Atrial Fibrillation

“Technique of Cryoablation”

Kaoru Okishige, M.D., F.H.R.S., F.A.C.C., F.J.C.S.

Heart center
Japan Red Cross Yokohama City Bay Hospital
Yokohama, Japan

2019 KHRS in Seoul
Grand Walkerhill Seoul Hotel
Settings and Procedures for Cryoballoon Ablation

• Total anesthesia
• Single atrial septal puncture
• 3D mapping system is not always required.
• Gap sites along PV ostium have to be ablated with spot RF ablation catheter.
“Pull Down Technique”

Leakage (+) → Cryo-adherence → Leakage (-) → Pull down
Pull-down technique
Nadir Temperature Differences between Successful And Unsuccessful PVI

![Graph showing nadir temperature differences between successful and unsuccessful PVI. The graph compares complete PVI with incomplete PVI, highlighting temperature plateaus at different freezing durations.](image)
Classification of Occlusion Grade

Grade 1 = poorest occlusion
Grade 2 = secondly poorest occlusion
Grade 3 = thirdly poorest occlusion
Grade 4 = complete occlusion

1620 cases (20\textsuperscript{th} in June, 2019)
Freeze and Thaw

Slope 1

Slope 2
Comparison by PV occlusion status

* $P < 0.001$  # $P = 0.002$  + $P = 0.001$

Grade 4 = complete occlusion, 3 = trivial leakage, 2 = moderate leakage, 1 = massive leakage

Clinical results according to the occlusion grade

Clinical Assessment of cryoballoon ablation for cases with left common pulmonary vein

Takatoshi Shigeta, Kaoru Okishige, Hideshi Aoyagi, Takehiko Keida, Yasuteru Yamauchi, Tetsuo Sasano, Kenzo Hirao.
Japan Red Cross Yokohama City Bay Hospital

J Cardiovasc Electrophysiol 2017;28:1021-1027
## Patients Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 501)</th>
<th>Group A (n = 28)</th>
<th>Group B (n = 473)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65±10</td>
<td>65±12</td>
<td></td>
<td>0.90</td>
</tr>
<tr>
<td>Gender (male; n, %)</td>
<td>19 (68)</td>
<td>335 (71)</td>
<td></td>
<td>0.83</td>
</tr>
<tr>
<td>Hypertension (n, %)</td>
<td>10 (36)</td>
<td>215 (46)</td>
<td></td>
<td>0.34</td>
</tr>
<tr>
<td>Diabetes mellitus (n, %)</td>
<td>4 (14)</td>
<td>53 (11)</td>
<td></td>
<td>0.55</td>
</tr>
<tr>
<td>Paroxysmal atrial fibrillation (n, %)</td>
<td>19 (68)</td>
<td>374 (79)</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>62±12</td>
<td>64±10</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>Left atrial diameter (mm)</td>
<td>41±7</td>
<td>41±7</td>
<td></td>
<td>0.92</td>
</tr>
</tbody>
</table>
The percentage of required touch-up ablation for successful PVI

p = 0.15

We were successfully able to isolate all left common PVs.
Total procedure time

Group A: 145 ± 24
Group B: 144 ± 28

p = 0.57

J Cardiovasc Electrophysiol 2017;28:1021-1027
Phrenic nerve injury (PNI)

Group A

Group B

PNI+ 11.1%
PNI- 16.4%

p = 0.78

J Cardiovasc Electrophysiol 2017;28:1021-1027
The clinical outcomes of the ablation

<table>
<thead>
<tr>
<th>Group</th>
<th>LCPV(+)</th>
<th>LCPV(-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>11</td>
<td>24</td>
</tr>
<tr>
<td>Group B</td>
<td>8</td>
<td>25</td>
</tr>
</tbody>
</table>

**p = 0.02**
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Univariate</th>
<th></th>
<th>Multivariate</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>P</td>
<td>B</td>
<td>P</td>
</tr>
<tr>
<td>Age</td>
<td>1.01</td>
<td>0.65</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Gender</td>
<td>1.03</td>
<td>0.93</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.90</td>
<td>0.76</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.18</td>
<td>0.74</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td>1.00</td>
<td>0.88</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Left atrial diameter</td>
<td>1.04</td>
<td>0.12</td>
<td>1.05</td>
<td>0.08</td>
</tr>
<tr>
<td>The presence of a LCPV</td>
<td>2.62</td>
<td>0.04</td>
<td>3.03</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Cox regression analysis for predicting atrial tachycardia.
Esophageal Injury by CB

Clinical investigation of esophageal injury from cryoballoon ablation of persistent atrial fibrillation

Takatoshi Shigeta MD¹,² ID | Kaoru Okishige MD¹ ID | Hideshi Aoyagi MD¹
Takuro Nishimura MD¹ ID | Rena A. Nakamura MD¹ | Naruhoiko Ito MD¹
Yusuke Tsuchiya MD¹ | Mitsutoshi Asano MD¹ | Tsukasa Shimura MD¹
Hidetoshi Suzuki MD¹ | Manabu Kurabayashi MD¹ | Yuichi Fukami MD³
Shinya Sakita MD³ | Takehiko Keida MD⁴ | Tetsuo Sasano MD² | Kenzo Hirao MD²
Yasuteru Yamauchi MD¹

DOI: 10.1111/pace.13578
Let = luminal esophageal temperature

A. LET (°C)

- ELs+ (p=0.17)
- ELs-

B. LET (°C)

- GH+ (p=0.23)
- GH-

EL = esophageal lesion
GH = gastric hypomotility
## Logistic regression analysis for ELs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age</td>
<td>0.98</td>
<td>0.92-1.04</td>
</tr>
<tr>
<td>Male gender</td>
<td>3.04</td>
<td>0.37-25.20</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2.44</td>
<td>0.57-10.50</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.76</td>
<td>0.60-0.97</td>
</tr>
<tr>
<td>Left atrial diameter</td>
<td>0.99</td>
<td>0.90-1.10</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td>0.97</td>
<td>0.92-1.02</td>
</tr>
<tr>
<td>touch up ablation for PVI</td>
<td>0.46</td>
<td>0.06-3.87</td>
</tr>
<tr>
<td>touch up ablation for the LAPW</td>
<td>0.50</td>
<td>0.06-4.20</td>
</tr>
<tr>
<td>nadir LET</td>
<td>0.90</td>
<td>0.77-1.05</td>
</tr>
<tr>
<td>Premature termination of ablation due to low LET</td>
<td>1.31</td>
<td>0.37-4.61</td>
</tr>
</tbody>
</table>
Thromboembolic events
Incidence of silent cerebral infarctions after catheter ablation of atrial fibrillation utilizing the second-generation cryoballoon

Tomofumi Nakamura¹*, Kaoru Okishige¹, Toshiro Kanazawa², Mitsumi Yamashita¹, Naohiko Kawaguchi¹, Nobutaka Kato¹, Hideshi Aoyagi¹, Yasuteru Yamauchi¹, Tetsuo Sasano³, and Kenzo Hirao³

¹Heart Center, Yokohama City Bay Red Cross Hospital, 1-12-3 Shin-yamashita, Naka-ward, Yokohama, Japan; ²Department of Neurology, Yokohama City Bay Red Cross Hospital, 1-12-3 Shin-yamashita, Naka-ward, Yokohama, Japan; and ³Heart Rhythm Center, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo, Tokyo, Japan

Received 24 February 2016; accepted after revision 29 May 2016
Representative Cases with asymptomatic CI

- DWI
  - 3-4 mm
- FLAIR
- DWI
  - 4 × 7 mm
- FLAIR
Comparative study of hemorrhagic and ischemic complications among anticoagulants in patients undergoing cryoballoon ablation for atrial fibrillation

Kaoru Okishige (MD)\textsuperscript{a,*}, Tomofumi Nakamura (MD, FACC)\textsuperscript{a}, Hideshi Aoyagi (MD)\textsuperscript{a}, Naohiko Kawaguchi (MD)\textsuperscript{a}, Mitsumi Yamashita (MD)\textsuperscript{a}, Manabu Kurabayashi (MD)\textsuperscript{a}, Hidetoshi Suzuki (MD)\textsuperscript{a}, Mitsutoshi Asano (MD)\textsuperscript{a}, Tsukasa Shimura (MD)\textsuperscript{a}, Yasuteru Yamauchi (MD)\textsuperscript{a}, Tetsuo Sasano (MD)\textsuperscript{b}, Kenzo Hirao (MD)\textsuperscript{b}

\textsuperscript{a}Heart Center, Yokohama-city Bay Red Cross Hospital, Yokohama City, Japan
\textsuperscript{b}Arrhythmia Center, Tokyo Medical and Dental University, Tokyo, Japan
Silent Cerebral Ischemic Events among DOAC Tx

P=0.7472

Okishige, K et al., J Cardiology 2017;69:11-15
Anticoagulation strategy during perioperative period
DOACs were administered depending on the status of consciousness.

(A) conventional interrupted DOACs

- rivaroxaban
- edoxaban
- dabigatran
- apixaban

**Day 1**: Initial DOAC administration

**Day 2**: Catheter ablation and Heparin bridge

**Day 3**: MRI

**Day 4**: Discharge

(B) uninterrupted dabigatran

- rivaroxaban
- edoxaban
- dabigatran
- apixaban

**Day 1**: Initial DOAC administration

**Day 2**: Catheter ablation with dabigatran administration

**Day 3**: MRI

**Day 4**: Discharge

## Results

<table>
<thead>
<tr>
<th></th>
<th>Conventional way</th>
<th>Uninterrupted DB way</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A n=229</td>
<td>Group B n=42</td>
<td></td>
</tr>
<tr>
<td>Cerebral Embolism (%)</td>
<td>69 (30)</td>
<td>4 (9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>symptomatic, (%)</td>
<td>1 (0.004)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding events, (%)</td>
<td>17 (7)</td>
<td>4 (9)</td>
<td>0.54</td>
</tr>
<tr>
<td>bleeding at puncture site</td>
<td>10</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>pericardial effusion</td>
<td>6</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>hemorrhagic gastric ulcer</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Idarucizumab for cardiac tamponade

“Clinical Experience of Idarucizumab Use in Cases of Cardiac Tamponade under the Uninterrupted Anticoagulation during Catheter Ablation for Atrial Fibrillation.”

Data from 14 institutions in Japan

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age</th>
<th>Creatinine level (mg/dL)</th>
<th>Creatinine clearance (mL/min)</th>
<th>DOACs before ablation (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>female</td>
<td>84</td>
<td>0.58</td>
<td>49</td>
<td>apixaban (5)</td>
</tr>
<tr>
<td>2</td>
<td>female</td>
<td>51</td>
<td>1.34</td>
<td>99</td>
<td>dabigatran (300)</td>
</tr>
<tr>
<td>3</td>
<td>female</td>
<td>73</td>
<td>0.62</td>
<td>48</td>
<td>edoxaban (30)</td>
</tr>
<tr>
<td>4</td>
<td>male</td>
<td>88</td>
<td>0.82</td>
<td>49</td>
<td>apixaban (5)</td>
</tr>
<tr>
<td>5</td>
<td>male</td>
<td>67</td>
<td>0.88</td>
<td>97</td>
<td>rivaroxaban (15)</td>
</tr>
<tr>
<td>6</td>
<td>male</td>
<td>77</td>
<td>0.71</td>
<td>78</td>
<td>dabigatran (220)</td>
</tr>
<tr>
<td>7</td>
<td>female</td>
<td>54</td>
<td>0.80</td>
<td>122</td>
<td>edoxaban (60)</td>
</tr>
<tr>
<td>8</td>
<td>female</td>
<td>80</td>
<td>0.53</td>
<td>56</td>
<td>apixaban (5)</td>
</tr>
<tr>
<td>9</td>
<td>female</td>
<td>78</td>
<td>0.79</td>
<td>55</td>
<td>dabigatran (220)</td>
</tr>
<tr>
<td>10</td>
<td>female</td>
<td>78</td>
<td>0.72</td>
<td>59</td>
<td>dabigatran (220)</td>
</tr>
<tr>
<td>11</td>
<td>female</td>
<td>71</td>
<td>1.09</td>
<td>40.88</td>
<td>dabigatran (220)</td>
</tr>
<tr>
<td>12</td>
<td>female</td>
<td>69</td>
<td>0.67</td>
<td>63.6</td>
<td>dabigatran (300)</td>
</tr>
<tr>
<td>13</td>
<td>female</td>
<td>70</td>
<td>0.48</td>
<td>86</td>
<td>dabigatran (220)</td>
</tr>
<tr>
<td>14</td>
<td>female</td>
<td>82</td>
<td>0.70</td>
<td>56.7</td>
<td>edoxaban (30)</td>
</tr>
<tr>
<td>15</td>
<td>female</td>
<td>73</td>
<td>0.76</td>
<td>68</td>
<td>dabigatran (220)</td>
</tr>
<tr>
<td>16</td>
<td>male</td>
<td>72</td>
<td>1.09</td>
<td>55.45</td>
<td>rivaroxaban (15)</td>
</tr>
<tr>
<td>17</td>
<td>male</td>
<td>85</td>
<td>0.83</td>
<td>53</td>
<td>dabigatran (220)</td>
</tr>
<tr>
<td>18</td>
<td>female</td>
<td>75</td>
<td>1.06</td>
<td>43.4</td>
<td>apixaban (5)</td>
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<tr>
<td>19</td>
<td>female</td>
<td>61</td>
<td>0.48</td>
<td>95</td>
<td>edoxaban (30)</td>
</tr>
<tr>
<td>20</td>
<td>female</td>
<td>84</td>
<td>0.79</td>
<td>71.5</td>
<td>dabigatran (220)</td>
</tr>
<tr>
<td>21</td>
<td>female</td>
<td>74</td>
<td>0.70</td>
<td>62.8</td>
<td>dabigatran (300)</td>
</tr>
</tbody>
</table>

Successful hemostasis was obtained in all patients except for one.

Change of parameters after Idarucizumab

PT-INR

\[ P = 0.8950 \]

aPTT

\[ P = 0.0020 \]

ACT

\[ P = 0.0313 \]

Blood coagulation status during freezing

**Blood sampling**

Blood was obtained from the FlexCath where blood temperature was lowest during freezing.
Figure 2. The schema of coagulation cascade

Thrombin antithrombin complex (TAT):
TAT is formed following the neutralization by antithrombin III and reflects thrombin generation.
normal value: <3-4ng/ml

Prothrombin fragment F1+2 (PF 1+2):
PF 1+2 is an activation peptide released from prothrombin during thrombin formation.
normal value: 50-170bM
ACT > 300 sec!

Presented at HRS in Boston, 2018
CMAP Measurement
(compound motor action potential)

Useful tool for the prevention of phrenic nerve injury
Clinical Usage of CMAP in Neurology

**NORMAL**
- Compound action potential
- No decrement in amplitude in response to repeated stimulation

**MYASTHENIA GRAVIS**
- Decline in amplitude with repeated stimulation because fewer muscle fibers in motor unit are firing action potentials
Surface ECG Electrodes

CMAP Electrodes

(Heart Rhythm 2014;11:369–374)
CMAP Amplitude (mV)

Ablation Time (sec)

P<0.001

Patients without PNP

Patients with PNP

(Heart Rhythm 2014;11:369–374)
Left phrenic nerve injury during electrical isolation of left-sided pulmonary veins with the second-generation cryoballoon

Kaoru Okishige MD, FACC, FHRS
Hideshi Aoyagi MD
Takurou Nishimura MD
Takatoshi Shigeta MD
Takehiko Keida MD
Yasuteru Yamauchi MD
Tetsuo Sasano MD
Kenzo Hirao MD

PACE 2017;40:1426-1431
Variation of anatomical course of left phrenic nerve
Consecutive patients with paroxysmal AF
N=448

No PN injury patients
N=419

Transient PNP patients
N=21

PN injury patients
N=29

Persistent PNP patients
N=8

8/448=1.8%
Novel method for earlier detection of phrenic nerve injury during cryoballoon applications for electrical isolation of pulmonary veins in patients with atrial fibrillation

Kaoru Okishige, MD, FHRS,* Hideshi Aoyagi, MD,* Naohiko Kawaguchi, MD,* Nobutaka Katoh, MD,* Mitsumi Yamashita, MD,* Tomofumi Nakamura, MD,* Manabu Kurabayashi, MD,* Hidetoshi Suzuki, MD,* Mitsutoshi Asano, MD,* Kentarou Gotoh, MD,* Tsukasa Shimura, MD,* Yasuteru Yamauchi, MD,* Toshirou Kanazawa, MD, † Tetsuo Sasano, MD, ‡ Kenzo Hirao, MD‡

From the *Heart Center, Yokohama-City Bay Red Cross Hospital, Yokohama City, Japan, †Department of Neurology, Yokohama-City Bay Red Cross Hospital, Yokohama City, Japan, and ‡Arrhythmia Center, Tokyo Medical and Dental University, Tokyo, Japan.

Heart Rhythm 2016;13:1810–1816
Time to occurrence of PNP

Okishige K et al., Heart Rhythm 2016;13:1810-1816
Time required for recovery from PNP

Okishige K et al., Heart Rhythm 2016;13:1810-1816
Max output stimulation concealed PNP.
Quick, safe, and effective maneuver to \textit{prevent phrenic nerve injury} during cryoballoon ablation of atrial fibrillation.


\textit{J. Interv Card Electrophysiol} 2018;53:233-238
Right-sided PN

“pull-back” maneuver

J. Interv Card Electrophysiol 2018;53:233-238
Change of CMAP amplitude

* : p<0.01
Dormant conduction
by
Cryoballoon Application
Study Population (n=864 PVs) (n=216 patients)

- Isolated PVs solely by CB (n=795 PVs) (n=199 patients)
- Waiting time and adenosine-challenge
  - PV reconnections (n=8 PVs) (n=8 patients)
    - No AF recurrence (n=6 patients)
    - AF recurrence (n=2 patients)
  - Persistent PVI (n=856) (n=208 patients)
    - No AF recurrence (N=173 patients)
    - AE recurrence (N=35 patients)

Isolated PVs by touch-up RF (n=68 PVs) (n=17 patients)

Dormant conduction = 3.7 %

Okishige K, et al., J Cardiol 2018;71:577-582
Distribution of dormant conduction sites

LS=left superior PV; LI=left inferior PV; RS=right superior PV; RI=tight inferior PV
a=anterior; p=posterior; s=superior; c=carina; b=bottom
★ =location of the DCs

Okishige K, et al., J Cardiol 2018;71:577-582
The Clinical Implication of electrical isolation of the left atrial posterior wall created by the cryoballoon application in patients with persistent atrial fibrillation.

1) Department of Cardiology, Japan Red Cross Yokohama City Bay Hospital
2) Heart Rhythm Center, Tokyo Medical and Dental University

Takuro Nishimura\textsuperscript{1)}, Kaoru Okishige\textsuperscript{1)}, Naruhiko Ito\textsuperscript{1)}, Yusuke Tsuchiya\textsuperscript{1)}, Takatoshi Shigeta\textsuperscript{1)}, Rena Nakamura\textsuperscript{1)}, Mitsutoshi Asano\textsuperscript{1)}, Hidetoshi Suzuki\textsuperscript{1)}, Tsukasa Shimura\textsuperscript{1)}, Hideshi Aoyaghi\textsuperscript{1)}, Manabu Kurabayashi\textsuperscript{1)}, Yasuteru Yamauchi\textsuperscript{1)}, Kenzo Hirao\textsuperscript{2)}

(submitted)
(1) PVI by Cryoballoon
(2) Roof line construction by CB
(3) Bottom line construction by CB
LA posterior ablation
Rapid ventricular pacing (RVP) and balloon temperature

Blood pressure

RVP

Temperature
Proximal Inner Balloon

Nishimura T, Okishige K, et al (submitted)
1st session

<table>
<thead>
<tr>
<th></th>
<th>acute success rate</th>
<th>average CB temp.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PV isolation</strong></td>
<td><strong>100%</strong> (50/50)</td>
<td></td>
</tr>
<tr>
<td><strong>Roof block line creation</strong></td>
<td><strong>99%</strong> (49/50)</td>
<td><strong>-44 ± 5°C</strong></td>
</tr>
<tr>
<td><strong>Bottom block line creation</strong></td>
<td><strong>75%</strong> (39/50)</td>
<td><strong>-41 ± 5°C</strong></td>
</tr>
<tr>
<td><strong>EI of the LA-PW</strong></td>
<td><strong>74%</strong> (38/50)</td>
<td></td>
</tr>
</tbody>
</table>

The successful block lines was defined as a continuous scar lesion (<0.1mV) connecting bilateral PVs by the voltage map.

A successful electrical isolation (EI) of the LA-posterior wall (PW) was defined as a scar (<0.1mV) covering the entire posterior area of the LA.
AF or AT recurrence-free survival probability without anti-arrhythmia drug

Follow up period: range 3 – 17.5 months
Median: 10 months

1 year: 81.0%

N=234 patients

Nishimura T, Okishige K, et al (submitted)
Comparison to previous reports

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>N</th>
<th>Procedure for EI of the LA-PW</th>
<th>Follow up duration</th>
<th>LA diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>Henn</td>
<td>227</td>
<td>Cox-Maze surgery</td>
<td>5y</td>
<td>N/A</td>
</tr>
<tr>
<td>2015</td>
<td>Kim</td>
<td>60</td>
<td>RF</td>
<td>12m</td>
<td>42.3 (6.4)</td>
</tr>
<tr>
<td>2016</td>
<td>Bai</td>
<td>32</td>
<td>RF</td>
<td>3y</td>
<td>48 (7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cryoballoon</td>
<td>10m</td>
<td>44 (5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>N</th>
<th>Procedure for EI of the LA-PW</th>
<th>Follow up duration</th>
<th>LA diameter</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>p=0.054</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>p=0.78</td>
<td></td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td>p=0.89</td>
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Nishimura T, Okishige K, et al (submitted)
Left Atrial **Posterior Wall** Isolation in Conjunction with Pulmonary **Vein** Isolation Using the Cryoballoon for Treatment of **Persistent Atrial Fibrillation**

*(PIVoTAL) –IDE* Trial

**International Multicenter Clinical Study**
12 institutions in USA
1 institution in Belgium (Brussels Univ.)
1 institution in Japan (Yokohama Red Cross)
Thank you for your attention

Yokohama-city Bay Red Cross Hospital
PV stenosis

p = 0.36

Group A: 7.4%
Group B: 4.4%

mild PV stenosis+

mild PV stenosis-

J Cardiovasc Electrophysiol 2017;28:1021-1027
Immediately after cryoablation

5 months after cryoablation

(Heart Rhythm 2015:12:2195–2203)
**FIGURE 1** The comparison of the nadir LET between that during the PVI and the linear ablation of the LAPW. **LET** = luminal esophageal temperature; PVI = pulmonary vein isolation.
<table>
<thead>
<tr>
<th></th>
<th>With ELs</th>
<th>Without ELs</th>
<th>P</th>
<th>With GH</th>
<th>Without GH</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of patients</strong></td>
<td>11</td>
<td>90</td>
<td></td>
<td>16</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td><strong>Procedure time, min</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>LA dwelling time, min</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Touch up ablation for the PVI, n (%)</strong></td>
<td>1 (10)</td>
<td>16 (21.6)</td>
<td>0.6</td>
<td>8 (15.4)</td>
<td>15 (21.1)</td>
<td>1.0</td>
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<tr>
<td><strong>Touch up ablation for the LAPW isolation, n (%)</strong></td>
<td>1 (9.1)</td>
<td>13 (14.4)</td>
<td>1.0</td>
<td>0</td>
<td>13 (15.3)</td>
<td>0.4</td>
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</tbody>
</table>

Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation

Karl-Heinz Kuck, M.D., Josep Brugada, M.D., Alexander Fürnkranz, M.D., Andreas Metzner, M.D., Feifan Ouyang, M.D., K.R. Julian Chun, M.D., Arif Elvan, M.D., Ph.D, Thomas Arentz, M.D., Kurt Bestehorn, M.D., Stuart J. Pocock, Ph.D., Jean-Paul Albenque, M.D., Ph.D., and Claudio Tondo, M.D., Ph.D., for the FIRE AND ICE Investigators*
A Primary Efficacy End Point

Hazard ratio, 0.96 (95% CI, 0.76–1.22)

P<0.001 for noninferiority

No. at Risk
Cryoballoon
RFC

<table>
<thead>
<tr>
<th></th>
<th>374</th>
<th>338</th>
<th>242</th>
<th>194</th>
<th>165</th>
<th>132</th>
<th>107</th>
<th>70</th>
<th>57</th>
<th>34</th>
<th>12</th>
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<tbody>
<tr>
<td>RFC</td>
<td>376</td>
<td>350</td>
<td>243</td>
<td>191</td>
<td>149</td>
<td>118</td>
<td>93</td>
<td>58</td>
<td>44</td>
<td>25</td>
<td>12</td>
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</tbody>
</table>
C Primary Safety End Point

Hazard ratio, 0.78 (95% CI, 0.52–1.18)

P=0.24

No. at Risk
Cryoballoon
RFC

<table>
<thead>
<tr>
<th>Days since Procedure</th>
<th>374</th>
<th>323</th>
<th>298</th>
<th>261</th>
<th>229</th>
<th>189</th>
<th>159</th>
<th>117</th>
<th>94</th>
<th>55</th>
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<tr>
<td></td>
<td>376</td>
<td>315</td>
<td>292</td>
<td>247</td>
<td>215</td>
<td>176</td>
<td>146</td>
<td>110</td>
<td>87</td>
<td>52</td>
<td>27</td>
</tr>
</tbody>
</table>
Pacing threshold before and after cryoapplication in individual PVs

![Graph showing pacing threshold comparison before (pre) and after (post) cryoapplication in different PVs (LSPV, LIPV, RSPV, RIPV). The graph includes error bars and indicates statistical significance with a * symbol for P < 0.05.](Okishige K et al., Heart Rhythm 2016;13:1810-1816)
Amplitude of CMAP

mV

LSPV  LIPV  RSPV  RIPV

Maximum
Threshold

* P < 0.05

Okishige K et al., Heart Rhythm 2016;13:1810-1816