New Strategies in AF Ablation
Are We There Yet?

Salwa Beheiry, RN MSN, CCRN
Director, EP and Arrhythmia Services
Texas Arrhythmia Institute
Austin, Texas
DISCLOSURES

No Disclosures
What is The Rationale For PV isolation
Foci Triggering Atrial Fibrillation

(Haïssaguerre M et al. NEJM 1998; 339: 659-66)
APC Initiated From RUPV Branch

39 y.o. w/ PAF
PV Triggers initiating AF
Thoracic Veins

- Pulmonary veins
- Superior vena cava
- Coronary sinus
- Ligament of Marshall
- Others (LA appendage, Septum....)
CMC (sequentially positioned at each PV ostium)

HAISSAGUERRE, 2000

2 CMCs (positioned at the ipsilateral PV ostia)

KUCK, 2004

CMC (multiple movements along the PV antrum)

NATALE, 2003

No CMC

PAPPONE, 2004
Beyond Ostial PV Isolation:
PV Antrum Isolation

More proximal ablation: the PV antrum

Time consuming mapping
Risk of new foci (35%)
Higher risk of distal stenosis
PVAI improves the outcomes

% free from recurrent AF/AT off AADs

Antral PVI

Ostial PVI

Log-rank P = 0.036

Months

Pulmonary veins and Antrum in Paroxysmal Atrial Fibrillation
Paroxysmal Atrial Fibrillation
PULMONARY VEIN ANTRUM ISOLATION IN PATIENTS WITH PAROXYSMAL ATRIAL FIBRILLATION: MORE THAN A DECADE OF FOLLOW-UP

Santangeli, Di Biase, Natale et al. Circ Arrhythm 2016
Original Article

Pulmonary Vein Antrum Isolation in Patients With Paroxysmal Atrial Fibrillation
More Than a Decade of Follow-Up

Yağın Gökoğlan, MD; Sanghamitra Mohanty, MD, MS, FHRS; Mahmut F. Güneş, MD; Chintan Trivedi, MD, MPH; Pasquale Santangeli, MD; Carola Gianni, MD; Issa K. Asfour, BS; Rong Bai, MD, FHRS; J. David Burkhardt, MD, FHRS; Rodney Horton, MD, FHRS; Javier Sanchez, MD; Steven Hao, MD; Richard Hong, MD; Salwa Beheiry, RN; Luigi Di Biase, MD, PhD, FHRS; Andrea Natale, MD, FHRS, FESC

Background—We report the outcome of pulmonary vein (PV) antrum isolation in paroxysmal atrial fibrillation (AF) patients over more than a decade of follow-up.

Methods and Results—A total of 513 paroxysmal AF patients (age 54±11 years, 73% males) undergoing catheter ablation at our institutions were included in this analysis. PV antrum isolation extended to the posterior wall between PVs plus empirical isolation of the superior vena cava was performed in all. Non-PV triggers were targeted during repeat procedure(s). Follow-up was performed quarterly for the first year and every 6 to 9 months thereafter. The outcome of this study was freedom from recurrent AF/atrial tachycardia. At 12 years, single-procedure arrhythmia-free survival was achieved in 58.7% of patients. Overall, the rate of recurrent arrhythmia (AF/atrial tachycardia) was 21% at 1 year, 11% between 1 and 3 years, 4% between 3 and 6 years, and 5.3% between 6 and 12 years. Repeat procedure was performed in 74% of patients. Reconnection in the PV antrum was found in 31% of patients after a single procedure and in no patients after 2 procedures. Non-PV triggers were found and targeted in all patients presenting with recurrent arrhythmia after 22 procedures. At 12 years, after multiple procedures, freedom from recurrent AF/atrial tachycardia was achieved in 87%.

Conclusions—In patients with paroxysmal AF undergoing extended PV antrum isolation, the rate of late recurrence is lower than what previously reported with segmental or less extensive antral isolation. However, over more than a decade of follow-up, nearly 14% of patients developed recurrence because of new non-PV triggers. (Circ Arrhythm Electrophysiol. 2016;9:e003660. DOI: 10.1161/CIRCEP.115.003660.)

Key Words: atrial fibrillation • non-PV triggers • paroxysmal AF • pulmonary vein isolation • recurrence

Atrial fibrillation (AF) is the most common sustained arrhythmia associated with a variety of adverse outcomes, including death, stroke, heart failure, reduced quality of life, and increased rate of hospitalizations.1 Because the initial observation of pulmonary veins (PVs) triggering AF was described by Haissaguerre et al2 in 1998, significant advances have been made in the catheter-based treatment of AF. Today, pulmonary vein antrum isolation (PVAI) is the cornerstone of catheter-based therapies in symptomatic, drug-resistant paroxysmal AF (PAF) patients.

See Editorial by Kumar and Michaud

Long-term arrhythmia-free survival after AF ablation is important and highly desirable because this would have beneficial effects on patient prognosis, clinical decision-making process, and economic policies. Long-term success is defined as freedom from AF/atrial flutter (AFL)/atrial tachycardia (AT) recurrences after the 3-month blanking period through a minimum of 36-month follow-up from the date of the ablation procedure in the absence of Class I and III antiarrhythmic drug (AAD) therapy according to the latest guidelines.3 Several published reports have provided information on the outcomes of AF ablation.4-30 A meta-analysis evaluating studies reporting >3 years of outcome after catheter ablation (CA) found that nearly 80% of patients remained in sinus rhythm at 3 years.31 Few series have reported long-term outcomes of AF ablation over 5 years.2,5-10,12-15 However, data on long-term follow-up of PVAI are limited, which would provide valuable information regarding the efficacy and safety of CA and necessity of repeat procedures. Therefore, we sought to assess the outcome of PVAI in patients with PAF over a follow-up period of more than a decade.

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For the author affiliations, please see the Appendix section.
Correspondence to Andrea Natale, MD, Texas Cardiac Arrhythmia Institute, St David’s Medical Center, 3000 N IH-35, Suite 720, Austin, TX 78705.
E-mail: d.natale@gmail.com
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Circ Arrhythm Electrophysiol is available at http://circ.ahajournals.org
DOI: 10.1161/CIRCEP.115.003660
### Table: Demographics and Comorbidities

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of Patients (N=513)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>374 (73%)</td>
</tr>
<tr>
<td>Age</td>
<td>54.4±10.6</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.0±5.2</td>
</tr>
<tr>
<td>BMI ≥30 kg/m²</td>
<td>176 (34.3)</td>
</tr>
<tr>
<td>Duration of AF</td>
<td>48 (24, 80.5)</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>180 (35.1)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>41 (8.0)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>228 (44.4)</td>
</tr>
<tr>
<td>CAD</td>
<td>85 (16.6)</td>
</tr>
<tr>
<td>History of Stroke/TIA</td>
<td>13 (2.5)</td>
</tr>
<tr>
<td>COPD</td>
<td>8 (1.6)</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>37 (7.2)</td>
</tr>
<tr>
<td><strong>Preprocedure echo parameters</strong></td>
<td></td>
</tr>
<tr>
<td>LAD, cm</td>
<td>4.3±0.6</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>54.4±7.6</td>
</tr>
<tr>
<td><strong>Procedural parameters</strong></td>
<td></td>
</tr>
<tr>
<td>Procedure time, min</td>
<td>137.3±55.5</td>
</tr>
<tr>
<td>Fluoroscopic time, min</td>
<td>43.7±21.5</td>
</tr>
<tr>
<td>Radiofrequency time, min</td>
<td>57.1±24.3</td>
</tr>
<tr>
<td>Presence of scar</td>
<td>125 (24.4%)</td>
</tr>
<tr>
<td>Cardioversion during the procedure</td>
<td>64 (12.5%)</td>
</tr>
<tr>
<td>Baseline INR</td>
<td>1.9±0.5</td>
</tr>
</tbody>
</table>

### Figure: Procedure Recurrence and Outcome

- 513 patients with PAF
- AF/AT recurrences: N = 212 (41.3%)
- Repeat Procedures: N = 156/212 (73.6%)
- Two procedures: 118 (75.6%)
- Three procedures: 32 (20.1%)
- Four procedures: 6 (3.8%)
- Cumulative AF/AT free: N = 446 (87%)

- PV reconnection
- Previous non-PV triggers
- New non-PV triggers
Patient History

- Female patient now 84 year old who had an ablation for paroxysmal atrial fibrillation 12 years ago and did well till a few months ago when she experienced recurrences of atrial arrhythmias requiring cardioversion
- She was considered for a repeat procedure
CASE 1
Voltage Map
CASE 1
Risk Factors of LA appendage Triggers in PAF

- Age (especially older female)
- Low EF
- Sleep apnea plus obesity
- Post mitral valve repair/replacement
- Hypertrophic Cardiomyopathy
- LA larger than 5 cm
The PW between the PVs IS ALL PV ANTRUM WHY?
ICE Guided Antrum Identification
Why isolate the PW between the PVs

The PW derives from the same tissue of the PVs

32 days

33 days

36 days

## Antral Triggers Disclosed by Isoproterenol Challenge

<table>
<thead>
<tr>
<th></th>
<th>Focal/Distal PVI</th>
<th>Proximal PVI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of pts</td>
<td>21</td>
<td>190</td>
</tr>
<tr>
<td>Age, ys</td>
<td>52 ± 10</td>
<td>53 ± 11</td>
</tr>
<tr>
<td>Females, %</td>
<td>38</td>
<td>25</td>
</tr>
<tr>
<td>PAF, %</td>
<td>16 (76)</td>
<td>102 (54)</td>
</tr>
<tr>
<td>LA diam, mm</td>
<td>4.1 ± 0.9</td>
<td>4.3 ± 0.6</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>56 ± 10</td>
<td>53 ± 6</td>
</tr>
<tr>
<td>Failed AADs</td>
<td>3 ± 1</td>
<td>3 ± 1</td>
</tr>
</tbody>
</table>

% AF induction (↑20 µg isuprel)

Marrouche, Natale et al. JACC 2002;40:464-474
“the endpoint for ablation was PV isolation and not only delay in left atrial to PV conduction time”
Isolation of the entire PW

Freedom from AF recurrence (%)

- **Entire posterior LA isolation (box lesion)**
- **Control (no box lesion)**

<table>
<thead>
<tr>
<th>Time</th>
<th>Entire Posterior LA Isolation</th>
<th>Control (no box lesion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>3 months</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>6 months</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>12 months</td>
<td>90</td>
<td>90</td>
</tr>
</tbody>
</table>

P values:
- 1 month: P = 0.004
- 3 months: P = 0.018
- 6 months: P = 0.011
- 12 months: P = 0.138

Comparative Effectiveness of Wide Antral Versus Ostial Pulmonary Vein Isolation
A Systematic Review and Meta-Analysis

Riccardo Proietti, MD, PhD; Pasquale Santangeli, MD; Luigi Di Biase, MD, PhD; Jacqueline Joza, MD; Martin Louis Bernier, MD; Yang Wang, MD; Antonio Sagone, MD; Maurizio Viecca, MD; Vidal Essebag, MD, PhD; Andrea Natale, MD

Total Supraventricular Arrhythmia Recurrence

Overall Complication Rate

Odds Ratio: 0.42; 95% CI: 0.32-0.56
p<0.00001

Odds Ratio: 0.72; 95% CI: 0.37-1.38
p=0.32
Can This Be Done With Balloons
Outcomes of Posterior Wall Isolation Using the Cryoballoon in Conjunction with Wide Area Pulmonary Vein Ablation Is Superior to Pulmonary Vein Isolation Alone in Persistent Atrial Fibrillation: A Multicenter Experience

**Short title:** Aryana et al., PVI+PWI versus PVI alone Using Cryoablation

Arash Aryana, MS, MD¹, James H. Baker, MD², Martin A. Espinosa, MD², Mark R. Bowers, MS, MD¹, P. Gearoid O’Neill, MD¹, Kenneth A. Ellenbogen, MD³, Luigi Di Biase, MD, PhD⁴, André d’Avila, MD, PhD⁵ and Andrea Natale, MD⁶
Cryoballoon Maneuvers for Ablation of the Left Posterior Wall Segments
A. Aryana et al, HR 2018
Persistent AF Patients
Adjuvant CFAE Ablation Improves the Outcome
Evidence from Meta-Analysis

Favors PVAI Alone  Risk Ratio  Favors PVAI + CFAE

Verma, 2007
Elayi, 2007
Lin, 2009
Oral, 2010
Verma, 2010

Pooled

RR = 1.32, 95% CI 1.05 to 1.65
P = 0.02

Hayward et al. Heart Rhythm 2011;8:994-1000
## Results - Baseline Characteristics

### STAR-AF2

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PVI</th>
<th>PVI+CFE</th>
<th>PVI+Lines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age - year</strong></td>
<td>58 ± 10</td>
<td>60 ± 9</td>
<td>61 ± 9</td>
</tr>
<tr>
<td><strong>Male sex – n (%)</strong></td>
<td>52 (78)</td>
<td>213 (82)</td>
<td>196 (76)</td>
</tr>
<tr>
<td><strong>Ejection fraction (%)</strong></td>
<td>55 ± 11</td>
<td>57 ± 10</td>
<td>57 ± 10</td>
</tr>
<tr>
<td><strong>Left atrial diameter (mm)</strong></td>
<td>44 ± 6</td>
<td>44 ± 6</td>
<td>46 ± 6</td>
</tr>
<tr>
<td><strong>Time from first AF diagnosis (yrs)</strong></td>
<td>4.3 ± 6.3</td>
<td>4.2 ± 5.0</td>
<td>3.6 ± 4.2</td>
</tr>
<tr>
<td><strong>AF burden at Baseline</strong></td>
<td>83 ± 36</td>
<td>85 ± 33</td>
<td>80 ± 37</td>
</tr>
<tr>
<td><strong>Constantly in AF &gt;6 months – n (%)</strong></td>
<td>52 (78)</td>
<td>207 (80)</td>
<td>186 (72)</td>
</tr>
</tbody>
</table>

### Medical history – n (%)

<table>
<thead>
<tr>
<th>Condition</th>
<th>PVI</th>
<th>PVI+CFE</th>
<th>PVI+Lines</th>
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</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>32 (48)</td>
<td>143 (55)</td>
<td>158 (62)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6 (9)</td>
<td>31 (12)</td>
<td>26 (10)</td>
</tr>
<tr>
<td>Coronary disease</td>
<td>2 (3)</td>
<td>21 (8)</td>
<td>29 (11)</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>6 (9)</td>
<td>14 (5)</td>
<td>19 (7)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>3 (4)</td>
<td>10 (4)</td>
<td>15 (6)</td>
</tr>
</tbody>
</table>

### CHADS<sub>2</sub> score - n (%)

<table>
<thead>
<tr>
<th>Score</th>
<th>PVI</th>
<th>PVI+CFE</th>
<th>PVI+Lines</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>31 (46)</td>
<td>93 (36)</td>
<td>81 (32)</td>
</tr>
<tr>
<td>1</td>
<td>25 (37)</td>
<td>126 (48)</td>
<td>127 (50)</td>
</tr>
<tr>
<td>2</td>
<td>6 (9)</td>
<td>31 (12)</td>
<td>29 (11)</td>
</tr>
<tr>
<td>&gt;2</td>
<td>5 (7)</td>
<td>10 (4)</td>
<td>19 (7)</td>
</tr>
</tbody>
</table>
Results - Primary Outcome

Documented AF > 30 seconds after one procedure with or without AAD

- Pulmonary vein isolation: 59%
- Isolation + Electrograms: 48%
- Isolation + Lines: 44%

p=0.15
Is Posterior Wall Enough?
Proven isolation of the pulmonary vein antrum with or without left atrial posterior wall isolation in patients with persistent atrial fibrillation

During the 1st procedure, PVAI alone was performed in 20 patients (Group 1) while in 32 patients (Group 2) PVAI was extended to achieve isolation of the entire LA posterior wall (PVAI+LAPW).

All patients regardless of atrial tachyarrhythmia recurrence underwent a 2nd procedure 3 months after the 1st procedure.

In patients with reconnection of PVs and/or LAPW, re-isolation was performed and a 3rd procedure was performed 3 months later to verify permanent isolation.

Patients entered follow-up only after PVAI or PVAI+LAPW isolation was proven in Group 1 and in Group 2, respectively.

Event recorder and 7-day Holter were used to evaluate atrial tachyarrhythmia recurrence.

Bai, Di Biase, Natale, HR 2015
Proven isolation of the pulmonary vein antrum with or without left atrial posterior wall isolation in patients with persistent atrial fibrillation

Bai, Di Biase, Natale, HR 2015
Proven isolation of the pulmonary vein antrum with or without left atrial posterior wall isolation in patients with persistent atrial fibrillation

Rong Bai, MD, FHRS, FESC, †† Luigi Di Biase, MD, PhD, FHRS, FACC, †††
Prasant Mohanty, MBBS, MPH, † Chintan Trivedi, MD, † Antonio Dello Russo, MD, †
Sakis Themistoclakis, MD, †† Michela Casella, MD, †† Pietro Santarelli, MD, ††
Gaetano Fassini, MD, † Pasquale Santangeli, MD, † Sanghamitra Mohanty, MD, FHRS, †
Antonio Rossillo, MD, † Gemma Pelargonio, MD, †† Rodney Horton, MD, † Javier Sanchez, MD, †
Joseph Gallighouse, MD, † J. David Burkhart, MD, FHRS, † Chang-Sheng Ma, MD, FHRS, †
Claudio Tondo, MD, † Andrea Natale, MD, FHRS, FACC, FESC †††††
Non PV triggers ablation improves the success rate of catheter ablation of Persistent Atrial Fibrillation after a single procedure: Results From A Prospective Multicenter Study

622 consecutive pts with persistent AF:
- Group I: PVAI+ PW (n=203)
- Group II: PVAI+PW+non-PV trigger ablation

Arrhythmia-free after 18 ± 9 month FU:
- Group I: 58.1%
- Group II: 67.5%

Di Biase, Natale, AHA 2014
Attention to Triggers
What is the Prevalence of Triggers?
PV triggers
- sustained: triggering AF or sustained AT
- non-sustained: repetitive consistent PACs

Non-PV triggers
- reproducibly triggering AF or sustained AT

Triggers elicited:
1. Spontaneously
2. Incremental ISO
   3 > 6 > 12 > 20 µg/min
3. RA pacing 15 beats @ 10 mV x 2 ms
   250 > 180 ms
PV triggers

Non-PV triggers

<table>
<thead>
<tr>
<th>Variable</th>
<th>PV triggers (n = 1975)</th>
<th>No PV triggers (n = 193)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>57 ± 10</td>
<td>53 ± 13</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sex: male</td>
<td>1500 (76)</td>
<td>136 (70)</td>
<td>.091</td>
</tr>
<tr>
<td>Hypertension</td>
<td>899 (51)</td>
<td>93 (48)</td>
<td>.525</td>
</tr>
<tr>
<td>Diabetes</td>
<td>189 (10)</td>
<td>17 (9)</td>
<td>.731</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>65 (3)</td>
<td>6 (3)</td>
<td>.892</td>
</tr>
<tr>
<td>Previous stroke/TIA</td>
<td>117 (6)</td>
<td>9 (5)</td>
<td>.475</td>
</tr>
<tr>
<td>CHADS2 score</td>
<td></td>
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<tr>
<td>0</td>
<td>845 (43)</td>
<td>96 (50)</td>
<td>.074</td>
</tr>
<tr>
<td>1</td>
<td>772 (39)</td>
<td>63 (32)</td>
<td>.049</td>
</tr>
<tr>
<td>≥ 2 or NA</td>
<td>358 (18)</td>
<td>36 (18)</td>
<td>.920</td>
</tr>
<tr>
<td>Type of AF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>1397 (71)</td>
<td>134 (69)</td>
<td>.874</td>
</tr>
<tr>
<td>Persistent</td>
<td>449 (23)</td>
<td>47 (24)</td>
<td>.874</td>
</tr>
<tr>
<td>Long-standing persistent</td>
<td>129 (7)</td>
<td>12 (6)</td>
<td>.874</td>
</tr>
<tr>
<td>LA diameter (cm)</td>
<td>4.3 ± 0.7</td>
<td>4.3 ± 0.8</td>
<td>.989</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>60 ± 9</td>
<td>59 ± 9</td>
<td>.356</td>
</tr>
</tbody>
</table>
Age and Non-PV Triggers

![Bar chart showing prevalence of non-PV triggers in paroxysmal and non-paroxysmal AF, with P-values and age groups.]
Pts with Non-PV Triggers = 63/226 (28%)
How Do We Locate Non PV Triggers?
Groups With Higher Prevalence of Non PV Triggers

- Severe left atrial scarring
- Non paroxysmal AF
- Females
- Sleep apnea/obesity
- Hypertrophic Cardiomyopathy
- Valve Surgery
- LV dysfunction
- Left atrial dilatation
- Older Age
Endpoints in Some of The Trigger Sites
Left Atrial Appendage
Arrhythmia/Electrophysiology

Left Atrial Appendage
An Underrecognized Trigger Site of Atrial Fibrillation

Luigi Di Biase, MD; J. David Burkhardt, MD; Prasant Mohanty, MBBS, MPH; Javier Sanchez, MD; Sanghamitra Mohanty, MD; Rodney Horton, MD; G. Joseph Gallighouse, MD; Shane M. Bailey, MD; Jason D. Zagrodzky, MD; Pasquale Santangeli, MD; Steven Hao, MD; Richard Hongo, MD; Salwa Beheiry, MD; Sakis Themistoclakis, MD; Aldo Bonso, MD; Antonio Rossillo, MD; Andrea Corrado, MD; Antonio Raviele, MD; Amin Al-Ahmad, MD; Paul Wang, MD; Jennifer E. Cummings, MD; Robert A. Schweikert, MD; Gemma Pelargonio, MD; Antonio Dello Russo, MD; Michela Casella, MD; Pietro Santarelli, MD; William R. Lewis, MD; Andrea Natale, MD, FHRS

Background—Together with pulmonary veins, many extrapulmonary vein areas may be the source of initiation and maintenance of atrial fibrillation. The left atrial appendage (LAA) is an underestimated site of initiation of atrial fibrillation. Here, we report the prevalence of triggers from the LAA and the best strategy for successful ablation.

Methods and Results—Nine hundred eighty-seven consecutive patients (29% paroxysmal, 71% nonparoxysmal) undergoing redo catheter ablation for atrial fibrillation were enrolled. Two hundred sixty-six patients (27%) showed firing from the LAA and became the study population. In 86 of 987 patients (8.7%; 5 paroxysmal, 81 nonparoxysmal), the LAA was found to be the only source of arrhythmia with no pulmonary veins or other extrapulmonary vein site reconnection. Ablation was performed either with focal lesion (n=56; group 2) or to achieve LAA isolation by placement of the circular catheter at the ostium of the LAA guided by intracardiac echocardiography (167 patients; group 3). In the remaining patients, LAA firing was not ablated (n=43; group 1). At the 12±3-month follow-up, 32 patients (74%) in group 1 had recurrence compared with 38 (68%) in group 2 and 25 (15%) in group 3 (P<0.001).

Conclusions—The LAA appears to be responsible for arrhythmias in 27% of patients presenting for repeat procedures. Isolation of the LAA could achieve freedom from atrial fibrillation in patients presenting for a repeat procedure when arrhythmias initiating from this structure are demonstrated. (Circulation. 2010;122:109-118.)

Key Words: atrial appendage ■ atrial fibrillation ■ catheter ablation
Figure 1. Flow chart showing the study design. PAF indicates paroxysmal AF; PER, persistent AF; and LSP, long-standing persistent AF.
Kaplan Meier curve showing probability of AF-free survival across different population subgroups
• 51 year old male with persistant atrial fibrillation presented to the EP laboratory. After isolation of three of the four PV antrum, the patient converted to sinus rhythm. The procedure was completed and isoproterenol was given up to 20 ug/min
Atrial Fibrillation From The CS with Isoproterenol
Example of firing from the coronary sinus during infusion of isoproterenol at 20 ucg/min.
Atrial Fibrillation Triggers From The Coronary Sinus: Comparison Between Isolation Versus Focal Ablation.

Luigi Di Biase, MD, PhD, Rong Bai, MD, Prasant Mohanty, MBBS, MPH, Javier E. Sanchez, MD, Sanghamitra Mohanty, MD, J. David Burkhardt, MD, Rodney Horton, MD, Shane Bailey, MD, Jason Zagrodzky, MD, G. Joseph Gallinghouse, MD, Pasquale Santangeli, MD, Antonio Dello Russo, MD, Michela Casella, MD, Gemma Pelargonio, MD, Stefania Riva, MD, Gaetano Fassini, MD, Richard Hongo, MD, Salwa Beheiry, RN, Dhanunjay Lakkireddy, MD, Subba Reddy Vanga, MD, Robert A. Schweikert, MD, Douglas Gibson, MD, Raimondo Massaro, MD, Domenico Potenza, MD, William R. Lewis, MD, Claudio Tondo, MD and Andrea Natale, MD.

- Texas Cardiac Arrhythmia Institute at St. David’s Medical Center, Austin, Texas, USA;
  - University of Texas, Austin, Texas, USA;
  - Department of Cardiology, University of Foggia, Foggia, Italy;
    - Monzino Hospital, Milan, Italy;
    - Catholic University Rome, Italy;
    - Kansas University, Kansas, USA;
  - California Pacific Medical Center, Austin, Texas, USA;
  - Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy
  - Scripps Clinic, San Diego, California, USA

Email: dibbia@gmail.com
A total of 225 consecutive patients undergoing PVI and showing triggers from the CS were included in the study.

Based on operator’s choice, CS was targeted with:

- Complete isolation (Group 1, n=140)
- Focal ablation (Group 2, n=85)

Di Biase, Natale et al, Abs HRS 2011
RESULTS: Follow-up

➢ No periprocedural complications were reported.

➢ After 21 ± 7 months of follow-up, 103 (74%) patients in group 1 and 43 (51%) in group 2 were recurrence free (log-rank p < 0.001).

Di Biase, Natale et al, Abs HRS 2011
Outcomes In Long Standing Persistent Patients
Long standing persistent (LSP) atrial fibrillation (AF) is the most challenging type of AF to treat with catheter ablation.
EDITORIAL COMMENT

Long-Standing Persistent Atrial Fibrillation

The Metastatic Cancer of Electrophysiology*

J. David Burkhardt, MD,†
Luigi Di Biase, MD, PhD, †‡§
Andrea Natale, MD†§

Austin, Texas; and Foggia, Italy
Left Atrial Appendage: An Underrecognized Trigger Site of Atrial Fibrillation


Figure 1. Flow chart showing the study design. PAF indicates paroxysmal AF; PER, persistent AF; and LSP, long-standing persistent AF.
EVIDENCE of the LAA as a TRIGGER for AF/AT

Localized reentry within the left atrial appendage: arrhythmogenic role in patients undergoing ablation of persistent atrial fibrillation

Mélèze Hocini, MD, Ashok J. Shah, MD, Isabelle Nault, MD, Prashanthan Sanders, MBBS, PhD, Matthew Wright, MBBS, PhD, Sanjiv M. Narayan, MD, FACC, Yoshihide Takahashi, MD, Pierre Jaïs, MD, Seiichiro Matsuo, MD, Sébastien Knecht, MD, Frédéric Sacher, MD, Kang-Teng Lim, MD, Jacques Clémenty, MD, Michel Haïssaguerre, MD

Management of focal atrial tachycardias originating from the atrial appendage with the combination of radiofrequency catheter ablation and minimally invasive atrial appendectomy

Xiao-gang Guo, MD, Jin-lin Zhang, MD, Jian Ma, MD, Yu-he Jia, MD, Zhe Zheng, MD, Hong-yue Wang, MD, Xi Su, MD, Shu Zhang, MD, F HRS

Left Atrial Appendage Ligation and Ablation for Persistent Atrial Fibrillation

The LAALA-AF Registry

Dhanunjaya Lakkireddy, MD, Arun Sridhar Mahankali, MD, Arun Kanmantareddy, MD, Randall Lee, MD, Nitish Badhwar, MD, Krzysztof Bartus, MD, PhD, Donita Atkins, BSN, Sudharani Bommana, MPH, Jie Cheng, MD, Abdi Rasekh, MD, Luigi Di Biase, MD, PhD, Andrea Natale, MD, Jayant Nath, MD, Ryan Ferrell, MD, Matthew Earnest, MD, Yeruva Madhu Reddy, MD
The clinical efficacy of left atrial appendage isolation caused by extensive left atrial anterior wall ablation in patients with atrial fibrillation

Hwan-Cheol Park¹ · DaeIn Lee² · Jaemin Shim² · Jong-II Choi² · Young-Hoon Kim²

Circulation Arrhythmia and Electrophysiology

Left Atrial Appendage Electrical Isolation and Concomitant Device Occlusion to Treat Persistent Atrial Fibrillation: A First-in-Human Safety, Feasibility, and Efficacy Study
Sanjeev Panikker, Julian W.E. Jarman, Renu Virmani, Robert Kurys, Shevish Halder, Eric Lim, Charles Butcher, Habib Khan, Lilian Mantzidis, Edward Nicol, John P. Foran, Vivas Markides and Tom Wong

Circ Arrhythm Electrophysiol. 2016;9;

Left atrial appendage isolation in addition to pulmonary vein isolation in persistent atrial fibrillation: One-year clinical outcome after cryoballoon based ablation

Running title: Cryoballoon based LAA isolation in persistent AF
Hikmet Yorgun, MD, Associate Professor
Ugur Canpolat, MD, Assistant Professor
Duygu Kosyigit, MD
Cem Çöreli, MD
Berna Evranos, MD, Assistant Professor
Kokret Aytemir, MD, Professor, FESC

Europace2017

Ablation success rates assessment

*12-lead ECG
*TEE
*24-h Holter
*7-day Event recorder if required
*TEE (to assess LAA flow)

3 month

6 month

12 month

AF Free Survival

Log-rank p<0.001

Follow-up (months)

P = 0.032

Group 3

Group 2

Group 1

Follow-up period (months)
Effect of Empirical Left Atrial Appendage Isolation on Long-term Procedure Outcome in Patients With Persistent or Long-standing Persistent Atrial Fibrillation Undergoing Catheter Ablation (BELIEF)

This study is currently recruiting participants.

Verified May 2011 by Texas Cardiac Arrhythmia Research Foundation

Sponsor:
Texas Cardiac Arrhythmia Research Foundation

ClinicalTrials.gov Identifier:
NCT01362738

First received: May 26, 2011
Last updated: May 31, 2012
Last verified: May 2011
Study Design

173 Patients Enrolled
(≥18 years, long-standing persistent AF refractory to antiarrhythmic drugs)

Randomized 1:1

Standard Ablation + Empirical LAA isolation (Group 1): n= 85

Standard Ablation alone (group 2): n= 88

Follow-up After Index Procedure

Ablation Success Assessed at 12 month

62 Patients underwent a second procedure (27 group 1 and 35 group 2). LAA isolation was performed in all patients during repeat ablation

Follow-up after Redo

Outcome Assessed at 24 month
Why we Designed This Study?

• Because in previous experience we had seen that long term in many of these patients the LA appendage had to be isolated

• And because this was the case even when no firing was detected with high dose of isoproterenol
At the 12 month follow-up, 48 (56%) in group 1 and 25 (28%) in group 2 were recurrence-free off-AAD after a single procedure. (Log-rank $p=0.001$, unadjusted HR 1.92 [1.3 to 2.9]).

Di Biase, Natale et al JACC 2016
Percutaneous alternative to the Maze procedure for the treatment of persistent or long-standing persistent atrial fibrillation (aMAZE trial): Rationale and design

Randall J. Lee, MD, PhD, a Dhanunjaya Lakkireddy, MD, b Sunee Pill, MD, c, d Christopher Ellis, MD, e Jason T. Connor, PhD, f, g Benjamin R. Saville, PhD, f, h and David Wilber, MD i San Francisco, CA; Kansas City, KS; New York, NY; Ridgewood, NJ; Nashville, TN; Austin, TX; Orlando, FL; and Chicago, IL.
Abnormal cells, which corresponded to the automaticity cells described by de Bakker et al., characterized by “amorphous, pale eosinophilic staining cytoplasm and the absence of nuclei.”

Source: [Heart Rhythm 2014; 11:17-25](https://doi.org/10.1016/j.hrthm.2013.10.017)

Debakker JM, Cardiovasc Electrophysiol.1994;5:335–344
What are the downsides to endocardial LAA ablation/Isolation?

- Complete electrical isolation may be difficult to accomplish
- Risk of perforation in the thin pits of the LAA wall
- Loss of LAA atrial contractility and effect on LA emptying and stroke volumes
- Loss of LAA contractility and high risk for thrombus formation and the need for prolonged anticoagulation

Can You Stop Anticoagulation After LA Appendage Isolation
Protocol To Assess Eligibility to Discontinue Coumadin

• 6 months following the procedure we assess:
  – Mitral inflow pattern
  – LA appendage velocity
  – LA appendage contractility
LAA isolation endocardially can cause significant LAA stasis and thrombus

A wide area isolation of the LAA with anterior and lateral line seems to be more commonly associated with LAA stasis and thrombus formation than with more circular closer isolation.

Circ Arrhythm Electrophysiol. 2016;9:e003461. DOI: 10.1161/CIRCEP.115.003461
Does Closing The LAA Surgically Eliminate Triggers?
Patients were alternately assigned to Tiger Paw System II (Maquet, Rastatt, Germany; 8 patients) or AtriClip (Atricure, Dayton, OH, USA; 7 patients)

- The early success of epicardial LAA occlusion is not dependent on LAA morphologic type or occluder used.
- A minimal remnant LAA stump not exceeding 1 cm in length without distal blood flow was observed in one-third of the cases.
Successful fluoroscopy ablation of an incessant atypical atrial flutter attributed to AtriClip usage during mini-MAZE surgery for persistent atrial fibrillation

The critical zone of the atypical flutter site was near the endocardial tissue underlying the AtriClip

Ablation of the Left Atrial Appendage ”Stump” to Cure Post Surgical Maze Patients

• 214 patients undergoing redo ablation for AF after a failed surgical ablation were enrolled in this study

• Out of the 214 patients with previous LAA amputation referred to our Institution, 169 demonstrated firing from LAA “stump” (79%)

• At 12 months of follow-up, 167 of the 169 patients with LAA “stump” ablated, were in sinus rhythm on or off AADs

• Ablation of the LAA “stump” may be necessary during repeat procedure following surgical ablation of AF to achieve freedom from AF.

• Ablation of the LAA “stump” appeared to be feasible and relatively safe

Di Biase L. et al. Circulation 2010
Can We Find Localized AF Sources?
Ablation at Inferior Left Atrial Rotor (Focal Impulse and Rotor Modulation, FIRM)

81 YO man, AF for 31 Years, Multiple Cardioversions; 1st ablation
Symptomatic AF undergoing RFA

N = 107 (paroxysmal 29%)

FIRM-guided ablation

PVAI ± lines (LA roof)

Freedom from AF

FU = median 8 months

82.4 vs 44.9% (p < 0.001)

79.3 vs 35.6% (p < 0.001)

We need... RCTs
LONG-TERM CLINICAL OUTCOMES OF FOCAL IMPULSE AND ROTOR MODULATION FOR TREATMENT OF ATRIAL FIBRILLATION: A MULTI-CENTER EXPERIENCE

Focal Impulse or Rotor Modulation (FIRM)

The Usual Suspects

Independent groups

Focal impulse and rotor modulation as a stand-alone procedure for the treatment of paroxysmal atrial fibrillation: A within-patient controlled study with cardiac resynchronization therapy

Focal impulse and rotor modulation: Acute procedural clinical follow-up

ROCKS vs SUCKS

Round 1

RESULTS: Rotor activation was observed in 11 patients (14.7%: 10 parsimonious and 1 persistent AF) (tachycardia cycle length 160.9 ± 19.8 ms). Rotors were observed transiently (duration 6128 ± 9094 ms) during AF at the roof (n = 5), septum (n = 3), and ostium of the left superior PV (n = 3). Five rotors circulate in clockwise and 6 in counterclockwise directions. The length of the block line at the poor efficacy, different from previously published studies. Randomized studies are needed to evaluate the efficacy and clinical utility of this ablation for treatment of AF.
Relative contribution of different ablation targets in the AF disease continuum

- **PV Triggers**
- **LAA**
- **Substrate ?**

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Atrial Fibrillation Patients on Drugs
…After Catheter Ablation