Right Ventricular Pacing Revisited
Unavoidable or to be Avoided

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Deleterious Effects of RV Pacing?

- Altered left ventricular electrical and mechanical activation:
  - Pacing-induced LV dyssynchrony secondary to the abnormal activation sequence, ventricular dyssynchrony may be present in up to 50% of the patients after long term RV apical pacing
  - Less work produced for given LVEDV
  - Delayed papillary muscle activation \(\rightarrow\) Valvular insufficiency thus causing MR
Deleterious Effects of RV Pacing?

- Remodeling
  - Modified regional blood flow patterns
  - Increased oxygen consumption without increase in blood flow
  - Abnormal thickening of LV wall

- Cellular disarray
  - Fibrosis (away from pacing lead location)
  - Fat deposition
  - Calcification
  - Mitochondrial abnormalities

Abnormal Activation Sequence
In RV Apical Pacing

Natural, Intrinsic Conduction Provides More Physiologic Contraction than RV Pacing
The amount of Pacing-induced LV dyssynchrony is related to the presence of LV dysfunction at Baseline
<table>
<thead>
<tr>
<th>Study</th>
<th>Details</th>
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</table>
| **Danish Pacemaker Study**                | Andersen HR, et al. Lancet 1997;350:1210-16  
AAI vs. VVI for SSS Danish pacemaker study: AAI had slightly better survival and was associated with lower occurrence of CHF (native AV conduction is better) |
| **CTOPPP Study**                          | Patients undergoing first IPG implant, n=2,568 32  
Canadian centers, Prospective, randomized                                                                                                                                                             |
| **DAVID Trial**                           | JAMA 2002;288:3115-23  
RV stimulation may be more deleterious in patients with advanced LV dysfunction (ICD candidates): DDDR-70 was worse than VVI-40; more pacing (60%) was seen in DDDR-70; however, only 30.8% of the patients had a QRS>130ms |
| **MOST Trial**                            | Sweeney M, et al. PACE 2002;25:690  
(mode selection trial in sinus-node dysfunction)  
Hospitalization was not associated with mode but with prevalence of more then 40% RV pacing                                                                                                         |
| **The PAVE Study**                        | J. Cardiovascular, Electrophysiology 2005  
Nov;16(11):1160-5 Left Ventricular-Based Cardiac Stimulation Post AV Nodal Ablation Evaluation                                                                                                                                 |
| **MOST Sub-Study**                        | There was a strong association between RV pacing and risk of heart failure hospitalizations as well as atrial fibrillation (AF) episodes                                                                                                                                 |
In the DANISH study, AAI was also associated with less Heart Failure and decreased mortality.


In patients with SND, atrial pacing is associated with a significantly higher survival, less atrial fibrillation and less heart failure compared to ventricular pacing.
MOST Study
Mode Selection Trial in Sinus Node Dysfunction

Patients Undergoing Initial IPG Implant for SND
n=2010

Dual-Chamber Pacing
n=1014

Ventricular Pacing
n=996

Follow for a median of 33 months and compare:

- Death from any cause or non fatal stroke
- Composite of death, stroke, or hospitalization for HF
- Atrial fibrillation
- Heart Failure score
- Pacemaker syndrome
- Quality of Life
MOST
Conclusions

- In patients with SND, dual-chamber pacing reduces newly diagnosed and chronic atrial fibrillation reduces signs and symptoms of heart failure and slightly improves quality of life.

- Dual-chamber pacing did not improve the rate of the primary endpoint of mortality or freedom from stroke.
DAVID Trial
Dual-Chamber and VVI Implantable Defibrillator Trial

760 assessed for eligibility
250 excluded
149 Did not meet Rx criteria
55 refused
46 Other

510 eligible
4 Not randomized
2 Required pacing
1 Inadequate defibrillation threshold
1 Decided not to implant

506 randomized

VVI-40 (n=256)
- 1 had pacing mode set to DDD
- 1 LTF
- 10 Discontinued intervention
- 5 Bradycardia
- 1 CHF and AF
- 1 Brady induced Torsade
- 1 Heart Tx workup
- 1 AF w rapid V response
- 1 multiple shocks due to double counting

DDD-70 (n=250)
- 3 had pacing mode set to VVI
- 2 LTF
- 5 Discontinued intervention
- 1 Angina
- 1 CHF and Lead Failure
- 1 CHF Hospitalization
- 1 Exacerbation of VT
- 1 Lead Migration

DAVID Conclusions

In ICD patients:
In Patients with intact conduction, RV pacing greater than 40% leads to an increase in death and Heart Failure Hospitalization.³

MOST Sub-study
Conclusions: Heart Failure Hospitalization (HFH)

• V-pacing is > 40%
  - HFH risk is constant

• V-pacing is < 40%
  - For each 10% reduction in V-pacing there is a 54% relative reduction in risk for HFH
  - 2% when pacing was minimized to < 10%
MOST Sub-study
Conclusions: AF

- Relationship between risk of AF and Cum%VP was similar between pacing modes:
  - Risk of AF showed a linearly increasing relationship with increased Cum%VP from 0% pacing up to 80-85% pacing in both pacing modes.
  - The risk of AF increased by 1% for each 1% increase in Cum%VP.

# Summary of Pacing Mode Clinical Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Mortality</th>
<th>Hospitalization for CHF</th>
<th>Atrial Fibrillation</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Danish AAIR vs. VVIR; All SND pts</td>
<td></td>
<td>But not until after 3 years FU</td>
<td>Both acute and chronic</td>
<td><strong>NS</strong></td>
</tr>
<tr>
<td>CTOPP Physiologic vs. ventricular pacing; ~40% of pts had SND</td>
<td></td>
<td></td>
<td>But not until 2 years FU</td>
<td></td>
</tr>
<tr>
<td>MOST Dual-chamber vs. single chamber; All SND pts</td>
<td></td>
<td>But still 10% at 36 months</td>
<td>But still 24-25% at 36 months</td>
<td></td>
</tr>
<tr>
<td>DAVID No indication for pacing</td>
<td>(Composite endpoint)</td>
<td></td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

**NS** = Not a studied endpoint

= No Difference Observed
Right Ventricular Pacing should be Avoided or to be Minimized
Strategies for reduction of RV Pacing

1. Use of AAI pacing mode
2. DDD pacing with a fixed long AV delay
3. DDD with search AV hysteresis
4. AAI(R)-DDD(R) mode switch Algorithms
AAI Pacing: Too Risky?

- AAI pacing preserves a normal ventricular activation sequence
- The incidence of progression to symptomatic AV block in SND patients been estimated at about 2% per year
- Supraventricular tachycardias can develop in as high as 50% of patients with SND
- AAI pacing is ineffectual for ventricular bradycardia during
  - Paroxysmal and permanent AF
  - AV block
Fixed Long AV Delays

- Long AV delays may reduce unnecessary ventricular pacing

- The main disadvantage of a fixed long AV delay are:
  - Total atrial refractory period (TARP) is prolonged, leading to exercise-induced AV block
  - Post-ventricular atrial refractory period (PVARP) is shortened to compensate and it can predispose to pacemaker-mediated tachycardia (PMT)
  - Abandonment of mode-switching or significantly delayed AF recognition
DDD with Search AV Hysteresis

- Automatically adjusts AV delay so that:
  - AV Delay > Patient’s intrinsic PR interval
  - Preserves normal ventricular depolarization if intrinsic conduction exists
  - Optimal AV delay when V pacing required
AV Search Hysteresis Algorithm

- Searches for intrinsic conduction by prolonging the AV delay interval regularly every five minutes
- If intrinsic ventricular activity is found during the extended AV delay, the pacemaker adjusts the AV delay settings (paced and sensed) to accommodate this intrinsic activity
- If no more intrinsic ventricular is sensed, the AV delays resume their previously programmed values
- Do not allow non-conducted beat
DDD with and without AV Search does not eliminate RV Pacing in many patients

% of patients with %VP ≥ 20%

DDD w fixed AV Delay=300ms

AV Search Hysteresis - INTRINSIC RV Pre Amendment

AV Search Hysteresis - INTRINSIC RV Post Amendment


*AVSH parameters were modified under a protocol amendment. Rate hysteresis was set at a 20bpm offset, which allowed the lower rate limit to approach 40bpm with intrinsic conduction. AVSH AV increase was changed from 50% to 100% pacing.
AAI(R)-DDD(R) mode switch Algorithms

- Managed Ventricular Pacing (MVP) algorithm by Medtronic
- RYTHMIQ algorithm by Boston Scientific
- SafeR algorithm by Sorin
- Vp Suppression algorithm by Biotronik
Managed ventricular pacing or MVP modes can be used in all patients, but is most effective in SND patients with reliable AV conduction.

- Unnecessary RV pacing can be reduced to less than 10%.
- Pacemaker can switch from AAI(R) to DDD(R) back depending on AV conduction.
Managed Ventricular Pacing (MVP) Algorithm

AAI(R) mode and mode-switches to DDD(R) or DDI(R) in case of conduction loss or AT/AF episodes.

Diagram:
- **Initialize**
  - **AAI(R)**
    - **Loss of Conduction**
      - **DDIR**
        - AT/AF Terminates
        - Detection Uses 4 of 7 Mode Switch Detection Criteria
    - Conduction Check Passed
      - **One Cycle AAI(R)**
    - Conduction Check Failed Increment Check Interval (1, 2, 4, 8 mins up to 16 hrs)
      - **DDD(R)**
        - AT/AF Episode
          - Conduction Check
            - AAI(R)
MVP Study Results: Reduction in %VP without Loss of Atrial Support

The Save Pace Trial
(Search AV Extension and Managed Ventricular Pacing for Promoting Atrioventricular Conduction)

1065 SND patients randomized – DDDR pacing versus DDDR Minimal Ventricular Pacing

Minimising RV pacing led to 40% reduction in relative risk of developing persistent AF

Reduction in persistent AF resulted in fewer invasive ablations and fewer heart failure hospitalisations

Primary Endpoint: Persistent AF

Time to Cardioversion, AVN Ablation or PVI for AF by Treatment Group

Hazard Ratio=0.60
95% Confidence Interval = 0.41-0.88
p=0.009

Hazard Ratio=0.62
95% Confidence Interval = 0.37-1.03
p=0.06
Options should be considered in patients with chronic RV apical Pacing

1. Alternative RV pacing sites
2. Upgrade of RV apical pacing to CRT
Alternative Pacing Sites

- RV septal pacing sites are the most studied as an alternative site for RV pacing.
- Recent clinical studies have suggested that RV septal pacing can potentially prevent the long-term adverse effects associated with RV apical pacing.
Shortest distance to Purkinje Fibers?

Right Ventricular Septum
Alternative Pacing Sites

- LV dysfunction induced by iatrogenic RV apical pacing is still reversible by upgrading to RV septal pacing even after a mean of 13 years of pacing.
Alternative Pacing Sites

- In patients with permanent RV apical pacing and preserved LV function in whom ventricular lead replacement is required, RV septal pacing is a feasible option.

- It remains unclear whether RV septal pacing upgrading can be used to treat patients with RV apical pacing induced heart failure.
RV septal Pacing upgrading

A

PA view

LAO view

B

RV Apical pacing

RV Septal pacing
Upgrade of RV apical Pacing to CRT

- For patients with conventional pacemaker who developed heart failure, upgrade to CRT should be considered.

- LV reverse remodeling after upgrade from RV apical pacing to CRT has been demonstrated and severity of MR may improve.

Laurens F. Tops, et al., JACC, Vol. 54, No. 9, 2009
2013 ESC Guidelines, Europace (2013) 15, 1070–1118
Conclusions

- RV pacing increases the risk for HF, AF and death
- AAI is superior to VVI and DDD for patients with intact conduction system
- **AAI(R)-DDD(R) mode switch algorithm** is the most effective algorithm to minimize RV pacing in pacemaker and ICD patients
- Selective pacing site appears promising
- Upgrade to CRT in heart failure patients should be considered