Catheter Based Therapy for AFIB

Why?
Epidemiology of Atrial Fibrillation

- Risk for developing AFIB is 1 in 4 men and women over >40 years of age
- Most common sustained cardiac arrhythmia
- AFIB is associated with more hospitalizations than any other arrhythmia
- Prevalence: AF affects > 2.9 million in USA
- Incidence: 160,000 new cases dx per year

Clinical Consequences of AFIB

- Symptomatic
  - Palpitations, dyspnea, fatigue, chest pain, lightheadedness

- Cerebrovascular accident
  - 15% of all strokes
  - Incidence of all cause stroke in AFIB is 5%
  - greater severity….2.23 Odds ratio for bedridden state
Clinical Consequences of AFIB

- Heart failure
  - Tachycardia mediated cardiomyopathy
  - Exacerbates heart failure

- Impaired quality of life

- Increased mortality
  - 2 to 3 fold increase in mortality

Treating Atrial Fibrillation

- 30% of all AF patients are left undiagnosed
- 70% of AF patients are suitable for treatment

- **Rhythm Control**
  - Suppressive (Anti arrhythmic Drug) Therapy
    - 50% effective

- **Rate Control therapy**
Treatment for Atrial Fibrillation

- Why are there more than 5 Antiarrhythmic Drugs for the treatment of AFIB?

- Answer: Not one of them is universally effective!

Drug Therapy for Prevention of Recurrent Atrial Fibrillation

Rate Control Strategy: AFFIRM

Flaws in Rate Control Strategy

- Minimize symptoms related to atrial fibrillation
- Committing young patients without heart disease to lifelong drug therapy and anticoagulation [outcome unknown!!]
- Forcing patients to accept rate controlling drug side effects [fatigue, ED, constipation, orthostasis]
- Organ toxicity [amiodarone] and proarrhythmia [dofetilide - SCD]
Rate-control vs. Rhythm-control Strategy

**AFFIRM: Predictors of Mortality**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Risk Ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus Rhythm</td>
<td>0.54</td>
<td>0.42 - 0.71</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Warfarin</td>
<td>0.47</td>
<td>0.36 - 0.61</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Digoxin</td>
<td>1.50</td>
<td>1.18 - 1.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AA Drugs</td>
<td>1.41</td>
<td>1.10 - 1.83</td>
<td>&lt;0.0005</td>
</tr>
</tbody>
</table>

*Other significant factors in model: age, CAD, CHF, smoking, stroke/TIA, normal LVEF, MR.*


The Promise of Catheter Ablation

- Curative procedure
  - Effectively maintain sinus rhythm
- Avoid side effects of AADs
  - Improve left ventricular function
  - Improve Quality of Life
  - Reduce mortality
What does Catheter Ablation Provide?

- Tissue destruction
  - Point lesions
  - Non-linear/non-contiguous lesions

Can AFIB be cured by destroying atrial tissue?

- What is the mechanism of AFIB?
- What tissue needs to be destroyed?
- Can catheter ablation lesions be?
  - Reliable
  - Reproducible
  - Safe
“Learning by Burning”

What do we know?
Natural History of Paroxysmal AF
PACs initiating Paroxysmal AF

SPONTANEOUS INITIATION OF ATRIAL FIBRILLATION BY ECTOPIC BEATS ORIGINATING IN THE PULMONARY VEINS.

M. HARADAIGUIRO, M.D., PIERRE JAN, M.D., DENN C. SHAM, M.D., ATSUSHI TAKAHASHI, M.D., MEEZE HOON, M.D., GILES QUINN, M.D., STEPHANIE GARRIGOU, M.D., ALAIN LE MOINE, M.D., PHILIPPE LE METAYER, M.D., AND JACQUES CLEMENTY, M.D.

Conclusion: The pulmonary veins are an important source of ectopic beats, initiating frequent paroxysms of atrial fibrillation. These foci respond to treatment with radio-frequency ablation. (N Engl J Med 1995;338:659-66.) ©1995, Massachusetts Medical Society.
**Mechanism of Paroxysmal AFIB**

**Focal Triggers**

This procedure ablates foci (trigger sites) thought to be responsible for initiation of AF.

Care must be taken to avoid ablating within pulmonary veins to avoid potential complication of pulmonary vein stenosis.

**Pulmonary Vein Isolation**

- This procedure ablates foci (trigger sites) thought to be responsible for initiation of AF.
- Care must be taken to avoid ablating within pulmonary veins to avoid potential complication of pulmonary vein stenosis.
**Encircling Ostial Ablation Isolating PV Triggers**
- Segmental or circumferential lesions placed at ostia of the pulmonary veins (PV)
- Highly effective ablation strategy for paroxysmal AFIB

**Persistent and Chronic AFIB**
- Why is Pulmonary Vein Isolation alone Less effective?
  - Technical issue
    - Unable to accomplish PVI
  - Mechanistic issue
Technical Innovations

- Visualization
  - 3D Mapping systems – ESI and CARTO
  - Merging with CT angiograms, MRI
  - Intracardiac ECHO

Advanced Mapping Tools
Technical Innovations

- Lesion creation
  - Large tip catheters – 8mm
  - Irrigated catheters – Chili and Thermocool
  - Balloon catheters – Cryocath, Laser, HIFU
  - Multipolar – Ablation Frontiers
  - Contact Force catheter

- Catheter Manipulation
  - Deflectable catheters and sheaths

- Robotics catheter
  - Hansen
  - Stereotaxis
**Mechanistic issues**

**Multiple Wavelet Hypothesis**

HRS Expert Consensus Statement 2007

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**Mechanistic issues**

**Non Pulmonary Vein Triggers**

Non PV triggers for atrial fibrillation

Marchlinski et al
Mechanistic issues

If PVI is inadequate what else can we destroy? “substrate modification”

- Multiple Wavelet Hypothesis
  - Linear lesions
    - Reproduce the MAZE
    - Destroy atrial tissue that may allow atrial tachycardias

- Continuous Fractionated Atrial Electrograms
  - Destroy atrial tissue displaying disorganized electrical activity
  - Constituting 40% of the atrium

- Non Pulmonary Vein Triggers
  - Other Thoracic Vein Triggers - LOM, SVC, Coronary sinus

- Destroy the ganglionic plexi
- Target Rotors
MAZE III for persistent AFIB

Critical number of reentrant wavelets

Critical mass of atrial tissue

Ablation Methods
Complex Fractionated Electrograms

Nademanee et al

GPs + CFAE
CAFE and Ganglionic Plexi

Anterior Right GP
Superior Left GP
Superior Left CFAE

Anterior Right CFAE
Inferior Left GP
Inferior Posterior CFAE
Inferior Right GP
If smart bombs do not work then...

- Resort to carpet bombs

Hybrid Approach
Complications

- Vascular access
- Coagulation
- Lesion delivery
- Collateral Damage

Pulmonary Vein Stenosis
Cardiac Tamponade

Phrenic nerve paralysis
Atrio-Esophageal Fistula

Ablating the Esophagus?
Cerebrovascular accident

What are the Outcomes?
Classification of Atrial Fibrillation

- **Paroxysmal**
  - Self-terminating, usually <48 hours

- **Persistent**
  - Lasts > 7 days, requires CVN

- **Long-standing persistent**
  - Lasts > 1 year

- **Permanent**
  - Presence of arrhythmia is accepted as permanent

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


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Efficacy of Catheter Ablation vs ADT Paroxysmal AFIB

Kaplan-Meier curve of time to recurrence of symptomatic atrial arrhythmia following second line antiarrhythmic drug therapy (ADT)

Patients who had catheter ablation have fewer episodes of Afib than patients who took medication.

RF Catheter Ablation is Safe and Effective in Octogenarians

- Up to 10% of people over 80 years of age have AF
- Up to 25% of strokes in this group are due to AF
- This study compared safety and efficacy of RF ablation in two groups: greater and less than 80 years of age
- Success rates and complications were similar between the two groups

Figure Legend:
Kaplan-Meier event-free survival curve after the first procedure (blue line) and after the last procedure (red line). Plus sign (+) indicates censored. Numbers at bottom indicate patients at risk. ATa = atrial tachyarrhythmia.

From: Catheter Ablation of Long-Standing Persistent Atrial Fibrillation: 5-Year Outcomes of the Hamburg Sequential Ablation Strategy


Kaplan-Meier Curve of Time to First Atrial Fibrillation/Atrial Flutter/Atrial Tachycardia Recurrence Through 12 Months

Investigators working in their selected ranges ≥80% of the time during radiofrequency application demonstrated a significant increase of 15% in the effectiveness success at 12 months compared to those working in their selected ranges <80% of the time (effectiveness cohort, n = 122).

Figure Legend:
Kaplan-Meier Curve of Time to First Atrial Fibrillation/Atrial Flutter/Atrial Tachycardia Recurrence Through 12 Months

Investigators working in their selected ranges ≥80% of the time during radiofrequency application demonstrated a significant increase of 15% in the effectiveness success at 12 months compared to those working in their selected ranges <80% of the time (effectiveness cohort, n = 122).
Why is RFA not more common?

- Complications: 5%
- Success: 33%
- Recurrence: 62%

Why is AF Ablation not always effective?

- Atrial fibrillation is not one disease
- We do not yet understand the underlying mechanism
- Technical challenge
Mechanism of AFIB 2015

- AF requires a trigger and susceptible substrate

- Goal of catheter ablation:
  - Eliminate the triggers and alter the arrhythmogenic substrate

Who is a Good Candidate for a Catheter –Based Ablation

- Frequent symptomatic atrial fibrillation

- Limited structural heart disease
  - LA < 5cm, no significant mitral valvular disease

- Younger patient

- Medically refractory/intolerant

- First line therapy [occupation or declines AAD Rx]
**Caution! Anticoagulation**

- AFIB ablation should not be performed with the sole intent to obviate the need for anticoagulation.

- AFIB ablation cannot be performed in patients who cannot be anticoagulated.

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**TABLE 1 Applying Classification of Recommendations and Level of Evidence**

<table>
<thead>
<tr>
<th>CLASS I</th>
<th>Benefit &gt;&gt; Risk</th>
<th>Procedure/Treatment SHOULD be performed/ administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLASS IIa</td>
<td>Benefit &gt;&gt; Risk</td>
<td>Additional studies with focused objectives needed</td>
</tr>
<tr>
<td>CLASS IIb</td>
<td>Benefit &gt;= Risk</td>
<td>IT IS REASONABLE to perform procedure/administer treatment</td>
</tr>
<tr>
<td>CLASS III</td>
<td>Benefit &lt;= Risk</td>
<td>Additional studies with broad objectives needed; additional registry data would be helpful</td>
</tr>
</tbody>
</table>

**SIZE OF TREATMENT EFFECT**

<table>
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<tr>
<th>LEVEL A</th>
<th>Multiple populations evaluated*</th>
<th>Data derived from multiple randomized clinical trials or meta-analyses</th>
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<tbody>
<tr>
<td>LEVEL B</td>
<td>Limited populations evaluated*</td>
<td>Data derived from a single randomized trial or nonrandomized studies</td>
</tr>
<tr>
<td>LEVEL C</td>
<td>Very limited populations evaluated*</td>
<td>Only consensus opinion of experts, case studies, or standard of care</td>
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**STRENGTH OF EVIDENCE/PRECISION OF TREATMENT EFFECT**

- Recommendation that procedure or treatment is useful/effective
- Sufficient evidence from multiple randomized trials or meta-analyses
- Recommendation in favor of treatment or procedure being useful/effective
- Some conflicting evidence from multiple randomized trials or meta-analyses
- Recommendation's usefulness/effectiveness less well established
- Greater conflicting evidence from multiple randomized trials or meta-analyses
- Recommendation that procedure or treatment is not useful/effective and may be harmful
- Sufficient evidence from multiple randomized trials or meta-analyses
- Recommendation that procedure or treatment is not useful/effective and may be harmful
- Evidence from single randomized trial or nonrandomized studies
- Recommendation that procedure or treatment is not useful/effective and may be harmful
- Only consensus opinion, case studies, or standard of care
Indications for Catheter Ablation of AF

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<th>Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication</th>
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<tr>
<td>Paroxysmal: Catheter ablation is recommended*</td>
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<tr>
<td>Persistent: Catheter ablation is reasonable</td>
</tr>
<tr>
<td>Longstanding Persistent: Catheter ablation may be considered</td>
</tr>
<tr>
<td>Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent</td>
</tr>
<tr>
<td>Paroxysmal: Catheter ablation is reasonable</td>
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<tr>
<td>Persistent: Catheter ablation may be considered</td>
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2014 AHA/ACC/HRS Guidelines for the Management of Patients with Atrial Fibrillation

*Class I indicates that the intervention is beneficial. |
**Class II indicates that the intervention is probably beneficial. |
***Class III indicates that the intervention is probably not beneficial. |

No Structural Heart Disease
- Dofetilide
- Dronedarone
- Flecainide
- Propafenone
- Amiodarone
- Catheter ablation
- Amiodarone

Structural Heart Disease
- CAO
- HF
- Dofetilide
- Dronedarone
- Flecainide
- Amiodarone
- Catheter ablation
- Amiodarone

*Figure 2 - Strategies for rhythm control in patients with paroxysmal* and persistent AF.

*Class I indicates that the intervention is beneficial. |
**Class II indicates that the intervention is probably beneficial. |
***Class III indicates that the intervention is probably not beneficial. |

*Denotes agents that are a Class IA or IIB antiarrhythmic agent.

AF indicates atrial fibrillation; AV, atrioventricular; CAO, coronary artery disease; HF, heart failure; and LVM, left ventricular hypertrophy.
**Case: Paroxysmal Atrial Fibrillation**

- 55 yo WM with PAFIB since 2005
  - Originally precipitated by ETOH
  - Recurrent ER visits with *symptomatic* AFIB
  - Tx: Propafenone, Diltiazem and Rivoroxaban
  - Increasingly frequent events [6 per month]

- ECHO:
  - EF 55%, LA 4.7cm, mild MR, PAP 35mmHG
Case: Paroxysmal Atrial Fibrillation

- 45 yo WM
- PMH:
  - Presented with persistent atrial fibrillation 10 years ago. Treated with Propafenone, Diltiazem and ASA. No DM, HTN or Vascular disease
- Present:
  - No symptoms
  - Feels skipped beats when taking his pulse
  - Normal ECHO
  - Medications expensive and inconvenient

Case: Persistent Atrial Fibrillation

- 54 yo WF
- PMH:
  - PAFIB since 2009 ppted by ETOH
- Present:
  - Palpitations, SOB/dizziness
  - Persistent AFIB – Unsuccessful CVN
  - Loaded with flecainide/CVN returned in AFL
  - CVN to sinus with EF 40% on ECHO
  - Prolonged QT with dofetilide
  - Maintaining sinus rhythm on amiodarone
Case: AFIB of Unknown Duration

- 68 yo WM
  - Asymptomatic atrial fibrillation
  - Controlled ventricular response rate
- PMH:
  - Hypertension, Type II DM, no CAD
- Medications
  - Metoprolol, Lisinopril, Apixaban, Glucophage
- ECHO
  - EF 55%, Mild MR and LA 5.6cm