Catheter Ablation of Atrial Fibrillation
2011

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Atrial Fibrillation 2010

- > 3 Million Patients
- >350,000 New Cases Annually
- Major Cause of Stroke
- One Billion Dollars in Annual Hospital Expenditures
- Medicare Patients >65 years of age
  Excess $1400-$3200 /Year
Mortality With Atrial Fibrillation

Framingham Study

- 2X All Cause Mortality
- 4X Age Adjusted Mortality >55 years
- Adjust for Risk Factors (HTN, DM, MI, CHF)
  - 3X Mortality
- Between 15% and 45% are actually anticoagulated
Impact of Atrial Fibrillation on Mortality in Framingham Study


Follow-up (yr)

Dead (%)
### Annual Stroke Risk

**AFASAK, BAATAF, CAFA, SPAF 1, SPINAF**

<table>
<thead>
<tr>
<th>RISK CATEGORIES</th>
<th>PLACEBO</th>
<th>WARFARIN</th>
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<tbody>
<tr>
<td>Age &lt; 65 years</td>
<td>1%</td>
<td>1%</td>
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<tr>
<td>Age &lt; 65 years One or More Risks</td>
<td>4.9%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Age 65-75 years</td>
<td>4.3%</td>
<td>1.1%</td>
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<tr>
<td>Age 65-75 years One or More Risks</td>
<td>5.7%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Age &gt; 75 years</td>
<td>3.5%</td>
<td>1.7%</td>
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<tr>
<td>Age &gt; 75 years One or More Risks</td>
<td>8.1%</td>
<td>1.2%</td>
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Antiarrhythmic Therapy/AFFIRM

- Restoration and maintenance of sinus rhythm were associated with a 47% reduction in the risk of death.
- The use of antiarrhythmic drugs and the presence of CHF significantly increased the risk of death, by 49% and 57%, respectively, thereby reversing the benefit of the restoration of sinus rhythm.
Atrial Fibrillation is \textit{NOT} a Benign Dysrhythmia and it is \textit{BETTER} to be in Normal Sinus Rhythm
LA/PV Musculature
Adult: Identical Vessel Wall in PV’s & Left Atrial Body

Pulmonary Vein

Posterior Left Atrium

Schematic of Atrial

Douglas, et al
AJC, 2006

- Red = vessel wall
- Blue = myocardium with smooth-walled inner aspect
- Brown = Atrial myocardium
Discontinuity
Intercellular Fibrosis
Arrhythmogenic Substrate

- Discontinuity and fibrosis, even when mild, will result in isolated myocardial clusters. The result is reduced myocardial coupling and reduced electrotonic inhibition, thus facilitating automaticity.

- The combination of poorly coupled cells, fibrosis, and cellular hypertrophy will lead to slow conduction and, thereby, facilitate local reentry within PV’s.
Initiation of Atrial Fibrillation
Simultaneous PV Mapping
Focal Ablation
Pulmonary Vein Angiography
Pulmonary Venous Mapping
RAO and LAO with CMC
Segmental Ostial Isolation
Oral, Morady; Circulation 2002

April, 2009
Schematic of Atrial

Douglas, et al
AJC, 2006

- **Red** = vessel wall
- **Blue** = myocardium with smooth-walled inner aspect
- **Brown** = Atrial myocardium
PV Ostium vs. Antrum
Image Registration

LAT
2-LAT > 136 Points

LAT
2-LAT > 136 Points

295ms
1.01 cm

PA
2.42 cm
Segmental Ostial PV vs. Left Atrial Circumferential Ablation

Cumulative proportion of patients free of paroxysmal atrial fibrillation

LACA (n=40)

SOCA (n=40)

\( p = 0.02 \)

April, 2009

NYU Results

- Success defined as Freedom from AF and ALL Atrial Tachyarrhythmias OFF Antiarrhythmics after a Single Procedure

- Success: 74 % SOCA + LACA
  62 % SOCA
Underlying Pathogenesis of Atrial Fibrillation

- Paroxysmal
- Persistent
- Permanent

Relative importance

Initiation substrate
Trigger
Substrate

AF/disease progression

Ablation Success
How Do You Get There?

Paroxysmal

PV isolation

Persist/chronic

Non-PV foci

Linear abl

Redo

Packer et al, 2007
Optical Mapping
Microreentrant Source of AF Dominant Frequencies

• Jalife; Circ. 2000; 101:194-199
Dominant Frequencies

Lazar et al; Circulation 2004
Dominant Frequency Map
Lazar et al; 2004
Defragmentation
Targeting Fractionated Electrograms

Oral 2004
Coronary Sinus Ablation
### SVC-RA Junction Ablation

<table>
<thead>
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<th>SVC-RA Junction</th>
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<tr>
<td>C9-10</td>
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<td>C11-12</td>
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<tr>
<td>D13-14</td>
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<tr>
<td>D15-16</td>
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<td>RAA</td>
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- **190 ms**

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<tr>
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<tr>
<td>RAA</td>
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- **240 ms**

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<td>C9-10</td>
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<tr>
<td>D15-16</td>
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<tr>
<td>RAA</td>
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</table>

- **304 ms**
Automated CFAE Map
Implementation and Deployment of the CFE Mapping Tool: How It Works

• Map Display Representation
  – Average interval represented with color scale (ms)
    • 1-8 second evaluation interval

• Activation Detection Criteria
  – Peak-to-peak voltage threshold
    • > Baseline noise floor
  – Duration threshold (slope)
    • Near field vs. far field
  – Refractory setting
    • Avoid double counting

April, 2009
Capacity of High Density Mapping
Detecting Continuous Fractionation
Septal Roof
CFAE in Isolated PV
AF Ablation

Structural Heart Disease
Vagal Denervation

- 297 patients undergoing AF ablation
- 34.3% with complete vagal denervation
  - Abolition of all evoked vagal reflexes around PVs
- Decreased recurrence of AF at 12 months
- Higher mean HR and attenuated HRV at 3 mos

(Pappone 2003)
Chronic AF (Randomized)
Success Rates With Ablation

**Worldwide Survey**

The graph shows the success rates with ablation over different ranges of follow-up (F/U) periods. The categories range from 0-3 years to >24 years. The graph compares success rates without AAD, success rates with AAD, and overall success rates.

- **Success without AAD**
- **Success with AAD**
- **Overall Success**

The data indicates a higher success rate for longer follow-up periods, particularly for success with AAD and overall success.
Single procedure, single center efficacy of ablation

*Calkins, 2006*

- 200 patients, 46% paroxysmal
- Long term success was 28%
- Long term success was 41% with repeat procedures
- Optimal candidates with paroxysmal AF achieved a 69% success
- Major complication in 7.9%
The methodology used to perform Catheter Ablation of Atrial Fibrillation is in Evolution (To say the least!)
AF Ablation

• True Efficacy of Catheter Ablation of AF Remains Unknown - No large prospective multicenter trials, nonrandomized, varied drug use, short f/u, varied definition of success, no survival data

• Techniques and tools employed for Catheter Ablation of AF continue to evolve rapidly
Catheter ABlration vs ANtiarrhythmic Drug Therapy in Atrial Fibrillation (CABANA) Trial

Douglas L. Packer, MD
Kerry L. Lee, PhD
Daniel B. Mark, MD
Richard A. Robb, PhD
CABANA Investigators

Mayo Clinic Rochester
Duke Clinical Research Institute
National Heart Lung and Blood Institute
Efficacy of Antiarrhythmic Drugs and Catheter Ablation in Patients with Atrial Fibrillation

**Antiarrhythmic Drug Therapy**
- **Treatment success**: 46% (40,1813)
- **Recurrent AF**: 18% (800)

**Catheter Ablation**
- **Single-procedure success off AAD**: 57% (21,2800)
- **Multiple-procedure success off AAD**: 71% (34,3481)
- **Single-procedure success on AAD or uncertain Catheter ablation**: 72% (52,4786)
- **Multiple-procedure success on AAD or uncertain Catheter ablation**: 77% (42,3562)

**Procedure Success with AF Ablation**

### Single Procedure
- Cheema, 2006 (n=64)
- Della Bella, 2001 (n=58)
- Della Bella, 2001 (n=40)
- Gerstenfeld, 2003 (n=226)
- Gerstenfeld, 2002 (n=41)
- Hocini, 2005 (n=45)
- Hocini, 2005 (n=45)
- Lemola, 2005 (n=60)
- Mansour, 2004 (n=40)
- Mansour, 2004 (n=40)
- Nademanee, 2004 (n=121)
- Nakashima, 2002 (n=42)
- Nilsson, 2006 (n=54)
- Nilsson, 2006 (n=46)
- Pappone, 2001 (n=251)
- Saad, 2003 (n=71)
- Scanavacca, 2004 (n=49)
- Stabile, 2005 (n=51)
- Thomas, 2004 (n=48)
- Vasamreddy, 2005 (n=70)
- Vasamreddy, 2004 (n=75)
- Verma, 2005 (n=42)
- Verma, 2005 (n=658)
- Yamada, 2006a (n=53)
- Yamada, 2006b (n=47)
- Yamada, 2006b (n=61)
- Yamada, 2006c (n=55)
- Oral, 2002 (n=70)
- Jais, 2004 (n=100)
- Jais, 2004 (n=100)
- Oral, 2006b (n=77)
- Overall (n=2,800)

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**Calkins et al:**
*Circ A & E 2:349, 2009*

**Single procedure success off AAD (%):**

- 02
- 04
- 06
- 08
- 10

---

### Multiple Procedure
- Arentz, 2003 (n=58)
- Bhargava, 2004 (n=106)
- Cheema, 2006 (n=64)
- Dixit, 2004 (n=62)
- Dong, 2005 (n=68)
- Dong, 2005 (n=83)
- Gerstenfeld, 2003 (n=226)
- Haissaguerre, 2005 (n=60)
- Haissaguerre, 2000 (n=90)
- Haissaguerre, 1998 (n=45)
- Kistler, 2006 (n=47)
- Kistler, 2006 (n=47)
- Kottkamp, 2004 (n=100)
- Kumagai, 2005 (n=50)
- Kumagai, 2005 (n=50)
- Liu, 2006 (n=55)
- Liu, 2006 (n=55)
- Macle, 2002 (n=136)
- Nademanee, 2004 (n=121)
- Nakashima, 2002 (n=42)
- Nilsson, 2006 (n=54)
- Nilsson, 2006 (n=46)
- Oral, 2006a (n=153)
- Ouyang, 2005 (n=40)
- Sacher, 2004 (n=115)
- Verma, 2005 (n=42)
- Verma, 2005 (n=658)
- Wnuk-Wojnar, 2005 (n=68)
- Yamada, 2006a (n=53)
- Yamada, 2006b (n=47)
- Yamada, 2006b (n=61)
- Yamada, 2006c (n=55)
- Hsieh, 2003 (n=227)
- Pappone, 2004b (n=297)
- Overall (n=3,481)

---

**Multiple procedure success off AAD (%):**

- 02
- 04
- 06
- 08
- 10
Outcome of Ablation and Drug Therapy in Randomized Trials

Freedom From Recurrent AF

- RAAFT\textsuperscript{1}: n=13, P<0.001
- CACAF\textsuperscript{2}: n=6
- APAF\textsuperscript{3}: n=21
- A4\textsuperscript{4}: n=4
- ORAL\textsuperscript{5}: n=57

\textsuperscript{1}JAMA 293:2634, 2005; \textsuperscript{2}Eur Heart J 27:216, 2006; \textsuperscript{3}JACC 48:2340, 2006; \textsuperscript{4}Circ 118:2498, 2008 5, 2006; \textsuperscript{5}NEJM 354:967, 2006
How Will CABANA Help Us?

- Minimize bias
- Reflect what is happening in the community
- Provide direct comparator information
- Optimize development of treatment recommendations
- Yield a treasure-trove of data
CABANA Trial
Primary Objective and Hypothesis

Treatment strategy of percutaneous left atrial catheter ablation for purpose of eliminating AFib is superior to current state-of-the-art medical therapy with either rate control or rhythm control drugs for reducing total mortality (primary endpoint) and decreasing composite endpoint of total mortality, disabling stroke, serious bleeding or cardiac arrest (key secondary endpoint) in patients with untreated or incompletely treated AF warranting therapy.

Packer: CABANA Investigator Meeting, 2009
CABANA Trial
Secondary Endpoint/Objectives

- Total mortality, disabling stroke, serious bleeding or cardiac arrest
- Cardiovascular total mortality or hospitalization
- Cardiovascular death
- Cardiovascular death or disabling stroke
- Arrhythmic death or cardiac arrest
- Heart failure death
- Freedom from recurrent AF
- Cardiovascular hospitalization
- Medical costs, resource utilization and cost effectiveness
- Quality of life
- Composite adverse events
- LA size, morphology and function

Packer: CABANA Investigator Meeting, 2009
CABANA Trial Inclusion Criteria

Subjects must meet all following criteria

• Documented AF episodes ≥1 hr in duration with ≥2 episodes over 4 mo with ECG documentation of 1 episode or ≥1 episode of AF lasting >1 week

• Warrant active therapy beyond simple ongoing observation

• Eligible for catheter ablation and ≥2 sequential rhythm control and/or ≥3 rate control drugs

• ≥65 years of age or <65 years with ≥1 of the following risk factors for stroke:
  Hypertension
  Diabetes
  CHF (including systolic or diastolic heart failure)
  Prior stroke or TIA
  LA size >5.0 cm (or volume index ≥40 cc/m²)
  EF ≤35

*Subjects <65 years of age whose only risk factor is HTN must have a 2nd risk factor or LVH to qualify

Packer: CABANA Investigator Meeting, 2009
Its so easy anybody can do it!

April, 2009
Risks of Catheter Based Therapy

- Embolization
- Atypical Left Atrial Flutter
- LA-Esophageal Fistula
- Pulmonary Vein Stenosis
- Pericarditis
- Tamponade
- Hematoma
- Deep Vein Thrombosis
Atrial Tachycardias
Atrial Tachycardia

Morady: Heart Rhythm Journal, 2009
Left Atrial Flutter Around Pulmonary Veins
Focal Atrial Tachycardia
Lesion Delivery
Collateral Lung Injury
Esophageal Anatomy

A

LV
CS
Eso
LA
RIPV
LSPV
LIPV

B

LV
CS
Eso
LA
RIPV
LSPV
LIPV

C

LV
CS
Eso
LA
RIPV
LSPV
LIPV

D

LV
CS
Eso
LA
RIPV
LSPV
LIPV

Oral, Circulation 2005
Tissue Sensing Technology for RF Ablation Therapy

Larry A Chinitz MD
NYU Heart Rhythm Center
New York University School of Medicine
The ablation power is distributed between reference patch, the myocardium, and the surrounding blood.

When measuring impedance resistive properties are assumed to predominate: A good approximation only.
RF Energy Delivery to Heart Tissue

- RF energy distribution between blood and tissue determined by proportion of ablation electrode in contact with tissue by the equivalent circuit shown below.

- ≈ 5 gm contact
- 25% electrode-tissue contact
- 4.5 W of 50 W setting delivered to tissue

- ≈ 1 gm contact
- 75% electrode-tissue contact
- 19 W of 50 W setting delivered to tissue
Resistor: Voltage and current in phase (0°)
Capacitor: Voltage lags current ¼ cycle (90°)
Resistor/capacitor: lag between 0° ~ 90°
Elements of Complex Impedance

Impedance Magnitude ($|Z|$) = Voltage ($|V|$) / Current ($|I|$)

Diagram showing the relationship between $V_{\text{sense}}$, $I_{\text{inject}}$, and the phase angle ($\phi$).
• Phase angle: increases as catheter moves into tissue
• This is a relative, normalized measurement
  – Baseline: 0 deg is measured when catheter in blood
  – Minimize effect due to tissue variations
  – Robust & Consistent coupling indication
Trabeculated Tissue Surface

- Represents electrode surface in contact with tissue
- Predicts energy delivery to tissue
TST vs Bipolar EGM: Perfused Ventricular Wedge

- Catheter electrode advanced from 4 mm above tissue to 4 mm into tissue.
- R wave magnitude does not correlate with degree of tissue contact.
- TST correlates with degree of tissue contact.
- This result was consistent for 7 hearts, 4 runs per heart.
TST Porcine Thigh Model

Contact force is not predictive of lesion depth in pseudo-trabeculated tissue.

TST more accurately predicts lesion depth, regardless of tissue surface morphology.

<table>
<thead>
<tr>
<th></th>
<th>Smooth</th>
<th>Trabeculated</th>
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<tbody>
<tr>
<td>Force</td>
<td>0.78</td>
<td>0.47</td>
</tr>
<tr>
<td>TST</td>
<td>0.92</td>
<td>0.91</td>
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</table>
Successful lesion creation criteria:

- Full 60 second run at 20 W without high temperature shut-off
- Ability to find the lesion at post mortem

Highest percentage of successful lesions created in TST range 5 – 9.

\[ n = 60 \text{ lesions in 5 swine} \]
TST Conclusions

• Based on ventricular wedge studies and whole swine model, TST is highly correlated with ablation electrode contact with the endocardium.

• TST is more sensitive than Contact Force for assessing the dose of RF energy to the endocardium.

• Real time TST measurements will allow the operator to more appropriately select ablation parameters based on the degree of contact and oscillation of signal during contact.

• Use of TST has the potential to avoid tissue pops during ablation and collateral damage.

• TST may allow the creation of more accurate geometry and improve 3-D mapping
Catheter Ablation is a reasonable alternative to pharmacological therapy to prevent recurrent AF in symptomatic patients with little or no LA enlargement (class 2A, level of evidence C)
Classification of Recommendations

- Class I: Conditions for which there is evidence and/or general agreement that a given procedure/therapy is beneficial, useful, and effective.
- Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of performing the procedure/therapy.
  - Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.
  - Class IIb: Usefulness/efficacy is less well established by evidence/opinion.
- Class III: Conditions for which there is evidence and/or general agreement that a procedure/therapy is not useful or effective and in some cases may be harmful.
Level of Evidence

- Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses.
- Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies.
- Level of Evidence C: Only consensus opinion of experts, case studies, or standard-of-care.
Pharmacological management of patients with newly discovered atrial fibrillation (AF)

NEWLY DISCOVERED AF

Paroxysmal
- No therapy needed unless significant symptoms (e.g., hypotension, HF, angina pectoris)
  - Anticoagulation as needed

Persistent
- Accept permanent AF
  - Anticoagulation and rate control as needed
  - Consider antiarrhythmic drug therapy
    - Cardioversion
    - Long-term antiarrhythmic drug therapy unnecessary

Rate control and anticoagulation as needed

Fuster, V. et al. Circulation 2006;114:e257-e354
Pharmacological management of patients with recurrent paroxysmal atrial fibrillation (AF)

RECURRENT PAROXYSMAL AF

- Minimal or no symptoms
  - Anticoagulation and rate control* as needed
    - No drug for prevention of AF

- Disabling symptoms in AF
  - Anticoagulation and rate control as needed
    - AAD therapy*
      - AF ablation if AAD treatment fails

Fuster, V. et al. Circulation 2006;114:e257-e354
Antiarrhythmic drug therapy to maintain sinus rhythm in patients with recurrent paroxysmal or persistent atrial fibrillation

Fuster, V. et al. Circulation 2006;114:e257-e354
Pharmacological management of patients with recurrent persistent or permanent atrial fibrillation (AF)

**RECURRENT PERSISTENT AF**
- Minimal or no symptoms
  - Anticoagulation and rate control as needed

**Disabling symptoms in AF**
- Anticoagulation and rate control
  - AAD therapy
    - Electrical cardioversion as needed

**PERMANENT AF**
- Anticoagulation and rate control as needed

- Continue anticoagulation as needed and therapy to maintain sinus rhythm
  - Consider ablation for severely symptomatic recurrent AF after failure of greater than or equal to 1 AAD plus rate control

Fuster, V. et al. Circulation 2006;114:e257-e354
Preventing Thromboembolism

Class I

- INR should be determined at least weekly during initiation of therapy and monthly when anticoagulation is stable. *(Level of Evidence: A)*

- Aspirin, 81-325 mg daily, is recommended as an alternative to vitamin K antagonists in low-risk patients or in those with contraindications to oral anticoagulation. *(Level of Evidence: A)*

- For patients with AF who have mechanical heart valves, the target intensity of anticoagulation should be based on the type of prosthesis, maintaining an INR of at least 2.5. *(Level of Evidence: B)*

- Antithrombotic therapy is recommended for patients with atrial flutter as for those with AF. *(Level of Evidence: C)*
Preventing Thromboembolism

- Class III

- Long-term anticoagulation with a vitamin K antagonist is not recommended for primary prevention of stroke in patients below the age of 60 y without heart disease (lone AF) or any risk factors for thromboembolism. *(Level of Evidence: C)*
HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: Recommendations for Personnel, Policy, Procedures and Follow-Up
Developed in partnership with the European Heart Rhythm Association (EHRA) and the European Cardiac Arrhythmia Society (ECAS); in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), and the Society of Thoracic Surgeons (STS).
Endorsed and Approved by the governing bodies of the American College of Cardiology, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, and the Heart Rhythm Society.
AF Definition

- Paroxysmal AF is defined as recurrent AF (≥2 episodes) that terminates spontaneously within 7 days.
- Persistent AF is defined as AF which is sustained beyond seven days, or lasting less than seven days but necessitating pharmacologic or electrical cardioversion.
- Longstanding persistent AF is defined as continuous AF of greater than one-year duration.
- The term permanent AF is not appropriate in the context of patients undergoing catheter ablation of AF as it refers to a group of patients where a decision has been made not to pursue restoration of sinus rhythm by any means, including catheter or surgical ablation.
Indications for Catheter AF Ablation

- Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication.
- In rare clinical situations, it may be appropriate to perform AF ablation as first line therapy.
- Selected symptomatic patients with heart failure and/or reduced ejection fraction.
- The presence of a LA thrombus is a contraindication to catheter ablation of AF.
Symptomatic AF patients undergoing other cardiac surgery.

Selected asymptomatic AF patients undergoing cardiac surgery in whom the ablation can be performed with minimal risk.

Stand-alone AF surgery should be considered for symptomatic AF patients who prefer a surgical approach, have failed one or more attempts at catheter ablation, or are not candidates for catheter
Pre-procedure Management

- Patients with persistent AF who are in AF at the time of ablation should have a TEE performed to screen for thrombus.
CT and MR Imaging of the Atrium and Pulmonary Veins

- Imaging the anatomic features of the PVs and LA preprocedurally
- Disclosing the anatomic relationship between the LA, esophagus and adjacent vascular structures
- Providing an understanding of the degree of morphological remodeling of the PVs and LA
- Assisting in the detection of post procedure complications.
Complications

- Major complications are those that result in permanent injury or death, require intervention or treatment, or prolong or require hospitalization (6% in world-wide survey)
- Cardiac Tamponade (1.2%), PV Stenosis (1.3%), Esophageal Injury (0.25%), Phrenic Nerve Injury (0-0.48%), Thromboembolism (0-7%), Atrial Tachycardias (25%), Vascular Complications (4%), Coronary Occlusion, Periesophageal Vagal Injury, Radiation Exposure, Mitral Valve Trauma
Post-procedure Management

- Low molecular weight heparin or intravenous heparin should be used as a bridge to resumption of systemic anticoagulation following AF ablation.
- Warfarin is recommended for all patients for at least two months following an AF ablation procedure.
- Decisions regarding the use of warfarin more than two months following ablation should be based on the patient’s risk factors for stroke and not on the presence or type of AF.
- Discontinuation of warfarin therapy post ablation is generally not recommended in patients who have a CHADS score ≥2. (CHF, HTN, age >75, DM, prior CVA)
- ASA or Warfarin is appropriate for patients with a CHADS score of 1 following an ablation procedure.
Unresolved Issues

- What are the long-term efficacy outcomes for ablation?
- What are the comparative success rates of various drug and ablative techniques?
- What are the outcomes of AF ablation in patients with persistent and longstanding AF?
- Does symptom state at enrollment contribute to trial outcomes?
- What is the impact of ablation on atrial size, morphology, and function?
- What is the benefit of AF ablation in patients with varying types of underlying cardiac and noncardiac disease?
- Do these interventions have an impact on the long-term occurrence of stroke or peripheral thrombo-embolic events?
Unresolved Issues

- In which patients can warfarin be safely discontinued following the ablation?
- Is there acceptable rationale for ablation applied as first line therapy for AF?
- Is ablative intervention cost-effective, or is drug therapy more economically efficient?
- Beyond placebo effect, what is the relative quality of life benefit of ablation vs. drug therapy?
- What is the optimal ablative strategy for treatment of persistent and longstanding persistent AF?
- What are the safety and efficacy outcomes of newer ablation technologies such as cryo, ultrasound, and laser ablation?
- What are the safety and efficacy outcomes of ablation strategies that target complex fractionated electrograms or autonomic ganglia when used alone or as an adjunctive procedure?