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

    - since the barriers function as discontinuities, they can be thought of as secondary sources of action potentials
    - 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 my 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

