Cardiac Devices and Technologies: Continued Rapid Rates of Development

44

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Abstract

The primary goals of this last chapter are to: (1) make note of the technologies mentioned earlier in this book, (2) describe some important changes in healthcare and global markets that could have an impact on the use rate of technologies being developed, and (3) discuss several other future opportunities in the cardiac device arena. It should be noted that the chapters of this third edition were updated, and new ones were added to specifically describe recent critical advances in cardiac device technologies and/or clinical applications. There are also other areas of importance in cardiac treatment such as biological approaches to disease management (stem cell therapy), genomics (diagnostics and gene therapy), proteomics, and/or tissue engineering, all of which may have a major impact on the future of cardiac clinical care; however, detailed discussions of these approaches are beyond the scope of this book.

Keywords

Medical device development • Implantable therapies • Catheter-delivered devices • Endocardial ablation devices • Device coating agents • Telemedicine • Implantable sensors Cardiac imaging • Surgical tools • Less invasive surgery

44.1 Introduction

Since the second edition of this book was published in 2009, much has changed in the field of cardiac devices. In response, several new chapters were added, and others were expanded in this third edition, so to accommodate the rapid growth and innovation in this field. In many of these chapters, the authors provided histories of cardiac device development and fairly thorough discussions of currently employed devices and/or assessment technologies. To appreciate how rapidly innovations in the area of cardiac disease continue to progress, one can simply perform a search on the United States Patent and Trademark Office website (www.uspto.gov). This search produces an impressive number of companies and/or individuals that are attempting to secure intellectual property protection in this clinical category. More specifically, Table 44.1 summarizes the number of published *patent applications* identified in October of 2015, 2008, and 2004, citing the following keywords: cardiac, cardiac surgery, cardiology, cardiac electrophysiology, cardiovascular stents, and cardiac repair.

Note that this list likely does not include all issued patents, as some may be foreign and many of these patents detail prospective future products. For example, in searching the same database mentioned above (at time of print for this book), the key word CARDIAC produces 93,942 *issued patents* in 2015 since 1976, compared to 49,017 patents issued in 2008 and 37,410 in 2004. This rapid increase includes only US patent applications, yet the same is true for the number of new international patent submissions. There are several other resources to locate information on emerging

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Table 44.1 Patent applications for various key words

Keyword	Number of patent applications		
	2015	2008	2004
Cardiac	93,942	46,946	18,920
Cardiac surgery	5,404	2331	1015
Cardiology	14,798	3961	1480
Cardiac electrophysiology	869	213	79
Cardiovascular stents	313	137	52
Cardiac repair	224	127	32

Source: United States Patent and Trademark Office website (www.uspto.gov)

cardiac devices, such as the Food and Drug Administration website (http://www.fda.gov), the Google™ patent search website (https://www.google.com/?tbm=pts&hl=en&gws_rd=ssl), and various other websites. It is important to note that, relative to medical devices, not all countries uphold patent protection to the same international standards; this is a major issue to consider as a corporation looks to expand globally. Discussion of these implications is beyond the scope of this text, but those developing cardiac devices need to be critically aware of this reality. For example, it was recently noted by Shara Aranoff, former Commissioner and Chairman of the US International Trade Commission [1], that "Over the past 20 years, the number of patent infringement disputes filed annually at the U.S. International Trade Commission (ITC) has more than tripled. Although typically associated with smartphones and semiconductor chips, the ITC has also seen quite a few disputes involving medical devices. Important trends are emerging in medical device patent litigation at the ITC."

Many novel ideas that eventually lead to new products, therapies, and/or training protocols often first occur through "basic" cardiac research or clinical patient management. Hence, in order for emerging technologies to continue to advance at a rapid rate, it is imperative that laboratories performing basic research in cardiac-related technological areas continue to receive necessary support. Furthermore, prototype testing and clinical trials are essential to insure that the best possible technologies are developed and eventually made available for general use. Yet, it is important to note that many critical lessons can be learned from trials that employ misdirected devices or technologies.

When considering the design of a medical device, there are typically a number of key processes or steps involved:

- A device sketch (e.g., on a cocktail napkin, iPad, or smartphone during a meeting with a clinician, with a signed nondisclosure agreement)
- Detailed drawings and intellectual property disclosures
- A critical study of the associated normal and pathologic anatomies
- The creation of an impressive animation of device design, its function, and/or its clinical delivery/placement
- Device prototype development (rapid, working, polished prototypes and/or computer simulations)
- Bench testing (safety, wear, and biocompatibility testing)
- Redesign: set on a final design freeze
- Preclinical research: animal testing
- Redesign (if needed) or initiation of clinical testing
- Simulation systems of device implantation
- Market release and/or corporate acquisition

Some devices can be employed as life-saving measures prior to approval for market release, if a *Humanitarian Device Exemption* is obtained. For more details on the design process, the reader is referred to Chap. 42.

As cardiac devices become more beneficial and help people live longer lives, we foresee that there will be a need to design devices that: (1) have even higher reliability and longevity; (2) can be upgraded, extracted, and/or replaced; and/or (3) allow for easy data retrieval (i.e., "big data" obtained remotely). More specifically, the retrieval of data and/or the reprogramming of implantable cardiac systems (sensor/pacing/defibrillation) should be accomplished with minimal need for patient training or education; they should function as seamlessly and simply as possible (*you just implant them!*). As these systems evolve, there will be growing interest from healthcare payers as well as the physicians and/or hospitals that monitor patients. Furthermore, data would ultimately and automatically be interfaced with *electronic health records* which are becoming commonplace in the USA and many global markets. Importantly, the increased use of home monitoring may be perceived as the only possible way to manage the growing amount of "big data" collected from the "baby boomer" patients receiving such therapies. This approach in turn may result in: (1) improved care, (2) greater levels of patient confidence, (3) better understanding of disease-specific therapies, and/or (4) overall cost savings for both the healthcare industry and consumers. It should also be noted that currently there are patient-owned medical records, as mandated in a Presidential order in 2004. Furthermore, with the passing of the *Affordable Care Act* in the USA, the future of cardiac device coverage will be affected, but at this time it is still not clear how and/or to what degree. To learn more about these policies, the reader is referred to http://www.hhs.gov/healthcare/facts/timeline/index.html. The Affordable Care Act was passed by Congress and then signed into law by President Obama on March 23, 2010; on June 28, 2012, the Supreme Court rendered a final decision to uphold the healthcare law. Important features of the Act include the following:

1. *Coverage*
    - Ends preexisting condition exclusions for children: health plans can no longer limit or deny benefits to children under 19 due to a preexisting condition.
    - Keeps young adults covered: individuals under 26 of age may be eligible for coverage under their parents'

health plan.
  - Ends arbitrary withdrawal of insurance coverage: insurers can no longer cancel coverage just because an individual makes an honest mistake.
  - Guarantees right to appeal: individuals have the right to ask their insurance provider to reconsider denial of payment.
2. *Costs*
  - Ends lifetime limits on coverage: lifetime limits on most benefits are banned for all new health insurance plans.
  - Reviews premium increases: insurance companies must publicly justify any unreasonable rate hikes.
  - Helps individuals get the most from their premium dollars: dollars spent on premiums must be spent primarily on healthcare, not administrative costs.
3. *Patient Care*
  - Covers preventive care at no cost: individuals may be eligible for recommended preventive health services without a copayment.
  - Protects choice of doctors: individuals may choose their own primary care doctors from the plan's network.
  - Removes insurance company barriers to emergency services: individuals can seek emergency care at a hospital outside of the health plan's provider network.

Within the last several years, we have again witnessed a fair number of cardiac device recalls due to the so-called *inherent failures*. However, this may be not so surprising, as the sophistication of these devices continues to increase and more and more clinicians have started to implant them. Nevertheless, it needs to be emphasized that human cardiac anatomy is highly variable and dynamic (ever changing, with reverse remodeling occurring with improved outcomes and survival); thus, we need to consider that the implant environment continues to change post-therapeutically (post-implant) and is a highly caustic environment. The human body has innate healing and foreign body response systems.

Despite the occurrence of failed devices, all designs were required to pass rigorous bench testing, animal trials, and human clinical trials before approval for market release. It is of interest to note that each company often designs their own bench testing equipment because, in most cases, the device designs are novel or unique. In fact, many times this testing equipment also becomes proprietary. Therefore, it is likely that bench testing of cardiac devices with high sales volumes will become regulated by governments sometime in the near future.

To provide greater perspective on the design and testing challenges facing the cardiac device industry, perhaps an example will suffice. A pacing lead moves approximately 100,000 times every day (or 37,000,000 times annually), and this can occur in multiple locations and with numerous degrees of freedom. Furthermore, when considering failure of the lead insulation alone, we must expect failures due to abrasions, the association with the fibrous device pocket, the potential for lead-to-lead interactions, anatomical considerations (bones, ligaments, etc.), and/or other complications. It is also interesting to note that some features of lead implantation (e.g., design of the anchoring sleeves) have received little attention or study, yet this may greatly influence the potential for lead failures. For a detailed review on the bench testing of cardiac valves, the reader is referred to Kelley et al. [2].

Again, several new chapters were added to this edition of the textbook, and others were updated to provide the reader with additional information on bench top (in vitro), preclinical, and clinical testing/research (e.g., Chaps. 27 and 41–43).

44.2 Resuscitation Systems and Devices

Even before the cardiac patient enters the emergency and/or operating room, there are many new technologies being developed to aid in resuscitation. Such innovations range from improvements of existing tools (e.g., automated application of cardiopulmonary resuscitation, the use of active compression–decompression devices) to novel mechanisms that accomplish better patient outcomes (e.g., impedance threshold valve, cerebral cooling, and inducing mild hypothermia). Furthermore, automated external defibrillators have become commonplace in the USA, with units being purchased for use in schools, health clubs, emergency vehicles, shopping malls, and even personal homes. Recent clinical trials describe the success of these emerging technologies (see Chap. 38).

44.3 Implantable Therapies

Advances in microtechnology have now made it possible to create implantable therapies that can be life saving, e.g., implantable defibrillators to detect and treat thousands of episodes of sudden cardiac fibrillation. For example recently, there has been a drive to implant vagal nerve stimulators for several proposed therapies including heart rate control, blood pressure control, dietary control, and/or even the reversal of depression. The need for such devices will likely increase at an exponential rate and will be directed specifically to all types of cardiac complications.

44.3.1 Left Atrial Appendage/Atrial Fibrillation Therapy

There are growing numbers of treatment for the side effects of atrial fibrillation which, in some patients, leads to crippling strokes. The focus of these devices is to modify the role of the left atrial appendage in pathologies associated with atrial fibrillation. More specifically, this tiny alcove of the heart has been described to service as a "starter heart" for the human embryo; it can be a site for blood to pool and subsequently form clots that can be expelled out of the heart and into the brain, causing strokes. Today, it is estimated that atrial fibrillation affects five million people worldwide and is considered to be responsible for up to 25 % of all strokes. It has been reported that, due to aging of the population, the number of patients with atrial fibrillation will likely increase by approximately 2.5-fold by the year 2050 [3].

At present, one of the most common treatments for atrial fibrillation is the administration of anticoagulant drugs; note that there are several new drugs available in addition to coumadin. From a device perspective, suggested approaches to treat this problem include tissue clamps, screens, and other methods to seal off the appendage; many of these approaches are being studied through ongoing clinical trials. Nevertheless, ablation is a critical tool for treating atrial fibrillation, and for more details the reader is referred to the new chapter in this textbook (Chap. 29), as well as Chap. 32 on the mapping of such arrhythmias.

44.3.2 Cardiac Remodeling

Chronic cardiac remodeling is a well-known response of dilated cardiomyopathy and is thought to play a central role in disease progression [4–6]. Associated heart chamber dilation and/or wall thinning will elevate overall wall stress which is considered to trigger the local release of neurohormones, thereby adversely affecting myocardial molecular biology and physiology [7]. Therapeutic approaches to treat heart failure have been described primarily as a means to inhibit or even induce reverse remodeling (e.g., beta-adrenergic blockade). More recently, mechanical unloading using left ventricular assist devices (see Chap. 39), extracorporeal pumps (Chap. 33), or portable whole heart support systems (e.g., EXCOR®, Berlin Heart, Berlin, Germany) have been employed as alternatives. Such interventions can profoundly unload a heart, leading to reverse remodeling and thus improved physiological performance [4]. The design of such pump systems has been ongoing, and the goal has been to transition from external (or partially external) to fully implantable pumps (e.g., external to internal pumps with small rechargeable battery packs). Furthermore, when system developers changed from pulsatile to continuous pumps, pump size was reduced by ~1/7, pump weight was reduced by ~1/4, and they were also quieter and more reliable (e.g., fewer moving parts); see Chap. 39 for further details.

44.4 Catheter-Delivered Devices

Since the first edition of this textbook in 2005, there has been a boom in the delivery of specialized cardiac devices that can be introduced intravascularly or via intracardiac methods. Such devices include stents, septal occluder devices, valves, leads, implantable pacemakers, and ablation tools (see Chaps. 8, 28, 30, and 35). Currently, the field of transcatheter-delivered valves is one of great interest and high competition within the medical device industry (Chap. 36). In addition, the team approach for the clinical delivery of such systems is becoming widespread, with cardiologists and cardiac surgeons working together in hybrid catheter lab/operating rooms to perform multi-tiered treatments on patients (e.g., implanting pacing/defibrillation systems, valves, and/or bypass grafts). As the number of these *centers of excellence* continues to increase to perform such procedures, it is likely that older individuals will be receiving implantable devices and/or other cardiac therapies. It should be noted that there are also cardiac catheters on the market to deliver stem cell or gene therapies (see Chap. 40).

44.4.1 Stents

An intraluminal coronary artery stent is a small wire mesh tube that is placed within a coronary artery to keep the vessel patent (open). Stents are commonly deployed: (1) during a coronary artery bypass graft surgery to keep the grafted vessel open, (2) after balloon angioplasty to prevent reclosure of the blood vessel, and/or (3) during other heart surgeries. For delivery, a stent is collapsed to a small diameter and put over a balloon catheter. Typically with the guidance of fluoroscopy, the catheter and stent are moved into the area of the blockage. When the balloon on the delivery catheter is inflated, the stent expands, locking it in place within the vessel and thus forming a scaffold which holds the artery open. Stents were originally intended to stay in the vessel permanently, keeping it open to improve blood flow to the myocardium and thereby relieving symptoms (usually angina). Note that a stent may be used instead of angioplasty. The type of stent to be deployed depends on certain features of the artery blockage, i.e., size of the artery and where the blockage is specifically located. Today bioabsorbable stents are being deployed. Often stents need to be placed at vessel bifurcations, and thus special techniques and/or stents need to be deployed. For example, a *provisional technique* is a generally accepted procedure for treating a bifurcation in a coronary artery. The main branch is stented first, with the stent deployed to a diameter matching the distal side of the target vessel. This is then followed by a *proximal optimization technique* which addresses the malapposition of stent struts resulting from sizing the stent using the distal side of the target vessel. Lastly, the use of a final *kissing balloon technique*, in which two balloons are simultaneously deployed into the main branch and side branch, is used in order to restore patency to the jailed side branch and obtain better strut apposition at the bifurcation (see: http://www.vhlab.umn.edu/atlas/device-tutorial/stents). It should be noted that at the Transcatheter Cardiovascular Therapeutics (TCT) meetings held in 2014 and 2015, a special session was dedicated to the discussion of various stenting techniques that can be utilized in various clinical situations (see: http://www.crf.org/tct).

44.4.2 Catheter-Delivered Leads or Pacemakers

One of the continuing challenges in the area of intracardiac lead development is to downsize lead diameters and, at the same time, minimize the possibility of fractures or failures. Similarly, there is growing practice in the placement of leads within the cardiac veins, as well as in the development of tools for cannulation of the coronary sinus. For a detailed discussion of left-sided leads and resynchronization therapy, the reader is referred to Chap. 31.

Although pacing systems with leads have been utilized since the inception of cardiac pacing, recent advances in miniaturization technology and battery chemistry have made it possible to develop a self-contained pacemaker small enough to be implanted entirely within the heart, while still aiming to provide similar battery longevity to conventional pacemakers. In general, leadless pacemakers (or transcatheter-delivered pacemakers) are self-contained devices designed to be implanted within the chambers of the heart directly at the desired site of pacing. By eliminating the need for a subcutaneous device pocket and insertion of a permanent lead within the vasculature, some of the complications associated with traditional pacing systems can be avoided, including pocket infection, erosion and/or hematoma as well as lead dislodgement, fracture and/or infection. For more details on these devices, see Chap. 30.

44.5 Implantable Sensors

Device and battery technologies continue to decrease in size and, at the same time, exhibit improved efficiency. Also, there have been rapid advances in printable and/or flexible micro-electronics. In turn, this creates increasing opportunities for novel approaches to long-term assessment of various physiological parameters from unique aspects of the entire cardiovascular system. Numerous innovations for the management and collection of "big data" have arisen in the field of medicine, including implantable computers and sensors, wireless data transmission, and web-based repositories for collecting and organizing information.

One such device, the Reveal LINQ™ Insertable Cardiac Monitor (Medtronic, Inc., Minneapolis, MN, USA), is an implantable monitoring system that records subcutaneous electrocardiograms and is indicated for human clinical use for: (1) patients with clinical syndromes or situations at increased risk of cardiac arrhythmias, and (2) patients who experience transient symptoms that may suggest a cardiac arrhythmia [8]. A common use of the system is for unexplained syncope (fainting), in which case the implanted device can capture episodes with impaired cardiac output, including bradycardias (unusually low heart rates), asystoles (long periods without a heartbeat), or tachycardias (unusually high heart rates). The Reveal LINQ is intended to continuously sense and collect unique and valuable information such as heart rate, physical activity, and body temperature from a sensor injected under the patient's skin. Subsequently, physicians can access these data via a controlled website at any time and review screens that present summaries from the latest downloads, trend information, and/or detailed records from specified times or problem episodes. Interestingly, these human clinical devices have been recently deployed in captive and free-ranging wildlife to aid in the characterization of normal physiology and the interaction of animals with their environment, including reactions to humans (Fig. 44.1) [9].

44.6 Procedural Improvement

With pressure on the healthcare system to continually reduce treatment costs and better document the outcome benefits of a given therapy, much effort will continue to be focused on procedural improvements for cardiac care.

44.6.1 Cardiac Imaging

Our ability to image internal and external features of the heart continues to improve at a rapid rate and, as indicated in Chaps. 22 and 24, the sophistication of such systems can be quite extreme. Yet, as the cost of computer hardware decreases and capabilities increase, opportunities to downsize and develop such technologies for widespread use continue to become more and more feasible.

44.7 Training Systems

As technologies have become more advanced, so has the need to teach students, residents, and physicians on how to use them. There are numerous education programs, conferences,

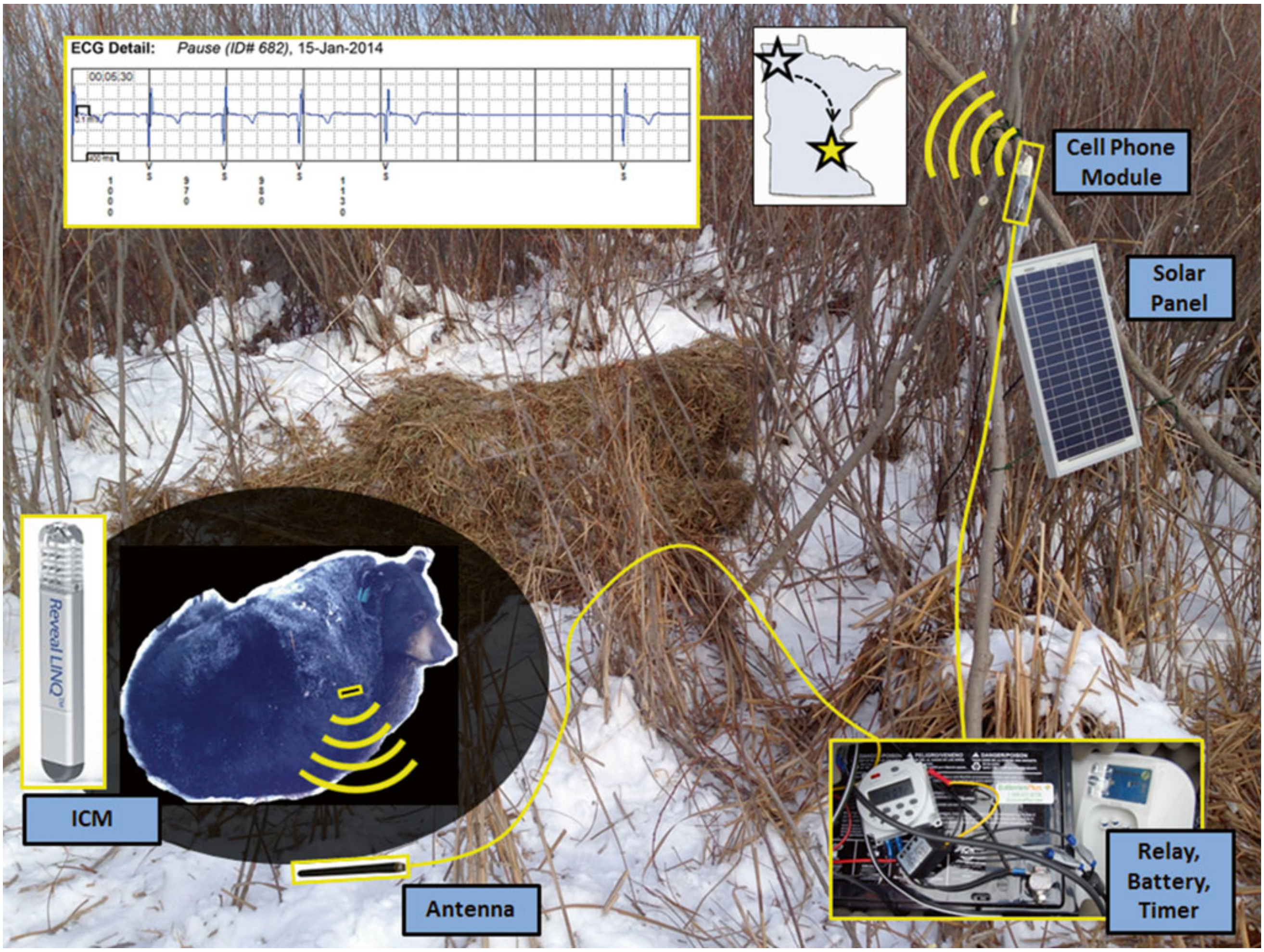

Fig. 44.1 The use of a wireless telemetry system at a bear den. The insertable cardiac monitor (Reveal LINQ™, Medtronic Inc., Minneapolis, MN, USA) communicated with a relay station housed in a waterproof container via an antenna buried under the bear. Transmissions to an Internet site were via a cellular module attached to a timber tripod fabricated at the site. The system was powered by 12 V batteries charged by a solar panel [9]. *ICM* insertable cardiac monitor

websites, teleconferences, and special courses offered. For example, our laboratory has developed a free access website dedicated to the education of functional cardiac anatomy, imaging, 3D models, and device deployment (see http://www.vhlab.umn.edu/atlas/).

44.8 Summary

Within this book, several devices utilized for cardiac electrophysiology, interventional cardiology, and cardiac surgery were discussed. The development of such innovative technologies continues to mature at a rapid rate and includes: (1) resuscitation systems and devices, (2) implantable therapies (pacemakers, implantable cardioverter defibrillators, stents, septal occluders, valves, annular rings, fibrin patches, etc.), (3) delivery systems/invasive therapies (angioplasty, ablations, catheters, etc.), (4) procedural improvements (noninvasive mapping systems, 3D echocardiography, magnetic resonance imaging, training simulators, etc.), (5) less invasive surgical approaches (off-pump, robotics, direct aortic transcatheter valve placements, etc.), (6) post-procedural follow-up/telemedicine (electrical, functional, adverse events, etc.), and (7) training tools. There is no doubt that continued improvement of these technologies, as well as advances in rehabilitation and other support services (patient education, training, home monitoring, etc.), will extend and/or save lives and enhance the overall quality of life for individuals with cardiovascular disease. Many of these developments are currently available, and the challenge for healthcare providers in the coming years will be to provide the best possible care in the most cost-effective way. Perhaps we will see the day of the family house call once again, where the healthcare provider visits the home and assesses and monitors all family members living there during a single visit (ECGs, electronic auscultations, pressure assessments, echocardiography, device reprogramming, blood and genetic analyses, etc.). It should be noted that it was not that long ago, in the 1960s, that medical students were still instructed on how to perform a "traditional house call."

In conclusion, it is exciting to think about the technologies that have been employed thus far as well as those that are being developed that will positively affect the overall healthcare of the cardiac patient. It continues to be an exhilarating era to be working in the field of cardiovascular sciences.

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