to 50 W to the RF catheter tip. Liquid nitrogen contained inside a canister (LD10 Taylor- Wharton) was delivered to the catheter tip through a custom made pressure pump driven by nitrogen gas.

Thermocouple Measurements

To verify the accuracy of thermal gradients shown in COMSOL simulation, the temperature of cardiac tissue was measured at the RF ablation site (r=0mm), an equidistant location between the two (r=3.875 mm) and underneath the cryogenic anchor (r=7.75mm). All temperature measurements were collected during 5s of initial cryogenic anchoring followed by 60s of concurrent RF ablation at 50W. The temperature of the tissue at the RF ablation site was measured with a built-in temperature sensor on the catheter tip, which was displayed on the RF generator console. Temperatures at the two other sites were measured through thermocouples placed 1 mm underneath the cardiac tissue (Fig 2b). A thermocouple was also placed directly on the cryogenic anchor. Data from the thermocouples were synced and recorded with data acquisition software (Omega, Stamford, CT).

Temperatures measured with thermocouples during simultaneous RF ablation and cryogenic anchoring over a period of 60 seconds are shown below (Fig 4). Average cryogenic anchor temperature at -26.3 ºC led to temperature of tissue underneath the cryogenic anchor to remain relatively constant at -15 ºC, which was sufficient for cryogenic anchoring. These temperatures were above the threshold for cryogenic damage of -30 ºC [17], indicating that tissue beneath the cryogenic anchor was not being cryoablated.

The tissue temperature between the RF tip and cryogenic anchor was predicted to remain constant at 37 ºC. However, the experimental temperature of tissue between the RF tip and cryogenic anchor remained constant at around 10 ºC. This suggests that the thermal gradient caused by cryogenic anchoring resulted in a much lower temperature than predicted. This unexpected thermal interference did not significantly affect RF ablation since the temperature underneath the RF tip was automatically compensated by the generator by increasing power. Thus, RF ablation temperature remained constant at 70 ºC, well above the minimum 45ºC threshold for ablation [6][7].

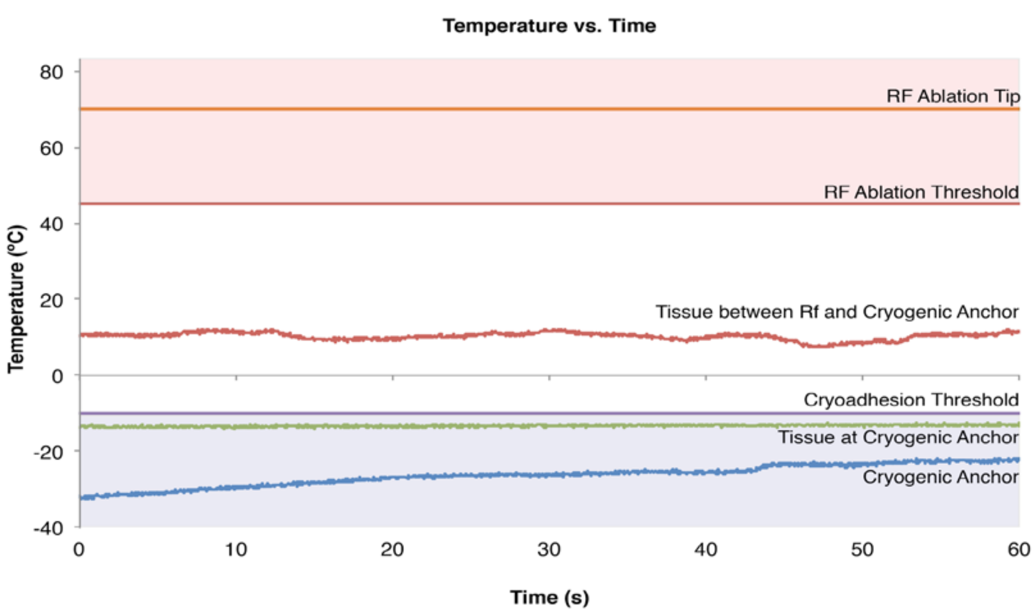

Figure 4: Temperature of cardiac tissue and cryogenic anchor during dual RF ablation and cryogenic anchoring for 60 seconds.

Cryogenic Anchor Adhesion Strength

The average adhesion strength on the endocardium was found to be 151.8±64 kPa. During simultaneous cryogenic anchoring and RF ablation, the average adhesion strength decreased significantly to 93.3±20 kPa (p=0.05) (Fig 6). This decrease in anchoring strength during simultaneous RF ablation could have resulted from undetected thermal interaction.

Although there is no published value for the anchoring strength required to maintain attachment, we estimated a value based on finite element stress analysis of left ventricular mechanics. A left ventricle model was chosen due to higher prevalence for arrhythmia in the left ventricle [20]. Guccione et al. determined that the maximum pressure exerted by cardiac fibers in the left ventricle is 59 kPa [21]. Both adhesion strength values exceeded this minimum threshold (Fig 5). Therefore, our results suggest that the cryogenic anchoring strength during simultaneous RF ablation would be large enough to maintain contact with endocardial tissue during a normal cardiac contraction.

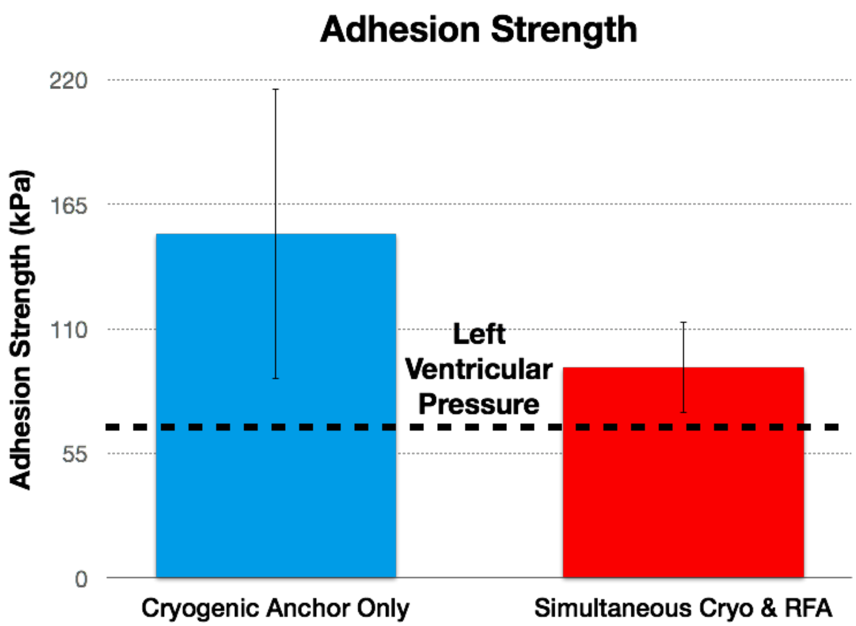

Figure 5. Average adhesion strengths comparing cryogenic anchor only and simultaneous cryogenic anchoring and RF ablation.

Conclusion

Our group developed and tested a cryogenic anchor to improve the stability of RF ablation in cardiac arrhythmia treatment. We demonstrated a cryogenic anchor without thermal interference from RF ablation based on finite element analysis with COMSOL Multiphysics. Our data suggests that the temperatures necessary for RF ablation and cryogenic adhesion can be obtained simultaneously in our proposed target dimensions. Additionally, the cryogenic anchor was demonstrated to have an adhesion strength sufficient to maintain attachment during normal cardiac contractions. These results indicate that cryogenic anchoring may be a viable method to stabilize RF ablation for cardiac arrhythmia treatment.

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