Chapter 18
Medical Electronics Design, Manufacturing, and Reliability

Mark Porter, Robert Erich, and Mark Ricotta

Abstract Medical devices cover a wide range of products and applications that can be as basic as a tongue press, or as complex as an implanted life-sustaining therapy delivery device such as an Implantable Pulse Generator (IPG), or Implantable Cardiac Defibrillator (ICD). This chapter will provide an overview of medical devices that have electronic content, and an in-depth review of implantable medical devices design, manufacturing, and reliability considerations. The authors will examine industry trends, discuss key design considerations, and provide a review of product development, manufacturing, and reliability considerations for implantable medical electronics.

18.1 Introduction

The electronics industry has seen decades of consistent growth spanning multiple generations and forever changing the landscape of product design and consumer expectations. From the advent of the transistor by Bell Labs in 1948 [1] to today's most complex deep miniaturization CMOS integrated circuits, electronics have transformed the way we live, work, communicate, shop, entertain, and interact. Electronics content has found its way into nearly every aspect of our daily routine. Major market segments include industrial, computing, consumer electronics, telecommunications, and the traditional high reliability markets of aerospace and automotive. Evolution in this space has seen increasing electronic content in market segments that have traditionally been mechanical application. For example, automotive electronics applications have evolved to include engine control, audiovisual, wireless controls, internet connectivity, and an array of sensors too large to list. Household electronics applications have expanded to include audiovisual, computing, wireless, numerous appliances, and a growing number of software application (app)-based controls such as heating/cooling, lighting, and security.

M. Porter • R. Erich (✉) • M. Ricotta
Medtronic Cardiac Rhythm and Heart Failure, 2343 West Medtronic Way,
Tempe, AZ 85281, USA
e-mail: Mark.Porter@Medtronic.com; robert.j.erich@medtronic.com;
Mark.Ricotta@Medtronic.com

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Medical devices of all types contain electronic content and just as in the examples from automotive and household electronics, medical devices are taking advantage of momentum in the electronics space.

Medical electronics enable products and applications that restore health, alleviate pain, and create the ability of active health management through advanced sensors and diagnostic tools. Consider the simple example of a thermometer; a traditional application may be a sealed glass tube containing a liquid that expands and contracts as temperature changes. A modern thermometer, however, may be a much more complicated electronic device consisting of a circuit board, a battery, and a digital display. In this example, an application was improved upon based on the availability of electronic content. There are also several examples of medical electronic applications that were made possible through the development of custom electronic circuits and materials.

Implantable Pulse Generators (IPGs)—more commonly called Pacemakers—and Implantable Cardiac Defibrillators (ICDs) are examples of medical application that drove the development of custom electronics materials and processes. The first implantable pacemaker was designed in 1959 by an electrical engineer named Wilson Greatbatch, with the assistance of Dr. William Chardack and Dr. Andrew Gage. The Chardack-Greatbatch implantable pacemaker was patented (patent number 3,057,356) and licensed to Medtronic for manufacturing in 1961 [2]. In that era, the concept of implantable electronics represented cutting-edge medical technology, and there was very little process, component, and material infrastructure to support growth in this area. Components and materials were engineered, evaluated, and tested by medical companies to verify and validate safety in these nontypical applications. This was the forefront of Class III medical electronics development.

Throughout this text are examples of today's state-of-the-art advanced materials and processes that will enable tomorrows most sophisticated electronics applications. In this chapter, the authors will examine how electronics development is being leveraged to drive next-generation medical electronics. Medical electronics, in general, will be enabled to grow through using a fast-follower approach to the development in consumer electronics. Technology platforms developed for applications such as portable electronics, computing, gaming, and telecommunication can be adopted for medical application. Industry wide reliability data for standard components, material, and processes can be leveraged to help narrow design choices and limit reliability testing to use condition-based requirements. This chapter will provide a background on medical electronics, share an overview of working in a regulated environment, examine key drivers for the medical electronics space, and provide an in-depth review of implantable medical electronics design, development, qualification, and manufacturing.

18.1.1 Review of Medical Electronic Products Classification

It is important to understand whether a product is classified as a medical device because there are restrictions and requirements for operating in this highly regulated space. In the early years of development for medical devices, no formal regulatory system existed. Companies were free to sell devices using their own internal oversight with market and clinical acceptance the de facto standard of product efficacy. In the United States, the FDA started regulating the introduction of medical devices in 1976 [3] and other government agencies in many regions around the world began providing directives as well.

The United States Food and Drug Administration (FDA) regulates a broad range of medical devices from low risk disposable applications such as tongue depressors, to medium risk products such as medical beds, and high-risk, life-sustaining applications like pulse generators and defibrillators. Within the FDA, the Center for Device and Radiological Health (CDRH) is responsible to provide oversight and regulation for companies who manufacture, repackage, relabel, and/or import medical devices within the United States. The Quality System Regulation (QSR) that defines this space is 21 CFR 820, and each manufacturer is responsible to establish and follow this quality system in support of their FDA registration. In Europe, there are several directives, including the Medical Devices Directive (MDD) and the Active Implantable Medical Devices Directive (AIMDD). Certification of conformity to these regulations is handled by the Technischer Überwachungsverein (TÜV), in English the Technical Inspection Association. In Japan, the Ministry of Health, Labor, and Welfare (MHLW) carries out regulatory functions. Other countries around the world may have their own formal system or rely upon the earlier agencies to ensure safe and effective use of implantable medical electronics. Outside of the U.S. and EU, other examples include Health Canada, the China Food and Drug Administration, the Japan Ministry of Health, Labour and Welfare.

There are also international standards organizations and working groups who help to drive standardization between the regulating bodies. The International Standards Organization (ISO) has created ISO standard 13485 "Medical Device Quality Management Systems—Requirements for Regulatory Purposes" to define requirements for a quality management system for the manufacture of Medical Devices. The Global Harmonization Task Force (GHTF) was created in 1992 to help drive alignment between various national and international standards. From the GHTF we get the standard process validation guidance for Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ). The GHTF served as the foundation for today's International Medical Device Regulators Forum (IMDRF). The IMDRF is a group of voluntary participants from international medical device regulating bodies who collaborate to drive standardization of international requirements and promote patient health and safety.

The FDA offers the following Medical Device Definition [4].

Medical devices range from simple tongue depressors and bedpans to complex programmable pacemakers with microchip technology and laser surgical devices. In addition, medical devices include in vitro diagnostic products, such as general purpose lab equipment, reagents, and test kits, which may include monoclonal antibody technology. Certain electronic radiation emitting products with medical application and claims meet the definition of medical device. Examples include diagnostic ultrasound products, x-ray machines, and medical lasers. If a product is labeled, promoted, or used in a manner that meets the following definition in section 201(h) of the Federal Food Drug and Cosmetic (FD&C) Act it will be regulated by the Food and Drug Administration (FDA) as a medical device and is subject to premarketing and postmarketing regulatory controls. A device is:

- "An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:
  - Recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
  - Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
  - Intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."

18.1.2 Class I Medical Devices

Class I medical devices are devices which meet the minimum requirements to be classified as a medical device and have the low to moderate potential to cause patient harm. Due to their low risk to patient safety, they generally require the lowest level of process controls. Most Class I medical devices are exempt from premarket approvals (classifications can be "with exemptions" or "without exemptions"). Typical controls for a Class I medical device would include manufacturer registration and device listing, labeling regulation, and following a quality system that demonstrates Good Manufacturing Practice (GMP).

Examples of Class I medical products: tongue depressors, tooth brush, manual stethoscopes, hospital beds, crutches, manual wheel chairs, and bandages.

18.1.3 Class II Medical Devices

Class II medical devices are similar to Class I medical devices in that they may or may not require any type of premarketing approval, depending on the exemption classification that is determined in the classification process. In general, Class II medical devices have a higher patient safety risk than Class I and are subjected to a higher level of process controls requirements. While the controls for Class I products still apply, additional controls may be warranted for a Class II product

based on the increased level of patient safety risk. These additional controls, or Special Controls, may include such requirements as product performance standards, special labeling, or postmarket surveillance.

Examples of Class II medical products: external pulse generators, catheters, thermometers, blood pressure cuffs, contact lenses, acupuncture needles, and powered wheel chairs.

18.1.4 Class III Medical Devices

Class III medical devices represent the highest level of potential risk to patient and have the highest level of controls applied. As with Class I and II, general controls and special controls apply. In addition, Pre-Market Approval (PMA) is required. Some requirements of a PMA include but are not limited to description of the device, indication(s) for use, a complete description including specifications, components, and materials, summary of manufacturing process and controls, performance standards, and clinical study results.

Examples of Class III medical devices include Implantable Pulse Generators (IPG), Implantable Cardioverter Defibrillators (ICD), heart valves, and coronary stents.

18.2 Key Drivers for Growth in Medical Electronics

To better understand growth in the medical electronics space, it is helpful to step back and consider some of the key drivers. Growth will likely be sustained in this space, and we will continue to see both evolutionary and revolutionary products and applications being developed as the global population and life expectancy both continue to rise. Medical electronic device designs will continue to push the envelope for product features and health benefits, and continue to blend expectations with consumer electronic functionality and performance. Product segments will continue to blur the line between medical devices and consumer health and well-being products.

18.2.1 Aging Population

It is commonly accepted that life expectancy and the global population continue to rise. With a substantial increase in the total number of elderly the overall need for medical care is following the same trend. The Federal Interagency Forum on Aging-Related Statistics publishes data and research of the rising population [5]. In this work, the growth of the U.S. population age 65 and over was

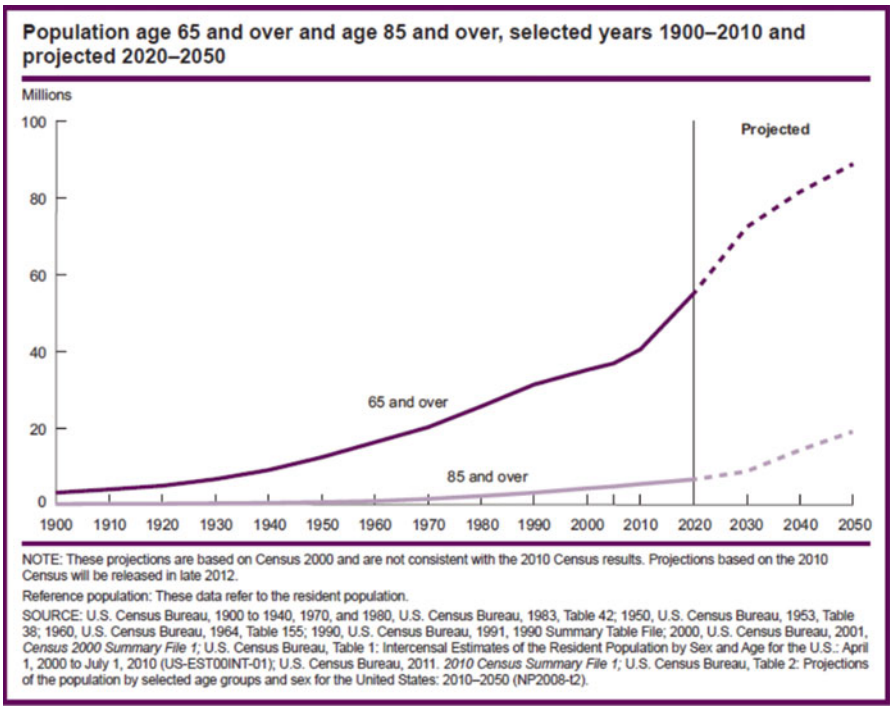


Fig. 18.1 Growth trend for population age 65 and over, 85 and over, in millions

documented from 1900 through current, and projected out to 2050, as shown in Fig. 18.1. This work shows substantial and ongoing growth in aging population. According to this research, the number of Americans aged 65 and over will double between 2010 and 2035. In addition to the rise in aging population, the cost for drug-based therapy is also on the rise, making medical device-based therapy an increasingly competitive alternative to medication.

18.2.2 Demographic Shift Toward Tech-Competent User Base

With the increase in population and elderly patients comes an increase in the likelihood that a patient has a basic operational understanding of electronics products. Email and the internet have been standard office tools for well over two decades, and handheld electronics have become ubiquitous in our daily lives. Whether it is derived from using a complicated cable television remote, or learning to use a tablet or personal computer to video chat with grandchildren, the tolerance for operating electronics has never been higher in the elderly population. This finds its way into the medical marketplace in the willingness and ability to monitor health

remotely, perform data download follow-up visits, or use simple health monitoring devices in situations where visits to the doctor standard of care are a thing of the past. App-based health monitoring is a growing trend because it can take advantage of existing infrastructure through smart phones and sensors and be delivered to a wide audience through a virtual marketplace of application downloads. The global network of cellular phone carriers has created the infrastructure so that anyone with cellular service can have access to a network of virtual medical care. In rural or developing areas, this infrastructure goes beyond those who have access to a traditional landline telephone. Examples of app-based health monitoring include motion sensing, heart rate sensing, step counters, and blood pressure readings.

18.2.3 Target Market Moving from Treatment to Detection and Prevention

At the same time electronics are becoming common place, advanced development with a variety of sensors has been on the rise. Doctors have been predicting an evolutionary state where proactive medicine would take the place of symptom-based care. This is a common believe in some medical fields, for example, osteopathic medicine and chiropractic care. Medical device technology has followed along this thought process with leading medical device manufacturing companies shifting focus from treatment to detection and eventually to prevention. Years of medical research has allowed doctors to study biometric outputs and link them to disease states for a predictive understanding of future disease states. No, it is not a crystal ball, but advanced statistics allow for enough correlation between biometrics outputs and disease states to substantiate behavior and lifestyle changes based on sensing and create meaningful outcomes for patient health and well-being.

18.2.4 Availability of Advanced Electrical Content

Medical electronics are poised to take advantage of the great opportunity provided by the explosion in growth of consumer electronics. Tremendous advances have been made in microelectronic materials, assembly equipment, assembly process, and component design. Advanced, miniaturized components are readily available from a variety of supplier and distributors. There is sufficient assembly infrastructure to keep costs low, and equipment platforms that serve high volume consumer electronics products can be leveraged for medical devices. Miniaturization in the portable electronics space has paved the way for downsized components, wafer fabrication geometry node shrinks, higher levels of silicon chip integration. Advanced substrate development allows aggressive interconnect circuit density between chips and components.

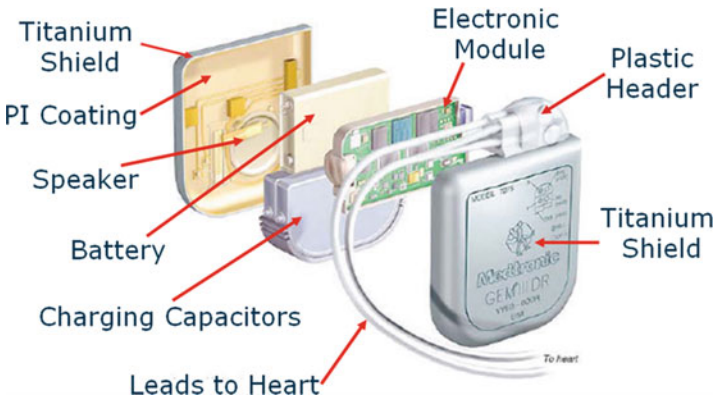


Fig. 18.2 Exploded view of implantable cardiac defibrillator

With the advent of the implantable pulse generator, electronic materials and components need to be developed for use in this advanced medical application. Early medical device companies were on the leading edge of electronic component and material design and development in this space, often taking on significant performance and reliability challenges that required extensive research and field performance evaluations. In today's market, medical companies have the ability to choose from a vast selection of materials that have well-documented field performance against standards, which allows simplified development testing that can focus on field use conditions.

Consider the example of an Implantable Cardioverter Defibrillator (ICD). Figure 18.2 shows the exploded view of a Medtronic ICD. The device consists of a titanium case and a plastic header that houses the lead connections. On the inside, there is an electronic module, a battery, and the charging capacitors that store and deliver high electrical pulses to the heart. The electrical circuit used in this application bares strong similarity to electronics that can be found in consumer electronics. It consists of a multilayer circuit board, using both surface mounted components and an array of wire bonded integrated circuits. Key assembly technologies include aluminum wedge bonding, gold themosonic ball bonding, flip chip assembly, and surface mount technology. The final electronic module is sized using a router. Medical device companies maintain a core competency in therapy development, device design, and device manufacturing. While the ICD itself is a highly sophisticated custom medical device, much of the electronic content and design elements are standard material and processes that are similar to what would be found inside of a smart phone or remote control.

18.3 Design Concepts and Enabling Technologies

Medical electronics share similar design concepts to other types of mainstream electronics. From consumer electronics, there is a similar drive for smaller, faster, lighter, and less expensive devices. From aerospace and automotive, medical electronics thrive off the same drive for reliability and predictable performance. Following find a brief review of several key design considerations for medical electronics.

18.3.1 Low Power Consumption

Looking specifically at implantable applications, battery life is paramount in device performance because it dictates how long a device can remain implanted and functional in the human body. Most implantable electronics are battery powered and hermetically sealed, so when a battery approaches end of life the device needs to be removed (explanted) and replaced. Because of the high impact to the patient battery longevity remains one of the key design features.

Power consumption requirements place severe constraints on implantable medical device design practices, technology choices, and applicable algorithms and therapies. Devices must operate for 5–10 year lifetimes on a single battery. Cardiac devices do not use rechargeable batteries due to the critical nature of applied therapies, although some spinal stimulation devices utilize inductive-coupled charging techniques to allow near-continuous high power output over extended periods of time, which would otherwise deplete the battery in a relatively short time frame.

In conflict with lifetime requirements, there is a desire to increase therapeutic efficacy through the use of new input sensors, advanced signal processing algorithms, large volumes of diagnostic data, and high data rate wireless communication [6]. Each of these desirable features contributes to battery depletion and must be managed through the use of integrated circuit design choices, ultralow leakage component selection, and power gating. These practices in turn place additional requirements on the selection, characterization, qualification, and validation of each element that goes into the implantable system.

18.3.2 Miniaturization

Downsizing implantable medical electronics is a significant driver for meeting challenging customer requirements and increasing product acceptance. Beyond just a matter of consumer preference, size, weight, and shape all drive patient safety and comfort. From the perspective of weight, implanted electronics sit in a tissue

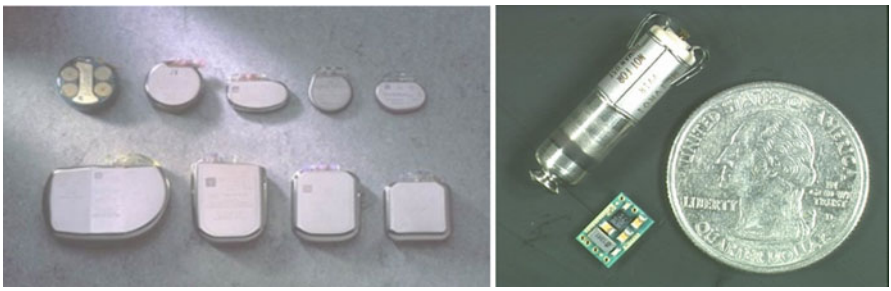


Fig. 18.3 View showing downsizing of IPG and ICD products, along with the leadless Medtronic Micra™

pocket cut just under the skin, and a patient can feel the weight of the device. Size is important for comfort level, overall mobility, and ease of motion. In addition to the feel, many patients have a strong appreciation for discretion and don't like an implanted device to be noticeable to a casual observer. Often patients do not like to be reminded that they have an implanted device assisting their health and wellness. Shape serves similar concerns of patient comfort, as angles and edges can poke out where as a more rounded shape can contour under the skin. Physicians typically put a high focus on product feature set, ease of programming, and operation (interrogation) and longevity. Patient inputs put a stronger emphasis on size, shape, and overall reliability.

Figure 18.3 shows the progression of downsizing in the IPG and ICD space, showing several generations of products with a 10–20 % reduction in size which is typical for each generation. The image on the right side of Fig. 18.3 shows the Medtronic Micra™ leadless pacemaker, which represents an evolutionary reduction in size. At the time of its launch, it was the smallest implantable pacemaker in the world, at just 24 cm in length, and less than 1 cm^3 in volume. This device does not use traditional leads to deliver the pacing therapy from the device to the heart. Instead, this device is implanted directly into the heart, through a catheter inserted in the femoral vein. This device represents an astonishing size reduction of 90 %, moving from approximately 10 cm^3 for a traditional pacemaker to under 1 cm^3 for this insertable device. Custom integrated circuit design, power management, downsized passive components, advanced organic substrate, and a significant level of silicon packaging integration make this design possible.

For portable medical devices, the demands for miniaturization are much more in line with consumer electronics. Patient feedback on device design includes a desire for downsizing, easy user interface, and an industrial design that is more in line with popular electronics rather than something that resembles a medical device and looks like it should be in a hospital or clinical setting. For patients who need to carry around a monitor device, it is much more comfortable to have it seem like a phone or video game than a medical device, helping maintain discretion for whatever medical condition they may be monitoring or treating. Figure 18.4 shows the progression in downsizing of the Medtronic Carelink home monitor

Fig. 18.4 View showing down sizing of desktop monitor products

family of products. These products are used to read electronic data from the implanted device and transmit that data to a patient management network that can be accessed by a physician. The device on the left is a landline-based wired device with a magnetic reader tethered to the bedside monitor base station. The center image shows a smaller, wireless version of the same monitor. The image on the right is the most recent design in this product family. Rather than using a base station, this reader transmits data to an App on the patient's smart phone or tablet, and the App then interfaces with the patient management network. The internal electronics in these applications are similar and not aggressively downsized. The dynamic driving of this product evolution is the advancement made in wireless technology and the proliferation of smart phones and tablets within the patient population.

18.3.3 Growth and Standardization of Wireless

Wireless communication has advanced to the point where it has become a standard design feature and a minimum consumer expectation for many types of product. This consumer expectation is now making its way into the medical space and is especially prevalent with desktop and body-worn applications. Cellular service growth drove the expansion of the global cellular network for telecommunications. WiFi has emerged as the Wireless Local Area Network (WLAN) standard, operating to the (Institute of Electrical and Electronics Engineers) IEEE 802.11 communication protocol. For Personal Area Networks (PANs) Bluetooth has emerged as the leader for wireless communication protocol for a wide array of consumer products. Bluetooth uses short wavelength Ultra High Frequency (UHF) radio frequency waves between 2.4 and 2.485 GHz, operating to the IEEE 802.15.1 communication protocol. Examples include computer peripheral devices, mobile phone peripheral devices, wireless speakers, and audio headsets. A key advancement in Bluetooth technology is the reduction in power needed to transmit and receive, making it increasingly attractive for medical electronic applications.

For early medical electronic wireless applications, dedicated frequency bands were identified. Medical Device Radiocommunication Service (MedRadio) is a

dedicated frequency band isolated between 401 and 406 MHz. There is a core band within MedRadio known as the Medical Implant Communication Services (MICS) band which operates between 402 and 405 MHz. These bands are isolated only for wireless communication of medical devices, which protects the bands from bandwidth limitations and interference issues. However, it also limits the ability for medical devices to communicate with standard electronics through WiFi or Bluetooth.

As Bluetooth and WiFi stabilize as the wireless communication protocols for our day-to-day electronic products, consumers expect the same from medical devices. Consumers are not willing to accept a device that cannot exchange information with their smart phones through Bluetooth or through their WiFi home networks. With design considerations including data security and transmission integrity, most of today's implantable electronic devices communicate with custom protocols within the MedRadio band. New home monitoring devices leverage Bluetooth to exchange information between the patient smart phone or tablet and the desktop monitor, allowing patience the convenience of initiating sessions and monitoring progress using a smart phone-based app. It is possible that next-generation devices may be able to exchange data directly with an implanted device.

18.3.4 Sensors, Accelerometers, and Medical Monitoring

Low cost consumer electronics content combined with wireless WLAN and PAN availability have led to growth in the area of portable and wearable health monitoring. Development of biometric sensors and accelerometers is paving the way for health monitoring applications to take advantage of the existing infrastructure for wireless portable electronics and offer consumers low cost fully integrated options to monitor health and well-being. This emerging area flirts with the boundary of medical product classification, with some products considered medical devices and others considered consumer health tracking, or wellness devices.

Sensor detection may include but is not limited to sound, temperature, pressure, light, color, energy, and magnetism. Accelerometers are a type of sensor that measure acceleration or a change in speed. Advanced accelerometers contain motion sensing elements that turn movement into a voltage, and the magnitude of the voltage change is calibrated to speed. This can be done in three dimensions so that the change can be defined as a vector. A popular example of the use of an accelerometer to detect motion is in wireless video game controllers, where movement in the game controller is taken as input to the video game emulating physical motion such as throwing motion, jumping motion, a golf swings, or a bowling throw. This same technology can be applied in a health care application which can track activities such as running, jumping, and climbing. Measuring and tracking changes in these (and other) types of biometric parameters can lead to the development of applications that can diagnose and/or treat a variety of medical conditions. Examples of conditions that can be monitored, treated, or even potentially

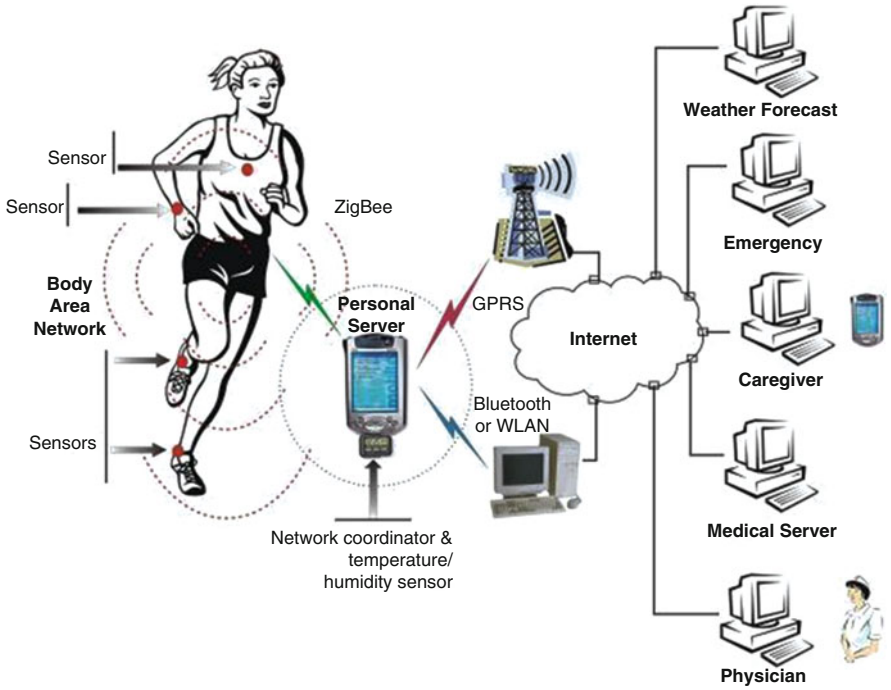


Fig. 18.5 Conceptual diagram of body area network

prevented through the use of sensing electronics include but are not limited to cardiovascular fitness, weight, heart rate, hypertension, heart arrhythmias, snoring, sleep apnea, seizures, blood oxygenation, or diabetic insulin levels.

Figure 18.5 shows a conceptual image of an athlete wearing multiple sensor devices that might detect and record metrics such as heart rate, motion, step count, body temperature, or altitude. The data taken on these sensors can be communicated through Bluetooth to a personal device such as a smart phone, and that device can communicate through the internet to a variety of data end users. These may include physicians, caregivers, or emergency contacts. In this example biometric data can be consolidated over a PAN, communicated to the internet over a WLAN or cellular network, and be provided to a variety of end users who can manipulate the data for virtually unlimited applications.

18.3.5 Advanced Wafer Fabrication Availability

The fabrication process to manufacture a semiconductor integrated circuit is a costly one. Fabrication equipment is expensive and the facilities requirements are extensive, including handling of corrosive chemicals and the need to ensure

extreme cleanliness with particulate-free manufacturing. As lithography features decrease in size, Class 1000 cleanrooms (less than 1000 particles greater than 5 μm per cubic foot) that were once standard in the early days of wafer fabrication have given way to fabrication cleanliness requirements as low as Class 1 (less than 1 particle greater than 5 μm per cubic foot). As a point of reference, a hospital operating room typically operates at Class 10,000. Normal fluctuations in environmental conditions must be controlled as variations in temperature, humidity, and vibration can all impact the wafer fabrication process. With the number of transistors on an integrated circuit extending into the millions or even billions, defect management is critical to yielding even a single good chip.

As wafer fabrication lithography nodes (standard feature size) scale downward, the cost of fabrication increases. It has become increasingly difficult for manufacturing companies to afford internally run wafer foundries, which has given rise to the fabless semiconductor model. There are now a wafer foundry companies whose sole business is subcontract wafer foundry service. Consolidation of advanced wafer foundries moving toward a subcontract service model allows design companies to shed the cost of operating a fab and focus on product development. There is mutual benefit from this subcontract model; it allows design companies access to state-of-the-art fab technology and design libraries at a competitive cost, while it also consolidates global demand from for device manufacturers allowing foundries to fill fab capacity and drive competitive operating costs.

For the medical device manufacturers, this means they have access to the worldclass wafer fab services without having to carry the cost of foundry operations. Quality is paramount for medical device manufacturing, but quality control for advanced wafer fabrication processes has been optimized through the economic impact of yield loss for high volume electronics applications. Medical device designers share in the availability of advanced processors, decreased cost of memory, and a wide range of fabrication technology for both analog and digital circuit design.

18.3.6 Silicon Integration and Electronic Packaging

Electronic packaging is the field associated with design and manufacturing of chip carriers which house and protect integrated circuits (IC). The electronic package creates the electrical, mechanical, and thermal interface between the IC and application circuit board. Common examples of electronic packages include the Dual Inline Packages (DIP), Standard Outline Transistor (SOT), Small Outline Integrated Circuit (SOIC), Ball Grid Array (BGA), Chip Scale Packages (CSP), System In Package (SIP), and Wafer Level Chip Scale Package (WLCSP), to name only a few.

There are several benefits of using an electronic package versus designing the IC directly onto the circuit board. The feature sizes capable to be achieved on a circuit board can be orders of magnitude larger than the feature sizes on the pad ring of an

IC, so the package acts as an interposer to fan out the IC interconnect to larger geometrics that will match circuit board feature sizes. It also allows the circuit board assembler to be able to focus on soldering the electrical interconnects instead of having to perform more complex IC attach methods like wire bonding or a complicated C4 (controlled collapse chip connection) soldering (flip chip soldering). Electronic packaging also may include mechanical reliability benefits, thermal interface improvements, and provide the ability to be able to rework complex ICs on the circuit board through reflow soldering.

Traditional circuit design for implantable medical electronics used a hybrid circuit approach; ICs were attached in ceramic cavities and wire bonded alongside of soldered components. There were several design and manufactuing challenges for using ceramic substrates: design features were coarse by today's standards leading to low compoent density, manufactuing costs were higher compared with laminate substrates, and assembly throughput was low. Following trends in consumer electronics, hybrid circuit assembly migrated toward surface mount assembly onto organic printed wiring board (PWB) substrates. This strategic technology platform change allowed for a significant improvement in size, cost, and manufacturability. Depending on design complexity, PWB substrates could be as simple as four-layer through-hole designs or as complex as multilayer high density interconnect (HDI) designs using microvia interconnect.

Figure 18.6 shows the progression in design of an ICD circuit over three generations of design evolution. On the top left, the image shows a PWB circuit that uses flip chip interconnect for the IC attach process. Flip chip interconnect was originally used because it allowed for the smallest IC footprint on the board because

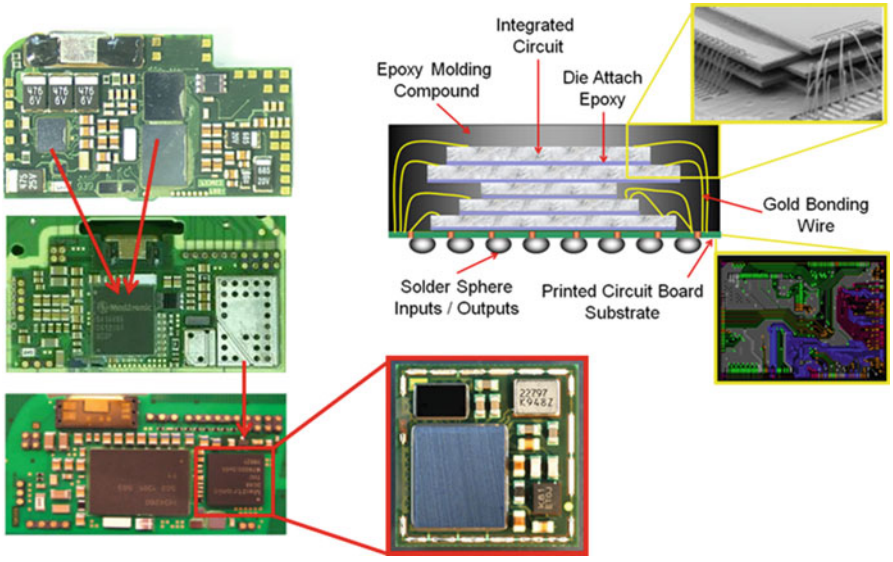


Fig. 18.6 Electronic packaging in an implantable ICD application

the wire bond pad ring can be eliminated in exchange for the flip chip solder interconnect. In the next evolution of design, those chips have been integrated into a fine pitch ball grid array (FBFA). The FBGA stacks the ICs vertically to further eliminate precious real estate on the PWB design. The blow up image to the left shows a depiction of a FBGA cross section, along with digital images of the actual stacked IC showing the wire bonds. In this design revision, the space saved by the move from flip chip to FBGA allowed for the inclusion of a telemetry radio to be added to the circuit with no size penalty. This is significant, because while it was important to add the wireless telemetry feature to the device, it was not acceptable to increase the overall device volume. In the third design evolution shown on the bottom left, again there is a FBGA housing all of the ICs, but the telemetry radio has moved from discrete component assembly on the PWB, to the use of a fully functional SIP radio module. The blow up to the right of the image shows the radio module with the overmold compound removed to expose the underlying components.

18.4 Implantable Medical Electronics Design and Reliability

18.4.1 Implantable Medical Electronic Applications

The first implantable pacemaker, or Implantable Pulse Generator (IPG), was developed in the late 1950s. Although solid-state transistors allowed the devices to be small enough to run on battery power, these first products were the size of a hockey puck, had a fixed output rate, and required frequent replacement due to battery wear-out. Over the decades since that time, improvements in available technology have allowed an ever wider array of therapies to be delivered to patients to treat many additional forms of illness.

As integrated circuit technology advanced, devices became smaller and more advanced. The displaced volume of pacemakers was a key factor affecting patient comfort, eventually resulting in the ability to implant the device in the pectoral region. In the early 1980s, the introduction of rate-responsive pacemakers meant that the device could now respond to the physiological needs of a patient during exercise, which gave rise to an increasing market size as doctors looked to provide better outcomes and quality of life for their patients.

At the same time that implantable pacemakers were being developed, it was recognized that high-energy shocks could reset a heart that had gone into abnormal rhythms, which otherwise often resulted in death within minutes. External defibrillators saw widespread use in emergency settings in hospitals and ambulances, but were not available in the settings where they were most needed: at the point of use where the onset of an arrhythmia occurred. By the early 1990s the first Implantable Cardioverter Defibrillators (ICDs) were introduced. Due to the requirements of high-energy delivery capacitors alongside the traditional electronics and batteries

of IPGs, the volume of these devices was quite large. Once again, advances in technology have allowed them to shrink to the point where pectoral implant is possible.

A major disease state that remained untreated by electrical stimulation until the mid-1990s was heart failure. In this condition, the heart muscle loses strength and begins degenerating, eventually resulting in patients becoming bedridden. In order to effectively assist the heart in regaining synchrony, both sides of the heart must be paced together. This required a lead that could be introduced into the left side of the heart, which is at much higher pressure than the traditional lead location in the right ventricle. With the introduction of left-heart leads and cardiac resynchronization therapy (CRT) devices, many patients saw quality of life improvements and a reduction in the severity of their condition.

Continued exploration of maladies that could be treated with electrical stimulation has resulted in deep-brain stimulation for dystonia, tremor, and Parkinson's disease, along with spinal cord stimulation for chronic pain. All of these devices are based in part on technologies that were developed to treat cardiac problems.

In addition to using devices to treat clinical conditions, recent advances in memory storage have enabled the use of small implantable devices to record heart rhythms over an extended period of time. These devices are used to help diagnose the presence of arrhythmias that result in syncopal episodes (fainting) where traditional methods such as halter monitors or tilt table tests are uninformative. Figures 18.7 and 18.8 show some examples of different generation implantable medical devices and the time when they were introduced to the market.

Fig. 18.7 Implantable electronic devices. *Top row*: pacemaker, drug pump, defibrillator. *Second row*: pressure monitor, neurostimulator. *Third row*: loop recorder, transcatheter pacemaker

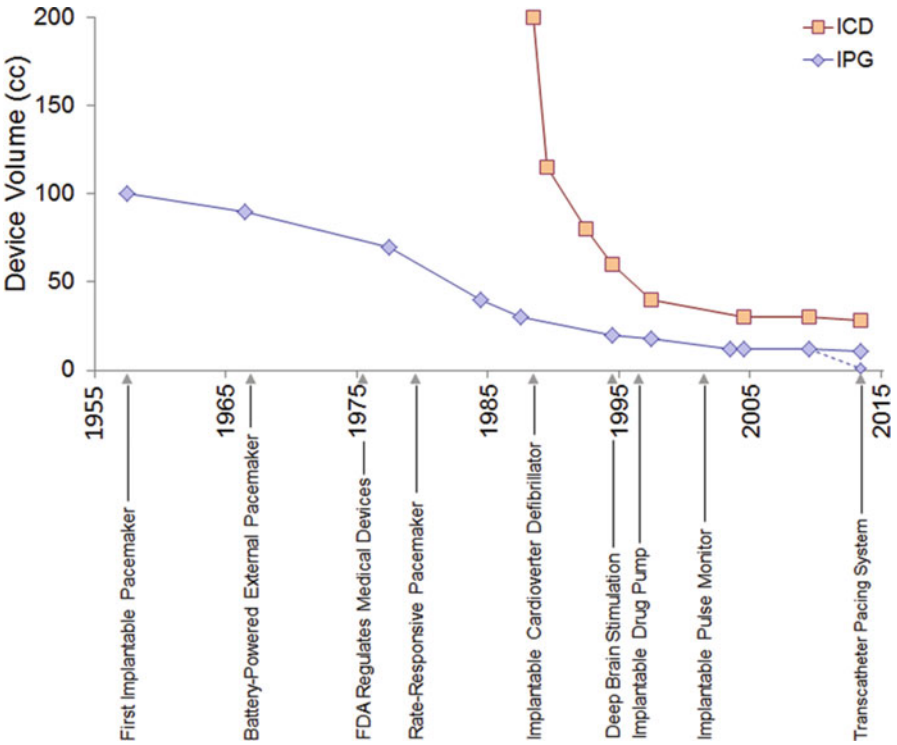


Fig. 18.8 Implantable device timeline

In all of the cases outlined before, advances in silicon, battery storage, capacitor performance, and manufacturing technologies have played key enabling roles. Similar to commercial electronic systems, increases in performance have accompanied decreases in size. The following figure shows the progression of shrinking device volumes, which is an important patient comfort consideration. These advances have created reliability challenges across many aspects of device design, qualification, and test.

18.4.2 Development Process

Figure 18.9 provides a high-level view of the implantable medical device development flow, along with the relationships among the major tasks. Qualification of each of the manufacturing processes and components that go into the design and construction of a medical device serves as a series of gates before each successively more complex system can be qualified. These constraints are shown by the gray, dotted lines in the figure.

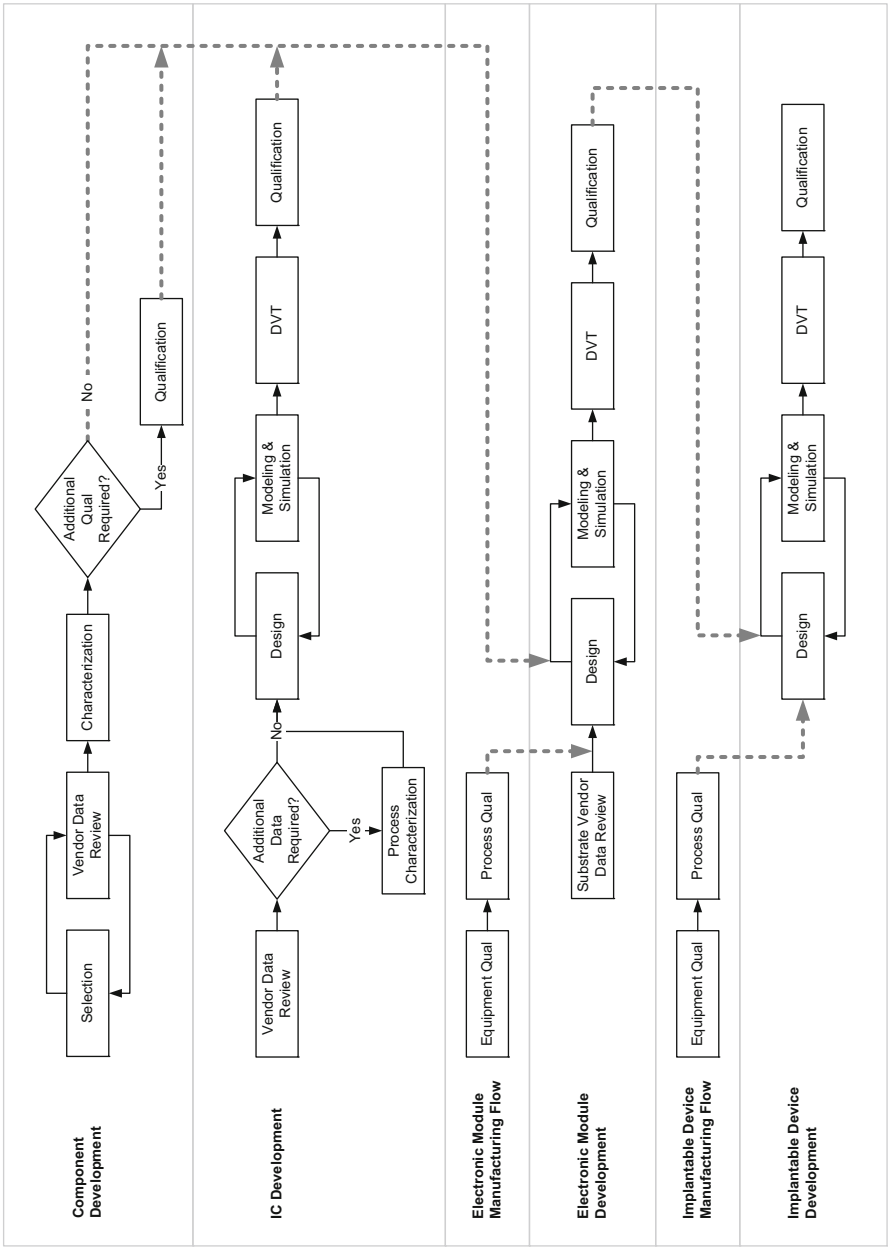


Fig. 18.9 High level implantable device product development flow

For components (integrated circuits, sensors, passives, substrates, FETs, batteries, high-energy capacitors, etc.), supplier qualification and reliability data is reviewed. In some cases there may be sufficient evidence of compliance to requirements that no additional effort is required to design the component into the system. More commonly, the specific use conditions of implantable electronics place constraints on component performance that are not investigated during supplier qualification procedures. In these circumstances, additional characterization and qualification tasks will be undertaken either by the implantable device manufacturer alone or as a joint effort between supplier and customer.

Component characterization consists of an in-depth assessment of performance metrics as provided by the supplier, as well as custom tests to medical device requirements. Accelerated life tests under applicable loads may be investigated at this stage, which provide an early indication of component reliability.

Integrated circuit development includes additional areas of focus. IC design may be performed internally, externally, or as a combination of both. In some cases, off-the-shelf designs may be used, but in general this is not common. As foundry technology continues to provide shrinking feature sizes in support of high-performance commercial applications, implantable design considerations often require additional process characterization on candidate test circuits to assess whether or not a new technology is capable of meeting the performance requirements for implantable devices. Investigations may include small subcircuits whose function in past technology nodes is well understood, such as SRAMs, voltage regulators, clock circuits, microcontroller cores, and output stimulation circuits.

Design Verification Test (DVT) is a significant effort at all the major subsystem and final system levels. In addition to validating that a design meets its requirements, independent verification of the tests themselves is accomplished. Extensive input and output measurements of the device under test are rigorously conducted and analyzed to ensure all design features perform as desired and can be tested to a level required to guarantee device performance.

When final device qualification is complete, clinical studies and subsequent submission to regulatory agencies for approval are undertaken. For minor changes to existing devices, the process may be accomplished in as little as 30 days. For major new products or therapies provided for new indications, the review process can last many months, with substantial evidentiary documentation showing clinical benefit, as well as compliance to internal and external manufacturing and reliability requirements.

18.4.3 Environmental Conditions and Constraints

Use conditions for implantable medical electronics in the final environment, the human body, are generally benign compared to other industrial and commercial applications. Temperature excursions are essentially nonexistent and mechanical

loads are not very severe. However, the requirement of between 5- and 10-year lifetime on a single battery places significant stress on overall design and performance considerations. Although power consumption is not usually thought of as an extreme environment, it is useful to consider it in this manner for implantable electronics. Because the circuits that perform therapeutic and diagnostic functions must operate at very low bias levels, noise immunity, both internal and external, as well as timing margin in digital circuits is challenged in similar ways to very high-speed circuits. This makes what would otherwise appear to be relatively simple design-for-reliability trade-offs into significant challenges.

With conservation of energy a significant consideration, much effort is spent characterizing defects that could cause increased current drain out of the battery. Failure mechanisms that result in marginally higher power consumption that go unnoticed in most applications can be the cause of low manufacturing yields and premature device explant. Qualification testing is designed to detect systematic problems of this nature, while rigorous screening techniques at the component, electronic module, and final device levels are employed to remove low-level defects from the population of shipped devices.

In addition, ICDs also require very high voltage circuits (~800 V) in close proximity to low power components. Although charge/discharge cycles are generally infrequent, in some patients multiple therapies in rapid succession can occur; these episodes are called tachy storms from the terminology of tachyarrhythmias describing dangerously fast heart beats. Implantable devices are designed for worst-case conditions like this.

18.4.4 Manufacturing Stresses

Implantable electronic systems are typically manufactured using equipment and processes that differ very little from standard commercial practices. Thermal stresses are the result of solder reflow and other high-temperature processes. Mechanical stresses arise due to handling requirements as assemblies move throughout the line. In particular, the nonrectangular shapes required of circuit boards that must fit into ergonomic form factors for implantable use result in clamping and routing operations that can place considerable force and vibration stresses on the module.

Although implantable medical electronics are currently exempt from the Pb-free RoHS and other hazardous materials requirements worldwide, suppliers of electronic components are moving quickly to eliminate lead from final metal termination finishes. This creates the requirement that solder reflow processes completely wet end terminations to reduce the likelihood of whisker growth.

Placement of the electronics into the titanium housing, called the “can,” is also a source of stress due to the high packing density of components and the need to press the assembly into a molded plastic frame with epoxy attachment.

Completing the final device assembly requires seam welding the titanium can and backfilling with a dry, nonreactive gaseous environment. Care is taken to ensure that melting the titanium does not impact any of the internal elements within. When assembly is complete, a sterilization process is used to ensure no bacterial agents remain on the exterior, and the device is packaged in a sealed, sterile box for shipping.

18.4.5 Shipping and Storage

Devices have an expiration date starting from the battery attach process, since at that point the device is in continuous operation using factory default settings. Precautions against vibration-induced damage are similar to those used for commercial electronics. The need to provide access to devices upon short notice at any hour of the day requires that some products be stored with technical sales and support personnel in uncontrolled environments. For this reason, devices are required to remain functional below −20 °C and above +50 °C.

18.4.6 Implant Conditions

Once a device is implanted, the thermal environment becomes quite benign, varying very little from 37 °C. Mechanically, there is essentially no chance for short-duration, high-g impacts, but flexing of the titanium due to muscle contraction or close proximity to bones can result in low-amplitude, high-cycle cumulative damage to connections that are made between the rigid electronic components within the device (e.g., circuit board, battery, and high-energy capacitors). Studies to measure this environment using human or animal phantoms have been undertaken and continue to be an area of research.

Although the body is a harsh chemical environment with blood and saline solutions constituting corrosive liquids, the electronics in an implantable device are housed within the inert ambient contained inside the can. Since compromised hermeticity of the can has not been a significant failure mode, no effort is made to coat the internal components or provide additional insurance against body fluid ingress.

As indications for device usage have increased, the population of patients with devices has also grown. Combined with reduced mortality overall due to better health care and lifestyle choices, the frequency of patients with comorbidities such as cancer has risen. This has resulted in higher probabilities that a device will be exposed to a relatively high dose radiation treatment regimen. Great care is taken to ensure devices are not exposed directly to the therapeutic beam, but scattered radiation can result in nonnegligible cumulative damage to oxides within ICs. In addition, photo-induced currents during treatment are at risk of swamping ultralow

bias currents that are used to maintain device functionality. Radiation hardened-by-design techniques that have been employed in the aerospace industry are now starting to see adoption in specific sensitive circuits within implantable devices.

In addition to x-ray flux within a cancer treatment suite, secondary particle generation during the process results in a very large concentration of thermal neutrons. For older IC technologies (critical dimensions ≥ 130 nm) the use of Boron-doped glasses (BPSG) for the first interlayer dielectric provides a mechanism for alpha particle generation due to nuclear reactions with ^{10}B nuclei. This has been shown to result in soft error rates on the order of 10^5 above the normal background [7]. Care must be taken to ensure devices do not become unsafe in this environment.

The use of CT and MRI techniques to help doctors diagnose illnesses can also have adverse effects on devices. Until recently, MRI in particular was not advised for patients with implanted devices due to the serious risk of field-induced currents heating the device and/or lead, and the likely result of permanent device malfunction. Much research has been performed over the past 5 years to both understand and mitigate issues arising from these treatments, especially since they have become much more common. Devices are now available that are able to withstand MRI sequences without permanent damage, opening up better diagnostic outcomes for patients who require them.

18.4.7 Longevity Requirements

Typical lifetime goals are targeted to 10-year performance, although actual longevities among nonrechargeable devices can vary significantly with applied therapy. Nominal models are used to predict battery performance and adjusted based upon device settings. Illnesses that require continuous pacing, rather than pacing on demand, will shorten device lifetime. In addition, ICDs may also have shortened longevity depending upon the number of high-energy defibrillation events that are applied.

18.4.8 Reliability Requirements

Reliability demonstration assessments target failure rates in the low single-digit FIT range (Failures In Time—defined as Failures/10^9 h) at 10-year application. System failure is partitioned into risk categories as shown later through a Fault-Tree Analysis (FTA) and/or Failure Modes and Effects Analysis (FMEA) process. A small portion of an example FMEA is shown in Fig. 18.10.

1. Failure to Deliver Therapy—This is the highest risk category. Any failures that fall into this category result in significant design mitigation efforts.

Component	Component Function	Potential Failure Mode	System Feature(s) Affected	Potential Effect(s) of Failure	Potential System Hazard Effect(s)	Sev	Potential Cause(s)	Occ	Design Requirement(s)	Det	RPN
C9	VREG	Open	Voltage Regulator	Noise and/or incorrect level for regulated supplies	POR	3	Defective solder joint; Defective, damaged or missing component, defective PWB / Vendor; Manufacturing	1	No special requirements	2	6
C9	VREG	Short	Voltage Regulator	ADC and tilt functions will be lost	Degraded pacing function	4	Defective or damaged component; Solder bridge; Wrong capacitor placed in that hybrid location, defective PWB / Vendor; Manufacturing	1	No special requirements	1	4
C9	VREG	Out of Tolerance High	Voltage Regulator	None	None	1	Defective or damaged component/ Vendor; Manufacturing	1	No special requirements	3	3
C9	VREG	Out of Tolerance Low	Voltage Regulator	Noise and/or incorrect level for VREG	POR	3	Defective or damaged component/ Vendor; Manufacturing	1	No special requirements	3	9
C9	VREG	High Leakage Current	Voltage Regulator	Voltage regulation loss	Degraded pacing function	4	Defective or damaged component; Flux or contamination on PC board; Solder bridge/ Vendor; Manufacturing	1	No special requirements	2	8
C11	VCPU	Open	Microprocessor supply	Possible POR	Possible POR	3	Defective solder joint; Defective, damaged or missing component, defective PWB / Vendor; Manufacturing	1	No special requirements	1	3
C11	VCPU	Short	Microprocessor supply	Core of the microprocessor will not run	Possible POR	3	Defective or damaged component; Solder bridge; Wrong capacitor placed in that hybrid location, defective PWB / Vendor; Manufacturing	1	No special requirements	1	3
C11	VCPU	Out of Tolerance High	Microprocessor supply	No detrimental effect	None	1	Defective or damaged component/ Vendor; Manufacturing	1	No special requirements	3	3
C11	VCPU	Out of Tolerance Low	Microprocessor supply	No detrimental effect	None	1	Defective or damaged component/ Vendor; Manufacturing	1	No special requirements	3	3

Fig. 18.10 Example extract from an electronic module (hybrid circuit) FMEA

2. Reduced Longevity—Failures in this category are typically handled either by design mitigation or system performance monitoring. Battery depletion curves under all applicable therapeutic regimens are well understood; deviations from this performance are monitored by the device, with a warning provided to the patient and clinician if necessary.
3. Diagnostic Data Storage—Patient health and device performance and parameter settings are logged on a frequent basis; as the volume of this data has increased, the likelihood of transient errors appearing in records has also gone up. Errors in this category are considered customer-impact failures and are also targeted for mitigation by design choices such as error correction codes (ECC) or memory block checks (CRC).

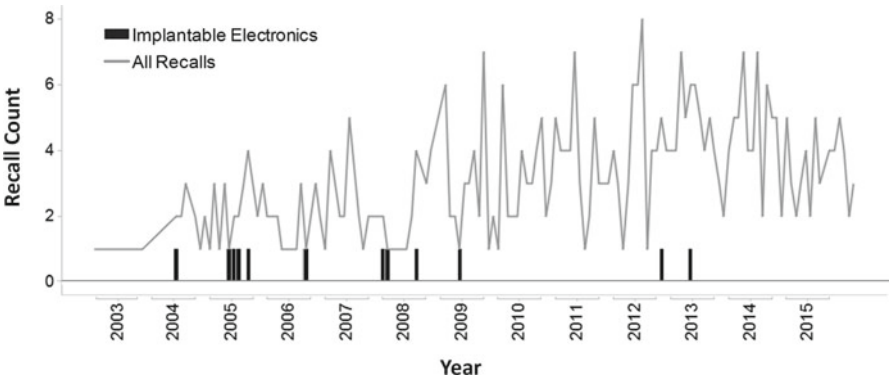
18.4.9 System Level Failure Modes

The FDA maintains a publicly accessible database of device recalls [8], which contains implantable and nonimplantable categories. Class 1 recalls are the most serious, defined as failures that have the potential to cause patient injury or death. Figure 18.11 plots the data from 2003 to the beginning of 2016 by month, where the counts are taken as event classes, that is, recalls of multiple device models for the same failure type are counted as a single event. Along with recalls of all devices, implantable electronics recalls are shown as the bars.

For implantable electronics, failure mechanisms that operate in CMOS integrated circuits have special consideration. The impact of defects that create low-level leakage paths that go unnoticed in many commercial applications are significant concerns for medical electronics. In particular, leakage paths in gate oxides, metallization, and vias are the focus of design and screening strategies. While defects of this type may not lead to failure to deliver therapy, they may become the source of premature battery depletion.

As mentioned in Sect. 18.4.6, radiation-induced malfunctions are the most commonly reported issues in the medical literature [9–11]. This is likely due to the clinically visible problems associated with radiation exposure of devices. In addition to effects caused by cancer radiotherapy and CT environments, soft errors in memory and logic are becoming more of a general concern for implantable electronics, much as they are in the commercial arena. Memory and logic gate count increases combined with low voltage operation have created a higher degree of susceptibility to upsets in newer devices, although system-level mitigations may render these events unobservable to the clinician (e.g., regularly performed memory scrubbing).

Another failure mode of concern is current drain increases due to passive component degradation. In most commercial applications, leakage increases on the order of microAmps are inconsequential for system performance, whereas they are significant contributors to early battery depletion in implantable electronics.



Date	Description
Jul, 2004	Some devices with suspect capacitors have had unexpected charge circuit time-outs or charge circuit inactive conditions.
Jun, 2005	Laboratory analysis of returned devices revealed that deterioration in a wire insulator within the lead connector block in conjunction with other factors resulted in an electrical short.
Jul, 2005	A hermetic sealing component utilized in the device may experience a gradual degradation resulting in a higher than normal moisture content within the pacemaker case late in the device's service life.
Aug, 2005	New information regarding the June, 2015 recall indicates that one of the original recommendations can increase the risk of a latching event.
Oct, 2005	Incorrect implantation may cause serious health complications.
Oct, 2006	The Catheter Access Port (CAP) on some products may detach from the main body of the pump which can interrupt drug flow to the target site.
Feb, 2008	Pump motor stall due to gear shaft wear.
Mar, 2008	Device/Drug Interaction - updated the labeling for the devices to include current patient management and treatment recommendations.
Sep, 2008	Disconnection or occlusion of the suture-less connector (SC) catheters from the catheter port.
Jun, 2009	One or more bond wire pairs will lift or separate from the bonding terminals on the device electronics.
Dec, 2012	Unapproved drugs may impact performance of the infusion pump system.
Jun, 2013	An electrical short circuit in a feedthrough may present as a motor stall or low battery reset/alarm and lead to a loss of or reduction in therapy.

Fig. 18.11 Medical device Class I recall event timeline

In addition to electronic component degradation or failure, reliability considerations of the battery; high-energy capacitors; header block; and lead connector, conductors, or insulators can also impact device performance. Qualification testing of these elements consists of accelerated battery depletion discharging, high-voltage capacitor charge/discharge testing, mechanical bend, and fracture testing

of leads. In addition, testing at the final device level ensures all subsystems perform as specified when combined together. Detailed description of qualification testing in this area is beyond the scope of this text.

18.4.10 Commonly Encountered Failure Mechanisms

Table 18.1 lists the failure mechanisms of concern for implantable electronics, the stresses that provide visibility into their frequency within a short time, the qualification tests that are performed to highlight their likelihood of occurrence, and the subsystem or system for which the testing takes place. Many of the items are common to any electronic system, while some are specific to implantable electronics. For the former category, once again the ultralow power requirements of implantable medical electronics may heighten or lower the impact the particular failure has on the system.

For example, SILC (Stress-Induced Leakage Current) and NBTI (Negative Bias Temperature Instability) have generally defined failure criteria used in the semiconductor industry as a 10 % shift in threshold voltage (V_t). Due to the exponential increase in subthreshold leakage current with V_t, these criteria may lead to excessive current drain in implantable applications. Depending on the detail supplied by the foundry in their qualification documentation, additional testing may be required to ensure degradation due to these mechanisms does not reduce battery longevity to an unacceptable level.

Electromigration on the other hand, which is initiated by high current densities, is not a serious issue for implantable cardiac devices. At the IC level, current densities are low enough that they are not a concern, and no joule heating takes place. At the module level the same holds true. The only circuitry that must be designed to withstand high currents is the high-power module that manages charge/discharge cycles for defibrillation therapy. These are stressed by repetitive cycling far beyond their intended design, during which any failure mechanism that may be present, including electromigration, is checked.

Neuromodulation devices may require additional electromigration testing and/or design mitigations due to the extended use of relatively high output voltages. As these devices continue to see increased use, the number of output channels is increasing, which puts further pressure on design margin.

18.5 Qualification

This section will discuss examine and discuss a qualification methodology to establish how a product may be evaluated to meet design and reliability requirements. Compliance-based requirements are discussed, and technical rigor is emphasized.

Table 18.1 Failure mechanisms of concern for implantable medical electronics

Failure mechanism	Accelerating stresses	Qualification test	Applicable to
Cautery/defib damage	Voltage	Saline tank high-voltage pulse testing	Final device
Ceramic capacitor cracking	Mechanical stress	Vibration testing, four-point bend, drop testing	Electronic module
CMOS failure mechanisms (SILC, NBTI, TDDB)	Temperature, voltage	HTOL	CMOS integrated circuits
Component fracture inside final device	Pressure	Barometric pressure testing	Final device
Corrosion	Temperature, relative humidity, contaminants	Hermetic environment of implantable device makes this an insignificant failure mechanism	NA
Creep	Mechanical stress, temperature	HTOL	Electronic module, final device
Current leakage increase due to component degradation	Temperature, voltage, ambient environment	HTOL, Bias/environmental testing	Component, electronic module
Delamination	Humidity, contamination, temperature cycling, mechanical stress	HTOL, temperature cycling, 85/85, vibration testing, four-point bend	Component, electronic module, final device
Dendritic growth	Temperature, voltage differential	Hermetic environment of implantable device makes this an insignificant failure mechanism	NA
Electromigration	Current density, temperature, temperature gradient	IC-level conducted by foundry. This is generally not a failure mechanism of concern in implantable cardiac devices due to low current densities. Neuromodulation devices may require additional testing	Component, electronic module, final device
ESD damage	Voltage	ESD testing	CMOS electronics, electronic module
Fatigue cracking	Mechanical stress, strain range	Vibration testing, four-point bend, drop testing, low-frequency/low-amplitude repetitive cycling	Electronic module, final device
High-voltage component failure	Temperature, voltage cycling	Repetitive defibrillator charge/discharge cycling	Electronic module, final device
Intermetallic formation (e.g. purple plague)	Temperature	HTOL	Electronic module

(continued)

Table 18.1 (continued)

Failure mechanism	Accelerating stresses	Qualification test	Applicable to
Popcorning due to moisture absorption (plastic packages or epoxy over-mold)	Temperature	MSL testing	Component, electronic module
Radiation degradation	Radiation intensity	X-Ray radiation testing, MRI susceptibility, CT testing	Component, electronic module, final device
Soft error upset	Particle impingement rate	Alpha foil testing, neutron beam, testing, proton beam testing	Component, electronic module

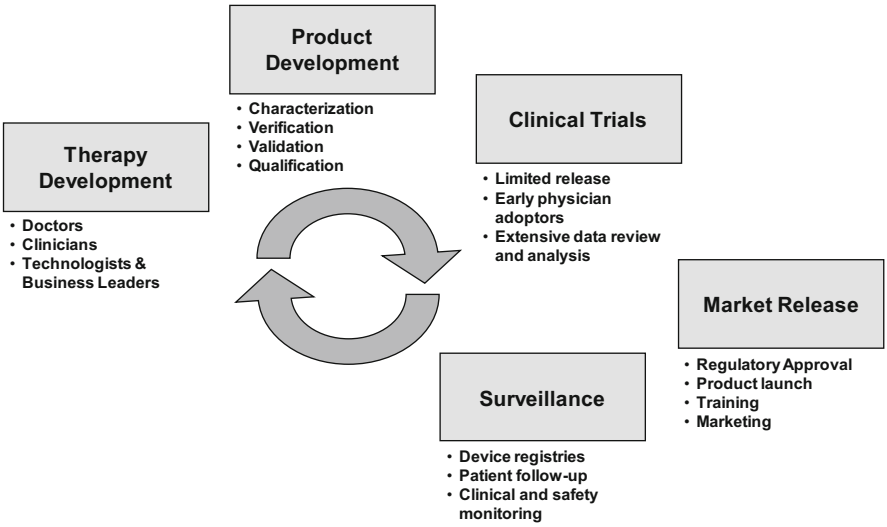


Fig. 18.12 Qualification activity in the overall product development and release process

18.5.1 Qualification Overview

Similar to other electronic applications, medical device qualification is embedded within a much larger development and release process, as shown in Fig. 18.12. Other industries may use a similar approach, with the main differences lying in the clinical trials, regulatory approval, and surveillance required for medical devices. Qualification takes place at the end of the product development cycle.

18.5.2 Qualification, Verification, and Validation

Regulations governing the design and use of medical devices are not prescriptive in their policies. In general, regulatory agencies are interested that manufacturers have a standard set of protocols and procedures that they follow, with demonstrated effectiveness in meeting internal and external requirements. For instance, the FDA provides the following guidance on design verification. Similar guidance information is provided by AIMDD and MHLW.

> Verification activities are conducted at all stages and levels of device design. The basis of verification is a three-pronged approach involving tests, inspections, and analyses. Any approach which establishes conformance with a design input requirement is an acceptable means of verifying the design with respect to that requirement. In many cases, a variety of approaches are possible [12].

Table 18.2 provides a list of activities that are commonly performed on each of the device subassemblies and the standards or requirements used. Unlike the auto industry, for example, implantable device manufacturers do not have a set of overarching documents that prescribe performance or reliability requirements to suppliers. This has resulted in the adoption of many external standards for specific functional blocks, as well as numerous internally developed requirements.

18.5.3 Manufacturing Process Controls

As indicated in Fig. 18.9, manufacturing processes used in the construction of implantable electronics are required to be separately characterized, validated, and qualified. Supplier audits are performed to ensure compliance with applicable standards such as ISO9001 or ISO13485, and processes controlled directly by the implantable device manufacturer must also meet these same standards.

The FDA provides guidance on expectations in this area through a system of documents that was previously known as Good Manufacturing Practices (GMP) and is now referred to as the Quality System Manual (QSM) [13]. For processes, the following definitions are given. Prior to manufacturing a system or subsystem of an implantable device, all processes must have completed the three tasks shown.

1. Installation Qualification/Operation Qualification (IQ/OQ): Establishing documented evidence that process equipment and ancillary systems are capable of consistently operating within established limits and tolerances.
2. Process Performance Qualification (PQ): Establishing documented evidence that the process is effective and reproducible.
3. Process Validation: Establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications.

Table 18.2 Qualification requirements for implantable medical electronics

System level	Reliability area	Requirements	Typical test method (and requirement)
IC	Design	Internal requirements	Design Rule Checks + DFR Checks (100 % compliance)
			Layout vs. schematic—LVS
			Redundant vias (design-dependent requirement)
			Soft Error Robust memory and logic in critical circuits (circuit functionality-dependent)
	Simulation	Internal requirements	Circuit block level simulation
			System modeling
			Power dissipation
	Test	Rigorously verify requirements	All performance requirements are verified
			Specification limits are verified
	Verification	Verify test implementation and IC functionality	All performance requirements are verified
			Specification limits are verified
			Statistical Post-Processing—SPP methodology assigned
	TDDB, NBTI, SILC, OVS, IDDq	JEDEC standards and internal requirements	Foundry data modeling
			SRAM performance testing
			Over-Voltage Stress—OVS life-time modeling
			IDDq distribution analysis
	HTOL	MIL-STD 883	Packaged part dynamic/static burn-in (168-h, 500-h, 1000-h @ 125 °C/150 °C)
			Delta analysis pre/postlife test (<10 % shift)
	MSL testing	JEDEC standards	Moisture level tested on PEM components, and epoxy over-mold (MSL 2 or 3)
	Mechanical testing	JEDEC standards and internal requirements	Wafer thinning to ~5 mil (no statistical changes in measured parameters)
			Package stress simulation (package/IC-dependent stress)
			Four-point bend testing (~2000 microstrain)
	Radiation effects	Internal requirements	Soft Error Rate—SER tested under accelerated conditions (circuit functionality-dependent)
			X-Ray radiation testing (circuit functionality-dependent)
	ESD	JEDEC standards and internal requirements	HBM pin testing (2000 V)
			CDM pin testing (500 V)

(continued)

Table 18.2 (continued)

System level	Reliability area	Requirements	Typical test method (and requirement)
Components	Component-specific testing	JEDEC standards and internal requirements	HTOL (500-h, 1000-h @ 125 °C/150 °C)
			Mechanical stress (component-dependent stress)
			High-Temperature Reverse Bias—HTRB (<100 nA leakage after stress)
			High-Voltage Withstand (~2000 V)
			Temp-Cycle (−55 °C to 125 °C)
	Supplier data	JEDEC standards and internal requirements	HTOL (500-h, 1000-h @ 125 °C/150 °C)
			Mechanical stress (component-dependent stress)
			High-Temperature Reverse Bias—HTRB (<100 nA leakage after stress)
			High-Voltage Withstand (~2000 V)
			Temp-Cycle (−55 °C to 125 °C)
	Monitoring	Internal requirements	Electronic data submission with Certificate of Compliance
			Online Out Of Control analysis
Electronic module	Design	Internal requirements	Design Rule Checks (Electrical and Mechanical—100 % compliance)
	Simulation	Internal requirements	System modeling
			Power dissipation
	Test	Rigorously verify requirements	All performance requirements are verified
			Specification limits are verified
	Verification	Verify test implementation and electronic module Functionality	All performance requirements are verified
			Specification limits are verified
	HTOL	MIL-STD 883	Electronic module dynamic burn-in (168-h, 500-h, 1000-h @ 125 °C)
			Delta analysis pre/postlife test (<10 % shift)
	Mechanical testing	JEDEC standards and internal requirements	Temp-Cycle (−55 °C to 125 °C)
			Four-point bend to failure (~2000 microstrain)
			Drop-Shock-Vibration (500 g RMS)
	Radiation effects	Internal requirements	X-Ray radiation testing

(continued)

Table 18.2 (continued)

System level	Reliability area	Requirements	Typical test method (and requirement)
Implantable device	Design	Internal requirements	Design Rule Checks (100 % compliance)
	Simulation	Internal requirements	System modeling
			Power dissipation
	Test	Rigorously verify requirements	All performance requirements are verified
			Specification limits are verified
	Verification	Verify test implementation and device functionality	All performance requirements are verified
			Specification limits are verified
	EMI	CENELEC standards	EMI testing
	Mechanical testing	JEDEC standards and internal requirements	Temp-Cycle (−25 °C to 55 °C)
			Drop-Shock-Vibration (500 g RMS)
	Radiation effects	Internal requirements	X-Ray radiation testing (device-dependant requirement, test to ~3000 Rad)
			MRI compatibility testing
			EMI testing
	Cautery/defib	Internal requirements	Saline Tank (repeated high-voltage deliveries)
	Hermeticity	Internal requirements	Vacuum leak rate
	Sterility	Internal requirements	Bacteria culture
	Performance testing and modeling	Internal requirements	Power dissipation
			Pacing Output
			Input signal chain integrity
			Defibrillation output testing
			Power-On Reset—POR parameters
			Memory address space uniqueness
			Battery performance
			Telemetry

18.5.4 Component and Material Qualification

Once all the processes used in the manufacturing flow have been qualified, component qualification can proceed. In this context, component refers to a single unit that is assembled onto the electronic module or within the final implantable device, and could include both monolithic entities such as diodes or capacitors, as well as complex subsystems such as Stacked Chip-Scale Packages (SCSP).

As shown in Fig. 18.8, component development starts with vendor selection and a review of their data. The latter may be provided as part of an audit or can be found through publications the supplier makes available to customers. Matching device requirements to performance characteristics of each component generally results in a series of evaluations among competing options until a small number of alternatives are chosen. Once the selection has reached this point, a more detailed characterization effort is begun. It is during this phase that component attributes are tested against implantable device requirements and may include testing beyond the original manufacturer's operating envelope or against limits that are relevant to medical devices.

In some cases, characterization uncovers performance attributes that make the component unsuitable for implantable use or require additional screening techniques to ensure reliable operation. An example can be found in tantalum capacitor technology. Many ratings of this highly reliable component are used in huge quantities throughout electronic systems, including implantable medical devices. Suppliers typically screen lots of material that will be used in medical applications, but even with this effort, small changes in leakage that can result from additional processing at the electronic module or final device manufacturing facilities may result in yield impact due to current drain that commercial applications do not experience.

Once the characterization process is complete, a final review of all available data is conducted to determine whether or not additional qualification is needed. Once again this is primarily driven by implantable requirements that do not align exactly with the component supplier qualification procedures. This work may be performed alone by the medical device manufacturer or as a joint effort with the supplier.

For integrated circuits, the development flow has special tasks that do not appear in the passive or monolithic component process. Because of the cost of developing a custom IC, before a new technology is chosen for implementation vendor data is reviewed in detail. This will include current drain and performance metrics, as well as a review of the IC design flow. As in the component data analysis, additional process characterization may be required to ensure designs can truly meet the current drain requirements of implantable electronics. When an IC design is complete and has been verified for correct functionality, qualification proceeds through protocols that involve HTOL and validation of screening processes.

18.5.5 Electronic Module Qualification

When all components and manufacturing processes have completed qualification, electronic module qualification is performed. Design work and early prototypes are built in parallel with component and module development, but final qualification cannot proceed until all processes and components have completed qualification, and applicable documentation is finalized.

Qualification of the electronic module is generally performed internally by the implantable device manufacturer, although some portions of the effort may be outsourced to previously qualified contractors. Electrical, thermal, and mechanical stresses are applied to the module and subsequent testing ensures performance meets requirements.

18.5.6 Finished Device Qualification

When all components, electronic module, and manufacturing processes have completed qualification, finished device qualification is performed. Design work and early prototypes are built in parallel with earlier development, but final qualification cannot proceed until all required processes and components have completed qualification, and applicable documentation is finalized.

Very few external standards exist to guide this work, which has resulted in a large number of internal requirements that have been developed to cover the gap. Many specialized tests are performed, such as barometric pressure testing to ensure that devices can be transported in unpressurized airline holds, as well as withstand higher pressures for scuba diving patients. Cautery/defib testing is performed in saline tanks to ensure high-voltage spikes associated with surgery or external defibrillation do not affect device performance.

18.5.7 Supplier Controls

Ensuring externally purchased materials and components that are used in implantable devices are reliable in this application is an important process. The characterization and qualification procedures previously described are designed to ensure that appropriate choices are made in the original device design, but intentional changes or process drift over time will not be uncovered.

Components may require additional acceptance specifications beyond those provided by the manufacturer on the data sheet. These are uncovered during the earlier work and negotiated as part of the contractual agreement between supplier and customer. In addition, formal change notification procedures are agreed upon, which may cover materials, processes, or manufacturing sites. Even where known performance attributes are matched before and after changes, additional work may be performed by the medical device manufacturer depending on the level of risk associated with the change, as described by the FMEA or FTA analysis. This could include a complete requalification of the component, which will prevent insertion of the new component in the finished device until the work is complete.

Because of the specialized requirements of implantable electronics, it is often the case that outgoing quality testing provided by the supplier is modified. Depending on the complexity of the component, this may include simple additions or

modifications to existing tests, or a complete set of custom tests. For example, simply screening to tighter leakage current limits for tantalum capacitors may be sufficient for this technology, whereas wireless telemetry modules that operate at ultralow power may require a complete suite of custom tests to ensure RF blocks operate with sufficient noise immunity and low bit-error rates. Any such customization is negotiated as part of the purchase agreement, with changes made during the life of a product requiring formal agreement.

Medical device manufacturers are required by the FDA to retain records for at least 10 years, whereas most commercial suppliers do not store data for that length of time. For this reason, supplier data may be transmitted to the device manufacturer and stored within their systems. In the past, much of this was accomplished through paper travelers or certificates of compliance. Recently, it has become more common for this data to be shared electronically, allowing medical device manufacturers to monitor supplier performance in a much more proactive fashion. Once again, the frequency and content of transmitted data is negotiated as part of the purchase agreement.

18.6 Manufacturing and Process Development

The competitive landscape in the medical device industry has changed in recent years. What once was a specialized market has shifted to a commodity model where innovation, cost, and speed to market are critical. As such, the strategy for process development has changed. In order to compress process development timelines, reuse of standard processes or rigorous, yet efficient development of new processes is required. However, that efficiency cannot be realized at the expense of compromising quality, reliability, or manufacturability. Transferring reliable, high yielding, and stable processes is necessary and requires adoption of new methods and tools.

18.6.1 Manufacturing Process and Materials

Medical device design and manufacturing trends now tend to follow the commercial electronics industry's roadmaps. Miniaturization and cost pressures are driving the use of packaging technologies that can maximize density. Designs that used to incorporate 2D packaging such as surface mount assembly or chip and wire attach on the main substrate have transitioned to more 2.5D type processes. Incorporating different packaging technologies into a design is now commonplace which puts greater emphasis on understanding process and material interactions across the entire value stream.

With the increased focus on cost and supply delivery, transferring processes with low manufacturing yields for medical device assemblies is no longer tolerated. Claiming that design complexity is reason for poor manufacturability is misguided.

While the decision to release a product or process at lower yields is clearly one for the business to make (based on competitive threats, market needs, or other constraints specific to that business), it should not be the norm. Any process can be developed and transferred with high yield given the proper development approach and focus. Manufacturability assessments and decisions must be an integral part of the process development activity, and the earlier, the better.

A common assessment should be the integration of processes and materials. Every process and material used will have an interaction with subsequent processes and materials. By considering these interactions during development, better predictions can be made of process performance at manufacturing volume. Upstream processes have maximum and minimum output requirements and operating ranges and those should be treated as input variables to the downstream processes. Additionally, the way with which material and/or product is introduced into a process is equally as important. Material handling conditions should be understood and opportunities for error become minimized or eliminated.

18.6.2 Beyond 6-Sigma: Developing Transfer Functions

The key to transferring a robust process is an understanding of how process inputs can influence the process outputs. A transfer function is the mathematical expression of this relationship and is developed through the use of Design of Experiment methodologies. The statistically derived expression then allows the engineer to predict a process's performance based on the equation. However, using the transfer function only as a mathematical expression is underutilizing its capability. The transfer function allows the development engineer to understand the significance of the individual inputs, the positive or negative impact to an output, and any potential interactions between the inputs themselves. This first principles understanding is the foundation for robust process development and stable manufacturing. As a foundation, it is meant to be built upon.

Robust process development needs not only the understanding of how the process inputs can influence the process outputs but also a fundamental understanding of the different sources of variation and their impact on the process. Variation comes in many forms, be it machine, human, material, environment, etc., and the development activities should be able to identify and reduce a process's sensitivity to them. This also can be accomplished by rigorous, disciplined use of Design of Experiments. The key, though, is ensuring a thorough review of risks, potential sources of variation, and potential critical input parameters prior to any experimentation. This may differ depending on the type of development activity being completed.

The principles before can be applied during any phase of development, from a new technology, to an existing technology used for a different product or against different requirements, or to a continuous improvement effort that looks to optimize a process window. Whichever flavor, the first step should be completing a thorough

risk assessment. Many tools exist to help with this activity, and while a Failure Mode Effects Analysis (FMEA) is the most common, any method will work as long as all interactions are considered. This is where an estimation of all sources of variation is important, because the risk assessment defines the focus of the development activity. This step in the process is critical and typically the most underrated.

For a new technology development, there is a good chance most of the risks are unknown. In these situations, an understanding of the product and process requirements is important. The risks are then defined around these requirements. In some cases requirements may be unknown or assumed, but that shouldn't deter the risk assessment activity. Since with any good risk assessment process there are review and update steps, the engineer can reassess the risk as the project moves forward if the requirements become better defined. There is really never a situation where a risk assessment occurs too soon. In fact, this is critical to the Design for Reliability and Manufacturing (DRM) methodology and is necessary to be truly predictive and proactive, which will be discussed more in the next section.

Most likely, the risk assessment for medical device manufacturing is more product focused than process, since the risk impact needs to be considered in the use condition state—which means at the customer or patient level. At the process level, the many sources of variation will impact the manufacturability or stability of the process. These should be treated as input variables similar to process parameters, such that they are varied in a controlled manner during the development process. What are the operating ranges of the upstream processes? What are the allowable process / product outputs of the upstream processes? What are the material parameters that may change and impact the process? Is there any variability in tooling or fixtures that could be significant? Do environmental conditions such as temperature or humidity have an impact on the process performance? These types of questions, and more, need to be asked and where appropriate, the variables should be included in any development experimentation. This could mean multiple lots of incoming material or intentional variation of material characteristics; variation in fixture or tooling design; long-term stability runs of a process over time or with varied environmental conditions. Whatever the identified sources of input variation, it is important to not disregard them and to instead explore the possible interactions with the process. Once understood, it is best to control the input variation, but in many cases this is not possible. That's when establishing a robust window for process parameters becomes important.

Establishing operating ranges for process parameters is rightly focused on being able to meet process output requirements. This is the traditional use of the transfer function. At the same time, process parameters should be developed such that they can account for and minimize the impact of the input variation, as discussed before. In effect, the process parameters are then used to help control the input variation by making the process insensitive to it. Any number of experimental methods can be used to understand, develop, and optimize process settings, but the key is collecting and using the right data. Early definition of the measurement method for process

outputs is critical to ensuring efficient, robust development of processes. And while collecting more data always seems the right approach, schedule and/or development cost pressures will impact those decisions.

The volume of samples and data to be collected should be a risk-based decision in order to maximize the benefit. A high risk process or critical process output should require larger samples sizes than a lower risk one, and the results need to be statistically significant at a given yield, reliability, or confidence level. Not all processes or process outputs are equal from this standpoint and this understanding is important in order to work within project constraints. Claiming manufacturing capability based on the results of a single experiment is tenuous compared with drawing the same conclusion based on multiple runs across multiple lots while including as much variation as possible.

The final point of this section deals with statistics. As already mentioned, all decisions should be data driven based on statistically significantly sample sizes. However, if it is not possible to generate large sample sizes based on cost or schedule, allow statistics to be your guide. There are many statistical analysis software packages available, for example, Minitab and JMP, that should be leveraged to help make decisions. And they all offer options to bound data sets with confidence intervals based on sample size. Don't ignore what the data are telling you.

18.6.3 Change Management

Throughout this chapter, the extent of development and qualification required to launch a medical product has been discussed. All of that development work is the foundational underpinning of the results and conclusions reported to regulated bodies to obtain approval to distribute product. It is important to consider the impact of making postsubmission changes. Changes can come in many different ways and can be initiated by the device manufacturer, or anywhere throughout the supply chain stemming down through multiple tiers of material and component suppliers. In many segments of the electronic industry, change is sought after and relied upon to ensure a product has incorporated the very latest in technology. In some industries, it is also common to release a product platform and continue to work through meeting cost targets and manufacturing yields during the product launch process. Finally, changes may be driven by product field performance surveillance and deemed necessary due to functionality or customer feedback. These are all valid and important reasons that change must be tolerated.

In the medical device environment, all changes must be reported to regulators and approved prior to implementation. There is typically a (sometimes significant) cost associated with implementing change because not only is there cost to establish appropriate supporting data, but there is cost to file the change request as well. All

changes must be justified with similar data and/or justification as the original product submission, such that there is objective evidence a product still meets its intended requirements and there are no patient safety risks associated with making the change. For these reasons, medical device manufacturers typically want to limit as much change as possible. This means when a device is developed, the manufacturing process must be mature and the BOM must be stable at the time the product makes the transition from development to manufacturing.

Managing change can go beyond the limitations of form, fit, and function. Many changes that need to be managed in the medical device world represent improvements or innovations to a material, component, or process, that are meant to have no measurable output on the performance of the product. There is, however, risk of unintended consequences due to changes that may not even be visible or detectable to an incoming component. This could manifest itself in a change in performance, or even just as a change variation of performance within specification. For example, the modification of a cleaning procedure could be intended to product the same result on a finished component, but leave an unintended residue on the surface that could impact downstream manufacturing, or even impact field reliability. Component and material suppliers may not know or understand all of the use conditions associated with what they are supplying. The burden of responsibility is on the medical device manufacturer to know about changes and have them evaluated appropriately. It is critical that the medical device requirements for change management are flowed down through the supply chain so that all changes can be brought forward and evaluated.

One challenge of medical device manufacturing is the use of consumer-grade electronic components, which are often referred to as Off The Shelf (OTS) components. Consumer-grade components can be thought of as a generic grade of industrial or medical-grade components. While form, fit, and function may be advertised as equivalent to their industrial or medical-grade counterparts, there may be subtle differences such as size or performance tolerance, missing verification steps such as performance testing or screening. From a design perspective, using consumer-grade components appears to be a favorable approach because selection of available components may be high, and price may be competitive. However, through the product lifecycle, it may become difficult to ensure continuity of supply or to ensure change is appropriately communicated. This is especially true for components that are being purchased through a distributor as opposed to the manufacturer. In many cases, consumer-grade components may be all this is available without having an industrial or medical grade equivalent. For a medical device manufacturer, it is important to understand the component supply chain infrastructure so appropriate steps can be taken, and risk can be mitigated. This may come in the form of supply agreements, added inspection steps, increased inspection frequency, or even performance testing.

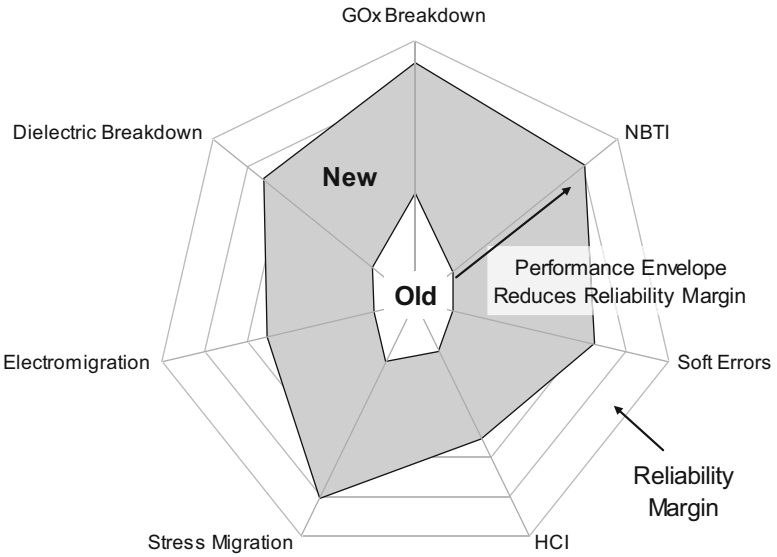


Fig. 18.13 Reliability margin shrinking

18.7 Implantable Medical Device Challenges

18.7.1 CMOS Scaling

CMOS scaling is a double-edged sword, providing both increased performance that leads to new therapies and data storage options, along with increased current drain that leads to early battery depletion. Managing trade-offs in this area, while still keeping several generations behind the leading edge and ensuring obsolescence is avoided, is a constant challenge. Figure 18.13 shows a schematic representation of shrinking reliability margins in CMOS electronics due to scaling and material changes [14]. In previous generations, sufficient margin existed that reliable medical electronics performance could be ensured through conservative design techniques. Although this is still true, there is less margin for error, requiring careful planning of technology adoption strategies, and a more complex suite of characterization and qualification practices.

18.7.2 Lead-Free Requirements Impact

Although the implantable medical device industry has been free from Pb-free regulations, the reality is that component manufacturers are shutting down Pb finishes on their parts. The medical device industry does not have high enough

volumes to enforce special considerations, so it is increasingly finding itself in a position of having to evaluate Pb-free component compatibility with Pb solder lines.

At present, this has meant ensuring that final finishes on all components are known and that manufacturing flows do not leave non-Pb surfaces exposed within the device. In the future, if Pb-containing solder pastes become increasingly difficult to procure, changes to Pb processes will be made, which will have an impact on component selection and qualification, especially as it relates to the higher reflow temperatures required.

18.7.3 Increasing Device Complexity

Physicians are asking for more automaticity, greater data storage capacity, more sophisticated algorithms and data processing, wireless telemetry, and new therapies that require additional complexity of the devices. This is true not only for the CMOS microcontrollers and memories but also of high-voltage delivery circuitry and external components. Managing this complexity, while still delivering devices to the market on schedule is creating the need for new processes and management practices in order to meet these needs.

18.7.4 External System Interfaces

With wireless telemetry now a reality in many devices, data streaming into the hands of a clinician creates new interfaces that need to be managed, both from a technology and security point of view. Current generations of devices require an external device that is either located within the patient's home or can be worn. A number of electronics companies have created divisions focusing on health care [15, 16], which includes wireless connectivity within the clinical setting to improve efficiency and patient outcomes. Future implantable devices may benefit from direct interaction with this environment, much as the use of pagers was replaced by cell phones, and now by WiFi-enabled smart phones that allow users to download information that is relevant to the context in which they find themselves. With the current drain constraints already mentioned throughout this article, the impact of such ubiquitous access on implantable device performance, as well as the need to provide extremely high levels of security will create interesting challenges.

18.7.5 Qualification Strategies for the Future

Given that device complexity will increase in the future, design and performance modeling early in the product development cycle is fast becoming a condition for success. Waiting until qualification to find serious design issues is no longer a viable approach. New tools and methods are being developed throughout many electronics applications, and the medical device community is adopting them as appropriate. This includes the following areas.

1. *Finite Element Analysis (FEA)*
   Techniques to model the impact of materials and design choices prior to building actual prototypes are now commonly employed. Mechanical and thermal stresses and the impact on generated strains within the device can be accurately modeled on a comparative basis. In the future, these models will become more sophisticated, capable of starting at the final device level and descending levels of hierarchy to the subcomponent interface level (e.g., solder bumps, copper traces in substrates, connector interfaces, etc.).

   Generating failure distributions through crack propagation, thermal stresses, or mechanical cycling will be required in order to minimize the necessity of qualification testing to ensure sufficient application margin. Although progress has been made in this area, especially in the aerospace and automotive industries where FEA has been extensively used for many years on metal structures [17], the challenge for electronics lies in successfully extrapolating failure mechanics within the highly nonlinear material sets that are used [18].
2. *System-Level Simulation*
   Performance simulation of electronic designs has progressed from simple Spice modeling to higher level digital methods. This has been driven largely by the integrated circuit industry, where the ability to model billions of transistors on a single piece of silicon is required to ensure designs are implemented correctly. Degraded transistor models are now routinely generated as part of process qualification, which include effects due to NBTI, Hot-Carrier Injection (HCI), and other important CMOS effects. The future will require that these capabilities be extended beyond the realm of silicon to include passive components, RF modules, sensors, energy sources, and external interfaces. Leveraging this infrastructure to support rapid prototyping and qualification test protocols will ensure both more reliable devices [19], the use of more advanced technologies, and improved patient outcomes.
3. *Bayesian Methods*
   Current qualification practices largely ignore information acquired during previous product development efforts. Although new technologies continue to be introduced with each new generation, many pieces of older designs are carried forward into new designs. Much work has been done in this area to provide a Bayesian framework for incorporating prior data into new analyses [20–23]. In addition to the efficiencies introduced by the possibility of reduced sample sizes,

more robust designs along with better institutional memory will be fostered by the adoption of these methods.

4. *Safety Standards*
   IEC 61508 was created to provide a framework that companies could use to both standardize processes and nomenclature around safety measurements, as well as certify compliance to a given safety level as required by customers, industry, or any external agency. The automotive industry is now making adherence to ISO 26262, a recasting of IEC 61508 to that application, a requirement for their suppliers. The medical device industry is looking into the use of this safety standard as well. In order to ensure that safety design goals are met, qualification procedures will need to accommodate procedures within the standard, as well as demonstrate compliance of final devices.
5. *Modular Design*
   To support new architectures, faster time to market, and the viability of early modeling, medical devices are increasingly being manufactured from subassemblies that have been fully characterized and qualified. This makes future designs more flexible and simplifies the overall qualification strategy. This strategy will continue into the future.

References

1. Gorton WS, Genesis of the transistor, written in December 1949 and intended for volume 3 of A History of Engineering and Science in the Bell System
2. Allan R (2003) A short history of the pacemaker. Electronic design (website). Penton Media, Inc. http://www.elecdesign.com/Articles/Index.cfm?AD=1&ArticleId=5950. Accessed 13 Mar 2005
3. U.S. Food and Drug Administration. http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/ucm095274.htm
4. U.S. Food and Drug Administration. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051512.htm
5. Federal Interagency Forum on Aging-Related Statistics (2012) Older Americans 2012: Key indicators of well-being. Federal Interagency Forum on Aging-Related Statistics, U.S. Government Printing Office, Washington, DC
6. Gerrish P et al (2005) Challenges and constraints in designing implantable medical ICs. IEEE Trans Dev Mater Reliab 5(3):435–444
7. Wilkinson JD et al (2005) Cancer-radiotherapy equipment as a cause of soft errors in electronic equipment. IEEE Trans Dev Mater Reliab 5(3):449–451
8. U.S. Food and Drug Administration. http://www.fda.gov/MedicalDevices/Safety/RecallsCorrectionsRemovals/ListofRecalls/default.htm
9. Rodriguez F et al (1991) Radiation-induced effects in multiprogrammable pacemakers and implantable defibrillators. Pacing Clin Electrophysiol 14(12):2143–2153
10. Thomas D et al (2004) Radiation-therapy induced electrical reset of an implantable cardioverter defibrillator device located outside the radiation field. J Electrocardiol 37 (1):73–74
11. McCollough CH et al (2007) Effects of CT radiation on implantable cardiac rhythm management devices. Radiology 143(3):766–774

12. U.S. Food and Drug Administration. Design control guidance for medical device manufacturers. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070627.htm#_Toc382720788
13. U.S. Food and Drug Administration. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/QualitySystemsRegulations/MedicalDeviceQualitySystemsManual/default.htm
14. Porter M, et al (2008) Reliability considerations for implantable medical ICs. In: IEEE international reliability physics symposium, Phoenix
15. Intel Mobile Point of Care Whitepaper. http://www.intel.com/corporate/healthcare/emea/eng/casestudy/whitepapers.htm
16. Texas instruments medical applications guide. http://focus.ti.com/lit/sg/slyb108d/slyb108d.pdf
17. Tryon RG et al (1996) Development of a reliability-based fatigue life model for gas turbine engine structures. Eng Fract Mech 53(5):807–828
18. Nasser L, et al (2005) Electronic material microstructural, variability-based, total life fatigue prediction approach. Vextec Corporation. http://www.vextec.com/images/_downloads/pdf_IPMM-final.pdf
19. CCC visioning study on cross-layer reliability. http://www.relxlayer.org
20. Pan R (2009) A Bayes approach to reliability prediction utilizing data from accelerated life tests and field failure observations. Qual Reliab Eng Int 25:229–240
21. Jiang M, Dummer DJ (2009) Bayesian reliability demonstration test in a design for reliability process. In: Annual reliability and maintainability symposium, Fort Worth, pp 31–36
22. Houben MJHA, et al (2009) Reliability prediction through Bayesian inference based on product change. In: Annual reliability and maintainability symposium, pp 292–297
23. Ion RA, et al (2006) Bayesian model for early reliability prediction. In: Annual reliability and maintainability symposium, pp 260–265