Spectral Analysis Techniques of Surface Electrocardiograms in Atrial Fibrillation Research and Clinical Management

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Is Analysis of Fibrillatory Waves Useful for Treatment of Atrial Fibrillation?

SHIH-ANN CHEN, M.D., and CHING-TAI TAI, M.D.

„As our increasing understanding of the mechanism of AF forms the basis for new treatment strategies, we believe that **noninvasive methods such as spectrum analysis of fibrillatory waves**, which is capable of detecting or monitoring changes in the characteristics of fibrillatory waves due to interventional procedures, **will be useful for treatment of AF**.“

J Cardiovasc Electrophysiol
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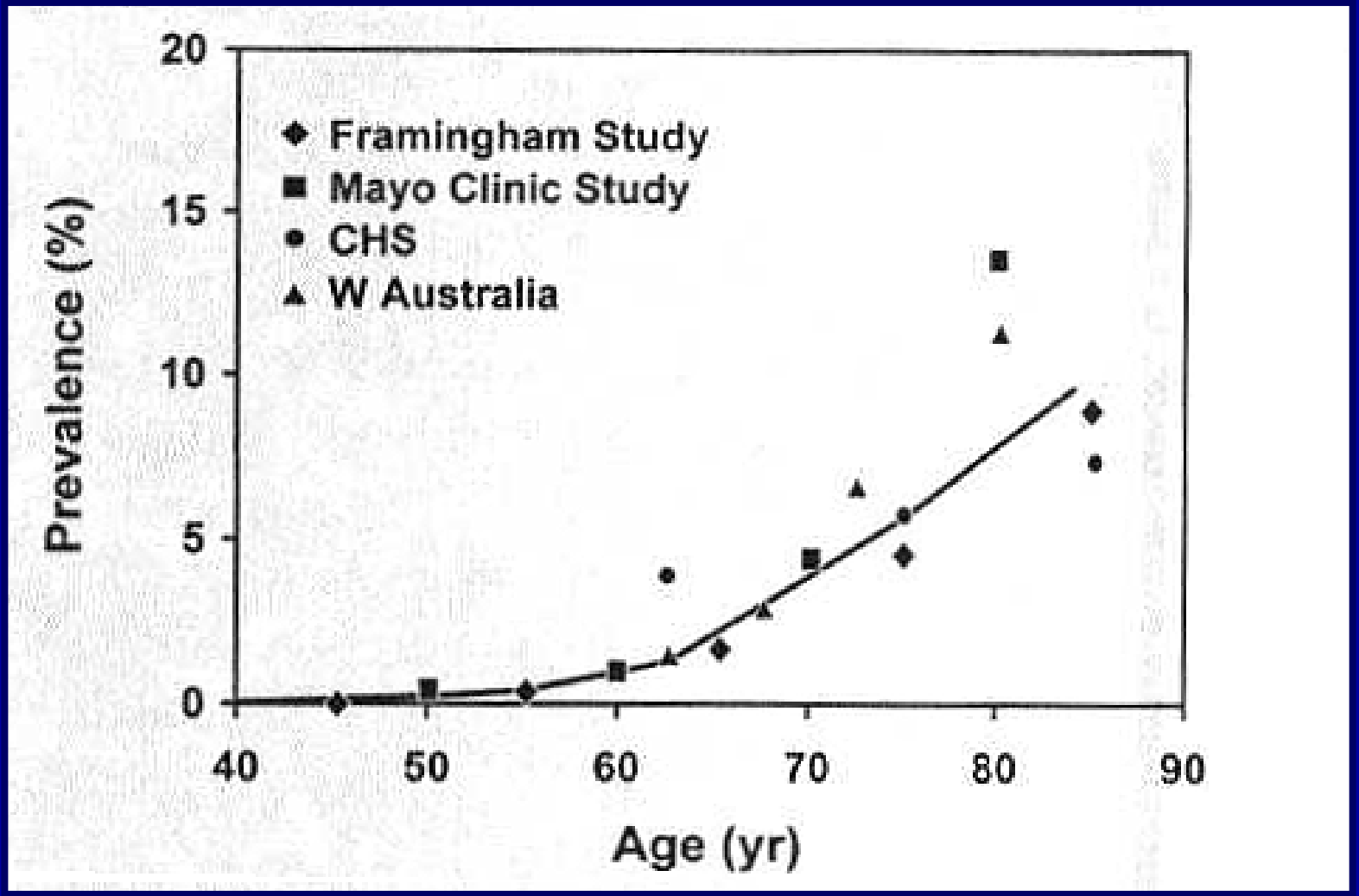
AF Prevalence



Feinberg et al. *Arch Intern Med* 1995

Significance of AF

- **Frequent Symptoms**
  - Palpitations (> 50 %)
  - Chest pain and Dyspnea (> 50 %)
  - Symptoms of cerebral hypoperfusion (25 %)
- **Increased Morbidity and Mortality**
  - 3 – 5-times increased risk for stroke
  - Development of heart failure
- **High Cost**
  - frequent office visits and hospitalizations
  - ca. 6.000 – 15.000 US Dollar per patient and year

General Treatment Options in AF

Restoration and Maintenance of SR

pharmacologic
vs
non-pharmacologic

Control of Ventricular Rate

pharmacologic
vs
non-pharmacologic

Anticoagulation

ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation 2001

General Treatment Options in AF

Restoration and Maintenance of SR

Control of Ventricular Rate

No treatment recommendations that *"take the various mechanisms and patterns of AF into account"*

Anticoagulation

ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation 2001

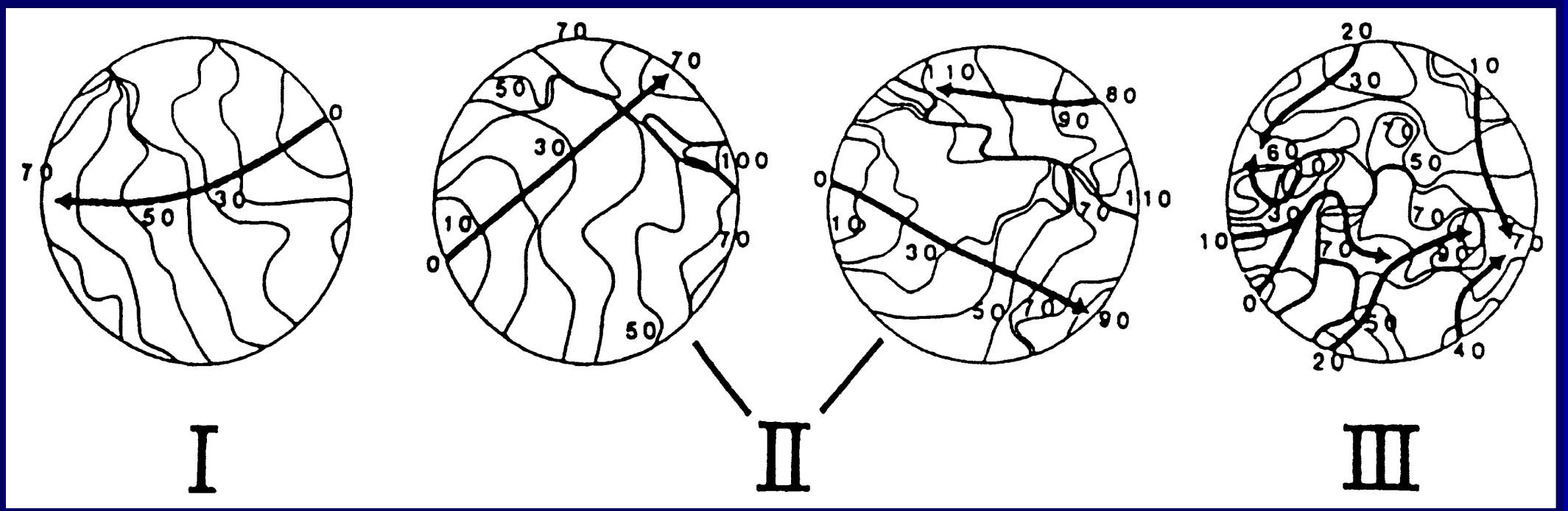
Issues in Clinical AF Management

How to quantify AF severity in the individual patient ?

How to choose among the different treatment options for the individual patient ?

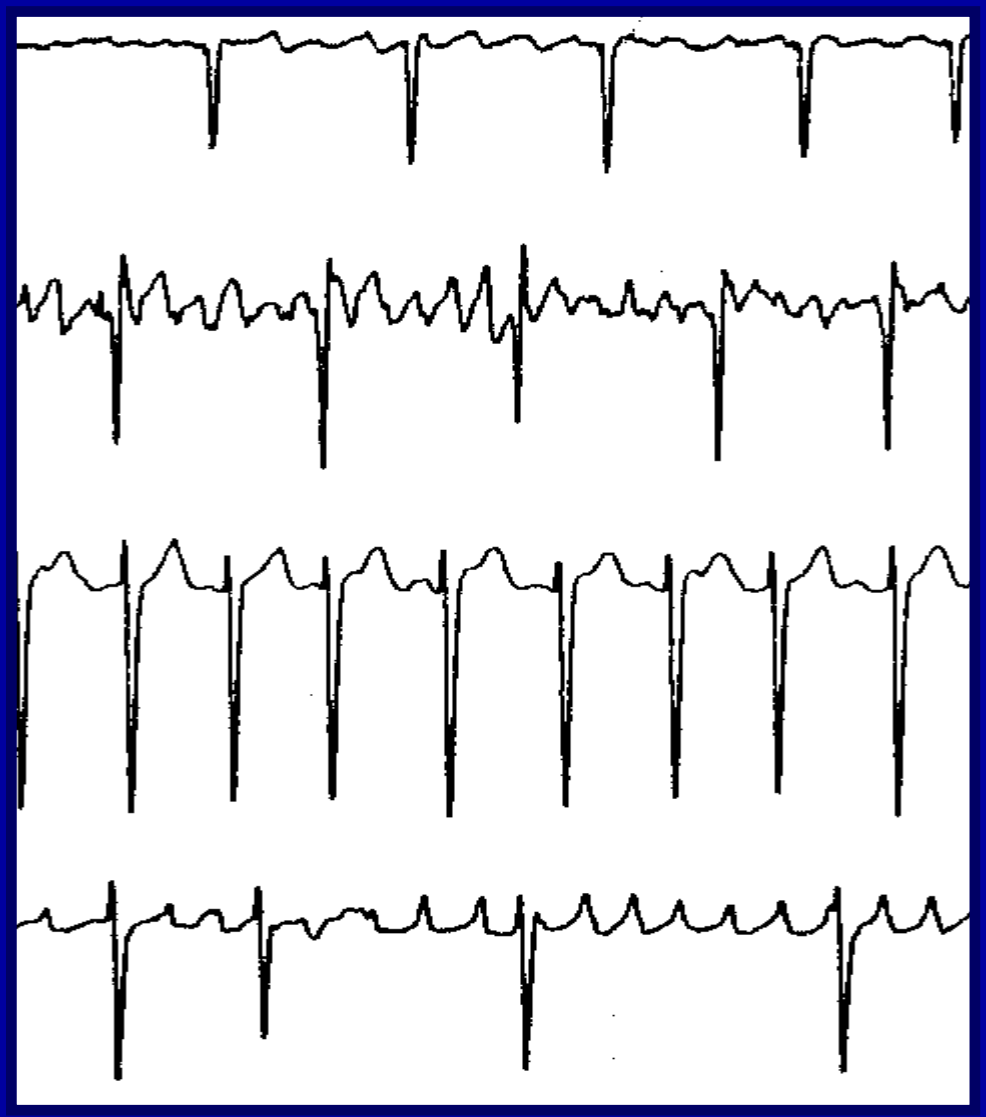
AF is not a Homogenous Arrhythmia

Evidence From Epicardial Mapping



Konings et al. *Circulation* 1994

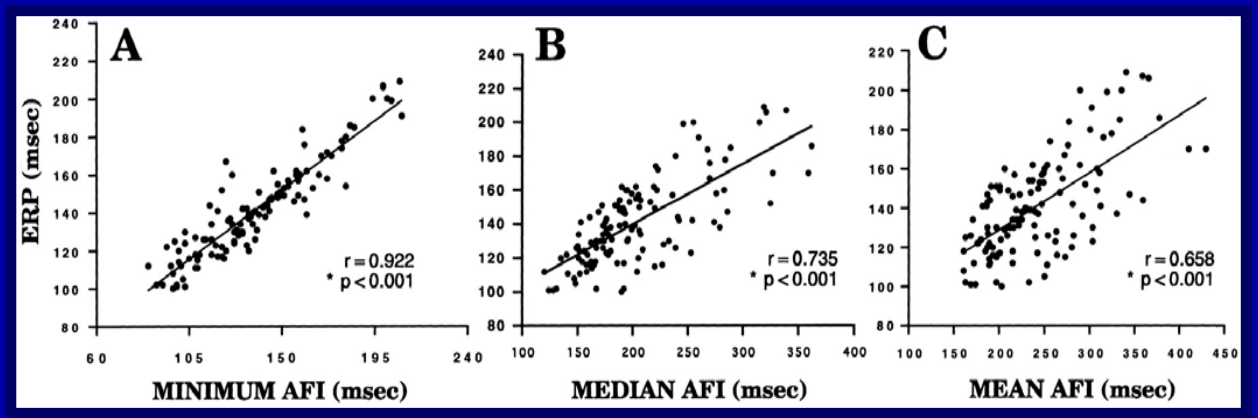
AF is not a Homogenous Arrhythmia
Evidence From Surface ECG



Holm, *Dissertation* 1997

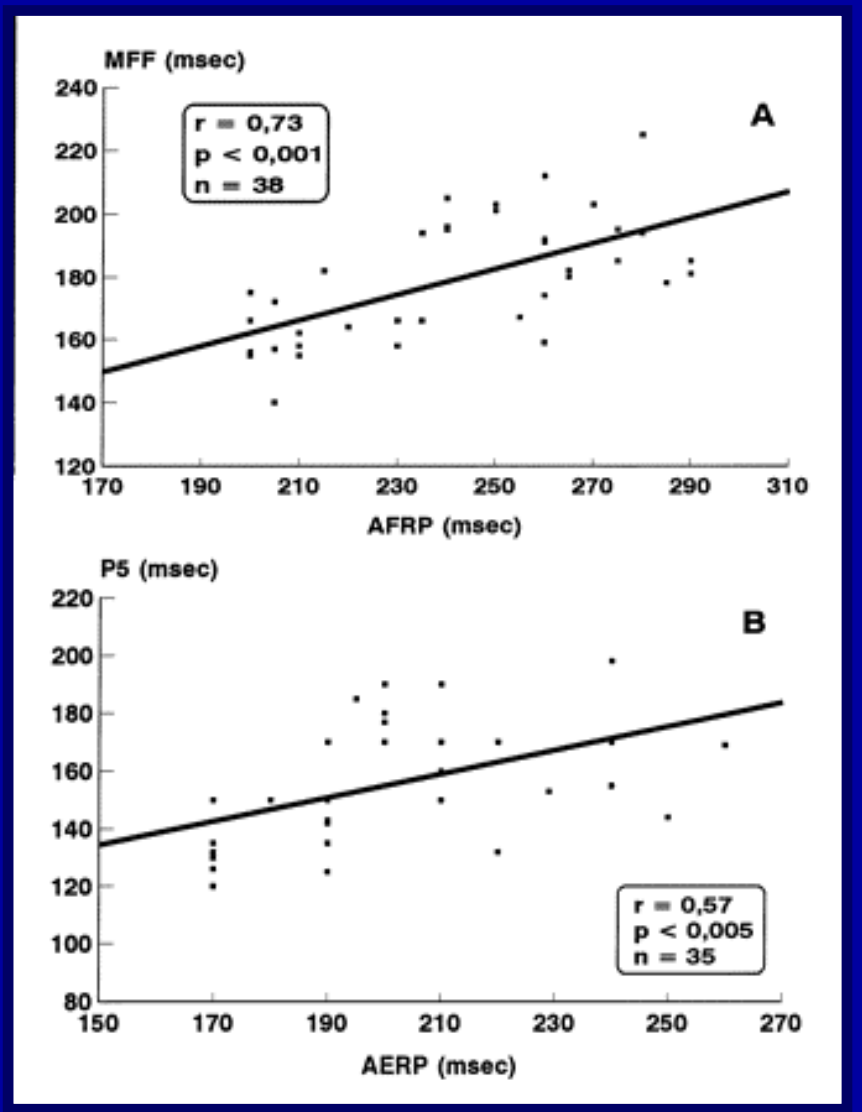
Fibrillatory Rate as a Measure of Atrial Refractoriness

AF in Isolated Canine Atria



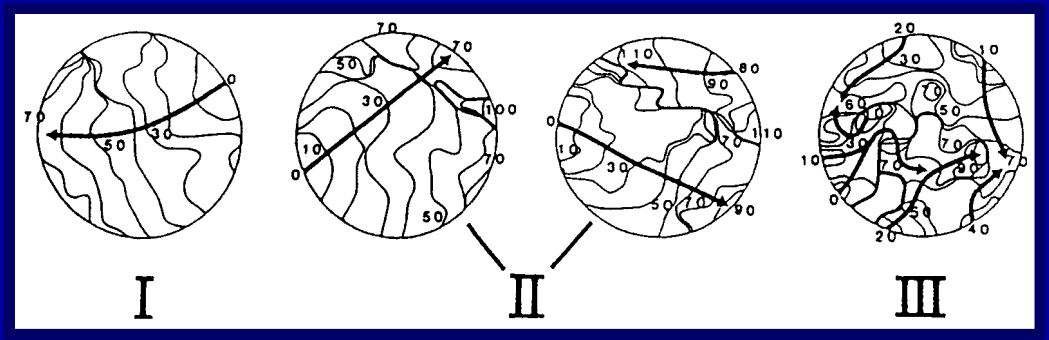
Kim et al. *Circulation* 1996

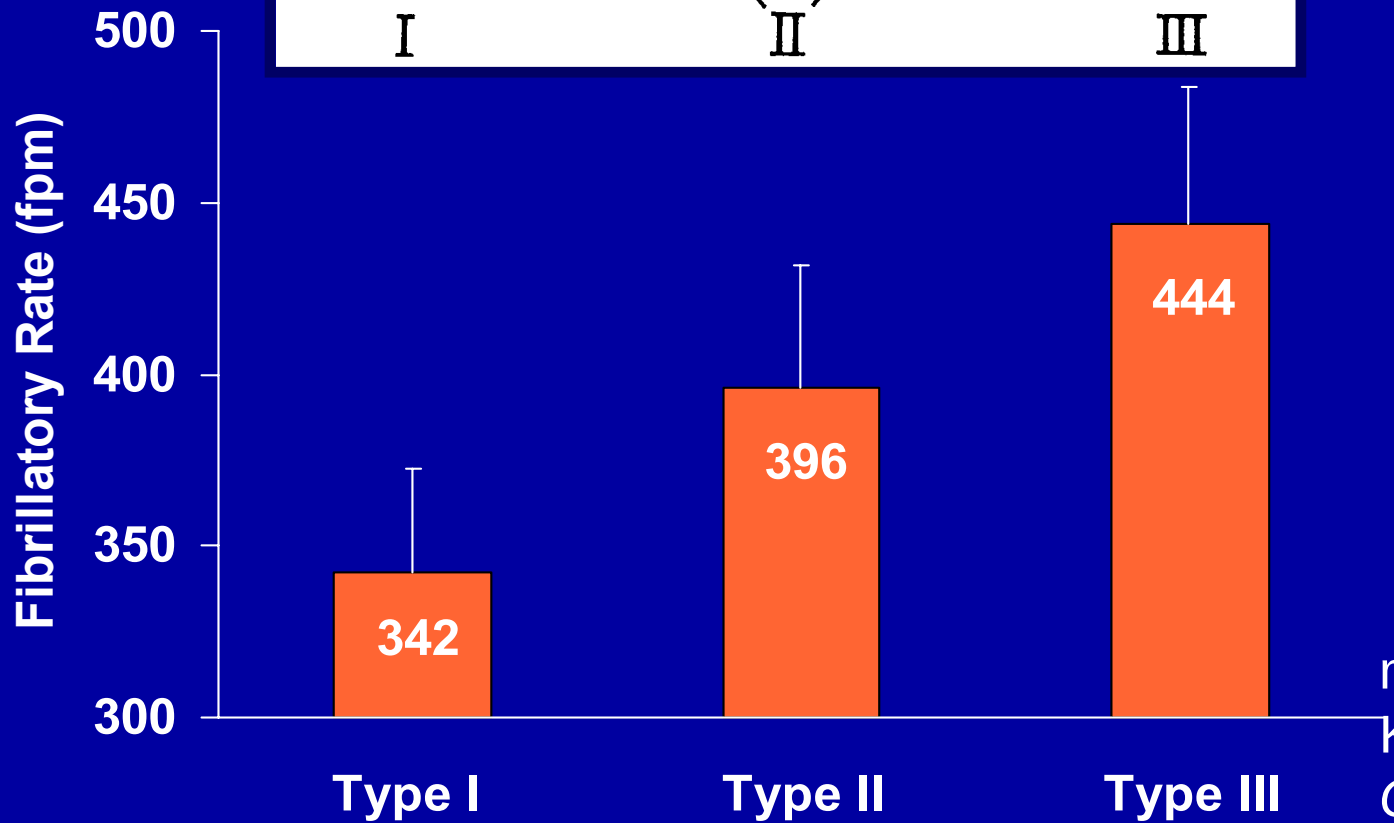
Induced Human AF



Capucci et al. *Circulation* 1995

Fibrillatory Rate as a Measure of AF Complexity

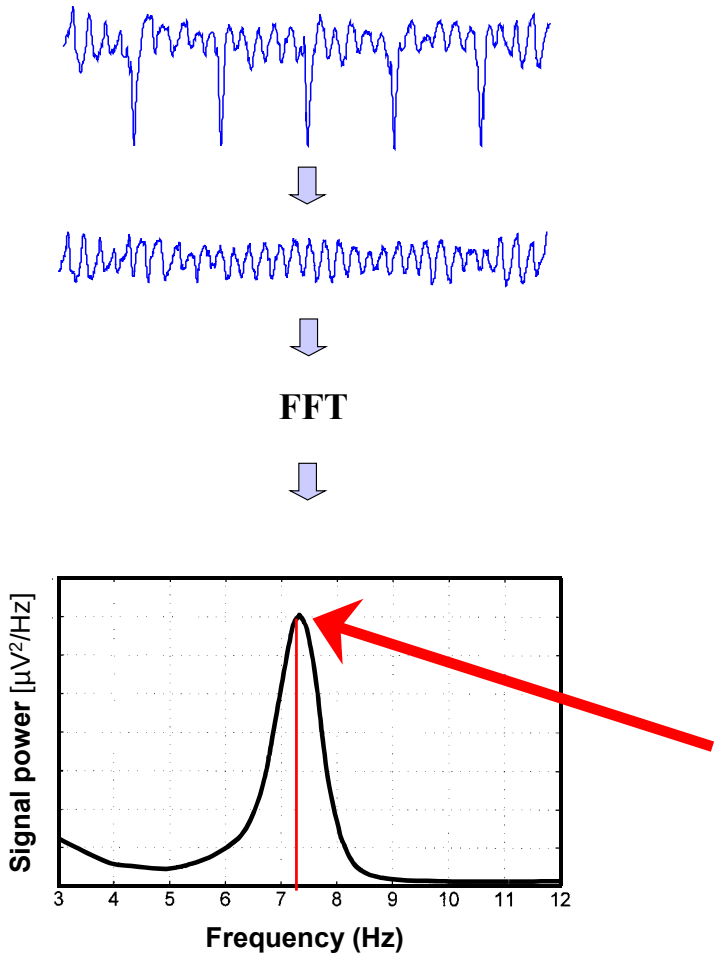




modified from Konings et al. *Circulation* 1994

FAF-ECG

*F*requency *A*nalysis of *F*ibrillation



Rate (fpm) = Frequency (Hz) x 60

Surface ECG lead

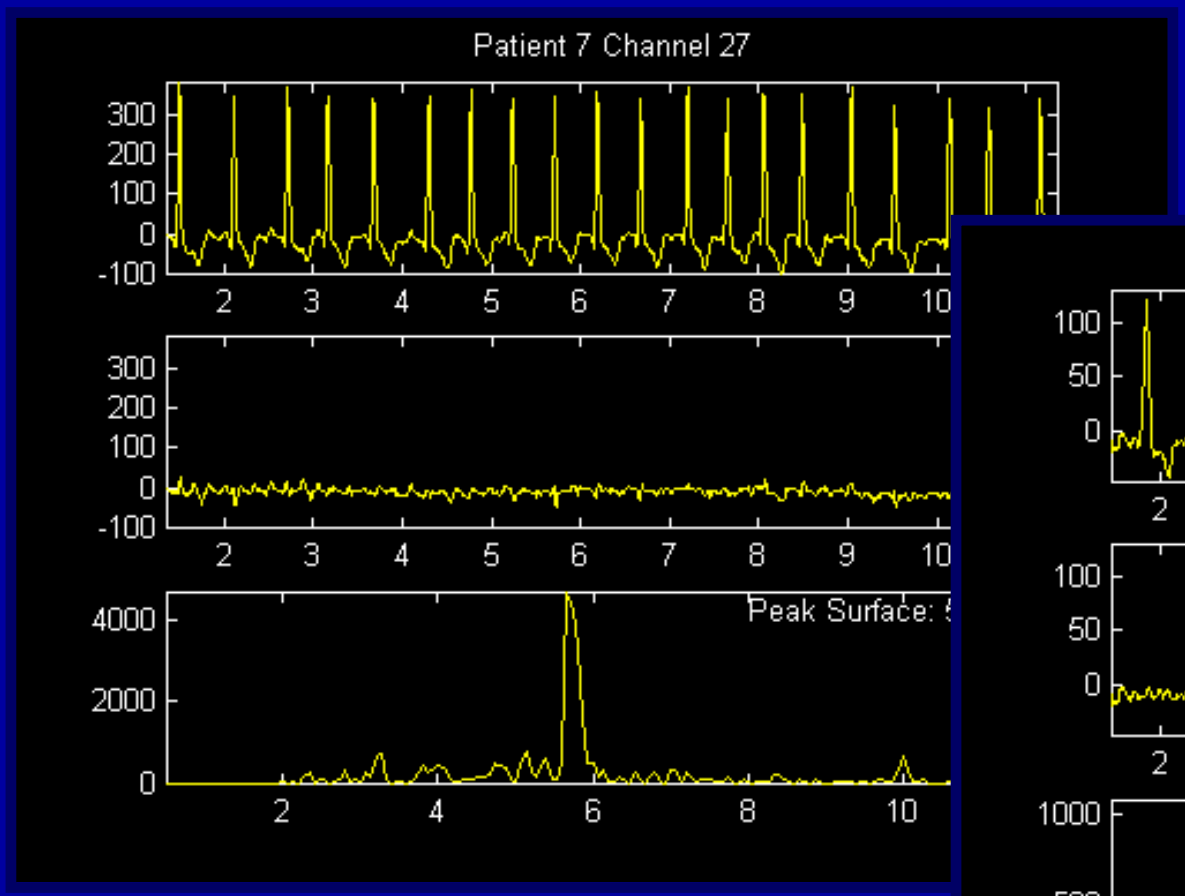
Fibrillatory signal after subtraction of averaged QRS-T-complexes

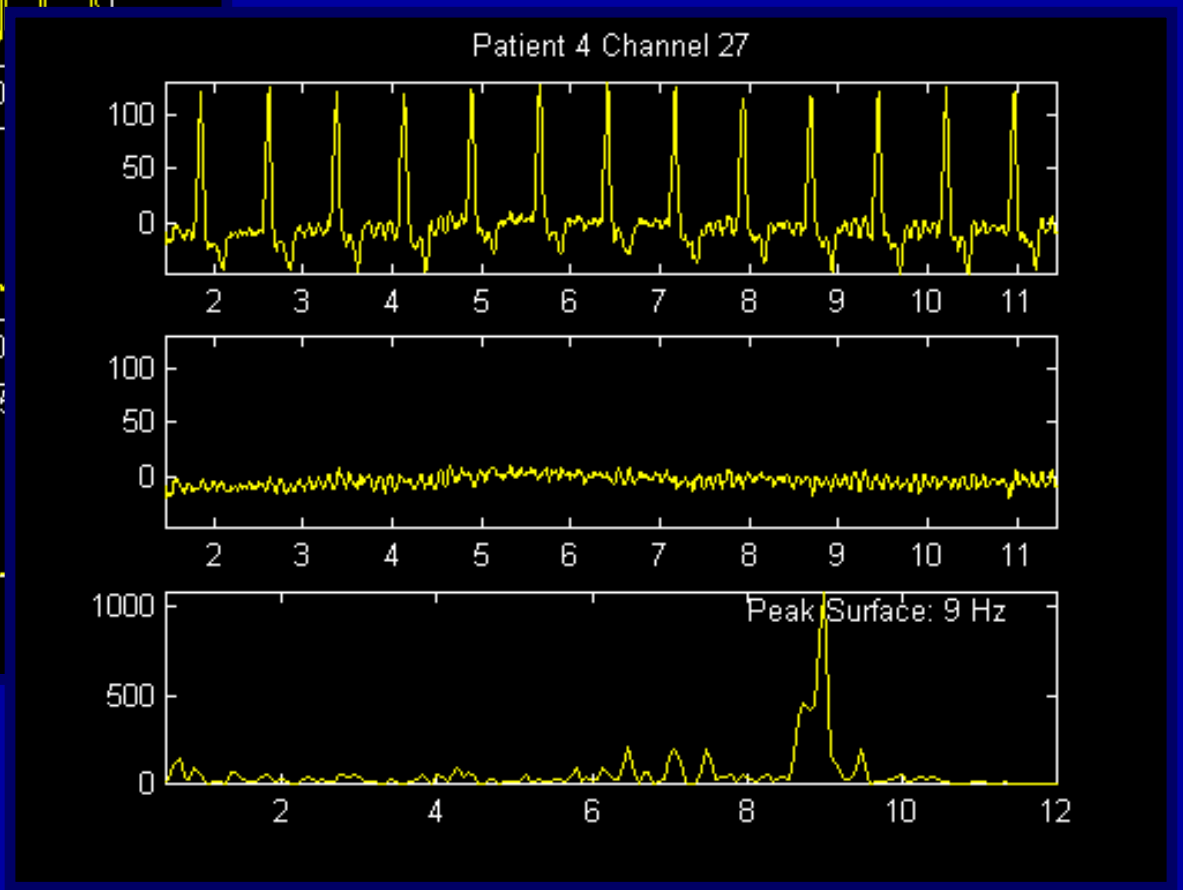
Frequency power spectrum

Determination of dominant fibrillatory rate

Holm et al. *Cardiovasc Res* 1998
Bollmann et al. *Am J Cardiol* 1998

FAF-ECG
Examples



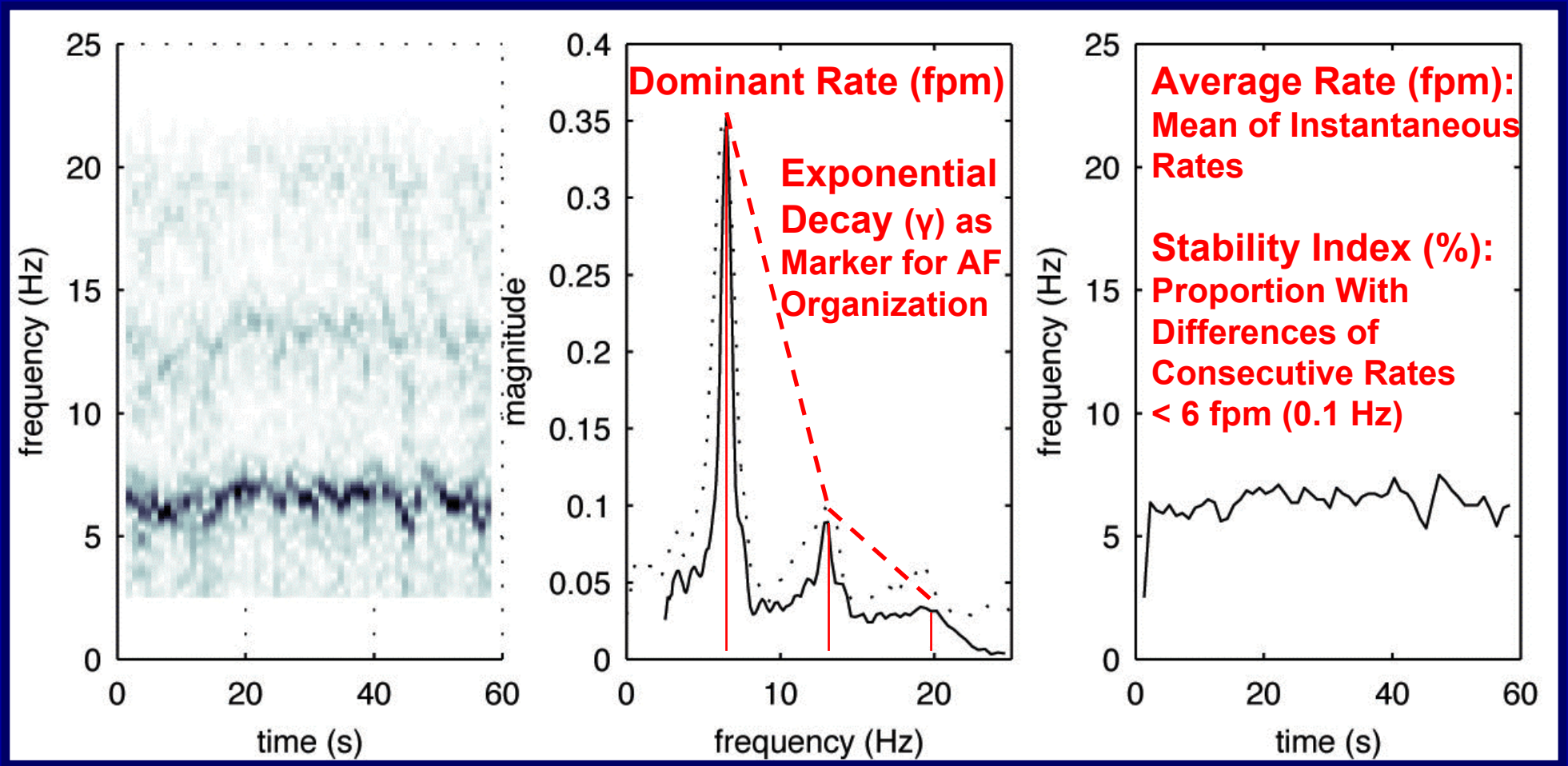


Atrial Fibrillatory Frequency, Atrial Fibrillatory Rate or Atrial Cycle Length – Does it Matter ?

	Patient A			*Patient B*		
	Frequency (Hz)	Rate (fpm)	Cycle length (ms)	Frequency (Hz)	Rate (fpm)	Cycle length (ms)
Pre-drug	6	360	166	9	540	111
Post-drug	5	300	200	8	480	125
Difference	**1**	**60**	**34**	**1**	**60**	**14**

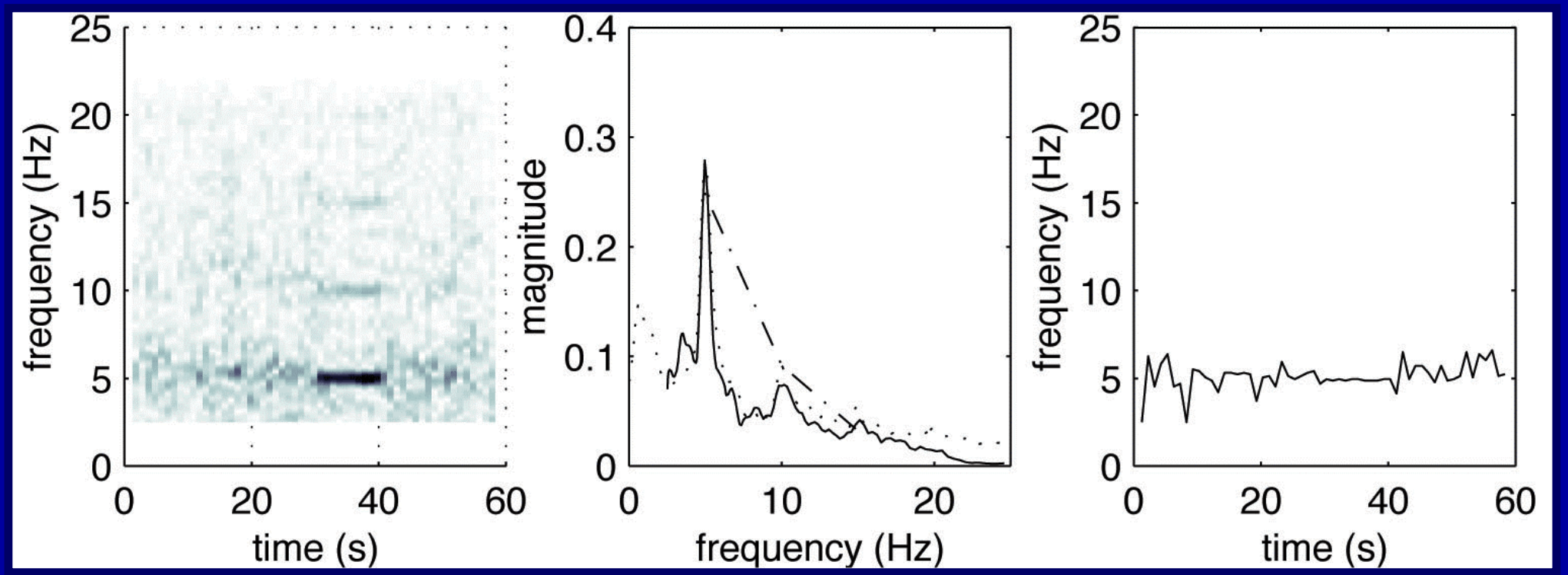
Bollmann et al. *Am J Cardiol* 2004

Time-Frequency Analysis



Stridh et al. *IEEE Trans Biomed Eng* 2001
Bollmann et al. *J Cardiovasc Electrophysiol* 2003

Time-Frequency Analysis
Example

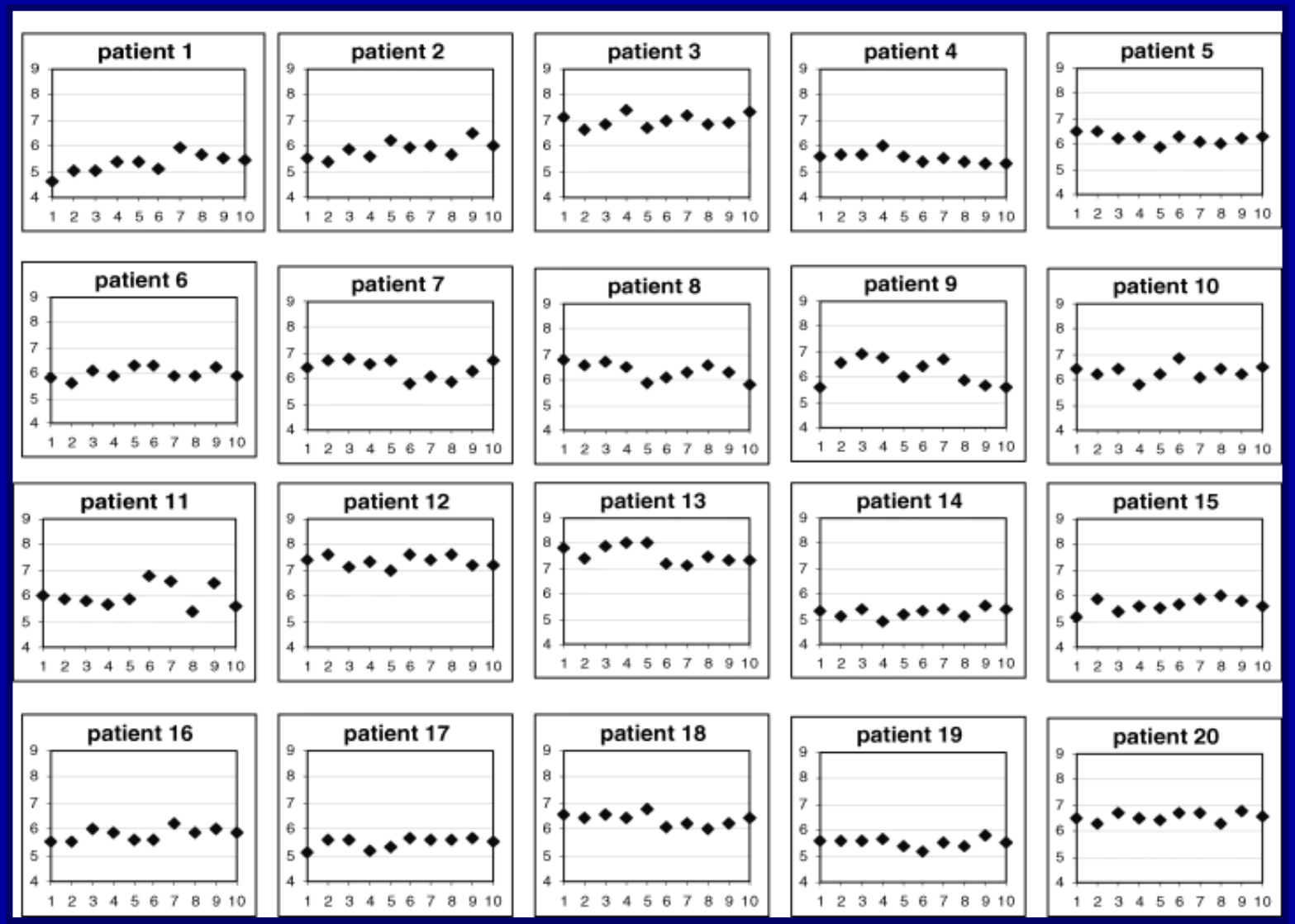


Stridh et al. *IEEE Trans Biomed Eng* 2001
Bollmann et al. *J Cardiovasc Electrophysiol* 2003

Primary Investigator Investigation	Bollmann	Olsson	Stridh & Sornmo	Others
Validation	Comparison with intracardiac EGM (N=54)	Comparison with intracardiac and esophageal EGM (N=8)		Comparison with asystolic ECG segment (N=12)
Method improvement			Spatiotemporal QRST cancellation Time-frequency analysis	
Reproducibility	Short-term-reproducibility (N=6)	Short-term-reproducibility (N=10) Long-term-reproducibility (N=10)		Short-term-reproducibility (N=5) 24-hour reproducibility (N=20)
Circadian rate variation	Every 6 hours (N=30)	Every hour (N=20)		
Spontaneous AF termination	Onset vs. mid-episode vs. termination (N=11)			10 min before termination vs. termination (N=19)
Monitoring and predicting atrial drug effects	i.v. ibutilide (N=15) p.o. amiodarone (N=5) p.o. sotalol (N=3) p.o. flecainide (N=18) p.o. verapamil (N=27)	i.v. sotalol (N=5) p.o. verapamil (N=10) i.v. MgSO4 (+GIK) (N=13)		i.v. cibenzoline (N=5) i.v. procainamide (N=3) p.o. bepidril (N=22) i.v. ibutilide (N=19)
Monitoring autonomic maneuvers	Carotid sinus massage (N=19)	Head-up tilt test (N=14)	Controlled breathing + i.v. atropine (N=8)	
Predicting ADFT	Internal CV (N=19)			External CV (N=29)
Predicting AF recurrence	Internal CV (N=19) External, internal and drug-induced CV (N=44)			
Heart rhythm differentiation				Sinus rhythm vs. atrial fibrillation

Husser et al. *Indian Pacing Electrophysiol J 2004*

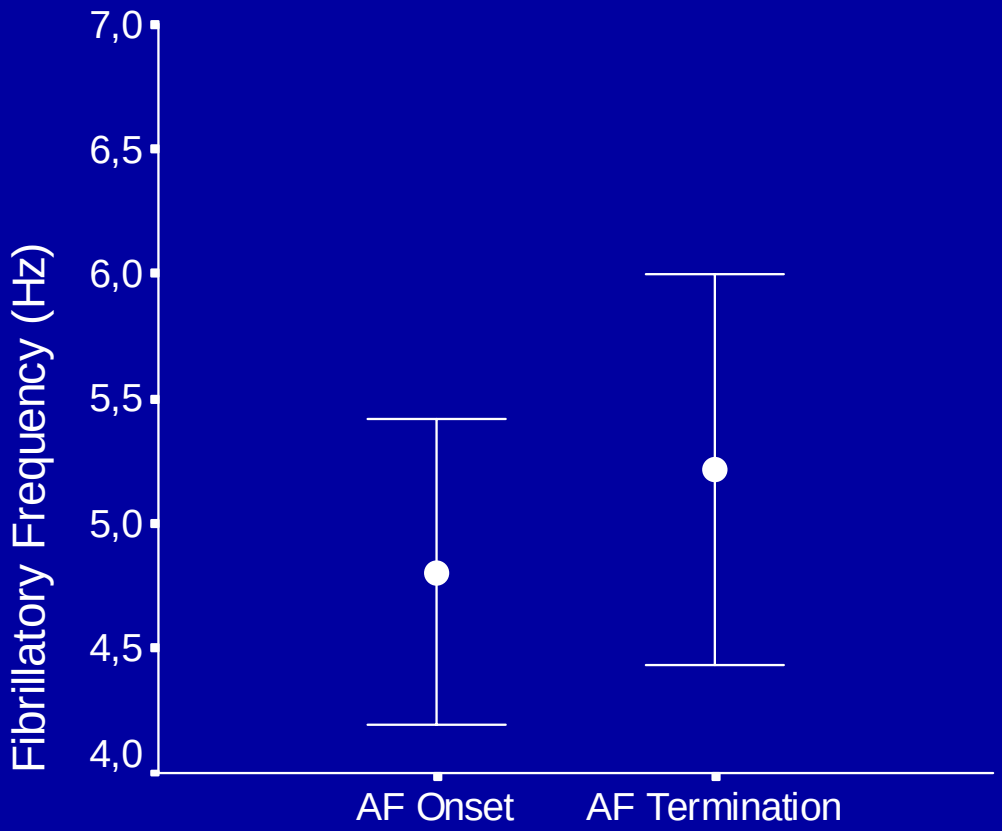
Reproducibility of Fibrillatory Rate



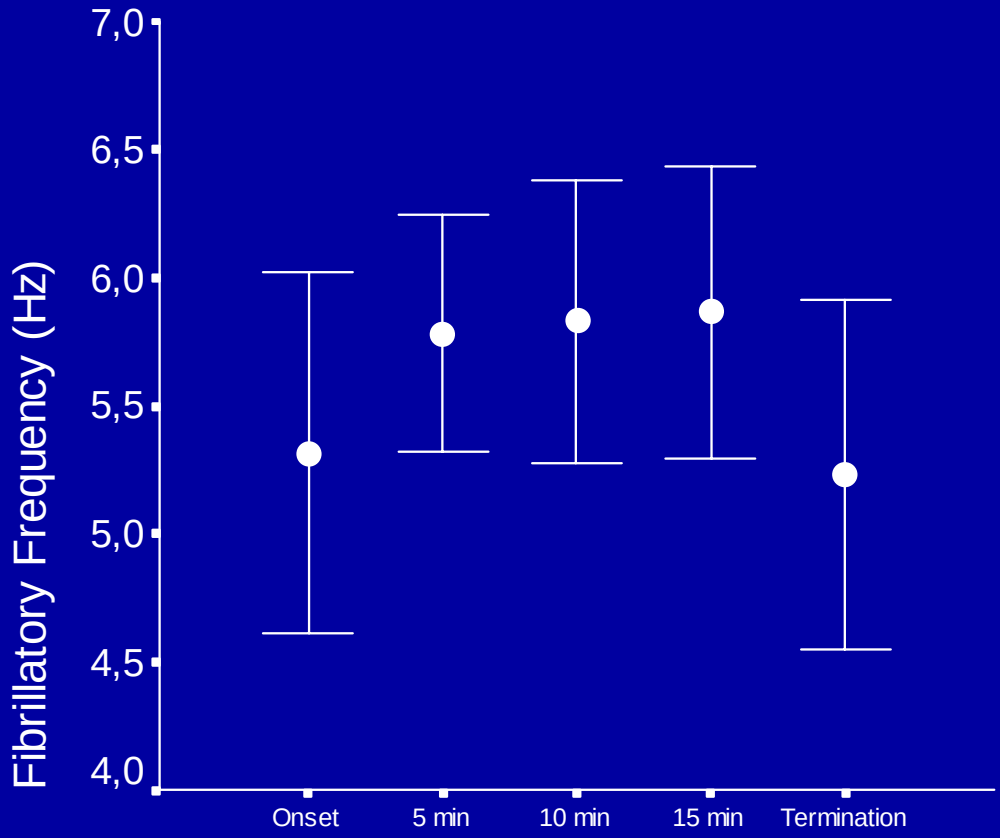
Xi et al.
J Cardiovasc Electrophysiol
2004

Fibrillatory Rate as Predictor for Spontaneous AF Termination

AF Duration < 15 min
N=13

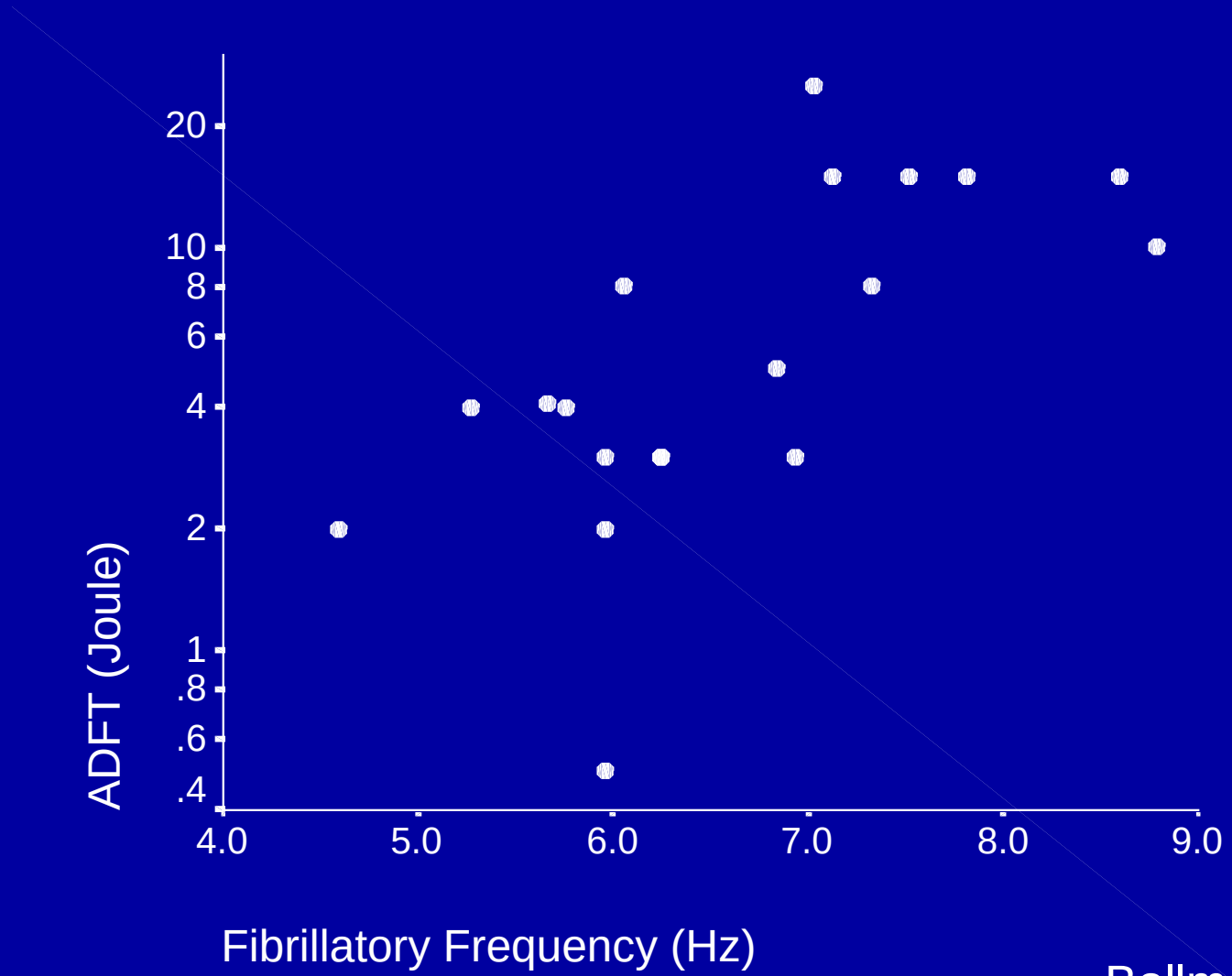


AF Duration ≥ 15 min
N=18



Bollmann et al. *Cardiovasc Res* 1999

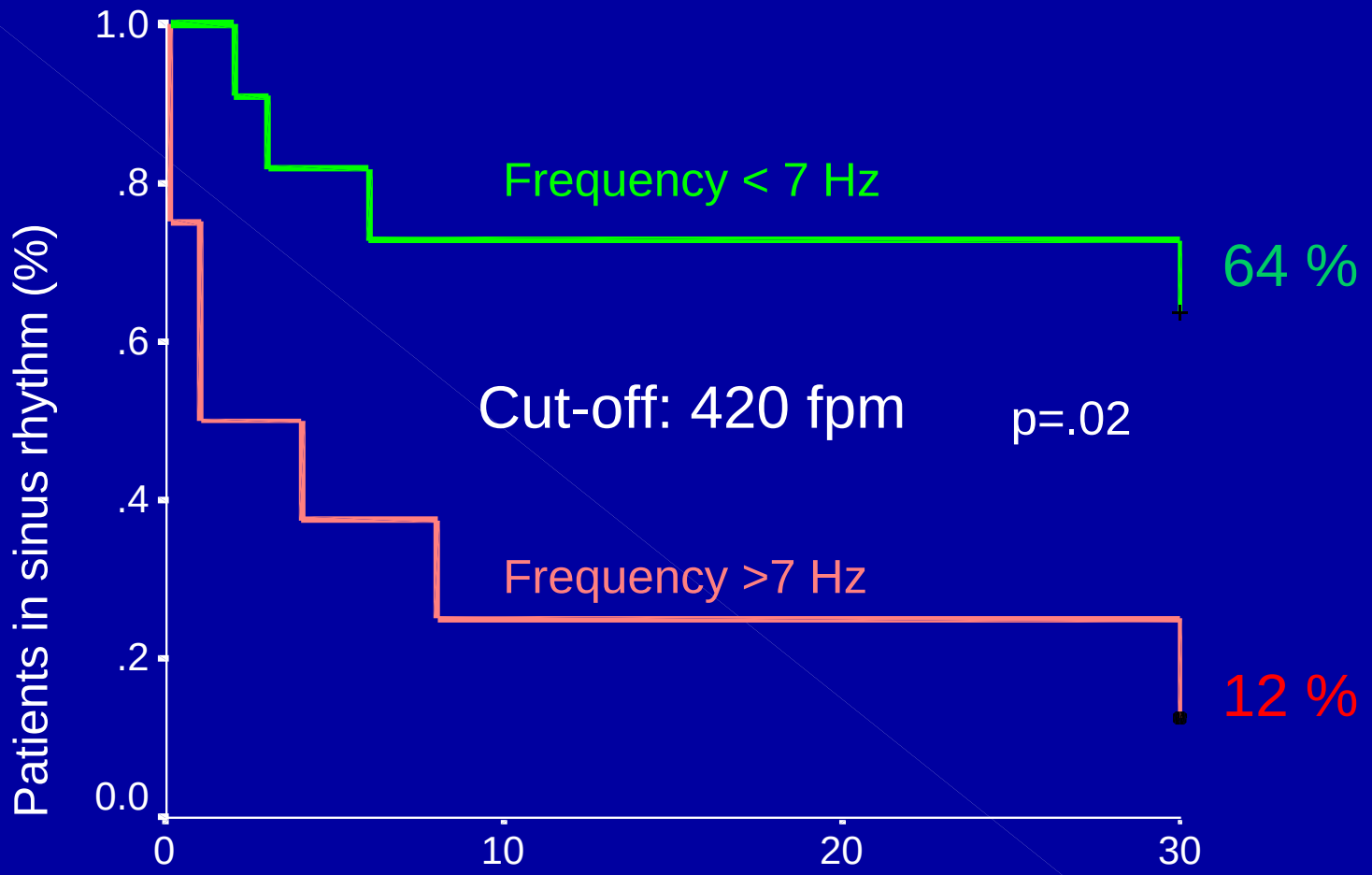
Fibrillatory Rate as Predictor for Internal Defibrillation Threshold



R=.71
p=.001

Bollmann et al. *PACE* 2002

Fibrillatory Rate as Predictor for AF Recurrence



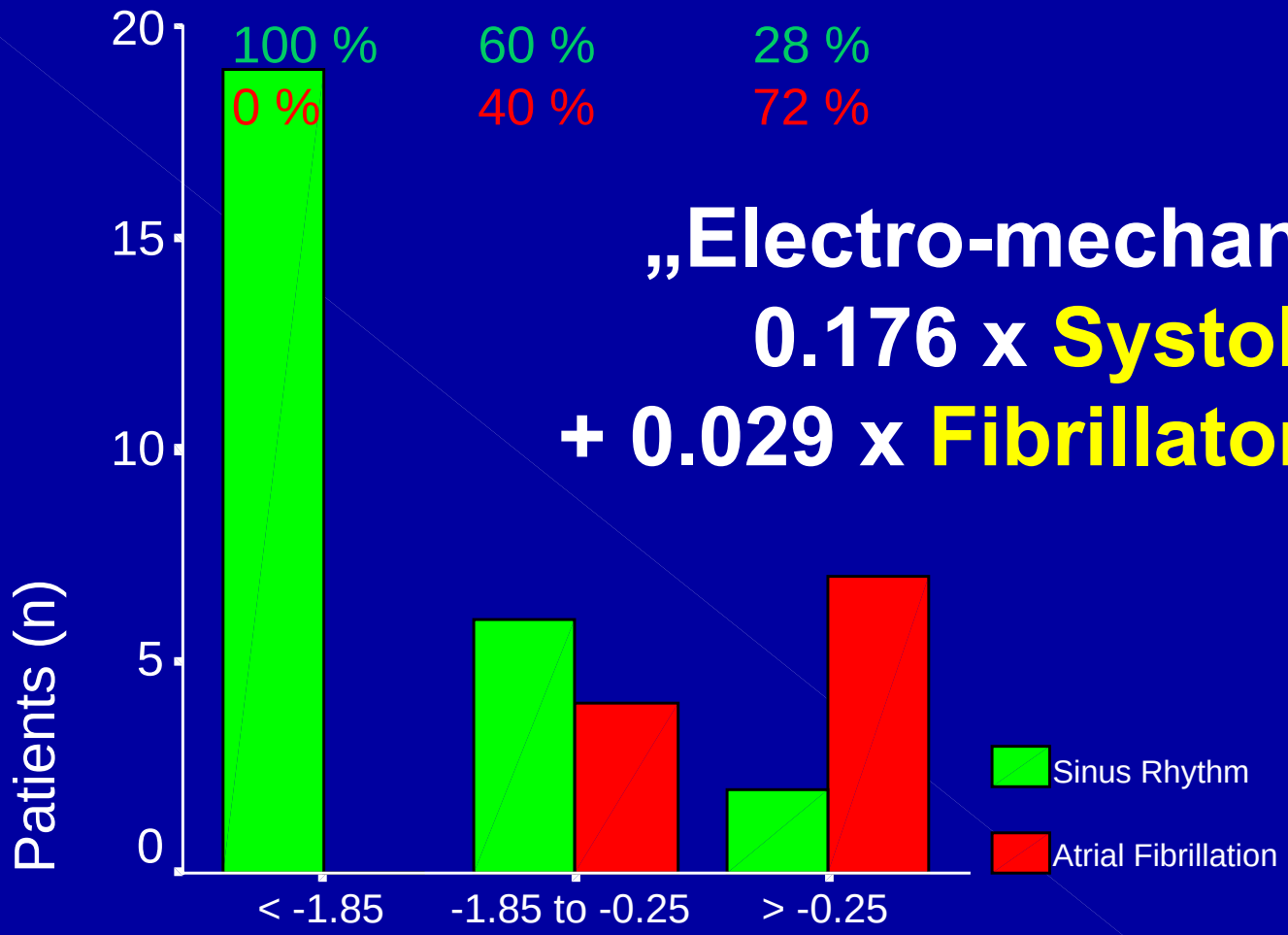
Bollmann et al. *PACE* 2002

Risk Stratification Based on Systolic LA Area and Fibrillatory Rate

	*SR * (n=29)*	*AF * (n=13)*	*p Value*
Age (years)	63 ± 12	61 ± 11	NS
Male/Female	15/14	10/3	NS
AF duration (months)	12 ± 20	30 ± 35	.11
Underlying heart disease			NS
None	7	3	
Systemic hypertension	16	5	
Coronary artery disease	2	1	
Dilated cardiomyopathy	1	2	
Valvular heart disease	3	2	
LA diameter (mm)	44 ± 5	47 ± 5	NS
Systolic LA area (cm^2) †	24.9 ± 6.6	31.5 ± 5.4	.006
Diastolic LA area (cm^2) †	19.6 ± 6.2	23.9 ± 5.5	.05
LVEF (%)	54±15	56 ± 14	NS
Class I or III antiarrhythmics			NS
Flecainide	17	7	
Amiodarone	11	6	
Sotalol	1	0	
Fibrillatory rate (fpm)	386 ± 33	420 ± 41	.007

Bollmann et al. *J Cardiovasc Electrophysiol* 2003

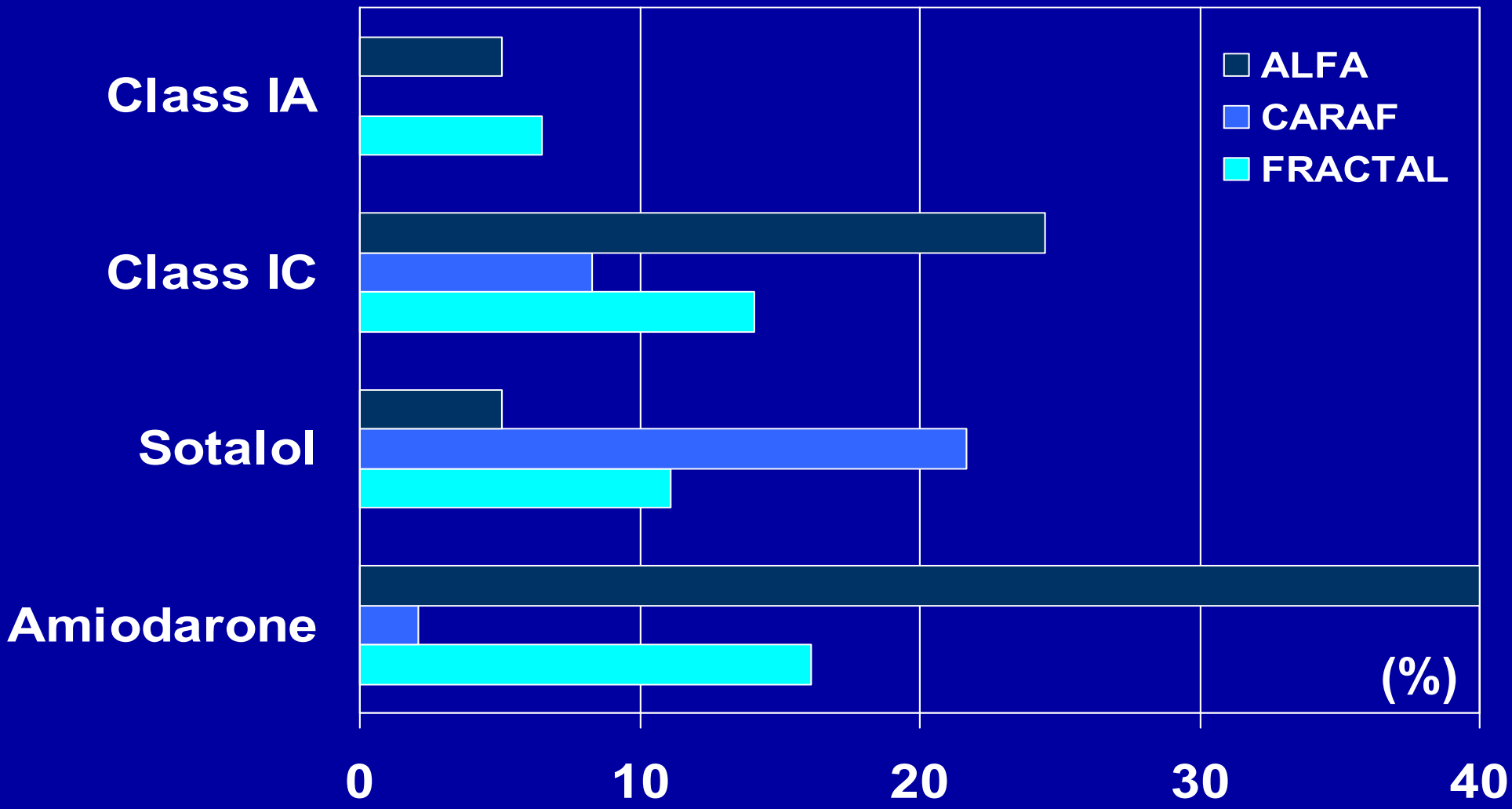
Risk Stratification Based on Systolic LA Area and Fibrillatory Rate



„Electro-mechanical Index“ =
0.176 x Systolic LA Area
+ 0.029 x Fibrillatory Rate – 17.674

Bollmann et al.
J Cardiovasc Electrophysiol
2003

Antiarrhythmic Drug Utilization in New-onset AF



Husser et al. *Cardiovasc Drugs Ther* 2004

Issues with Antiarrhythmic Drugs

Drug effects are not predictable in the individual patient

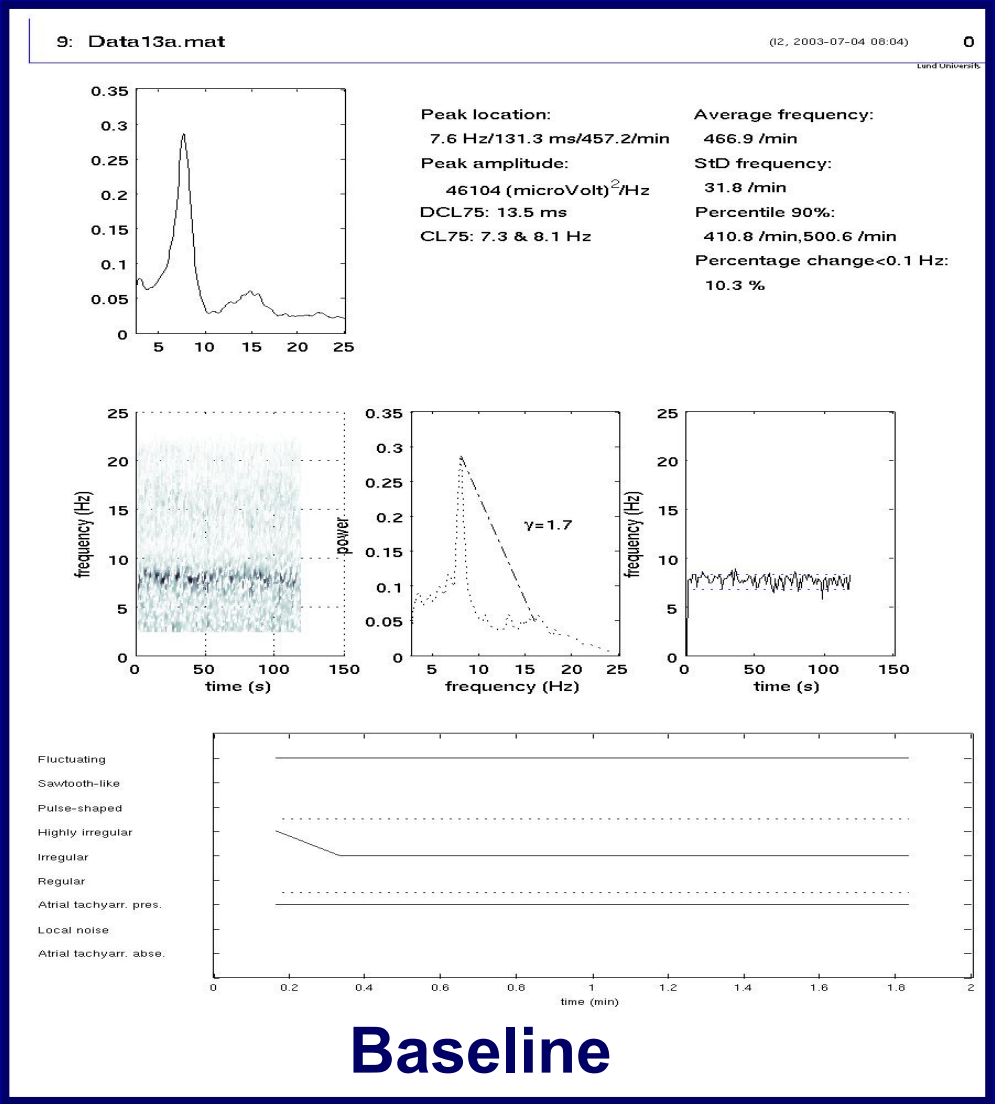
Drug monitoring is limited to plasma levels and ventricular ECG parameters (e.g. QT-Interval)

Monitoring and Predicting Antiarrhythmic Drug Effects

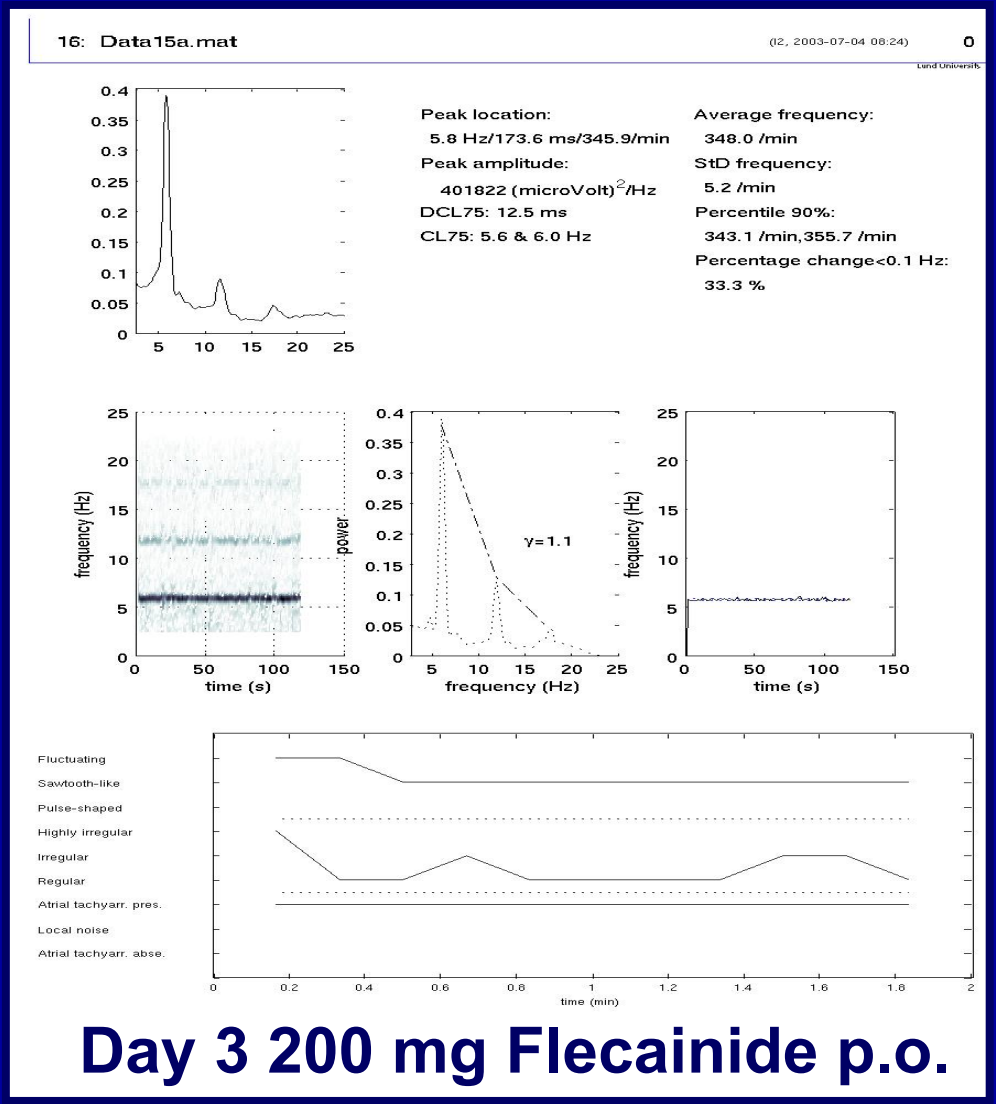
Drug(s)	*Dosage*	*Patients (N)*	*Drug effect (baseline vs after drug)*	*AF termination*	*Converters vs non-converters*
Flecainide	300 mg bolus + 100 – 200 mg/day p.o.	18	- 108 fpm (6.2 ± 0.5 vs 4.4 ± 0.4 Hz)	50 %	Baseline fibrillatory rate 354 vs 384 fpm (5.9 ± 0.4 vs 6.4 ± 0.4 Hz)
Cibenzoline **Procainamide**	1.4 mg/kg i.v. (N=5) 10 mg/kg i.v. (N=3)	8	- 102 fpm (151 ± 17 vs 203 ± 21 ms)	100 %	-
Amiodarone **Sotalol** **Flecainde**	600 – 1200 mg/day p.o. (N=5) 240 – 480 mg/day p.o. (N=3) 200 mg/day (N=1)	8	- 66 fpm (6.9 ± 0.5 vs 5.8 ± 0.4 Hz)	0 %	-
Bepidril	200 mg/day p.o.	32	-	69 %	Fibrillatory rate change 31 ± 10 vs 17 ± 5 %
Ibutilide	1 mg (+ 1 mg if required) i.v.	15	- 114 ± 42 fpm	60 %	Baseline fibrillatory rate 338 ± 55 vs 436 ± 67 fpm
Ibutilide	1 mg (+ 1 mg if required) i.v.	19	- 82 ± 57 fpm	35 %	Fibrillatory rate change 108 ± 60 vs 68 ± 52 fpm
Sotalol	80 mg i.v.	5	Atrial cycle length increased in all patients	0 %	-

Husser et al. *Cardiovasc Drugs Ther* 2004

Monitoring Antifibrillatory Drug Effects Using Time-Frequency Analysis (1)

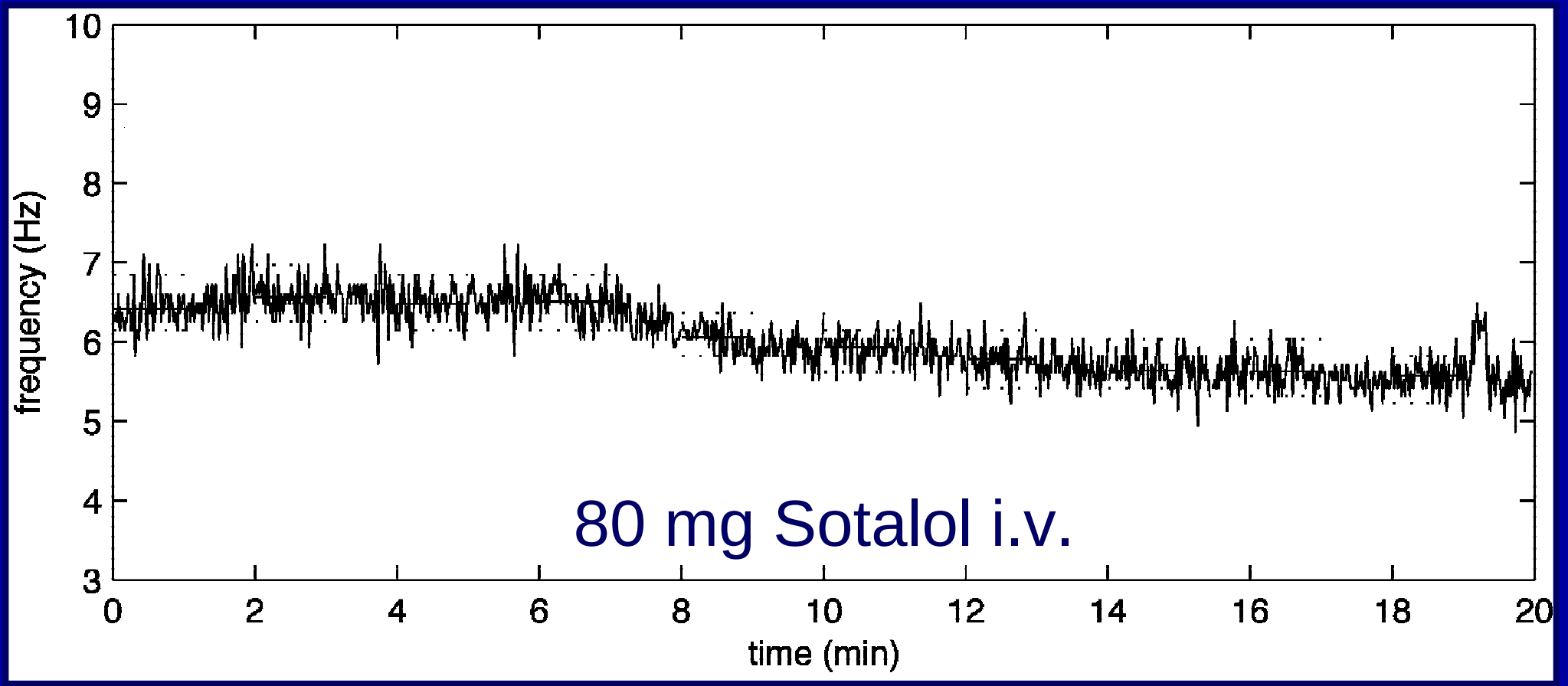


Baseline



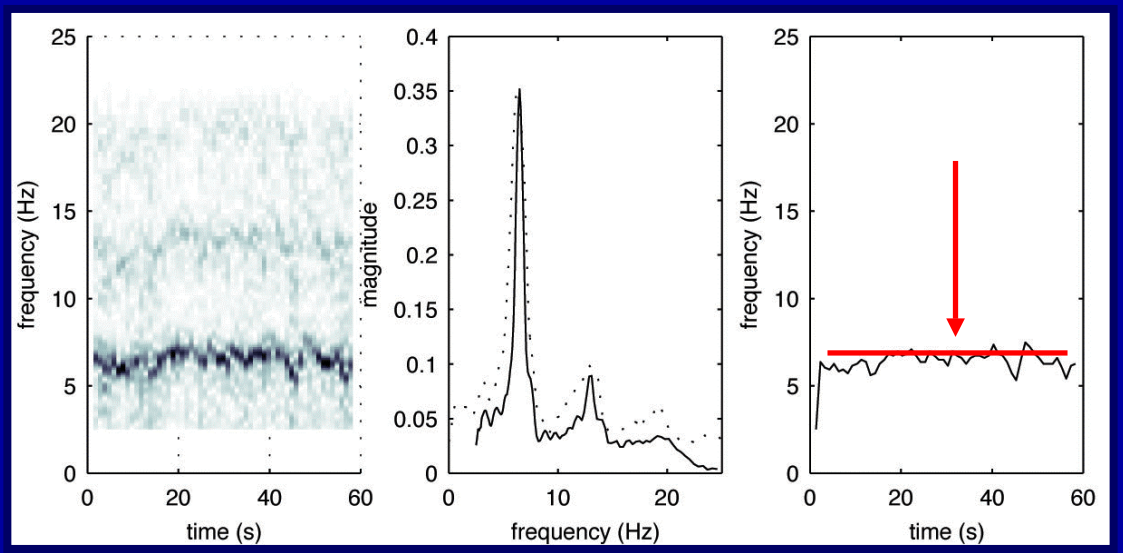
Day 3 200 mg Flecainide p.o.

Monitoring Antifibrillatory Drug Effects Using Time-Frequency Analysis (2)

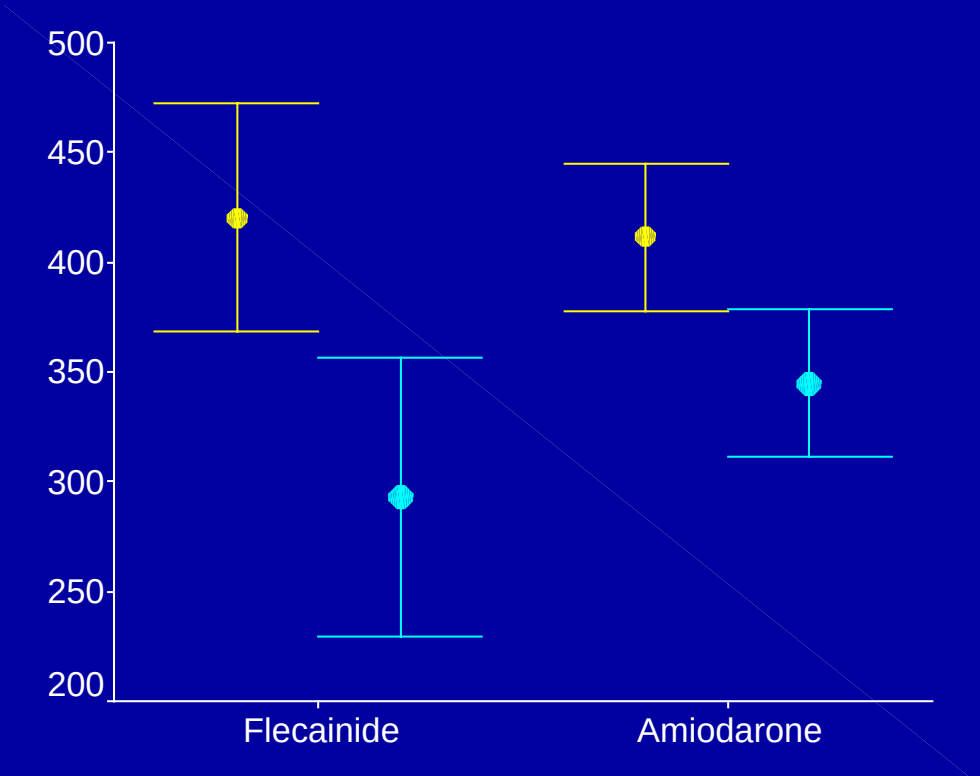


Husser et al. *Cardiovasc Drugs Ther* 2004

Influence of Antiarrhythmic Drugs on Fibrillatory Rate



Average Rate (fpm)

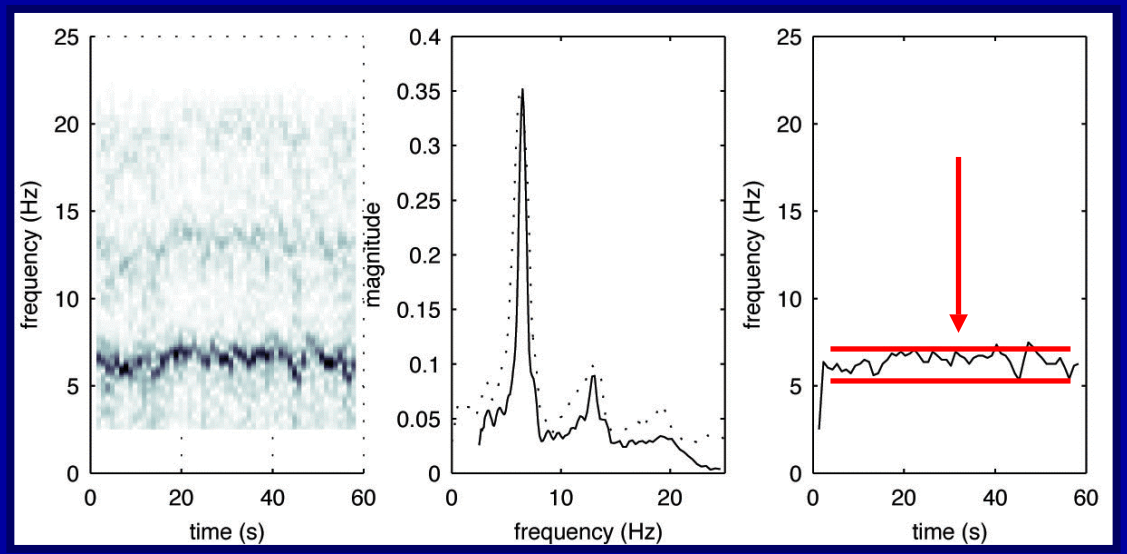


Baseline vs. Drug p<.001 for Flec; p<.001 for Amio

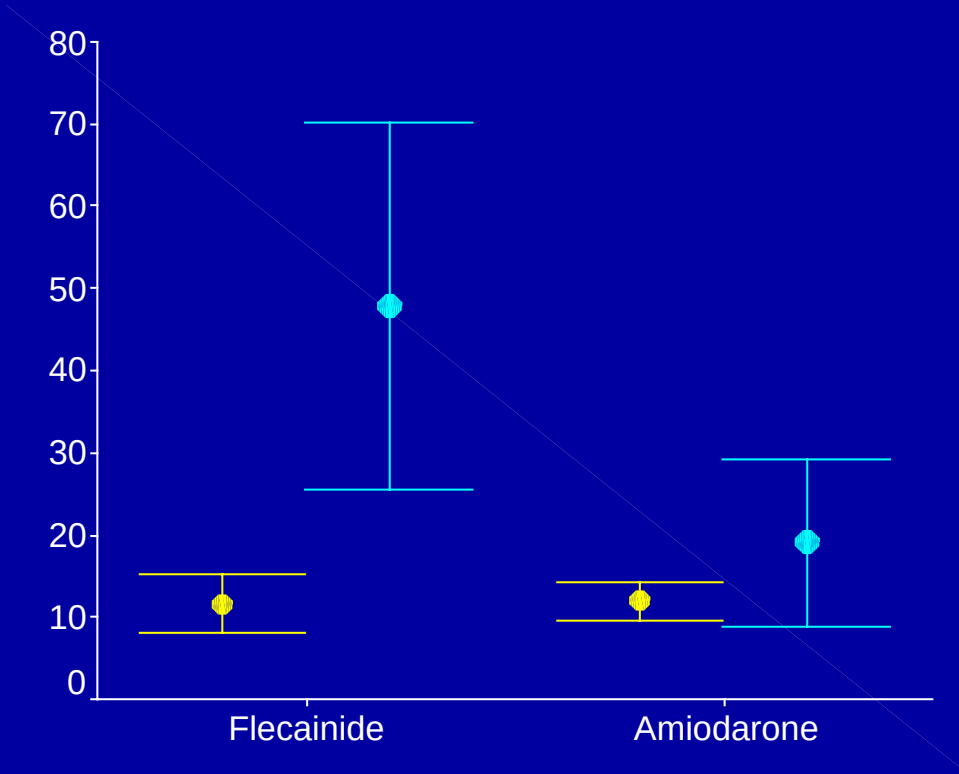
Change Flecainide vs. Amiodarone p=.015

Husser et al. *Am J Cardiol* 2005

Influence of Antiarrhythmic Drugs on Fibrillatory Rate Stability



Rate Stability (%)

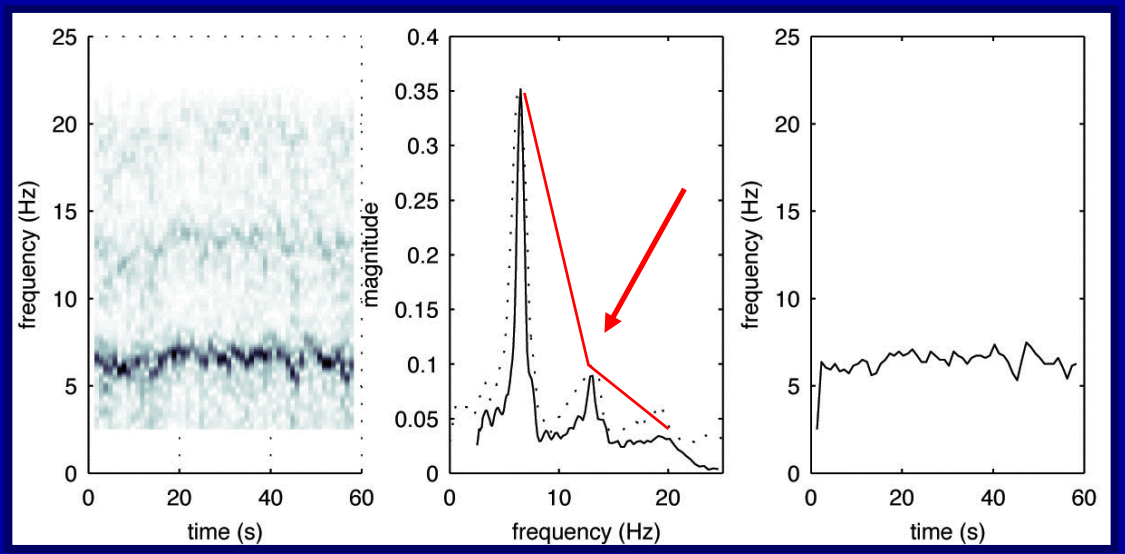


Baseline vs. Drug p=.001 for Flec; p=.011 for Amio

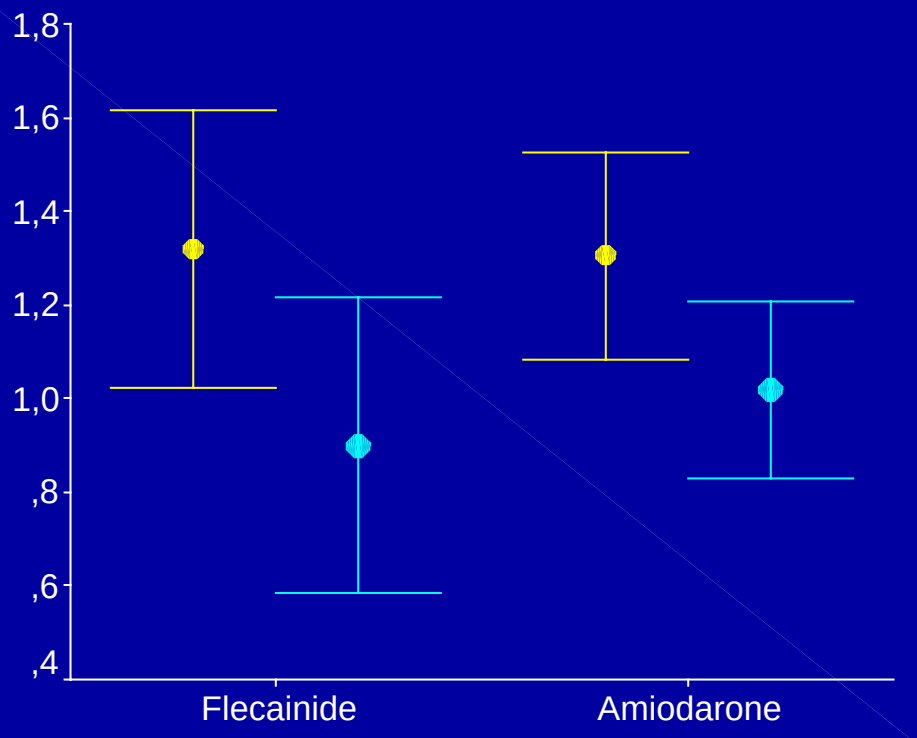
Change Flecainide vs. Amiodarone p=.002

Husser et al. *Am J Cardiol* 2005

Influence of Antiarrhythmic Drugs on Exponential Decay



Exponential Decay



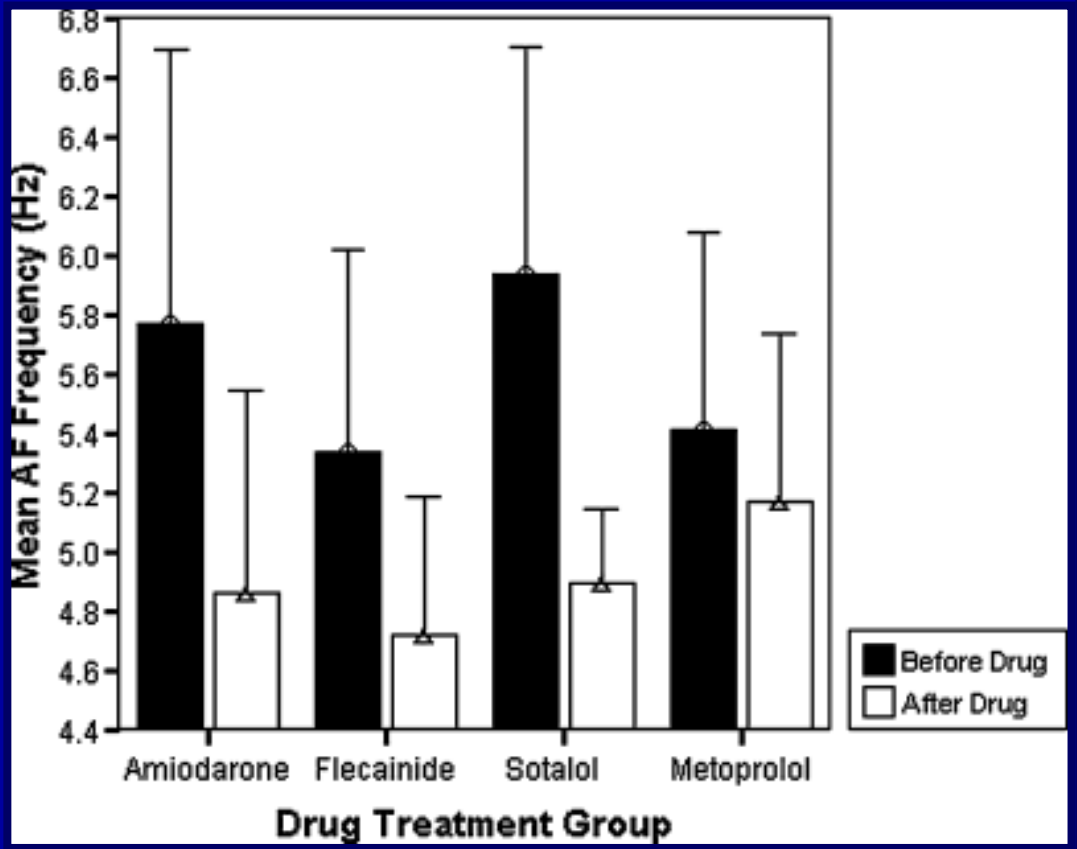
Baseline vs. Drug p=.001 for Flec; p=.001 for Amio

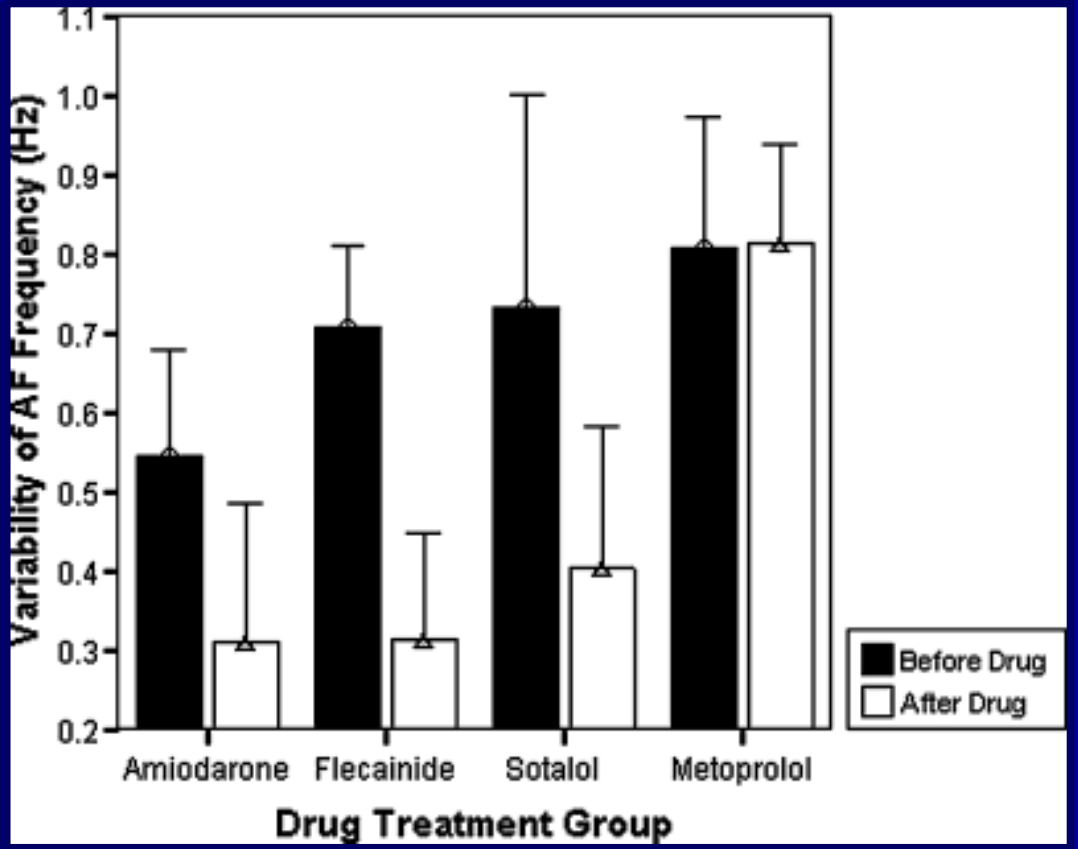
Change Flecainide vs. Amiodarone p=.272

Husser et al. *Am J Cardiol* 2005

Influence of Antiarrhythmic Drugs on Fibrillatory Rate and Its Variability

Results from Principal Component Analysis

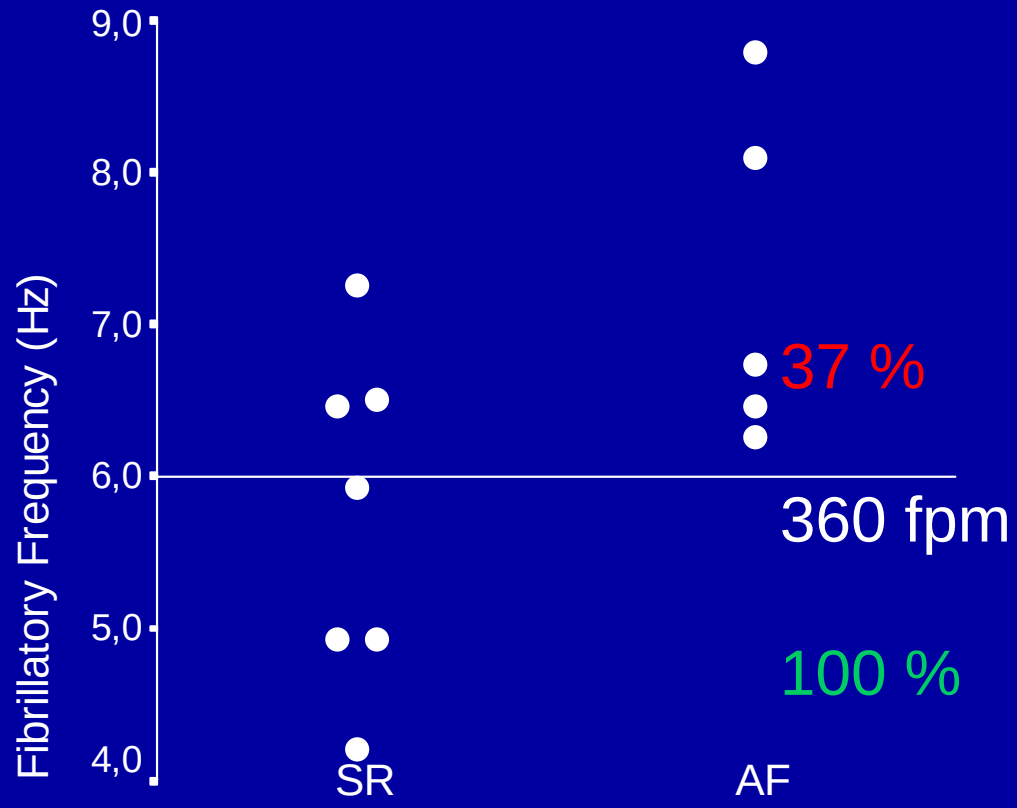




Raine et al. *J Cardiovasc Electrophysiol* 2004

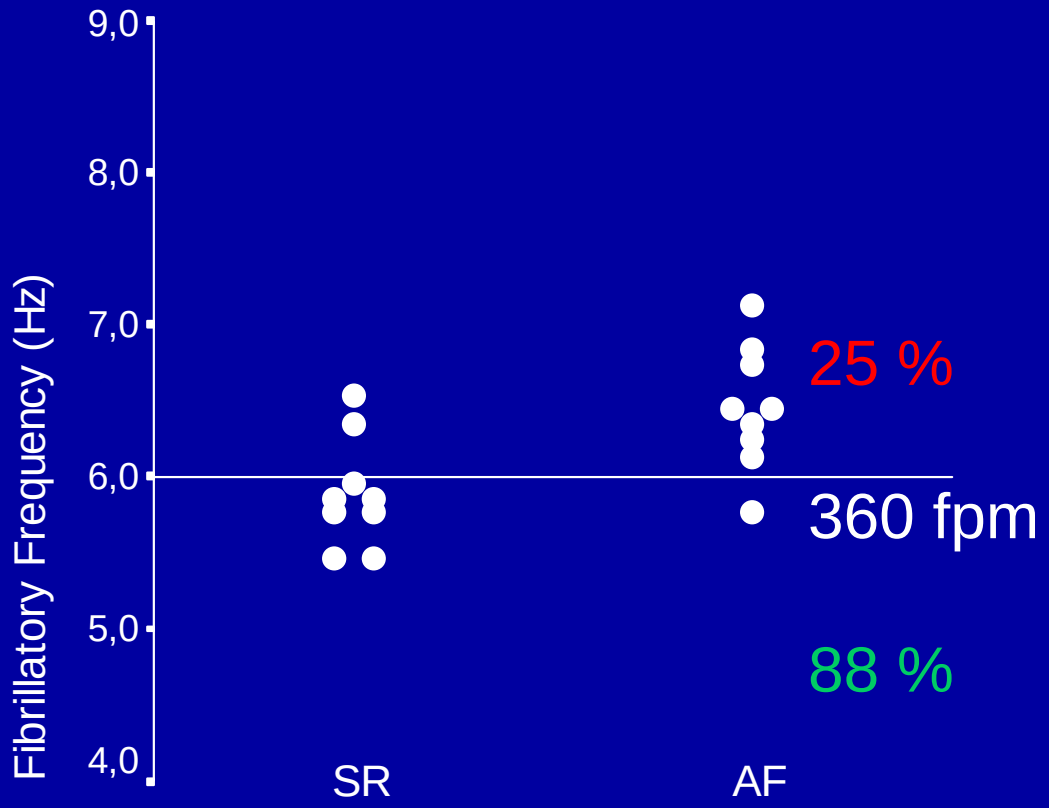
Fibrillatory Rate as Predictor for Drug-Induced AF Termination

Ibutilide 1g (+1g) i.v.



Bollmann et al. *Am J Cardiol* 1998

Flecainide 300 mg p.o.



Bollmann et al. *Am J Cardiol* 2002

Conclusions (1)

Determination of frequency measures from the surface electrocardiogram

- is possible in the vast majority of AF patients
- allows non-invasive monitoring of pharmacologic interventions
- seems to exhibit prognostic information

Conclusions (2)

AF with a low fibrillatory rate is more likely ...

- **to terminate spontaneously**
- **to terminate after antiarrhythmic drug administration**
- **to remain in sinus rhythm after cardioversion**

... than AF with a high rate