Managing Atrial Fibrillation in 2010

Jennifer Cummings, MD FACC
Director, Cardiac Electrophysiology
Akron General Medical Center

Disclosures

Company	Type
Boston Scientific	Speaker Honoraria
St. Jude Medical	Speaker Honoraria
	Atrial Fibrillation Advisory Board
Medtronic	Speaker Honoraria
Sanofi-Aventis	Speaker's Bureau
Corazon Consulting	Consultant

Objectives

- Atrial fibrillation continues to be a growing problem
  - Growing in population
  - Growing in cost
  - Growing in danger
- Therapeutic options do not appear to be keeping up with the disease process
  - Review current treatment options
  - Review future treatment options

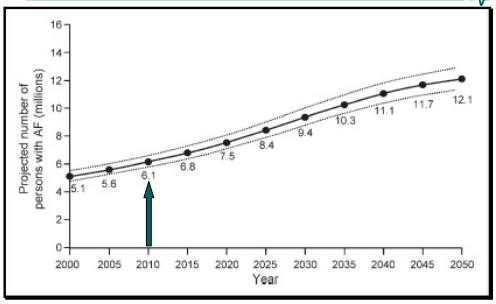
Atrial Fibrillation: A Growing Problem

Atrial Fibrillation: Prevalence Estimates

- AF is the most common form of arrhythmia[1]
- AF affects approximately
  - 2.3 million people in the United States
  - 4.5 million people in the European Union1
- AF is associated with high rates of morbidity and mortality[1,4]
  - 1 of every 6 stokes occurs in patients with AF[1]

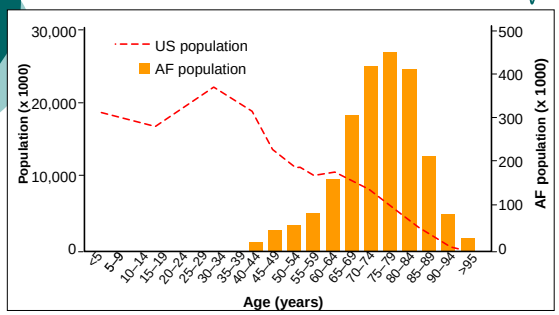
1. Fuster V et al. J Am Coll Cardiol. 2006;48:e149-246. 2. Fuster V et al. Nature Clinical Practice Cardiovascular Medicine. 2005;2:225. 3.Go AS et al. JAMA. 2001;285:2370-2375. 4. Wattigney WA et al. Am J Epidemiol. 2002;155:819-826.

Atrial Fibrillation: Prevalence Estimates



Turpie A. New oral anticoagulants in atrial fibrillation. EHJ 2007; 29:155-65

Atrial Fibrillation: a growing problem



Feinberg W, et al. *Arch Intern Med.* 1995;155:469-473.

Most Common Arrhythmia Admission

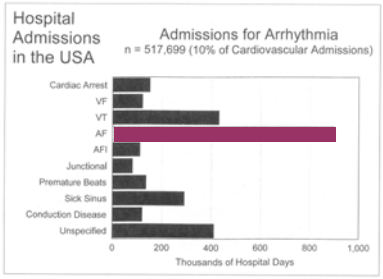


FIGURE 1. Number of hospital admission days in the United States for arrhythmias. (Modified with permission from *J Am Coll Cardiol*.[4])

Cost of Atrial Fibrillation

- Total annual costs for treatment of AF were estimated at US **$6.65 billion**
  - $2.93 Billion for hospitalizations
  - $1.95 billion for incremental inpatient cost as comorbid diagnosis
  - $1.53 billion for outpatient treatment
  - $235 million for prescription drugs

Coyne KS, Paramore C, Grandy S, et al., Assessing the direct costs of treating nonvalvular atrial fibrillation in the United States, Value Health, 2006;9:348–56.

Cost of Atrial Fibrillation

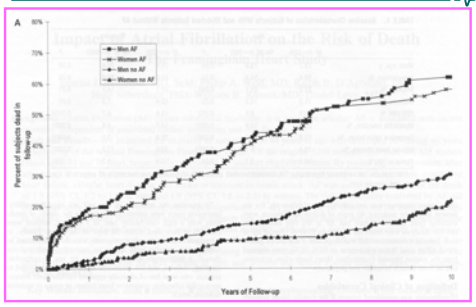
Atrial Fibrillation: Growing danger?

Atrial Fibrillation: Not a benign problem

- Atrial Fibrillation & Risk of Death Framingham Heart Study
  - 40 year follow-up patients with and without atrial fibrillation.
  - Adjustment for age, hypertension, diabetes, CHF, valvular disease & myocardial infarction.
  - Odds ratio for death: 1.5 in men, 1.8 in women

Circ. 1998;98:946-52

Atrial Fibrillation & Risk of Death Framingham Heart Study



Therapeutic options are not catching up to the growing problem of Atrial Fibrillation:

In fact for a while they seemed to go nowhere!

What are the cornerstones in the management of the patient with Atrial Fibrillation?

Stroke/Thromboembolism Prevention

Ventricular Rate Control

ythm Control

Management of Atrial Fibrillation: Ventricular Rate Control

- AV nodal blocking medications
- Beta-adrenergic blockers
- Calcium channel blockers
- Digoxin
- Ventricular pacing
- AV nodal modification/ablation with pacemaker implantation

The AFFIRM Trial

Is it worth struggling to maintain sinus rhythm?

4060 pts with AFib

Rate Control — ***Rhythm Control***

- No difference in mortality, stroke risk or quality of life
- More frequent hospitalization and adverse drug effects in Rhythm Control arm

Rate Control for All?

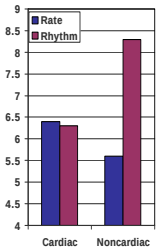
AFFIRM - N Engl J Med 2002;347:1825-33

Rate Control for ALL is really what halted progress…..

Problems with AFFIRM

- Mean age: 69.7 +/- 9 years
  - Young patients were underrepresented
- 45% of those screened declined enrollment
  - Were highly symptomatic patients underrepresented?
- AFFIRM was not a trial of sinus rhythm versus atrial fibrillation: It was a trial of the strategy
  - 62% of “Rhythm Control” patients were in NSR
  - 35% of “Rate Control” patients were in NSR

Problems with AFFIRM



- Total mortality in AFFIRM was not significantly different comparing Rhythm and Rate strategies
- Non cardiac mortality was different comparing the two groups:
  - Cancer (6% vs 4%)
  - Pulmonary disease (4% vs 3%)
- 63% of patients experienced amiodarone

Steinberg, 2004

AFFIRM did apply to

- Asymptomatic Patients
- Elderly Patients
- No CHF
- In THIS population:
  - Rate and rhythm control strategies result in similar outcomes with respect to
    - mortality
    - stroke
    - functional capacity*
    - quality of life*

Errors in Patient Management Due to Misinterpretation of AFFIRM Trial Results – “Rate Control for All”

- Dooming patient without heart disease to lifelong drug therapy and coumadin
- Not attempting cardioversion in patients with “New Onset” AF because rate control is “preferred therapy”
- Forcing patient to accept rate controlling drug side effects as “ part of aging process” (fatigue, loss of mental clarity, insomnia, constipation)

Relationships Between Sinus Rhythm, Treatment, and Survival in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Study

The AFFIRM Investigators*

Background—The AFFIRM Study showed that treatment of patients with atrial fibrillation and a high risk for stroke or death with a rhythm-control strategy offered no survival advantage over a rate-control strategy in an intention-to-treat analysis. This article reports an “on-treatment” analysis of the relationship of survival to cardiac rhythm and treatment as they changed over time.

Methods and Results—Modeling techniques were used to determine the relationships among survival, baseline clinical variables, and time-dependent variables. The following baseline variables were significantly associated with an increased risk of death: increasing age, coronary artery disease, congestive heart failure, diabetes, stroke or transient ischemic attack, smoking, left ventricular dysfunction, and mitral regurgitation. Among the time-dependent variables, the presence of sinus rhythm (SR) was associated with a lower risk of death, as was warfarin use. Antiarrhythmic drugs (AADs) were associated with increased mortality only after adjustment for the presence of SR. Consistent with the

Conclusions—Warfarin use improves survival. SR is either an important determinant of survival or a marker for other factors associated with survival that were not recorded, determined, or included in the survival model. Currently available AADs are not associated with improved survival, which suggests that any beneficial antiarrhythmic effects of AADs are offset by their adverse effects. If an effective method for maintaining SR with fewer adverse effects were available, it might be beneficial. (*Circulation.* 2004;109:1509-1513.)

Management of the patient with Atrial Fibrillation

Stroke/Thromboembolism Prevention

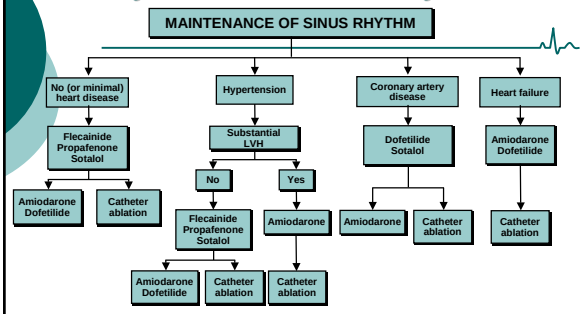
Ventricular Rate Control

Rhythm Control

Management of Atrial Fibrillation: Rhythm Control

- Antiarrhythmic drugs +/- DC cardioversion
- AF catheter ablation (PVAI)
- Atrial Segmentation
  - Surgical Maze procedure
  - Catheter Maze procedure: "Linear AF ablation"
- Pacing
  - Prevention/Suppression algorithms
  - Treatment (termination) algorithms

Rhythm Control: Anti-arrhythmics



LVH = left ventricular hypertrophy.
Fuster V et al. *J Am Coll Cardiol.* 2006;48:e149-246.

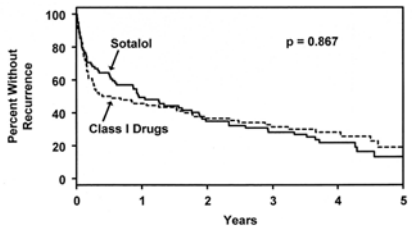
Antiarrhythmic Drugs for AF

Drug	Drug Class	Dosage	Adverse Events
Flecainide	Class 1C	200-300 mg	Ventricular tachycardia, heart failure, proarrhythmia
Propafenone	Class 1C	450-900 mg	Ventricular tachycardia, heart failure, proarrhythmia
Sotalol	Class III	160-320 mg	Asthma, bradycardia/heart block, heart failure, torsades de pointes
Amiodarone (off-label)	Class III	100-400 mg	Bradycardia/heart block, thyroid dysfunction, pulmonary and liver toxicity with long-term use
Dofetilide	Class III	500-1000 mcg	QT interval prolongation (need to monitor), torsades de pointes, conduction disturbances
Dronedarone		800mg	GI disturbance / Bradycardia / Use cautiously in Class 2-3 CHF

1. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation. J Am Coll Cardiol 2006;48:854-906. 2. Lim HS et al. Critical Care. 2004;8:271-279.

Problem? They aren't that effective

Time to recurrence of atrial fibrillation: Sotalol versus class I drugs

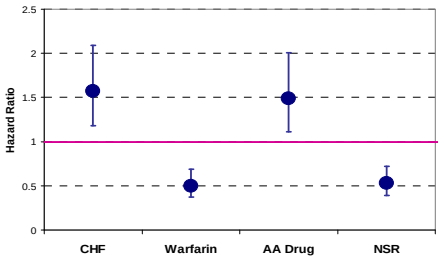


Number of Recurrences (% Without Recurrence)

Sotalol:	0 (100%)	41 (49%)	52 (35%)	57 (28%)	61 (22%)	64 (13%)
Class I:	0 (100%)	50 (46%)	58 (37%)	62 (31%)	64 (28%)	67 (19%)

The AFFIRM First Antiarrhythmic Drug Substudy Investigators, J Am Coll Cardiol 2003;42:20-29

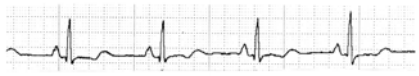
Problem? They aren't that safe



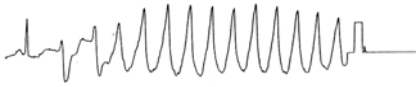
Epstein, et al, Circ, 2004

Drugs have inherent risks for their decreased efficacy. . .

This is your heart…



This is your heart on drugs…

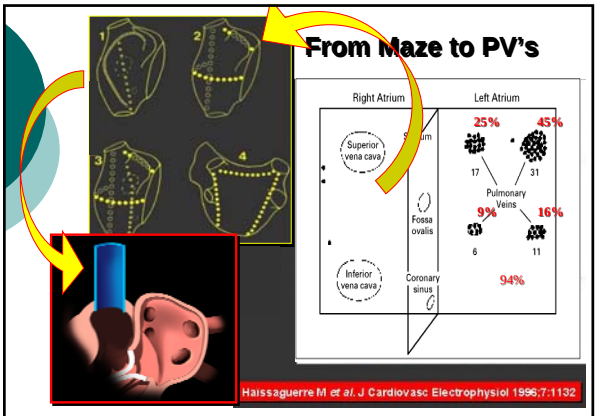


ANY QUESTIONS?

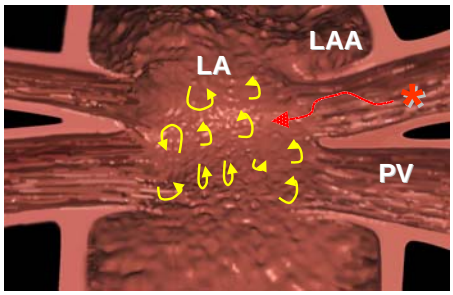
You're going to burn What? Where?

What is all this ablation about?

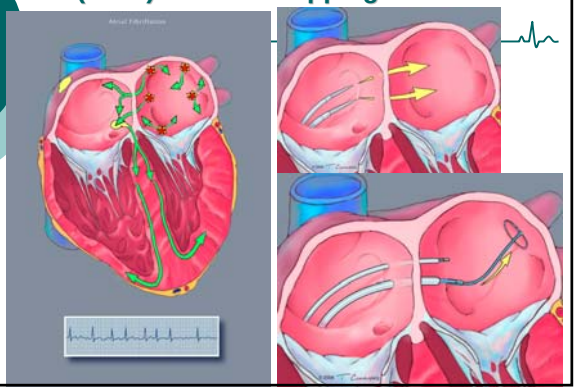
From Maze to PV's



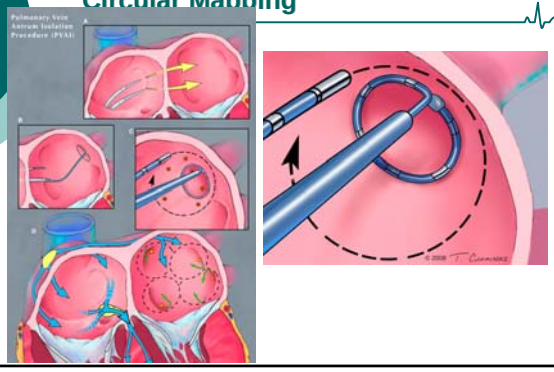
Pulmonary Vein Triggers Initiating Atrial Fibrillation



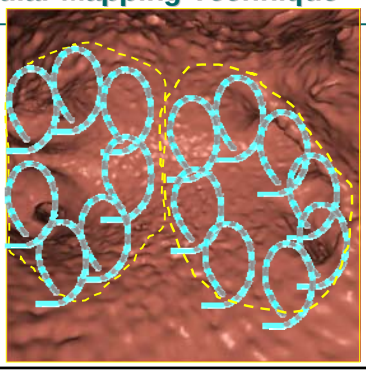
Pulmonary Veins Antrum Isolation (PVAI):Circular Mapping

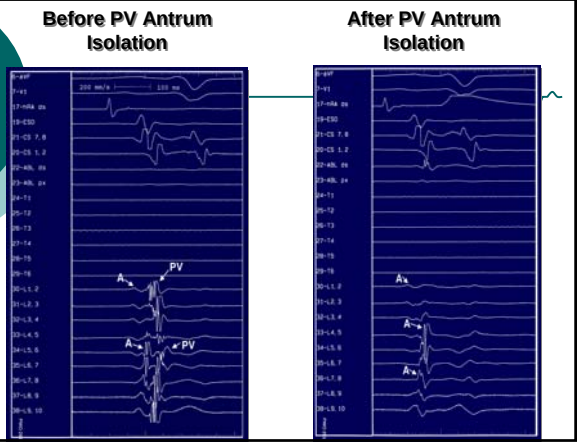


Pulmonary Veins Antrum Isolation (PVAI): Circular Mapping



Pulmonary Veins Antrum Isolation: Circular Mapping Technique





Impact of type of atrial fibrillation (AF) and repeat catheter ablation on long term freedom from AF: Results from a Multicenter Study

Mandeep Bhargava* MD, Luigi Di Biase*- # MD, Prasant Mohanty-, MBBS, MPH, Subramanyam Prasad* MD, David O. Martin* MD, MPH, Michelle Williams-Andrews* RN, Oussama M. Wazni* MD, J.David Burkhardt- MD, Jennifer E. Cummings* MD, Yaariv Khaykin** MD, Atul Verma** MD, Steven Hao- MD, Salwa Beheiry- RN, Richard Hongo-, MD, Antonio Rossillo-- MD, Antonio Raviele-- MD, Aldo Bonso--, MD, Sakis Themistoclakis--, MD, Kelly Stewart, RN, Walid I, Saliba*, MD, Robert A. Schweikert--, MD, Andrea Natale***, MD, FACC

*Cleveland Clinic, Cleveland, OH, USA;
-Sutter Pacific Heart Center, San Francisco, CA, USA;
--Umberto I Hospital, Mestre-Venice, Italy;
**Southlake Regional Medical Center, Newmarket, Ontario, Canada;
-Texas Cardiac Arrhythmia Institute at St. David's Medical Center, Austin, TX, USA;
--Akron General Medical Center, Akron, OH, USA;
Department of Cardiology, University of Foggia, Foggia, Italy;
*** Texas Cardiac Arrhythmia Center at St David Medical Center, Austin, TX, USA, Stanford University, Palo Alto, CA, USA, Case Western Reserve University, Cleveland, OH, USA

Bhargava M, ... Cummings JE, Schweikert R, Natale A. Heart Rhythm. 2009 Jun 9.

AF Ablation: Long term data

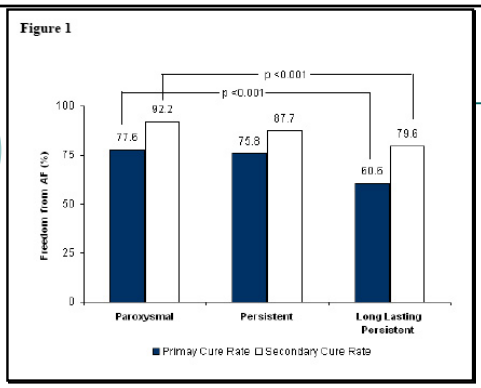
- N = 1,404 patients
  - 728 PAF
  - 676 non-PAF
    - 293 Persistent
    - 383 Long standing (chronic)
- 12 operators at 4 different centers
- Technique: intracardiac echo (ICE) guided circular mapping radiofrequency catheter ablation

Bhargava M, ... Cummings JE, Schweikert R, Natale A. Heart Rhythm. 2009 Jun 9.

Table 2: Freedom from AF after initial and repeat catheter ablations

SN	Variable	Paroxysmal (1)	NPAF (2)	P-value (1 vs. 2)	Persistent (3)	Long lasting persistent (4)	P-value (1 vs. 3 vs. 4)
1	Primary recurrence	163/728	222/676	/	71/293	151/383	/
3	Redo ablation done	121(74.2%)	166(74.8%)	0.904	51(71.8%)	115(76.2%)	0.782
4	Recurrence after redo (Sec)	13/121	52/166	/	15/51	37/115	/
5	Total recurrence (Sec)*	57/728	114/676	/	36/293	78/383	/

Bhargava M, ... Cummings JE, Schweikert R, Natale A. Heart Rhythm. 2009 Jun 9.



Bhargava M, ... Cummings JE, Schweikert R, Natale A. Heart Rhythm. 2009 Jun 9.

So what are the risks?

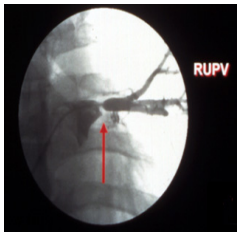
Atrial Fibrillation Ablation Complications
Cardiac Complications

Perforation / Effusion: Treatment / Prevention

- Intracardiac Echocardiography
- Rapid diagnosis
- Evaluate for RA / RV collapse

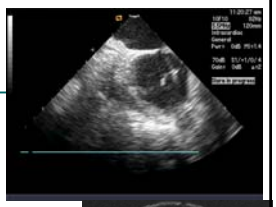
Pulmonary Vein Stenosis

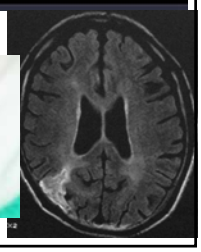
- 1-2% Incidence
- CT Scans
  - 3 months
  - 6 months if stenosis seen at 3 months
- Angioplasty / Stenting warranted in cases >70% or if Significant decrease in perfusion <25% in affected lung



Stroke

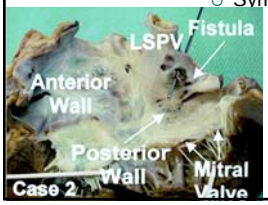
- 1-2% Incidence
- Char and/or Thrombus
- Intra-procedure echo
- Anticoagulation





Esophageal Complications

- <25 reported in the world
- Insidious Onset
- Late presenting
  - 10-16 days (mean 12.3)
- Symptoms: Vague Gradual
  - Fever / Chills
  - Leukocytosis
  - Microcytic Anemia
  - Embolic phenomenon



AF Catheter Ablation: Cleveland Clinic
Complications by Age Groups

	Group I (<50 years)	Group II (51-60 years)	Group III (>60 years)	P
Tamponade/Perforation	none	1 (0.86%)	2 (02%)	NS
TIA	1 (0.09%)	none	1 (01%)	NS
Stroke	none	none	3 (03%)	P<0.05
Severe PV Stenosis	2 (1.8%)	3 (2.6%)	1 (0.9%)	NS

Bhargava, Natale et al JCE 2004; 15(1): 8-13

When do you go to ablation?

- Though these risks are low, the invasiveness of the procedure still keeps it as second line therapy
- New ACC guidelines place ablation as second line therapy following an attempt at antiarrhythmic therapy

Can you predict who will do well and who won't?

AF Catheter Ablation :Cleveland Clinic

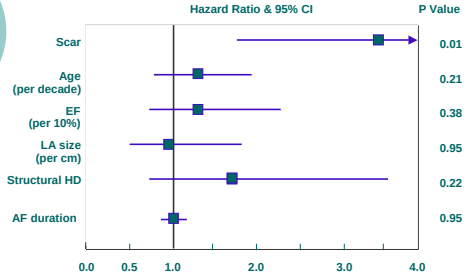
Results by Age Group

	Group I (<50 years)	Group II (51-60 years)	Group III (>60 years)	
Recurrences	16/106 (15.1%)	19/114 (16.7 %)	19/103 (18.4%)	NS; P=0.8
Paroxysmal	6/64 (09.3%)	8/56 (14.3%)	8/54 (14.8%)	NS; P=0.7
Persistent	2/11 (18.2%)	3/16 (18.8%)	2/08 (25.0%)	NS; P=0.9
Permanent	8/31 (25.8%)	8/42 (19.0%)	9/41 (21.9%)	NS; P=0.8

Bhargava, Natale et al JCE 2004; 15(1): 8-13

AF Catheter Ablation: Cleveland Clinic

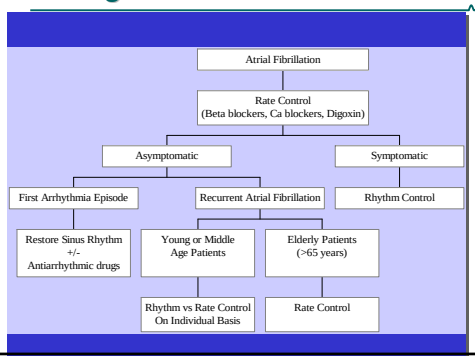
Multivariate Predictors of AF Recurrence Post PVAI



Verma, Natale et al JACC 2005;45(2):285-92

So how do get your rhythm?

AF Algorithm



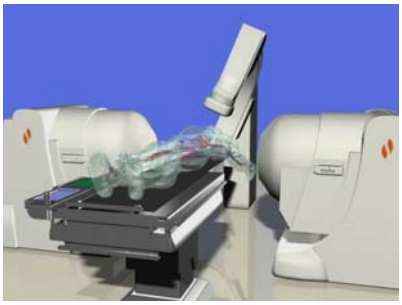
AF Catheter Ablation: Candidates

- Symptomatic AF (paroxysmal or persistent)
- At least one antiarrhythmic medication failure
- Younger patients with "lone" paroxysmal AF are the best candidates, but patients with persistent AF, older patients and those with co-morbidities such as structural heart disease and heart failure may also be appropriate candidates

AF Catheter Ablation: Potentially Poor Candidates

- Asymptomatic or minimally symptomatic AF
- No trial of antiarrhythmic drug
- Left atrial cardiomyopathy
- Goal of undergoing ablation is to get off warfarin
- Frail, elderly patients
- Severe structural heart disease, mechanical mitral valve, etc.

So what is new in 2010? Robotic Navigation



So whats new in 2010 Robotic Navigation

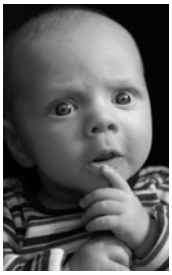
So what is new in 2010 Better Imaging

What is new in 2010 Safer tools: Cryotherapy

Whats new in 2010 New Antiarrhythmic

- Dronedarone (Multaq)
  - Class III antiarrhythmic drug (multiple channels)
  - Amiodarone congener: noniodinated amiodarone derivative
    - Lacks the iodine moiety, among other differences
    - Perhaps less risk for thyroid toxicity, amiodarone toxicity
  - "one dose fits most": 400 mg twice daily

Questions?



You ready for some cases???

Case 1

- WL is a 50 y/o man with no significant past medical history presented to his PCP with increased fatigue especially with exertion. He was found to be in atrial fibrillation and referred to your office for evaluation
  - PMHx: none
  - Meds: PCP started on Toprol XL 25mg
  - Social: EtOH: occasional; denies smoking

Case 1

- Exam
  - HR 88 bpm BP 105/60 RR 14 SaO2 100%
  - Normal physical with the exception of irregular heart beat no m/r/g
- Echocardiogram: EF 50% left atrium 3.8cm, septum 1.0cm.
- What is your plan from here?

Case 1: Continued

- So he remains in sinus rhythm for a couple months but then returns to you and he is back in atrial fibrillation with a rate of 100 bpm.
- This time he feels more symptomatic. He is short of breath with minimal exertion and is having palpitations
- What are his options?

Case 2

- MG is a 70 y/o woman with a past medical history of
  - CAD – status post CABG
  - Systolic CHF (Chronic) EF 30%
    - Status post ICD
  - Diabetes
  - Hypertension
- She presents to device clinic and complains she is more tired and has been feeling bad.

Case 2

- Device check demonstrates stable function, however she has mode switched and has been in atrial fibrillation for about one week. Heart rates are in the 80s.
- What do you do?

Case 2

- She is on
  - Coreg 12.5 bid
  - Lisinopril 5 mg
  - Insulin
  - Aspirin 81mg daily
  - Imdur
- Her last blood work shows
  - Na 135 K 4.0 BUN/Cr 22/1.5
  - WBC 6 H/H 13/36

Case 2

- What do you do?
  - Does she need to be admitted?
  - What are your short term goals?
  - What are your long term goals?
- What are her options
  - Short term?
  - Long term?

The end!