Recurrent ICD shocks are associated with

- Reduced quality of life
  - (Mark DB et al, NEJM 2008;359:999-1008)

- Increased mortality rate
  - (Poole JE et al, NEJM 2008;359:1009-1017)

- 5% rate of ICD–unresponsive SCD
  - (Mitchell LB et al, JACC 2002;39;1323-1328)
In 1980, Dr. Michel Mirowski and his team inserted the first ICD in a patient.
ICD Therapy
Life Extension and Quality of Life

• Approximately 20% of patients in primary prevention and 45% of patients in secondary prevention receive an appropriate ICD intervention within the 2 years following ICD implantation.
ICD Therapy
Life Extension and Quality of Life

• Despite the technological evolution of ICD systems, more than 20% of shocks are due to supraventricular arrhythmia (inappropriate).
ICD Therapy
Life Extension and Quality of Life

• VT storm, defined as 3 or more appropriate ICD therapies within a 24-hour period, may affect 4% and 20% of the patients in the primary and secondary prevention.

• ICD shocks decrease quality of life, increase patient’s anxiety and increase the risk of morbidity and a higher 3-month mortality.
Therapeutic options to reduce ICD shocks and increase survival

- Antiarrhythmic drugs (AADs)
- VT catheter ablation
Benefits of Adjuvant AADs Therapy in ICD Patients

1. Decrease in appropriate ICD shocks due to suppression of recurrent VT/VF
2. Decrease in inappropriate ICD shocks due to reduced frequency and better rate control of SVT
3. Slowing of tachycardia leading to improved hemodynamic tolerance
Benefits of Adjuvant AADs Therapy in ICD Patients

4. Slowing of rate of tachycardia facilitating successful termination by ATP
5. Decrease in frequency of symptomatic non-sustained ventricular arrhythmias
6. Prevention and better treatment of electrical storm
Benefits of Adjuvant AADs Therapy in ICD Patients

7. Improved control of maximal sinus rate
8. Improved quality of life and sense of well-being
9. Reduced rate of recurrent ICD related hospitalizations
10. Prolongation of ICD battery life
<table>
<thead>
<tr>
<th>Study</th>
<th>Drug/Dose</th>
<th>No. per Group</th>
<th>Follow-Up</th>
<th>Primary End Point</th>
<th>Secondary End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pacifico et al</td>
<td>Sotalol (207 +55 mg) vs placebo</td>
<td>150</td>
<td>12 mo</td>
<td>All-cause death or all-cause ICD shock: Sotalol: 44% (HR: 0.52) Placebo: 56%</td>
<td>Mean frequency of shocks due to any cause: Sotalol: 1.433 ± 53 Placebo: 3.89±10.65</td>
</tr>
<tr>
<td>Kuhlmann et al</td>
<td>Sotalol (80 to 400 mg) vs placebo</td>
<td>46</td>
<td>12 mo</td>
<td>Recurrence of VT/VF: Sotalol: 32.6% Placebo: 53.2%</td>
<td>Total mortality: Same across the groups</td>
</tr>
<tr>
<td>Singer et al</td>
<td>Azimilide 35, 75, or 125 mg vs placebo</td>
<td>35–46</td>
<td>374 d</td>
<td>Frequency of appropriate ICD shocks and ATP: Placebo: 36 35 mg AZ: 10 75 mg AZ: 12 125 mg AZ: 9 per patient-year (HR: 0.31)</td>
<td></td>
</tr>
</tbody>
</table>
Clinical Trials Summarizing Benefits of Adjuvant AADs Therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>Drug/Dose</th>
<th>No. per Group</th>
<th>Follow-Up</th>
<th>Primary End Point</th>
<th>Secondary End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorian et al</td>
<td>Azimilide 75, 125 mg vs placebo</td>
<td>199-214</td>
<td>1 y</td>
<td>All-cause shock and ATP: 75 mg AZ: HR0.43 125 mg AZ: HR0.53 as compared with placebo</td>
<td>Appropriate ICD therapy: 75 mg AZ: HR0.52 125 mg AZ: HR0.38 as compared with placebo</td>
</tr>
<tr>
<td>Kettering et al</td>
<td>Metoprolol (108±44 mg) vs sotalol (31991 mg)</td>
<td>50</td>
<td>727 d</td>
<td>Recurrent VT/VF requiring ICD therapy: Metoprolol: 66% Sotalol: 60% Event-free survival not different between groups</td>
<td>Total mortality: Metoprolol: 8 deaths Sotalol: 6 deaths Not different between the 2 groups</td>
</tr>
</tbody>
</table>
Amiodarone Plus Beta-Blocker Reduces ICD Shocks

Conolli et al. JAMA. 2006;295

- 412 patients with dual-chamber ICD for inducible or spontaneously occurring VT or VF
- Randomized 1 year of treatment to BB, BB+amio, Sotalol
- BB therapy consisted of either metoprolol (100 mg/day), carvedilol (50 mg/day) or bisoprolol (10 mg/day)
## OPTIC Study

<table>
<thead>
<tr>
<th>Event Rate</th>
<th>Beta-Blocker</th>
<th>Amiodarone + Beta-Blocker</th>
<th>Sotalol</th>
</tr>
</thead>
<tbody>
<tr>
<td>All shock (%)</td>
<td>38.5</td>
<td>10.3</td>
<td>24.3</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.27 (0.14-0.52)</td>
<td>0.61 (0.37-1.01)</td>
<td></td>
</tr>
<tr>
<td><em>P</em> value</td>
<td>&lt; .001</td>
<td>.055</td>
<td></td>
</tr>
<tr>
<td>Appropriate shock (%)</td>
<td>22</td>
<td>6.7</td>
<td>15.1</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.30 (0.14-0.68)</td>
<td>0.65 (0.36-1.24)</td>
<td></td>
</tr>
<tr>
<td><em>P</em> value</td>
<td>.004</td>
<td>.18</td>
<td></td>
</tr>
<tr>
<td>Inappropriate shock (%)</td>
<td>15.4</td>
<td>3.3</td>
<td>9.4</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.22 (0.07-0.64)</td>
<td>0.61 (0.29-1.30)</td>
<td></td>
</tr>
<tr>
<td><em>P</em> value</td>
<td>.006</td>
<td>.20</td>
<td></td>
</tr>
</tbody>
</table>

Amiodarone: 73% Reduction in all shocks
Adverse effects of AADs

1. Cardiac
   A. Bradyarrhythmia
   B. Torsades de pointes
   C. Impairment of myocardial function

2. Extracardiac toxicity
Adverse effects of AADs

1. Interference in ICD function due to
   A. Increase in defibrillation threshold
   B. Increase in pacing threshold

2. Interference in accurate arrhythmia detection due to
   A. Slowing of rate of ventricular tachycardia
   B. Decrease in amplitude of electrocardiogram interfering with sensing
   C. Limiting effectiveness of rate stability criterion
Summary and Recommendations

• **Could be the first line therapy** to treat recurrent ventricular arrhythmias that precipitate frequent ICD shocks
  
  A. Optimizing β-blocker therapy
  B. If they do not work or cannot be tolerated, amiodarone, azimilide or sotalol may provide benefit

• **Do not reduce mortality** in patients surviving AMI (CAMIAT, EMIAT)

• Some actually **increase** mortality (CAST, CAST-II)
  • proarrhythmia
Why do we need ablation in patients with ICD?

1. Multiple ICD shocks: Incessant VT, Arrhythmia Storm
2. Negative effect of shocks and AADs in survival and quality of life
3. Probability of inappropriate therapies if slow VT zone programmed
# Catheter Ablation for the Treatment of Sustained Monomorphous VT

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgent catheter ablation is recommended in patients with scar-related heart disease presenting with incessant VT or electrical storm.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Catheter ablation is recommended in patients with ischaemic heart disease and recurrent ICD shocks due to sustained VT.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Catheter ablation should be considered after a first episode of sustained VT in patients with ischaemic heart disease and an ICD.</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>
Ablation in Patients with ICD and shocks

- In most studies, catheter ablation has been performed in patients with ischemic heart disease after multiple ICD interventions, including patients with incessant VT (secondary VT ablation).

- In almost all of these studies, patients were included after failure of 1 or multiple AADs.
VT ablation Trials

- **Secondary VT ablation trials:**
  - Thermocool trial
  - Cooled RFC trial
  - Euro-VT trial

- **Prophylactic or primary VT ablation trials:**
  - SMASH trial
  - VTACH trial
Catheter Ablation After Multiple ICD Interventions

- The **2 largest prospective** multicenter trials using irrigated RFC included more than 350 patients with structural heart disease, predominantly CAD:
  - Thermocool trial
  - Cooled RFC trial
Thermocool VT Ablation Trial

• Patients with multiple VTs, unmappable VTs, and a history of prior failed VT ablation were included.

• The acute success rate was 49% when elimination of all inducible VT was used as the end point.

• In 142 patients with ICDs who survived 6 months, VT episodes were reduced from median of 11.5 to 0.
Thermocool VT Ablation Trial

1-year mortality 18%
Causes of Mortality

- Procedure: 10%
- In Hospital Arrhythmia: 17%
- Late Arrhythmia: 8%
- Heart Failure: 34%
- Other Cardiac: 13%
- Noncardiac: 13%
- Unknown: 10%
- VT/SD: 21%
Cooled RFC study

• Patients with a hemodynamically stable VT were included
• The acute success rate was 71% when the end point was elimination of all mappable VTs and 41% when the end point was elimination of VT of any type.

• In the cooled RFC study, a 75% reduction in the VT frequency in the two months after ablation compared to the two months before ablation was observed in 99 of 122 patients (81%), of whom 115 had an ICD.
Euro-VT Study

• In 63 patients with recurrent scar-related ventricular tachycardia at 8 centers in Europe.

• 42 patients (66.7%) had an ICD before ablation, and another 9 patients (14.3%) received an ICD thereafter.
Euro-VT Study

• At least 1 VT successfully ablated in 81%, all inducible VTs ablated in 50%
• At 6 months F/U, 51% remained free of any recurrent VT
• Mean number of ICD therapies reduced from 60 pre-RFA to 14 post-RFA for the 6 months after ablation
• No procedural mortality
• Non-fatal adverse events occurred in 5%

Tanner, H et al 2009 Europace
Catheter Ablation of VT/VF Before ICD Interventions

Prophylactic Catheter Ablation for the Prevention of Defibrillator Therapy

Vivek Y. Reddy, M.D., Matthew R. Reynolds, M.D., Petr Neuzil, M.D., Ph.D., Allison W. Richardson, M.D., Milos Taborsky, M.D., Ph.D., Krit Jongnarangsin, M.D., Stepan Kralovec, Lucie Sediva, M.D., Jeremy N. Ruskin, M.D., and Mark E. Josephson, M.D.
SMASH VT
Substrate Mapping and Ablation in Sinus Rhythm to Halt Ventricular Tachycardia Trial

Aim of study

To assess the efficacy of prophylactic VT ablation in preventing ICD therapy in patients with:

- Previous myocardial infarction
- Undergoing ICD implantation for life-threatening arrhythmic events.

Reddy et al, NEJM 2007;357:2657-65
SMASH VT

128 patients in 3 centres:
Planned or recent ICD for
- Ventricular fibrillation
- Unstable ventricular tachycardia
- Syncope with inducible VT during EP

Ablation group No:62
Substrate ablation in sinus rhythm

Control group No:64
No further therapy

Exclusion criteria:
Class I and III antiarrhythmic drugs
Incessant or multiple episodes of VT

Mean follow up 23 months

Reddy et al, NEJM 2007;357:2657-65
SMASH VT

Endpoints

I. ) Survival free from any appropriate ICD therapy

II.)Freedom from

- any appropriate ICD shock
- death
- ICD storm

Reddy et al, NEJM 2007;357:2657-65
SMASH VT: Results

Events over a mean 22 month follow up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ablation Group (N=64)</th>
<th>Control Group (N=64)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICD events*</td>
<td>8 (12)</td>
<td>21 (33)</td>
<td>0.35 (0.15–0.78)</td>
<td>0.007†</td>
</tr>
<tr>
<td>ICD shocks</td>
<td>6 (9)</td>
<td>20 (31)</td>
<td>0.27 (0.11–0.67)</td>
<td>0.003†</td>
</tr>
<tr>
<td>ICD storms</td>
<td>4 (6)</td>
<td>12 (19)</td>
<td>0.30 (0.09–1.00)</td>
<td>0.06‡</td>
</tr>
<tr>
<td>Death</td>
<td>6 (9)</td>
<td>11 (17)</td>
<td>0.59 (0.22–1.59)</td>
<td>0.29†</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>3 (5)</td>
<td>6 (9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventricular tachycardia storm</td>
<td>0</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>1 (2)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1 (2)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (2)</td>
<td>4 (6)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Implantable cardioverter–defibrillator (ICD) events include ICD shocks and antitachycardia pacing.
† The P value was calculated by the log-rank test.
‡ The P value was calculated by Fisher’s exact test.
SMASH VT

Prophylactic catheter ablation

No Change in Survival

Reddy et al. NEJM 2007
Catheter ablation of stable ventricular tachycardia before defibrillator implantation in patients with coronary heart disease (VTACH): a multicentre randomised controlled trial

Karl-Heinz Kuck, Anselm Schaumann, Lars Eckardt, Stephan Willems, Rodolfo Ventura, Etienne Delacrétaz, Heinz-Friedrich Pitschner, Josef Kautzner, Burghard Schumacher, Peter S Hansen, for the VTACH study group*
To assess the efficacy of prophylactic VT ablation in patients with:

- Previous MI, LVEF <50%
- Before ICD implantation for first episode of stable VT (SBP>90mmHg, no syncope or cardiac arrest)

Kuck et al, Lancet 2010;375:31-40
VTACH STUDY

107 patients in 16 centres
Documented stable VT, previous MI, EF <50%

Follow up at least 1 year, mean 22 months

Kuck et al, Lancet 2010;375:31-40
VTACH STUDY

PRIMARY END POINT
Time from ICD implantation to recurrence of any sustained VT or VF

SECONDARY END POINTS
Survival free from
• Death
• Syncope
• Hospital admission for cardiac reasons
• VT storm

Number of appropriate ICD interventions

Kuck et al, Lancet 2010;375:31-40
VTACH STUDY
Primary Endpoint

TIME TO FIRST VT OR VF (MONTHS) - ABLATION: 18.6, CONTROL: 5.9

Kuck et al, Lancet 2010;375:31-40
### VTACH STUDY RESULTS

<table>
<thead>
<tr>
<th>24-mo event-free survival estimates</th>
<th>Ablation, n=52 (%)</th>
<th>Control, n=55 (%)</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT recurrence</td>
<td>46.6</td>
<td>28.8</td>
<td>0.61 (0.37–0.99)</td>
</tr>
<tr>
<td>Hospital admission for cardiac reasons</td>
<td>67.4</td>
<td>45.4</td>
<td>0.55 (0.30–0.99)</td>
</tr>
<tr>
<td>VT storm</td>
<td>75.0</td>
<td>69.7</td>
<td>0.73 (0.36–1.50)</td>
</tr>
<tr>
<td>Syncope</td>
<td>96.2</td>
<td>85.4</td>
<td>0.36 (0.07–1.81)</td>
</tr>
<tr>
<td>Death</td>
<td>91.5</td>
<td>91.4</td>
<td>1.32 (0.35–4.94)</td>
</tr>
<tr>
<td>ICD shock (n [%])</td>
<td>17 (32.7%)</td>
<td>29 (52.7%)</td>
<td>..</td>
</tr>
<tr>
<td>Inappropriate ICD shock (n [%])</td>
<td>4 (7.7%)</td>
<td>6 (10.9%)</td>
<td>..</td>
</tr>
<tr>
<td>≥2 appropriate shocks per year (n [%])</td>
<td>4 (7.7%)</td>
<td>12 (21.8%)</td>
<td>..</td>
</tr>
</tbody>
</table>
VTACH STUDY

Kuck et al, Lancet 2010;375:31-40
Safety of prophylactic ablation

<table>
<thead>
<tr>
<th>Study</th>
<th>Complications</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ablation related death</td>
<td>No death</td>
<td></td>
</tr>
<tr>
<td>VTACH</td>
<td>2 complications</td>
<td>3.8%</td>
</tr>
<tr>
<td>SMASH VT</td>
<td>3 complications</td>
<td>4.7%</td>
</tr>
</tbody>
</table>

- Transient ischemic ST-elevation
- Transient cerebral ischemic event
- Pericardial effusion
- Exacerbation of HF
- Deep venous thrombosis
This pilot randomized clinical trial to determine the feasibility of a large clinical trial aimed at testing whether early use of catheter ablation of ventricular tachycardia (VT) is superior to antiarrhythmic medications at reducing mortality.

**STAR-VT Study**
(Substrate Targeted Ablation using the FlexAbility™ Ablation Catheter System for the Reduction of Ventricular Tachycardia)
Heart Center of Leipzig VT (HELP-VT) Study

- The short-term success rates after VT ablation in NIDCM and ICM patients were similar, the long term outcomes in NIDCM patients were significantly worse.
Conclusions

- Catheter ablation is an effective way of treating VT in ICD patients including (ICM, NIDCM?)
- Both hemodynamically stable and unstable VTs can be successfully mapped and ablated by experienced operators
- With the growing population of patients with ICDs, the impact of ICD shocks on quality of life and side-effects of AADs, there is a growing need for more aggressive use of catheter ablation for VT
Conclusions

• **Prophylactic ablation** should be Strongly considered before implantation of a cardioverter defibrillator

  KH Kuck et al Lancet 2010;375:40

• The rate of procedure-related complications is low

• Evidence of a positive effect on survival, hospital admission or quality of life is needed before this strategy can be recommended for routine use

  WG Stevenson, U Tedrow, Lancet 2010;375:6
Epi-Endo Approach
Multiple VTs