Dear Nam Nguyen and two peer reviewers,

Thank you for the thoughtful comments. We have elected to accept all comments and have made revisions to the manuscript accordingly. Reviewer #1 is especially well versed in the cryoablation literature, and we thank this reviewer for the insightful comments. Below are our descriptions of the changes that can be found in the new manuscript version. We believe that comment #7 was important, but we simply did not collect the data in this manner. Our hope is that we have addressed this comment #7 to the satisfaction of the reviewer.

Best regards,   
Hae Lim and Dr S. Adler

From Nam:  
1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues. The JoVE editor will not copy-edit your manuscript and any errors in the submitted revision may be present in the published version.

* Thank you. We have proof read the manuscript.

2. 1.3.2: Please express the centrifugation speed in terms of x g. file.

* We have now expressed this measurement as Xg and RPM.

3. Visualization: Please provide an SW file for all highlighted material in the protocol to orient the scriptwriter regarding any images/screenshots to be included in the video in addition to videographer footage.

* The SW file is now attached.

4. Formatting:

-3.7 should be reorganized to include timing and cycles in the appropriate position in the substeps.

* The steps have been reorganized in order.

-Figure 5 legend – Please describe what is shown the figure rather than describing the outcome. (What is shown in 1-10?)

* The legend has been corrected.

5. Discussion: What troubleshooting/modifications could be performed?

* The 2nd to last paragraph of the discussion now contains some troubleshooting guidance.

6. Continuity: Are steps 3.1, 3.2, 3.6, and 4.2 nonessential? There is room to incorporate more steps into the protocol if the authors wish to film them.

* Thank you. With the room available, these steps have been selected for incorporation.

From reviewer #1:  
1) On page 2 in the introduction section it is stated, that radiofrequency catheter ablation is the typical method when a surgical intervention is necessary.   
A catheter ablation is an electrophysiological interventional catheter based treatment, not a surgical one.

* Thank you for this catch. The sentence has been rewritten.

2) The number of enrolled patients is low, what is significant limitation stated in the manuscript. It is mentioned, that in all patients a 3D EAM system was used to guide the cryofocal catheter. Please describe in detail, which system was used and how the anatomical reconstruction of the RA model was performed, and which catheter was used. The use of a 3D EAM system in Cryoballoon ablation procedures for pulmonary vein isolation is not standard of care, however, it is exceptional to use it in the described setting. Please comment also on the economic aspects of using the described setting, especially in combination with the use of ICE.

* Thank you for this suggestion. Section 4.7 now includes more details of the RA mapping using 3D EAM.
* Also, the last paragraph of the discussion now including careful thoughts about the economic aspect.
* Specifically, the 3D EAM system used here is an Ensite Velocity system with the Precision mapping module and NavX guidance system. However, the journal format rules do not allow the usage of specific products names within the text of the manuscript.

3) On page 5 it is described how to introduce the transseptal sheath. Rather introducing a guide wire into the LA I would recommend to introduce the guide wire into the left superior pulmonary vein.

* Thank you, we agree and have made this change.

For the introduction of the cryoballoon catheter this guidewire was used. An intraluminal circular mapping catheter, which can be used instead of a guide wire, is available. Why was that catheter not used?

* The Achieve mapping catheter can be used here in replacement of the guidewire. Although this is not Dr Adler’s usage protocol, this has now been noted in the manuscript as an alternative or option.

What specific circular mapping catheter was used to confirm isolation of the pulmonary veins? Please describe the "pace and capture" protocol used in detail.

* Thank you, we have described the mapping catheters used by their generic description based on journal rules. Additionally, we have further described the entrance and exit block testing (pace and capture protocol). Lastly, we have given a reference for more extensive testing techniques as described by Andrade et al 2015.

4) On page 6 (3.9) it is described how the monitoring of the phrenic nerve function was monitored during the freeze. Why has the technique of CMAP not been used for more intensive monitoring of the nerve function?

* Thank you. While we did not CMAP monitor phrenic nerve function during this protocol, we do agree that this method is important and have put it into the protocol as an additional usage.

5) In 3.6.4 it is described how PV occlusion with the cryoballoon was assessed. Because ICE has been used in each of the patients, it would have been elegant to demonstrate possible leaks during cryoballoon positioning at the PV using ICE imaging. Please comment.

* Yes, we agree. The usage of ICE is now included with directions.

6) On page 11 it is mentioned that the catheter used in the CryoCor study is a novel cryoablation catheter. As far as I am informed the CryoCor catheter is not available any more since years. The study was published in 2008, however, further safety and efficacy aspects will not be available in the future. Please comment.

* Thank you. We have edited this paragraph more carefully and in agreement with your comment.

7) It is stated by the authors, that this study records the shortest mean procedure time of 30 minutes. In table one the total procedure time including cryofocal and cryoballoon ablation is 240.6 min, so approximately 4 hours. In recent publications reporting of PVI using the Cryoballoon system procedure times for PVI were approximately 100-120 minutes. Please provide detailed data of exact procedure times for PVI using Cryoballoon and for the Isthmus ablation using cryofocal ablation. A procedure time of 30 minutes is not plausible due to the fact, that total cryofocal ablation time for atrial flutter was 29.7 minutes. This needs to be clarified. In table 1 total procedure times in total, for PVI only and for AFlut only should be stated, also cryoablation times in the same manner.

* We feel that there is some data confusion here, due to our terminology usage. So we have tightened the language throughout the manuscript.
  + We absolutely agree that upon retrospective examination of the data that we should have separately collected a PVI procedure time and an AFL procedure time during the collection of data. However, we did not collect this data.
* Consequently, below are our clarifying statements.
* The ~30 minute cryoapplication time (29.7 min) to complete an AFL ablation is amongst the shortest reported thus far with Montenero and Kuniss reporting 45 and 40 min, respectively.
* The ~240 minute is the total procedure time (skin to skin; femoral puncture to last catheter exit).
  + We agree that there have been more recent balloon protocols with AFAdv that use shorter application times to achieve 120 minute procedures, but we were not using these shorter protocols during this study.
  + And we are not sure (or convinced) that everyone is reporting skin to skin time which is more akin to total physician time.
* We did not record our PVI time in this study, as it was not our original design intent of the study. Admittedly, our table will be missing a PVI procedure time and an AFL procedure time.
  + This study is not trying to report a short cryoballoon usage time, and it does not give protocol advice that would promote short cryoballoon times.
    - As an example, we did not use Achieve and instead used a conventional circular mapping catheter which did add time (during PVI) due to exchange between balloon and circular catheter to confirm block at each PV.
* Instead, some physicians feel that usage of cryofocal ablation for AFL is not possible because of the lengthy procedure and we wanted to offer a protocol that may shorten the procedure (a bit).
  + By reducing the AFL ablation time by ~15 minutes, this protocol achieves the original study goal of finding a protocol that is closer to an RF ablation time of AFL while still maintaining safety and efficacy.

8) Please describe the new methodology how to place the cryofocal lesion sets more in detail. Is the use of a 3D EAM system possibly of greater advantage compared to the novel lesion set? Please comment on that in the discussion section.

* Yes, the 3-D EAM is critically important, and the first discussion paragraph now reflects this comment.

**Reviewer #2:**   
*Manuscript Summary:*  
It is a nice paper even though it describes an old technique.