Programming ICDs to Reduce Appropriate and Inappropriate Shocks

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Introduction

• ICD shock therapy improves survival of patients at risk for sudden cardiac death.

• The high sensitivity of ICDs to detect tachycardia events is accompanied by reduced specificity resulting in inappropriate and unnecessary shocks.

• Up to 30% of ICD patients may experience inappropriate shocks
Causes of inadequate ICD shock therapy

1. Fast VT that could have been pace-terminated
2. Non-sustained VT
3. Supraventricular tachycardia
4. Ventricular oversensing of cardiac signals
5. Electromagnetic interference
6. Lead fracture

Evolution of ICD Shock Reduction Strategies

- Non committed shocks
- Antitachycardia pacing
- SVT discrimination algorithms
- ATP for FVT and during charging
- Strategic programming
- Delayed treatment

PainFree Rx
WAVE, Gem DR
EnTrust, PainFree Rx II
EMPIRIC, PREPARE
ADVANCE III, MADIT-RIT

Survival rates:
- No VA (93.8%)
- ATP-only (94.7%)
- Shock therapy (88.4%)

• Shocked VT/VF episodes are associated with a 20% increased mortality risk per event, while ATP-terminated VT/VF was not associated with higher mortality risk.

ATP in the Fast VT zone - PainFREE Rx
(ischemic CMP, NID 12/16, 2 seq.of Burst)

VF Zone (NID = 12/16)
Fast VT Zone
Optional VT Zone

240 ms 320 ms
250 bpm 188 bpm

ATP in the Fast VT zone - PainFREE Rx

### TABLE 2. Outcome of ATP Therapy for FVT (n=446 Episodes)

<table>
<thead>
<tr>
<th>Terminating Therapy</th>
<th>Efficacy</th>
<th>Acceleration*</th>
<th>Syncope</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP therapy (1st or 2nd sequence)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw, n (%)</td>
<td>378 (85)</td>
<td>10 (4)</td>
<td>3 (0.6)</td>
</tr>
<tr>
<td>Adjusted†, % (95% CI)</td>
<td>77 (68–83)</td>
<td>7 (3–14)</td>
<td>...</td>
</tr>
<tr>
<td>Shock, n (%)</td>
<td>48 (11)</td>
<td>...</td>
<td>6 (1.3)</td>
</tr>
</tbody>
</table>


ATP in the Fast VT zone – PainFREE Rx II
(ischemic & non-ischemic CMP, NID 18/24)

### TABLE 2. Outcomes Related to Patient Safety

<table>
<thead>
<tr>
<th>Outcomes Related to Patient Safety</th>
<th>ATP Arm</th>
<th>Shock Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceleration (episodes), n (%)</td>
<td>4 (2)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Arrhythmic syncope (episodes), n (%)</td>
<td>2 (0.7)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Median episode duration, s</td>
<td>10.0</td>
<td>9.7</td>
</tr>
<tr>
<td>Mortality (patients), n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>32 (10)</td>
<td>24 (7)</td>
</tr>
<tr>
<td>Sudden cardiac</td>
<td>1 (0.3)</td>
<td>2 (0.6)</td>
</tr>
</tbody>
</table>

**Physical and Mental QoL: Baseline to 12 months**

- **ATP arm (n=43 pts)**
- **SHOCK arm (n=55 pts)**

<table>
<thead>
<tr>
<th>Physical Subscales</th>
<th>Mental Subscales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical function</td>
<td>Vitality</td>
</tr>
<tr>
<td>Role physical</td>
<td>Social functioning</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>Role emotional</td>
</tr>
<tr>
<td>General health</td>
<td>Mental health</td>
</tr>
</tbody>
</table>

- **p<0.05**

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**PREPARE Primary Prevention Parameter Evaluation**

- **700 patients, 1 year follow-up**
- **The key Strategies to ↓ shocks:**
  - avoid detecting slower tachycardia, non-sustained events
  - employing SVT discriminators
  - ATP as first therapy for fast VT
  - high output 1\textsuperscript{st} shock

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*Wilkoff et al. JACC 2008;52:541-50.*
PREPARE Primary Prevention Parameter Evaluation (NID 30/40)

Control: patients from EMPIRIC and MIRACLE-ICD


VF zone Programming

• VF zone can safely be programmed to high rates (≥ 250 bpm)

PREPARE – time to first shock


Long NID (30/40)

- RELEVANT study:
  A prospective, parallel, nonrandomized multicenter study, non-ischemic CMP, primary prevention
  - N=324 pts implanted with CRT-D devices (2004-7)
    - protect group=164 pts with Medtronic Insync III Protect devices, long NID (39/40) with “monitor only” VT zone (32 beats detect)
    - Control group=160 patients utilizing other Medtronic CRT-Ds NID (12/16)
  - The extended NID led to 91% of FVT not needing treatment because of spontaneous termination

ATP programming

1. Type of ATP therapy (Burst, Ramp, Scan)
2. Number of pulses in each train
3. Number of ATP therapies
4. RV ATP vs. BIV ATP

Type of ATP

- Limited data on efficacy of Burst vs. Ramp vs. Scan configurations
- Some evidence suggests Ramp and Scan can be more pro-arrhythmic
- Recommended initial therapy be Burst with Ramp and Scan reserved for Burst ATP failures
ADVANCE - D Trial

• Atp DeliVery for PAinless ICD ThErapy

• Does ATP duration affect outcome?
  - 925 patients randomized to receive 8 or 15 pulses for FVT (320-240 ms)
  - FVT Termination
    • 64% in 8 pulse group
    • 70% in 15 pulse group (p=ns)
  - No difference in pro-arrhythmia

Number of ATP

• Too few can limit success of ATP
• Too many can lead to delays in VT termination

• If a slow, hemodynamically stable VT is present, and particularly if ATP has proven successfully previously, more ATP schemes may be appropriate
• 2-3 ATP therapies typical in VT zone
ADVANCE CRT-D

- Is BIV ATP better than RV ATP?
- 526 patients randomized to RV or BIV ATP
- No difference in efficacy between both approaches
- BIV ATP was associated with a lower incidence of syncope

Gasparini M Am Heart J 2010;159:1116

PROVE (Programming Atitachicardia pacing for Primary Prevention in Patients with ICD for ATP use)

- 830 pts., primary prevention, ICDs and CRT-Ds

PREPARE trial → the safety and effectiveness of ATP were not endpoints and were not reported.

PROVE trial –

ATP (very modest: only two bursts) was highly effective for terminating VT, regardless of the tachycardia cycle length


...but the price to pay

• Beneficial effect of ATP in VT zone with 92% of true VT episodes successfully terminated

• 45.8% of shocks → VT/VF termination
  (2.5% of pts affected)

• 54.2% of shocks → causes other than VT/VF
  (2.9% of pts affected)

  → SVT discriminator left up to individual physician
High-rate cut-off programming – shock only zone ("shock box")

- 365 pts, ischaemic or non-ischaemic cardiomyopathy and left ventricular dysfunction, primary prevention (single ch., dual ch., biv)
- Registry-based study, non-controlled

<table>
<thead>
<tr>
<th>170 bpm</th>
<th>220 bpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO DETECTION</td>
<td>MONITORING ZONE</td>
</tr>
<tr>
<td></td>
<td>Nominal NID</td>
</tr>
<tr>
<td></td>
<td>SVT Discrimination ON</td>
</tr>
<tr>
<td></td>
<td>Timers OFF</td>
</tr>
<tr>
<td>1</td>
<td>VF</td>
</tr>
<tr>
<td>2</td>
<td>VF</td>
</tr>
<tr>
<td>3</td>
<td>N/Q</td>
</tr>
<tr>
<td>4</td>
<td>N/O</td>
</tr>
<tr>
<td>5</td>
<td>N/Q</td>
</tr>
<tr>
<td>6</td>
<td>N/Q</td>
</tr>
<tr>
<td>7</td>
<td>N/Q</td>
</tr>
</tbody>
</table>


- 11.2% appropriate shocks (SCD-HeFT 22.4% - 188 bpm, 18/24)
  ~34% of the fast VT episodes terminated spontaneously during capacitor charging (PainFREE Rx II)
- 6.6% inappropriate shocks (MADIT II 11.5%, PainFREE Rx II 15%, SCD - HeFT 17.4%)

High-rate cut-off programming – shock only zone (“shock box”)

Event – free survival for appropriate and inappropriate shocks

- mortality 17% over 40 months
- mortality rates in other trials shorter follow-up
- in line with recently published survival rates for heart failure pts with an ICD (Poole JE et al. N Engl Med 2008)


Based on these suggested parameters should we use tailored individual therapy?
EMPIRIC Study

• Goal: To test empiric testing to tailored physician guided therapy for a large group of patients with ICDs (900).

• Empiric strategy:

<table>
<thead>
<tr>
<th>Zone</th>
<th>Rate</th>
<th># beats</th>
<th>Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>VF</td>
<td>&gt; 250 bpm</td>
<td>18 of 24</td>
<td>30J x 6</td>
</tr>
<tr>
<td>FVT</td>
<td>201 - 250</td>
<td>&quot;</td>
<td>Burst(1), 30J x 6</td>
</tr>
<tr>
<td>VT</td>
<td>≤ 150 - 200</td>
<td>16</td>
<td>Burst(2), Ramp(1), 20J, 30J x 3</td>
</tr>
</tbody>
</table>

• Tailored Therapy left to discretion of Physician

Results: % Episodes Shocked

% Episodes Shocked | Difference of % Shocked
-------------------|--------------------------
Rhythm             | Empiric | Tailored | Non-inferiority margin
VT/VF              | 22.3%   | 28.7%    |
SVT                | 11.9%   | 26.1%    |

Empiric statistically non-inferior for both VT/VF and SVTs

Wilkoff B. JACC 2006
### MADIT-RIT

**Three Treatment Arms (abbreviated)**

<table>
<thead>
<tr>
<th></th>
<th>Arm A (Conventional)</th>
<th>Arm B (High-rate)</th>
<th>Arm C (Duration-delay)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone 1:</td>
<td>Zone 1: &gt;170 bpm, 2.5s delay</td>
<td>Zone 1: &gt;170 bpm, 60s delay</td>
<td>Zone 1: &gt;170 bpm, 60s delay</td>
</tr>
<tr>
<td></td>
<td>Onset/Stability Detection Enhancements ON</td>
<td>Monitor only</td>
<td>Rhythm ID® Detection Enhancements ON</td>
</tr>
<tr>
<td></td>
<td>ATP + Shock</td>
<td></td>
<td>ATP + Shock</td>
</tr>
<tr>
<td></td>
<td>SRD 3 min initial</td>
<td></td>
<td>SRD Off</td>
</tr>
<tr>
<td>Zone 2:</td>
<td>Zone 2: &gt;200 bpm, 1s delay</td>
<td>Zone 2: &gt;200 bpm, 2.5s delay</td>
<td>Zone 2: &gt;200 bpm, 12s delay</td>
</tr>
<tr>
<td></td>
<td>Quick Convert™ ATP + Shock</td>
<td>Quick Convert™ ATP + Shock</td>
<td>Rhythm ID® Detection Enhancements ON</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ATP + Shock</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SRD Off</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Zone 3:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;250 bpm, 2.5s delay</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Quick Convert™ ATP + Shock</td>
</tr>
</tbody>
</table>

*All programming is within approved labeling. Rhythm ID® and Quick Convert™ are trademarks of Boston Scientific Corporation.

Slides adapted from those presented by Arthur J Moss, MD at AHA 2012, Los Angeles, CA USA.
### Cumulative Probability of Death by Treatment Group

![Cumulative Probability of Death by Treatment Group](image)


### Frequency and Hazard Ratios for Inappropriate Therapy, Death, and Syncope by Treatment Group

<table>
<thead>
<tr>
<th>Events</th>
<th>Treatment Groups</th>
<th>Treatment Group Comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A (n=514)</td>
<td>B vs A</td>
</tr>
<tr>
<td></td>
<td>B (n=500)</td>
<td>Hazard Ratio</td>
</tr>
<tr>
<td></td>
<td>C (n=486)</td>
<td></td>
</tr>
<tr>
<td>1st Inapp Therapy</td>
<td>105</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>34</td>
<td>16</td>
</tr>
<tr>
<td>1st Syncope</td>
<td>23</td>
<td>22</td>
</tr>
</tbody>
</table>

PainFree SST Trial

(SmartShock Technology)

Study Objectives

The study was designed to evaluate the inappropriate shock rate using the SmartShock discrimination algorithms with out-of-the box nominal settings.

Primary Objectives
Inappropriate shock free rate at 1y post implant in Medtronic ICDs:

1. Dual (DR) and Triple Chamber (CRT) ICDs [presented HRS 2013]
2. Single Chamber ICDs [presented Europace 2013]

Pre-specified sample size of VR-ICD Cohort
At least 519 subjects with 1-year follow-up to obtain 2% precision assuming 92.5% shock free rate.
### SmartShock Algorithms in VR-ICD

<table>
<thead>
<tr>
<th>Algorithms</th>
<th>Feature description</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wavelet</td>
<td>QRS morphology discrimination. SVT limit moved to 260ms</td>
<td>SVT rhythms</td>
</tr>
<tr>
<td>T-wave Discrimination</td>
<td>Recognize T-wave oversensing and prevent detection/therapy</td>
<td>T-wave oversensing</td>
</tr>
<tr>
<td>Lead Noise Discrimination</td>
<td>Recognize lead noise oversensing and prevent detection/therapy; provide alert</td>
<td>Lead failures</td>
</tr>
<tr>
<td>Lead Integrity Alert</td>
<td>Provide an alert when there are early indication of lead failure</td>
<td>Lead failures</td>
</tr>
<tr>
<td>Confirmation+</td>
<td>Improved recognition of rhythm termination during charging</td>
<td>Non-sustained VT</td>
</tr>
</tbody>
</table>

### Primary results - Patients free from inappropriate shock at 1 year

<table>
<thead>
<tr>
<th>VR</th>
<th>97.6%</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR, CRT-D</td>
<td>98.2%</td>
</tr>
</tbody>
</table>
Effect of VT Therapy Zone

VT Therapy Zone did not increase the risk of an Inappropriate Shock

375 out of 709 patients (53%) have VT shocks enabled

<table>
<thead>
<tr>
<th></th>
<th>Median</th>
<th>Quartiles</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT initial NID</td>
<td>20</td>
<td>16-24</td>
<td>12-100</td>
</tr>
<tr>
<td>VT Max cycle length</td>
<td>350</td>
<td>340-360</td>
<td>300-600</td>
</tr>
</tbody>
</table>

Summary: Programming Shock Prevention

- Program VF zone up to 250 bpm
- Apply (several) ATP in the Fast VT Zone
- Prolong detection (18/24 – 30/40 cycles instead of 8/12 – 12/16 cycles)
- Empiric ICD programming is safe, equally effective compared to the “standard” ICD programming. It significantly reduces the morbidity associated with ICD therapy, and may improve mortality
Summary: Programming Shock Prevention

- It is remarkable how good science exposes the weaknesses of expert opinion. We were all so convinced that ventricular tachyarrhythmia required fast and aggressive action, like what is done in a CCU. Science now shows it's the opposite: the best way to approach ventricular arrhythmia with an ICD is with patience and nuance.