Overview of Cardiac Arrhythmias and Treatment Options

William H. Sauer, MD
Chief, Cardiac Arrhythmia Services
Brigham and Women’s Hospital
Harvard Medical School
Road Map

• Overview of Cardiac Arrhythmias and Treatment Options
  • Antiarrhythmic Medications
    • AFFIRM 1999
    • EAST AF 2019
  • Implantable Devices
    • SCD-HeFT 2005
  • Catheter Ablation
    • CABANA 2019
    • PAUSE-SCD 2021

• Summary
Cardiac Arrhythmias

- Too Fast (Tachyarrhythmias)
  - Atrial Fibrillation and Atrial Flutter
  - Supraventricular Tachycardia (SVT)
  - Ventricular Tachycardia (VT) and Ventricular Fibrillation (VF)
- Too Slow (Bradyarrhythmias)
  - Sinus Node Dysfunction
  - Heart Block and Conduction System Disease
  - Premature Ventricular Contractions (PVCs)
Norman J. Holter (1914 – 1983)  
"Father" Of Ambulatory ECG Monitoring First Holter 1947:  
Weight 85 pounds
Dr. Sauer:

As you requested, attached is a copy of an ECG report I took today. I started to taking the apixaban yesterday. Can you please advise as respects to the Flecainide?

**Patient:** Brooks Martin, 5/4/62 (57yrs)

**Recorded:** Thursday, September 12, 2019 at 11:34:42 AM

**Heart Rate:** 68 BPM

**Duration:** 30s

**Instant Analysis:** Normal

---

**Enhanced Filter, Mains Frequency:** 60Hz  **Scale:** 25mm/s, 10mm/mV
Irregular Pulse Notification Algorithm

Tachogram = Periodic, opportunistic measurements

Positive triggers frequent measurements
Not confirmed ⇒ return to usual sampling

The algorithm does not use the watch ECG feature
# Initial Irregular Pulse Notifications

<table>
<thead>
<tr>
<th>Age</th>
<th>Notified / Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>2,161 / 419,297</td>
<td>0.52</td>
</tr>
<tr>
<td>≥ 65</td>
<td>775 / 24,626</td>
<td>3.2</td>
</tr>
<tr>
<td>55–64</td>
<td>556 / 42,633</td>
<td>1.3</td>
</tr>
<tr>
<td>40–54</td>
<td>488 / 132,696</td>
<td>0.37</td>
</tr>
<tr>
<td>22–39</td>
<td>341 / 219,179</td>
<td>0.16</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>Notified / Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>461 / 177,087</td>
<td>0.26</td>
</tr>
<tr>
<td>Male</td>
<td>1,672 / 238,700</td>
<td>0.70</td>
</tr>
</tbody>
</table>

Perez, MV et al. NEJM 2019; 381.20: 1909-1917.
Heart Rate Over 120 — 200 BPM
Average
This ECG was not checked for AFib because your heart rate was over 120 BPM.

If you repeatedly get this result or you're not feeling well, you should talk to your doctor.

Reported Symptoms
- Rapid, pounding, or fluttering heartbeat
- Chest tightness or pain
- Fainting

iOS 12.1.4, watchOS 5.1.3, Watch4.2
Arrhythmia Treatment Options

• Medical Therapy
  • Antiarrhythmic Drug Therapy
  • Anticoagulation for Stroke Prevention

• Pacemakers
  • Conduction System Pacing
  • Cardiac Resynchronization

• Implantable Cardiac Defibrillators
  • Identification of high risk patients (primary prevention)

• Catheter Ablation
Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

Antiarrhythmic Medications

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AFFIRM – Study Overview

• Randomized comparison of two treatment strategies
  • Rate control + anticoagulation
  • Rhythm control +/- anticoagulation

• Subjects without symptoms, but with risk factors for stroke
• Enrollment 1995 - 1999

The AFFIRM investigators. NEJM 2002; 347.23: 1825-1833.
Patients

• Age = 69.7 +/- 9.0 years
• 39% Women
• Abnormal LV function: 26%
  • NYHA HF Class > 2: 9%
• HTN: 51%

• Rate Control
  • Digoxin: 48%
  • Beta-blockers: 47%
  • Ca++ blockers: 39%

• Rhythm Control
  • Amiodarone: 38%
  • Sotalol: 31%
  • Propafenone: 9%
  • Others (<5%): Flecainide, Disopyramide, Quinadine, Moricizine

The AFFIRM investigators. NEJM 2002; 347.23: 1825-1833.
Primary Endpoint: All cause mortality

The AFFIRM investigators. NEJM 2002; 347.23: 1825-1833.
Secondary Endpoint-Death, Disabling Stroke or Anoxic Encephalopathy, Major Bleed, or Cardiac Arrest

Rhythm
Rate

\( p = 0.33 \)

The AFFIRM investigators. NEJM 2002; 347.23: 1825-1833.
Warfarin Use

% Using Warfarin at Follow-up Visit

<table>
<thead>
<tr>
<th>Time</th>
<th>BL</th>
<th>2 M</th>
<th>4 M</th>
<th>1 Y</th>
<th>2 Y</th>
<th>3 Y</th>
<th>4 Y</th>
<th>5 Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate</td>
<td>80</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Rhythm</td>
<td>80</td>
<td>80</td>
<td>80</td>
<td>80</td>
<td>80</td>
<td>80</td>
<td>80</td>
<td>80</td>
</tr>
</tbody>
</table>

Legend:
- Yellow: Rate
- Grey: Rhythm
Limitations of AFFIRM

• Patients with any symptoms of AF were not enrolled
• The mean follow-up of 3.5 years is not long-term.
  • AF begets AF – this makes cross-over to rhythm control difficult
  • AF symptoms could develop over time
• AFFIRM did not evaluate low risk patients
• AFFIRM did not evaluate patients with heart failure
The Case for Rhythm Control within AFFIRM

• Rhythm control arm was only successful at sinus rhythm maintenance 60% of the time
  • Not truly a comparison of strategies
  • Actually, there was significant survival benefit in those patients able to maintain sinus rhythm
• The apparent increase in stroke and mortality risk in the rhythm control arm is entirely explained by lack of anticoagulation

Summary of AFFIRM (as I see it)

• Rate control is an acceptable strategy for treatment of *asymptomatic* AF
• Rhythm control should be considered if there is a decent chance for long-term sinus rhythm maintenance
• Anticoagulation should be continued in patients with risk factors for stroke – even in those who appear to maintain sinus rhythm
• Patients with any symptoms attributable to AF should be treated with a rhythm control strategy
Fast forward 20 years to EAST-AF
• Enrollment
  • Study population – key characteristics
    • Median age 70, >mild cognitive impairment 44%
    • First episode: 38%, paroxysmal: 36%; 26% persistent
    • 30% asymptomatic, 54% in NSR at enrollment
    • Median days since AF diagnosis: 36
    • CHA2DS2-VASc 3.4
    • CHF: 29%
    • 90% anticoagulated
    • 80% on beta blockade

• Outcomes
  • Enrollment stopped early due to efficacy of treatment arm, median followup 5.1 years.
  • Choice of rhythm control in treatment arm:
    • At enrollment: 36% flecainide, 20% amio, 8% ablation
    • After 5 years: 19% ablation
  • Primary composite #1: 3.9 vs. 5.0/100 person-years (P-Y) (hazard ratio [HR] 0.79, 95% confidence interval [CI] 0.66-0.94, (p 0.005)
  • Primary composite #2: LOS 5.1 vs. 5.8 days (p 0.23). AFFIRM and AF-CHF each reported increased LOS with rhythm control.
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Early Rhythm Control</th>
<th>Usual Care</th>
<th>Treatment Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First primary outcome — events/person-yr (incidence/100 person-yr)</strong></td>
<td>249/6399 (3.9)</td>
<td>316/6332 (5.0)</td>
<td>0.79 (0.66 to 0.94)†</td>
</tr>
<tr>
<td><strong>Components of first primary outcome — events/person-yr</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(incidence/100 person-yr)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>67/6915 (1.0)</td>
<td>94/6988 (1.3)</td>
<td>0.72 (0.52 to 0.98)‡</td>
</tr>
<tr>
<td>Stroke</td>
<td>40/6813 (0.6)</td>
<td>62/6856 (0.9)</td>
<td>0.65 (0.44 to 0.97)‡</td>
</tr>
<tr>
<td>Hospitalization with worsening of heart failure</td>
<td>139/6620 (2.1)</td>
<td>169/6558 (2.6)</td>
<td>0.81 (0.65 to 1.02)‡</td>
</tr>
<tr>
<td>Hospitalization with acute coronary syndrome</td>
<td>53/6762 (0.8)</td>
<td>65/6816 (1.0)</td>
<td>0.83 (0.58 to 1.19)‡</td>
</tr>
<tr>
<td><strong>Second primary outcome — nights spent in hospital/yr</strong></td>
<td>5.8±21.9</td>
<td>5.1±15.5</td>
<td>1.08 (0.92 to 1.28)¶</td>
</tr>
<tr>
<td><strong>Key secondary outcomes at 2 yr</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in left ventricular ejection fraction — %</td>
<td>1.5±9.8</td>
<td>0.8±9.8</td>
<td>0.23 (−0.46 to −0.91)¶</td>
</tr>
<tr>
<td>Change in EQ-5D score</td>
<td></td>
<td>-1.0±21.4</td>
<td>-2.7±22.3</td>
</tr>
<tr>
<td>Change in SF-12 Mental Score**</td>
<td>0.7±10.6</td>
<td>1.6±10.1</td>
<td>1.20 (−2.04 to −0.37)¶</td>
</tr>
<tr>
<td>Change in SF-12 Physical Score**</td>
<td>0.3±8.5</td>
<td>0.1±8.2</td>
<td>0.33 (−0.39 to 1.06)¶</td>
</tr>
<tr>
<td>Change in MoCA score</td>
<td>0.1±3.3</td>
<td>0.1±3.2</td>
<td>−0.14 (−0.39 to 0.12)¶</td>
</tr>
<tr>
<td>Sinus rhythm — no. of patients with feature/total no. (%)</td>
<td>921/1122 (82.1)</td>
<td>687/1135 (60.5)</td>
<td>3.13 (2.55 to 3.84)† †</td>
</tr>
<tr>
<td>Asymptomatic — no. of patients with feature/total no. (%)</td>
<td>861/1159 (74.3)</td>
<td>850/1171 (72.6)</td>
<td>1.14 (0.93 to 1.40)† †</td>
</tr>
</tbody>
</table>
• AFFIRM did not show superiority for rhythm control
  • Inconsistent Anticoagulation
  • Low efficacy of antiarrhythmic medications
• EAST-AF be viewed as a correction of the present-day problems with AFFIRM
  • Ablation included (~20% patients)
  • Improved anticoagulation adherence
  • Improved medical therapy for non-arrhythmic therapy
Implantable Devices for Arrhythmias

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• Summary
Implantable Cardiac Rhythm Devices - Pacing
Options for Pacing

Dual Chamber Pacer

Biventricular Pacer

His Bundle Pacer
## Historical perspective

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1958</td>
<td>First External Pacemaker</td>
</tr>
<tr>
<td>1960</td>
<td>First Implantable Pacemaker</td>
</tr>
<tr>
<td>1970</td>
<td>Pediatric Asynchronous Pulse Generator</td>
</tr>
<tr>
<td>1979</td>
<td>Rate response</td>
</tr>
<tr>
<td>1986</td>
<td>Radically smaller size</td>
</tr>
<tr>
<td>1989</td>
<td>1st Microprocessor-based, Mode switching</td>
</tr>
<tr>
<td>1990</td>
<td>Full automaticity</td>
</tr>
<tr>
<td>1991</td>
<td>1st MRI-Conditional</td>
</tr>
<tr>
<td>1995</td>
<td>Rate response via activity &amp; minute ventilation</td>
</tr>
<tr>
<td>1998</td>
<td>MVP™, Full automaticity</td>
</tr>
<tr>
<td>2004</td>
<td>MRI-Conditional</td>
</tr>
<tr>
<td>2006</td>
<td>MVP™, Full automaticity</td>
</tr>
<tr>
<td>2011</td>
<td>MRI-Conditional</td>
</tr>
<tr>
<td>2016</td>
<td>Transcatheter Pacing System</td>
</tr>
<tr>
<td>2013</td>
<td>MRI-Conditional</td>
</tr>
</tbody>
</table>
Cardiac Resynchronization Therapy (CRT)
Typical LBBB pattern randomized to His corrective pacing

Tung, et al. JACC 2019 and LBCT HRS 2019
**Results - Per-Protocol Analysis**

**BiV-CRT**
- Baseline LVEF: 29.6%
- Follow-up LVEF: 33.9%

**His-CRT**
- Baseline LVEF: 26.3%
- Follow-up LVEF: 33.6%

Tung, et al. JACC 2019 and LBCT HRS 2019
Electrocardiographic outcomes

Lack of QRS narrowing during:

- BiV-CRT: 20.6%
- LOT-CRT: 3.3%

Jastrzębski, M et al. Heart Rhythm 2021
Echocardiographic outcomes

Baseline CRT

Super-response 24.4%

Jastrzębski, M et al. Heart Rhythm 2021
Treatment Options - ICDs
Hypothesis and Primary Endpoint

• To determine, by intention-to-treat analysis, if amiodarone or a conservatively programmed shock-only single lead ICD reduces all-cause mortality compared to placebo* in patients with either ischemic or non-ischemic NYHA Class II and III CHF and EF ≤ 35%.

*Double-blind for drug therapy
Kaplan-Meier Estimates of Death from Any Cause

<table>
<thead>
<tr>
<th>Treatment Comparison</th>
<th>Hazard Ratio (97.5% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone vs. placebo</td>
<td>1.06 (0.86–1.30)</td>
<td>0.53</td>
</tr>
<tr>
<td>ICD therapy vs. placebo</td>
<td>0.77 (0.62–0.96)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Placebo  
(244 deaths; 5-yr event rate, 0.361)

Amiodarone  
(240 deaths; 5-yr event rate, 0.340)

ICD therapy  
(182 deaths; 5-yr event rate, 0.289)

Bardy G et al. NEJM 2005; 352:3
Hazard Ratios for the Comparison of Amiodarone and ICD Therapy with Placebo

<table>
<thead>
<tr>
<th>Amiodarone vs. Placebo</th>
<th>Subgroup</th>
<th>ICD Therapy vs. Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 398</td>
<td>Hazard ratio (97.5% CI)</td>
<td>No. 382</td>
</tr>
<tr>
<td>1.17 (0.72–1.90)</td>
<td>Female sex</td>
<td>0.96 (0.58–1.61)</td>
</tr>
<tr>
<td>1.04 (0.83–1.30)</td>
<td>Male sex</td>
<td>0.73 (0.57–0.93)</td>
</tr>
<tr>
<td>1.00 (0.76–1.32)</td>
<td>Age &lt;65 yr</td>
<td>1.098</td>
</tr>
<tr>
<td>1.13 (0.83–1.52)</td>
<td>Age ≥65 yr</td>
<td>0.578</td>
</tr>
<tr>
<td>1.06 (0.84–1.34)</td>
<td>White race</td>
<td>1.283</td>
</tr>
<tr>
<td>1.08 (0.71–1.62)</td>
<td>Nonwhite race</td>
<td>0.75 (0.48–1.17)</td>
</tr>
<tr>
<td>1.04 (0.84–1.29)</td>
<td>LVEF ≤30%</td>
<td>1.390</td>
</tr>
<tr>
<td>1.24 (0.66–2.31)</td>
<td>LVEF &gt;30%</td>
<td>285</td>
</tr>
<tr>
<td>1.06 (0.80–1.41)</td>
<td>QRS &lt;120 msec</td>
<td>977</td>
</tr>
<tr>
<td>1.05 (0.78–1.41)</td>
<td>QRS ≥120 msec</td>
<td>699</td>
</tr>
<tr>
<td>517</td>
<td>1.61 (1.17–2.23)</td>
<td>6-Min walk test</td>
</tr>
<tr>
<td>547</td>
<td>0.82 (0.56–1.20)</td>
<td>&lt;950 ft</td>
</tr>
<tr>
<td>545</td>
<td>0.72 (0.46–1.12)</td>
<td>950–1275 ft</td>
</tr>
<tr>
<td>1.10 (0.85–1.42)</td>
<td>Beta-blocker</td>
<td>1157</td>
</tr>
<tr>
<td>530</td>
<td>0.98 (0.69–1.38)</td>
<td>No beta-blocker</td>
</tr>
<tr>
<td>514</td>
<td>1.20 (0.87–1.65)</td>
<td>Diabetes</td>
</tr>
<tr>
<td>1178</td>
<td>1.00 (0.77–1.30)</td>
<td>No diabetes</td>
</tr>
</tbody>
</table>
SCD-HeFT: Primary Conclusions

• In class II or III CHF patients with EF < 35% on good background drug therapy, the mortality rate for placebo-controlled patients is 7.2% per year over 5 years

• Simple, single lead, shock-only ICDs decrease mortality by 23%

• Amiodarone, when used as a primary preventative agent, does not improve survival
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Catheter Ablation

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Arrhythmia Treatment Options – Ablation
Cardiac Ablation Volume

CAGR 2010 – 2020

- **AF**: 16.6%
- **VT**: 5.8%
- **AFL**: 3.9%
- **SVT**: 2.7%
- **ALL**: 9.8%

Cardiac Ablation Volume (2010-2020):

- **2010**: 142,740
- **2011**: 150,480
- **2012**: 163,420
- **2013**: 179,580
- **2014**: 194,010
- **2015**: 213,060
- **2016**: 235,810
- **2017**: 262,480
- **2018**: 293,190
- **2019**: 327,830
- **2020**: 366,020
Consider the Alternative -- Antiarrhythmic Drugs
(Amiodarone HCl) Tablets

DESCRIPTION

(Amiodarone HCl) Tablets are a member of a new class of antiarrhythmic drugs with predominantly Class III (Vaughan Williams' classification) effects. Tablets are available in three strengths, containing 100 mg, 200 mg, and 400 mg amiodarone hydrochloride, for oral administration. The 100 mg tablets are white tablets with the following inactive ingredients: anhydrous lactose, colloidal silicone dioxide, corn starch, magnesium stearate and povidone. The 200 mg tablets are pink, scored tablets with the following inactive ingredients: lactose monohydrate, magnesium stearate, povidone, pregelatinized corn starch, sodium starch glycolate, stearic acid, FD&C Red 40 and FD&C Yellow 6. The 400 mg tablets are light yellow, scored tablets with the following inactive ingredients: colloidal silicon dioxide, corn starch, lactose monohydrate, magnesium stearate, povidone and D&C Yellow 10 Aluminum Lake.

Amiodarone hydrochloride, the active ingredient in Tablets, is a benzofuran derivative: 2-butyl-3-benzofuranyl 4-[2-(diethylamino)-ethoxy]-3,5-diiodophenyl ketone hydrochloride. It is not chemically related to any other available antiarrhythmic drug.

The structural formula is as follows:

\[
\text{C}_2\text{H}_3\text{I}_2\text{NO}_3\cdot\text{HCl}
\]

Molecular Weight: 681.8
PRECAUTIONS

Impairment of Vision
Optic Neuropathy and/or Neuritis
Cases of optic neuropathy and optic neuritis have been reported (see “WARNINGS”).

Corneal Microdeposits
Corneal microdeposits appear in the majority of adults treated with amiodarone. They are usually discernible only by slit-lamp examination, but give rise to symptoms such as visual halos or blurred vision in as many as 10% of patients. Corneal microdeposits are reversible upon reduction of dose or termination of treatment. Asymptomatic microdeposits alone are not a reason to reduce dose or discontinue treatment (see “ADVERSE REACTIONS”).

Neurologic
Chronic administration of oral amiodarone in rare instances may lead to the development of peripheral neuropathy that may resolve when amiodarone is discontinued, but this resolution has been slow and incomplete.

Photosensitivity
Amiodarone has induced photosensitization in about 10% of patients; some protection may be afforded by the use of sun-barrier creams or protective clothing. During long-term treatment, a blue-gray discoloration of the exposed skin may occur. The risk may be increased in patients of fair complexion or those with excessive sun exposure, and may be related to cumulative dose and duration of therapy.

Thyroid Abnormalities
Amiodarone inhibits peripheral conversion of thyroxine (T₄) to triiodothyronine (T₃) and may cause increased thyroxine levels, decreased T₃ levels and increased levels of inactive reverse T₃ (rT₃) in clinically euthyroid patients. It is also a potential source of large amounts of inorganic iodine. Because of its release of inorganic iodine, or perhaps for other reasons, amiodarone can cause either hypothyroidism or hyperthyroidism. Thyroid function should be monitored prior to treatment and periodically thereafter, particularly in elderly patients, and in any patient with a history of thyroid nodules, goiter or other thyroid dysfunction. Because of the slow elimination of amiodarone and its metabolites, high plasma iodide levels, altered thyroid function and abnormal thyroid-function tests may persist for several weeks or even months following Pacarone® (Amiodarone HCl) Tablets withdrawal.
The following side-effect rates are based on a retrospective study of 241 patients treated for 2 to 1,515 days (mean 441.3 days).

**The following side effects were each reported in 10 to 33% of patients:**
- Gastrointestinal: Nausea and vomiting.

**The following side effects were each reported in 4 to 9% of patients:**
- Dermatologic: Solar dermatitis/photosensitivity.
- Neurologic: Malaise and fatigue, tremor/abnormal involuntary movements, lack of coordination, abnormal gait/ataxia, dizziness, paresthesias.
- Gastrointestinal: Constipation, anorexia.
- Ophthalmologic: Visual disturbances.
- Hepatic: Abnormal liver-function tests.
- Respiratory: Pulmonary inflammation or fibrosis.

**The following side effects were each reported in 1 to 3% of patients:**
- Thyroid: Hypothyroidism, hyperthyroidism.
- Neurologic: Decreased libido, insomnia, headache, sleep disturbances.
- Cardiovascular: Congestive heart failure, cardiac arrhythmias, SA node dysfunction.
- Gastrointestinal: Abdominal pain.
- Hepatic: Nonspecific hepatic disorders.
- Other: Flushing, abnormal taste and smell, edema, abnormal salivation, coagulation abnormalities.
What is the most important information I should know about amiodarone Tablets?

Tablets can cause serious side effects that can lead to death including:

- lung damage
- liver damage
- worse heartbeat problems
- thyroid problems

Call your doctor or get medical help right away if you have any symptoms such as the following:

- shortness of breath, wheezing, or any other trouble breathing; coughing, chest pain, or spitting up of blood
Catheter Ablation

• Continued advancements with improved technology leading to improved outcomes
  • Electroanatomical mapping
  • Intracardiac echocardiography
  • Force sensing catheters
  • Automated signal processing
  • Introduction of varied energy sources
Identification of an AF trigger

Preliminary Findings

<table>
<thead>
<tr>
<th>Sinus Rhythm with 1st Degree AVB Blocked PAC and Atrial Fibrillation/Flutter Onset</th>
</tr>
</thead>
</table>

Blocked PAC
Resets Sinus Node

Same PAC Initiates AF
Equipment and Personnel in the Ablation

- Fluoroscopy
- Electroanatomical Mapping System
- Ultrasound catheter
- Ablation catheter
- Mapping catheter(s)

- MD Assistant
- Technicians
- Nurses
- Anesthesiologist
- Electrophysiologist
Catheter Positions for Identification of AF initiation
Before Ablation

Sinus rhythm

Before Ablation

Pulmonary Vein begins fibrillating...

... which triggers Atrial fibrillation

Atrial Fibrillation
Electroanatomical Mapping
Sinus rhythm (on surface)

After Ablation

Left Superior PV Fibrillation (after isolation)

Atrium in Sinus Rhythm
Electroporation and Pulsed Field Ablation

**Abstract**

**BACKGROUND** Catheter ablation of atrial fibrillation using thermal energies such as radiofrequency or cryotherapy is associated with indiscriminate tissue destruction. During pulsed field ablation (PFA), subsecond electric fields create microscopic pores in cell membranes—a process called electroporation. Among cell types, cardiomyocytes have among the lowest thresholds to these fields, potentially permitting preferential myocardial ablation.

**OBJECTIVES** The purpose of these 2 trials was to determine whether PFA allows durable pulmonary vein (PV) isolation without damage to collateral structures.

**METHODS** Two trials were conducted to assess the safety and effectiveness of catheter-based PFA in paroxysmal atrial fibrillation. Ablation was performed using proprietary bipolar PFA waveforms: either monophasic with general anesthesia and paralytics to minimize myocardial contraction, or biphasic with sedation because there was minimal muscle stimulation. No ischaemic protection strategy was used. Real-time electrophysiological mapping was repeated after 2 months to assess the durability of PV isolation.

**RESULTS** In 81 patients, all PVs were acutely isolated by monophasic (n = 15) or biphasic (n = 66) PFA with a mean delivery/activation time of 3.2 ± 2.4 min, and fluoroscopy time of 11.1 ± 7.6 min. With no subsequent wavefront reentry, durability at 3 months improved from 18% to 100% of patients with all PVs isolated. Beyond 1 procedure-related pericardial tamponade, there were no additional primary adverse events over the 120-day median follow-up, including stroke, phrenic nerve injury, PV stenosis, and myocardial injury. The 12-month Kaplan-Meier estimate of freedom from any adverse event was 87% ± 5.6%.

**CONCLUSIONS** In first-in-human trials, PFA preferentially affected myocardial tissue, allowing facile ultra-rapid PV isolation with excellent durability and chronic safety. IMPULSE: A Safety and Feasibility Study of the IONIA Approach Endocardial Ablation System to Treat Atrial Fibrillation [NCT03230388]; and PRESS: A Safety and Feasibility Study of the PAF/PULS Endocardial Ablation System to Treat Paroxysmal Atrial Fibrillation [NCT03744779].
## Electroporation: Tissue Specificity

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>PEF Ablation Threshold (V/cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nerve</td>
<td>3800</td>
</tr>
<tr>
<td>Vascular smooth muscle</td>
<td>1750</td>
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<tr>
<td>Red blood cell</td>
<td>1600</td>
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<tr>
<td>Myocardium</td>
<td>400</td>
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</tbody>
</table>

Adapted from Reddy et al., JACC EP 2018
How well does ablation work?
Patient Randomization

Subjects 2204

Ablation Therapy 1108
- Ablated 1006 (90.8%)
  - Repeat ablation 215 (19.4%)
- Not ablated 102 (9.2%)
- Completed FU 1002 (90.4%) 48.9 mo

Drug Therapy 1096
- Drug Treated 1092 (99.6%)
  - Rhythm control 953 (87.2%)
  - Rate control only 126 (11.5%)
- Cross Over Ablated 301 (27.5%)
- Completed FU 966 (88%) 48.2 mo

Crossovers

* Withdrew <3 years

Packer DL et al. CABANA. JAMA 2019
Primary Endpoint (Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest (Per Protocol)

Ablation vs. Drug
Hazard ratio: 0.73 (95% CI, 0.54–0.99)
P=0.046

Number at risk
Drug  
Ablation

<table>
<thead>
<tr>
<th>Months since randomization</th>
<th>Event rate (%)</th>
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<tr>
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<tr>
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<td>3</td>
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<tr>
<td>48</td>
<td>0</td>
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</tbody>
</table>

Packer DL et al. CABANA. JAMA 2019
Ablation vs. Drug
Hazard ratio: 0.53 (95% CI, 0.46–0.61)
P<0.0001
Freedom from any ICM documented ATA at 2 years follow-up

- **All patients**
- **Patients with documented ATA before PVI**

<table>
<thead>
<tr>
<th>Months</th>
<th>Number at risk</th>
<th>Without ATA after PVI (N = 72)</th>
<th>ATA burden</th>
<th>N = 84</th>
<th>ATA burden</th>
<th>AF burden reduction</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>105</td>
<td></td>
<td>(0, 0) %</td>
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<td>100</td>
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<tr>
<td>3</td>
<td>105</td>
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<td>(1.71, 6.58)</td>
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<tr>
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<td>(1.71, 17.24)</td>
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<td>100, 100</td>
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</tbody>
</table>

Duytschaever et al. CLOSE to CURE Study. Heart Rhythm 2020
Catheter Ablation and 1 Year Freedom of AF

- Paroxysmal: ~85%
- Persistent: ~70%
- Longstanding Persistent: ~50%

Why not 100%?

- Pulmonary veins can electrically “reconnect” (The heart can heal!)
- There can be other sources for AFib besides the pulmonary veins.
Study Design

Secondary prevention or primary prevention with inducible scar-mediated MMVT, EF<50%

Refuse randomization

ICD + ABLATION
(VF >230, VT-10 bpm, ATP3)

Substrate-based ablation of targeted VTs and scar homogenization (Epicardial encouraged/discretionary)

Primary outcome: Recurrent VT, CV rehospitalization, and death at 2 years

Secondary: Primary outcome vs. Registry Recurrent VT/ CV rehospitalization/ death individually

ICD
(VF >230, VT-10 bpm, ATP3)

ABLATION only
Registry

Results - Ablation Techniques

- Epicardial approach in 52%
- Multielectrode catheters in 88%

- Predominant strategies: Pacemapping 40%, ILAM 30%, VT activation 30%, entrainment 22%, LP elimination 67%
- Termination of at least 1 VT 59% of cases, noninducibility 80%
- Stable VTs in 41%, multiple 50%
- Median RF time: 45 min (30-60 min), procedural duration: 240 min (166-280 min)
Results- Primary Outcome

Cardiac Arrhythmias: Concluding Remarks

William H. Sauer, MD
Chief, Cardiac Arrhythmia Services
Brigham and Women’s Hospital
Harvard Medical School
Road Map

• Overview of Cardiac Arrhythmias and Treatment Options
  • Antiarrhythmic Medications
    • AFFIRM 1999
    • EAST AF 2019
  • Implantable Devices
    • SCD-HeFT 2005
  • Catheter Ablation
    • CABANA 2019
    • PAUSE-SCD 2021
• Summary
Summary

• Cardiac arrhythmias are increasingly being recognized by patients
• Treatment options continue to evolve
• Catheter ablation is superior to medications for controlling arrhythmias
Thank You
Thank You - Brigham and Women's Hospital Cardiac Arrhythmia Service

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