Atrial Fibrillation: Interventional Approaches

Tyler Taigen, MD
Eric Espinal, MD
Discussion Outline

• Review current treatment of atrial fibrillation
  • Pathophysiology
  • Risk assessment and treatment to reduce thromboembolic events
  • Rhythm control strategies
  • Review of evidence for catheter based ablation of AF

• New concepts
  • Alternative treatment options for persistent AF
  • Role of autonomic innervation in AF
  • Focal impulse and rotor modulation
  • Hybrid surgical/endovascular approach
Classification of AF

**New Onset**: First episode of atrial fibrillation of at least 30 sec or is present throughout the ECG.

**Paroxysmal**: > 1 Episode, Duration is < 7 days if self-limited, or < 48 hours if cardioverted

**Persistent**: > 1 Episode which is sustained beyond 7 days, or requires cardioversion after > 48 hours

**Long standing persistent**: Continuous AF despite efforts to restore sinus rhythm for more than 12 months. Note the term “permanent AF” is reserved for patient in whom the decision has been made to not attempt restoration of sinus rhythm.

**Lone**: Any type in a patient with structurally normal heart and younger than 60 yrs – term is no longer used in literature

Definitions from HRS consensus document on Catheter Ablation of Atrial Fibrillation.
AF Treatment goals

- Rate Control
- Rhythm Control
- Stroke Prevention
AF Treatment goals

Rate Control
- **Pharmacologic** (goal resting HR < 110)
  - BBBlockers
  - CCB
  - Amiodarone
- **Nonpharmacologic**
  - AV node ablation and implantation of PPM, BiV if EF < 50% (Block-HF)

Rhythm Control
- **Pharmacologic**
  - First line for many patients with paroxysmal AF and most with persistent AF
- **Non-pharmacologic**
  - Catheter Ablation (PVI)
  - Surgery (MAZE)
  - Hybrid Procedures (Atricure, Convergent)

Stroke Prevention
- **Pharmacologic**
  - Warfarin
  - NOAC (dabigatran, rivaroxiban, apixiban, endoxaban)
- **Non-Pharmacologic**
  - Surgical: LAA Ligation
  - Interventional: LAA occlusion device (i.e. Watchman)
OAC: Scoring Calculators

Risk of Stroke

**CHADS2**
- CHF (1)
- Hypertension (1)
- Age ≥ 75 years (1)
- Diabetes Mellitus (1)
- Prior stroke or TIA (2)

**CHA\textsubscript{2}DS\textsubscript{2}-VASc**
- CHF (1)
- Hypertension (1)
- Age ≥ 75 (2)
- Diabetes Mellitus (1)
- Prior Stroke or TIA (2)
- Vascular disease (1)
- Age 65-75 years (1)
- Female (1)

Risk of Bleeding

**HAS-BLED**
- Hypertension (1)
- Abnormal renal function (1)
- Abnormal liver function (1)
- Stroke (1)
- Bleeding (1)
- Labile INRs (1)
- Elderly (age > 65) (1)
- Drugs (1)
- Alcohol (1)
A 48 year old man presents to the emergency department with palpitations and shortness of breath that had suddenly began 3 hours earlier. Following administration of IV metoprolol, the patient’s rhythm converts to normal sinus rhythm and his symptoms resolve.

An echo demonstrates asymmetric septal hypertrophy (interventricular septal thickness 1.7cm, posterior wall thickness 0.9cm), mid systolic anterior motion of the mitral valve, mild left atrial enlargement and a 10mm Hg across the LV outflow tract at ret. LV systolic function is normal. A presumptive diagnosis of hypertrophic cardiomyopathy (HCM) is made.

Which of the following would be the next best step in management?

A. Warfarin for a goal INR 2-3  
B. Aspirin 325mg daily  
C. Holter monitor to decide AF burden  
D. AV node ablation and DDD pacemaker
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A. Warfarin for a goal INR 2-3

Patients with HCM and AF are at an increased risk of stroke and systemic thromboembolism and anticoagulation is recommended regardless of the CHADS-VASc score. In some series the risk of embolic stroke is as high as 50% in HCM patients with AF.
Stroke Risk: Additional Considerations

High
- Hypertrophic cardiomyopathy
- Systemic embolization
- Thyrotoxicosis until euthyroid
- Rheumatic Disease

Moderate
- Female
- CAD/Vascular Disease
- Age (>65-75)
- Renal Dysfunction

Minimal to No risk
- Severe Mitral Valve Regurgitation
New Oral AntiCoagulants (NOACs)

- Extrinsic Pathway
  - Factor Vila
  - Tissue Factor
  - Phospholipids

- Intrinsic Pathway
  - Factor IX – Factor IXa
  - Factor VIIIa
  - Phospholipids

- Factor X
  - Indirect Factor Xa
  - Inhibitors – Antithrombin
  - Fondaparinux
  - Idraparinux

- Factor Xa
  - Direct Factor Xa Inhibitors
  - Rivaroxaban
  - Apixaban

- Phospholipids
  - Factor Va – Factor Xa

- Prothrombin
  - Thrombin
  - Fibrinogen
  - Fibrin
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<tr>
<th>Trial</th>
<th>Patients (n)</th>
<th>CHADS2 (mean)</th>
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# NOAC Trial Comparison

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- 1° endpoint: Stroke or systemic embolism
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- **1° endpoint**: Stroke or systemic embolism
- **Major Bleeding**: Reduction in hemoglobin of 2gm/dl, transfusion of at least 2 units of PRBCs, symptomatic bleeding in critical area, or death

**Summa Cardiovascular Institute**
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- 1° endpoint: Stroke or systemic embolism
- Major Bleeding: Reduction in hemoglobin of 2gm/dl, transfusion of at least 2 units of PRBCs, symptomatic bleeding in critical area, or death
- GI bleeding: Trend toward less only in apixaban
PVI Anticoagulation protocol

• Conflicting data on peri-procedural use of NOACs
  • May have higher incidence of bleeding with dabigatran

• Summa protocol:
  • Patient takes last dose of NOAC 24 hours prior to ablation then receives dose within 2 hours after sheath pull following PVI
  • Continue coumadin, uninterrupted with INR 2-3
  • All patients continue anticoagulation for minimum of three months following PVI
  • Decisions regarding anticoagulation > 3mos post ablation are based on stroke risk independent of rhythm control strategy (ie CHADS2VASC score)
Alternative option?

What if patient can’t take anticoagulation?

Emerging technology to occlude the left atrial appendage
1. Surgical ligation (good evidence, longest track record)
2. Watchman (FDA advisory panel approved, again…)
3. Amplatzer device
4. Lariet suture delivery device
Watchman Trial

FDA approval for alternative in patients with indication for anticoagulation for prevention of thromboembolic events
Strategies for rhythm control in patients with paroxysmal* and persistent AF.†

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive Summary
Evidence for rhythm control with RFA

Solid evidence for PVI in paroxysmal atrial fibrillation:

Following failed antiarrhythmic medication:

- APAF Trial *J Am Coll Cardiol* 2006;48:2340-7
- Thermocool AF Study *JAMA*. 2010;303(4):333-340
- STOP-AF Trial *J Am Coll Cardiol* 2013;61:1713-1723

As first line treatment:

- MANTRA-PAF *NEJM* 10/2012;Vol367,No17
- RAAFT -2 *JAMA*. 2014;311(7):692-700
EXPEDITED REVIEW

A Randomized Trial of Circumferential Pulmonary Vein Ablation Versus Antiarrhythmnic Drug Therapy in Paroxysmal Atrial Fibrillation

The APAF Study

Carlo Pappone, MD, PhD, FACC,* Giuseppe Augello, MD,* Simone Sala, MD,* Filippo Gugliotta, BEng,* Gabriele Vicedomini, MD,* Simone Gulletta, MD,* Gabriele Paglino, MD,* Patrizio Mazzone, MD,* Nicoleta Sora, MD,* Isabelle Greiss, MD,* Andreina Santagostino, MD,* Laura LiVolsi, MD,* Nicola Pappone, MD,† Andrea Radinovic, MD,* Francesco Manguso, MD, PhD,* Vincenzo Santinelli, MD*

Milan and Telese Terme, Italy
198 patients age 18-70 presenting with paroxysmal atrial fibrillation >6 months and qualifying atrial fibrillation burden >2 episodes per month despite AAD
Randomized.
33% female, mean age 56 years, mean follow-up 12 months

Circumferential pulmonary vein ablation (CPVA)
n=99

Antiarrhythmic medical therapy
n=99
  with flecainide (n=33)
  with sotalol (n=33)
  with amiodarone (n=33)

Following a 1-month run-in phase to uptitrate antiarrhythmic medical therapy in both arms, ablation was performed in patients randomized to CPVA to encircle all 4 PVs with 3 additional lines to prevent atrial tachycardias (ATs) using either a 8mm or a 3.5mm irrigated tip catheter and with the guide of CARTO or NavX system. Medical therapy was discontinued in the CPVA group. Crossovers were allowed after 3 months.

Primary Endpoint: Freedom from recurrent atrial arrhythmias
At 9 months, a greater number of patients in the CPVA group were free from recurrent AF and AT (all CPVA patients in the absence of antiarrhythmic drug therapy) (87% vs 29%; p<0.001)
Cryoablation of AF: STOP AF Trial

Cryoballoon Ablation of Pulmonary Veins for Paroxysmal Atrial Fibrillation

First Results of the North American Arctic Front (STOP AF) Pivotal Trial

Douglas L. Packer, MD,* Robert C. Kowal, MD,† Kevin R. Wheelan, MD,† James M. Irwin, MD,‡ Jean Champagne, MD,§ Peter G. Guerra, MD,|| Marc Dubuc, MD,|| Vivek Reddy, MD,¶ Linda Nelson, RN,# Richard G. Holcomb, PhD,** John W. Lehmann, MD, MPH,†† Jeremy N. Ruskin, MD,‡‡ for the STOP AF Cryoablation Investigators

Rochester, Minnesota; Dallas, Texas; Tampa, Florida; Quebec, Canada; New York, New York; Minneapolis, Minnesota; and Wayland and Boston, Massachusetts
Cryoablation PVI: STOP AF Trial

**Primary Effectiveness Analysis**

**Treatment Success**

- **CRYO**: 69.9% (114/163)
- **DRUG Rx**: 7.3% (6/82)

P < 0.001

KM estimate 68.6% (SE 3.9%) vs 7.3% (SE 2.9%)

(0, 100, 200, 300, 400, 500 days)

Blanked 30 days
### Table 2: Summary of Adverse Events On-Treatment Analysis

<table>
<thead>
<tr>
<th>Type of Adverse Event</th>
<th>Drug Treatment (N = 82)</th>
<th>Cryoablation (N = 163)</th>
<th>All Cryoballoon-Treated (N = 228)</th>
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<tr>
<td></td>
<td>No. of Events</td>
<td>%</td>
<td>No. of Cryoablation Events</td>
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<tr>
<td>Stroke</td>
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PV = pulmonary vein; TIA = transient ischemic attack.
Radiofrequency Ablation as Initial Therapy in Paroxysmal Atrial Fibrillation

MANTRA-PAF

294 Patients Randomized

146 Assigned to RFA
140 Underwent RFA (96%)

- 69 underwent repeated RFA
- 665 7D Holter recordings

After 24 months
- N=140; 223 RFA procedures (1.6±0.7)
- On AAD: N=13/138 (9%) (IC: 10, III: 3)
- Withdrawn N=5
- Died N=3

148 Assigned to AAD
146 Started AAD (99%)

- 666 7D Holter recordings
- Treatment with 1.24±0.48 AAD’s

After 24 months
- N=54; 87 RFA procedures (1.6±0.7)
- On AAD: N=100 /137 (73%) (IC: 86, III:14)
- Withdrawn N=7
- Died N=4
MANTRA-PAF: Response according to Rx
Radiofrequency Ablation vs Antiarrhythmic Drugs as First-Line Treatment of Paroxysmal Atrial Fibrillation (RAAFT-2) A Randomized Trial

Carlos A. Morillo, MD, FRCP; Atul Verma, MD, FRCP; Stuart J. Connolly, MD, FRCP; Karl H. Kuck, MD, FHEART; Girish M. Nair, MBBS, FRCP; Jean Champagne, MD, FRCP; Laurence D. Sterns, MD, FRCP; Heather Beresh, MSc; Jeffrey S. Healey, MD, MSc, FRCP; Andrea Natale, MD, for the RAAFT-2 Investigators

**Importance.** Atrial fibrillation (AF) is the most common rhythm disorder seen in clinical practice. Antiarrhythmic drugs are effective for reduction of recurrence in patients with symptomatic paroxysmal AF. Radiofrequency ablation is an accepted therapy in patients for whom antiarrhythmic drugs have failed; however, its role as a first-line therapy needs further investigation.

**Objective.** To compare radiofrequency ablation with antiarrhythmic drugs (standard therapy) in treating patients with paroxysmal AF as a first-line therapy.

**Design, Setting, and Patients.** A randomized clinical trial involving 127 treatment-naïve patients with paroxysmal AF were randomized at 16 centers in Europe and North America to receive either antiarrhythmic therapy or ablation. The first patient was enrolled July 27, 2006; the last patient, January 29, 2010. The last follow-up was February 16, 2012.

**Interventions.** Sixty-one patients in the antiarrhythmic drug group and 66 in the radiofrequency ablation group were followed up for 24 months.
From: Radiofrequency Ablation vs Antiarrhythmic Drugs as First-Line Treatment of Paroxysmal Atrial Fibrillation (RAAFT-2): A Randomized Trial


**Summary**

127 Randomized

- **66** Randomized to undergo ablation during 90-day blanking period
  - **63** Underwent ablation as randomized
    - **2** Did not undergo ablation
      - **1** Procedure aborted
      - **1** Withdrew before procedure
      - **1** Underwent reablation

- **61** Randomized to receive antiarrhythmic drug therapy during blanking period
  - **60** Received 90-day drug therapy as randomized
    - **1** Withdrew
    - **3** Underwent ablation

**21-mo Follow-up Period**

- **57** Completed follow-up period with 75% adhering to transtelephonic recording
- **9** Underwent reablation
- **6** Crossed over to receive antirrhythmic drug therapy

**21-mo Follow-up Period**

- **48** Completed follow-up period with 75% adhering to transtelephonic recording
- **26** Crossed over to undergo ablation
- **24** Discontinued drug therapy

**Included in the primary analysis**

- **66** Included in the primary analysis

- **61** Included in the primary analysis
From: Radiofrequency Ablation vs Antiarrhythmic Drugs as First-Line Treatment of Paroxysmal Atrial Fibrillation (RAAFT-2): A Randomized Trial

Kaplan-Meier Curves of Time to First Recurrence of Any Atrial Tachyarrhythmias (A) and Time to First Recurrence of Symptomatic Atrial Tachyarrhythmias (B). Tachyarrhythmias include atrial fibrillation, tachycardia, and flutter. HR indicates hazard ratio.

Figure Legend:

Kaplan-Meier Curves of Time to First Recurrence of Any Atrial Tachyarrhythmias (A) and Time to First Recurrence of Symptomatic Atrial Tachyarrhythmias (B). Tachyarrhythmias include atrial fibrillation, tachycardia, and flutter. HR indicates hazard ratio.

PVI: Technique in APAF, Thermocool AF
PVI: ESI-NAVX (paroxysmal lesion set)
Key to define: Pulmonary vein isolation

Endpoint is to achieve electric isolation of all PVs.

- **Entrance Block**: confirmed with absence of electrograms at the os of veins (along plane of ablation). Adenosine infusion-hyperpolarize membrane which results in conduction when line of block is incomplete. May confirm with distal pacing (ie from appendage, coronary sinus or right atrium)
- **Exit Block**: Less critical to define, but involves pacing from lasso catheter and monitoring for capture outside of vein
- **Drug testing and programmed stimulation:**
  - Adenosine: 6-18 mg IV push with lasso at os of each vein (hence administer four times)
  - Isuprel: 10-20 mcg/min with lasso in place to look re-induction of AF and non-pulmonary vein triggers
  - Search for dual AV node physiology, AP, or inducible arrhythmia
- In total 30 minute monitoring period following final ablation
Pre-Isolation
LEFT SUPERIOR OS, POST RFA

PRINT REVIEW FIT

HRA 9-10
HRA 1-2
CS (9-10)
CS (1-2)
ABL 1-2
ABL 3-4
LS 1,2
LS 2,3
LS 3,4
LS 4,5
LS 5,6
LS 6,7
LS 7,8
LS 9,10
LS 10,1
STIM
PV reconnection with Adenosine
Adenosine wears off – but need to treat
Post RF ablation – no reconnection
PVI vs antiarrhythmic medical therapy?

When to consider a patient with AF for PVI ablation?

Paroxysmal AF after failed AADs
• APAF Trial
• Thermocool-AF Study
• STOP-AF Trial

Paroxysmal AF as initial therapy
• Mantra-PAF
• RAAFT-2
• CABANA should be definitive trial

➢ Ablation is best suited when relatively low risk of stroke (CHADS2 score) and recurrent, self-limited symptomatic episodes of atrial fibrillation in particular when occur on medical therapy i.e. Paroxysmal AF refractory to an antiarrhythmic drug (AAD)
When to refer a patient with AF for ablation?

Solid evidence for Paroxysmal AF

- APAF Trial
- Thermocool-AF Study
- STOP-AF Trial
- MANTRA-PAF
- RAAFT-2

- Ablation is best suited for patient with relatively low risk of stroke (CHADS2 score) and recurrent, self-limited symptomatic episodes of atrial fibrillation

- The time to consider AF ablation is soon after symptomatic recurrences. Risk of waiting is progression to more persistent nature of AF with more LA scarring and decrease opportunity for long-term rhythm control
### Indications for Catheter Ablation of AF

<table>
<thead>
<tr>
<th>Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal: Catheter ablation is recommended *</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Persistent: Catheter ablation is reasonable</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Longstanding Persistent: Catheter ablation may be considered</td>
<td>IIb</td>
<td>B</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal: Catheter ablation is reasonable</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Persistent: Catheter ablation may be considered</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Longstanding Persistent: Catheter ablation may be considered</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

*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*
2015: Ablation Candidates

• Symptomatic Paroxysmal AF refractory to ≥ 1 AAD:
  • Freedom from AF for 1 year is ~75%-85% (APAF, ThermoCool)

• Symptomatic Paroxysmal AF as first line treatment (MANTRA-PAF, RAAFT1/2):
  • Freedom from any recurrence over 2 years is ~55%

• Symptomatic Persistent AF refractory to ≥ 1 AAD
  • Freedom from AF for 1 years is ~50% (Oral et al, NEJM 2006)
  • Efficacy of ablation in Long standing atrial fibrillation, in particular when left atrium is severely dilated and/or scarred
Classic Paper defining AF Triggers

Possible mechanism of Atrial Fibrillation

A.

Ectopic focus

B.

Single-circuit reentry

C.

Multiple-circuit reentry

D.

Relationship to Clinical Forms

<table>
<thead>
<tr>
<th>Paroxysmal</th>
<th>Persistent</th>
<th>Permanent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time course and progression of underlying (heart) disease</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pulmonary Vein

Atria

Triggers/Drivers

Functional reentry substrate

Structural reentry substrate
Mechanism of AF

• Haissaguerre et al. demonstrated that ectopic beats from PV may trigger AF, however underlying mechanisms which supports and sustains AF are not well understood

• 2 prevailing hypotheses:
  1. Multiwavelet hypothesis: continuously meandering, random electrical wavelets create an unorganized atrial rhythm (AF)
  2. Localized source hypothesis: organized reentrant circuits are stable and self-sustained to cause high frequency activation which results in complex patterns of activation that characterize AF – so called rotors
Rotors

Hurricane

Atrial Fibrillation

“Eye” of the Storm

Atrium

Summa Cardiovascular Institute
Sustained arrhythmia requires substrate

**Trigger** + Accessory Pathway, Cavotricuspid Isthmus, Slow Pathway, Ectopy → SVT

Ablation → >85% success¹ (one procedure)

**Trigger** + Sustaining Mechanisms (Stable Rotors/Focal sources) → AF

¹Data from [source].
Treatment of Atrial Fibrillation by the Ablation of Localized Sources

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

Sanjiv M. Narayan, MD, PhD,*† David E. Krummen, MD,*† Kalyanam Shivkumar, MD, PhD,‡ Paul Clopton, MS,† Wouter-Jan Rappel, PhD,§ John M. Miller, MD||

San Diego and Los Angeles, California; and Indianapolis, Indiana
Does PVI knock off AF Rotors?

Conclusion: AF Ablation Succeeds if Rotors are Eliminated (Directly or Coincidentally)

Follow-up from CONFIRM, Narayan et al. JACC. 2013 epub.
Summa Cardiovascular Institute
Characteristics of AF

1. Triggers and substrate appear to originate from the same type of tissue
2. AF requires a combination of focal firing and reentry
3. “AF begets AF”
   \[ \text{AF} \rightarrow \text{Inflammation} \rightarrow \text{AF} \rightarrow \text{Fibrosis} \rightarrow \text{AF} \]
   Perhaps
   \[ \text{AF} \rightarrow \uparrow \text{Autonomic Tone} \rightarrow \text{AF} \]
What causes this PV PAC?
Ganglionic Plexi relative to PVI ablation
Role for therapy directed toward modulation of ANS?

• Evidence that modulation of autonomic nervous system during PVI improves outcomes
• Technology development geared toward easier localization of GPs
• Renal denervation as adjunctive therapy for patients with refractory hypertension and AF
  • JACC paper (Pokushalov et al. April, 2012) demonstrating improved freedom from AF vs PVI alone
Current Understanding of MOA

Electrophysiologic Mechanisms

- Microre-entrant circuits
- PV foci
- LOM
- Vagal Ganglia
- Dominant Spiral Wave

Summa Cardiovascular Institute
Overview

- Pulmonary vein isolation is effective in treatment of paroxysmal Afib, although plenty of room for improvement
- The pathophysiology underlying AF is complex, involving not only pulmonary vein triggers
  - Rotors, spiral waves, and atrial substrate changes
  - Autonomic innervation
  - Fibrosis and stretch
  - Even with respect to paroxysmal AF, as much as 20% of electical impulses arising from the PVs might propagate through pathways other than venoatrial continuity at the PV ostium (primarily via epicardial connections)
ESI – Ablation of Persistent AF
Surgical Approach

Dr. Espinal

MAZE
Atticure
Combined valve and Atticure etc
Summa AF ablation experience

- Posterior wall and/or extra linear lesion sets in patients with persistent AF
- Very few “Long-standing Persistent” cases to date

- How might we expand treatment options to patients with more difficult to control persistent AF or patients with recurrence despite medications and PVI?
Convergent Procedure

1. Epicardial ablation performed through transdiaphragmatic access
2. Endovascular ablation performed via transseptal access with pulmonary vein isolation and confirmatory testing
Dr. Espinal
# Initial Data from Single Center Trials

<table>
<thead>
<tr>
<th>Author &amp; Institution</th>
<th>Society Meeting</th>
<th>N</th>
<th>% Persistent or Longstanding Persistent</th>
<th>Mean AF Duration</th>
<th>Mean Sinus Rhythm at Follow-Up</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr. Nick Child</td>
<td>Heart Rhythm Congress UK</td>
<td>19</td>
<td>100%</td>
<td>7.8 yrs</td>
<td>90% at 1 year</td>
<td>Holter</td>
</tr>
<tr>
<td>Guy’s &amp; St. Thomas’, UK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dr. Dmitri Pajitnev</td>
<td>European Society of Cardiology Barcelona, Spain</td>
<td>28</td>
<td>100%</td>
<td>4.6 yrs</td>
<td>80% at 1 year</td>
<td>Reveal 24/7</td>
</tr>
<tr>
<td>Kerckhoff Klinik, Germany</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dr. Michael Zembala</td>
<td>American Association for Thoracic Surgery, Toronto, Canada</td>
<td>54</td>
<td>100%</td>
<td>4.4 yrs</td>
<td>85% at 1 year</td>
<td>Holter 7-day</td>
</tr>
<tr>
<td>Silesian Center for Heart Diseases, Poland</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dr. Borut Gersak</td>
<td>International AF Symposium Orlando, Florida</td>
<td>60</td>
<td>100%</td>
<td>6.2 yrs</td>
<td>83% at 1 year</td>
<td>Reveal 24/7</td>
</tr>
<tr>
<td>University Medical Center Ljubljana, Slovenia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reference (# Subjects)</th>
<th>% NPAF</th>
<th>Type of Monitoring</th>
<th>Freedom from AF/AFL/AT (Follow-up)</th>
<th>Repeat Ablations</th>
<th>Adverse Event Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Civello(^{1}) (n=104)</td>
<td>73 %</td>
<td>72 hours to 14 days Holter</td>
<td>92.0 % (8.0 months)</td>
<td>4 %</td>
<td>5.8 %</td>
</tr>
<tr>
<td>Gilligan(^{2}) (n=39)</td>
<td>79 %</td>
<td>72 hours Holter</td>
<td>94.0 % (12.6 months)</td>
<td>6 %</td>
<td>2.6 %</td>
</tr>
<tr>
<td>Golden(^{3}) (n=61)</td>
<td>88 %</td>
<td>72 hours Holter</td>
<td>79.0 % (11.0 months)</td>
<td>8 %</td>
<td>3.3 %</td>
</tr>
<tr>
<td>Gersak(^{4})ultrathin (n=50)</td>
<td>94 %</td>
<td>Revele(^{Y}) XT</td>
<td>91.0 % (12.0 months)</td>
<td>2 %</td>
<td>10.0 %</td>
</tr>
<tr>
<td>Gehi(^{5}) (n=101)</td>
<td>83 %</td>
<td>24 hour Holter</td>
<td>70.5 %* (12.0 months)</td>
<td>6 %</td>
<td>6.0 %</td>
</tr>
</tbody>
</table>

AF = atrial fibrillation; AFL = atrial flutter; AT = atrial tachycardia; NPAF = Non-paroxysmal atrial fibrillation. *Arrhythmia free survival.
Low Rate of Atrial Fibrillation Recurrence Verified by Implantable Loop Recorder Monitoring Following a Convergent Epicardial and Endocardial Ablation of Atrial Fibrillation

BORUT GERSAK, M.D., Ph.D.,* ANDREJ PERNAT, M.D., Ph.D.,† BORIS ROBIC, M.D.,* and MATJAZ SINKOVEC, M.D., Ph.D.,†

From the *Department of Cardiovascular Surgery, and †Department of Cardiology, University Medical Center Ljubljana, Zaloska, Ljubljana, Slovenia

Implantable Loop Recorder Monitoring Outcomes for the Convergent AF Procedure. 
Objective: Evaluate long-term outcomes in patients undergoing the Convergent procedure (CP) for the treatment of atrial fibrillation (AF).

Background: The CP provides a multidisciplinary approach, combining endoscopic creation of epicardial linear lesions followed by endocardial mapping and ablation and targets persistent and longstanding persistent AF patients who are at increased risk of heart failure, stroke, and mortality.

Methods: Outcomes from a prospective nonrandomized study were recorded for consecutive patients by interrogation of implanted Reveal® monitors. Rhythm status and AF burden were quantified 6–24 months postprocedure, and compared relative to AF type, gender, age, body mass index, left atrial size, left ventricular ejection fraction, and congestive heart failure, hypertension, age >75 years, age between 65 and 74 years, stroke/TIA/TE, vascular disease (previous MI, peripheral arterial disease or aortic plaque), diabetes mellitus, female (CHA2DS2-VASc).

Results: A total of 50 patients were enrolled with 94% having persistent or longstanding persistent AF. There were 2 atrioesophageal fistulas reported. In one patient, the fistula resulted in death at 33 days postprocedure; in the second, the fistula was surgically repaired but patient died 8 months postprocedure from a CVI. After CP, 95% of patients were in sinus rhythm at 6-month follow-up; 88% at 12 months; and 87% at 24 months. The median AF burden recorded with Reveal XT monitors was 0.0%, 0.1%, and 0.1% at 6, 12, and 24 months with 81%, 81%, and 87% of patients reporting a burden less than 3%, respectively.

Conclusion: Using 24 × 7 continuous loop recording, the CP demonstrated success in treating persistent and longstanding persistent AF patients. Endocardial mapping and catheter ablation with diagnostic confirmation of procedural success complemented the endoscopic creation of epicardial linear lesions in restoring sinus rhythm. (J Cardiovasc Electrophysiol, Vol. 23, pp. 1059-1066, October 2012)
Methods:
Prospective, nonrandomized

Enrollment:
1/2009-7/2011

50 patients underwent procedure at the University of Ljubljana Medical Center in Solvenia

### TABLE 1
Demographic Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
<td>N = 50</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>42 (84%)</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>56.4 (10.8)</td>
</tr>
<tr>
<td>Range</td>
<td>31, 79</td>
</tr>
<tr>
<td>BMI (kg/m²), mean (SD)</td>
<td>28.8 (3.9)</td>
</tr>
<tr>
<td>Range</td>
<td>20, 42</td>
</tr>
<tr>
<td>Preoperative LA (cm), mean (SD)</td>
<td>4.8 (0.5)</td>
</tr>
<tr>
<td>Range</td>
<td>3.2, 5.7</td>
</tr>
<tr>
<td>Preoperative LVEF (%), mean (SD)</td>
<td>58.6 (10.5)</td>
</tr>
<tr>
<td>Range</td>
<td>40, 80</td>
</tr>
<tr>
<td>Atrial fibrillation type, N</td>
<td></td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Persistent</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>Longstanding persistent</td>
<td>39 (78%)</td>
</tr>
<tr>
<td>AF duration (years), mean (SD)</td>
<td>5.0 (4.7)</td>
</tr>
<tr>
<td>Range</td>
<td>1, 25</td>
</tr>
<tr>
<td>Type of procedure, N</td>
<td></td>
</tr>
<tr>
<td>Staged epicardial and endocardial hybrid</td>
<td>16 (32%)</td>
</tr>
<tr>
<td>Single setting convergent procedure</td>
<td>34 (68%)</td>
</tr>
<tr>
<td>Preexisting conditions, N (%)</td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>37 (74%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Stroke/TIA/thromboembolic event</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Vascular disease (CAD, PAD)</td>
<td>2 (4%)</td>
</tr>
</tbody>
</table>
Gersak et al: Major Adverse Events

<table>
<thead>
<tr>
<th>MACE</th>
<th>Total # (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural mortality (1 and 8 month postprocedure resulting from esophageal fistulas)</td>
<td>2/50 (4.0%)</td>
</tr>
<tr>
<td>Stroke/CVA</td>
<td>1/50 (2.0%)</td>
</tr>
<tr>
<td>Transient ischemic attack (TIA)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Tamponade</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>1/50 (2.0%)</td>
</tr>
<tr>
<td>Phrenic nerve palsy</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Newly developed 3rd degree AV block</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Acute limb ischemia</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Excessive bleeding requiring &gt;2 units of blood transfusion</td>
<td>1/50 (2.0%)</td>
</tr>
<tr>
<td>Major complications were observed in 5 patients</td>
<td>5/50 (10.0%)</td>
</tr>
</tbody>
</table>

- Initially esophageal temperature was not measured
Amiodarone was initiated for all patients post-procedure then AAD therapy was directed by referring physician.

Rhythm followed by Implantable Loop Recorders.

**TABLE 3**

<table>
<thead>
<tr>
<th>Clinical Measure</th>
<th>Percent Responders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus rhythm</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>95% (41/43)</td>
</tr>
<tr>
<td>12 months</td>
<td>88% (28/32)</td>
</tr>
<tr>
<td>24 months</td>
<td>87% (13/15)</td>
</tr>
<tr>
<td>SR and No AADs†</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>67% (29/43)</td>
</tr>
<tr>
<td>12 months</td>
<td>75% (24/32)</td>
</tr>
<tr>
<td>24 months</td>
<td>67% (10/15)</td>
</tr>
</tbody>
</table>

†Includes patients off amiodarone.
### TABLE 4
Reveal Monitoring AF Burden at 6, 12, and 24 months

<table>
<thead>
<tr>
<th>AF Burden Threshold</th>
<th>6 month</th>
<th>12 month</th>
<th>24 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.2%</td>
<td>72% (31/43)</td>
<td>56% (18/32)</td>
<td>53% (8/15)</td>
</tr>
<tr>
<td>≤0.5%†</td>
<td>74% (32/43)</td>
<td>66% (21/32)</td>
<td>60% (9/15)</td>
</tr>
<tr>
<td>≤1.0%‡</td>
<td>77% (33/43)</td>
<td>75% (24/32)</td>
<td>73% (11/15)</td>
</tr>
<tr>
<td>≤2.1%§</td>
<td>79% (34/43)</td>
<td>73% (24/32)</td>
<td>80% (12/15)</td>
</tr>
<tr>
<td>&lt;3.0%¶</td>
<td>81% (35/43)</td>
<td>81% (26/32)</td>
<td>87% (13/15)</td>
</tr>
<tr>
<td>≤4.2%††</td>
<td>81% (35/43)</td>
<td>84% (27/32)</td>
<td>87% (13/15)</td>
</tr>
</tbody>
</table>

†7 min/day. Threshold based on published Reveal XT outcomes in drug refractory paroxysmal AF prospective randomized study.\(^{22}\)
‡14 min/day. Threshold based on published catheter ablation outcomes comparing continuous monitoring at 10 min/day to 24-hour, 48-hour, and 7-day Holters.\(^{23}\)
§30 min/day. Threshold based on cutting HRS recommendations of cumulative AF time in half; the duration of each individual episode was not available.\(^{12}\)
¶43 min/day.
††1 hour/day. Threshold based on HRS recommendations of cumulative AF time since the duration of each individual episode was not available to compare against the 30 seconds limit.\(^{12}\)
RESEARCH ARTICLE

Combined Endocardial and Epicardial Ablation for Symptomatic Atrial Fibrillation: Single Center Experience in 100+ Consecutive Patients

KENNETH C. CIVELLO, MD, MPH, FACC, CHARLES ANDREW SMITH, MD, FACC and WILLIAM BOEDEFELD, MD

Our Lady of the Lake Hospital, Baton Rouge, LA

ABSTRACT. Our aim was to document and evaluate the outcomes of the first 100+ patients who underwent the convergent procedure at Our Lady of the Lake Hospital. Between May 2010 and December 2011, 104 symptomatic atrial fibrillation (AF) patients underwent the convergent procedure combining surgical epicardial radiofrequency ablation and endocardial ablation. Antiarhythmics were discontinued at 8 weeks. Arrhythmia episodes were detected by electrocardiogram at 1 month, 3 months, 6 months, and 1 year. A≥72-hour patient monitoring or interrogation of Permanent Pacemaker/Implantable cardioverter-defibrillator was performed at 6 and 12 months. Of the 104 patients (age 60.9 years, 77% males, body mass index 32.7, ejection fraction 56.1%, left atrial diameter 4.1 cm) paroxysmal AF was present in 27% and persistent/longstanding persistent AF in 73%. AF duration was 5.2 years. At 12-month follow-up 87.5% (63/72) of patients were in sinus rhythm (SR) ± antiarrhythmic drugs (AADs). At last follow-up 89.0% (92/104) of patients were in SR ± AADs. Three patients underwent repeat catheter ablation for atypical atrial flutter. No complications <7 days, no atrio-esophageal fistulas, myocardial infarction, or death were reported. The convergent procedure, bringing together the strengths of the endoscopic epicardial ablation and endocardial catheter ablation, provides a viable and promising treatment option for patients with symptomatic AF.

KEYWORDS. atrial fibrillation, convergent, endocardial ablation, epicardial ablation, radiofrequency.
**Methods**: Between May 2010 and December 2011, the first 104 AF patients underwent hybrid epicardial and endocardial ablation. Patients were excluded if they had prior open heart surgery or major abdominal procedure.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All subjects (n=104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>80 (77)</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>60.9 (8.6)</td>
</tr>
<tr>
<td>Range</td>
<td>37–79</td>
</tr>
<tr>
<td>Body mass index (kg/m²), mean (SD)</td>
<td>32.7 (5.8)</td>
</tr>
<tr>
<td>Range</td>
<td>22.5–46.7</td>
</tr>
<tr>
<td>Preoperative left atrium (cm), mean (SD)</td>
<td>4.1 (0.6)</td>
</tr>
<tr>
<td>Range</td>
<td>3.1–6.1</td>
</tr>
<tr>
<td>Preoperative left ventricular ejection fraction (%)</td>
<td>56.1 (9.1)</td>
</tr>
<tr>
<td>Atrial fibrillation type, N (%)</td>
<td>28 (27)</td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>31 (30)</td>
</tr>
<tr>
<td>Persistent</td>
<td>45 (43)</td>
</tr>
<tr>
<td>Longstanding persistent</td>
<td>5.2 (4.9)</td>
</tr>
</tbody>
</table>
Civello et al : Major Adverse Events

- One CVA in patient with longstanding persistent AF and EF = 30%
- One pericardial effusion >30 days after procedure
- Two pleural effusions, one PV stenosis

Table 2: Major adverse cardiac event rates (<7 days post procedure) and at last follow-up (>7 days post procedure)

<table>
<thead>
<tr>
<th>Major Adverse Cardiac Events</th>
<th>&lt;7 days post procedure</th>
<th>&gt;7 days post procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural mortality</td>
<td>0/104 (0.0%)</td>
<td>0/104 (0.0%)</td>
</tr>
<tr>
<td>Stroke/Cerebrovascular Accident</td>
<td>0/104 (0.0%)</td>
<td>1/104 (1.0%)</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>0/104 (0.0%)</td>
<td>1/104 (1.0%)</td>
</tr>
<tr>
<td>Tamponade</td>
<td>0/104 (0.0%)</td>
<td>0/104 (0.0%)</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>0/104 (0.0%)</td>
<td>1/104(1.0%)</td>
</tr>
<tr>
<td>Phrenic nerve palsy</td>
<td>0/104 (0.0%)</td>
<td>0/104 (0.0%)</td>
</tr>
<tr>
<td>Pulmonary vein stenosis</td>
<td>0/104 (0.0%)</td>
<td>1/104(1.0%)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>0/104 (0.0%)</td>
<td>2/104(2.0%)</td>
</tr>
<tr>
<td>Esophageal fistula</td>
<td>0/104 (0.0%)</td>
<td>0/104 (0.0%)</td>
</tr>
<tr>
<td>Excessive bleeding requiring &gt;2 units of blood transfusion</td>
<td>0/104 (0.0%)</td>
<td>0/104 (0.0%)</td>
</tr>
</tbody>
</table>
Civello et al: Results

Antiarrhythmic drug (AAD):

- Dofetilide 65%
- Flecanide or propafenone 13%
- Amiodarone 8%
- Dronedarone 3%
- Sotalol 1%
- No AAD 6%

AAD for minimum of 8 weeks
Convergent Lesion Sets
CONVERGE - Epi/Endo Ablation For Treatment of Persistent Atrial Fibrillation (AF)

This study is currently recruiting participants. (see Contacts and Locations)

Sponsor:
nContact Surgical Inc.

Information provided by (Responsible Party):
nContact Surgical Inc.

ClinicalTrials.gov Identifier:
NCT01984346

First received: November 7, 2013
Last updated: September 23, 2014
Last verified: September 2014

Tracking Information

First Received Date: November 7, 2013
Last Updated Date: September 23, 2014
Start Date: December 2013
Estimated Primary Completion Date: June 2016 (final data collection date for primary outcome measure)

Current Primary Outcome Measures:
AF/AT/Flutter (AF) free absent class I and III AADs except for a previously failed or intolerant class I or III AAD with no increase in dosage. [ Time Frame: 12 Months ] [ Designated as safety issue: No ]
The primary efficacy endpoint is success or failure to be AF/AT/Flutter free absent class I and III AADs except for a previously failed or intolerant class I or III AAD with no increase in dosage following the 3 month blanking period through the 12 months post procedure follow-up visit.

Original Primary Outcome Measures:
Same as current