Anatomy, Physiology and Ablation of Atrial Fibrillation

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Disclosure

• Medtronic, Inc. (Clinical Events Committee, consultant)
• Biosense-Webster, Boston Scientific, Medtronic, St. Jude (UF EP Fellowship Support)
Strategies in AF Ablation

• Mechanisms of atrial fibrillation
• Pulmonary vein isolation
  – Radiofrequency techniques
  – Cryoballoon techniques
• Strategies for ablation of persistent AF
• Surgical AF ablation approaches
• Focal impulse and rotor mapping/ablation
Mechanisms of AF

Extracardiac Factors:
- Hypertension
- Obesity
- Sleep apnea
- Hyperthyroidism
- Alcohol/drugs

Atrial Structural Abnormalities:
- Fibrosis
- Dilation
- Ischemia
- Infiltration
- Hypertrophy

Inflammation
- Oxidative stress

AF

Atrial tachycardia remodeling

RAAS activation

Genetic Variants:
- Channelopathy
- Cardiomyopathy

Atrial Electrical Abnormalities:
- ↑Heterogeneity
- ↓Conduction
- ↓Action potential duration/refractoriness
- ↑Automaticity
- Abnormal intracellular Ca²⁺ handling

Autonomic nervous system activation

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation
Mechanisms of Arrhythmogenesis

Triggers ↔ Substrate

Modulating Factors

e.g. autonomic, electrolyte, ischemia
Pathophysiology of AF

Triggers

PV/non-PV Triggers

Substrate

Electrophysiologic  Anatomic

Calkins et al. Heart Rhythm 2007
Length of the myocardial sleeves extending over the veins (mm)

<table>
<thead>
<tr>
<th></th>
<th>Pulmonary veins</th>
<th>Venae cavae</th>
</tr>
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<tbody>
<tr>
<td>Range</td>
<td>5 - 25</td>
<td>15 - 33</td>
</tr>
<tr>
<td>Average</td>
<td>13</td>
<td>24</td>
</tr>
<tr>
<td>RS</td>
<td>1 - 17</td>
<td>8 - 10†</td>
</tr>
<tr>
<td>LS</td>
<td>8 - 24*</td>
<td></td>
</tr>
<tr>
<td>RI</td>
<td>1 - 19</td>
<td></td>
</tr>
<tr>
<td>LI</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

Nathan and Eliakim.
Circulation 1966;34:412-422
Angiogram of a Left Inferior Pulmonary Vein Depicting the Source and Exit of Ectopic Activity
AF Ablation Efficacy Depends On Patient Population

- Paroxysmal
- Persistent
- Long-standing persistent
Lesion Sets for Paroxysmal AF Patients

• Most paroxysmal AF patients should receive only PV isolation
  – Wide antral, not just ostial

• A minority of paroxysmal AF patients may need more extensive lesion sets
  – Concomitant atrial flutter
  – Long AF episodes
  – Large atria
  – Structural heart disease
    • HTN, obesity, etc.
  – Re-do procedures

• Should we manage “recently-persistent” AF the same as paroxysmal?
Catheter Ablation of Atrial Fibrillation
Catheter Ablation For Paroxysmal AF

Cryoballoon

RF Ablation Catheter

Mapping Catheter

POSTERIOR VIEW

LSPV

RSPV

LIPV

RIPV

Left Atrium

Catheter Ablation Versus Antiarrhythmic Drugs for Atrial Fibrillation

Early Studies

The APAF Study

The A4 Study

Early studies limited by small study populations, variable entry criteria and definitions of success, and were conducted in a single or limited number of centers.
Atrial Fibrillation Ablation
Systematic Literature Review and Meta Analysis

Figure 3. Efficacy of catheter ablation in patients with AF.

Calkins et al. Circ Arrhythmia Electrophysiol 2009;2:349
Comparison of Antiarrhythmic Drug Therapy and RF Catheter Ablation in Patients With Paroxysmal Atrial Fibrillation

Trial data from:
1) Wilber, D. J. et al. JAMA 2010;303:333-340
2) FDA website
Comparison of Antiarrhythmic Drug Therapy and RF Catheter Ablation in Patients With Paroxysmal AF: 

**Thermocool Study**

![Graph showing comparison of Thermocool Study results](image)

- Symptomatic Atrial Arrhythmia
- Freedom From Symptomatic Atrial Arrhythmia
- HR, 0.24; 95% CI, 0.15-0.39; Log-rank P < .001

Follow-up, mo:

106 88 84 79 75 75 73 71 57

61 37 27 21 15 12 11 10 7 4

New Advances in RF Ablation – Contact Force
EFFICAS II: optimization of catheter contact force improves outcome of pulmonary vein isolation for paroxysmal atrial fibrillation

Pulmonary vein isolation at 3-month remapping. Comparison of durable isolation rates per vein in EFFICAS I, without CF guidelines, and EFFICAS II, with CF guidelines.  

Kautzner et al. Europace 2015;17:1229
Balloon Catheters

Gentlemen, I give you the Cardiac Catheter 8,000!
Cryoballoon Freezing of the Left Inferior Pulmonary Vein
Voltage Maps Pre- and Post Cryoballoon Ablation

Pre-Ablation

Post-Ablation
Procedural Success in the STOP AF Trial

A

Continued treatment success (%)

Days

0 100 200 300 400 500

CRYO = 69.9% (114/163)
68.6% KM estimate
(APS + freedom from CT)

p < 0.001 (exact binomial test of proportions)
p < 0.001 (log rank test, all follow-up)

BLANKED

DRUG = 7.3% (6/82)
7.3% KM estimate
(Freedom from CTF)

Cryo, n= 163 156 123 120 74 1
Drug, n= 82 71 11 6 5

Packer et al. JACC 2013;61:1713
Increased Incidence of Esophageal Thermal Lesions Using the Second-Generation 28-mm Cryoballoon

Metzner et al. *Circ Arrhythm Electrophysiol*. 2013;6:769-775
Single Procedure Freedom from AF, AT and AFL
Arctic Front Advance Cryoballoon Single Center Published Studies

Single Procedure Freedom From AF

Cryoablation vs. RF Ablation

“C’mon, c’mon — it’s either one or the other.”
Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation

Kuck et al, NEJM 2016
Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation

Kuck et al, NEJM 2016
A Randomized Comparison of Drug Therapy Versus Reablation *After a Failed Initial Ablation Procedure* in Patients With Paroxysmal Atrial Fibrillation

\[ \text{Number at risk} \]

<table>
<thead>
<tr>
<th>Group 1</th>
<th>77</th>
<th>62</th>
<th>56</th>
<th>53</th>
<th>49</th>
<th>46</th>
<th>45</th>
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<tbody>
<tr>
<td>Group 2</td>
<td>77</td>
<td>43</td>
<td>25</td>
<td>21</td>
<td>15</td>
<td>13</td>
<td>9</td>
</tr>
</tbody>
</table>

\[ P < 0.0001, \text{Log-Rank test} \]
A Randomized Comparison of Drug Therapy Versus Reablation After a Failed Initial Ablation Procedure in Patients With Paroxysmal Atrial Fibrillation

Pokushalov E et al. Circ Arrhythm Electrophysiol 2013;6:754-760
Long-Term Outcome Following Successful Pulmonary Vein Isolation: Pattern and Prediction of Very Late Recurrence

Complications of AF Ablation

- Thromboembolism/air embolism
- Cardiac tamponade
- Pulmonary vein stenosis
- Atrio-esophageal fistula
- Vascular access-related complications
  - Hematoma, pseudoaneurysm, AV fistula
- Left atrial flutters/atrial tachycardia
- Mitral valve trauma/catheter entrapment
- Phrenic nerve injury
- Radiation exposure/skin burns
- Acute coronary artery occlusion
- Periesophageal vagal injury
LUPV Stenosis
Necrotic ulcer within the anterior wall of the oesophagus in close proximity to the left atrial posterior wall 24 h after PVAI.

Left Atrial–Esophageal Fistula After Pulmonary Vein Isolation
Phrenic Nerve Palsy

Pre-Ablation

Post-Ablation
AF Ablation Efficacy Depends On Patient Population

- Paroxysmal
- Persistent
- Long-standing persistent
Atrial Fibrillation Begets Atrial Fibrillation

Wijffels, Circulation 1995;92:1954-68
Atrial Fibrillation Begets Atrial Fibrillation

Atrial Remodeling

• Remodeling is an adaptive regulatory process of cardiac myocytes that occurs over time in order to maintain homeostasis against external stresses
  – Electrophysiological (ionic)
  – Structural (extracellular)
  – Cellular
  – Neurohumoral
  – Genomic
• If left untreated, it may become irreversible (apoptosis, necrosis, and fibrosis)
• May be maladaptive and deleterious
Relationship of AF Mechanism to Clinical Forms

Ablation of Persistent AF

• Pulmonary vein isolation

  Plus??

• “Extensive substrate modification”
  – Ablation of CFEAs
  – Left-sided linear lesions (roof line, mitral isthmus line), posterior LA “box” lesions, appendage ablation
  – Cavo-tricuspid isthmus line, coronary sinus lesions, other right atrial lesions
  – Ablation of ganglionated plexi

• Rotor ablation
Ablation Strategies for Persistent or Long-Standing Persistent AF

- PVI
- PVI + linear lesions
- PVI + complex fractionated atrial electrograms (CFAEs)
- PVI + linear lesions + CFAEs
- PVI + ablation of focal sources and rotors
- PVI + isolation of LAA
- PVI + ablation of autonomic ganglia
- PVI + isolation of area of fibrosis
- PVI + ......
Catheter Ablation for Persistent AF

Stepwise Ablation Approach to Persistent AF

Haissaguerre et al

- Stepwise progression of lesions until AF terminates:
  - PVI
  - LA defragmentation
  - CS defragmentation/isolation
  - RA defragmentation

- Linear lesions only for macroreentry

- The longer the AF duration (especially >6 mo):
  - The more rotors are present
  - More linear lesions are needed
Standard Circumferential pulmonary vein isolation

Extensive pulmonary vein antrum isolation including the entire left atrial posterior wall down to the coronary sinus, and to the left side of the interatrial septum
Box Isolation of Fibrotic Areas

Figure 1. Left atrial voltage mapping in four patients with recurrences of paroxysmal atrial fibrillation despite durable pulmonary vein isolation (PVI) showing the variable severity and localization of left atrial fibrosis. Box isolation of the fibrotic areas (BIFA) is done in all cases with connection to the previous PVI lines. Color coding: red for substantially reduced voltages <0.5 mV and purple >1.5 mV. LPV and RPV = left and right pulmonary veins.
Approaches to Catheter Ablation for Persistent Atrial Fibrillation (STAR AF II)

Approaches to Catheter Ablation for Persistent Atrial Fibrillation

P=0.15 for the overall comparison, by the log-rank test

<table>
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<th>No. at Risk</th>
<th>0</th>
<th>1</th>
<th>3</th>
<th>5</th>
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<th>9</th>
<th>11</th>
<th>12</th>
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<th>19</th>
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<td>Pulmonary-vein isolation</td>
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<td>60</td>
<td>50</td>
<td>41</td>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation plus electrograms</td>
<td>244</td>
<td>242</td>
<td>161</td>
<td>137</td>
<td>124</td>
<td>72</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation plus lines</td>
<td>244</td>
<td>240</td>
<td>152</td>
<td>133</td>
<td>115</td>
<td>57</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Circumferential pulmonary vein isolation as index procedure for persistent atrial fibrillation

Freedom from ATa recurrences after 1 year follow-up according to ablation strategy (RFCA turquoise line; CB-AdvA red line) off drugs, considering (right panel) or not (left panel) a 3 months blanking period.

Giuseppe Ciconte et al. Europace 2015;17:559-565
How Can We Improve the Management of Persistent AF?

• **Better ablation strategies for persistent AF**
  - More aggressive catheter ablation
    • New catheter systems under development
  - Hybrid catheter/surgical (endocardial/epicardial) ablation
  - More targeted catheter ablation
    • FIRM ablation
  - Promotion of reverse remodeling before and after ablation

• **Prevention of persistent AF**
  - Earlier ablation for paroxysmal AF
Ablation of Persistent AF Using Multielectrode Catheters and Duty-Cycled Radiofrequency Energy
Lesions of the Standard Maze III
Surgical Procedure for AF

Cox JL. J Thorac Cardiovasc Surg 2003;126:1693
The Cox-Maze Procedure for Lone AF: A Single-Center Experience Over 2 Decades

Kaplan-Meier analysis of freedom from atrial fibrillation for the Cox-Maze procedure (III+IV)

Weimar T et al. Circ Arrhythm Electrophysiol 2012;5:8-14
Thoracoscopic Pulmonary Vein Isolation
Pulmonary Vein Isolation
Thoracoscopic Video-Assisted Pulmonary Vein Antrum Isolation, Ganglionated Plexus Ablation, and Periprocedural Confirmation of Ablation Lesions

Atrial Appendage Exclusion

Atriclip

Appendage
Minimally-Invasive Surgery and Catheter Ablation for Persistent AF

“Hybrid” Procedure

May be particularly useful for ablation of persistent atrial fibrillation, where the results of each technique alone are sub-optimal.
Hybrid Thoracoscopic Surgical and Transvenous Catheter Ablation of AF

Pison et al. JACC 2012;60:54
“Convergence” Procedure

Trans-Diaphragmatic Cardioscopy
Pericardial Access Through Diaphragm and Behind the Heart
“Convergence” Procedure

Gersak et al. J Thorac Cardiovasc Surg 2014;147:1411
European Experience of the Convergent Atrial Fibrillation Procedure: Multicenter outcomes in consecutive patients

FIGURE 2. Arrhythmia and intervention-free survival analysis.

Gersak et al. J Thorac Cardiovasc Surg 2014;147:1411
European Experience of the Convergent Atrial Fibrillation Procedure: Multicenter outcomes in consecutive patients

<table>
<thead>
<tr>
<th>Serious adverse event</th>
<th>No. (%) of 73</th>
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<tbody>
<tr>
<td>Operative mortality</td>
<td>0 (0)</td>
</tr>
<tr>
<td>&lt;30-d Mortality</td>
<td>0 (0)</td>
</tr>
<tr>
<td>&gt;30-d Mortality</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Stroke/CVA</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>TIA</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Tamponade</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Phrenic nerve palsy</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Esophageal fistula</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Newly developed third-degree AV block</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Acute limb ischemia</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Bleeding requiring transfusion</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td>Bleeding with conversion to sternotomy</td>
<td>2 (2.7)</td>
</tr>
</tbody>
</table>

Serious adverse events were observed in 8 patients (8 of 73; 11%); CVA, Cerebrovascular accident; TIA, transient ischemic attack; AV, atrioventricular.

Gersak et al. J Thorac Cardiovasc Surg 2014;147:1411
Mechanisms of Arrhythmogenesis

Triggers → Modulating Factors (e.g. autonomics, electrolytes, ischemia) → Substrate

Modulating Factors

e.g. autonomics, electrolytes, ischemia
Mechanisms of AF

• **Triggers** initiate AF

• **Drivers and rotors** perpetuate AF
  – Triggers that fire incessantly are drivers
Rotors and Spirals

Sandeep V. Pandit, and José Jalife Circulation Research. 2013;112:849-862
AF Ablation Paradigm Shift

Triggers $\rightarrow\rightarrow\rightarrow$ Substrate

- Focal impulse and rotor modulation (FIRM) hypothesis \textit{(Narayan et al)}:
  - AF is a substrate disease driven by a small number of drivers/rotors
    - Spatially stable over many cycles
Mapping of Focal Impulses and Rotors in Human AF

- **Invasive**
  - **Topera**: endocardial FIRM

- **Noninvasive**
  - **Cardioinsight**: epicardial FIRM
  - **EP Solutions**: endo- and epicardial FIRM
Basket Mapping Catheter

Yamada T. Indian Pacing Electrophysiol J 2007;7:97-109
Atrial Basket Catheter Mapping

Right Atrium

Left Atrium
FIRM Ablation
CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) Trial

![Graph showing freedom from atrial fibrillation over days with event-free survival for different groups.

- FIRM-Blind
- FIRM-Guided
- FIRM-Blind, 1st Ablation
- FIRM-Guided, 1st Ablation

Statistical significance:
- p = 0.016 for 1st Ablation
- p = 0.006 for all cases

Narayan et al. JACC 2012;60:628]
The number of driver regions ablated to terminate AF increases with the duration of persistent AF.

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Michel Haissaguerre et al. Circulation. 2014;130:530-538
Summary of Complex AF Mechanisms

Calkins et. al. Heart Rhythm 2007;4:816-861
Indications for Catheter Ablation of AF

- Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication
  - Paroxysmal: Catheter ablation is recommended* I
  - Persistent: Catheter ablation is reasonable IIa
  - Longstanding Persistent: Catheter ablation may be considered IIb

- Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent
  - Paroxysmal: Catheter ablation is reasonable IIa
  - Persistent: Catheter ablation may be considered IIb
  - Longstanding Persistent: Catheter ablation may be considered IIb

*Catheter ablation of symptomatic paroxysmal AF is considered a Class 1 indication only when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced center.
Catheter Ablation for Atrial Fibrillation

Class III: Harm

1. AF catheter ablation should not be performed in patients who cannot be treated with anticoagulant therapy during and following the procedure

2. AF catheter ablation to restore sinus rhythm should not be performed with the sole intent of obviating the need for anticoagulation

2014 AHA/ACC/HRS AF Guidelines
Atrial Fibrillation Management

AF drugs and ablation are the tip of the iceberg

- Obesity
- Sleep apnea
- Hypertension
- CHF
- Diabetes
- Alcohol
- Exercise
- Atrial myopathy
- Genetics
Long-Term Effect of Goal-Directed Weight Management in an Atrial Fibrillation Cohort

**FIGURE 2** Atrial Fibrillation Freedom Outcome According to Group

(A) Kaplan-Meier curve for AF-free survival without the use of rhythm control strategies. (B) Kaplan-Meier curve for AF-free survival for total AF-free survival (multiple ablation procedures with and without drugs). Abbreviations as in Figure 1.
Treatment of Obstructive Sleep Apnea Reduces the Risk of Atrial Fibrillation Recurrence After Catheter Ablation

Fein et al. JACC 2013;62:300
Questions?