Appendix 2.5.2
Sample Need Specification

An improved, long-term way to defibrillate the ventricle

Problem

- Defibrillation is the use of energy to "reset" normal rhythm
  - mainly used to terminate ventricular fibrillation (VF), a fatal arrhythmia
- Only long-term way to defibrillate is via an implantable cardioverter defibrillator (ICD)
- There are numerous limitations to the use of an ICD
  - amount of energy required to defibrillate with an ICD usually causes pain
  - ICD batteries last <3-7 years so ICD generators need replacement
  - though small, ICDs are placed in the chest resulting in cosmetic effects
  - getting “shocked” (defibrillated) can be psychologically traumatic

Burden of VF

- ICD statistics can serve as a surrogate for burden of potential and real VF
  - >260,000 patients with ICD indications, including those at risk (prophylactic)
  - >150,000 ICDs implanted annually in U.S.
  - cost >$3 billion worldwide currently
  - medications have been shown not to be as effective as ICDs
- Patients types
  - higher risk of VF in patients with low ejection fraction (EF), usually <30-35%
    - candidates for primary prevention ICD implantation (prophylactic)
  - patients who have had documented VF or survived cardiac arrest
    - candidates for secondary prevention ICD implantation

Mechanisms of VF

- VF is theorized to occur and persist via a four-stage mechanism
  - stage I (tachysystolic stage): premature ventricular beats can induce initial wavebreak with large reentrant wave; usually lasts 1-2 sec
  - stage II (convulsive incoordination): multiple wavelets and reentry over smaller regions of myocardium; lasts 15-40 sec
  - stage III (tremulous incoordination): wavelets and independent contraction in even smaller areas; lasts 2-4 min
  - stage IV (atonic fibrillation): slow passage of wavelets over very small distances with loss of all visible contractility
- VF most often seen in the setting of structural heart disease or ischemia
  - these can promote reentry and VF stages III and IV
ICDs deliver defibrillation energy in stage II

**Mechanism of defibrillation**

- Exact mechanism of why administration of a pulse of energy “resets” heart unknown

- Hypothesized to be due to cessation of most of the multiple wavelets and reentrant areas in VF, thereby permitting resumption of coordinated excitation and contraction
  - requires rapid induction of changes in transmembrane potential of myocytes
    - prolonging of refractoriness of action potential may be important
  - requires a critical mass of myocardium (>75%) to be involved
  - must not reinitiate fibrillation
    - if only part of the heart affected, heterogeneity of refractoriness can occur leading to reentry and eventual fibrillation
    - shock that halts VF must not reinitiate VF through same mechanism by which a shock of same strength during vulnerable period can initiate VF (upper limit of vulnerability)
  - exact ionic mechanisms of changes in transmembrane potential not known

- Defibrillation can be achieved using various waveforms
  - biphasic waveforms require less current and energy than monophasic waveforms to defibrillate and are usually more successful
  - waveform duration, waveform shape, electrode impedance, and defibrillator capacitance all important in success of defibrillation

- Energy required to defibrillate is based on minimum potential gradient that needs to be created in a sufficient amount of myocardium
  - location of defibrillation electrodes play significant role
    - from body surface, usually need 200-360 Joules for defibrillation
      - only 4-20% of current reaches heart, due to loss through tissue
      - with leads in heart, usually only need 20-34 Joules
  - distance between electrodes, amount of heart “within” circuit, size of electrodes, respiration, etc… also play role
    - large epicardial patches require less energy for defibrillation
  - mathematical formulations model how a pulse of energy in one area can affect transmembrane potential at a distance away from electrode
    - the cell membrane and gap junctions are viewed as a high-resistance barriers while the intra- and extracellular spaces are low-resistance spaces
    - current is forced to “go around” these high-resistance barriers
      - this exit and reentry of current causes various degrees of depolarization or hyperpolarization in different parts of the intracellular space
o since the barriers function as discontinuities, they can be thought of as secondary sources of action potentials
o this causes perpetuation of the current at a distance from the electrode

• **Methods of defibrillation**
  
  § ICD – only current long-term solution
  • circuit is from coil on lead in ventricle (usually right) to a second coil more proximal on lead, to ICD generator, or to subcutaneous array on patient’s side/back
  • may also be attached to epicardial patches, but uncommon
  § LifeVest – for short-term use outside hospital
  • usually if temporary risk of VF or as bridge to ICD
  § External pads or paddles – for emergency or while in hospital
  • circuit formed by paddles or two patches
  § Internal paddles placed on surface of heart – usually only during open heart surgery

• **Patient issues with ICDs**
  
  § Pain
  • defibrillation feels like being “kicked in the chest”
    § likely due to activation of skeletal muscles and nerves in the chest and abdomen
  • patient can feel even 1-2 Joules of energy
  • changes in sensing require re-testing of defibrillation threshold
    § requires induction of VF and potential risk of death and sensation of “shock”

  § Generator implantation and replacement
  • internal leads require permanent implantation in venous system and fixation to heart
    § can become infected requiring removal, which carries significant risk
    § leads may fail, requiring additional leads which can reduce lumen of vessel
  • current ICD batteries last <3-7 years leading to need for generator changes
    § generator changes expose patient to risks of additional procedure and infection
    § requires re-testing of defibrillation threshold

  § Cosmetic
  • though ICDs small, implantation in the chest results in small scar
  • in thin patients, may often see outline of device

  § Psychological
  • sensation of being “shocked” can be very traumatic
- increases thoughts about potentially lethal events and possible death
- increases fear of performing activities that may lead to VF and “shock”

- Other
  - devices may be affected by magnets and may limit ability to get MRIs
  - devices can only be interrogated with programmer
    - sometimes difficult to ascertain device settings in emergency setting

- New approaches being developed to treat arrhythmias
  - Subcutaneous, leadless ICDs only for defibrillation
    - sensing may be an issue requiring methods beyond sensing only rate
    - may require very high energy to successfully defibrillate
  - Intravascular ICD
    - could be low-cost and implanted in many patients
      - possible first-line therapy prior to permanent ICD
    - few shocks only
    - may be thrombogenic
  - Cell therapy
    - May be able to reconstitute damaged, non-functioning tissue thereby preventing VF

- Need criteria – for Fibrillation Fiona: A 64 year old active, currently asymptomatic female with a history of ischemic cardiomyopathy who underwent prophylactic ICD implantation after medications optimized

- Absolute requirements
  - must improve at least one of the four main limitations of current ICDs without leading to new limitations or worsening of current benefits or limitations of ICDs:
    - pain from defibrillation
    - need for replacement every <3-7 years
    - cosmetic effects
    - psychological effects
  - if affects procedure, should not be any more invasive than current implantation or replacement procedures
  - should have no effect on current medical therapy and should not be affected by medications

- Desirable requirements
  - no effect on cardiac function
  - easy-to-use/learn for average electrophysiologist
  - patient-friendly