

Implantable defibrillators: 30 years of history

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The first concept of an implantable defibrillator was published in 1970 by Dr. Michel Mirowski and his colleague and friend Dr. Morton Mower. Within 30 years implantable defibrillator therapy has gone through a breathtaking development. However, it started with a vision and a concept of one man, who went through difficult times, personally, and in his intention to make his idea of a device that prevents sudden death come true.

As with other innovative approaches in medicine, in the beginning there were more opponents than supporters of the concept. Device technology has impressively improved, but the principal concept remained the same: automatic shock delivery to a fibrillating heart by an implanted defibrillator will restore normal heart rhythm and save the life of the patient.

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Introduction

When the first concept of an implantable cardioverter-defibrillator (ICD) was published in 1970 by Dr. Michel Mirowski and his colleague and friend Dr. Morton Mower¹ it was unimaginable that the ICD would lead to a completely new approach to overcome sudden death in patients who have survived a cardiac arrest or are considered at high risk of life-threatening arrhythmic events.

Today a few million patients have received an ICD which protects their lives, and its effectiveness is unquestioned. Like other therapies that revolutionized medicine, the way from the theoretical concept to the first implantation of a defibrillator in a patient was long and not without obstacles, criticism and disbelief. Even after significant technological improvement of the implantable device, acceptance of the life-saving therapy increased only slowly, although it was obvious that antiarrhythmic drugs had not fulfilled their expectations. It took more than 20 years after the first implantation of an ICD that guidelines cautiously recommended the use of defibrillator therapy. This article aims to describe the fascinating history of the defibrillator. It is a story of a physician with an unbreakable vision and a demonstration of a fascinating technical development of a device that prevents countless patients from dying suddenly.

A brilliant extraordinary physician and visionary

Dr. Michel Mirowski, the inventor and father of the ICD^{2,3}, was born October 1924 in War-

saw as Mordechai Frydman. Shortly after the German invasion into Poland September 1939, and the death of his mother, at the age of 15 he left Warsaw to escape the Nazi Terror, and by this became the only survivor of his family from the Holocaust. He moved east, first to Lvov in the Ukraine, then to Rostov in the Soviet Union with the intention to enlist in the army to fight against the Germans. He changed his name to get a Russian passport to Mieczyslaw Mirowski (later named Michel Mirowski), but he was too young to become a soldier in the Soviet army. Only at the end of the war, after escaping further to Krasnodar and Andijan, he could volunteer for the army. When the war was over he came back to Poland and registered for one year as a medical student at the University of Gdansk. After a short stay in Palestine he went back to Europe and attended Medical School in Lyon, France. After finishing medical school he had his first contact with cardiology in Lyon where he received his doctor degree in 1953 writing a thesis on mitral commissurotomy. Here he also met his wife Anna. In 1954 he started his medical training at the Tel Hashomer hospital in Tel Aviv in Israel. There he met Dr. Harry Heller, the chief of medicine who became his best teacher and friend who later died of sudden death (1966). This stimulated Dr. Mirowski's idea to build a device to overcome the inevitable destiny of patients who develop ventricular fibrillation.

But before doing so he spent two years (1958-1960) at the Cardiological Institute of Dr. Sodi-Pallares in Mexico City, working in the field of vectorcardiography with Dr. Enrique Cabrera. Thereafter he spent two years in Baltimore, USA for a fellowship working

with Dr. Helen Taussig, a famous cardiologist in congenital heart disease. From 1963-1968 Mirowski went back to Israel to work as chief of cardiology in a small community hospital in Asaf Harofeh, but in 1968 he returned to Baltimore to become the director of the coronary care unit at the Sinai Hospital. This was the place where his visionary mission began.

A profound friendship between colleagues and scientists

The Sinai Hospital in Baltimore was a teaching hospital of Johns Hopkins Medical School, giving Dr. Mirowski the possibility to have a close link between clinical work and research. There he met Dr. Morton Mower, Dr. Bernard Tabatznik and Dr. Albert Mendeloff. The idea of building an automatic implantable defibrillator (AID) was born and needed to be realized despite heavy objections and disputes of leading cardiologists at this time. But it was the deep friendship, the mutual respect and the close cooperation between Dr. Mirowski and Dr. Mower that helped to overcome the technical challenges and the disbelief of the others^{4,5}. After the first publication of the "Standby automatic defibrillator" in 1970¹, later accompanied by a contradicting editorial of Dr. Bernard Lown⁶ and a rejected patent offer by a pacemaker company, another brilliant physician and engineer, Dr. Stephen Heilman, joined the group and helped with his small medical device company MEDRAD in Pittsburgh to build a defibrillator, implantable in dogs in 1975⁷. Even before this could be accomplished, further support came from Dr. Arthur Moss, who later became the "father of the MADIT trials"⁸ (Figure 1).

It took five more years with many chronic dog experiments until the first device was ready to be implanted in patients. In February 1980 Dr. Mirowski's dream became true. At the Johns Hopkins Hospital in Baltimore Dr. Levi Watkins, a cardiac surgeon, together with the cardiologist Dr. Philip Reid implanted the first AID in a 57-year-old woman who had survived a cardiac arrest after a myocardial infarction⁹. Her cardiologist was Dr. Roger Winkle, a well known cardiologist from Stanford, who later became a strong supporter of the new approach to treat ventricular tachyarrhythmias and fight sudden death.

But even after this pioneering event, therapy with an ICD was not easily accepted, and during many conferences

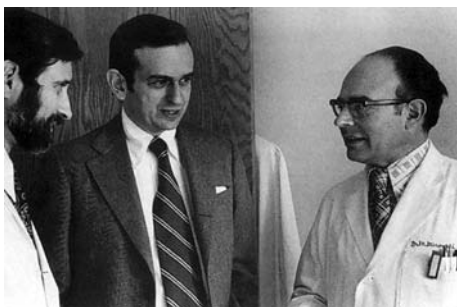


Figure 1. The three friends Dr. Michel Mirowski (right), Dr. Morton M. Mower (left) and Dr. J. Arthur Moss (center) meet in Baltimore (around 1972).



Figure 2. Dr. Michel Mirowski (14.10.1924-26.3.1990) during a discussion at a Symposium in Hannover, Germany 1988.

within the following years Mirowski and his friends had to convince disbelievers and to overcome general skepticism of many colleagues, medical societies and healthcare authorities (Figure 2). Until 1985 worldwide only 800 patients received an ICD, but Dr. Mirowski's reward is the undeniable role as one of the medical heroes of the last century who turned his vision into reality, and by this wrote medical history. He died of myeloma at the age of 66 in March 1990, survived by his wife and three daughters.

Technical development of the implantable defibrillator

The first defibrillator (AID) was relatively bulky (289 g, 150 ml) which had to be implanted subcutaneously in the abdominal region¹⁰ (Figure 3). It needed a median sternotomy to open the pericardium to place and fix a large and a small patch electrode on the epicardial surface (Figure 4). Sensing was done via two screw-in leads. Noteworthy to mention that Mirowski already from the very beginning had in mind to use endocardial leads for defibrillation and sensing, but this was technically impossible at this time.

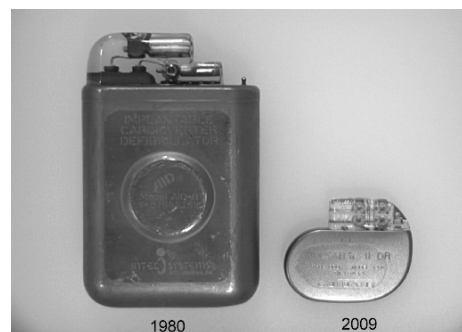


Figure 3. An example of the early automatic defibrillator (left) with 289 g weight and 150 ml volume (1984); an example of the fully programmable dual chamber implantable defibrillator 2009 (right) with 70 g weight and 31 ml volume.



Figure 4. Implanting of the electrode patch leads after sternotomy during the first automatic defibrillator implantation in Hannover 1984.

Intraoperative defibrillation threshold testing was simple because the first devices were not programmable. Sensing of ventricular fibrillation used an interesting algorithm of "probability density function". Initially shocks with monophasic waveforms were asynchronously delivered, but two years later adding synchronous shock delivery allowed cardioversion for ventricular tachycardia. The only programmable feature at this time was the cut-off rate for ventricular tachycardia or fibrillation (VT/VF). Patient follow-up needed an external magnet over the implanted generator and a monitor unit that indicated the charge time and the number of delivered shocks (Figure 5).

Five years (1985) after the first defibrillator implant the Food and Drug Administration approved the ICD after about 500 implanted devices. In 1988 the combined endocardial-subcutaneous patch lead system was introduced which made thoracotomy unnecessary. Sensing was now done from the right ventricular lead and defibrillation was performed between the right ventricular coil and the left lateral subcutaneous patch electrode. In 1991 the biphasic shock waveform was introduced, and devices became fully programmable. At this time about 10 000 devices had been implanted by five different ICD manufacturers. Around 1995 all devices had exclusively endocardial sensing and defibrillation leads and allowed subcutaneous pectoral implantation of the pulse generator. After 1996 all defibrillators could deliver antitachycardia pacing prior to shock delivery, and provided the full range of anti-bradycardia pacing. In 2000 all ICD devices contained sophisticated tachycardia detection algorithms, reliable discrimination be-



Figure 5. Follow-up of a patient with an abdominally implanted automatic defibrillator in 1984. A magnet is placed over the implanted generator. The monitor was connected to a sensing device, also held over the implanted generator. Retrievable were the number of delivered shocks and the charge time for the shock.

tween supraventricular and ventricular rhythms, used the "hot can" as one defibrillation pole, had retrievable electrogram storage capacity, fully programmable antitachycardia pacing features, and a variety of different lead systems were offered by all manufacturers. Devices now offer an enormous versatility, however, programming and patient follow-up became rather complex. Since 2003 ICD therapy was combined with cardiac resynchronization therapy (CRT) to treat heart failure. The concept of CRT has also been developed and was introduced into clinical practice by Dr. Morton Mower in 1990^{11,12}, and since then CRT went through comparably fast technological progress than ICD therapy.

In order to improve patient surveillance and to make device control and interrogation easier and more comfortable for the patient, about five years ago telemonitoring via telephone, modem, call center and internet has been introduced. It is predictable that the technological progress of ICD and CRT therapy will further increase, but time has come to mandate more device simplicity instead of complexity.

From the first defibrillator implant to multicenter trials

The first defibrillator in Europe was implanted 1982 in Paris by Dr. Philippe Coumel; in Italy in September 1984 by Dr. Critelli in Naples, preceded by other European countries in the same year. This would not have happened without the technical and scientific support of Seah Nisam, a brilliant engineer and personal friend of Michel Mirowski. European acceptance of the ICD was low in the eighties and implants were performed in few centers of each country. Interest increased significantly in the nineties, and Italy is currently the second largest ICD implant country in Europe with about 250 devices/million inhabitants. In 2007 the mean implant rate per million in Europe was 155 devices/million inhabitants, however with a considerable variation between European countries. Although the number of patients with an ICD indication is difficult to assess, it is estimated that less than 20% of potential ICD candidates currently receive these devices. The explanation for this discrepancy is difficult to find, requires careful analysis, but may be due to various reasons, different healthcare systems as well as economic disparities between individual countries.

Although Mirowski was strongly convinced that the defibrillator saves lives, and more so after long-term follow-up reports until 1995¹³⁻¹⁵ scientific societies as well as healthcare authorities asked for prospective, multicenter randomized ICD trials. The first trials compared antiarrhythmic drugs with ICD treatment in patients that had survived a cardiac arrest or had experienced episodes of rapid ventricular tachycardia. Actually, the first randomized trial was published from a European group in Utrecht, in The Netherlands¹⁶. Secondary prevention study results in patients after aborted cardiac arrest were published between 1997 and 2000, the largest study being the AVID (Antiarrhythmics Versus Implantable Defibrillators) trial which showed a risk reduction of overall mortality between 39% and 27% of the ICD compared with amiodarone¹⁷, followed by the CASH (Cardiac Arrest Study

Hamburg) study¹⁸ and the CIDS (Canadian Implantable Defibrillator Study) trial published in 2000¹⁹.

Primary prevention of sudden death initially focused on patients after myocardial infarction with inducible, but not suppressible VT/VF. The MADIT (Multicenter Automatic Defibrillator Implantation Trial) study, published 1996, showed a 75% risk reduction of arrhythmic death and a 54% risk reduction of overall mortality²⁰. The MUSTT study (Multicenter Unsustained Tachycardia Trial), published 1999, demonstrated a similar beneficial outcome²¹.

The MADIT-II trial²² investigated 1232 patients after myocardial infarction with a left ventricular ejection fraction of $\leq 30\%$, but did not require provocation of VT/VF. The results were published in 2002, and they demonstrated again the benefit of the ICD with a significant risk reduction of overall mortality (31%).

Two trials, the DINAMIT (Defibrillator in Acute Myocardial Infarction Trial), published 2004²³, and recently (2009) the IRIS (Immediate Risk Stratification Improves Survival) study²⁴ both revealed that ICD implantation within the first month after an acute myocardial infarction may reduce sudden death, but does not decrease overall mortality, the reason explaining this finding is still a matter of debate. The SCD-HeFT trial (Sudden Cardiac Death-Heart Failure Trial), published 2005, confirmed that ICD therapy is able to reduce overall mortality including also patients with non-ischemic structural heart disease who have poor ventricular function and clinical symptoms of heart failure²⁵.

Two large trials, COMPANION (Comparison of Medical Therapy, Pacing, And Defibrillation in Heart Failure), published 2004²⁶, and MADIT-CRT, published 2009²⁷, demonstrated that combining CRT with ICD treatment can reduce overall mortality and sudden death compared with drug treatment alone in moderate to severe heart failure (COMPANION), and prevents progression of heart failure and diminishes heart failure hospitalization in patients with mild or no heart failure symptoms but poor ventricular function and delayed ventricular activation (wide QRS complex) when compared with ICD alone (MADIT-CRT). These trial results, together with other studies, provide the scientific background of currently updated guidelines for ICD²⁸ and CRT therapy²⁹, and recommend the ICD as class I with a level of evidence A for patients considered at high risk of sudden arrhythmic death.

Summary

Within 30 years ICD therapy has gone through a breathtaking development. It started with a vision and a concept of one man, who went through difficult times, personally, and in his intention to make his idea of a device that prevents sudden death come true. As with other innovative approaches in medicine, in the beginning there were more opponents than supporters of the concept. But with the help of brilliant engineering and a friendship of visionary physicians, Mirowski wrote medical history. Device technology has impressively improved, but the principal concept remained the same: automatic shock delivery to a fibrillating heart by an implanted defibrillator will restore normal heart rhythm and save the life of the patient. The fact that uncounted lives have been saved by a wonderful device is more than a Nobel-Prize can describe.

Riassunto

Il primo concetto di defibrillatore impiantabile (ICD) fu pubblicato nel 1970 da Michel Mirowski e dal suo collaboratore ed amico Morton Mower. Nell'arco degli ultimi 30 anni, l'ICD ha subito uno straordinario sviluppo tecnologico. Tuttavia, l'invenzione di questo dispositivo resta legata all'intuito di un singolo scienziato, che andò incontro a momenti di grande difficoltà anche dal punto di vista personale, e dalla sua volontà di realizzare un dispositivo in grado di prevenire la morte improvvisa.

Come altre idee innovative in Medicina, all'inizio lo sviluppo dell'ICD ha incontrato molti più oppositori che sostenitori. La tecnologia dei dispositivi si è sviluppata in modo impressionante, ma il concetto di base è sempre rimasto lo stesso: erogare uno shock in modo automatico ad un cuore fibrillante attraverso un ICD è in grado di ripristinare il ritmo sinusale e salvare la vita al paziente.

Parole chiave: Defibrillatore impiantabile; Morte improvvisa.

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