What is the Endpoint of AF Ablation?

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**Presenter Disclosure Information**

Within the past 12 months, the presenter has received financial support from the organizations identified below for the relationships listed.

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<thead>
<tr>
<th>Company Name</th>
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<tbody>
<tr>
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<td>Consultant / Lecture Honorarium</td>
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<td>Boston Scientific</td>
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*No organization has prepared, altered or influenced content of any lecture material*
Why Pulmonary Vein Isolation?

1. Based on strong physiological rationale
   - PVs represent the main trigger site for all types of AF
   - PV reconnection invariably found at repeat procedures

2. Treatment proven effective in multiple RCTs against both drug therapy and other ablation approaches (lines, CFAE, HF sources)

3. Efforts to achieve more durable PVI translate into better outcomes in RCTs (adenosine, pace and capture, steerable sheaths, GA, contact force catheters)
Why SHOULD we adopt PVI and Trigger Ablation?

**Physiological Rationale**

Prevalence of PV Triggers Across Different Types of AF – N=2,168

![Bar Chart](chart.png)

- Paroxysmal
- Persistent
- Longstanding Persistent

P=0.67
Why SHOULD we adopt PVI and Trigger Ablation?

Physiological Rationale

PV reconnection invariably found at repeat procedures

PV Reconnection (3rd and 4th Procedure)

N. Patients

0 10 20 30 40 50 60 70 80 90 100

4 PVs 2 PVs 2 PVs 1 PVs All disconnected

Lin, Marchlinski et al. JCE 2015;26:371-7
**RCTs** More Durable PVI Increases Success

**Adenosine-guided PVI ↑ Success**


**Steerable Sheaths ↑ Success**


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**General Anesthesia ↑ Chronic PVI & Success**

Di Biase et al. Heart Rhythm 2011;8:368-72

- Long-term success (P < 0.001)
- PV reconnection rate at redo procedure (P = 0.003)
Why SHOULD we adopt PVI and Trigger Ablation?

RCTs against other ablation approaches

# Efficacy of PVA + linear substrate modification for non-paroxysmal AF

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>RCT</th>
<th>N</th>
<th>AF Type</th>
<th>Follow-up (mos)</th>
<th>Primary Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral et al.</td>
<td>2005</td>
<td>X</td>
<td>40</td>
<td>LSP (&gt;6 mos)</td>
<td>10 ± 3</td>
<td>48%</td>
</tr>
<tr>
<td>Vasamreddy et al.</td>
<td>2005</td>
<td></td>
<td>27</td>
<td>LSP (ns)</td>
<td>-</td>
<td>52%</td>
</tr>
<tr>
<td>Oral et al.</td>
<td>2006</td>
<td></td>
<td>77</td>
<td>LSP (&gt; 6 mos)</td>
<td>12</td>
<td>74%</td>
</tr>
<tr>
<td>Willems et al.</td>
<td>2006</td>
<td>X</td>
<td>62</td>
<td>Pers.</td>
<td>16 (14-19)</td>
<td>69%</td>
</tr>
<tr>
<td>Elayi et al.</td>
<td>2008</td>
<td>X</td>
<td>47</td>
<td>LSP (&gt;12 mos)</td>
<td>17 ± 2</td>
<td>11%</td>
</tr>
<tr>
<td>Earley et al.</td>
<td>2006</td>
<td></td>
<td>42</td>
<td>LSP (ns)</td>
<td>8 (2-29)</td>
<td>38%</td>
</tr>
<tr>
<td>Gaita et al.</td>
<td>2007</td>
<td></td>
<td>13</td>
<td>LSP, HCM</td>
<td>18 ± 12</td>
<td>15%</td>
</tr>
<tr>
<td>Seow et al.</td>
<td>2007</td>
<td></td>
<td>56</td>
<td>Pers./LSP</td>
<td>22 ± 9</td>
<td>48%</td>
</tr>
<tr>
<td>Miyazaki et al.</td>
<td>2008</td>
<td></td>
<td>25</td>
<td>LSP (&gt;6 mos)</td>
<td>6</td>
<td>40%</td>
</tr>
<tr>
<td>Fiala et al.</td>
<td>2008</td>
<td></td>
<td>100</td>
<td>LSP (&gt;6 mos)</td>
<td>26 ± 14</td>
<td>57%</td>
</tr>
<tr>
<td>Estner et al.</td>
<td>2011</td>
<td>X</td>
<td>116</td>
<td>Pers.</td>
<td>24 ± 14</td>
<td>54%</td>
</tr>
</tbody>
</table>

- Without PV isolation confirmation
- PV isolation confirmed with a CMC
Cumulative Primary and Secondary Success Rates of Different Ablation Techniques in Non-PAF

DATA SOURCES:

**PVAI**: Pappone 2001; Cheema 2007; Elayi 2008; Oral 2009

**PVAI/PVA+LIN**: Oral 2005; Vasamreddy 2005; Oral 2006; Willems 2006; Elayi 2008; Earley 2006; Seow 2007; Miyazaki 2008; Fiala 2008; Estner 2011

**PVAI/PVA+CFAE**: Schmitt, 2007; Estner 2008; Li 2008; Porter 2008; Elayi 2008; Oral 2009
Arm 1: PVI
Arm 2: PVI + Empiric Trigger Sites
Arm 3: PVI + CFAE

No Benefit Of Complex Fractionated Atrial Electrogram (CFAE) Ablation in Addition to Circumferential Pulmonary Vein Ablation and Linear Ablation: BOCA Study

Freedom from AF/AT after first ablation procedure

Arhythmia free survival (%)

No. at risk

<table>
<thead>
<tr>
<th></th>
<th>CFAE</th>
<th>CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at risk</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>3 months</td>
<td>53</td>
<td>59</td>
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<tr>
<td>6 months</td>
<td>42</td>
<td>45</td>
</tr>
<tr>
<td>9 months</td>
<td>33</td>
<td>37</td>
</tr>
<tr>
<td>12 months</td>
<td>30</td>
<td>37</td>
</tr>
</tbody>
</table>

$p=0.20$
Focal Impulse and Rotor Modulation
The Jury is Still Out!

Ablation of Rotor and Focal Sources Reduces Late Recurrence of Atrial Fibrillation Compared With Trigger Ablation Alone


Initial Independent Outcomes from Focal Impulse and Rotor Modulation Ablation for Atrial Fibrillation: Multicenter FIRM Registry

JOHN M. MILLER, M.D., ROBERT C. KOWAL, M.D., PH.D., VIJAY SWARUP, M.D., JAMES P. DAUBERT, M.D., EMIL G. DAUD, M.D., JOHN D. DAY, M.D., KENNETH A. ELLENBOGEN, M.D., JOHN D. HUMMEL, M.D., PH.D., TINA BAYKNAER, M.D., DAVID E. KRUMMEN, M.D., SANJU N. NARAYAN, M.D., PH.D., YVKE V. REDDY, M.D., KALYANAN SHIVKUMAR, M.D., PH.D., JONATHAN S. STEINBERG, M.D., M.R.C.P., and KEVIN R. WHEELER, M.D.

The success of pulmonary vein isolation (PVI) for atrial fibrillation (AF) may be improved by targeting AF sources identified by Focal Impulse and Rotor Mapping (FIRM) and ablation of common triggers of AF. Although the time course of AF is dependent on the interference of atrial tissue, the use of FIRM-guided ablation has been shown to be effective in reducing AF recurrence.

Methods—A prospective, multicenter registry evaluated 78 consecutive patients (81 ± 10 years) undergoing FIRM-guided ablation for persistent AF (n = 48), inoperable AF (n = 7), or paroxysmal AF (n = 23). AF recordings from the left atrium and 64-lead basket catheter were analyzed using a novel mapping system (RhythmView™, Epica Inc., CA, USA). Ablation of focal sources was performed, followed by PVI.

Results—Of the 78 patients, 76% had 3 or more sources identified by FIRM. In total, 109,131 points were analyzed, with 7,856 points identified as sources of atrial activation. Ablation of these sources resulted in a 90.5% reduction in AF burden at 1 year.

Conclusions—Ablation of focal sources may be a useful adjunct to PVI for the treatment of persistent AF, reducing the burden of AF.

Background: Focal Impulse and Rotor Modulation (FIRM) has been shown to be an effective novel treatment approach for the treatment of atrial fibrillation (AF) through the use of novel mapping techniques and targeted ablation.

Methods: A total of 17 patients were evaluated using FIRM to target and ablate AF sources. The study was performed at a single medical center and included patients with paroxysmal AF, persistent AF, and atrial flutter.

Results: Significant reduction in AF burden was observed in all patients, resulting in a cumulative 85% reduction in AF burden at 1 year.

Conclusion: Focal impulse and rotor modulation is a promising technique for the treatment of atrial fibrillation and may provide a novel approach for reducing AF burden.

The majority of sources were rotors (86%). The total source burden decreased by 33.0% and the proportion of AF burden was reduced from 99.0% to 13.0%.

Keywords: FIRM, Ablation, Atrial Fibrillation, Mapping, Rotor, Rhythm, Characterization.

FIRM Ablation
The Jury is Still Out!

Narayan et al. JACC 2012;60:628-36
Sensitivity and Specificity of Periprocedural AF Termination in Predicting Long-Term Success

Area Under the Curve
0.68 (95% CI 0.64 to 0.72)
Lack of Association Between AF Termination and Long-Term Success
Is Non-Inducibility of AF or Change in Inducibility Status a Procedural Endpoint?

305 Pts Undergoing PVI+Non-PV Trigger Ablation

Log-Rank $P = 0.236$

Non-Inducible for AF/AT After Ablation

Inducible for AF/AT After Ablation
Is Non-Inducibility of AF or Change in Inducibility Status a Procedural Endpoint?

305 Pts Undergoing PVI+Non-PV Trigger Ablation

Log-Rank P = 0.232

Any Additional Role for Extra-PV Targets?
What is the Relevance of Non-PV Triggers?

*Ignoring Non-PV Triggers Worsens AF-Free Survival*

175 pts (88 w/ non-PV Triggers Abl.)

304 pts (59 w/ non-PV Triggers)

• Programmed stimulation (including V pacing) to screen for Accessory Pathway / AVNRT

• Initiation of PV and non PV atrial triggers for AF
  – Cardioversion if persistent/permanent AF - *ERAF/sustained AT*
  – If sinus rhythm give isoproterenol – Increments of 3, 6, 12, 20 mcg/min infusion (Median dose 12 mcg/min) – *AF/sustained AT*
  – Cardioversion of AF initiated by burst pacing – *ERAF/sustained AT*
  – Cardioversion of AF initiated with burst pacing during infusion of 2-3 mcg of isoproterenol - *ERAF/sustained AT*

Santangeli and Marchlinski. Heart Rhythm 2017: S1547-5271
Non-PV Trigger Mapping – Catheter Position

Santangeli and Marchlinski. Heart Rhythm 2017: S1547-5271
Prevalence of Non-PV Triggers and AF Type

\[ N=2357 \text{ 61\% PAF } \]

P=0.79

Santangeli, Marchlinski et al, Manuscript in preparation
Distribution of Non-PV Triggers

Total Group=2357
Patients with Non-PV Trigger = 245
# of Non-PV Triggers = 277

RAA=right atrial appendage
TV=tricuspid valve
CT=crista terminalis
ER=eustachian ridge
SVC=superior vena cava
AVNRT=AV node reentrant tachycardia

LAA=left atrial appendage
MV=mitral valve
CS=coronary sinus
LOM=ligament of Marshall
LLAP=left lateral accessory pathway
PW=posterior wall

RAA 4/0.17%
TV 8/0.34%
CT/ER 79/3.4%
SVC 39/1.7%
AVNRT 46*/2.0%
LIAS 11/0.47%
RSPV 13/0.55%
LSPV 8/0.34%
LLAP 8/0.34%
LIPV 13/0.55%
PW 13/0.55%
CS/MV/LOM 46/2.0%

# of Non-PV Triggers = 277
Gender and Prevalence of Non-PV Triggers

Santangeli, Marchlinski et al, Manuscript in preparation
Distribution of Non-PV Triggers and AF Type

*Higher Prevalence of LA Triggers in Non-PAF*

RAA=right atrial appendage
TV=tricuspid valve
CT=crista terminalis
ER=eustacian ridge
SVC=superior vena cava
AVNRT=AV node reentrant tachycardia

LAA=left atrial appendage
MV=mitral valve
CS=coronary sinus
LOM=ligament of Marshall
LLAP=left lateral accessory pathway
PW=posterior wall

*includes 4 pts with longstanding persistent AF*
Long-Term Outcomes

Overall Group
N=2357 pts

P = 0.083

Follow-up (days)

Freedom from AF-AT

Blanking period

PVI only  PVI + Non-PV Trigger
Long-Term Outcomes

Only Non-PV Triggers (N=31)

Blanking period

90%
AF Type and Outcomes

PAF 1-year AF/AT free survival 63%
Non-PAF 1-year AF-AT free survival 56%

• Patients with non-PAF had more LA triggers
• Non-PV triggers effectively targeted in all patients (i.e., trigger suppression w/ lack of AF reinduction)
Factors Associated with Recurrences Post Ablation For Persistent AF

Differences in Persistent Group
N=921

<table>
<thead>
<tr>
<th></th>
<th>No Recur N=520 (56%)</th>
<th>Recur N=401 (44%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M, %)</td>
<td>441 (85)</td>
<td>315 (79)</td>
<td>0.014</td>
</tr>
<tr>
<td>LS Persistent (%)</td>
<td>123 (24)</td>
<td>98 (24)</td>
<td>0.78</td>
</tr>
<tr>
<td>Non-PV trigger</td>
<td>39 (8)</td>
<td>52 (13)</td>
<td>0.0058</td>
</tr>
<tr>
<td>HTN (%)</td>
<td>302 (58)</td>
<td>227 (57)</td>
<td>0.65</td>
</tr>
<tr>
<td>DM (%)</td>
<td>68 (13)</td>
<td>55 (14)</td>
<td>0.78</td>
</tr>
<tr>
<td>OSA (%)</td>
<td>113 (22)</td>
<td>79 (20)</td>
<td>0.45</td>
</tr>
<tr>
<td>CAD (%)</td>
<td>63 (12)</td>
<td>39 (10)</td>
<td>0.25</td>
</tr>
<tr>
<td>TIA/CVA (%)</td>
<td>34 (9)</td>
<td>28 (7)</td>
<td>0.28</td>
</tr>
<tr>
<td>HCM (%)</td>
<td>5 (1)</td>
<td>18 (4)</td>
<td>0.0007</td>
</tr>
<tr>
<td>LA size, cm</td>
<td>4.7 ± 0.6</td>
<td>4.8 ± 0.7</td>
<td>0.03</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>57 ± 10</td>
<td>57 ± 12</td>
<td>0.6</td>
</tr>
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</table>

Redo Procedures - 28 pts in Non PV Trigger Group
Reconnected veins at second procedure (96%) (3.4 +/- 0.9 PVs per pt)
Non-pv trigger at second procedure - 8 (29%) / New nonPV trigger in 7/8 (25%)
What is the Endpoint of AF ablation?

1. PVI remains the main endpoint (physiological rationale, RCTs against AADs/other ablation strategies)

2. Targeting inducible non-PV triggers enhances success, although in non-PAF more non-PV triggers can emerge over time.

3. Empirical extra-PV ablation has unclear physiological rationale (linear ablation, CFAE, GPs, target scar, HF sources) and all the head-to-head comparisons with PVI in the setting of RCTs have shown negative results with potential for harm.

4. The role of driver/rotor mapping and ablation requires further investigation.