

# Cardiac Pacing and Defibrillation

2019/02/26

## What you can expect to learn today

- Wrapping up cardiac pacing
  - Anodal vs. Cathodal pacing
    - Activating function/virtual electrodes
  - CRT
    - HBP
    - PITA
  - Antitachycardia pacing
- Defibrillation
  - A brief primer on fibrillation
    - Unidirectional block
    - S1-S2
    - Vulnerable window (remember that T-wave pacing concept)
  - Revisit some theories of defibrillation
    - Virtual Electrode Hypothesis
  - Toward the future?
    - Optogenetics?
    - Multisite pacing for defibrillation?
- What about AF?
  - Do we treat that the same way we treat VF?

## Heart Failure

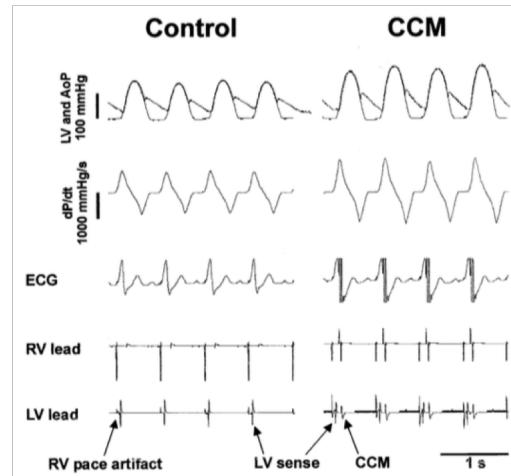
- What is it?
  - Pump dysfunction that results in an inability to meet the metabolic demands of the body.
  - Commonly caused by coronary artery disease (including prior MI), high blood pressure, AF, alcoholism, infection, cardiomyopathy.
  - Two primary types:
    - Preserved ejection fraction (HFpEF) – inadequate filling.  $EF=SV/EDV =50-70\%$
    - LV dysfunction ( $EF<40\%$ )
  - Also characterized in other ways:
    - Left vs. right sided
    - Systolic vs. diastolic dysfunction (same as before).
    - Increased preload vs. increased afterload.
    - Low CO with high resistance vs. high CO with low resistance
    - Graded by the degree of exercise tolerance. (NYHA functional classification).
  - Characterized by stable low-level performance punctuated by periods of acute decompensation.

| NYHA Class | Symptoms   |
|------------|--|
| I          | Cardiac disease, but no symptoms and no limitation in ordinary physical activity, e.g. no shortness of breath when walking, climbing stairs etc.           |
| II         | Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity.   |
| III        | Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g. walking short distances (20–100 m). Comfortable only at rest. |
| IV         | Severe limitations. Experiences symptoms even while at rest. Mostly bedbound patients.   |

## Non-Pharmacological Treatment

- AICD – purely to reduce mortality. Does nothing for symptoms (HF with  $EF<35\%$  has much higher rates of VT)
- Cardiac Contractility modulation – for patients NYHA II-IV. Best for patients with normal QRS duration (<120 ms). Improves symptoms QoL, and exercise tolerance.
- CRT uses biventricular pacing to ‘resynchronize’ the heart.
  - ~1/3 of HF with  $EF<35\%$  have significant ventricular dyssynchrony, particularly in LBBB.
  - NYHA II or IV, QRS duration >120 ms.
  - In the remaining 2/3 of HF patients it may be harmful.
- Pacing-induced transient asynchrony
  - Could be used in remaining 2/3 of patients without dyssynchrony

## Cardiac Contractility Modulation

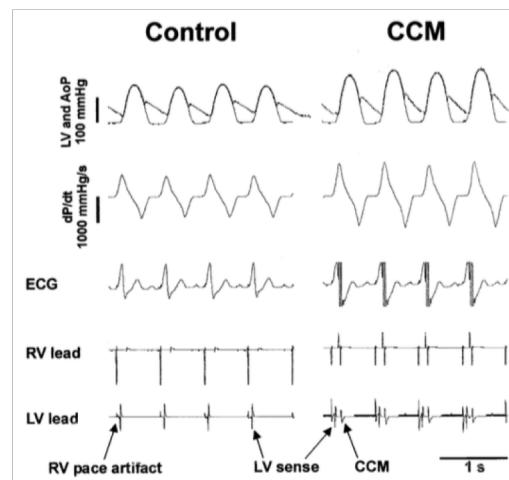


How might this work?

- Propose a mechanism.
- Are there any side-effects?

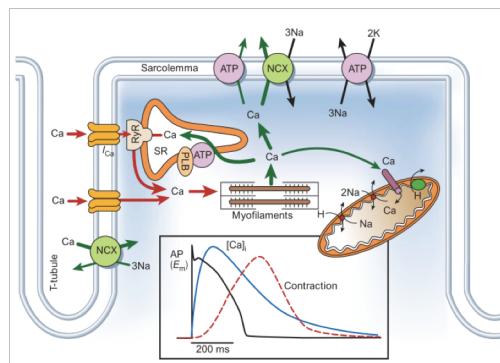
## Safety?

- Current delivery is coupled to sensed or paced events by adaptive CCM timing and safety algorithms which inhibit signal generation when irregular activation is detected.
- CCM stimulation is suppressed on ectopic beats and resumed only after 3 consecutive normal beats.

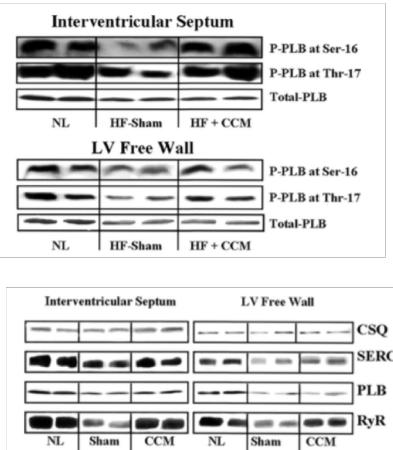


## Mechanisms?

### Acute

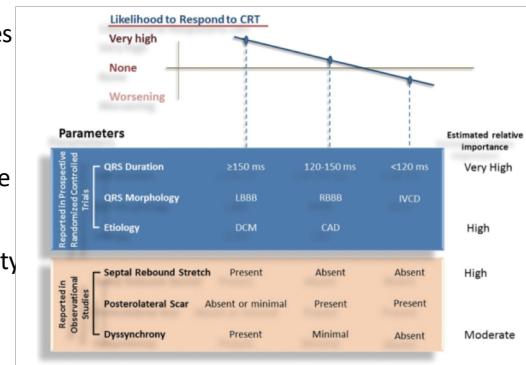


### Chronic



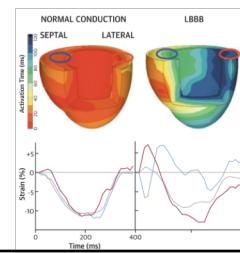
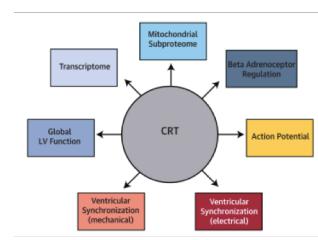
## CRT

- Cardiac resynchronization therapy (CRT) is one of the most successful HF therapies in the last 25 years but it is applicable to 25–30% of patients with symptomatic heart failure.
- Large randomized trials have demonstrated that CRT improves (QoL), reduces HF hospitalizations and mortality, and reverses the structural remodeling of the heart.
- Responders vs Non-responders (~30%)

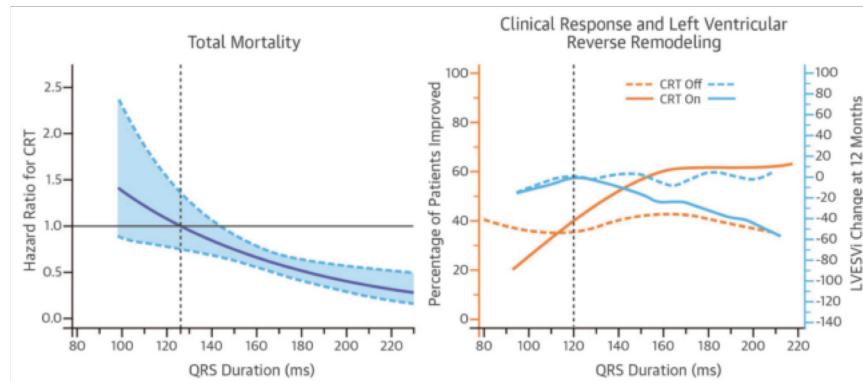


## CRT

- Increased regional **heterogeneity** in gene expression within the left ventricle is **reduced** with CRT
- CRT increases pyruvate carboxylation and branched-chain amino acid oxidation, increasing the pool of Krebs cycle intermediates and **fuels oxidative phosphorylation**
- CRT also improves rest and beta-adrenergic-stimulated myocyte function and calcium handling, up-regulating **beta-1 receptors** and adenylate cyclase activity and suppressing Gi-coupled signaling
- APD prolongation** in DHF in the lateral vs. anterior wall is **reduced** by CRT, particularly in the lateral wall
- CRT induces a pattern of activation different from LBBB, with the RV activation proceeding from apex to base. The base of the RV and of the interventricular septum is activated later than in a left bundle branch block, whereas the LV free wall is activated early
- DHF involves **disparities in the timing of shortening and reciprocal shortening/stretch** in the anterior and lateral LV walls, which are **corrected** by CRT
- AV synchronization: when the LV is pre-excited with pacing, the start of pressure development in the left ventricle occurs earlier. Shortening long AV delay by CRT increases pulse pressure and LV dP/dtmax. An optimal pulse pressure occurs when peak left atrial systole coincides with the start of LV contraction
- A leftward shift in pressure-volume loops reflects **reverse remodeling**

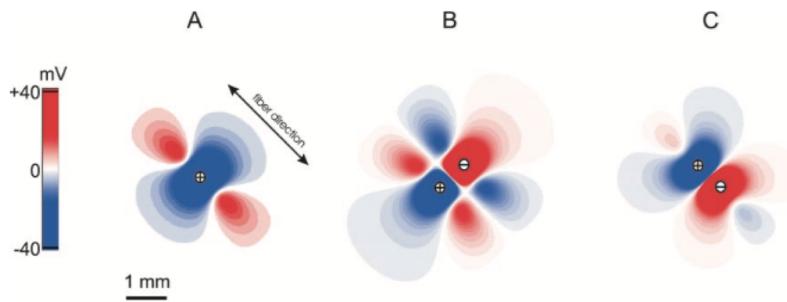


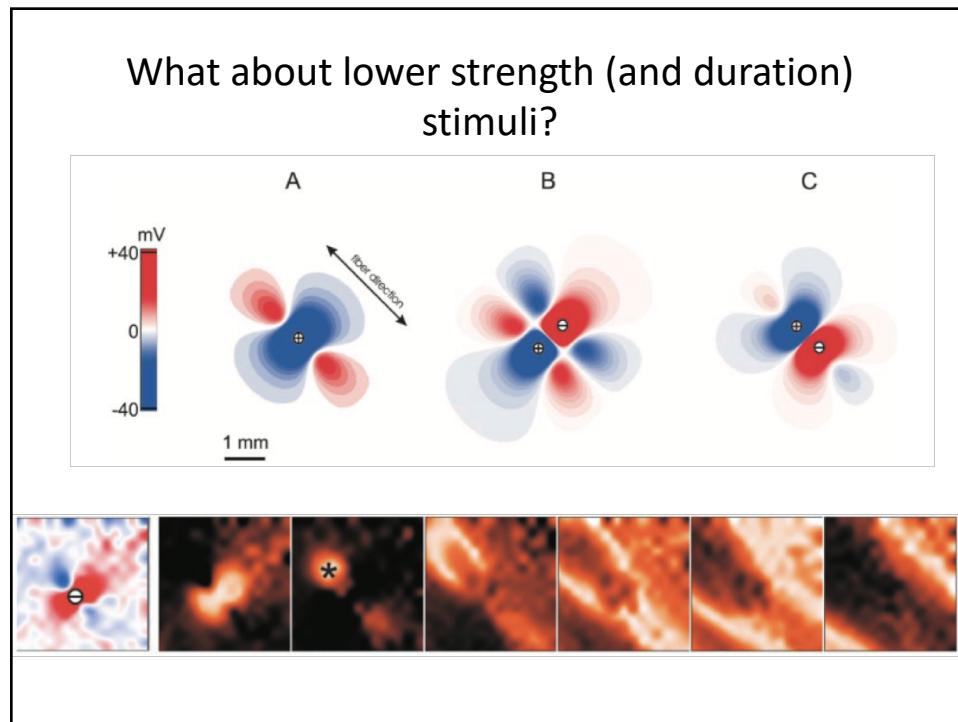
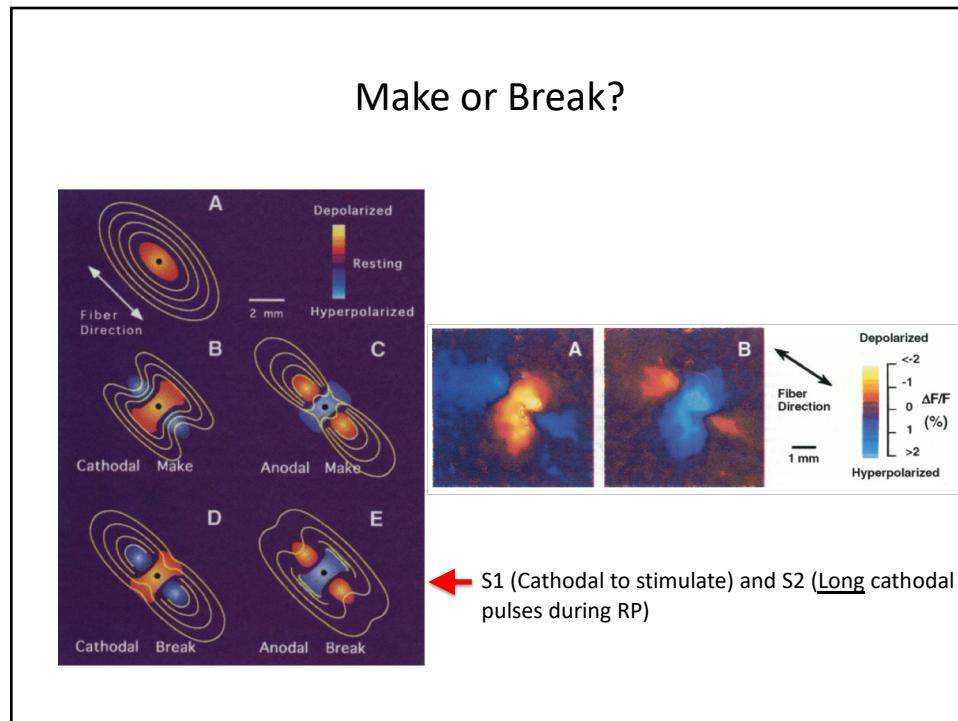
## More on suitability for CRT



## Let's predict activation patterns!

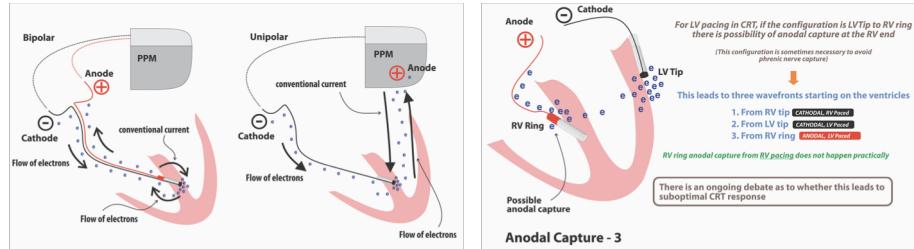
- Consider a 2D anisotropic environment.
  - What will the activation wavefront look like for cathodal stimulation?
  - Anodal?





## Biventricular Anodal Stimulation

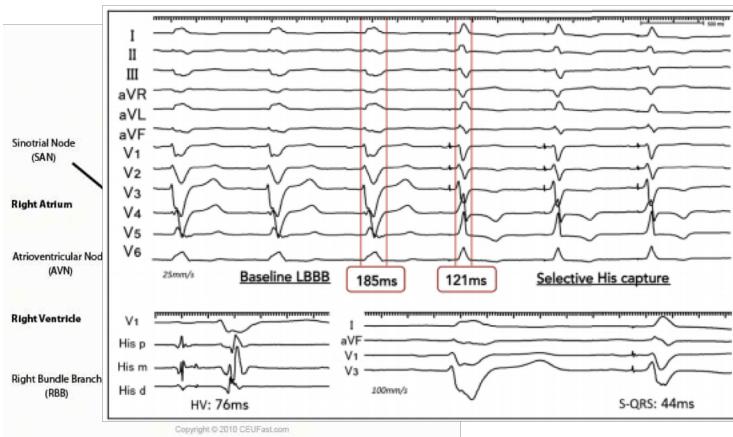
- In modern CRT systems, “*bipolar*” LV pacing can be achieved by pacing between two LV electrodes or from one of the electrodes on the LV lead to the RV ring (shared ring configuration).



- Could be better or worse:
  - The third activation site could increase pacing area and cause better resynchronization
  - The anodal site is intermittent, and is timed with the LV, not RV pacing, eliminating the ability of adjusting the interval between RV and LV

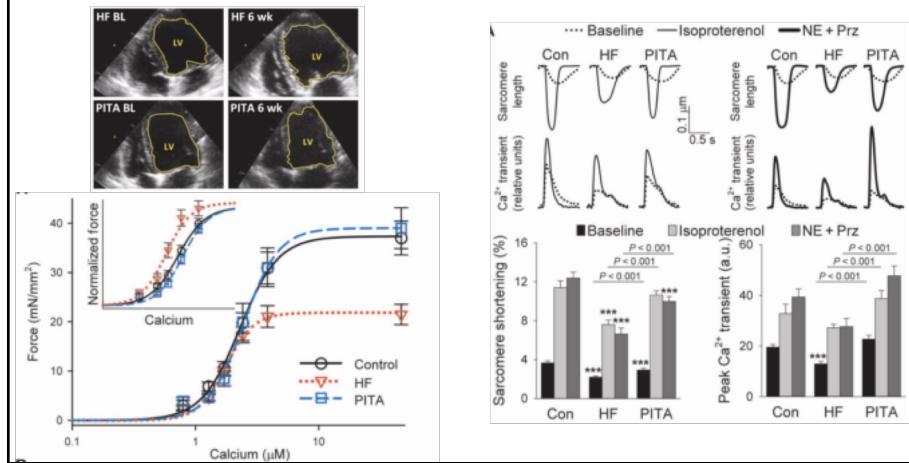
## His Bundle Pacing

- What if instead of pacing both ventricles we could pace the bundle of His?



## Pacemaker induced transient asynchrony

- Animals were tachypaced at 200 bpm, 24 hours/day, in VVI mode for 2 weeks to induce HF
- For the next 4 weeks they were either the same or PITA (RV tachypaced)
- Right ventricular free-wall pacing induces left ventricular dyssynchrony similar to that with a left bundle branch block



## CRT-D

- Most CRT is CRT-D. What about leadless pacemakers?
- What modes can be used?



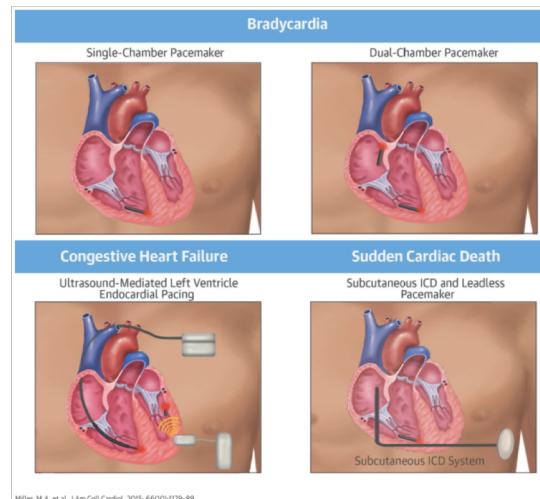
FIGURE 2. Leadless pacemakers (A) Nanostim and (B) Micra.

| Overview of leadless pacemakers Nanostim and Micra based on completed human trials |                           |                             |
|--|---------------------------|-----------------------------|
|  | Nanostim                  | Micra                       |
| Manufacturer   | St. Jude Medical          | Medtronic                   |
| Size (height × width)  | 42.0 × 6.0 mm             | 25.9 × 6.7 mm               |
| Volume   | 1.0 mL                    | 0.8 mL                      |
| Mass   | 2 g                       | 2 g                         |
| Delivery sheath size   | 18 F                      | 23 F                        |
| Primary fixation mechanism   | Helix                     | Tines                       |
| Projected battery life*  | 15.0 years                | 12.5 years                  |
| Remote monitoring  | No                        | Yes                         |
| Rate-responsive pacing   | Yes,<br>temperature-based | Yes,<br>accelerometer-based |
| Retrieval system   | Yes                       | No                          |

\*Based on reported projections at 3 months.  
Data from references 21–27.

## Leadless pacing configurations

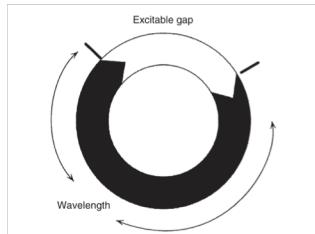
- Most CRT is CRT-D. What about leadless pacemakers?
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## What causes cardiac arrhythmia

| Abnormal impulse formation   | Alterations in the conduction of the impulse  |
|--|---|
| Enhanced normal automaticity   | Reentry   |
| Abnormal automaticity  | Reflection  |
| Triggered activity (delayed and early afterdepolarizations)                                    |   |
| <p>(a) Baseline<br/> (b) Decreased threshold<br/> (c) Decreased MDP<br/> (d) Increased DDR</p> | <p>(a) EAD (phase 2)<br/> (b) EAD (phase 3)<br/> (c) DAD</p>                            |
|  | <p>(a) Normal beat<br/> (b) Premature beat<br/> (c) Reentrant beat<br/> (d) a, b, c</p> |

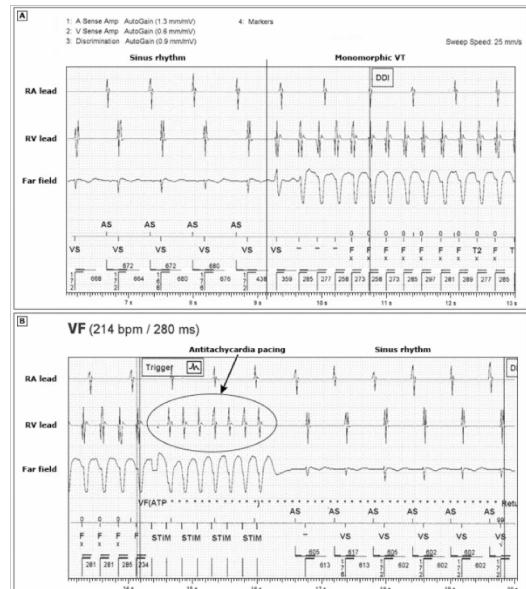
## More on Reentry -> VT



- Need for an intact predetermined anatomic circuit.
- Unidirectional block for the onset of the activity.
  - Typically occurs in the region of longest refractory period resulting from increased heart rate. Can result from:
    1. Increase in sinus rate.
    2. Rapid/premature atrial pacing.
    3. Retrograde activation from a ventricular extrasystole.
    4. Autonomic input
    5. Drugs and ischemia.
- Slow conduction in part of the circuit.
- $WL < PL$ .
  - Excitable gap has implications:
    1. Reentry is more stable with EG because it never hits refractory tissue.
    2. Possible to entrain or interrupt with stimulation ("Leading Circle Model").
      1. An externally initiated impulse may invade the circuit during the excitable gap and thus advance the activation front. Depending on the timing or the rate of external stimulation, the wave front may be advanced enough to collide with the repolarizing tail and thus terminate the activity.
    3. Drugs that increase RP must do it enough to eliminate EG

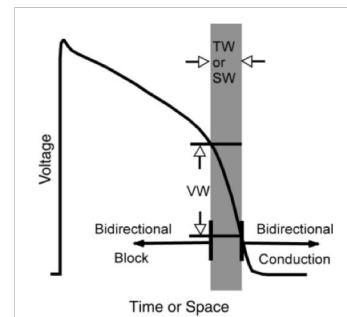
## Antitachycardia Pacing

- ATP is typically the first line of defense because both appropriate (5x) and inappropriate (2x) shocks of VT/VF increase mortality.
- Especially true with structural heart disease. Why?
- Programmed with at least 8 pulses at 84-88% of the VT CL. Why? How do we know what 88% is?
- Reduces both appropriate and inappropriate shocks.
- Side effects?
  - Inappropriate delivery with SVT!



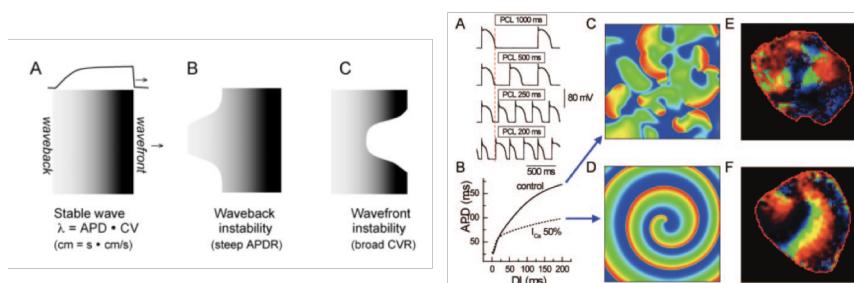
## What is the substrate for arrhythmia?

- Slow conduction – how do we get it
  - Reduced excitability (e.g. reduced Na channels in ischemia)
    - When there are too few channels the cell becomes inexcitable and conduction fails completely
  - Reduced cell-to-cell coupling (e.g. reduced gap junctions)
  - $\lambda = \theta * RP$
- Unidirectional block
  - How do we get it?
  - Remember triggered activity?

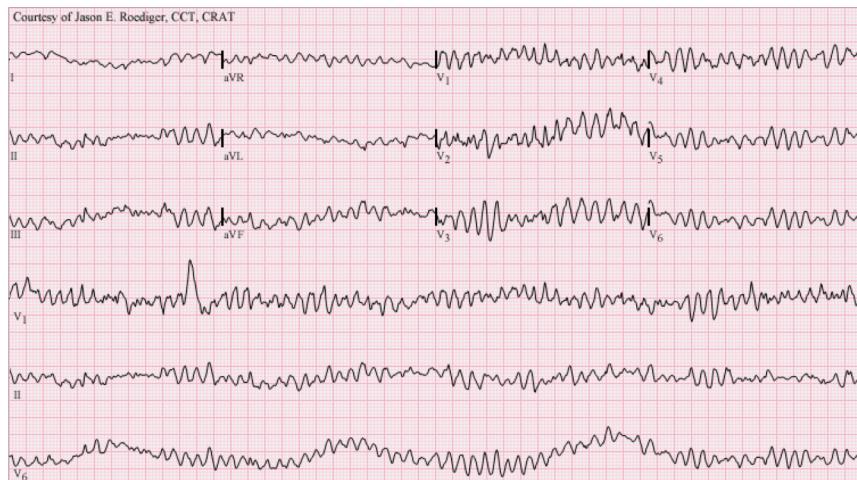


## That's reentry, what about fibrillation?

Wavebreak and Restitution

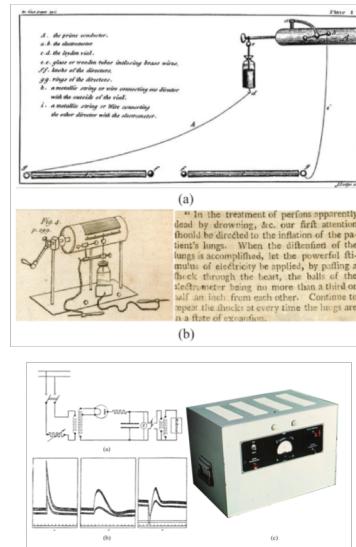


## ECG



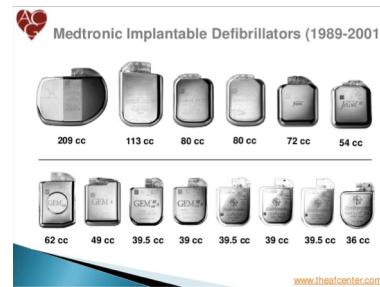
## Defibrillation: Historical overview

- 1788: Charles Kite reported a successful resuscitation with external shock.  
– Voltaic pile was in 1800!
- 1933: Kouwenhoven, Langworthy, and Hooker terminate VF in a dog with 60 Hz AC “countershock.”
- 1939: Gurvich and Yuniev propose capacitor discharge DC shock for defibrillation.
- 1947: Claude Beck completed the first open-chest human defibrillation



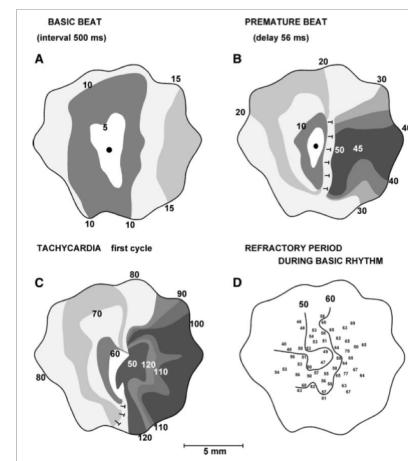
## Defibrillation: Historical overview

- 1956: Paul Zoll completed the first closed-chest human defibrillation
- DC defibrillators were demonstrably safer and gained acceptance.
- 1970: Mirowski and Mower (Sinai Hospital, Baltimore) first test automatic defibrillator in dogs.
- 1980: **Mirowski, Mower, Watkins et al. first ICD in human.**
- 1993: First ICD with biphasic waveform.



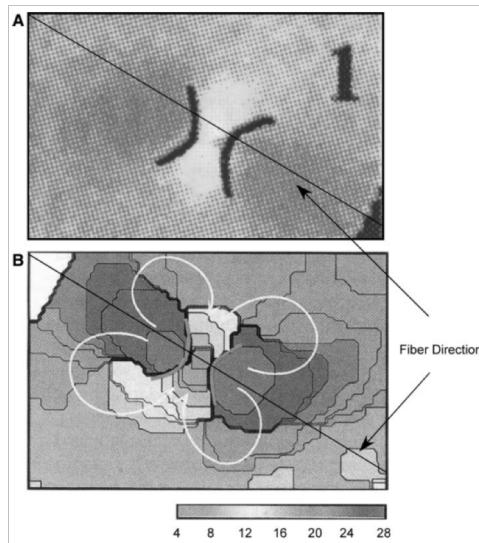
## What are the conditions again? Let's consider stimulation

- Tissue heterogeneity
  - Cause by stress (e.g. ischemia, drugs, MI, etc.)
  - Majority of VF is in ischemic heart disease.
- Triggered beat (e.g. PVC...EAD/DAD)
  - Usually benign
  - 3 or more PVCs = VT



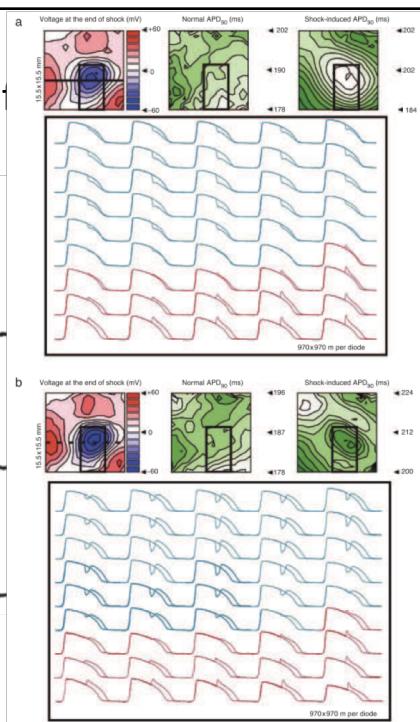
## VEP and the initiation of arrhythmia

- Under the right conditions a single stimulus can initiate a reentrant circuit (or several!)
- Is this anodal or cathodal?
- What would you expect to happen?



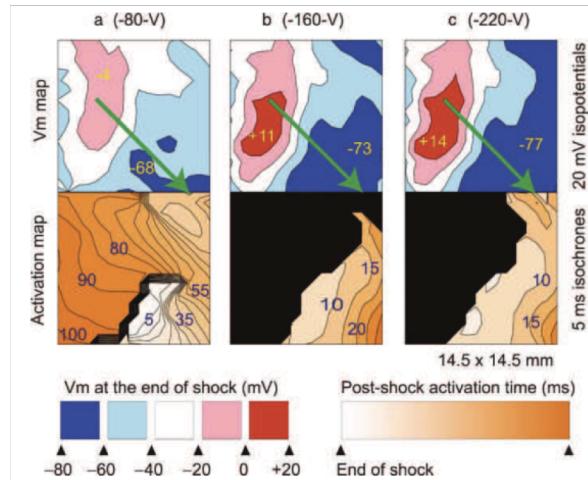
## How do we detect VEP?

- When we apply a shock we get VEP. We know this causes depolarization and hyperpolarization
- De-excitation occurs at the virtual anode or cathode?
  - Shortens the APD/RP
- Prolongation of the APD can occur at the virtual cathode.
- Partial de-excitation:
- What are the consequences?
  - Can partially or fully restore excitability at the virtual anode
  - If the virtual cathode is within a space constant, re-excitation can occur.



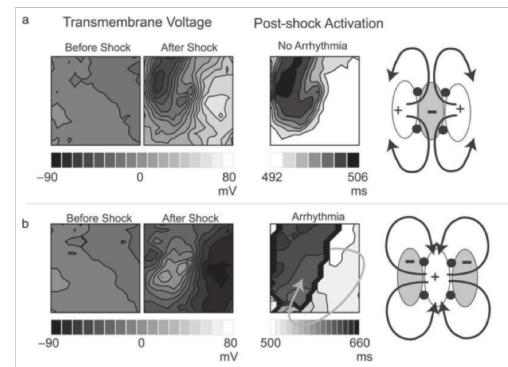
## Upper and Lower limits of Vulnerability

- ULV is defined as the weakest shock strength at or above which VF is not induced.
- LLV is the shock strength at or below which VF is not induced.
- What causes this? VEP!
  - Stronger negative polarization results in more complete recovery of Na inactivation and faster conduction of postshock reexcitation.

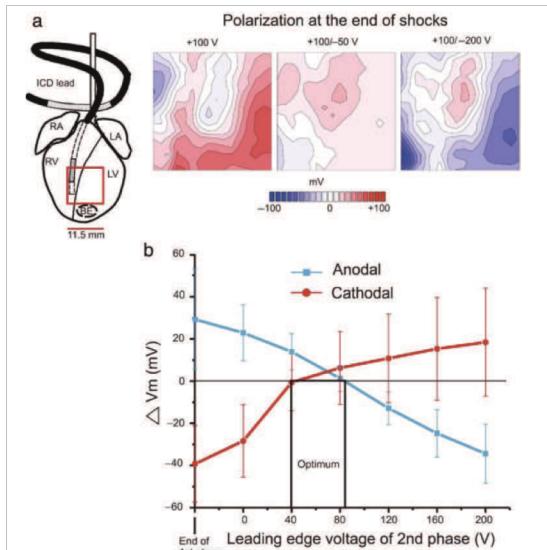


## Should we use anodal or cathodal defibrillation shocks?

- Anodal shocks create virtual cathodes farther away – implications for post-shock conduction.
- In clinical studies anodal ICD shocks had a 14.8% lower DFT than cathodal shocks, resulting in a lower DFT in 83% of patients.
  - Likely due to reinitiation!



## Why biphasic shocks?



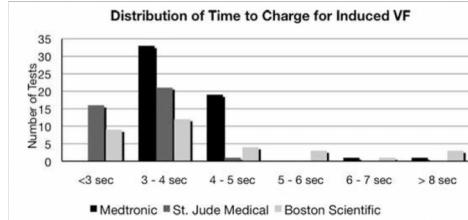
Ratio of 0.2-0.7 is optimal.  
Why is this?

## ICD Overview

- ICDs are indicated for two groups:
  1. Secondary prevention of SCD in patients with prior VT, VF, or resuscitated SCD thought to be caused by VT/VF
  2. Primary prevention of SCD in at-risk patients for VT/VF
    - Patients with prior MI and EF<30%
    - Cardiomyopathy NYHA class II-III and EF<35%
    - Syncope with structural heart disease and inducible sustained VT
    - Congenital LQT with recurrent symptoms
- Contraindicated for:
  - VT due to reversible, non-structural cause (e.g. drugs, electrolyte imbalance)
  - No reasonable survival with function for at least one year
  - Severe psychiatric illness that may be exacerbated
  - Active infections
  - Patients amenable to ablation

## ICD Overview

- What's inside?
  - Recording of EGM events
  - Remote monitoring
  - Pacing/sensing/defibrillation electrodes



| Performance Characteristics for Induced Ventricular Fibrillation                      |                                     |                             |                                    |         |
|---|-------------------------------------|-----------------------------|------------------------------------|---------|
|   | Boston Scientific<br>(n = 32 tests) | Medtronic<br>(n = 54 tests) | St. Jude Medical<br>(n = 38 tests) | P value |
| VF zone cycle length  | >250 BPM                            | >240 ms                     | >240 ms                            |         |
| Detection duration  | 1 second                            | 18/24 beats                 | 12 beats                           |         |
| Rapid VT cycle length   | 185–250 BPM                         | 240–320 ms                  | 240–320 ms                         |         |
| Detection duration  | 2.5 seconds                         | 18/24 beats                 | 12 beats                           |         |
| Mean time to ICD charging:<br>seconds ( $\pm$ SD)                                     | 4.24 $\pm$ 1.46                     | 3.99 $\pm$ 1.03*            | 3.00 $\pm$ 0.4                     | <0.05   |
| ICD charge starts >5 seconds: n (%)   | 6 (19)                              | 2 (4)*                      | 0 (0)                              | <0.05   |
| Number of tests with ATP as first<br>therapy for induced VF: n (%)                    | 3 (9.4)                             | 0                           | 0                                  | <0.05   |
| Mean time to charging when ATP is<br>first therapy for induced VF:<br>seconds (range) | 10.1 (8.2–13)                       |                             |                                    |         |

\*Includes event which was adjudicated as VT.



## ICD Programming

- Typically capable of pacing and CRT (if Bi-V) as well.
- Arrhythmia detection:
  - Basic algorithms rely on duration and rate.
    - Duration of arrhythmia must be long enough to warrant a response
    - Arrhythmia detection is based primarily on rate.
      - Rate cutoff of 220 bpm is safe.
      - Two groups: one with high rate cutoff and one without:
        - » 20% without received inappropriate shock, 4% with did.
        - » All-cause mortality was double without!
  - SVT is slower than VF but can be similar to slow VTs
    - Need discriminators for SVT -- many based on QRS templates
    - AV dissociation in VT
    - Atrial rate vs Ventricular rate (but careful with VT + AF)
    - Interval stability (if AF driven)
    - Chamber of onset (abrupt in ventricle vs gradual)
  - Noise detection
    - Physiological (e.g T/P-wave oversensing)
      - High bandpass filters, pattern matching
    - Non-physiological (e.g. electromagnetic interference)
      - Frequency content is non-physiological
      - Typically from lead failure (can monitor impedance)
  - ICD HR Zones: VT <180 bpm, VT>250 bpm, VF/VT>250
  - Cardioversion vs. Defibrillation