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The Bourner Lecture: Electrochemical power sources — an important contributor to modern health care

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Abstract

The invention of the cardiac pacemaker thirty-nine years ago marked the beginning of the era of the treatment of health disorders by battery powered implantable devices. Since that time several different battery-powered implantable devices have been developed and are in use. Batteries play an important role in external medical devices as well, ranging from surgical tools to motorized wheel chairs. As both battery technology and device development progress, the use of batteries in the treatment of disease will continue to be an important feature of medical care.

Keywords: Applications/medical; Reviews

1. Introduction

April 1997 marks the 39th anniversary of the implantation of the first experimental cardiac pacemaker in an animal. These tests proved successful, and the implantation of cardiac pacemakers in human beings became reasonably common in the 1960s. The technology progressed, and the number of pacemakers implanted annually exceeds 450 000 today. This development has led to the invention of other battery powered devices. Implantable defibrillators save thousands of lives annually. Drug delivery systems provide the carefully controlled administration of medication inside the patient. Neurostimulators which relieve severe pain and treat conditions such as epilepsy are in routine use. Left ventricular assist devices provide a life-saving 'bridge' for patients awaiting heart transplants.

In addition to these internal devices, batteries have long played an important role in powering external medical devices. Portable external defibrillators powered by rechargeable batteries are present in most emergency response vehicles. Holter devices for cardiac monitoring rely on batteries for energy. Ambulatory external drug delivery systems are powered by batteries. Motorized wheel chairs, increasingly common, rely on secondary batteries for their power. Surgical tools without cords enable surgeons to operate with less inconvenience. The list goes on and on.

The development of the devices mentioned above has been made possible in part by the advances in battery technology in the last 40 years. We have seen the evolution of implantable biomedical devices proceed as the development of advanced primary lithium batteries has evolved. The advances currently under way in the field of secondary batteries provide the promise of lighter, smaller, and longer lasting power sources for external medical devices. Specialty batteries using unique materials will allow the development of medical devices for demanding environments such as the magnetic resonance treatment arena.

Power sources for medical devices share many important features. Size and weight are always important considerations, particularly for implantable devices. Longevity is a crucial factor. Most important of all, however, is the requirement for the highest standards of quality and reliability. Life-saving devices simply must work right, and the battery is a crucial component in ensuring reliable performance. Methods of assessing quality and reliability of medical batteries have been developed and are used to ensure that power sources meet the requirements.

The following sections of this paper will discuss the history of devices using medical batteries and will provide a look at the future. The use of batteries to treat human health problems has a proud heritage and a bright future, and continued progress in this field is anticipated.

2. The cardiac pacemaker

The first successful cardiac pacemaker, developed by Greatbatch and Chardack between 1958 and 1960, used zinc/

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mercuric oxide batteries as the power source [1]. Early pacemakers used as many as ten of these batteries in a series/parallel combination. This cell, invented by Ruben [2], was used in most pacemakers during the first 10 years of the use of such devices. While this system helped make possible the development of the pacemaker, significant drawbacks were present.

The cell generated hydrogen gas as a by-product of the cell reaction, and this prevented hermetic sealing of the pacemaker. The cell showed significant self-discharge at body temperature. The end of cell longevity was rather abrupt, with little or no indication that cell depletion was imminent.

Whereas later versions of the cell, made by scientists in companies such as Leclanché, Mallory, and General Electric showed some improvement in longevity and self-discharge [3], the battery remained the significant contributor to pacemaker failure, and alternate power sources were sought.

A rechargeable pacemaker was developed in the 1970s, using a specially designed nickel/cadmium battery [4]. The cell was recharged through the skin by an alternating field. This pacemaker system was a technical success (some few remain implanted today!), but patient compliance was a problem and subsequent success in developing primary batteries rendered the system unattractive in the marketplace.

Nuclear batteries were developed for pacemakers. These cells used plutonium to generate heat, which was converted into electrical energy by thermopiles [5]. Again, this system was reliable and successful, but the regulatory burden associated with tracking patients implanted with these devices led to their demise in the marketplace.

The first real progress in achieving a truly long-lived pacemaker which was generally acceptable to the marketplace came with the development and commercialization of lithium primary batteries in the late 1960s and early 1970s. Lithium metal, which offers 3.86 ampere hours of capacity per gram, made possible the development of pacemakers with years of longevity which could be hermetically sealed and whose approach to cell depletion could be easily detected by the circuitry of the device.

The first lithium battery to be used in a cardiac pacemaker was the lithium/iodine-polyvinylpyridine (PVP) system, invented by Schneider and Moser [6,7] and improved by Greatbatch, Mead and Rudolph [8]. The first such battery was implanted in Italy in 1972 [9]. Several other lithium-based systems saw significant use in pacemakers, notably the lithium/silver chromate system [10], the lithium/cupric sulfide system [11], and the lithium/thionyl chloride system [12].

Gradually the other systems gave way to the lithium/iodine-PVP system, and today virtually all cardiac pacemakers use this system. This system solved several problems inherent in the earlier zinc/mercuric oxide battery. There is no gas generation, so the cell and the pacemaker can be hermetically sealed. The energy density approaches 1.0 Wh cm^{-3}, providing the possibility of greater longevity in a much smaller package, and the self-forming, self-healing electrolyte/separator (the lithium iodide formed during the cell reaction) provides inherent reliability. Over three million pacemakers using this system have been implanted in the last 25 years, and the system has shown an excellent record of reliability and safety [13].

There are two features of the lithium/iodine system which have motivated the consideration of alternative chemical systems for the pacemakers of the future. Because the system contains a solid electrolyte which grows thicker as the cell is discharged, the resistance of the cell is rather high and increases with discharge. This results in a voltage drop under load which increases as the cell is depleted and results in current-delivery limitations near end of service. Whereas the cell shows excellent volumetric energy density, the gravimetric energy density is not as advantageous, since iodine itself is rather dense and the cell is encased in a stainless steel case.

It has been proposed that using a solid cathode, liquid electrolyte system could help to alleviate these drawbacks. The lithium/carbon monofluoride system has been proposed for future pacemakers. This system can be encased in a titanium enclosure, resulting in a cell which retains the volumetric energy density of the lithium/iodine-PVP system while doubling the gravimetric energy density. The resistance of the cell remains well under 50 ohms throughout discharge, unlike the lithium/iodine-PVP system which exhibits a resistance of thousands of ohms in the final stage of discharge. These solid cathode liquid electrolyte systems, including lithium/carbon monofluoride and lithium/manganese dioxide, are likely to see service in pacemakers of the future [14].

3. The implantable cardioverter/defibrillator

The implantable defibrillator was developed by Morowski et al. in the 1970s [15]. Morowski believed that ventricular fibrillation, a major cause of death, could be treated by an implantable device which could detect the onset of the condition and provide a shock to the heart, stopping the fibrillation and restoring normal cardiac rhythm. It had long been recognized that an electrical shock could reverse ventricular fibrillation, and external defibrillators, which provided the shock through the skin and muscles of the patient, were in common use in the 1970s. It remained to develop an implantable device which could provide the same therapy directly to the heart. By 1980 a working model was implanted in a human.

This device places a challenging demand on the battery. The power source must operate efficiently at the low current drains necessary to power the monitoring circuitry and, when ventricular fibrillation is sensed, must provide a very high energy pulse (up to 35 joules) to charge the capacitors and provide the shock to the heart.

The first power source used in this application was a lithium/vanadium pentoxide cell developed by Horning and Viswanathan at the Honeywell Corporation [16]. Early units

powered by this device showed somewhat shorter longevities than needed, and this source was soon replaced by batteries using a cathode material known as silver vanadium oxide, based on original technology developed by Liang et al. at Wilson Greatbatch Ltd. [17,18] and adapted for the implantable defibrillator application by Keister et al. [19]. Cell development has also been reported by Crespi et al. [20]. The lithium/silver vanadium oxide energy source has been used in over 75 000 implantable defibrillators and has proven to be an effective battery for this application [21,22].

More modern versions of the implantable defibrillator provide bradycardia pacing, advanced monitoring, and 'tiered therapy', which attempts to pace the patient out of tachycardia, resorting to the high energy shock only if these lower energy treatments fail to reverse the tachycardia.

Recent advances in both battery design and capacitor technology have produced implantable defibrillators which are much smaller and lighter than the original large 'shock boxes' in use in the mid-1980s. Today's units can record diagnostic clinical data for telemetering to the physician. The development of the transvenous lead has eliminated the need for a thoracotomy to attach the lead to the heart. Recent clinical studies have established the effectiveness of the device in prevention of sudden cardiac death, providing an additional tool for the physician to treat serious arrhythmia.

4. Implantable neurostimulators

Some types of chronic intractable pain can be effectively managed by electrical stimulation of the spinal cord [23]. Implantable neurostimulators have been used for several years for this purpose. More advanced models of these devices, which operate electrically much like cardiac pacemakers, permit the patient to control the level of stimulation in response to the level of pain involved.

Recent studies have shown that direct stimulation of the brain may be effective in controlling the tremors associated with Parkinson's disease [24]. This application of stimulation is in use in Europe today and is under evaluation in the United States.

A unique application of neurostimulation has been developed to treat epilepsy. A multi-programmable implantable pulse generator delivers electrical signals to the left vagus nerve via bipolar electrodes. These electrical signals have been shown in clinical trials to be effective in reducing the frequency and severity of epileptic seizures [25].

The above-mentioned devices currently are powered by lithium/thionyl chloride batteries, which can provide the milliampere-level current drains necessary for effective stimulation [26]. It is likely that the future will see the use of solid cathode, liquid electrolyte batteries in these devices.

5. Implantable drug delivery systems

The development of implantable drug delivery systems began in the 1970s. The first such units used a bellows pump activated by liquefied freon [27]. The device provided a constant flow of a drug through the expansion of the bellows. Upon transcutaneous refilling of the device, the freon was reliquefied, the bellows was contracted, and the process continued. There were no electronics or batteries in the device, so no control of the drug administration other than that provided by the mechanical pump was possible.

It was recognized that more sophisticated devices using electrically powered pumps and advanced electronics could provide a more controlled administration of drugs. In the case of insulin delivery, a prime candidate for the use of this device, a programmable unit could mimic more closely the natural administration of insulin, providing better glucose control and the possibility of reduced side effects [28].

Such pumps are now in various stages of development or production. The use of implantable pumps for administration of several different drugs has been approved by the US Food and Drug Administration. Among the conditions treated with this therapy today are cancer, multiple sclerosis, cerebral palsy, and injuries [29]. Thousands of such pumps have been implanted.

The use of implantable pumps to administer insulin is still under clinical investigation at this writing. Over one thousand insulin pumps have been implanted worldwide, and evaluation and optimization continue [30].

The most commonly used battery system for these devices is the lithium/thionyl chloride system. This system offers the ability to deliver the milliampere-level current drains required by the device and the higher voltage (3.65) needed by the electronics. This system has proven effective in this application. As is the case with the neurostimulators mentioned above, drug pumps of the future may utilize solid cathode, liquid electrolyte systems such as lithium/manganese dioxide or lithium/carbon monofluoride.

6. Implantable atrial defibrillators

Atrial fibrillation is an arrhythmia in which rapid, irregular atrial impulses and ineffective atrial contractions occur. The atria can quiver at a very high rate, and cardiac rhythm and intensity are grossly irregular. Unlike ventricular fibrillation, which is always fatal in the absence of interventional treatment, this condition does not normally result in patient fatality, particularly if the patient has good ventricular function. Because all the blood is not pumped out of the atrium, blood can pool and clot. Thus the threat of stroke is greatly increased in patients suffering from atrial fibrillation.

A device has been developed which treats atrial fibrillation by electrical stimulation [31]. This device, which resembles a cardiac pacemaker in appearance, is implanted pectorally. The detection and stimulating leads are placed transvenously

into the heart. The device detects the onset of atrial fibrillation, and, after careful diagnosis of the appropriate electrophysiological signals, applies electrical pulses to the heart. Units are currently in clinical evaluation [32].

Typically, energy levels of about three joules or less are necessary to achieve reversal of the condition. These energy levels are adequately provided by implantable batteries capable of delivering milliampere-level pulses. Solid cathode, liquid electrolyte cells such as the lithium/silver vanadium oxide system are used in these devices.

7. Left ventricular assist devices/total artificial hearts

For more than 10 years the development of implantable left ventricular assist devices (LVAD) and totally artificial hearts (TAH) has been under way [33]. These devices are now beginning to see clinical use.

The left ventricular assist device is designed to provide long-term circulatory support to patients with critical heart disease often in need of a heart transplant. The heart of the patient remains in place, and the device takes on some or all of the pumping action normally done by the heart itself.

These devices are often used as a temporary treatment for patients awaiting the availability of a replacement human heart. The more advanced of these devices permit the patient to leave the hospital and return to some semblance of a normal life during the waiting period.

In addition to the LVAD, development is under way for a totally artificial heart which will replace a severely diseased natural heart. This device will also be totally implanted and will also act primarily as a 'bridge' to transplant.

The power requirements for such devices preclude the use of totally implantable batteries at the time of writing. The main power source for the ambulatory devices is normally an external battery pack (lead–acid rechargeables in some cases) which is worn like a vest or purse by the patient. The power is transmitted through the skin.

Some, but not all, such devices also contemplate the use of an implantable secondary battery pack as a backup to the external system. This will allow the patient between 30 and 60 min each day for changing the external pack and will protect against external battery failure.

Nickel/cadmium batteries are typically used in those devices which include an implantable battery. Current progress in lithium-ion secondary battery technology offers the promise of lighter, smaller battery packs in future versions of this type of device.

8. External medical devices

It would require many pages to contain the list of all external medical devices which rely on battery power. Batteries allow patients to be equipped with portable monitoring or therapeutic devices while remaining ambulatory. They allow surgeons to use electrical tools and visualization devices without the encumbrance of power cords attached to house power. Batteries make it possible for wheelchair users to travel about without providing manual propulsion of their devices. Uninterruptable power sources prevent the loss of line power from causing severe problems in hospitals. Indeed, it would be hard to imagine modern health care without the use of electrochemical power sources. The following paragraphs will discuss four specific examples of the many types of external devices which rely on batteries not only for their power but for the particular usefulness imparted by electrochemical power sources.

Holter monitors are devices which are worn for 24 h by patients with suspected heart problems. They provide a continuous electrocardiogram which is recorded and analyzed by cardiologists after the recording period. The intent is to provide a long-term monitoring of the heart under 'normal' conditions, i.e. as the patient goes through a typical 24 h routine. The first such units, used in the 1950s, were worn as backpacks and were heavy and cumbersome, due to the bulky electronics and batteries of that time. Such a device would obviously interfere with a normal 24-h activity period. Today, because of advances in both batteries and electronics, Holter monitors are no larger than a portable cassette tape player, and patients can wear them with little or no inconvenience as they go about their daily activities [34]. Most are powered by either rechargeable commercial batteries or by 'AA'-size alkaline cells.

Ambulatory drug delivery systems provide those in need of carefully controlled doses of medication over a long period of time with the ability to have those drugs delivered while they go about their daily lives. These systems can be worn on a belt and are small enough not to be overly obtrusive. The drug is administered into the body through a needle attached to a tube leading from the device. The early units, developed in the 1960s, resembled a backpack and were thus quite cumbersome. Today's models are worn on a belt and are about the size of a pager [35]. Many insulin-dependent diabetics use these external drug delivery systems [36]. Again, most are powered by commonly available commercial primary or secondary batteries.

External defibrillators have been used for many years to revive patients in cardiac arrest. They are used in hospitals and are carried on many emergency response vehicles where trained paramedics can administer defibrillation shocks on site as needed. These units were in the past quite heavy and bulky, since very high energy pulses must be administered through the chest of the patient to stop ventricular fibrillation. Recent advances in the design of portable external defibrillators have produced units with advanced shock-delivering algorithms (designed originally for implantable defibrillators) which have reduced the total power required to achieve defibrillation. Thus the size and weight of the units have been dramatically reduced [37]. Defibrillators normally rely on secondary batteries such as sealed lead–acid for their portable

power, although more recent devices use primary lithium cells.

One of the major advances in medical science in the last decade has been the development and increased use of magnetic resonance imaging as a visualization tool. Today the magnetic resonance theater is used not only to create images but also to perform procedures while the surgeon uses the magnetic resonance device for real-time visualization during surgery. Because of the presence of a strong magnetic field in this environment, the surgical tools must have a very low magnetic signature. Many such tools are electrically powered, and the desire to have a cord-free surgical device has led to the development of battery-powered tools for use in this arena. This in turn has led to the need for batteries with very low magnetic signatures. Such batteries have been developed [38] and are beginning to see use in this environment which poses very specific, unique requirements.

9. Summary

It has been the purpose of this paper to present an overview of the contributions which battery powered devices have made to medical science. From the first pacemakers, miraculous at the time but judged crude by the standards imposed by the progress of science in the last thirty years, to today's much smaller and more powerful devices, the progress in medical devices has mirrored the progress in battery technology, microelectronics, and medical science. As battery technology continues to evolve, the use of more advanced battery systems, e.g. of lithium-ion rechargeable cells for left ventricular assist devices, will continue to enable the development and use of smaller, more useful devices. Just as we have seen the evolution of implantable pacemakers from devices which weighed 240 g, occupied 123 cm^3 of volume, and lasted 1.5 years to those which weigh 12.8 g, occupy 5.9 cm^3 of volume, and last between 6 and 8 years today [39], the future will continue to surprise us as the devices in use 30 years from now will render those of today as crude-appearing as those of the 1960s seem to us now.

Batteries indeed contribute in a very important way to the maintenance of health and the saving of lives. We can look forward with confidence to even more exciting applications of battery-powered medical devices as scientists, engineers, and physicians continue to make progress.

References

[1] W. Greatbatch and W. Chardack, A transistorized implantable pacemaker for the long-term correction of complete atrioventricular block. *Proc. New England Research and Eng. Meet. (NEREM) 1:8, 1959.*

[2] S.R. Ruben, *US Patent No. 2 422 045* (1947).

[3] A. Salkind and S. Ruben, in B.B. Owens (ed.), *Batteries for Biomedical Implantable Devices,* Plenum, New York, 1986, p. 261.

[4] R.E. Fischell and J.H. Schulman, A rechargeable power system for cardiac pacemakers, *Proc. 11th Intersociety Energy Conversion Eng. Conf., 1976,* p. 163.

[5] D.L. Purdy, Nuclear batteries for implantable applications, in B.B. Owens (ed.), *Batteries for Biomedical Implantable Devices,* Plenum, New York, 1986, p. 285.

[6] J.R. Moser, Solid state lithium iodine primary battery, *US Patent No. 3 660 163* (1972).

[7] A.A. Schneider and J.R. Moser, Primary cells and iodine-containing cathodes therefor, *US Patent No. 3 674 562* (1972).

[8] C. Holmes, Implantable power sources, in G. Pistoia (ed.), *Lithium Batteries — New Materials, Developments, and Perspectives,* Elsevier Science, Amsterdam, Netherlands, 1994, p. 383.

[9] G. Antonioli, F. Baggioni, F. Consiglio, G. Grassi, R. LeBrun and F. Zanardig, Stimulatore cardiaco impiantabile con nuova battaria a stato solido al litio, *Minerva Med., 64* (1973) 2298.

[10] J.P. Gabano, M. Broussely and M. Grimm, Lithium solid cathode batteries for biomedical implantable applications, in B.B. Owens (ed.), *Batteries for Implantable Biomedical Devices,* Plenum, New York, 1986, p. 209.

[11] A.J. Cuesta and D.O. Bump, The lithium/cupric sulfide cell, in B.B. Owens and N. Margalit (eds.), *Proc. Symp. Power Sources for Biomedical Implantable Applications and Ambient Temperature Lithium Batteries,* The Electrochemical Society, Princeton, NJ, 1980, p. 95.

[12] D. Morley and R.J. Solar, The $Li/SOCl_2$ cell as an effective power source, in *Proc. 28th Power Sources Symp., Cherry Hill, NJ,* The Electrochemical Society, Princeton, NJ, 1978, p. 232.

[13] W. Greatbatch and C. Holmes, The lithium/iodine battery: a historical perspective, *Pacing Clin. Electrophysiol., 15* (1992) 2034.

[14] W. Greatbatch, C.F. Holmes, E.S. Takeuchi and S.J. Ebel, Lithium carbon monofluoride: a new pacemaker battery, *Eur. J. Cardiac Pacing Electrophysiol. (Abstr. Cardiostim '96 Meet.), 6* (1996) 156.

[15] M. Mirowski, M.M. Mower and P.R. Raid, The automatic implantable defibrillator, *Am. Heart J., 100* (1980) 1089.

[16] R.J. Horning and S. Viswanathan, High rate lithium cell for medical application, in *Proc. 29th Power Sources Conf., Cherry Hill, NJ,* The Electrochemical Society, Pennington, NJ, 1980, p. 64.

[17] C.C. Liang, M.E. Bolster and R.M. Murphy, Metal oxide composite cathode material for high energy density battery, *US Patent No. 4 310 609* (1982).

[18] C.C. Liang, M.E. Bolster and R.M. Murphy, Metal oxide composite cathode material for high energy density battery, *US Patent No. 4 391 729* (1982).

[19] P. Keister, R.T. Mead, B.C. Muffolotto, E.S. Takeuchi, S.J. Ebel et al., Nonaqueous lithium battery, *US Patent No. 4 830 940* (1989).

[20] A.M. Crespi, F.J. Berkowitz, R.C. Buchman, M.B. Ebner, W.G. Howard, R.E. Kraska and P.M. Skarstad, The design of batteries for implantable cardioverter defibrillators, in A. Attewell and T. Keily (eds.), *Power Sources 15,* International Power Sources Committee, Crowborough, UK, 1995, p. 349.

[21] R. Dreher and P. Haefner, Batteries for implantable defibrillators and advanced pacemakers, in R. Das (ed.), *Proc. Fourth Annual Battery Conf. Applications and Advances,* California State University, Long Beach, CA, 1989, p. VII-3.

[22] C.F. Holmes and M. Visbisky, Long-term testing of defibrillator batteries, *Pacing Clin. Electrophysiol., 14* (1991) 341.

[23] A.J. Salkind, A.J. Spotnitz, B.V. Berkovits, B.B. Owens, K.B. Stokes and M. Bilitch, Electrically driven implantable prostheses, in B.B. Owens (ed.), *Batteries for Biomedical Implantable Devices,* Plenum, New York, 1986, p. 25.

[24] Medtronic Inc., *Annual Shareholders Rep.,* 1996, p. 45.

[25] R. Terry, W.B. Tarver and J. Zabara, An implantable neurocybernetic prosthesis system, *Epilepsia, 31* (1990) Suppl. 2:S33.

[26] P.M. Skarstad, Lithium-liquid oxidant systems, in B.B. Owens (ed.), *Batteries for Biomedical Implantable Devices*, Plenum, New York, 1986, p. 215.

[27] P.J. Blackshear, F.D. Dorman, P.L. Blackshear, Jr., R.L. Varco and H. Buchwald, A permanently implantable self-recycling low flow constant rate multipurpose infusion pump of simple design, *Surg. Forum, 21* (1970) 136.

[28] C.D. Saudek, J.L. Selam, H.A. Pitt, K. Waxman, M. Rubio et al., A preliminary trial of the programmable implantable medication system for insulin delivery, *NEJM, 321* (1989) 574.

[29] Medtronic Inc., *Annual Shareholders Rep.*, 1996, p. 46.

[30] C.D. Saudek, W.C. Duckworth, A. Globbie-Hurder, W.G. Henderson et al., Implantable insulin pump versus multiple-dose insulin for non-insulin dependent diabetes mellitus, *J. Am. Med. Assoc., 276* (1996) 1322.

[31] J. Adams, Safety and design philosophy of an atrial defibrillator, *Eur. J. Cardiac Pacing Electrophysiol. (Abstr. Cardiostim '96 Meet.), 6* (1996) 61.

[32] C.P. Lau, H.F. Tse, K. Lee, N.S. Lok, D.S. Ho, M. Soffer and A.J. Camm, Initial clinical experience of a human implantable atrial defibrillator, *Pacing Clin. Electrophysiol. (Abstr. NASPE Meet.), 19* (1996) 625.

[33] L. O'Conner, Engineering a replacement for the human heart, *Mech. Eng.*, (July) (1991) 36.

[34] P. Gerr and R.J. Simpson, *Nationwide 24-Hour Holter Event and Pacemaker Monitoring*, <URL:http://www.holtera.htm>, (accessed Oct. 1996).

[35] A.O. Marcus and M.P. Fernandez, Insulin pump therapy, *Postgrad. Med., 99* (1996) 7.

[36] B.W. Bode, R.D. Steed and P.C. Davidson, Reduction in severe hypoglycemia with long-term continuous subcutaneous insulin infusion in Type 1 diabetes, *Diabetes Care, 19* (1996) 324.

[37] Anon. Heartstream wins Food and Drug Administration approval for its automatic external defibrillator for treating sudden cardiac arrest, *The Wall Street Journal, CCXXVIII*, No. 53, Sept. 13, 1996, p. B5.

[38] P.W. Krehl and H.A. Hornung, *IEEE J. Oceanic Eng.*, (1987) 271.

[39] C. de Gheldere, *Quelques Pacemakers*, Groeninghe S.A., Courtrai, Belgium, 1996, p. 14.