

Treatment to Suppress Ventricular Ectopy in Heart Failure

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Device Issues in Heart Failure & Heart Muscle Diseases

Heart Rhythm Congress 2011

Ventricular arrhythmias in heart failure

- Ventricular arrhythmias common in patients with heart failure
 - Ventricular premature beats 70-95%
 - Non-sustained VT 50-70%

Ventricular arrhythmias in heart failure

- Teerlink et al. Circ 2000,101
 - PROMISE study
 - Multivariate analysis did not show any ventricular arrhythmias predictive of SCD
 - PVCs predictive of non-sudden CD

1080 Patients	EF <35%
CAD	54%
PVCs >30/Hr	60%
Couplets	85%
NSVT	61%
>5 episodes	29%
>10 beats	10%

Ventricular ectopics and mortality

- Drögmüller et al. Z Kardiol 2003;92
 - 2420 patients post MI
 - NSVT only when combined with frequent ventricular ectopy associated with increased CV mortality
- Le et al. Ann Noninvasive Electrocardiol 2010;15
 - 352 patients with history of HF
 - 29 (8%) had PVCs
 - 5.5 fold increase in CV mortality ($p < 0.004$)

Ventricular ectopics and CRT

- Estimated 90% biventricular pacing recommended to achieve clinical response
- Frequent ventricular ectopy prevent adequate bi-ventricular pacing
- Important cause of non-response

Ventricular ectopics as cause of heart failure

- Chugh SS et al. J Cardiovasc Electrophysiol 2000;11
 - First report of ventricular ectopy as cause of LV dysfunction
- Frequency of ventricular premature beats >20% associated with development of heart failure
- Only affects ~5% of those with frequent ectopy

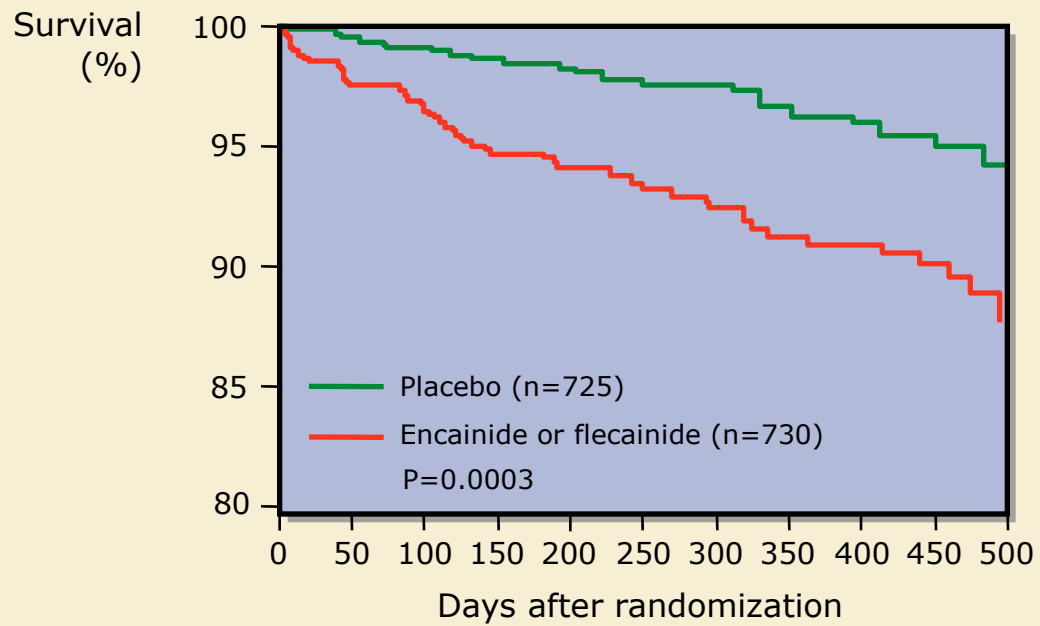
Why treat ventricular ectopy

- Symptoms
 - Palpitations
 - Pre-syncope/*Syncope*
 - Breathlessness
- Cardiac resynchronization therapy
 - Ensure adequacy of biventricular pacing
- Prevent deterioration in heart failure
- Prognosis

Cardiac Arrhythmia Suppression Study

- Double-blind study to investigate suppression of ventricular ectopy and NS VT in post MI patients
- Flecainide versus ecainide versus placebo
- Stopped after 10 months follow-up due to an excess of deaths in treatment arm

All-cause mortality



CAST Investigators. *N Engl J Med* 1989;**321**:406-12.

Cardiac Arrhythmia Suppression Study

- Double-blind study to investigate suppression of ventricular ectopy and NS VT in post MI patients
- Flecainide versus ecainide versus placebo
- Stopped after 10 months follow-up due to an excess of deaths in treatment arm
- **Flecainide and ecainide effective in suppressing ectopics**

Treatment Options

- Pharmacology
 - Heart failure
 - Anti-arrhythmics
- Cardiac Resynchronization Therapy
- Ablation

Diuretics

- Loop/Thiazide
 - Hypokalaemia/hypomagnasaemia
 - Increased frequency of ectopy
- Potassium sparing (aldosterone antagonists)
 - Correction of potassium losing effects of diuretics
 - Reduced expression of HCN channels

ACE Inhibitors (*ARBs*)

- Heart failure studies demonstrated the antiarrhythmic affects of ACE inhibitors
- ACE inhibitors reduce the risk of SCD
- Related to:
 - Off-loading of ventricles
 - Reduction in release of nor-adrenaline
 - Repletion of potassium
- Reduction in ectopic activity paralleled reduction in mortality
- ARBs less beneficial

Statins

- DEFINITE trial
 - Arrhythmic events in non-ischaemic cardiomyopathy
 - Lower rates of arrhythmic SCD when treated with a statin

Beta-Blockers

- Survival benefit from treatment of heart failure driven by reduction in SCD rather than from heart failure death
- MERIT-HF
 - Metoprolol versus placebo
 - SCD reduction (3.6% versus 6.6%)

Digoxin

- Improves symptoms in heart failure
- Reduction in hospitalization
- No mortality benefit
 - Reduction in heart failure death offset by increase in arrhythmic deaths
- Other inotropic agents may also be proarrhythmic

Anti-arrhythmic medications

- No consistent mortality benefit demonstrated from anti-arrhythmic medications
- Useful adjunct for symptomatic relief with ICD
 - Amiodarone
 - Sotalol

Antiarrhythmics medications

- Amiodarone
 - Less proarrhythmic
 - Effective symptom control
 - Recommended as adjunct to ICD therapy
- Sotalol (and other beta-blockers)
 - Less effective
 - Recommended as adjunct to ICD therapy
- Flecainide
 - Exacerbates heart failure
 - Increased mortality

Cardiac resynchronization therapy

- Reduction in mortality
 - Companion trial
 - Reduction in all cause mortality when combined with ICD
 - CARE-HF
 - Reduction in mortality attributable to CRT alone
 - Reduction in heart failure and sudden cardiac death

Cardiac resynchronization therapy

- Ventricular arrhythmias
 - Despite reduction in all cause mortality, heart failure and sudden cardiac death no clear reduction in ventricular arrhythmias
 - Pro-arrhythmic effect

CRT Delivery

Benefits of CRT depend on maintaining consistent Bi-V capture and preventing intrinsic conduction

Methods to manage intrinsic conduction in CRT include (amongst others):

- Appropriate upper rate and AV delay programming
- Avoidance of unilateral loss of capture
- Maintenance of higher pacing rates during mode switch
- Special algorithms to maintain Bi-V capture (e.g. VRR, Bi-V Trigger)
- Use of various pharmacological and ablative measures

Biventricular Trigger

Purpose:

- Designed to promote synchronised RV and LV pacing
- A Bi-V pace (LVP & RVP) is triggered after an RV sensed event
- Operates between the LRL and MPR
- Intended for use **during AT/AF**

Availability:

- Available at all times in any ventricular pacing mode
 - other than asynchronous modes
- May operate during an ATR mode switch, independent of an ATR mode switch, or both
- Programmable ON – OFF, with programmable MPR (30-185bpm)

Tracking Preference

Purpose:

Promotes delivery of CRT by temporarily reducing PVARP in order to re-establish atrial-tracked ventricular pacing (i.e. DDD(R) and VDD(R) modes)

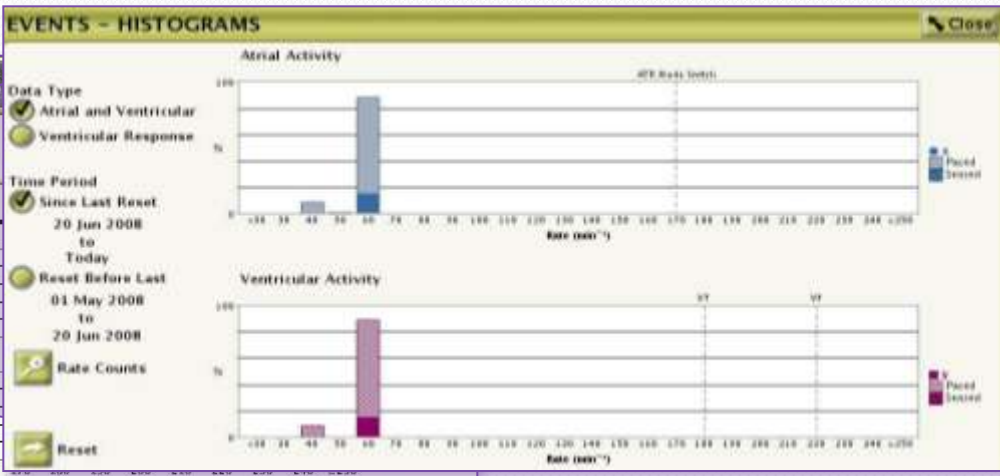
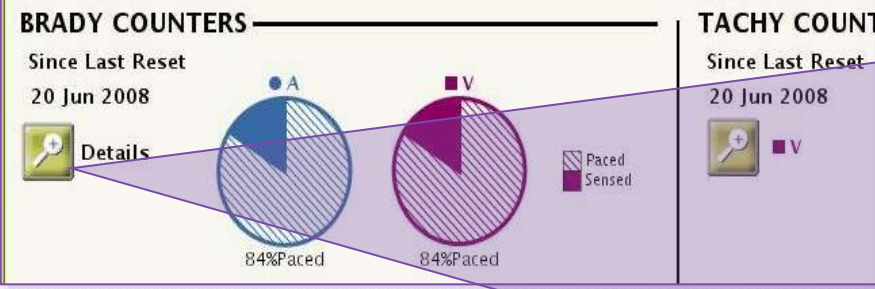
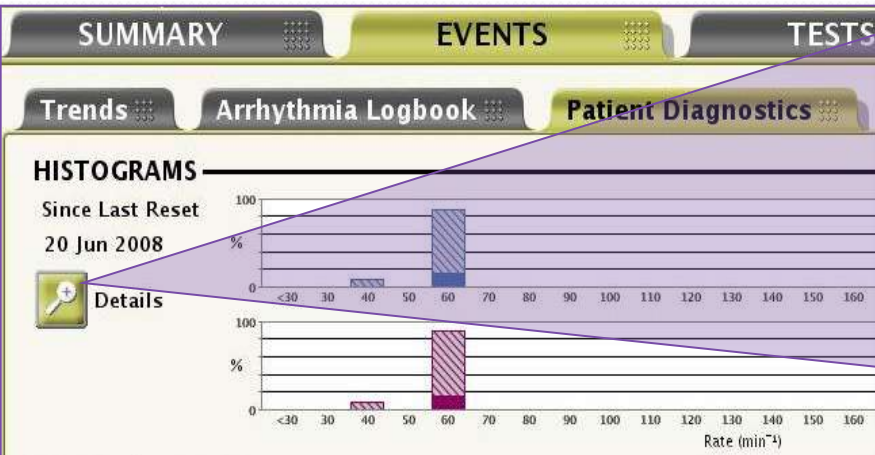
Atrial tracking may be lost when any of the following result in an atrial sense within PVARP:

- PVCs, PACs, Atrial rates above MTR, rate smoothing

Tracking Preference identifies atrial events below but near the MTR that should be tracked, but fall within PVARP

If two consecutive (AS)-VS cycles occur, PVARP is temporarily shortened to resume atrial-tracked ventricular pacing

Patient Diagnostics Histograms & Counters



EVENTS - BRADY COUNTERS

Counters	20 Jun 2008 to Today	01 May 2008 to 20 Jun 2008	20 Jun 2008 to Today	01 May 2008 to 20 Jun 2008
% A Paced	84	94		
% V Paced	84	95		
Intrinsic Promotion				
AV Search +				
% Successful	<1	<1		
Rate Hysteresis				
% Successful	0	0		

Atrial Burden	20 Jun 2008 to Today	01 May 2008 to 20 Jun 2008
Episodes by Duration		
< 1 minute	20	1
1 min - < 1 hr	0	1
1 hr - < 24 hr	0	0
24 hr - < 48 hr	0	0
> 48 hr	0	0
Total PACs	524	258
Ventricular Counters		
Total PVCs	551	103
Three or More PVCs	20	8

Catheter ablation

- Improvement in EF observed following successful ablation
 - Improvement in end-systolic and end-diastolic dimensions
 - Including patients with minimal/mild LV dysfunction
EF>50%

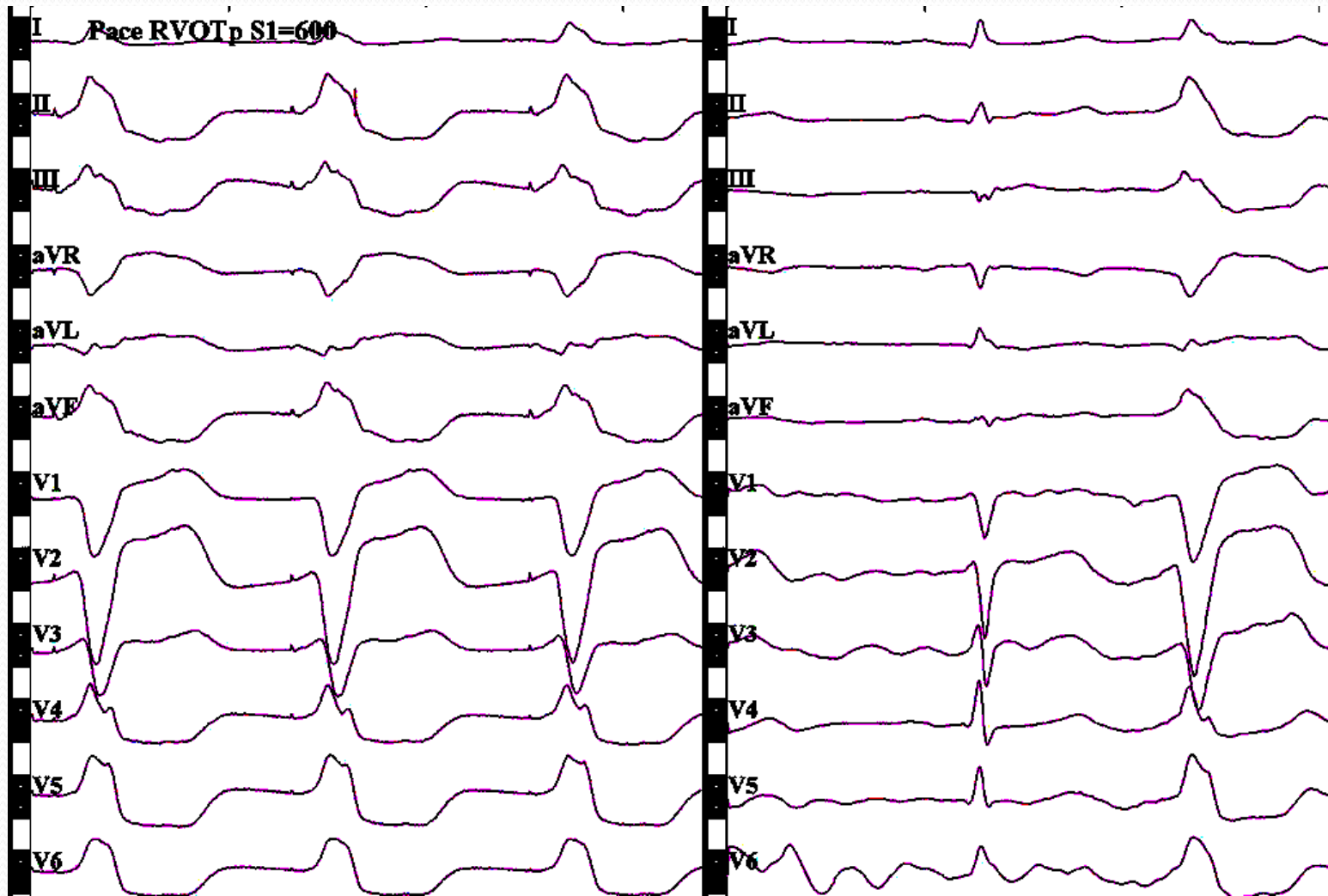
Catheter ablation

- Monomorphic ventricular ectopics arising from the outflow tracts
 - May arise from RVOT or LVOT
 - Catheter ablation successful in ~90%

Catheter ablation

- Localization
 - Contact mapping
 - Requires frequent ectopy during procedure
 - Pace mapping

Pace Mapping



Paced

Spontaneous

Catheter ablation

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 - Site of origin may be 1-2cm away from perfect pace map

Catheter ablation

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 - Pace mapping
 - Site of origin may be 1-2cm away from perfect pace map
 - Non-contact mapping
 - Non-contact array may be arrhythmogenic in outflow tract

Other considerations

- Ubiquitous distribution of ectopy
- Multifocal ectopy
- Epicardial site of origin

Summary

- Ventricular ectopics are common in patients with heart failure
 - Symptoms include palpitations, presyncope, syncope
 - May exacerbate/cause LV dysfunction
 - Prevent adequate biventricular pacing

Summary

- Treatment strategy
 - Treat underlying heart failure
 - Specific anti-arrhythmic medications (+/- ICD)
 - CRT optimization/specific algorithms
 - Catheter ablation