Best Practice Guide for Cryoballoon Ablation in Atrial Fibrillation: The compilation experience of over 3000 Procedures

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Best Practice Guide for Cryoballoon Ablation in Atrial Fibrillation: The compilation experience of over 3000 Procedures

Short title: Best Practice Guide for Cryoballoon Ablation

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Cryoballoon, atrial fibrillation, cryoablation, paroxysmal atrial fibrillation, pulmonary vein isolation, second generation cryoballoon, balloon, phrenic nerve, practice guidelines

Abbreviations
AF=atrial fibrillation
PVI= pulmonary vein isolation
PV=pulmonary vein
RF=radiofrequency
TTI=time-to-isolation
CB=cryoballoon
CB1=first generation cryoballoon; Arctic Front
CB2= second generation cryoballoon; Arctice Front Advance
ICE= intracardiac echocardiography
Abstract

Background: Since the release of the second generation cryoballoon (CB2; Arctic Front AdvanceTM) and the design modification with improved cooling characteristics, technique, dosing, and complication profile is significantly different compared to that of first generation cryoballoon. A comprehensive report of CB2 procedural recommendations has not been published.

Objective: To review the current best practices from a group of experienced centers to create a user's consensus guide for CB2 ablation.

Methods: High-volume operators with a combined experience of over three thousand CB2 cases were interviewed, and consensus for technical and procedural best practice was established.

Conclusion: Comprehensive review of the CB2 ablation best practice guide will provide the detailed technique of achieving safer and more effective outcome for CB2 AF ablation.

Introduction

Catheter ablation is an established tool in treatment of patients with atrial fibrillation (AF), and pulmonary vein isolation (PVI) has been a cornerstone strategy of the percutaneous management of paroxysmal AF. Unfortunately, long-term success has been constrained by the time-consuming and unpredictable nature of point-by-point focal ablation and the technical limitations on the effectiveness of ablation lesions to create a durable PVI. These procedural complexities have been historically notable with non-irrigated radiofrequency (RF) catheters and only marginally improved with external irrigation.
While focal RF catheters have been the standard-of-care for AF ablation \(^1\) balloon-based technologies were developed in an attempt to deliver ablative energy in a more continuous pattern without conduction gaps during cardiac tissue isolation. \(^3,4\) Since the USA release of the first-generation cryoballoon (CB1; Arctic Front™) in 2010, data from both single center studies and multicenter registries have demonstrated acute PVI and freedom from AF at comparable rates to RF. \(^1,5,6\)

The cryoballoon ablates with minimal disruption of the endothelium, creates relatively discrete lesions, and preserves the myocardial architecture, followed by replacement with fibrous tissue through the Joule-Thomson effect. \(^7\) The basic biophysical steps that result in cell death include formation of intracellular and extracellular ice crystals, causing withdrawal of intracellular water. Additional cell death is caused by consequences of cell thawing with the return of fluid into the cell causing cell membrane rupture.

The second generation cryoballoon (CB2; Arctic Front Advance™) was released in 2012, and it was designed to achieve more uniform cooling across the entire distal hemisphere of the balloon using eight injection tubes versus the original four-port design in CB1. \(^8,9\) Acutely, the time to achieve PVI has shortened and acute PV reconnection is rare, and chronically, freedom from AF seems to be higher in non-randomized studies. \(^10-18\) Also, the rates of PV reconnection in patients with recurrent AF are remarkably low compared with historic controls. \(^19\)

While research has indicated consistent patient outcomes with CB2, a comprehensive report of CB2 procedural recommendations has not been published. In an effort to drive consistent outcomes and minimize complications, this report serves to review the current best practices from a group of experienced centers to create a user’s consensus guide for cryoballoon ablation.
Best Practices: The Cryoballoon Ablation Procedure

Femoral and Left Atrial Access

The current Flexcath™ (Medtronic, Minneapolis, MN) sheath for the delivery of CB2 has an outer size of 15F, therefore the authors recommend initial femoral vein access has a shallow angle of entry, and then pre-dilation with a 14F short dilator. The Flexcath™ can be exchanged over a long stiff guidewire using a corkscrew motion or rotation for initial engagement. Full anticoagulation with IV heparin bolus should be given before initial transseptal access, as unacceptable incidences of thrombus formation has been observed via intracardiac echocardiography (ICE) shortly after any sheath placement in the left atrium even if heparin was given immediately after transseptal access. The target activated clotting time is recommended between 350-400 seconds. Patients who are already on warfarin typically would continue on therapeutic INR level. However, management of patients on novel oral anticoagulants management does vary, and most agree that until reversal agents are available, 12-24 hours freedom from the novel oral anticoagulants should be done. In general, anticoagulation management should not be different than prior AF ablation practices.

Initial left atrial access is best achieved using a standard transseptal sheath (both Mullins and SL-1 curve have been used), and then exchanged for FlexCath™ steerable sheath over a long stiff wire. We recommend a low anterior transseptal puncture that is near or on the limbus of the septum to allow more space for the balloon to be rotated posteriorly to the right inferior PV as well as mechanical advantages while accessing other PV [Figure 1]. Without sufficient distance between the puncture site and the RIPV, optimal balloon positioning and occlusion may be difficult. Also, a low puncture location improves balloon contact with the inferior aspects of the
PVs. We highly recommended using ICE to improve the safety of transseptal catheterization. ICE will also provide early detection of complications (e.g., catheter related thrombus and pericardial) in ablation cases. The location of the transseptal is best at the lower third of the septum, and anterior reach at the plane of ICE where the mitral valve is in view. [Figure 2] Bending of the distal 15cm portion of the typical transseptal needle can improve the transseptal needle engagement with the anterior portion of the septum.31

While monitoring with ICE and maintaining a steady manual pressure, a simple “clock” and “counter-clockwise” movement of the handle can ease the sheath across the septum. Slowly remove the dilator and exchange it for a guidewire. Occasional difficulties may be encountered pushing the Flexcath™ sheath across the septum especially at the transition of the dilator to the sheath. Some have found that option for placing the stiff exchange guidewire in left superior PV or maneuvering the guidewire to the right superior PV, will allow an easier push from inferior vena-cava directory across the septum and up toward the right superior PV in a straighter manner thereby overcoming the tougher septal transition. Next, aspirate (by syringe) approximately 15-20 cc to remove any possible air in the sheath while tapping the handle to release trapped air. Flush and connect the sheath to a low flow drip saline bag (1-3 cc/min).

After preparing the balloon and balloon-sleeve in heparinized saline, insert the cryoballoon into the sheath using the protective sleeve. Slowly advance the cryoballoon catheter over the entire length of the sheath. Advance the Achieve™ (Medtronic, Minneaplis, MN) mapping catheter using the cryoballoon shaft markers to confirm appropriate positioning. The mapping catheter should always lead the cryoballoon catheter to avoid trauma from the stiffer cryoballoon catheter tip. Fluoroscopy can be minimized by using markers on the cryoballoon body. When the first white band is at the valve of the sheath, this indicates that the balloon is at the distal tip.
of the sheath. The second white band indicates the cryoballoon is out of the sheath and ready for full inflation.

**Positioning and Occluding the Vein**

We describe six simple but critical maneuvers that can be utilized: to improve outcomes, to reduce complications, to ensure circumferential lesion creation, and to create substantial antral LA substrate modification. An antral level of isolation contributes to the success of the cryoballoon PVI, and it may reduce complications by maximizing the distance between the balloon and collateral structures beyond the LA chamber. The six critical maneuvers are given in chronological order, which include the following:

1. **When maneuvering the sheath to the desired PV, always lead the balloon with the soft tipped mapping catheter to avoid sheath trauma in the LA or PV.** Contrary to the focal RF catheter technique where the majority of catheter maneuvering is at the ablation handle, the majority of cryoballoon positioning is dependent on the sheath and maintenance of forward pressure on the balloon shaft. Since the cryoballoon sheath is stiff, there is a predictable 1:1 transference of movement force. Thus, the cryoballoon tool sets are easier to master and require shorter “learning” periods.

2. **Distal positioning of the Achieve™ (in the PV) will facilitate advancement of the balloon to the respective PV.** We recommend using the lower PV branch for isolation of inferior veins to provide the best angle for balloon engagement of the lower portion of the PV ostium, which is frequently the worst area of balloon-to-PV contact. Navigation of the Achieve™ into each of the PVs is best facilitated with the use of ICE, which can reduce
the need to use fluoroscopy. The PVs, FlexCath™, and Achieve™ are easily visualized with ICE.

3. Advance the balloon outside the sheath toward the PV ostium, while taking precautions not to deep seat the balloon. The sheath should be aligned with the angle of the targeted PV. Since balloon inflation occur using low pressure, it is unlikely to cause mechanical trauma to the PV; however, inadvertent inflation inside the PV should still be avoided.

4. Achieve™ can provide additional support for the cryoballoon, but majority of the control of the balloon-PV engagement is via the deflectable FlexCath™ sheath should be used to provide the primary support during PV occlusion, and the sheath can be advanced against the proximal hemisphere of the balloon during cryoablation for both support and catheter advancement for better occlusion. Achieve™ positioning relative to the balloon is not critically important as long as good balloon to PV antrum contact is maximized.

5. PV isolation is best achieved through the application of forward pressure to ensure the optimal balloon-to-PV ostium contact, which will result in successful isolation of the respective vein. With full occlusion of the PV, a 1-2 cc initial injection of radiopaque contrast will provide venographic evidence of balloon occlusion or leak detection.

   a. If the venogram does not reveal a leak at the ostium, do not immediately ablate. If no leak is visible on venogram, withdraw the cryoballoon slightly, and allow a leak around the PV-balloon interface to better define the PV ostium and ensure a proximal ablation. In some cases, this technique will reveal that the balloon was inside the PV and not at the PV ostium. Only re-apply the minimal amount of pressure needed to regain occlusion before ablation. This technique is often
denoted as the “proximal-seal” technique. Ablation can also be initiated prior to advancing the balloon to increase the balloon pressure and assist in keeping the balloon more proximal antrum, and thereby achieving a lesion set with closer resemblance to the typical wide-area-circumferential ablation. This technique also lessens the risk for phrenic nerve injury at the right superior PV. [Figure 3a and 3b]

b. If the venogram detects a leak, small adjustments with additional pressure toward the side of the leak will often secure occlusion at an optimal location. If complete occlusion cannot be made, then the PV antrum cross-section is likely more ovoid. In this case, separate application of ablation at different angle should be performed. Keeping in mind the area of best contact and the summation of the contact should surround the PV antrum. Performing Color-flow Doppler imaging to search for leak and poor contact may be used in place of contrast injection with a sweep of the array across the balloon. Utilizing ICE in Doppler mode imaging is particularly important consideration in patients with renal insufficiency or a history of contrast agent intolerance/allergic reaction(s).

6. Upon the best-fit occlusion above, the Achieve™ mapping catheter should be used to obtain PV potential recordings for real-time monitoring prior to initiation of the ablation. Torque can be applied to the Achieve™ mapping catheter to prolapse the circular mapping poles toward the antrum to be able to record approximately over 90% of all PV potentials to assess the time-to-isolation (TTI). Optimal Achieve™ position are demonstrated in Figure 1 and 3. One of the most critical indicators and predictors of permanent PV isolation is the TTI (best if less than 90 seconds). Reduction of the ablation time is also considered when a short TTI
is seen (less than 30 seconds) by reducing the total ablation time to 150 seconds. If desired, exit block from the PV can also be established during the ablation by pacing from the Achieve™. Rarely is Achieve™ required to provide distal cryoballoon anchoring for optimal positioning as a trade-off for the inability to record proximal PV electrogram-- most of the support to the balloon should be provided by the Flexcath™ sheath. In this setting, PV recording on the Achieve™ can be re-established after the initiation of a freezing cycle within approximately 10 seconds with a pull-back on the Achieve™ until the PV electrogram can be seen. After approximately 15 seconds into the freezing cycle, the central lumen is frozen, and wire cannot be moved.

**Pulmonary Vein Antrum Ablation**

Once the balloon is in the correct position at the PV antrum, the ablation process is initiated at the cryoconsole interface. Although a single operator technique is possible, a dual operator method is more common whereby the second operator is typically a nursing staff member who will assist in operations more distal to the cryoballoon catheter, including cryoconsole operation. The following five steps highlight the procedural period that is encompassed during the cryoballoon ablation.

1. Before ablation, prepare a small 1cc injection of contrast to ensure continued occlusion after freeze initiation. In some cases, the onset of freezing and balloon compliance change can dislodge the balloon and create a leak.

2. We recommend a 180s initial ablation with CB2, at a minimal temperature no colder than -55°C.
3. Maneuvering of the cryoballoon after initiation of ablation should be avoided. A “post-cryo initiation” maneuver may increase the risk of mechanical trauma and provide a false sense of durable ablation. Within the first 15 seconds of ablation, a layer of ice can be observed on the surface of the balloon which will act as a thermo-barrier and decrease energy transfer to the tissue. The acute block that may be observed before initiating a pull-down technique is transient. If a lower positioned seal is challenging, it is better to improve the ablation by ablating the upper portion of the PV ostium and then the lower portion of the PV ostium in two full separate applications. This situation does occur frequently as the majority of the PV antrum cross-sections are ovoid.

4. After freeze application, allow the balloon and tissue interface to thaw. The post-ablation thawing process can be slow. Do not move the balloon catheter until the catheter temperature reading reaches 35°C (even though the balloon automatically deflates at 20°C). The balloon may remain attached to tissue after balloon deflation in a phenomenon known as “late-adhesion” and mechanical manipulation might result in tissue damage or even perforation.

5. Before the second freeze, initiate the freeze and allow the balloon to enlarge and stiffen, then engage the PV ostium. The ostium should be fully engaged on the second ablation. This maneuver can help expand the antral location of the intended lesion and can be confirmed on ICE with the equator of the balloon outside of the vein yielding the “golf ball on a tee” appearance.[Figure 4]

To enhance the time-saving advantage of cryoballoon ablation, parallel processing and planning can be performed during the freeze cycle. Review the venogram of the current ablation to assess contact and determine if another ablation at a different angle is needed. The operator
can also review the PV venogram and plan the next ablation site, balloon angle, or target branches for placement of the Achieve™ catheter. Also, while ablating the left-sided PV, the operator can identify an optimal pacing location for the right phrenic nerve. This will save procedure time when transitioning from left- to right-sided PV.

**Cryoballoon Dosing and Temperature**

Various dosing regimens exist with recommendations from 2 to 5 minute per freeze. Historically, four minutes was the standard for CB1 based on procedures in the STOP AF clinical trial protocol.\(^5\) Since the release of CB2, shorter application times have been explored as a strategy to avoid collateral tissue injury without compromising efficacy. For example, a recent investigation by Ciconte et al. demonstrated an 80% freedom from AF in 143 consecutively enrolled subjects treated with a single 3 minute freeze using CB2.\(^18\)

The operator must understand the physiology of cryoenergy transfer to understand dosing. In brief, cryoballoon energy transfer is dependent on the source of cryoenergy, balloon-tissue contact area, collateral warming, and time. The two most important operator controlled factors are time and balloon-tissue contact. These two factors (along with nadir temperature) will have a direct impact on lesion depth in an exponentially decrementing manner. Simply, longer ablation time will correlate to a deeper lesion; however, the final ablation time is shortened when considering the balance of safety and collateral tissue freezing. Lastly, this longer ablation time to deeper lesion correlation is not completely linear. There is a penultimate depth of lesion penetration (regardless of time) that is established by the limitation of heat dissipation over space.
While the operator does not directly control nadir temperature, it is important for operators to understand and monitor temperature during the procedure. Importantly, the operator does determine when to terminate a freeze. The temperature displayed on the CryoConsole is not tissue temperature, and it is instead a return gas temperature measurement. The balloon-tissue interphase temperature is typically -70 to -80°C, but the temperature on the CryoConsole is the return gas temperature, and it often ranges between -40 to -50°C for optimal lesions. Therefore, the only conclusion that can be made from the return gas temperature is: if the temperature is cold, e.g. below -40°C, it likely reflects good tissue ablation. A steep, and rapid descent in temperature (colder than -40°C at 30 seconds), and nadir temperatures of -55 to -60°C are potential indicators of a distal cryoballoon location (rather than an antral position). The authors recommend that the ablation be terminated in either scenario and cryoballoon positioning confirmed.

The most important physiologic endpoint to predict successful PVI is TTI as identified by the Achieve™ catheter, as this is the only true tissue physiology that can be monitored. PV potentials should be closely monitored at the initiation of the freezing cycle, during the freeze, and after the ablation is complete. While data is needed to clearly correlate long term outcomes with abbreviated freeze protocols, our experience supports a more conservative dosing time of 150s if TTI is achieved at 30s or less. If the PV is not isolated within 180s, we recommend against increasing time or advancing the cryoballoon deeper into the PV. Rather, the operator should modify the cryoballoon-tissue contact.

To allow deep tissue warming, maximize cryoablation efficiency, and reduce risk of collateral damage, the authors recommend against an immediate follow-up application if the cryoballoon nadir ablation temperate reach below -55°C. This tissue re-warming time may potentially reduce
the risk of phrenic nerve or esophageal injury. If desired, ablation can be performed at another target PV while allowing warming.

In regards to dosing, esophageal temperature monitoring, as discussed later in this paper may also be helpful. For example, application of a 180s first lesion is rarely associated with an esophageal temperature below 25°C. Reducing application duration during a repeat freeze to 150s, or less, may be warranted due to the faster temperature decline on the repeat freeze thus avoiding deeper tissue injury. Repeated ablations for more than two times at a similar location should be avoided to prevent collateral injury.

Safety Considerations

As demonstrated in recently published studies, the improved cooling characteristics of CB2 translate into improved acute and long-term efficacy. However, enhanced cooling characteristics may also result in a greater potential for collateral damage to non-cardiac structures such as the phrenic nerve and the esophagus. The authors recommend closely monitoring temperature, application duration, contact force, anesthesia, TTI, type of esophageal tissue, and distances between the catheter and collateral structures (the phrenic nerve, lungs, and esophagus). We discuss techniques to avoid phrenic nerve injury and esophageal damage, below.

Prevention of Phrenic Nerve Injury

Right phrenic nerve (PN) palsy is the most common complication associated with cryoballoon ablation; persistent phrenic nerve injury (PNI) lasting post-procedure has been reported as high as 8.3%. Our experience suggests that the risk for persistent PNI can be minimized by ensuring the cryoballoon position is as antral as possible as described in above ablation section. Most importantly, actively monitoring the phrenic nerve during ablation, and terminating
ablation immediately at the first sign of hypothermic effect. To pace and monitor PNI, paralytics should not be administered during cryoablation—if paralytics have been administered during the induction of general anesthesia, sufficient time should be allowed for the paralytic effect to reverse prior to ablation, or neostigmine may be used as a reversal agent.

To monitor PN function, the nerve should be paced at twice the capture threshold using a deflectable catheter. We recommend that the pacing catheter be placed in the superior vena cava (SVC) and above the level of the ablation. A consistent site for PN capture is near the junction of the SVC and the right subclavian vein or the anterolateral portion of the SVC, near the atrial-SVC junction.

Palpation of the strength of diaphragmatic excursion during PN pacing, below the costal margin is the most common method of monitoring PN function. In addition to palpation, the monitoring of diaphragmatic compound motor action potential (CMAP) can increase the sensitivity of PNI early detection [Figure 5]. Combining CMAP and palpation had decreased the incidents of PNI to less than 1.5%. Several other methods have been proposed to monitor the PN in conjunction with CMAP and palpation as ICE, fetal heart monitor and external thoracic pressure monitor (Table 1) A detailed review of all the methods of monitoring of PN had been reported by Kowalski et.al. The ICE catheter can also provide confirmation of correct positioning of the balloon by visualizing the main portion of the balloon outside of the vein reduces the risk of freezing deeply in the vein and reducing the risk of PNI [Figure 4].

Once PNI occurs the operator should immediately stop ablation by “double stop” technique, or immediate balloon deflation. Ghosh et al. concluded that rapid balloon deflation results in more rapid tissue rewarming resulting in preventing persistent PNI, with no adverse events.
Continues pacing of the PN could assist in evaluating the time for recovery of function. If the
duration of recovery is short, another ablation can be attempted after wiring a different PV
branch and with more antral position of the balloon. If palsy persists after the procedure, it is
recommended to perform an inhalation-exhalation chest x-ray to establish a baseline for PNI for
comparison at later time to assess recover. Intravenous steroids may be administered to decrease
inflammation.

**Prevention of Esophageal Injury**

Esophageal injury is a complication observed in both RF and cryoablation procedures, and it
is a direct result of the proximity of the esophagus and the posterior wall of the left atrium. The
severity of the injury can vary, and manifests as esophageal erythema, esophageal ulcer/lesion, or
atrioesophageal fistula. Recent research has demonstrated CB2 esophageal lesion rates of 3.2 to
19%, as observed through post procedure endoscopies with the lowest rates (3.2%) reported
when a LET cut-off of 12-15°C is used. When LET, and other measures are used, damage
can be limited to esophageal lesions, which frequently heal in a few weeks. If unmonitored,
esophageal damage may result in rare and generally fatal, atrioesophageal (AE) fistulas. The
reported rate of AE fistula with CB1 and CB2 is approximately 1 out of 10,000, while the
incidence of AE fistula with RF varies between 0.1% (1 out of 1,000) and 0.25% (1 out of
400). While the root cause has not been determined, caution should be used when treatment
time exceeds four minutes, more than two freezes are applied to a PV, and balloon nadir
temperatures exceed -60°C.

The impact of CB2 ablation on esophageal thermal injury was recently investigated by two
different groups. Freeze-cycles of 240s were followed by a safety freeze-cycle of another 240
sec. While Metzner et al. did not have a predefined temperature cut-off, Fürnkranz et al.
stopped the freeze cycles at an esophageal endoluminal temperature of \(<5^\circ\text{C}\)\(^{26}\). The lowest temperature in the esophagus and the lowest temperature in the CB were noted. Post ablation all patients were treated with pantoprazol 40mg daily for 6 weeks, an endoscopy was performed two days post ablation. Metzner \textit{et al.} demonstrated an incidence of esophageal thermal injury of 12\% (6/50 patients),\(^{25}\) while the publication by Fürnkranz \textit{et al.} reports an incidence of 19\% (6/32 patients).\(^{26}\) As compared to esophageal thermal lesions after radio-frequency based ablation, lesions after CB ablation tend to be more superficial as most patients were completely asymptomatic and all lesions were resolved during repeat endoscopies. Importantly, none of the patients developed an atrial-to-esophageal fistula.

Based on their statistical analysis of correlating the lowest esophageal temperature and the endoscopic findings Metzner \textit{et al.} recommend an esophageal temperature cut-off of 10\(^\circ\text{C}\) (sensitivity 100\%, specificity 93\%),\(^{25}\) while Fürnkranz \textit{et al.} suggest a cut-off of 12\(^\circ\text{C}\) (sensitivity 100\%, specificity 92\%) for causing esophageal fistula injury.\(^{26}\) While this research brings us closer to better understanding techniques to prevent esophageal injury, it is very important to understand that no direct correlation has been made between esophageal fistula formation and temperature. There may be other predisposing factors, which are more important than temperature alone. The suggested endoluminal esophageal temperature cut-off values will have to be evaluated prospectively in future studies; however, consideration of the currently recommended minimal esophageal temperatures may contribute to safer use of CB2.

In the interim, as outlined in the 2012 HRS/EHRA/ECAS expert consensus statement, the authors reinforce luminal esophageal temperature monitoring, a barium swallow to outline the
esophagus, duration of energy application, prescription of proton pump inhibitors, and reduced contact force as options to minimize esophageal injury.\textsuperscript{1}

**Post-ablation Care**

Immediate post-ablation testing should be similar to that of the other AF ablation methods, however authors experience to date finds the use of adenosine to assess PV connection recovery has had limited use and rarely positive. Post-procedure groin management is also not different compared to traditional radiofrequency ablation. There has not been any increased rate of groin access complication due to larger sheath size. Post-ablation anticoagulation duration, with the consideration of less endocardium injury with cryoablation, is considered to be adequate at 1 month time-- this duration correlates with the complete tissue healing time observed in animal and \textit{in vivo} experience.

**Outcomes**

Cryoablation is a safe and effective tool for the treatment of paroxysmal AF with a high rate of durable procedural PVI,\textsuperscript{19} and long-term freedom from AF.\textsuperscript{10-18} Eight single center studies published on CB2, have demonstrated single procedure, off AADs, freedom from AF equal to or better than 80\%.\textsuperscript{10-18} Whereas, Freedom from PAF in recent, large RF multi-center studies and surveys (since 2010), including clinical study results from recent RF technology advancements, is reported to be 61-74\%.\textsuperscript{1,30} Also, RF catheter studies evaluating PVI durability at remapping procedures have reported between 23-35\% of patients had complete PVI at 3 months and only 8\% of patients at 12 months.\textsuperscript{1} The safety profile for the two therapies is similar. In a large multi-center registry (German Ablation Registry),\textsuperscript{6} the overall rate of major complications were similar
for cryo (CB1) and RF (4.6% for both groups); with PNP nearly half of cryo complications (2.1%).

**Conclusion**

In summary, cryoballoon ablation of atrial fibrillation is a useful tool for pulmonary vein isolation and antral modification. Specific technical recommendations were discussed in detail, which will make the cryoballoon procedure a safer and more effective tool for the treatment of atrial fibrillation.

**References:**


Figure Legends:

**Figure 1:** RAO view of right inferior PV cryoballoon engagement angle when transseptal site is lower and more anterior. Example of patient with atrial septal occlusion device at the secundum defect location is shown to better demonstrate the transseptal location.

**Figure 2:** A) ICE demonstrating lower and more anterior transseptal access (Arrow). RA= Right Atria, LA= Left Atria, MV= Mitral Valve, and arrow is the transseptal site. This demonstrates the transseptal sheath through the inferior septum location with thicker inferior limbus, as well as the anterior position with MV seen on ICE. B) Anatomical layout of optimal transseptal site (in white oval). Image modified courtesy of Visible Heart Lab, University of Minnesota. Associated movie clip shown.

**Figure 3:** The Proximal Seal Technique: Instead of initiating ablation after initial venogram, CB is first gently pulled back to reveal the real PV ostium by noting contrast leak. Notice the true antrum is much further back than initially realized. a) CB at left superior PV and venogram b) CB pulled back to reveal the real PV ostium. Associated movie clip shown.

**Figure 4:** Intracardiac ultrasound image of CB at left inferior PV and color Doppler revealing flow from left superior PV. CB outside of the PV antrum forming the “golf ball on tee” image. Associated movie clip shown.

**Figure 5:** Recordings of the diaphragmatic compound motor action potential (CMAP) during pacing from the CS catheter at 60 bpm located in the SVC and during application of cryo-energy to the right superior pulmonary vein. The CMAP amplitude (*) significantly decreased at 180 seconds of cryoballoon application. Notice that the pulmonary vein is isolated. At the time of phrenic nerve palsy the CMAP amplitude is a fraction of the baseline CMAP amplitude. The CMAP amplitude increased after the cryo-energy was discontinued but did not return to its original value. A decrease in CMAP amplitude by 35% from baseline predicted and prevented PNI. (Lakhani M, Saiful F, Parikh V, Goyal N, Bekheit S, Kowalski M. Recordings of diaphragmatic electromyograms during cryoballoon ablation for atrial fibrillation accurately predict phrenic nerve injury. Heart Rhythm. 2014 Mar;11(3):369-74. doi: 10.1016/j.hrthm.2013.11.015.)
Table 1: Pros and cons of various PN monitoring strategies


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<th>Method</th>
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<th>Disadvantages</th>
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<td>Fluoroscopy</td>
<td>Direct visualization of diaphragmatic motion</td>
<td>• Sensitive method for monitoring diaphragmatic motion</td>
<td>• Additional radiation exposure to the patient and the operator • Does not predict PN injury</td>
</tr>
<tr>
<td>Palpation</td>
<td>Palpation of diaphragmatic excursion</td>
<td>• Reliable and practical method for monitoring diaphragmatic motion</td>
<td>• Requires additional staff member • The palpable strength of diaphragmatic excursion may vary with respiration</td>
</tr>
<tr>
<td>Electromyography</td>
<td>Recording of diaphragmatic compound motor action potential (CMAP) by two standard surface electrodes positioned across the diaphragm or by advancing a quadripolar catheter in the right-hepatic vein during PN pacing</td>
<td>• Earliest detection of PN injury • Simple reliable and easily applicable • The only technique that predicts PN injury</td>
<td>• CMAP signals might be susceptible to respiratory variations. • The baseline amplitude must be adequate • Affected by paralytic agents</td>
</tr>
<tr>
<td>Auditory cardiotocograph</td>
<td>Decrescendo pitch on fetal heart monitor (placed across patient’s chest that can detect diaphragmatic contractions)</td>
<td>• Auditory cue to the operator • May portend PN injury prior to palsy</td>
<td>• Extra equipment difficult to record in obese patients</td>
</tr>
<tr>
<td>Intracardiac echocardiogram (ICE)</td>
<td>Direct visualization of diaphragmatic excursion</td>
<td>• minimal radiation exposure to the patient and the operator</td>
<td>• Requires additional venous access and intra-cardiac ultrasound</td>
</tr>
</tbody>
</table>
Baseline CMAP | Decrease in CMAP during Freeze | Prenic Nerve Palsy | Recovery
---|---|---|---
Modified 1 | * | * | *
V1 | | | |
aVF | | | |
CS 1,2 | | | |
LS 1,2 | | | |
LS 2,3 | | | |
LS 3,4 | | | |
LS 4,5 | | | |
LS 5,6 | | | |
LS 6,7 | | | |
LS 7,8 | | | |

Fig 5