From Bench to Bedside

Cardiac Pacing, 1960–1985
A Quarter Century of Medical and Industrial Innovation
Kirk Jeffrey, PhD; Victor Parsonnet, MD

Eugene Braunwald has compared the intense activity in cardiology between 1950 and 1990 to the systolic phase of the heartbeat. In the present paper, we discuss one important aspect of the broader transformation of cardiovascular medicine: the development of pacemaker technology to treat bradyarrhythmias. (Tachypacing and the implantable cardioverter-defibrillator, innovations of the 1980s, are beyond the scope of this discussion.) We are particularly interested in the sources of innovation in pacing, a field known for rapid shifts in hardware and techniques. After the first pacemaker implants (1958 and 1960), physicians guided technological change in pacing for about a decade. Beginning in the 1970s, pacemaker manufacturers supplanted physicians as the dominant influence on the technology of the field.

A new invention ordinarily goes through a period of uncertainty when it is not clear which of several variants will succeed. Eventually a dominant design, a standard version of the technology “synthesized from individual technological innovations introduced independently in prior product variants,” may emerge. By the late 1960s, physician-innovators had created a dominant design in pacing; we call it “the reliable pacemaker.” After 1970, device manufacturing firms introduced further innovations, leading to a new dominant design that we will call “the multifunctional pacemaker.”

We will use common descriptive labels to refer to specific pacing modes (noncompetitive, AV sequential, etc). At the request of the Inter-Society Commission for Heart Disease Resources, a Pacemaker Study Group (Drs S. Furman, N.P.D. Smyth, and Parsonnet) proposed a standard three-position (later five-position) pacemaker code that has now become part of the language of the field. We mention the appropriate code when first referring to a particular pacing mode. The code is summarized and the most important pacing modes are diagrammed in Figs 1 and 2.

The 1960s: Toward Reliability in Pacing
The invention of cardiac pacing in the 1950s is well documented. The classic papers of Callahan and Bigelow, Zoll, Weirich et al, Elmqvist and Senning, Furman and Robinson, and Chardack et al memorably describe the advances in understanding and technology that led to permanent pacing of the heart. Several of these pioneers later published first-person accounts of their work. Historical papers have also discussed the steps that led to permanent pacing.

The quarter century after 1960 saw many advances in the understanding of arrhythmias and in pacemaker technology, among them the definition of the spectrum of arrhythmias arising from atrial disease and known collectively as the “sick sinus syndrome,” the earliest clinically effective pacemakers able to sense electrical activity in the heart as well as pace, use of a transvenous endocardial lead for chronic pacing, and the introduction of lithium batteries and programmable pacemakers. In just 20 years, the number of patients carrying implanted pacemakers rose from half a dozen to an estimated half-million, while the number of manufacturers and implanting physicians also grew substantially.

The First Implantable Pacemakers
In 1958, Åke Senning, a thoracic surgeon at the Karolinska Hospital in Stockholm, implanted myocardial electrodes and a pulse generator with a rechargeable nickel-cadmium battery in a 40-year-old patient. Senning and his associate, Rune Elmqvist, an engineer with the Swedish firm Elema Schönander, had developed and tested this pacemaker between 1956 and 1958. The pulse generator failed within a few hours; a successor lasted about 6 weeks. Yet the patient survived, received another pacemaker in 1960, and is still living today. He has had 26 pacemakers altogether.

Two years later, William M. Chardack, chief of thoracic surgery at the VA Hospital in Buffalo, NY, carried out the first successful implantation of a battery-powered pacemaker with a myocardial lead. Engineer Wilson Greatbatch had worked with Chardack in designing the device. Chardack used a two-stage surgical procedure: he implanted the lead first, then the pulse generator after 2 months of successful pacing with stable thresholds of stimulation. His 77-year-old patient, Frank Henefelt, had suffered so many Stokes-Adams attacks that he customarily wore a football helmet! Once under pacemaker control, this gentleman was able to leave the hospital and lived a moderately active life for 2½ years, according to a story in a popular magazine, with no more “fainting spells.” The achievement of Chardack and Greatbatch has been recognized then and since as a defining event in the history of cardiac pacemaker implantation. A few weeks afterward, Paul M. Zoll and associates implanted a pacemaker of somewhat similar design at Beth Israel Hospital in Boston. Clearly, the idea for the implantable pacemaker...
was not the exclusive property of any one group but was “in the air.”

The 1960s were a time of incremental improvements in the early hardware and procedures of cardiac pacing. In the first year or two after Chardack’s case, no more than a few dozen physicians carried out implants in the United States. Implantation required a left anterior thoracotomy and exposure of the myocardium; thus, training in thoracic or cardiovascular surgery was a necessity. Almost all candidates for pacemakers presented with syncopal attacks, the acute symptoms of complete heart block. As often happens with a completely new treatment, pacing was clinically tested on patients close to death from numerous complex conditions. For the surgeon, implanting a pacemaker was a somewhat frightening procedure, but it was exciting to see patients who had been pale and continually passing out from Stokes-Adams seizures sit up after the operation, pink and rosy and ready to return to normal activities.

By the standards of the 1990s, the earliest implanted pacemakers appear large and ungainly. Powered by zinc-mercuric oxide cells, the pulse generators delivered stimuli at a preset rate, regardless of any intrinsic electrical activity in the heart. Hence, this early kind of pacing was known as asynchronous (later VOO) pacing. Pacemaker output was typically several times what was required. “The objective was simply to drive the heart,” Greatbatch later wrote, “without much regard for economy of battery life” or other refinements. The lead usually consisted of a pair of multistrand stainless steel epicardial wires in a Teflon sleeve.

Figure 3 lists the critical problems that received heaviest attention and indicates how they had been resolved by the end of the 1960s. In most cases, improvement in pacemaker performance and longevity flowed from an accumulation of small changes in hardware and procedure.

Critical Problems in Pacing During the 1960s

Manufacturers predicted that the pulse generators would function for 3 to 5 years, but the devices often failed unexpectedly much sooner. Unpredictable failures of life-sustaining devices required many emergency replacement procedures. Some of the early pacemaker recipients underwent two, three, or more reoperations because of broken wires or pulse generators that accelerated wildly or stopped suddenly. As they managed their patients through crises, physicians identified and helped solve a variety of critical problems that stood in the way of routine use of the pacemaker. Innovation in pacing during this decade was clearly driven by this pressing need to make the pacemaker a reliable device.

Fig 3 lists the critical problems that received heaviest attention and indicates how they had been resolved by the end of the 1960s. Every implanting physician faced them time and again. Chardack et al reported 11 broken leads in his first 16 patients and a range of other problems, including 11 cases of battery depletion before 24 months in a larger series of 60 cases. Kantrowitz reported 9 lead failures from broken wires, 3 dislodgements of the myocardial lead, and 2 cases of fluid in the pulse generator in a series of 43 patients. And from Newark Beth Israel Hospital, Parsonnet et al noted that their group had performed 22 complete reoperations and numerous minor operations on their first 93 patients (1961–1966), although 54 of these patients had required nothing beyond the original implant. Lead fractures were the group’s most common postimplant problem, followed by pulse generator failure and high pacing thresholds.

Addressing a Critical Problem: New Power Sources

Rather than review the solutions to all of the critical problems listed in Fig 3, we will discuss battery technology as an example of the problems and solutions of that day. Virtually all pacemakers of the 1960s drew their power from mercury-
zinc cells that had originally been developed during World War II for military applications. One firm supplied all the pacemaker manufacturers. Assured that batteries would function for 5 years, clinicians were dismayed to find that the pacemaker lasted <2 years on average. The cells were depleted nearly as much from self-discharge as from pacing, but of greater concern was that they emitted hydrogen gas as a byproduct and thus the pulse generator could not be sealed hermetically against the intrusion of body fluids. "If a really good power source were available," Parsonnet41,42 wrote in 1970, "the great majority of pacemaker replacements could be avoided."

The manufacturer made incremental improvements,43,44 but unhappiness with the mercury-zinc cells also induced a flurry of inventive activity involving completely different concepts: rechargeable pacemaker batteries,45–47 a biogalvanic cell,48 bioenergy sources such as driving a pacemaker off the mechanical action of the aorta or the diaphragm, nuclear generators, and batteries based on lithium chemistry (discussed below). Investigators in some cases devoted years of work to these possibilities.

Bioenergy
The group at Newark Beth Israel Hospital investigated biological processes within the human body that might be harnessed to power a pacemaker.49 What moved within the body that would produce energy? Pulsation of the thoracic aorta was a possibility. One member of the group knew a little about piezoelectric crystals, and a second was an amateur jeweler. In their first attempt, they obtained matchstick-sized ceramic blades to generate electricity. Circuitry within the pulse generator modified this energy and released it as timed electrical current. (From US Atomic Energy Commission. Generic environmental statement on the wide-scale use of plutonium powered pacemakers. January 1975.)

Figure 4. Diagram of thermoelectric nuclear generator in the version developed by Numec Corporation (later ARCO Medical). The generator used a tiny slug of Pu-238. Heat generated by decay of the plutonium was converted by a thermopile into an electrical current. (From US Atomic Energy Commission. Generic environmental statement on the wide-scale use of plutonium powered pacemakers. January 1975.)

In a second version, the Beth Israel group used two thin wafers or blades of a piezoelectric ceramic that were encapsulated in metal plates hinged together at one end like a clothespin; they clamped this mechanism around the descending aorta. The expansion and contraction of the vessel moved the ceramic blades to generate electricity. Circuitry within the pulse generator modified this energy and released it as timed electric impulses. This unit paced animals’ hearts for as long as 25 days at a time.51

They also considered other ideas such as pacing off the motion of the diaphragm by means of an apparatus like a watch spring (designed and supplied by E. Van Haaften of Bulova Watch Co). As the spring unwound, it turned a cam whose teeth snapped against wafers of piezoelectric material to produce output pulses. However, the investigators found that when something was attached to the apex of the dia-

Figure 4. Diagram of thermoelectric nuclear generator in the version developed by Numec Corporation (later ARCO Medical). The generator used a tiny slug of Pu-238. Heat generated by decay of the plutonium was converted by a thermopile into an electrical current. (From US Atomic Energy Commission. Generic environmental statement on the wide-scale use of plutonium powered pacemakers. January 1975.)

Physicians and Manufacturers in the 1960s
In the 1960s, most implanters of pacemakers were affiliated with academic medical centers and engaged in research and publication on pacing. Physicians and medical device manufacturing firms cooperated in a variety of ways, and both contributed important innovations.50–61 Physicians generally left to the engineers certain highly technical areas having to
do with implantable biocompatible materials, battery chemistry, and the design of pacemaker circuitry. Then as now, doctors often made suggestions to device manufacturers in rather general terms: We need smaller pulse generators, or Can you not give us a longer-lived battery? Sometimes physicians not only identified problems but described plausible solutions and tried to enlist others to build prototypes. For example, the initiative for the nuclear pacemaker came from Parsonnet in the form of a letter to the Atomic Energy Commission in 1965, suggesting that the agency look into this possibility.55

Several hospital-based research groups, working on their own or in close association with device manufacturers, made contributions as inventors during the 1960s. Such was the case with Chardack’s helical-coiled conduction wire, a vital advance over earlier lead designs when introduced by Medtronic, Inc in 1962.62 In Miami, cardiologist David A. Nathan and surgeon Sol Center approached Cordis Corporation with the idea for an atrial synchronous (or VAT) pacemaker and worked with engineer J. Walter Keller in developing and testing the device.22,63,64 Seymour Furman and his associates at Montefiore Hospital were active from the mid-1960s on in designing instruments that would help the physician assess the functioning of the pacemaker at implant and afterward. From this work, the Montefiore group went on in 1969 to describe the first practical techniques for the routine monitoring of pacemaker rate by telephone.55,66

Another important case of innovation reveals the complex and shifting nature of the relationship between physicians and the device manufacturing companies during the early days of cardiac pacing. It was clear that even in complete heart block, many patients had occasional conducted beats. Some physicians feared that pacemaker stimuli might occasionally induce ventricular fibrillation if they competed with intrinsic pulses. Others found that fixed-rate asynchronous pacing had negative hemodynamic effects in some patients, with fluctuations in cardiac output and blood pressure as the artificial pacemaker traded capture with the sinus node.67–69

Clinical researchers in England and Germany had earlier described experimental pacing devices that delivered impulses to the ventricle only when AV conduction failed.70,71 Medtronic, American Optical Co of Boston (AO), and Cordis announced pacemakers that avoided competition with conducted heartbeats. AO’s “demand” pacemaker and a similar unit from Medtronic recycled when they sensed ventricular depolarization. Designed by Barouh Berkovits, the AO pacer was first implanted in 1966 by Dwight Harken at Peter Bent Brigham Hospital in Boston.23 The Cordis “standby” pacer used a slightly different method in that a sensed R wave triggered the pacer stimulus with no AV delay, so that it fell into the refractory period of the QRS complex.24 (Today, these pacing modes are designated VVI and VVT: ventricular inhibited and ventricular triggered; the term noncompetitive encompasses both.)

If electrodes could be developed to sense spontaneous cardiac depolarizations, then it would be possible to design pacemakers able to respond appropriately to a variety of arrhythmias.72 Noncompetitive pacing was important as a step toward the dual-chamber pacemakers of a later era—devices that can sense and pace in one or both chambers and are thus capable of treating more complex arrhythmias.

Physicians had made substantial though indirect contributions to the invention of noncompetitive pacing. They had characterized the problem of pacemaker competition and had helped design and test experimental devices. However, embodying the concept in a reliable and fully implantable pulse generator required engineering skills in circuit design and a knowledge of the new silicon transistors. Once the manufacturing firms had built prototypes of the new pacers, they approached medical research groups and invited them to carry out animal and clinical evaluations of the devices.24,73

Doctors and engineers worked together in a variety of arrangements during the 1960s, but the pattern of noncompetitive pacing, in which doctors described a problem and engineers came up with a technological solution, would become the norm in the next decade.

Innovations in Procedures and Organization

In the 1960s, many physician contributions focused on implant procedures and the organization of services in the hospital. Temporary transvenous pacing is a good example of a procedural innovation. In the early 1960s, a number of implanting teams began the practice of routinely managing the patient on a transvenous lead and an external pulse generator for a few days or weeks to reduce congestive and cerebral symptoms and prepare the patient for the stresses of a thoracotomy and myocardial implant. This practice also reduced the risk of the patient’s experiencing a Stokes-Adams episode in the operating room that might then require an emergency thoracotomy.74–77

Furman’s transthoracic monitoring equipment, mentioned earlier, did not come into use as an isolated piece of hardware but as a basic step in the creation of routine procedures for postimplant follow-up of patients. At first, “follow-up” typically meant diagnosing and resolving various forms of premature and apparently random component failure that could leave the patient without pacemaker support,35,39 but as the number of patients grew, the need for routine and systematic surveillance became apparent. The earliest pacemaker clinics sought to estimate the remaining battery life of the pacemaker and identify those units about to fail before a problem became evident to the patient. This would make possible a scheduled rather than an emergency replacement.78–82 A decrease in pacing rate was the most important sign that the battery was approaching the end of its working life; this indicator could be detected by transthoracic monitoring.

The growing volume of patients with implanted pacemakers was an impetus for physicians to gather data on the behavior of the various pacemaker models, identify common types of pacemaker failure,83 and establish protocols for responding to different situations that could arise. In 1974, the Pacemaker Study Group of the Inter-Society Commission for Heart Disease Resources published the earliest set of formal guidelines for follow-up procedures and facilities; these have been updated periodically, most recently through a Policy Conference sponsored by the North American Society of Pacing and Electrophysiology (NASPE) in 1994.1,84
The transvenous endocardial lead gained rapid acceptance because it made the implantation of a pacemaker a less taxing procedure for both implanters and patients. Physicians have been more reluctant to adopt dual-chamber pacing, in part because of the difficulties of using an atrial lead and the more complex programming and follow-up that a dual-chamber device requires. See References 88, 90, 91, 104, 122, and 123.

These examples illustrate the point that the inventive activities of physicians and engineers did not conform to a single pattern in the 1960s. In general, physicians contributed ideas from their domain of clinical experience. They helped identify a variety of critical problems and as a response invented, or more often proposed or evaluated, possible solutions. They added not just new things but new ways of doing things.

Transvenous Pacing: A Radical Innovation

During the 1960s, most important innovations in cardiac pacing built on what physicians already knew and improved on existing technology. One important exception stands out: Transvenous catheter pacing was more than an incremental improvement. Furman had demonstrated in 1958—2 years before the first successful myocardial implant—that it was possible to maintain patients for many weeks with a temporary transvenous catheter electrode.9,14 and as already noted, some surgeons used a transvenous pacing lead with an external pulse generator to stabilize the patient for a few days before performing the definitive myocardial implant. The experience with temporary transvenous pacing helped acquaint surgeons with the techniques of catheterization.

Permanent transvenous pacing first appeared in the early 1960s,25,26 but did not gain general acceptance in the United States until after 1965 (Fig 5). A growing number of reports of successful long-term transvenous pacing in Sweden, the United States, and England85–87 and Medtronic’s introduction of a flexible transvenous lead in 1965 contributed to a shift toward the transvenous technique. Most experienced implanters shifted to the transvenous approach in the late 1960s, while surgeons new to the field accepted it as the normal path to the ventricle.88

Transvenous pacing encouraged the development of intra-cardiac diagnosis of arrhythmias,89 this in turn fostered the growth of clinical electrophysiology and led to the invention of new technologies such as implantable defibrillators with transvenous leads and endocardial ablation of aberrant conduction pathways. As Parsonnet and Bernstein18 put it, the transvenous pacing lead “spawned new specialties and industries.”

The catheter lead opened the field of pacemaker implantation to nonsurgeons, but until the late 1970s, surgeons continued to perform most implants.90 Then a gradual transition got underway: In the 1990s, fewer than half of the implanters are surgeons.90 A major impetus behind this shift was the development of an introducer, a peel-away sheath that provided access to a central vein through which a pacing lead could be passed. First described by Littleford et al,92 this device was a modification of the Seldinger sheath that had been used in cardiac catheterization for many years. The new design had a metal hub that could not be torn off, a necessity to allow passage of the larger connector terminal of a pacing lead. Once it was discovered that a central vein could be accessed without the need for exposing the cephalic vein in the delto-pectoral groove, nonsurgeons soon learned that they, too, could implant pacemakers.92

The Reliable Pacemaker of the Late 1960s

Over the first decade of implantable pacemakers, the expected longevity of the devices increased from a few months to 2 years or more. By 1970, companies and implanters had settled on the main features of a standard pacemaker design, including a transvenous lead and the capacity to sense as well as pace. Noncompetitive transvenous pacing became established as safe and effective for treating various forms of heart block. It seems to us, therefore, that the invention of a reliable pacemaker together with procedures for its implantation and use—the dominant design—was the overarching achievement of that era. Although Chardack93 believed that pacemaker “performance still falls short of . . . theoretical capabilities,” indications for implantation were becoming more liberal because the risks and complications associated with transvenous pacing now seemed “relatively trivial to most.”42

Innovation in the 1970s: Roots of Complexity

During the second decade of permanent cardiac pacing, device manufacturing firms created a regime of continuing and rapid technological change. By the early 1980s, the implantation and management of a cardiac pacemaker had become a far more complex procedure from the physician’s standpoint. There was a profusion of new indications for implantation and a stream of new pacemaker models with new capabilities. Many of the innovations in pacing hardware rendered physicians’ skills obsolete and required that they develop new competencies. A dominant design did not emerge until the diffusion of dual-chamber “universal” (DDD) pacemakers into general use during the mid-1980s.94

Surveys of pacing practice suggested that new indications (ie, in addition to complete heart block) accounted for one-quarter to one-half of new implants during the 1970s.90,95,96 The most important indication that emerged was the so-called “sick sinus syndrome,” a phrase introduced in
that covered a variety of disorders of impulse formation. Adding new indications for pacemaker implantation meant, of course, that the universe of potential patients expanded. Medicare, which had gone into operation in 1966, further encouraged the growth in the number of implants between the late 1960s and the advent of the prospective payment system in 1983 (Fig 6).

Pacemaker implantation had gained a reputation for being a safe and relatively simple procedure. Almost any surgeon or internist who wished to implant pacemakers in the United States could do so, regardless of subspecialty or training. In contrast to prevailing practices in Europe, no national accrediting boards and few hospitals defined and enforced implantation privileges in the United States. The total number of implanters is not known for certain, but it certainly was increasing rapidly during the 1970s. Many of the new pacemaker physicians implanted only a few devices each year as one aspect of broader practices in cardiology, internal medicine, or surgery.

The market for pulse generators and leads grew at an estimated annual rate of 45% during the decade. Medtronic and Cordis held about three-quarters of the US market for pacemakers, with Cordis specializing in advanced products for large pacemaker clinics and Medtronic firmly established among physicians who implanted relatively few pacemakers. But the lure of high profit margins and strong market growth also attracted new manufacturing firms. These newcomers sought to differentiate themselves from the more established companies by introducing many novel (patentable) features and by frequently announcing new and improved models. The manufacturers’ struggle for market share upset the stability of the pacemaker industry.

Doris Escher and her colleagues reported in 1978 that the 16 manufacturers active in the American market were then offering about 130 pulse generator models. (Most of the new entrants to the US pacemaker industry in the 1970s have since left the industry or have been absorbed by the larger companies. After a recent wave of acquisitions, five major American manufacturers remain: Medtronic; Sulzer Intermedics, which is owned by the Swiss conglomerate Sulzer; Cardiac Pacemakers, Inc [CPI], a division of Guidant Corp; and Pacesetter and Teletronics, both acquired by St Jude Medical in 1996.) Presented with this proliferation of devices, many of the newer implanting physicians came to rely heavily on the manufacturers’ “technical specialists” who were, in some cases, indistinguishable from sales representatives. From that day to this, close relationships between physicians and sales representatives have characterized the field of cardiac pacing.

Key Innovations of the 1970s

Several major technological innovations rendered obsolete the dominant pacemaker design of the late 1960s (Fig 7). First, manufacturers resolved the problem of pacemaker longevity by embracing the lithium battery, a long-lived power source free of the problems associated with the nuclear generator. Soon afterward, the device companies introduced noninvasively programmable pacemakers—and then multiprogrammable units with bidirectional telemetry. Implanting physicians accepted the lithium battery immediately but proved more cautious in their reaction to multiprogrammable devices and a third major innovation, dual-chamber pacing.

The Lithium Battery

The invention of a long-lived pacemaker battery based on lithium chemistry precipitated a cascade of radical changes in cardiac pacing. Engineers at Catalyst Research, a small battery manufacturer in Baltimore, Md, had invented a cell with a lithium anode and a cathode of iodine in 1967, but the company did not find a commercial use for it until word of the invention reached Wilson Greatbatch, designer of the circuitry for the first implanted pacemaker. Greatbatch perceived at once that its properties would make it suitable for implanted pacemakers. By 1973, his own firm of Wilson Greatbatch, Ltd, was manufacturing lithium batteries based on the Catalyst design. Because of his prestige in the pacing community and his ability to persuade, he single-handedly
turned the pacemaker industry to lithium. A survey of pacing practices in 1978 indicated that only 5% of newly implanted pulse generators still used mercury-zinc batteries.

CPI, a new company founded by a group of former Medtronic employees, released the first clinically reliable lithium pacemaker as its initial product in 1973. CPI was typical of several companies attracted to the pacemaker business in the 1970s that offered new technology in hopes of weaning physicians away from their accustomed suppliers. Most pacemaker manufacturers introduced lithium-powered pacers in 1975 to 1976.

The various batteries based on lithium chemistry had somewhat different properties and varied actuarial survival performance, but all enjoyed significant advantages over mercury. The high energy density of the lithium battery enabled the manufacturers to downsize their pulse generators. The output voltage of the lithium-iodine cell decreased gradually rather than abruptly as in the mercury-zinc cell, giving the physician ample warning of the need to replace the pulse generator. Finally, the new battery generated no gas as a chemical byproduct, so the entire pulse generator could last be hermetically sealed. Between 1972 and 1976, several companies had been forced to issue product advisories when moisture caused some of their mercury-powered pacemakers to short-circuit. The national publicity and unsympathetic reaction from Congress and the Food and Drug Administration were intensely unpleasant to the entire industry and drove one manufacturer, General Electric, out of pacing. These product failures no doubt accelerated the transition from mercury to lithium.

Programmable Pacemakers

Pacemaker manufacturers introduced hybrid circuitry and then completely integrated circuitry during the 1970s; this permitted them to design far more complex pacemakers with numerous parameters that the physician could noninvasively adjust by using a programmer that transmitted coded instructions on a carrier signal through the patient’s chest to the implanted pulse generator. In effect, the manufacturers were empowering physicians to individualize the behavior of the pacemaker for each patient. Innumerable variations in pacing could be achieved by noninvasive programming. Some of the concepts developed were not intuitively comprehensible, however; they required more study to achieve competence in the exploding field.

The external pulse generators of the 1950s had permitted adjustment of the impulse rate and amplitude. Between 1966 and 1972, device firms had designed several methods of modifying pacemaker function, but some of these required minor surgery, and all were (by later standards) crude in design. For example, one model from 1962 had two nipples in the pacemaker housing that the physician could enter with a Hagedorn needle to turn potentiometers and change the output or rate. Two firms offered dual-rate pacers in which a magnet applied externally would temporarily increase the pacing rate from its base value, and the output of another device could be adjusted by amputating a resistor housed in the end of a pacemaker “tail.”

In 1972, Cordis introduced the Omnicor line of pacemakers, the first adjustable pacers under noninvasive electronic control. The Omnicor was based on more advanced microelectronics than earlier pacers; it included an integrated sensing amplifier and two integrated digital logic circuits in an overall hybrid design. Parsonnet et al reported that it could be noninvasively reprogrammed for rate (six choices) and output (four choices). The Omnicor also contained a miniature magnetic reed switch that Cordis engineer Vincent Cutolo had developed. By means of a handheld device (the ancestor of today’s external programmers), the physician transmitted a series of magnetic pulses that vibrated the switch. A counter noted the number of changes in the position of the switch and associated this number with a corresponding value for rate or output.

Just as in the case of CPI and the lithium battery, Cordis enjoyed a brief monopoly on programmable pacers, but eventually the other firms, led by CPI, worked around the company’s patent. In 1978, five companies introduced multiprogrammable units (defined as programmability on at least three parameters). The most important of these devices was the Cyberlith from Intermedics, Inc, one of the new firms in the pacemaker industry. This pacer could be reprogrammed on four parameters, giving the physician a choice of 15 pacing rates, 14 impulse durations, and 7 sensitivity settings. But its truly distinctive feature was a novel two-way telemetry system, the product of a collaboration between engineer Robert R. Brownlee and surgeon G. Frank Tyers. Bidirectional communication meant that the doctor or a technician could not only adjust the pacemaker but download information about the stimulation rate, battery voltage and impedance, and the integrity of the encapsulation in the implanted device.

Programmable features and telemetry transformed the pacemaker from an appliance with a limited range of preconceived applications into an extraordinarily flexible tool adaptable to many applications, including some that its inventors had not envisioned. As Parsonnet and Bernstein later wrote, the pacemaker was becoming “essentially an implanted microcomputer that can be adapted noninvasively to any type of stimulation or sensing that is required.”

Reprogramming the output of the pacemaker extended its life, sparing the patient excessive reoperations. Pacing specialists also welcomed programmability because pacemakers could now be applied for a wider range of conduction diseases, thereby expanding the utility and further raising the profile of pacemaker therapy. Cardiologist Leonard S. Dreifus found “the programmable aspect of pacemakers ... increasingly attractive” in the effort to move beyond heart block and “pace patients with other electrophysiological derangements such as rapid tachycardias, AV junctional tachycardias, Wolff-Parkinson-White tachycardias, and ... other complex problems related to the sinus node and atrium.” Programmability was useful even in the more routine cases of heart block and the sick sinus syndrome because the programmable features enabled the physician to fine-tune the pacemaker repeatedly to accommodate pacing to the patient’s changing condition. In light of the long
pacemaker life expectancy, this flexibility seemed particularly important.

But while physicians definitely wanted long-lasting and adjustable devices, they had not expressed a clear demand for the great range of choices that multiprogrammable pacemakers actually gave them. The typical physician implanted a relatively small number of pacemakers. As the number of implanters rose, the mean number of annual implants declined.30,121 A survey from the early 1980s revealed that most respondents used either simple programmable or multiprogrammable pacemakers and declared these devices to be “clinically important,” yet some 47% of the programmable pacemakers were not reprogrammed within the first 3 months after implantation and 30% were never reprogrammed.122 This was not a transitory finding: subsequent surveys including the most recent, conducted in 1993, yielded similar percentages.31,125 Apparently, many physicians viewed programmability as a tool for troubleshooting pacemaker problems that might arise after implant but assumed that for most cases, the standard ventricular inhibited (VVI) pacing mode performed adequately.124,125

Given the number of implanting physicians who had entered the pacemaker field after 1970 and who implanted only a few pacers, simplicity and reliability remained important desiderata.97 The single-chamber programmable pacemakers of the mid-1970s offered the physician noninvasive control of pacing rate, output, and in some models, sensitivity to intrinsic cardiac signals. For the time being, that was about as much as the community of pacing physicians seemed to require, especially because programmable pacemakers were more expensive and entailed more complex record-keeping procedures. Did they also contribute to patient satisfaction, well-being, and longevity? In the absence of formal clinical trials, it was difficult to say for certain.29

**Dual-Chamber Pacing Before 1980**

A third important innovation, dual-chamber pacing, had been discussed for years but finally moved to center stage around 1980. Dual-chamber pacing was a physicians’ concept and by no means a new one. From the earliest days of long-term pacing, doctors had been interested in restoring the hemodynamic benefits of a functioning atrium synchronized with the ventricle. Nevertheless, it was a radical innovation like the transvenous pacing lead in the 1960s because it required that physicians inhibit the pacemaker.

In an effort to emulate the heart’s conduction system, several groups experimented in the 1950s and early 1960s with “P synchronous” or AV synchronous (VAT) pacemakers.5,11,126–128 Just 3 years after the first implantation of a fixed-rate pacemaker, Cordis announced an AV synchronous pacemaker called the Atricor that used epicardial electrodes. Essentially, this device bridged the AV node by stimulating the ventricle after sensing an atrial depolarization. In the face of atrial tachycardia, the pacer would revert to 2:1 or 3:1 conduction.21,22 This was a highly sophisticated concept for the mid-1960s, but it proved difficult to embody the idea in a fully satisfactory device. The complexity of the circuitry necessitated a bulky pulse generator and reduced the life of the battery. There were reports of problems with erratic sensing of the P wave and some unhappiness with the occasional abrupt drops in pacing rate that occurred when upper rate limits were reached.129

Yet dual-chamber pacing remained an intriguing possibility, particularly as the hemodynamic benefits of providing AV synchrony came to be more widely recognized. A few years after the Atricor, cardiologists Louis Lemberg and Agustin Castellanos, Jr, and engineer Barouh Berkovits announced a “bifocal” (AV sequential or DVI) pacer with endocardial electrodes that sensed only in the ventricle but paced both chambers.130,131 In the presence of atrial standstill or a very slow atrial rhythm plus heart block, the bifocal pacemaker (manufactured by American Optical) could deliver a stimulus to the atrium and then, after an appropriate interval, to the ventricle. If the patient had a sinus bradycardia with intact AV conduction, the pacemaker would pace the atrium alone. Normal sinus rhythm and AV conduction inhibited the pacemaker.

Despite physicians’ growing interest in pacing as a treatment for the sick sinus syndrome and claims that the bifocal pacer was more “physiological,”122 very few of these pacemakers were implanted. AV sequential pacing was appropriate for a small segment of the patient population, particularly those afflicted with both heart block and sinus bradycardia. The pulse generator was bulky and placed a high demand on its battery. In its earliest version and in a later model introduced after Berkovits moved from American Optical to Medtronic, AV sequential proved to be an interim step on the way to the more advanced forms of dual-chamber pacing.133

**The 1980s: The Multifunctional Pacemaker**

**Dual-Chamber “Universal” (DDD) Pacemakers**

At the end of the 1970s, the great majority of implanted pacemakers still functioned in the ventricular inhibited (VVI) mode.90 But advances in microcircuitry and clinical conceptions had created a climate in which dual-chamber pacing seemed to be the inevitable next step. Without seriously compromising service life, manufacturers could readily design in programmable functions for sensitivity, refractory period, and AV delay, along with stimulus rate, amplitude, and duration.10 These parameters had been fixed in the circuit designs of the earlier dual-chamber pacemakers and hence were identical for all patients; now physicians would be able to individualize the settings and revise them later as necessary. Some specialists were suggesting that dual-chamber pacing was preferable to ventricular inhibited for most patients.134–136

The third generation of dual-chamber pacemakers, introduced in 1980 to 1981, incorporated the major design innovations of the previous decade: long-lived lithium batteries, bidirectional communication between physician and pulse generator, and dual endocardial leads. It is perhaps less obvious that this new generation of pacers was founded on ideas and clinical experience extending back to the 1960s and even earlier, especially the concepts of altering the action of the pacer depending on sensed electrical activity within the heart and of trying to restore physiological response. The dual-chamber universal pacemaker was able to sense and pace in both atrium and ventricle. It paced...
the two chambers sequentially when atrial rates were slow but stimulated the ventricle synchronously with the atrium when atrial rates were faster. Designation of the upper rate limit also was a programmable function.29

Barriers to Physician Acceptance
Implanting a second lead via a separate vein and maintaining it stably in the atrium had always been a challenge; this was probably the greatest impediment to wide acceptance of all dual-chamber pacemakers.137 The tined atrial electrode with a fixed J curve pioneered by Nicholas Smyth proved to be a breakthrough.138,139 The device manufacturers later came out with a number of variants (eg, screw-in tips) intended to anchor the electrode tip in the atrium.140 Other improvements in lead technology prepared the way for wider use of two leads. The use of polyurethane as an insulating material resulted in strong, fatigue-resistant leads with a diameter somewhat less than that of silicone leads. Because polyurethane is slipperier than silicone, the implanter had an easier time introducing two leads through a single vein.141 If not wholly satisfactory, leads had come to be less of an impediment by 1980.142

Although further improvements in atrial sensing still were needed,143 advances in lead technology and implantation procedure led Parsonnet137 to assert that routine implantation of a second lead was "a technique whose time had come." But eventual acceptance of dual-chamber pacing in the large and growing community of pacemaker implanters did not depend solely on improvements in devices and surgical procedure. Just as with multiprogrammability around the same time, physicians who treated cardiac arrhythmias needed to have a clearer idea of the benefits that the second lead might confer on their patients. "Lack of understanding of system characteristics, indications for use, and clinical behavior" remained a significant barrier (Figs 5 and 8).144

As Furman and others145,146 had noted, dual-chamber pacing emulated physiological response; it provided "an approximation of the normal AV sequence, with the atrium contracting first, a delay of approximately normal duration . . . and then a ventricular contraction." In pacing the ventricle alone without a rate response, as had been the practice in earlier days, cardiac output was maintained by increasing cardiac contractility. This ability depended on myocardial viability that often diminished with age or the progression of the underlying disease. But now, as long as the inherent atrial rate was chronotropically competent,147 a dual-chamber pacemaker would be able to respond to the patient's varying needs for cardiac output by accelerating or slowing the ventricular rate.148 The major contraindication was chronic atrial fibrillation or flutter.146

The Multifunctional Pacemaker of the 1980s
With the invention of pacemakers that were long-lived, multiprogrammable, and capable of sensing and pacing in both chambers, clinicians were equipped to pace and manage virtually any form of bradycardia. Three such pacers came onto the market in 1981 from Cordis, Medtronic, and the West German firm Biotronik, with other models following.29 It seems clear that a new dominant design had supplanted the familiar ventricular-inhibited transvenous pacer of the late 1960s and early 1970s. The new pacemakers of the 1980s embodied a quest for multifunctionality (Fig 9), but this came at a price. The extraordinary flexibility of the new generation of pacemakers depended on external programming. Transvenous pacing had simplified the clinician's task by obviating the need to perform a thoracotomy; in contrast, dual-chamber universal pacemakers added new and daunting elements of complexity. The new generation of devices could produce ECGs that were difficult to interpret.149 They could oversense and self-inhibit, and there was some danger that an inappropriately configured DDD pacer could induce a pacemaker-mediated tachycardia.150 Managing these pacers required that the physician thoroughly understand pacemaker timing cycles.151

Despite these imperfections, a strong consensus in favor of DDD pacing took shape among pacemaker experts. In 1984, a task force of NASPE suggested that DDD pacing was indicated in 60% to 80% of all cases.146 Surveys of pacing practice reveal a gradual shift from single-chamber to dual-chamber pacing modes since about 1980, reflecting manufacturers' improvements in dual-chamber pacemakers and the growth of physician understanding and skill (Figs 5 and 8).
Actually, industry leaders had thought that DDD pacemakers would gain physician acceptance more quickly. In an interview, one executive recently commented that “it just took a long time for [many physicians] to really believe that the benefits were worth the hassles. You have to put in an atrial lead, atrial lead dislodgments are a little more of a problem, more programming of the device, more things that can go wrong. Perhaps PMTs [pacemaker-mediated tachycardias] early on discouraged people.” Today, nonsurgeons, electrophysiologists, and implanters at academic institutions tend to favor DDD and other dual-chamber pacing modes most strongly. Bernstein and Parsonnet\(^{41}\) hypothesized that these implanters are more heavily involved in follow-up and more interested in optimizing hemodynamics and avoiding the symptoms of the pacemaker syndrome.

**Pacemaker Complexity and NASPE**

During the 1970s, a few of the senior specialists in pacing founded the journal *PACE* and organized a professional society, the NASPE.\(^{152,155}\) These physicians had shared similar careers in cardiac pacing: they had begun in the 1960s or even the late 1950s, which meant that they were usually surgeons by training; and they worked at large teaching hospitals where they supervised residents and conducted laboratory and clinical research. As experienced implanters, they had been uneasy for several years about the level of training that some more-recent entrants brought to the field of pacing and believed that a specialty society was needed in a field that was growing almost explosively.\(^3\)

The presence of manufacturers’ sales representatives during implant procedures caused some consternation among this senior group. Speaking for many others, Seymour Furman commented that “the dependence of an implanting physician on a salesman for routine procedures is unwholesome”; he cited the rapid technological changes in cardiac pacing as the root of the problem and chided hospitals that “apparently remain unwilling to provide pacer technical assistance as they do for a host of other medical efforts.”\(^154\) Despite these concerns, the practice is now almost universal; a manufacturer’s representative is present for the implantation of the pacemaker in 95% of cases.\(^9\)

In announcing the formation of NASPE, the founding group mentioned a “growing concern over the increasing complexity of pacemaker systems, maintenance of quality control and good manufacturing practices by the manufacturers . . . and the proper surveillance of an ever-expanding recipient population.”\(^153\) Through policy conferences and special reports, NASPE sought to exercise a shaping influence on pacing practices by codifying a set of standards against which every implanting doctor or hospital administrator could measure his or her facility and practice.\(^154,155\) The NASPE leadership also began to push for formal training requirements and certification procedures for all physicians who implanted pacemakers.\(^156,157\) For the past decade, the society (through a subsidiary organization) has sponsored an annual national examination leading to a certificate of special competence for physicians and associated professionals.\(^158,159\) In 1998, some 8700 physicians participate in pacemaker implantation in the U.S. Only 1461 are NASPE members (according to sources at NASPE), but the number is growing steadily.\(^91\)

**Discussion**

By the mid-1980s, the pacemaker—an implanted electronic device that managed bradyarrhythmias—had attained technological maturity, though not perfection.\(^{161}\) Parsonnet and Bernstein\(^{111}\) predicted in 1985 that the next generation of electronic devices would carry multifunctionality to new levels. The “implantable multipurpose electronic system” of the future would “pace the heart, diagnose and interrupt tachyarrhythmias, identify and correct its own internal electronic problems, and adjust its output and sensing levels. . . .”

Much of this has come to pass. The past 15 years have seen the immense impact of the incorporation of sensors into the devices to adapt pacing rate and other functions to the activities of daily life. We have focused on bradycardia management in this paper, but atrial and dual-chamber pacing evolved into recognized treatments for many supraventricular tachycardias; this development is another indication of the remarkable flexibility of modern pacemakers. Indications for pacing now extend beyond conduction system disease to include AV nodal ablation (which produces AV block), while pacing has shown promise as a treatment for hypertrophic and end-stage dilated cardiomyopathy, vasovagal syncope, long-QT syndrome, and prevention of paroxysmal atrial fibrillation in some patients.\(^{162}\) The industry is presently investigating numerous refinements in pacing technology, among them improved atrial tachycardia discrimination and algorithms to change the pacing mode automatically in response to a tachycardia; elaboration of alternate sensors including Q-T interval, temperature, right ventricular pressure, right ventricular dP/dt, and pH; self-diagnostic techniques with automatic adjustment of thresholds for pacing and sensing in both chambers; and multisite pacing with electrodes in three or four chambers. In these developments the manufacturers have played the leading role, with clinicians peripherally involved until the stage of clinical evaluation.

The tiny devices of the 1990s are increasingly self-diagnostic, adjusting their function to the physiological demands of the body, the changes in stimulation and sensing threshold. Pacemakers began as appliances but are becoming fully automated machines. We will shortly see the complete integration of pacemakers with defibrillators in the same can. The uses of these devices have become so varied and complex that there is an even greater need for recognition of pacing as a subspecialty worthy of dedicated training and credentialing.\(^{156,163}\) Each of these developments is worth an extended discussion, but they are beyond the scope of this paper.

At the outset, we asked how physicians had contributed to the process of innovation in cardiac pacing and, more broadly, what groups and forces had driven the engine of technological change. We have discussed the innovations that most decisively influenced the development of cardiac pacing as a field of medical practice and reshaped the experience of doctors and their patients. We hazard some concluding thoughts about innovation in pacing during the era from 1960 to the mid-1980s:

1. At first, the modest size of the field of cardiac pacing and of its manufacturing firms made it possible for innovative men and women to bridge the normally separate worlds of medical research and corporate research and development.\(^{60}\) That informal and face-to-face quality of the field of pacing
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is more difficult to maintain today because of institutional growth (Medtronic had 45 employees in 1963 but has nearly 14,000 today) and the entrance of new parties: the Food and Drug Administration, the Health Care Financing Administration, and the hospital chains and managed-care organizations.  

2. After about 1970, physicians played a less central role in invention but continued to influence the technology of pacing by advising the manufacturers on needed improvements, by broadening the list of indications for pacemaker therapy, and by focusing on the training and certification of physicians and allied specialists for pacemaker work. In unexpected ways, the introduction of complex and multifunctional pacemakers has accentuated the differences in outlook between specialists and occasional implanters.6,164

3. Once launched, innovations diffuse into general use at very different rates. In the first quarter century of chronic pacing, physicians’ eagerness or reluctance to adopt new technology was generally a function of two factors: the simplicity or complexity of the new device and the adequacy of supporting technology. In the case of dual-chamber pacing, the “bench to bedside lag” was particularly striking.164

4. Between 1960 and 1985, what drove innovation in bradycardia pacing? Two factors were paramount. First, new knowledge from cardiology and electrophysiology added repeatedly to the list of arrhythmias for which pacing was thought to be an appropriate treatment. Second, the device manufacturers, in their struggle for market share in a rapidly growing industry, introduced new devices and components that helped burnish their reputations for high-tech excellence and cement their relationships with doctors. Extrapolating from recent developments, J. Warren Harthorne has suggested, with perhaps a touch of whimsy but with citations to the scientific literature, that the future will give us “implantable computers that will serve as an electronic service center” able to communicate with various organ systems “to arouse flagging performance of cerebral, respiratory, gastrointestinal, genitourinary, and musculoskeletal function.” Electrostimulation has evolved so far since 1960 that this description does not seem entirely outside the realm of the possible.18

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