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Michel Mirowski and the beginning of a new era of fighting sudden arrhythmic death

Younger colleagues may think that 35 years of implantable cardioverter–defibrillator (ICD) therapy means a "long time ago," while older colleagues will say: "is it already 35 years ago that we have ICD therapy available?" Indeed, anti-arrhythmic treatment of life-threatening ventricular arrhythmias has changed dramatically since the first implantation of a defibrillator in 1980 in a 57-year-old woman with frequent episodes of ventricular fibrillation 8 years after an inferior myocardial infarction [1]. At that time, anti-arrhythmic drugs were the only weapons to fight sudden arrhythmic death. However, effectiveness was mostly based on hope rather than effectiveness, although numerous drugs were available. Very few patients with life-threatening ventricular tachycardia events underwent surgical treatment with the intention to remove the arrhythmic substrate, but this approach was limited for those expected to survive the surgical intervention and patients who were considered "drug refractory" [2]. Therefore, the introduction of an implantable defibrillator may be considered as a "disruptive technology" to overcome sudden arrhythmic death. Yet, it took another 10 years after the first implantation of a defibrillator in patients to convince the majority of physicians, despite rapid technological progress of the device, that an implantable defibrillator is not a "bomb in the body of a patient" but a life-saving device, successfully terminating episodes of ventricular tachycardia (VT) or ventricular fibrillation (VF) [3].

Defibrillator development

The history of the development of the defibrillator therapy is fascinating; it tells about the vision and unbreakable strength of one man, Michel Mirowski, the long-lasting friendship of scientists and a difficult development of a device that was supposed to prevent sudden arrhythmic death. But it also tells us that even highly respected scientists can be wrong with their critique and warnings when predicting that "the implanted defibrillator system represents an imperfect solution in search of a plausible and practical application" [4]. In addition, it teaches that making us believe that "some electronic gadget manufacture" developing devices "because it was possible" turned out to be wrong, and warning that "indication and contraindication of standby automatic defibrillators should be defined before social energies are expended and scarce health resources are dissipated" are hasty conclusions [4].

Who was Michel Mirowski?

Michel Mirowski was born in Warsaw, October 1924, as Mordechai Friedman. His parents owned a fine food store. At the age of 15 years, shortly after his mother's death and Germany's invasion of Poland, he moved east to escape the German troops, first to Lvow, then to Rostov and Krasnodar with the intention to join the Soviet Union army to fight against the Germans. However, he was too young to become a soldier, but, moving to Russia, he changed his name to Mieczyslaw Mirowski and learned to fluently speak Russian. He worked in cigarette manufacturing, an airplane factory, became an administrator of a musician band, but finally was able to join the Polish communist army as a junior officer in 1944 [5].

Although he had registered as a medical student in October 1945 at the University of Gdansk, Poland, he left Gdansk and went to Tel Aviv in Palestine to work as a shoe salesman. In October 1947, he returned to Europe and continued Medical School in Lyon, France. In 1953, Michel Mirowski graduated from Medical School in Lyon and wrote his doctor's thesis on 29 cases of mitral stenosis, treated with commissurotomy. Three years before, he married his wife Anna, whom he had met in Lyon; the couple has three daughters, Ginat, Ariella, and Doris, who all became physicians.

In 1954, Mirowski returned to Israel and performed his residency term at the Tel Hashomer Hospital in Tel Aviv. The Chief of Medicine at that time was Dr. Harry Heller. Michel Mirowski and Dr. Heller became good friends. Michel once reported that Dr. Heller was a "typical German professor," but the best internist he ever met. Four years later, in 1958, Mirowski accepted a research fellowship position at the most famous Cardiology Institute in Mexico City where he worked with Dr. Sodi-Pallares and Dr. E. Cabrera. A few months after his arrival in Mexico, he wrote his first manuscript in Span-

ish, dealing with vector electrocardiography. Then, from 1960–1963, he accepted a fellowship position in Baltimore, USA, where he worked with the well-known Dr. Helen Taussig. During his time in Baltimore, he wrote 14 manuscripts on electrocardiology, particularly in congenital heart disease. In 1963, Mirowski returned to Israel, where he became Chief of Cardiology in a small community hospital in Asaf Harofeh [6].

Important dates for Michel Mirowski were the introduction of the direct current external defibrillator by Dr. Bernard Lown in 1962 [7], and the sudden cardiac death of his teacher and friend Dr. Harry Heller, who died suddenly in 1966 due to many episodes of ventricular tachycardia after myocardial infarction. In 1968, Mirowski decided to return to Baltimore where he accepted a half time position as director of the coronary care unit, a new concept at this time at the Sinai Hospital in Baltimore, with close affiliation to Johns Hopkins University Hospital.

This new position gave him the opportunity to work on his project of an implantable device that would be able to defibrillate a fibrillating heart. There was no hope that he would be able to achieve this goal all on his own and with limited resources available. However, he was fortunate to meet physicians and friends at Sinai Hospital who were open for his vision and concept of an implantable defibrillator. In Baltimore, Dr. Morton Mower was working on the heart station of the hospital and Dr. Albert Mendeloff, a gastroenterologist, was the Chief of Medicine of the Sinai Hospital. Importantly, the hospital had an animal laboratory and a biomedical engineering division, headed by William Staewen.

The initial concept of such a defibrillator consisted of a battery-operated defibrillating device that would be able to monitor in a stand-by mode and to recycle in case more than one shock would be needed to terminate induced ventricular fibrillation. Already from the very beginning in 1969, Mirowski and Mower had the idea of a single catheter system, positioned in the right ventricle with a distal electrode placed subcutaneously on the lateral chest wall. This was amazingly visionary and predicted what many years later was realized with the can of the implanted battery. The first sensing system in the experimental dog model used blood pressure monitoring in the right ventricle, measured by an intraventricular pressure transducer, mounted on the tip of the right ventricular catheter. The subcutaneously placed chest electrode consisted of a small external defibrillator paddle; the electrical circuit was derived from an old photoflash unit. After extensive bench testing and successful acute animal testing with induced ventricular fibrillation by low voltage alternating current, automatic capacitor (16 µF) charging up to 2500 V started after 6 s of no measurable right ventricular (RV) pressure and discharged 30–50 J to successfully terminate ventricular fibrillation after about 50 s, and returning the device to a standby condition. Mirowski and Mower called the system a "standby automatic defibrillator" and predicted that in the future it may be implanted temporarily or even permanently in selected patients, considered at high risk to develop ventricular fibrillation.

The concept of a potential implantable defibrillator was born, and it was published in 1970 [8]. However, soon thereafter one of the most prominent scientists at this time, Bernard Lown, wrote the remarkable editorial addressing the idea of an implantable standby defibrillator [4]. Lown did not believe that an exponential waveform used for external defibrillation would be suitable for internal defibrillation. He was concerned about deleterious effects on the myocardium, doubted that sensing of VF would be possible and questioned the operational readiness and reliability of a standby device. Lown felt ethical constrains to deliberately induce VF to test appropriate sensing of VF. His major argument against Mirowski's idea was the unclear clinical indication of an implantable defibrillator. He argued that "there is currently no precise method for identifying the susceptible subject; obviously there is little justification in burdening a large group in order to possibly save very few." Instead, Lown strongly promoted an effective anti-arrhythmic program in a coronary care unit. He called an implantable defibrillator an "imperfect solution in search of a plausible and practical application."

This was a devastating critique, but both, Mirowski and Mower, were not discouraged by Lown's opinion. The editorial rebuttal continued over 1 year [9]. Today, these pro and contra arguments on the future of the implantable defibrillator represent a memorable medical history.

Valuable help for Mirowski and Mower came from another visionary physician, Dr. Arthur Moss from Rochester, NY, who questioned whether Lown would be "so clairvoyant that they can see the ultimate impracticability of someone else's research energy?" [9]. Dr. Moss' helpful letter to the Editor [9] started another life-long friendship and clinical cooperation between Drs. Moss, Mirowski, and Mower.

Besides the intense discussion for whom an automatic defibrillator would be useful, particularly because of the newly introduced coronary care units with the possibility of using Lown's invented external defibrillators, Mirowski was convinced that defibrillating within the heart would significantly reduce the amount of required energy, and with this provide the possibility to reduce the size of the capacitors so that it could be built in an implantable defibrillator. He believed that successful defibrillation would be feasible by means of only one intravascular/intracardiac lead containing a right ventricular (RV) pressure transducer and two defibrillation coils. Absence of RV pressure would close a relay, allowing the capacitor to charge, and after about 50 s discharge predetermined energy via the electrodes. Successful defibrillation would return the device into a standby mode, whereas unsuccessful defibrillation would recharge the capacitor automatically to deliver further shocks.

The first clinical prototype consisted of an intravascular lead [superior vena cava (SVC)/RV] with the electronic components and power supply outside the body [10]. However, the unreliable sensing pressure transducer had to be abandoned and was replaced by a new contraction sensor, integrated into the defibrillation lead with an additional electrical R-wave sensing system. The first discharge energy was set to relatively low defibrillation energy, but in case of failed defibrillation the subsequent four discharges yielded the maximum energy level. The shock wave form

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H.U. Klein · S. Nisam

Michel Mirowski and the beginning of a new era of fighting sudden arrhythmic death

Abstract

Prior to the implantable cardioverter–defibrillator (ICD), life-threatening ventricular arrhythmias were treated using anti-arrhythmic drugs. The concept of an implantable defibrillator to prevent sudden arrhythmic death was first published by Michel Mirowski in 1970. Despite critical opinions by leading physicians, Michel Mirowski continued development of his vision. Hallmarks in the development of the ICD include the following: internal–external defibrillator used during surgery on humans in 1971/1972; fully implantable defibrillator tested in canines in 1975; defibrillator successfully implanted in a 57-year-old woman in 1980; second generation devices introduced in 1982; US Food and Drug Administration device approved in 1985. Today it is hard to imagine modern medicine without ICD therapy. This article provides the reader a history of the development of the ICD.

Keywords

Implantable defibrillators · Tachycardia, ventricular · Ventricular fibrillation · Myocardial infarction · Cardiac arrest

Michel Mirowski und der Beginn einer neuen Ära im Kampf gegen den plötzlichen Herztod

Zusammenfassung

Bevor es implantierbare Kardioverter-Defibrillatoren (ICD) gab, wurden lebensbedrohliche ventrikuläre Arrhythmien mit antiarrhythmischen Medikamenten behandelt. Das Konzept des implantierbaren Defibrillators zur Prävention des plötzlichen Herztods wurde erstmals von Michel Mirowski im Jahr 1970 publiziert. Trotz kritischer Stimmen von führenden Ärzten entwickelte Michel Mirowski seine Vision weiter. Meilensteine in der Entwicklung des ICD sind: Einsatz von internen/externen Defibrillatoren (1971/1972 während Operationen beim Menschen), voll implantierbare Defibrillatoren (1975 bei Hunden getestet), erfolgreich implantierter Defibrillator (1980 bei einer 57-jährigen Patientin), Einführung von Geräten der zweiten Generation (1982), Zulassung eines Geräts von der US-amerikanischen Arzneimittelzulassungsbehörde FDA (1985). In der heutigen Zeit ist eine moderne medizinische Versorgung ohne ICD-Therapie kaum vorstellbar. Dieser Beitrag bietet dem Leser einen geschichtlichen Überblick zur Entwicklung des ICD.

Schlüsselwörter

Implantierbare Defibrillatoren · Kammertachykardie · Kammerflimmern · Myokardinfarkt · Herzstillstand

was changed to a monophasic truncated exponential waveform, described by Schuder et al. [11] for transthoracic defibrillation.

The first testing of feasibility and effectiveness of low energy catheter defibrillation with the prototype of an internal–external defibrillator was performed 1971/1972 in 11 patients during coronary artery bypass graft surgery at the Johns Hopkins Hospital. In 9 out of 11 patients, one to three shocks successfully terminated ischemic arrest-induced ventricular fibrillation with 5–15 J [12].

To build a completely implantable automatic defibrillator had to overcome high hurdles. Mirowski and Mower filed a patent on their idea of an implantable defibrillator in 1970 which was granted in 1971. However, forming their own company to realize the concept needed significant amounts of money. They tried to sell their patent to Medtronic, at that time already a well-known pacemaker company. However, the company felt that there was no profitable future for such a device and did not buy the patent. Mirowski was informed about the company's "wise" decision by a friendly letter.

"Dear Dr. Mirowski:
We have conducted a complete and careful review of the current status of the defibrillator program. Unfortunately the technical obstacles in the program are quite severe. In addition, our marketing estimates for any product developed under the program do not appear to be very promising. Therefore we have decided to terminate the project…."[1]

During a 1972 cardiology conference in Singapore, Mirowski met Dr. Stephen Heilman, a physician and engineer who owned a small company, MEDRAD (MEdical Device Research And Development), that produced devices for angiographic imaging. Heilman decided to cooperate with Mirowski in order to build an implantable defibrillator. The technical cooperation with Mirowski and Mower led to deep friendship and mutual respect. They hired a young electrical engineer, Alois Langer, who specialized in multidimensional electrocardiographic analysis and test device construction. Soon after he started to work for MEDRAD, Langer invented a new electrical detection algorithm to sense ventricular fibrillation, the probability density function (PDF) feature, a sensing algorithm that distinguishes ventricular fibrillation from sinus rhythm, based on the amount of time the electrical signal spends on the isoelectric line [13]. With the backup of a small device company, highly motivated young engineers, and the strength and unchangeable vision of an implantable defibrillator, the first fully implantable defibrillator was ready in 1975 for canine experiments.

Although Mirowski initially insisted on the concept of a single intravascular (RV/SVC) lead defibrillator, he finally agreed to first use an intracardiac sensing lead with a SVC coil together with a RV apical cup or RV epicardial patch defibrillation electrode. The implanted defibrillator consisted of a hermetically sealed titanium case (250 g, 145 ml in volume), the intravascular catheter with RV sensing of PDF and the cup electrode at the apex of the heart placed via a left thoracotomy. The capacitor could deliver four shocks of truncated exponential pulses up to 30 J about 15–20 s after onset of ventricular fibrillation. After the fourth shock,

[1] Text of the letter Dr. Michel Mirowski received by Medtronic 1972, rejecting to buy the patent of Dr. Mirowski for an implantable defibrillator.

Fig. 1 ◀ Michel Mirowski and his colleagues involved in the first defibrillator implantation in humans. Baltimore 1980. **a**–**c** Dr. Michel Mirowski (1985–1988); **d** Dr. Morton Mower (1980); **e** Dr. Stephen Heilman (2010); **f** Dr. Levi Watkins. (**Fig. 1b and d** by courtesy of Il Pensiero Scientifico Editore)

35 s of normal rhythm was required to reset the counter to allow a new shock delivery. The projected life of the lithium batteries was 3 years or had a discharge capacity of about 100 shocks. In addition, a fibrillator with a conventional catheter in the RV to induce VF in active anesthetized dogs via a magnet placed over the implanted device was implanted applying 20 mA of 60 Hz current. A magnet over the implanted defibrillator inactivated the defibrillator as long as the magnet was left in place. The defibrillator had already a built-in test mode circuit that allowed charging the capacitor and discharge energy into a test-load resistor. The charging time was monitored by a small electromagnetic transducer held over the implanted device.

Already in 1975, the defibrillator was implanted in five anesthetized mongrel dogs. Induced VF was successfully terminated in 17 out of 18 VF episodes. Later, the device was tested in three awake dogs on seven occasions 4–9 months after implantation; almost all induced VF episodes were terminated by a single shock. Results of these experiments were first published in *Circulation* in 1978 [14]. Some of the dog experiments were filmed, and the movie was shown during some national and international cardiology congresses. A few colleagues in the audience accused Mirowski of having used Pavlovian techniques to train the dog to collapse and get up again. Only when an additional ECG with induced and terminated VF was added to the movie could they be convinced of the truth of the experiment. Later, animal rights people were very upset about these "cruel" experiments, so that Mirowski, deeply hurt by this argument, never showed the movie again in public. After altogether 25 successful long-term implantation experiments, a new company, INTEC Inc., under the corporate structure of MEDRAD Holdings was founded in 1979 specifically focusing on the industrial development of the implantable defibrillator for use in humans. A few committed engineers and physicians, Drs. Stan Bach and Steve Kolenik, joined the new INTEC Company. The main task was to obtain US Food and Drug Administration (FDA) approval of the device and to build a device with sufficient manufacturing quality.

Due to the close connection of Mirowski and Mower to Johns Hopkins University Hospital the whole project was moved over to this institution. The Chief of Cardiology at this time was Dr. Myron Weisfeldt; Dr. Philip Reid became the principal investigator of the project, joined by the young cardiac surgeon Dr. Levi Watkins. The FDA and the Institutional Review Board at Johns Hopkins Hospital had just approved the first human implantation of the device, and on 4 February 1980, the first defibrillator (called AID—automatic implantable defibrillator) was successfully implanted by Dr. Watkins in a 57-year-old woman, a patient of Dr. Roger Winkle from Stanford, CA [1].

The author (H.U. Klein) just learned that Dr. Levi Watkins died a few weeks ago. He is far too less recognized as the first surgeon to implant a defibrillator in a patient. Dr. Watkins was a very friendly, wonderful person originally from Alabama. It seems worth mentioning that Dr. Watkins' minister for his wedding ceremony was Dr. Martin Luther King.

One defibrillator electrode coil was placed in the SVC near the right atrium; the other electrode had a form of a cup or rectangular flexible patch electrode that had

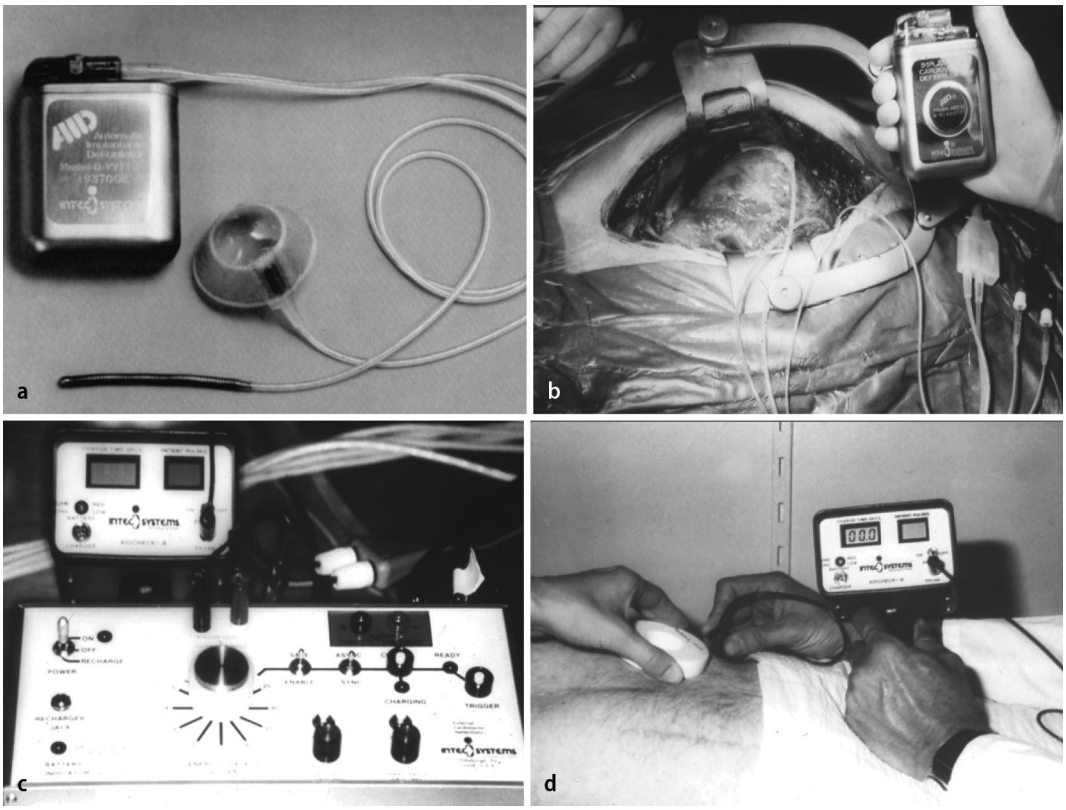

Fig. 2 ◀ **a** The first implantable defibrillator (AID) in humans with superior vena cava (SVC) lead and ventricular cup lead (1980). **b** AID-B implantation (1984) after median sternotomy and placing of two rectangular defibrillation patch electrodes (small on the right ventricle, large on left ventricle); the bipolar screw-in rate sensing lead is not visible. **c** Intraoperative test defibrillator (ECD) with charge-time monitoring device (AIDCHECK; 1984). **d** Defibrillator follow-up system (1985) with AIDCHECK, electromagnetic transducer and magnet

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Cedars-Sinai Med. Center, **LOS ANGELES, CA**
Ochsner Clinic, **NEW ORLEANS, LA**

Fig. 3 ▲ List of US and European centers that had implanted defibrillators within the first 10 years after the first implantation in 1980

to be placed on the epicardium over the apex of the heart. The detection algorithm used the PDF concept, the delivered shock was a truncated exponential monophasic shock of 25 J with the possibility of recycling three times in case of ineffective preceding shock delivery, with a strength of 30 J with the third and fourth shock. Additional equipment consisted of the external analyzer (AIDCHECK) which was initiated with a magnet. An external recording system was able to store a 20 s ECG prior to shock delivery and 1 min after the shock. The SVC lead needed positioning with fluoroscopy; the RV apical electrode was implanted via a left thoracotomy at the fifth intercostal space. The generator was placed in a subcutaneous abdominal pouch.

The first report of human implantations described three patients [1]. The first was the 57-year-old woman long after myocardial infarction with many episodes of VF and aborted sudden death, the second patient was a 16-year-old boy with normal left ventricular (LV) function, no coronary abnormality but many episodes of VF, the third patient was a 43-year-old man with episodes of VF after

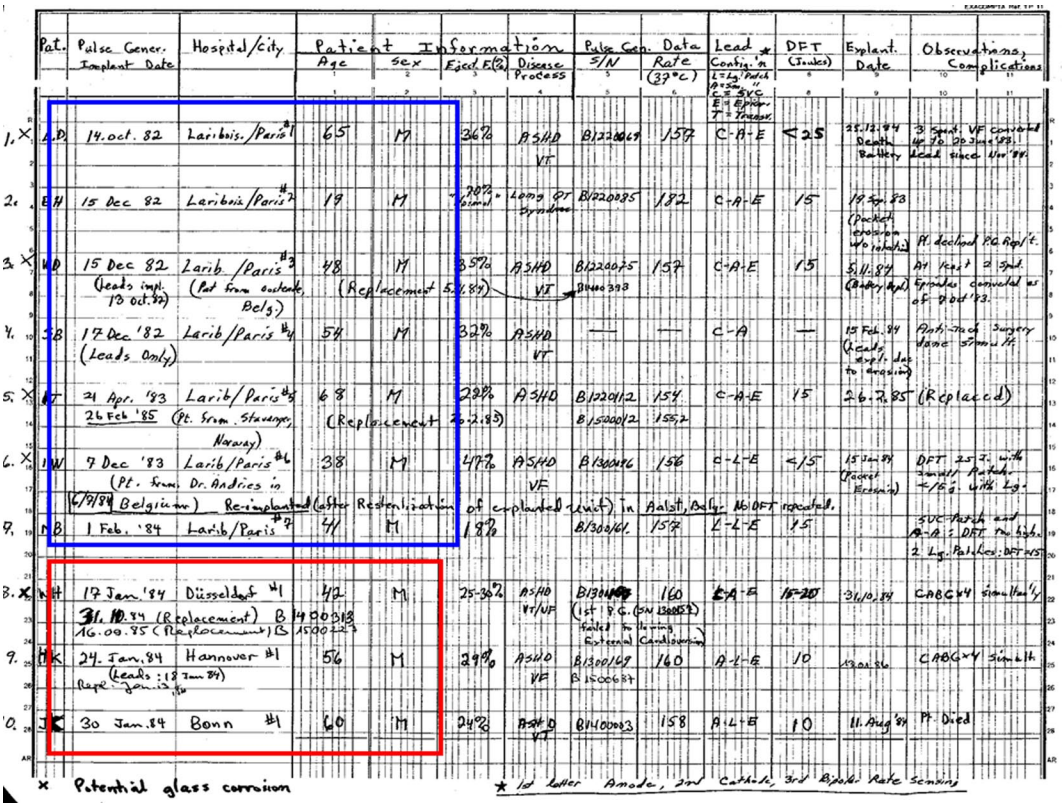


Fig. 4 ◀ Seah Nisam's personal notes from the first ten defibrillators implanted in Europe; *blue frame* first seven French centers; *red frame* first three defibrillators implanted in Germany

septal myectomy because of asymmetric hypertrophic cardiomyopathy. All three patients experienced successful termination of VF episodes after defibrillator implantation despite uninterrupted anti-arrhythmic drug therapy (◘ **Fig. 1**).

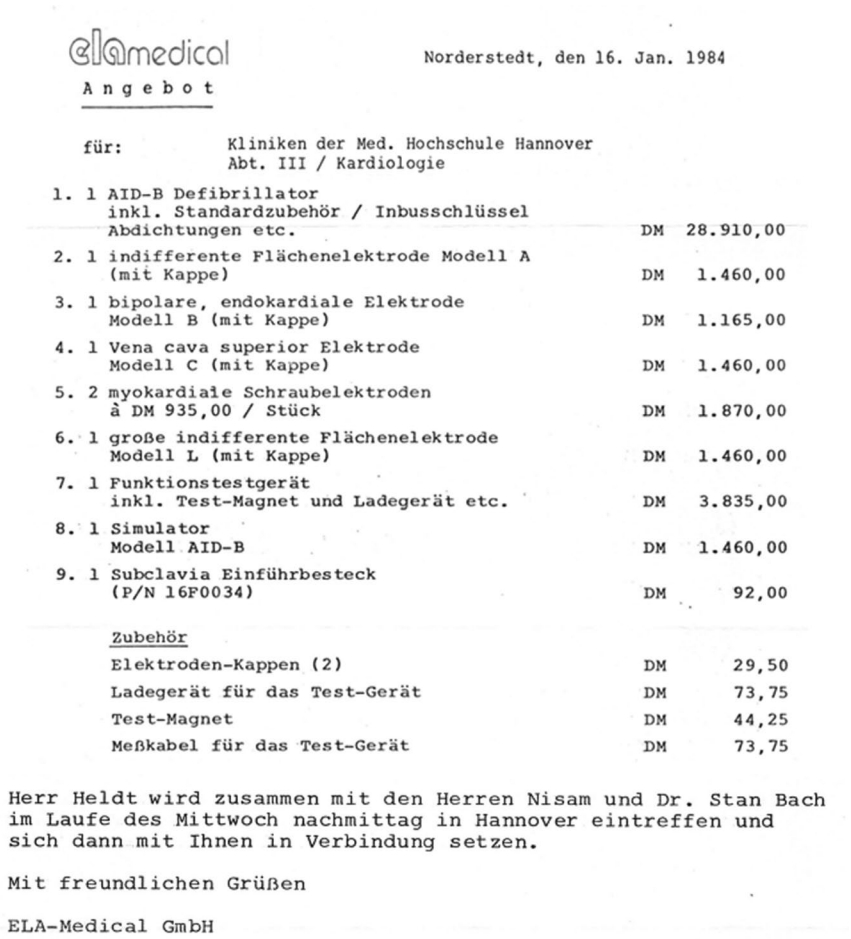
Development of next generation defibrillators

The AID was a nonprogrammable, committed device and contained about 280 discrete components with two hybrid circuits and two semicustom integrated circuits. Since it treated only ventricular fibrillation, it was obvious that future devices had to be improved in order to trigger also VT by means of a synchronizing circuit with reliable bipolar rate sensing. Soon after the first implantations in patients, it was clear that there was a need for shock counting, monitoring of capacitor charge time as well as external deactivation (◘ **Fig. 2a**).

After about 20 implantations of the original device, the second generation, the AID-B or AID-B/BR, was introduced in1982. Rate sensing was achieved by an epicardial bipolar screw-in lead. The apical cup was replaced by two flexible right angular patch electrodes sewn on the right and left ventricular wall. However, this needed now a complete median sternotomy (◘ **Fig. 2b**). The external monitor device, AIDCHECK, was used to test battery strength by capacitor charge time and counted the number of delivered shocks. The second generation device also had limited bradycardia pacing features. During device implantation an external defibrillator (ECD) was used to perform defibrillation energy threshold (DFT) testing (◘ **Fig. 2c, d**). This device had also special monitoring leads to record signals from the rate sensing and shocking leads after they were connected to the AID-B/BR pulse generator [15].

In 1985 the MEDRAD/INTEC company was acquired by a large pacemaker company, CPI (Cardiac Pacemaker Inc.), located in St. Paul, MN, USA, resulting in a rapid refinement of the defibrillator, then called Ventak®. At that time, about 400 devices had been implanted. In the same year, the device received FDA approval for routine clinical use, five years after the first implantation in patients. Hybrid electronic modules with integrated circuit technology were used but still with fixed rate sensing parameters. Only in 1988 was the new Ventak-P® device built with multiprogrammable parameters for rate detection and defibrillation energy delivery. Finally, also in 1988, a complete transvenous lead system was introduced (Endotak System), preventing the thoracotomy and epicardial patch electrode positioning. The generator (Ventak 1550®) could be implanted subcutaneously in the pectoral region similar to normal pacemakers [16]. Prior to switching to a complete intravascular SVC–RV electrode system, for a short time the intravascular electrode system was combined with a subcutaneously positioned patch electrode at the lateral chest wall.

It was not before the early 1990 that "tiered" ICD therapy was introduced, providing anti-tachycardia pacing (ATP), more sophisticated tachycardia detection algorithms, programmable shock energy delivery, and better anti-bradycardia pacing features. Another important improvement at this time was the introduction of biphasic waveforms which change the output polarity of the capacitor in mid-discharge. The new biphasic



elamedical

Norderstedt, den 16. Jan. 1984

Angebot

für: Kliniken der Med. Hochschule Hannover
Abt. III / Kardiologie

1.	1 AID-B Defibrillator inkl. Standardzubehör / Inbusschlüssel Abdichtungen etc.	DM	28.910,00
2.	1 indifferente Flächenelektrode Modell A (mit Kappe)	DM	1.460,00
3.	1 bipolare, endokardiale Elektrode Modell B (mit Kappe)	DM	1.165,00
4.	1 Vena cava superior Elektrode Modell C (mit Kappe)	DM	1.460,00
5.	2 myokardiale Schraubelektroden à DM 935,00 / Stück	DM	1.870,00
6.	1 große indifferente Flächenelektrode Modell L (mit Kappe)	DM	1.460,00
7.	1 Funktionstestgerät inkl. Test-Magnet und Ladegerät etc.	DM	3.835,00
8.	1 Simulator Modell AID-B	DM	1.460,00
9.	1 Subclavia Einführbesteck (P/N 16F0034)	DM	92,00

Zubehör

Elektroden-Kappen (2)	DM	29,50
Ladegerät für das Test-Gerät	DM	73,75
Test-Magnet	DM	44,25
Meßkabel für das Test-Gerät	DM	73,75

Herr Heldt wird zusammen mit den Herren Nisam und Dr. Stan Bach im Laufe des Mittwoch nachmittag in Hannover eintreffen und sich dann mit Ihnen in Verbindung setzen.

Mit freundlichen Grüßen

ELA-Medical GmbH

Fig. 5 ▲ Price offer for the first defibrillator system implanted in Hannover (1984)

waveform was able to reduce the defibrillation threshold (DFT) of more than 30 % when compared with monophasic shocks. At the same time, the generator can, implanted at the infraclavicular pectoral position, could be used as an "active" can, which further reduced the DFT.

Ten years after the first defibrillator implantation, Michel Mirowski passed away at the age of 66 on 26 March 1990, survived by his wife Anna and their three daughters. At that time, about 12,000 defibrillators in 22 countries had been implanted during these 10 years, produced now by five different defibrillator companies (**Fig. 3**).

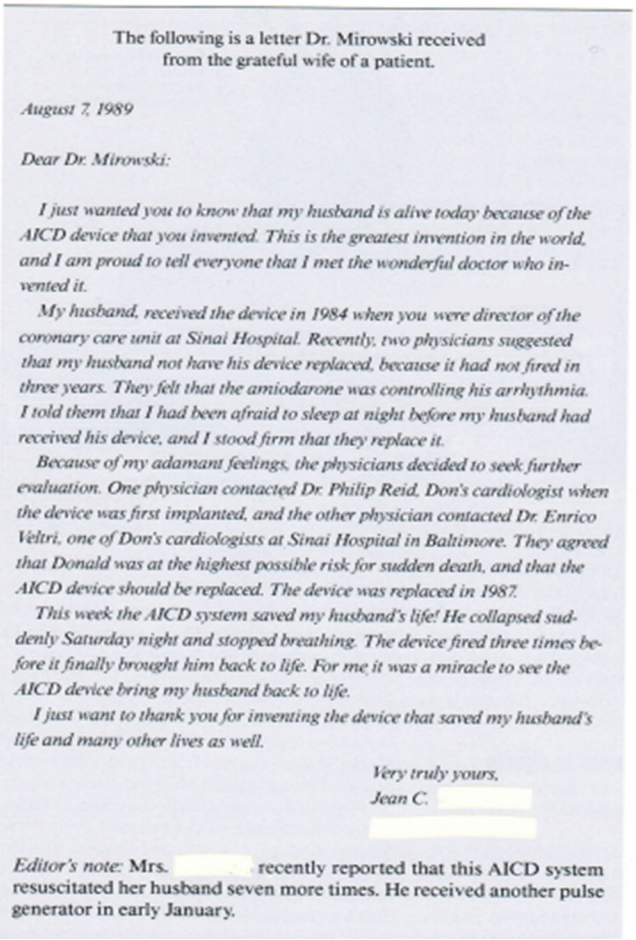
First years of ICD therapy in Europe

After the brief overview of the fascinating history of the development of defibrillator therapy, initiated by a courageous vision of a physician and scientist with an impressive will, realized by a group of inseparable friends as well as wise decisions of a small medical device company and despite strong opposition of leading electrophysiologists from the very beginning, it needs to be described how defibrillator therapy developed in Europe.

This would not have been possible without one man, Seah Nisam, who is involved in this field for more than 40 years. He received his electrical engineering degree from the Ohio State University. As a young engineer he started his professional career at the Medtronic pacemaker company. In 1971/1972, he met Michel Mirowski and Morton Mower for the first time when Medtronic was considering—but then refused—to acquire Mirowski's patents for the defibrillator concept. Very soon, he was "infected" by Mirowski's ideas and plans, and he remained in close contact with him over the years, until 10 years later, 1981/1982, under the agreement with Ela Medical, another pacemaker and medical device company, INTEC planned to introduce defibrillator therapy in Europe. It was certainly the decision of Michel Mirowski, who was a member of the Board of Directors of INTEC, that Seah Nisam was selected to run the scientific and technical program of the defibrillator therapy in Europe. He assisted and helped with defibrillator implantations in more than 30 European centers, beginning in France 1982 at the Lariboisiere Hospital, Paris, directed by Prof. Robert Slama and Philipp Coumel. It is easy to understand that Mirowski decided to start defibrillator implantation in France because he had attended Medical School in France and was married to a French lady. Therefore, the first seven AID and AIDB devices were implanted in Paris (**Fig. 4**).

Seah Nisam put together a group of very committed engineers and a strong team of technical specialists that assisted during the first 10 years of defibrillator therapy in Europe. One of the successful team members, Peter Heldt, was particularly helpful for Germany's beginning of defibrillator therapy (**Fig. 5**). Besides this, Seah Nisam became a well-known and highly respected scientist in the whole field of ICD therapy. He joined the scientist group at CPI in 1985, later Guidant Inc., and finally Boston Scientific Inc. in 2006. He was involved in the designing, planning, and performance of almost all landmark clinical trials (CASH, CABG-Patch, all MADIT trials, MUSTT, CAT, COMPANION, the Netherlands cost-effective study, BEST-ICD and many more). He is the author and co-author of more than 100 peer-reviewed manuscripts and book chapters dealing with defibrillator therapy [17]; he has given numerous talks at many international conventions, and he is a recipient of the prestigious Mirowski Award of Clinical Excellence. A highly recommendable paper written by Seah Nisam is the review of the history of defibrillator leads which was recently published in Europace, March 2015.

Besides his valuable impact on the development and progress of ICD therapy worldwide, his friendship with Michel Mirowski was the "door opener" for many scientific projects. It seems fair to speculate that without Medtronic's rejection of



The following is a letter Dr. Mirowski received from the grateful wife of a patient.

August 7, 1989

Dear Dr. Mirowski:

I just wanted you to know that my husband is alive today because of the AICD device that you invented. This is the greatest invention in the world, and I am proud to tell everyone that I met the wonderful doctor who invented it.

My husband, received the device in 1984 when you were director of the coronary care unit at Sinai Hospital. Recently, two physicians suggested that my husband not have his device replaced, because it had not fired in three years. They felt that the amiodarone was controlling his arrhythmia. I told them that I had been afraid to sleep at night before my husband had received his device, and I stood firm that they replace it.

Because of my adamant feelings, the physicians decided to seek further evaluation. One physician contacted Dr. Philip Reid, Don's cardiologist when the device was first implanted, and the other physician contacted Dr. Enrico Veltri, one of Don's cardiologists at Sinai Hospital in Baltimore. They agreed that Donald was at the highest possible risk for sudden death, and that the AICD device should be replaced. The device was replaced in 1987.

This week the AICD system saved my husband's life! He collapsed suddenly Saturday night and stopped breathing. The device fired three times before it finally brought him back to life. For me it was a miracle to see the AICD device bring my husband back to life.

I just want to thank you for inventing the device that saved my husband's life and many other lives as well.

Very truly yours,
Jean C.

Editor's note: Mrs. recently reported that this AICD system resuscitated her husband seven more times. He received another pulse generator in early January.

Fig. 6 ◀ Thank-you letter to Dr. Mirowski from the wife of a patient who received a defibrillator in 1984

the Mirowski/Mower patents in 1972, the development of ICD therapy would have taken a different direction and most likely would not have made Seah Nisam the "father of European ICD therapy."

Personal address to Michel Mirowski

Those who were fortunate to get to know Michel Mirowski personally—the author met him first 1979—and became friends with him will confirm that Michel was an extraordinary man who was enthusiastically committed to his vision of a device that was designed to save the life of thousands of people at risk of sudden arrhythmic death (◘ **Fig. 6**). He was very strong minded, convincing, straight forward, and certainly not a man of compromise. Despite his difficult life as a young man, he never let others feel it; he never showed prejudice to anyone, was full of humor, loved jokes, and was most interested in culture and history, always open to learn new things. Sometimes he lost his patience but never lost his temper or became offending. He was not the typical scientist but more the visionary and tried to simplify things. The secret of the success of ICD therapy was that Mirowski's "other half"—except his wonderful wife Anna—was Morton Mower, who consequently and more "mathematically" performed and completed what Mirowski had in mind [18]. And when Stephen Heilman joined the group, the "dream team" was complete [19].

Michel Mirowski was so convinced about the success of defibrillator therapy that he did not feel that it would need prospective or even randomized studies to prove that defibrillators would be effective and beneficial. He strongly argued that "one does not need studies because I know that they work." Of course, he was not completely serious about that, but it somewhat reflects his indestructible belief in defibrillator therapy, in particular his idea of primary prevention ICD indication.

There is one funny story that demonstrates his attitude to primary prevention defibrillator therapy. During one congress meeting, someone asked Mirowski whether he would let a 50-year-old gentleman drive a car when having a defibrillator implanted. Mirowski immediately dropped a clear and straight forward answer: "Of course; only those people over 50 who have a defibrillator implanted should drive cars." Although obviously stated partially in jest, this answer, it not only shows Mirowski's sense of humor, but reflects his strong commitment to primary prevention ICD therapy. At the beginning technically not feasible, Michel Mirowski envisioned defibrillator therapy with a single intravascular lead, and in some way his early experimental dog experiments using a subcutaneous electrode position predicted the recently developed S-ICD technology.

Very few physicians revolutionized medical therapy as dramatically as Michel Mirowski did. Some of them later received the Nobel Prize Award that is given only to living scientists. Mirowski's early death excluded him from becoming a Nobel Prize Award winner. The value of his contribution to mankind certainly would have qualified him for the Nobel Prize. It is difficult to imagine what would have happened if Mirowski would have given up his project after the strong opposition of the most established medical opinion leaders more than 40 years ago. However, his character and attitude did not allow "to give up" or "give in," but strengthened him to "beat the bastards." This was one of Dr. Michel Mirowski's often mentioned philosophic attitudes. The authors of this review are grateful of having known him personally and they may be allowed to consider him a good friend. We will keep his memory in honor and respect.

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Compliance with ethical guidelines

Conflict of interests. H.U. Klein was previously a consultant for Boston Scientific and has received speaker's honoraria from Boston Scientific. S. Nisam has no conflict of interest.

This article does not include studies on humans or animals.

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