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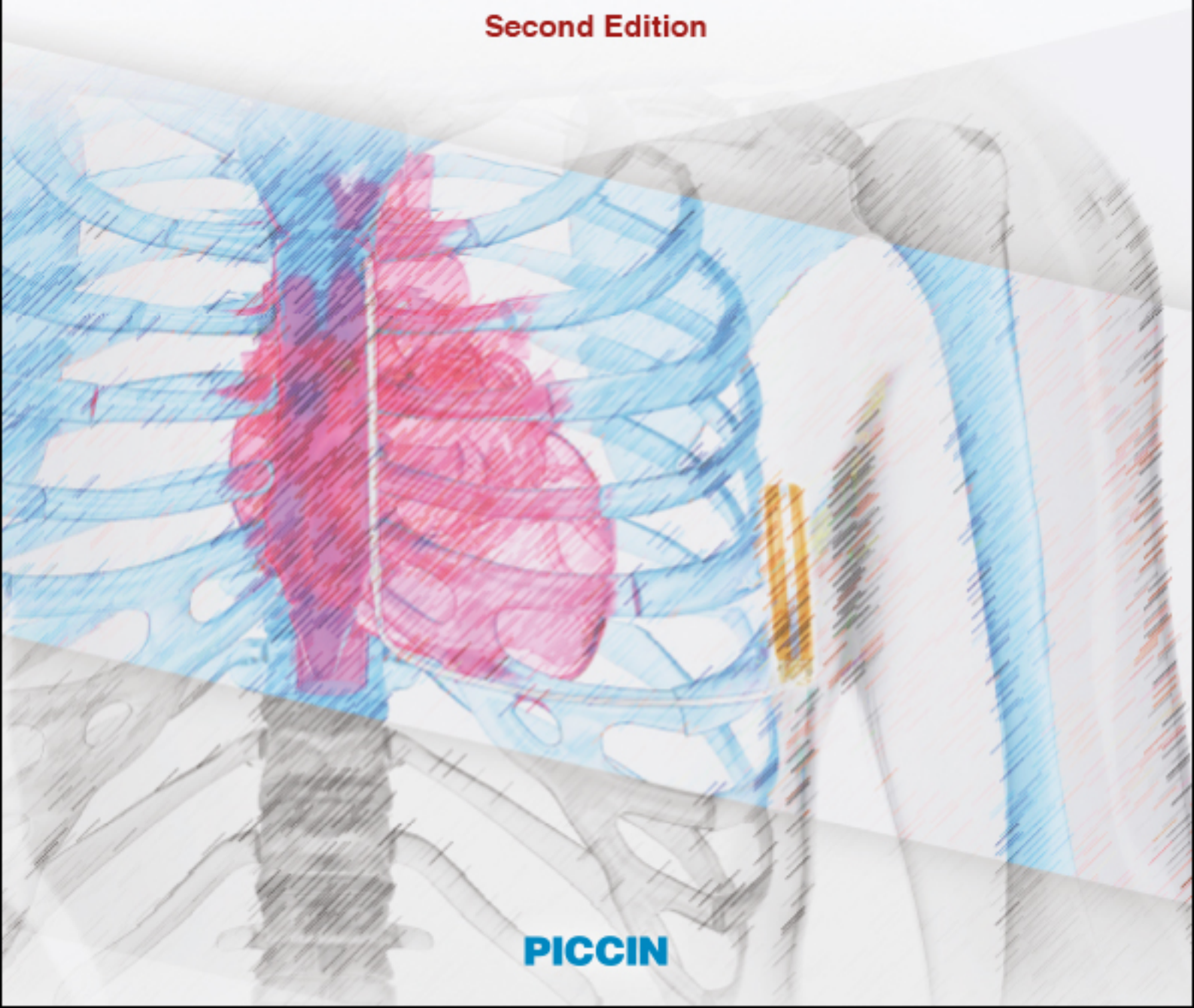
The Subcutaneous Defibrillator S-ICD

History, Evolution and Clinical Practice

Second Edition



PICCIN

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Foreword by
Ciro Indolfi
Antonio D'Onofrio

Introduction by
Riccardo Cappato

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Dedicated to those who have made the impossible possible, to those who experience the new without denying the old, to those who are dear to us for enriching our life with the gift of 'novelty'.

Foreword to the First Edition

It is a great honour for me to introduce this innovative book entitled: '*The Subcutaneous Defibrillator: History, Evolution and Clinical Practice*' by Giovanni Bisignani and co-authors. It is a two-fold pleasure because I have known Giovanni for the past twenty years and we are bound by a sincere friendship. I am especially pleased to announce the acknowledgement of his great scientific and organisational qualities.

The implantable cardioverter/defibrillator (ICD) is unquestionably one of the greatest discoveries of medicine contributing to the extension of the average lifespan. The first scientific report that documented the effectiveness of this device was the MADIT study, which demonstrated the benefits of ICD in significantly reducing 'sudden death', a syndrome, that accounts for about 50% of the total number of cardiovascular deaths. However, one possible complication of the use of the ICD are infections caused by the device. They occur in 1–2% of cases and lead to difficult and risky therapeutic questions, such as the antibiotic therapy to treat endocarditis and transvenous mechanical extraction of leads. The subcutaneous defibrillator surpasses these limitations without detriment to antiarrhythmic therapeutic options.

Potential patients eligible for traditional ICD and, therefore, also for subcutaneous ICD can be divided into two groups. The first group includes patients with structural heart disease in whom the risk of potential lethal arrhythmias is fundamentally linked to the degree of left ventricular dysfunction. Most of patients in this group present post-infarction left ventricular dysfunction. There are, however, three more categories of patients, such as those with primary dilated cardiomyopathy, hypertrophic cardiomyopathy, or arrhythmogenic right ventricular dysplasia, who may also be candidates for ICD and, subsequently, for subcutaneous ICD. In patients with severe left ventricular dysfunction, ICD has been shown to be the best protection against sudden arrhythmic death.

The second group includes patients who have no obvious structural heart disease but a genetic syndrome associated with a risk of sudden

death. In many cases, a family history of sudden death and electrocardiographic abnormalities lead to the diagnosis. Typical patients are ones with hereditary arrhythmogenic cardiopathies due to Brugada syndrome, catecholaminergic polymorphic ventricular tachycardias, etc.; they are often young and have a long life expectancy. For the latter, subcutaneous ICD is an attractive therapeutic option, considering the advantages related to the absence of electrodes inside the cardiac chambers. In subcutaneous ICD, the lack of a direct connection between the ICD and the heart (the shock electrode is also subcutaneous) prevents any infection of the electrode system from spreading to the endocardium, thus avoiding the need for extraction in case of malfunction, risks of damage to cardiac sections or to intrathoracic venous axis.

Furthermore, recent 2017 AHA/ACC/HRS guidelines for the prevention of sudden cardiac death recommend the subcutaneous defibrillator in all patients who need an implantable defibrillator but lack adequate vascular access, or have a high risk of infection, or when there is no need of bradycardia, antitachycardia or cardiac resynchronisation stimulation (class I indicators).

This book is the first ever written on this subject. It provides correct indications for the subcutaneous defibrillator, the implantation technique, information about recent innovations in the anaesthetic field and the possibility of remote control, all with finely detailed iconography. Last but not least, there is a very interesting chapter on cardiac magnetic resonance in patients with a subcutaneous defibrillator. In my opinion it is essential for electrophysiologists as it provides a road map to modify the device in 'MRI protection mode', helping patients with a subcutaneous defibrillator and allowing them to perform (or repeat, when necessary) the examination safely.

I wish to congratulate to Giovanni Bisignani and the co-authors for having filled, with this detailed book, the void of information on this new extraordinary procedure. Indeed, the subcutaneous defibrillator allows for the effective treatment of lethal cardiac arrhythmias by having no physical continuity with the cardiac chambers, thus protecting the patient from serious complications.

Ciro Indolfi
Professor of Cardiology
President-Elect of the Italian
Society of Cardiology (SIC)

Foreword to the Second Edition

Presenting the book of a dear friend and colleague hides many unknowns and pitfalls. It can yield to exceptional appreciations, obvious considerations, or to particularly detailed or inadequate reviews.

However, I do not hide the difficulty of facing this task due to the inherent prejudice of considering a book 'old' right after its publication.

The rapid evolution of ideas and scientific evidence of our times, quickly disclosed and made patrimony to all, is well known and can hardly be summarized and photographed. It is perhaps with this idea in mind that Giovanni Bisignani and his collaborators in the text on '*The Subcutaneous Defibrillator: History, Evolution and Clinical Practice*' describe in great detail all the historical, scientific, clinical and practical stages that led to the use of the subcutaneous defibrillator.

As a man of Magna Graecia Giovanni appreciates Cicero who appealed to history as a teacher of life and light of truth with his sentence '*Historia vero testis temporum, lux veritatis, vita memoriae, magistra vitae, nuntia vetustatis*'.

The authors, in fact, start from the sad experience of Michel Mirowski, who suddenly lost a dear friend as a result of cardiac arrest.

Mirowski, deeply embittered and distraught, set out to prevent others from experiencing the same intense sense of frustration and helplessness that he suffered from unexpectedly losing a close friend.

A motivation so strong that led him commit to many years of sacrifices, disappointments, hopes until the realization and implantation of the first cardioverter defibrillator. The device represents the most significant advancement in the management of patients with life-threatening cardiac arrhythmias.

From that moment on, a long journey characterized by scientific evidence aimed at identifying and selecting the patients who can best benefit from the technology began.

In the long years that follow, despite the use of more advanced materials and methods, the most common drawbacks related to the use of an

intravascular and intracardiac electrode such as dislocations, ruptures and infections of the intracardiac catheter were also highlighted.

In the light of these, a need for a new device arose. The said device should have the prerogative of avoiding the inconveniences related to the catheter and should not demand the use of any transvenous electrode, but with the same efficacy and safety for treating malignant ventricular tachyarrhythmias: S-ICD.

The authors accompany us in the various phases on the use of the subcutaneous device which range from patient screening to the evolution of the different surgical implantation techniques, from anesthetic management to the recommendations of the international guidelines, and from remote monitoring to cardiac magnetic resonance. A well-defined path enriched by wonderful as well as illustrative images accompanied by a vast and selected bibliography.

I believe that the authors have the merit of having combined what is new in literature without denying the old, that is, the story with a narrative verve that attracts the reader.

This makes the book timeless, without the danger of becoming obsolete, everything becomes pleasantly simple and interesting.

Giovanni Bisignani must be recognized for his firm determination, the will to carry out a work of dissemination in a difficult social context such as ours (South Italy), which is sometimes indifferent, hostile and prone to non-constructive criticism.

It is with great pleasure that I wish the authors every satisfaction for the finished work.

To future readers, I recommend this book for its clarity. It is reader frendly for lay users, doctors of different sectors and cardiologists. It may also prove useful to those who want to learn and deepen their awareness on a topic as interesting as the non-pharmacologic therapy of sudden death.

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Prefaces

We have long wanted to publish a book on S-ICD to help all those who approach the use of this new device. Thanks to the publisher Piccin, it is a great privilege for us to publish the first book on this topic. It crowns the efforts made to achieve it.

It is a dream come true.

The volume stems from clinical 'experience' and is aimed at the clinician, who is regularly engaged in the prevention of sudden cardiac death.

Reading the book clearly reveal the standard of expertise required of those who perform the implantation of an S-ICD. They not only need the necessary manual and technical skills, but also in depth cultural and clinical knowledge.

The first chapters present the history and evolution of the defibrillator, precisely outlining the hopes, difficulties, disappointments and challenges faced by those who have hoped for a different future in the worst of times, despite the scepticism and derision of many.

As Michel Mirowski liked to say: *'it was a road with many bumps, but it was the right one, and here we are'*.

Knowing the various stages and the often tortuous path of the history of the fight against sudden cardiac death makes us reflect, with gratitude, on the enormous amount of work behind our daily and apparently obvious gestures that are taken for granted, and it helps us accept and appreciate the present in order to build a better future.

Like all new things, S-ICD was initially looked on with scepticism and there was some difficulty introducing it into clinical practice. Pirandello considered it *'a new type of object that does not do or say anything'*, especially since there was a readily available transvenous defibrillator. After several positive clinical trials, use of the subcutaneous defibrillator became widespread.

Extensively illustrated, the book can be a valid, theoretical and practical aid for all those who want to familiarise themselves with S-ICD before implantation.

The aim is to provide an essential, quick and easy to use reference guide.

With these intentions, we have set ourselves to create a piece of work that is not only significant but also useful, a far more difficult task.

Our hope is that the readers and users of this book will recognise themselves in it, and wish to enter and become part of it.

Giovanni Bisignani, Silvana De Bonis, Antonio Bisignani

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It was with immense pleasure that I accepted the invitation of Giovanni Bisignani to collaborate with him together with Silvana De Bonis, Antonio Bisignani and Luca Auricchio to write this book. It is a great privilege to be able to present in a single manuscript all of the experience that I have gained in recent years with the S-ICD implanting technique.

The fascination of technological innovation in the medical community that applies to the prevention of sudden deaths gave me great passion and in 2014, I was involved for the first time with the installation of an S-ICD. I quickly realized the importance of collaborating with arrhythmologists (Drs. Patrizia Pepi and Albino Regiani) in our hospital.

Although the implantation of a defibrillator is an anomalous specialist field due to the usual activity of a thoracic surgeon, I immediately noticed how appropriate this request was, completely free from fears of loss of skills or possible professional jealousies, with the sole aim of ensuring the best possible result for the patients. This new device is in fact needed to be implanted on the chest wall in an anatomical location that is not easily accessible by a cardiologist with confidence but instead through a well-known approach by a chest surgeon. From that moment on, a long path of understanding began, study and development of the technique and supportive technology that has enabled the transformation of a subcutaneous procedure of 3 incisions, hence the name Subcutaneous-ICD, to a version of technique I would say 2.0, that is, with only 2 skin incisions and with intermuscular allocation of the device, which is now the gold standard designed to reduce the incidence of implant complications and improve the functional efficiency of the system itself.

The evolution of the technique has also involved the anesthetic management of patients who qualify for S-ICD implant. In fact, also in this

arena, we have contributed and witnessed a real revolution of care protocol, abandoning the original clinical practice of general anesthesia with intubation to move to a management approach that is characterized by the use of loco-regional anesthetic-antalgic blockings of the chest in awakened patients, aided with just superficial and cooperative sedation, with significant clinical and organizational improvements.

After the development of Version 2.0 of the implantation technique and the anesthetic management, the great passion continue to spread around the implant technique and the anesthetic management teaching methodologies to theoretical-practical courses in Cad Lab and with Proctorship-On Site in Italy, Europe and the Middle East. We have come a long way since 2014 and still want to continue with progress in the field; we are constantly studying improvements and innovation techniques to optimize the procedure and technology, which today represents a pivotal turning point in the care of patients with a risk of sudden death from cardiac arrest.

Andrea Droghetti

Introduction

The approach to medicine is a process subject to the common laws of the relationship between man and the universe. The attraction towards this science progresses in an uncontrolled manner when sustained by passion alone. Hence, except for those who choose to study medicine for reasons of self-interest, which clearly does not apply to what we are talking about, we have become doctors almost through the natural unfolding of events. We identify a discipline, study it as apprentices, develop it and, finally, decide to make it our 'companion' of life, thus refining the knowledge of matter to the point of predicting the development of events before they occur. In medicine, this kind of relationship translates into the famous saying 'prevention is better than cure', but it also happens in couples with deeply established relationships!

A fundamental part of medicine, as in every science, is based on research, which generates the knowledge that enriches the 'vocabulary' or dictionary the physician uses to interpret and solve the patient's disorders. Medical researchers are rare, compared to clinical doctors, and clinicians conducting research are even rarer. This is the case because research is difficult, expensive and most often frustrating. The clinician has little time for research and the researcher has almost no time (and often little inclination) for the clinic. To make matters worse, and this applies to cases of effective research, results lead to new knowledge but their applicability in clinical practice is more the exception rather than the rule.

This book deals with the certainly unusual path followed by clinicians who want to be researchers, who end up introducing a new therapy that is already being quite successfully used and shared by tens of thousands of people today. I consider it a fortune rather than talent to have personally been a significant part of this journey. In the book, the author traces the phases that characterised the conception, growth and maturation of the subcutaneous implantable defibrillator. This new therapy has been introduced to streamline the necessary procedures for implantation and management of this same technology that was the prerogative of very effective

and impressive transvenous systems until recently. The book meticulously and competently describes all the logical steps the implantable subcutaneous defibrillator had to face and overcome in order to be fit for the challenge with its predecessors. Citations refer to the history of defibrillation therapy and early experiments, to technical characteristics and indications, to implantation modalities and limitations. The presentation closes with an enlightened vision of the imminent challenges this new therapy will have to face in order to optimise its functions in the continuous and strenuous fight against sudden arrhythmic death.

Personally, I think that there are fundamentally two challenges that make the subcutaneous implantable defibrillator an instrument within the reach of all clinical indications. Firstly, to verify the efficacy and safety of this apparatus compared to the transvenous defibrillator, as not inferior to this technology, whose use has prevailed until the recent introduction into clinical practice of the subcutaneous implantable defibrillator. Secondly, the endowment of complementary instrumentation that, in addition to the currently supplied electric shock, is capable of subcutaneous pacing in order to stimulate the heart, if needed, in bradyarrhythmia, regular tachycardia or multi-chamber stimulation. Science is currently moving in these directions and, hopefully, we shall soon have the necessary information to answer these questions. Until then, the text of this book will accompany us into the intricacies of this new science, providing those interested with the information they need for a deep and passionate 'relationship' with it. Enjoy reading!

Riccardo Cappato

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Contents

CHAPTER 1

The Implantable Defibrillator: History, Technological Evolution and Limitations of the Transvenous System

A. Bisignani, G. Bisignani, S. De Bonis

The implantable defibrillator (ICD) is consolidated treatment for the prevention of sudden death. ICDs available today are the outcome of insight underpinned by innovation, good science and excellent engineering skills, but also of investments by industry. However, the invention of this device is associated with the intuition and vision of a single scientist who, despite experiencing hard times, was determined to create a device that could prevent sudden death[1].

Michel Mirowski came up with the idea of making an implantable cardioverter-defibrillator in the late 1960s, after a friend of his, Harry Heller, died of ventricular tachycardia.

When the first concept of an ICD by Michel Mirowski (Figure 1.1) and his colleague and friend Dr Morton Mower was published in 1970, it was unimaginable that the ICD would lead to a new approach to stop sudden death in patients who survived a cardiac arrest or who were considered to be at high risk of arrhythmic events, also because his research and ideas were ridiculed by the scientific community.

On 4 February 1980 a large group of people crowded into one of the operating rooms at the Johns Hopkins Hospital in Baltimore to observe the installation of the first automatic defibrillator in a human[2].

The patient was a 57-year-old woman who had suffered myocardial infarction and was undergoing aortic coronary bypass surgery for angina. She had lost consciousness several times due to tachycardia and ventricular fibrillation, and the therapy of antiarrhythmic drugs was no longer able to control the episodes. It was only a matter of time until one of the episodes would have been fatal.

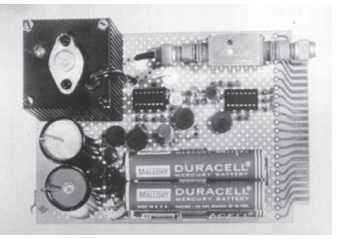

FIGURE 1.1
Dr Mirowski: 1966 concept of the ICD.

The patient was flown to the Johns Hopkins Hospital from California for the procedure along with her cardiologist, Dr Roger Winkle of Stanford University Medical School.

The operation was performed by the young cardiac surgeon Dr Levi Watkins, assisted by Dr Philip R. Reed, an electrophysiologist, and by Dr Morton Mower, a cardiologist at Mount Sinai Hospital in Baltimore and one of the developers of the defibrillator.

Near the operating table and unaccustomed to the surgical mask was Dr Michel Mirowski, 55, who witnessed his dream come true, all his efforts to build the electronic device. Once the catheters were positioned and connected to the generator, ventricular fibrillation was induced in the patient. It was recognised 45 seconds later by the defibrillator, which delivered the shock, restoring the normal heartbeat[2]. A few days later, the patient was discharged from hospital and sent home.

Thus began a new era to fight sudden death.

The first defibrillator was relatively cumbersome (289 g, 150 mL) and had to be implanted subcutaneously in the abdominal region. Since it was large, it needed a median sternotomy to open the pericardium in order to place and fix two electrode patches, one large and one small, on the epicardial surface (Figure 1.2).

However, Mirowski had already hypothesised the use of endocardial terminals for defibrillation and sensing, though it was technically impossible at that time.

Michel Mirowski, a Polish Jew, was born in Warsaw in 1924. He graduated in Lyon in 1953 and in 1954 began his internship at Tel Hashomer Hospital in Tel Aviv where he met Harry Heller, the Chief of Medicine who became his teacher and friend. It was the sudden death of his friend Harry Heller, preceded by repeated episodes of ventricular tachycardia, which helped him conceive the idea that his friend would not have died if he had had an implanted defibrillator.

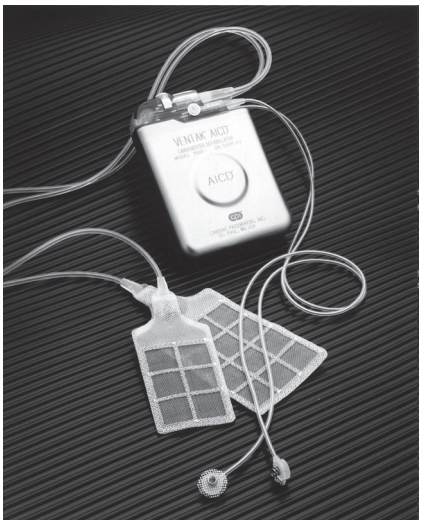

FIGURE 1.2
ICD: first human implantation, 1980.

In 1968, Mirowski was called to lead the coronary unit of Mount Sinai Hospital, where he continued to develop the ICD. At first, the cardiology community looked on his idea with great scepticism. In 1975, Mirowski's group made a film showing a dog who, after induced ventricular fibrillation, collapsed and lost consciousness. After the implanted defibrillator had discharged and terminated the PV, the dog woke up and started wagging its tail.

Physicians were sceptical and asked if they had used a dog who was trained for the purpose. To dispel any doubt, and without losing heart, the experiment was repeated. This time, both dog and ECG track were filmed in real time. This new film, presented in 1979 by Mirowski at the World Symposium on Cardiac Stimulation in Montreal, convinced many of the reliability and validity of the work.

Despite this pioneering event, ICD therapy was not easily accepted. Over the next few years, Mirowski and his colleagues had to convince non-believers and overcome the general scepticism of peers, medical societies and health authorities.

Although, up to 1985 only 800 patients had received an ICD worldwide, it was undeniable that Dr Mirowski felt rewarded and proud because he had turned his vision into reality.

In 1990, Mirowski died of myeloma, a type of blood cancer, at the age of 66. However, his intuition lives on in the many lives that have been saved by implanted devices.

In 1985, the Food and Drug Administration (FDA) approved the ICD. This was five years after the first defibrillator was implanted and more

than 500 additional implantations had been performed. The subcutaneous patch system was introduced in 1988, and thoracotomy was no longer necessary.

The first defibrillator in Europe was implanted by Dr Philippe Coumel in Paris in 1982; by Dr Critelli in Naples, Italy, in September 1984, preceded by other European countries in the same year[3].

Like other innovative ideas in medicine, initially the development of the ICD met many more opponents than supporters. Device technology has developed hugely but the basic concept has always been the same: to deliver an automatic shock through an ICD to a heart in tachycardia or ventricular fibrillation in order to restore sinus rhythm and save the patient's life (Figure 1.3).

It was a long and bumpy ride, as Michel Mirowski used to say. However, in the end it proved to be the right path.

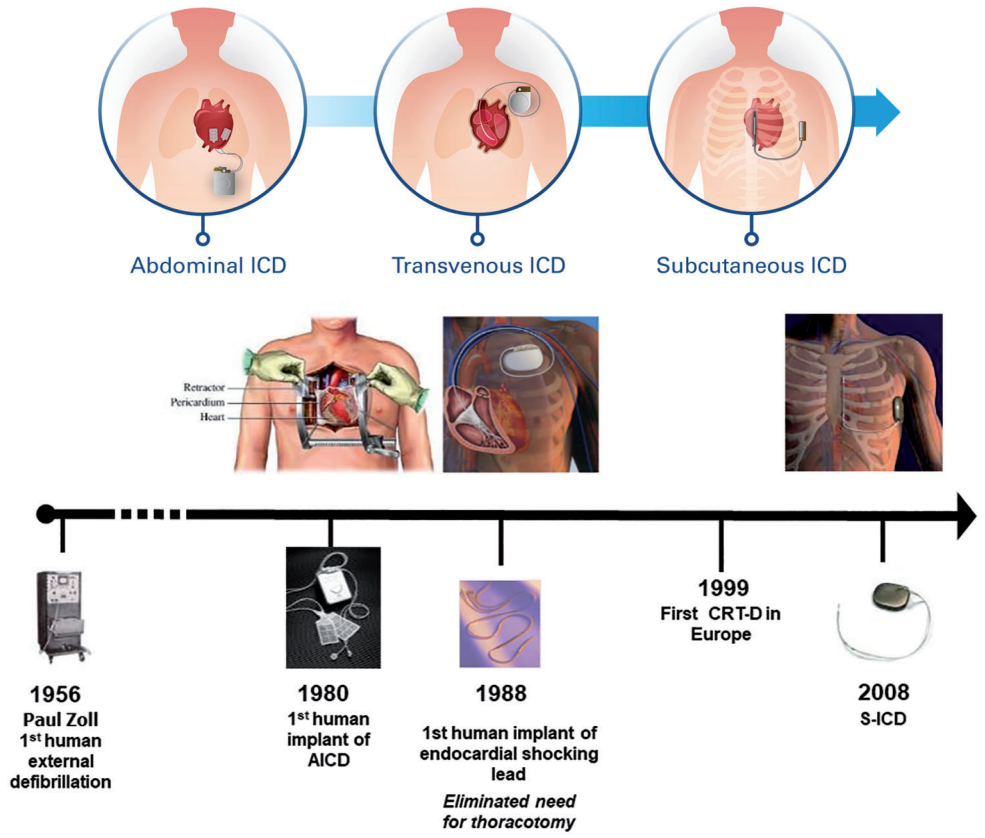

FIGURE 1.3

Evolution of the ICD for the prevention of sudden cardiac death.

TABLE 1.1

Key events in the development and industrialisation of the implantable defibrillator

Year	Event
1966	Conception of the device by Mirowski, after the death of his friend Harry Heller.
1969	First experimental model of the ICD. Michel Mirowski and Morton Mower defibrillated the heart of a dog with a transvenous catheter and subcutaneous electrode.
1975	Prototype of the defibrillator implanted successfully in dogs (250 g).
1978	Intec was established and started to produce a basic ICD for clinical studies.
1980	First automatic defibrillator implanted in a human at Johns Hopkins Hospital in Baltimore.
1985	The FDA approves the ICD for marketing in the US. Cardiac Pacemakers, Inc./Eli Lilly acquires Intec.
1988	First implantation of hybrid ICD in a human.
1988	First implantation of transvenous electro-catheter ICD without thoracotomy.
1995	First implantation of an ICD in the pectoral area.
1997	First generation ICD with a volume less than 50 cm^3.
2009	First subcutaneous implantable defibrillator, S-ICD.

Numerous large randomised and registry studies using this type of device, called transvenous ICD (T-ICD), have reported its superiority compared to any other treatment known to reduce the risk of sudden arrhythmic death, in secondary prevention, i.e., in patients who have already experienced ventricular tachyarrhythmia or who have survived cardiac arrest due to ventricular tachyarrhythmia, in primary prevention, i.e., in patients who, despite not having sustained ventricular tachyarrhythmia or related cardiac arrest, show signs of the risk of ventricular arrhythmia[4–9]. Indications for its clinical use have remained essentially the same since 2006–2008. The attention of the recent European Society of Cardiology (ESC) guidelines is mainly focused on possible concomitant contraindications and on difficulties involved in managing the follow-up of patients undergoing implantation[10].

Evaluation of the Survival Benefit of the ICD

Early studies compared antiarrhythmic drug treatment with ICD in patients who survived a cardiac arrest or who had sustained episodes of ventricular tachycardia. In fact, the first randomised study published was conducted by a European group from Utrecht, in the Netherlands[11].

The survival benefit conferred by T-ICD, compared to the best drug therapy for the same treatment of any underlying disease, is significant for all pathological conditions in which it was tested, ranging from a 20–30% reduction in total mortality in primary prevention to about 50% in subgroups and in secondary prevention. Each evaluation of the benefit risk for the use of ICD is based on accurate staging of the basic pathologies, both for the prognostic and overall treatment of the individual patient and to evaluate a choice of intervention, such as the ICD implant, generally the last resort after optimisation of every other treatment because the survival benefit determined by the ICD solely results from its very high capacity to prematurely discontinue any threatening ventricular tachyarrhythmia. An analysis of the net benefit of ICD and its cost-benefit depends on the overall mortality rate, from the extent of arrhythmic and non-arrhythmic components, pump deficiency or other origin, all that contributes to total mortality.

The most striking example is the syndrome of heart failure in myocardial disease with reduced ventricular kinetics. According to the MERIT study of the 1990s[12], sudden arrhythmic mortality accounts for 64% of total mortality in the NYHA functional class II, which reports a mortality of 10–15% at two years that decreases to about 30% in class IV. The cause of death due to pump deficiency (over 50%) prevails in the latter case, currently with a total mortality rate of 30% at one year, also as a result of optimised pharmacological and non-pharmacological therapies[13]. The effect of the ICD is likely to become pointless when the prognosis is unfavourable for other reasons in the short term. Conversely, if there is a good functional class and if, more generally, the prognostic classification of the basic pathology, heart and non-cardiac, indicates a favourable prognosis in the medium-long term, the benefit of the ICD is more pronounced concerning relative risk reduction. The absolute reduction in total mortality might be modest, if there is concomitant low total mortality: this entails the need for a higher number of implants to save a life, and introduces problems of individual risk stratification, including the risks of complications related to the ICD, which is still under extensive research and debate.

The pathological conditions in which sudden cardiac death (SCD) can

occur can be divided into: 1) structural heart diseases (cardiomyopathies, ischaemic and post-infarction cardiopathy, valvulopathies); 2) primitive electrical diseases (long QT syndrome, Brugada syndrome, other genetic arrhythmic syndromes of unknown origin, and ventricular tachycardia of the healthy heart without a genetic cause). Essential stratifiers of the risk of SCD in all forms presenting structural cardiac disease include left ventricular pump function and the presence of cardiac insufficiency, both of which increase risk with severity depending on the state of advancement of functional impairment.

Prevention of SCD in Cardiac Structural Disease: Major Studies

The benefits of ICD have been initially demonstrated for patients who have survived SCD or who have severe ventricular tachyarrhythmia at cardiac arrest. The risk of relapse in these patients is very high. Three major trials randomised the antiarrhythmic therapy (The Antiarrhythmic Versus Implantable Defibrillators trial [AVID][5], The Canadian Implantable Defibrillator Study [CIDS][6], and The Cardiac Arrest Study Hamburg [CASH][7]). These three trials showed a 3.6% reduction in the absolute risk of arrhythmic death (AVID and CASH) as early as the 1990s. AVID in particular, which was the most suitable in terms of number and design, demonstrated an absolute decrease of 5.6% in global mortality in the ICD arm, taking for granted the early interruption of the study due to evidence of the superiority of the ICD over amiodarone. A meta-analysis of the three studies highlighted a relative reduction of 28% in overall mortality and of 50% for SCD, mainly attributed to the subgroup of patients with a moderate reduction in left ventricular kinetics (with a cut-off value of 35% in Vsx ejection fraction [EF]), while poor benefit was found in patients with better kinetics (i.e., with EF >35%), and none in those with severe and uncorrectable kinetic Vsx impairment (EF <20%)[14]. The ESC guidelines are based on these results and have, therefore, included the indication of an ICD in secondary prevention for many years. Indeed, a distinction between aborted or equivalent SCD (badly tolerated or syncopal VT) persists in the last update of 2015, where the ICD is recommended with indication class IA and ventricular tachyarrhythmia that is not equivalent to SCD or with a severe clinical picture of intolerance occurring in a heart with normal left ventricular kinetics, where the indication is placed for class IIA[10].

In primary prevention, the role of ICD was supported by substantial evidence 5–10 years after the identification of its efficacy in secondary pre-

vention. Moreover, in the 90s, the MADIT I study showed that ICD implantation after a positive endocavitary provocative test for inducibility of major ventricular arrhythmias resulted in a significant advantage over total mortality in patients with post-infarction cardiopathy, reduced residual EF and non-invasive risk markers, and who were completely asymptomatic[18,19]. These data, which were confirmed by subsequent research investigations, together with the evidence from secondary prevention studies regarding the fundamental discriminating role of left ventricular kinetics in predicting the greatest net benefit of the ICD, developed the hypotheses for further studies aimed at a large population of patients with myocardial disease but with no previous ventricular tachyarrhythmia; patient who were, therefore, at lower risk of developing ventricular arrhythmic events than subjects in secondary prevention. Several large randomised trials on subjects with reduced EF, usually less than 30–40%, both ischaemic and non-ischaemic myocardial disease, were enrolled after a certain period of time after an acute myocardial infarction, a revascularisation intervention, or an initial diagnosis, if the cardiomiopathy was non-ischaemic. They concluded that ICD confers an independent and significant benefit compared to the best medical therapy, variously optimised in the different stages of the study[8,9,21–24]. Additionally, a cumulative analysis of the various primary prevention trials in hypokinetic left ventricular heart disease, both ischaemic and non-ischaemic, confirmed a decrease in relative risk that was similar between the two causes of left ventricular dysfunction (33% vs 26%, respectively)[25].

When discussing the 'best therapy', re-evaluation of the benefits of ICD on populations with a particular clinical profile might be recommended, especially in the primary prevention of patients with heart failure from hypokinetic and not ischaemic cardiopathy. The DANISH randomised study conducted in 2016 on a population of more than 1,000 patients, almost two thirds of whom were treated with cardiac resynchronisation therapy showed no benefit of ICD on overall mortality. However, sudden death was 50% lower with ICD. Moreover, a net benefit of the ICD also emerged on total mortality in the subgroup of younger patients (aged under 60 years)[26].

However, the decision to implant an ICD must also take into consideration the stratification of the risk of death for other causes, not just sudden death and age.

ICD in Primitive Electric Disorders

All known genetic syndromes are included in this broad field of arrhythmic diseases, those still of undetermined cause as well as those with idiopathic ventricular arrhythmogenic conditions. Some typical common characteristics are the absence of a structural myocardial disease, and the occurrence/diagnosis in subjects on average younger than those with primary structural heart disease. The distinction between absence/presence of structural disease is empirical and fragile. It is known that various genetic forms of high arrhythmic risk, such as arrhythmogenic right ventricular cardiomyopathy or lamina mutation cardiomyopathy, present an evolutionary progressive involvement of the ventricular myocardium that might initially be unnoticed and undetectable even with very sophisticated methods, whereas the first sign might be given by potentially malignant ventricular tachyarrhythmia. Research on ICD treatment in these patients consisted of non-randomised studies, and indications were mainly based on informed consent and small registries[27–31].

With regard to secondary prevention, data and opinions are consistent when indicating a substantial benefit from the ICD in patients with genetic arrhythmias such as, Brugada syndrome, long QT syndrome, short QT syndrome, and catecholaminergic polymorphic tachycardia. The occurrence of ventricular tachyarrhythmia or cardiac arrest has led to a class I indication in the latest European guidelines[10]; in the same syndromes, in the absence of major arrhythmic events, there is still an indication for ICD implantation, mainly in class IIA, in the case of syncopal episodes, particularly if the patient is already under targeted antiarrhythmic therapy and presents multiple clinical risk factors. The case is different for ventricular tachycardia of the healthy heart, with no inherited syndromes; it is usually well tolerated and has fairly well defined pathognomonic morphologies in terms of origin and mechanism, mainly from right ventricular or left ventricular outflow tract or fascicular ventricular arrhythmias. Although there may be diagnostic overlapping with certain forms related to initial cardiomyopathy, probably not as good a prognosis, this type of tachyarrhythmia, which is not related to any cardiopathy or genetic disease, is necessarily treated with ablation therapy combined with drugs.

Primary prevention in genetic arrhythmic syndromes is much more complex. In these cases, ICD indications arise from a multi-parametric approach focused on clinical risk factors and on certain special conditions, such as the presence of more malignant mutations in asymptomatic carriers of the KCNH2 or SCN5A mutation in long QT syndrome, and usually has a class II indication[28–31]. It should be noted that in this balance

of risks and benefits, and in the face of not strong evidence, a very important role is played by the procedural and post-procedural complications of long-term ICD implantation and by the disadvantages posed by the condition of the recipient of the device, in particular in subjects with very long life expectancies of several decades.

Complications and Risks of the Transvenous Defibrillator

The major limitations of the use of transvenous ICD (T-ICD) arise from the need to place at least one electrode inside the right ventricle through access to the intrathoracic venous shaft. The cardiac surgeon's epicardial location remains reserved for a minimal number of patients, during cardiac surgery or as an extreme ratio in cases of multiple insufficiencies or very unfavourable anatomies.

Among the complications or adverse events typical of T-ICD, those associated with the use of a transvenous electrode dominate: complications related to vascular access, those related to the performance and function of the electrode over time, and serious infectious complications caused by the presence of the transvenous electrode. Adverse problems due to malfunction of the generator or circuits, along with other difficulties related to inappropriate interventions of the ICD and some of the infectious complications are not attributable to the use of the transvenous electrode.

The complications of T-ICD, especially vascular problems and those of the electrode itself, are relevant both from the clinical perspective of morbidity and mortality, as well as from their impact on the health system and use of resources, which can be considerable if you project their impact on the life expectancy of a patient carrying a T-ICD system. It has taken some time to prove these concepts by performing cumulative analyses of the major randomised trials completed in the early 2000s, and by using large prospective registers created for various purposes and with different structures. There are administrative ones like Medicare in the US, and others created by scientific societies and regulatory authorities. Differences in the access to medical documentation, the type of record and the manner in which records and registers are kept appear to influence how clinical events are both reported and attributed. Registers with data from the early 2000s show ICD complications ranging between 3% and 16%, taking into account the wide diversity of follow-up duration and the heterogeneous definitions of complications[32–35]. At the same time, Medicare administrative data show a higher average rate, between 11% and 16% with each type of ICD, including those with CRT (cardiac resynchronisa-

tion therapy)[36,37], with an incidence of acute intra-hospital complications of 2.1% and 3.1% for mono-chamber and bicameral devices, respectively (Figure 1.4). Instead, in 2013 and 2014 Medicare USA published remarkable data regarding medical records from among 240,000 and 259,000 patients who were followed by the NCD Registry. They concluded that 30-day procedural complications decreased between 2.1% and 1.8%, while the more medium-term electron-related complications were 2.8% and the haemorrhagic and mechanical complications were less than 1%[38,39].

Even though Medicare registers assure reliable data, such as the tendency to slowly reduce complications over time, other studies report results that are less comforting and probably more realistic where the verification of the clinical source is either mandatory or frequent and regular. A meta-analysis of 18 randomised ICD studies published by 2011, including a total of nearly 6,800 patients, showed a 9.1% incidence of global complications, including those related to electrode and vascular access, which were 5.3%, the most part of which manifested early on[40]. Similar values have been reported in two other recent national registries. The national registry of Denmark, with a total of 1,075 ICD procedures, most of which are first implantations recorded over a 12-month period in 2010–2011. They showed a major global complication rate of 5.4% at six months with a single-chamber device, and of 6.7% with a bicameral device, with the addition of 3.2% and 7.7%, respectively, of minor complications[41].

In particular, within this very complete cohort, interventions on the electrodes (revision or new electrode implantation, upgrade) showed the

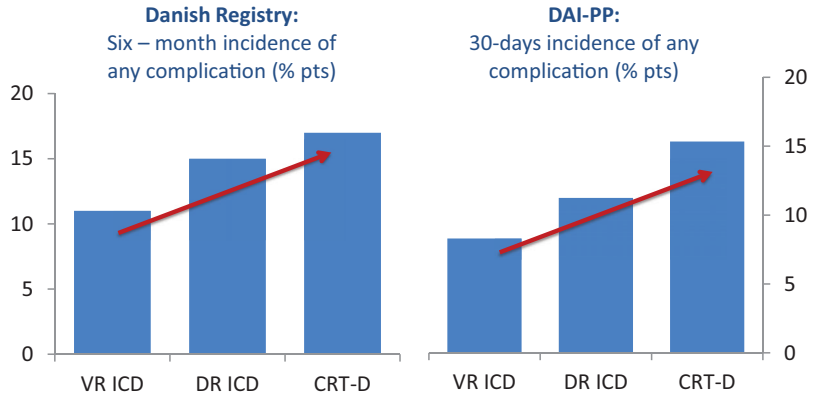

FIGURE 1.4

The tranvenous leads are an important source of complications.

highest incidence of complications with each type of device (pacemaker or ICD, with or without CRT), both major and minor (8.4% and 7.3%, respectively)[41]. For the years 2002–2012, in 5,539 patients who underwent a first ICD implantation (each type), the French DAI-PP register (Défibrillateur Automa- tique Implantable-Prévention Primaire) detected a 13.5% incidence of early complications within the first month mainly related to the electrode and to vascular access (57%), and 15.5% late complications at an average of 3.1 years of follow-up, 41% of which were related to the electrode[42]. Moreover, early probabilities seem to place a greater risk of late adverse events that are temporally far beyond the resolution of a periprocedural complication.

The impact of complications is certainly increased by a long life span, as also in the case young patients with genetic arrhythmic syndromes. These patients are exposed to the benefits and risks of ICD therapy for decades, resulting in a cumulative risk of complications due to an extended period of therapy[43] (Figures 1.5, 1.6).

The risk of complications associated with the transvenous (TV) lead increases by ~2% per year.

The ELECTRA register reported a 6.5% mortality rate one year after TV lead extraction. Age ≤65 is an independent predictor of lead malfunction[52].

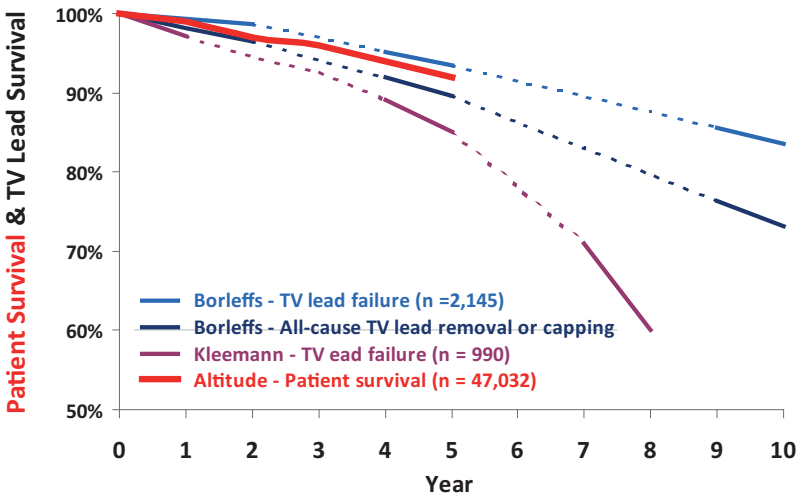

FIGURE 1.5

The graph shows how a young patient lives longer than a transvenous lead.

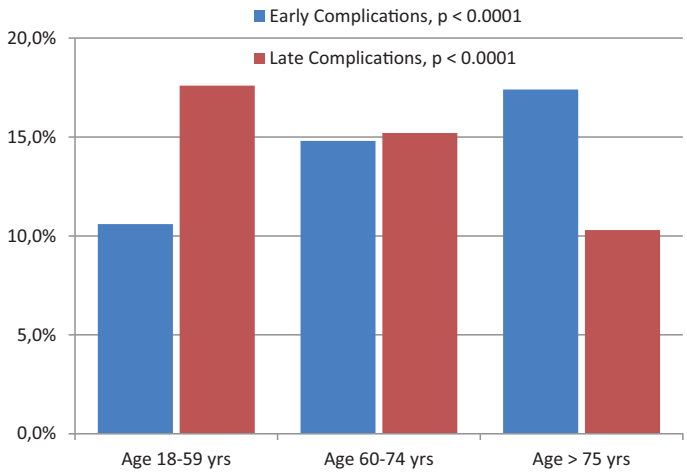

FIGURE 1.6

Due to their longer life span, young patients have more complications than older ones.

The variation observed in the survival of the ICD lead results from several factors, including: the variable definitions of the study relate to TV-lead malfunction, the variable performance of the different ICD lead models, and the impact of patient characteristics and surgeon implantation techniques on TV-lead performance.

The risk of therapy is further increased by circumstantial and unavoidable factors, such as a more active lifestyle (which puts greater stress on the electrode, and greater risks of high frequency ventricular beats) and the thoracic growth of paediatric and adolescent patients.

In this context, adverse events linked to wear and tear of the electrode and to repeated substitutions of the generator take on increasing significance. A recent meta-analysis involving 4,916 patients with arrhythmic syndromes acquired at a mean age of 39 years, showed a cumulative rate of 20% of inappropriate shocks and 22% of system-related complications, with a 4.4% incidence year-on-year, where the electrode malfunction was the most consistent, being detected in 10% of cases at a follow-up of slightly over four years[44].

Performance of the transvenous electrode over time is also a problem for older patients and or for those who do not have a very long life expectancy. Although the functional trend of the transvenous electrode

over time is improving, and looking beyond the impact of evidence of the unexpected defects of two very popular and widely used T-ICD electrodes[40,41], case reports up to 2007 report a 15% electrode malfunction rate at five years, with an estimated electrode survival of 85% and 60% at five and eight years, respectively[47].

It should also be noted that the major cumulative registries and analyses with ICD 'generalist' reports, most of which are hypokinetic cardiopathies, probably underestimate the impact of vascular and electrode complications in particular subgroups of patients, such as those with advanced anatomical complexities that amplify the risks. Examples of such cases include congenital heart disease, cases of previous major surgery on the heart and large thoracic vessels, normal procedures, and situations where revision surgery is performed to upgrade the device or due to malfunction of the electrode in previously re-implanted cardiac electrical devices[48,49].

Lastly, a quick reference to infectious complications: reported in the range of 1.5% in the early post-procedure phase (30–180 days), and probably under reported both in the past and even today due to the late or very late onset of infection, they constitute a considerable problem due to their increasing trend and because they are often untreatable with conservative therapy[40–42,50]. The causes and modality of primitive infection are surgical placement and electric 'prosthesis', besides the additional independent risk of the transvenous electrode associated with vascular access that favours infections, with the electrode itself that acts as an anchor and penetration point for infectious agents found in circulating blood, and with the ICD implantation site that reaches the heart.

ICD infections are more likely to be found in patients with peri-implant complications, who need to be reoperated to replace the device, and also in patients with comorbidities. Of the 200,909 implants performed, 3,390 patients (1.7%) developed an ICD infection. The infection rate was 1.4%, 1.5% and 2.0% for single catheter ICDs, ICDs with double catheter and biventricular ICDs, respectively ($p < 0.001$). Replacing the generator had a higher infection rate than the initial implant (1.9% vs 1.6%, $P < 0.001$). Factors associated with the infection were: adverse events during implantation requiring reoperation (odds ratio [OR], 2,692, 95% confidence interval [CI], 2.304–3.145), previous valve surgery (OR, 1,525, 95% CI, 1.375–1.692), reimplantation for device update, malfunction, (OR, 1,354, 95% CI, 1.196-1.533), renal failure undergoing dialysis treatment (OR, 1,342, 95% CI, 1.123–1.604), chronic lung disease (OR, 1,215; 95% CI, 1.125–1.312), cerebrovascular disease (OR, 1,172, 95% CI, 1.076-1.276), warfarin therapy (OR, 1,155, 95% CI, 1.060-1.257)[51].

Table 1.2 summarizes the results of various meta-analyses on the predictors of infections.

TABLE 1.2

Some Clinical and Instrumental Conditions that May Increase the Risk of Getting Infections after the ICD

Repositioning of the device
Early re-intervention to implant the device
Pocket haematoma
Very complex implantation
Temporary pacing
Previous implantation procedure
Previous infection of the device
Systemic infection/fever
Renal insufficiency
Haemodialysis
Chronic skin disease
Treatment with corticosteroids
Depressed immunity
Diabetes
Male gender
Young age
Low body mass indexes
Heart failure
Antithrombotic/anticoagulant therapy
Lengthy procedures
Doctor with limited experience

The Path to the Defibrillator without Electrodes

ICD is an irreplaceable therapeutic tool, but the need for intrathoracic electrodes has unveiled a wide range of unwanted and difficult treatment consequences. The transvenous electrodes are undoubtedly the most vulnerable critical point of the system, which generate the less problematic clinically relevant problems. We cannot conceal the fact that some circuit malfunctions have caused major problems for the ICD carrier community and for cardiologists who treat them.

Over the past 20 years, despite the use of more advanced materials and methods (surgical techniques, venous access, electrodes and devices), the incidence of electrode-related complications, from implantation to long follow-ups, has changed moderately, with the subsequent need to consider the hard to reduce relative risk inherent to the use of an intravascular and intracardiac electrode. Moreover, the absence of alternatives to T-ICD, where there is a documented and unacceptable risk of SCD, has produced a subspecialty with skills and technologies dedicated to management of the problems of electrical devices, particularly transvenous electrodes. Unlike other inactive prostheses, total system integrity is an essential condition for it to function and to save lives within a matter of seconds. Hence the need for an alternative that did not require the use of any transvenous electrode, but which ensured the same efficacy and safety for the treatment of malignant ventricular tachyarrhythmia. The subcutaneous defibrillator was eventually established. This represents the product in its most advanced state, and is now available in the clinical practice of every qualified centre.

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CHAPTER 2

The Subcutaneous Defibrillator: Historical Background, Design and Early Experiments

G. Bisignani, A. Bisignani, S. De Bonis

Historical Background

The first subcutaneous defibrillator was implanted in New Zealand in 2009. The procedure was performed at the Auckland City Hospital by Dr Margaret Hood on a 50-year-old patient presenting severe dilated cardiomyopathy with 15% EF. Dr Riccardo Cappato, Dr Gust Bardy and Jay Warren, President and General Manager of Cameron Health were also present during the procedure.

Subsequently, the S-ICD defibrillator was implanted in fourteen patients as part of the trial conducted to obtain authorisation to use the CE trademark.

The trial period continued with a study involving 55 patients in 10 centres based in Europe and in New Zealand. In New Zealand the implantation procedures were performed by Dr Margaret Hood at the Auckland City Hospital, and by Dr Ian Crozier at the Christchurch Hospital. The first implantation procedures carried out in Europe were performed under the guidance of Dr Riccardo Cappato at the Policlinico di San Donato Milanese, Italy, and of Professor Luc Jordaens at the Erasmus Medical Center in the Netherlands.

Referring to the clinical trial in question regarding the authorisation for the CE marking and to the first patient who underwent implantation of the S-ICD defibrillator in New Zealand, Dr Hood commented: "*Our first experience with this new technology has produced positive results. The whole procedure was quite easy from a surgical point of view. Once implanted, the S-ICD defibrillator can be programmed in such a way as to automatically optimise the parameters of the device to monitor heart rhythm, allowing*

to reduce the intrinsic complexity of traditional systems. Just the fact of not having to wear a protective lead coat to avoid radiation exposure during the procedure is a remarkable to be enthusiastic. All patients have resumed their normal life and are doing well."

Darryl Ward, one of the first patients who underwent implantation of the S-ICD defibrillator produced by Cameron Health, said: *"I feel fortunate to have been able to use this innovative technology because the defibrillator I had implanted previously was not working anymore. I feel relieved that there is nothing inserted in my heart."*

The S-ICD system received the CE trademark in 2009, and was approved by the U.S. Food and Drug Administration (FDA) in 2012.

In one of our interviews Riccardo Cappato, co-inventor of the S-ICD together with Gust Bardy, told about how the concept of this technology was first discussed at the Hilton Hotel in Chicago during the annual Heart Rhythm session (then NASPE) in May 1999. *"I sat at a table in a café with Gust Bardy, and we were discussing the present and future concepts of Arrhythmology as usual. I remember saying on that occasion,* continues Cappato, *that I consider the future of defibrillators to be a Chip that could be placed in the subcutaneous region so that way many more types of patients could use the device. It would be suitable for a larger patient population. At that point, Gust Bardy suddenly stood up and hugged me, saying that he had been thinking the same thing for some time now. Within a few months, thanks to his connections with the industrial world, he was able to file a request in Delaware to start up Cameron Health. This led to the approval of the subcutaneous defibrillator twelve years later."*

Cameron Health, named in honour of Gust Bardy's son, founded by Cappato and Bardy in 2000 in San Clemente, California, United States, was later purchased by Boston Scientific in 2012, which had a right of first refusal because it had already invested 30 of the 80 million dollars necessary to develop the company.

Cappato continued, saying that *at the Green Lane Hospital in Auckland City the first acute tests were performed on 15 patients, mainly to evaluate the defibrillation threshold, which had to be, on average, 10–12 J internally, and 110–115 J externally. New Zealand was chosen because, despite being a country with Western standards, it had few economic resources for health. Green Lane, which is the main hospital in Auckland City, had a limited budget that sufficed for only a few transvenous defibrillators. Using this information we requested the authorisation of the national ethics committee,* continued Cappato, *and it was easy to get the approval. You could say they were enthusiastic because our company paid for transvenous defibrillators in subjects with the indication for the device, who would otherwise not have been able to afford it.*

So the protocol was written as follows: indications for the transvenous device, the New Zealand National Health system's lack of equipment, request made by New Zealand doctors to Cameron for the appliance, Cameron's request to perform an acute study on the subject, which clearly required an unnecessary cut in the lead and generator case positioning regions in order to define, through that simulation, the right energy delivered by the device to ensure effective defibrillation, which was identified as 80 J. Sometime elapsed between the calculation of the defibrillation threshold and the creation of the first device. It was not easy because the initial studies on the transvenous defibrillator could afford to fail as there was no alternative, but studies with S-ICD presented a much more difficult challenge as there was already a device on the market, the T- ICD, which was 99.9% safe. The studies continued and, finally, 12 years later, we obtained the FDA approval in 2012 and an investment of 80–90 mil lion dollars from the company. Cameron had become an important company with 80 employees and 35 consultants. Another important, vital but underestimated aspect of this story, said Cappato, that has generated the most excitement was being able to see and observe that an important production facility had been created from our initial small 5 rooms, a company made up of people who enthusiastically believed in this project.

We had won the challenge.

Subcutaneous Cardiac Defibrillation

The ability to defibrillate the heart without introducing electrodes through the venous system is a hypothesis that has always fascinated defibrillation studies over the years. The possibility of cardiac defibrillation with a non-venous endocavitary system was proposed rather early on, deriving almost consequentially from research on defibrillation carried out on animals, and also from reports of dangerous solutions in isolated clinical cases in which the endocavitary or thoracotomy modality was not feasible.

The main technological and biophysical problems can be summarised in three types:

1. feasibility and predisposition of cardiac defibrillation with reasonably low energy and via electrode/electrodes only in the subcutaneous tissue;
2. feasibility and predisposition of subcutaneous sensing of ventricular tachyarrhythmia and, particularly, of ventricular fibrillation (VF) through a subcutaneous electrode/electrodes;
3. harmonisation, in the same device to be inserted subcutaneously, of the characteristics of the sensing and the pacing with the actual features of

the technology in relation to the battery, connections, circuits and pace and shock electrode.

Understanding the mechanisms of heart defibrillation has been the subject of intense research for years. An important contribution was provided by modelling and computer simulation studies, both investigating biophysical assumptions and theoretical validations of projects. Using the various methods concomitantly defined to record electrical activity, the modelling of ventricular fibrillation currents and defibrillation waves completed knowledge on the role of myocardial tissue components (intra and extracellular) and of the cell membrane in determining both the effectiveness of the defibrillation shock and the electrical conditions to avoid re-triggering potentially arrhythmogenic currents[1,2]. On this basis, the first shock systems were investigated, both intrathoracic and, above all, extra thoracic, defining constructive-mechanical, biophysical and functional principles.

Studies on the preparation and in vivo studies on animals have been developed in parallel, testing the knowledge of biophysics and modelling, and acquiring clinical experience on humans, in extreme empiricism in a few particular complex patients.

The idea of the subcutaneous electrode was proposed even before the introduction of the implantable defibrillator, during preliminary animal research studies in the early 1970s[3]. Since the 1990s, technological development of the transvenous defibrillator along with its wide clinical use have established the theoretical foundations and extensive hands on experience already acquired with intrathoracic and transvenous defibrillation, besides selecting rare but not exceptional cases of patients presenting insurmountable technical difficulties for conventional approaches, in whom an attempt could be made by experimenting with new modalities. Some papers published in the early 2000s reported the efficacy of defibrillation with a subcutaneous system. A first paper on two children with congenital heart disease demonstrated the efficacy of a defibrillation threshold (DFT) of 20 J average energy between a subcutaneous electrode in the left hemi-thorax and the case generator located in the abdominal region[4]. Another paper significantly confirmed the DFT in a newborn in whom the coil was located in the posterior extra thoracic region. In both papers, the chronic DFT maintained stable values[5]. In another case, of a child with hypertrophic CMP, the shock was tested between the active abdominal case and the subcutaneous coil, using an epicardial electrode for sensing[6].

The initial approach to defibrillation systems prepared when needed only in particular cases was then systematised by the work of Berul[7],

who, using only defibrillation coil and active case, reported both effective defibrillation with overlapping thresholds to previous cases-reports, and implant safety, first in experiments in vivo on small animals, and then in a case of a small-bodied child with congenital cardiopathy. However, the problem encountered was that of DFT in the adult animal, that exceeded the generator's maximum limit of 40 J. The scattered reports were then revised in a large retrospective work, which showed the practical feasibility of only subcutaneous defibrillation in children. Twenty-four subjects with an average age of 8.9 years presenting complex cardiovascular pathologies were examined in several studies. In fourteen there was a subcutaneous coil, in addition to an intrathoracic catheter, venous or epicardial for pace/sensing, and a case for active shock. The subcutaneous coil, through which shock was delivered, was associated with higher DFT but at a level that could be reasonably attained and used in practice (19 J)[8].

The crucial issue highlighted by case reports and research on defibrillation models was constituted by the DFT and by the shock configuration in the subcutaneous systems, precisely how to obtain low effective energies and stable performance over time of the defined acute requirements, with safety margins comparable to the T-ICD. Various computer modelling studies on electric fields generated by electrodes positioned in places with an arbitrary orientation in the human thorax have been validated to measure the relative effectiveness of defibrillation in relation to the orientation of the electrodes, showing the interrelations between the position of the case, electrode length and anterolateral-laterolateral or anteroposterior positions[9,10].

The question has been defined by various studies. The in vivo experiments on an acute animal and on an animal implanted with an aggregate investigative model of the S-ICD system, carried out by Cappato et al., take into consideration both the characteristics of the shock and the sensing modalities[11]. First of all, eleven different configurations of shock were located in the left hemithorax between a sternal electrode and a sub-axial lateral electrode (so-called dual electrode), whose conductive surface was varied, being able to evaluate at the same time the different positions of the sternal electrode. All defibrillations were effective with energies below 80 J, and the larger surfaces of the dual electrode were associated with the lower DFT. Some of the animals were implanted with the aggregated S-ICD system, which consisted of a left lateral case and a large surface parasternal electrode, which was then tested again: a shock of 65 J was effective on VF in 90% of cases[11].

Evidence related to defibrillation derived from these pioneer studies of Cappato supported the design of a model for industrial manufacturing.

Experimentation on humans provided other data about DFT and shock; the work of Burke et al. was among the first to report the results of a hybrid investigational system with an external defibrillator in a cohort of 15 patients during T-ICD implantation[12]. DFT with a single shock vector between pectoral case and a cutaneous electrode was 50 J in most patients, and only one in nine DFT models were greater than 70 J[12].

Another acute study in patients during T-ICD implantation showed low DFT energies using a case emulator in the anterior thoracic cavity, and a posterior coil: the energy was less than 35 J in 81% of patients[13].

From Subcutaneous Defibrillation to the Subcutaneous Defibrillator

The passage from the feasibility of only subcutaneous defibrillation to the complete S-ICD system required the conception and construction of:

- a software, which can be inserted into a CIED box and which contains, in addition to the battery and the condenser, the identification algorithm for ventricular tachyarrhythmia;
- an appropriate electrode suitable for detection and delivery of shock.

A considerable contribution to define subcutaneous sensing the modalities came from data accumulated on the use of the intracardiac detection algorithms, drawn up and perfected for the T-ICD.

Since the surface ECG waves correlate extensively and subcutaneously with the subcutaneous electrograms[14], preliminary studies have used skin electrodes to simulate the evaluation of the subcutaneous signal when 'designing' the S-ICD. It was thus possible to detect, through subcutaneous positioning of the sensing system, how the tachyarrhythmia discrimination system already constructed and implemented in the T-ICD could be used with high efficiency. With this technique, Burke et al.[15], interfacing subcutaneous electrodes to the detection and discrimination algorithms for tachyarrhythmia of conventional T-ICD, demonstrated that the cardiac electric signals recorded subcutaneously were different and easy to distinguish from the sinus rhythm and signals of ventricular fibrillation[15]. A subsequent presentation by Gold et al. proposed a cutaneous sensing model, equivalent to the subcutaneous one, comparing the perception achieved by a conventional single-chamber T-ICD. Correct recognition of the subcutaneous signal for ventricular tachyarrhythmia was found to be more than 98% more sensitive[16]. Another larger study confirmed and detailed these findings, after the S-ICD had been tested and approved for clinical purposes[17]. This study, called Subcutaneous versus Trans-

venous Arrhythmia Recognition Testing (START), involved simultaneous recording and cataloguing of a large series of arrhythmias induced by T-ICD implantation with both subcutaneous and transvenous electrodes. The recordings were identified and catalogued again, offline, by any type of T-ICD device in order to evaluate the comparative effectiveness of the algorithms in distinguishing ventricular arrhythmia from supraventricular arrhythmia. Appropriate distinction of ventricular tachycardia occurred in 100% of cases for the simulated S-ICD system, whereas the specificity for supraventricular tachycardia was (98%) higher in the S-ICD system than in the T-ICD system (average 76%)[17].

The detection algorithms, derived from the comparative experiences with T-ICD and validated in preclinical studies, were implemented in the first model of combined S-ICD, preliminarily tested in vivo on the whole animal, acknowledging complete success and recognition[11]. The essential elements of S-ICD sensing function were already defined in this technological precursor: analysis of the frequency and morphology of the rhythm recorded by subcutaneous ECG to identify the level of tachycardia. After identifying a rhythm in the conditional intervention zone, which is not subjected to the frequency filter alone, the QRS morphology was compared with QRS templates already registered at rest as reference. If there was a high correspondence of the QRS interval, the rhythm was catalogued as supraventricular. Otherwise, a further beat-by-beat analysis was performed to identify either a QRS polymorphism or its width greater than the conditions leading to recognition of the ventricular form and treatment activation, over time and with the programmed modes.

Development and Experiences of the Current Model of the Subcutaneous Defibrillator

The series of studies that demonstrated the feasibility and safety of the use of a device for cardiac defibrillation with a complete and exclusive subcutaneous position progressively defined its construction features. The manufacturing industry has constantly adapted the manufacture to the biophysical, clinical and technological evidence provided by scientific research. The preliminary experience with the first S-ICD[18] was proposed already in the first published report, in 2009, but studies in humans with an 'aggregate' experimental device began in 2001. As already mentioned, Cappato's experiments on animals, both acute and chronic, anticipated studies on prospective evaluation in humans[11]. The aggregate S-ICD system described above showed the effectiveness of defibrillation with a 65 J shock in 90% of cases, and with less energy than 80 J in 100% of cases;

it was effective on VF in 90% of cases; in the 5 chronic systems in animals 'of the aggregate' S-ICD there was no malfunction at a follow-up of 7–24 months[11]. The S-ICD already designed and assembled by the manufacturing industry was then tested in humans in a large synchronised multicentre work group, which included some leading research centres[19], through a series of studies first in acute patients and then in chronic ones. Two short-term studies were carried out using a single electrode-device system temporarily inserted subcutaneously, followed by two long-term studies that employed a finalised fully developed device that is still used today. The first studies on acute cases were carried out quickly, from 2001 to 2005, using a subcutaneous defibrillator temporarily inserted in humans during T-ICD implantation according to the current guidelines. The parasternal position of the electrode and its composition represented the technological product of all theoretical elaborations and previous individual practical experiments. There was an electrode connected to an active impulse generator, a three-pole structure with an 8 cm shock coil and two sensing poles, of which the distal one was positioned adjacent to the junction between the rib cage and the sternum, and the proximal one was adjacent to the xiphoid process[19]. In the first study on acute cases, DFTs were evaluated in 78 patients according to four different shock configurations, revealing that the best configuration had the generator in a left lateral position and the shock coil parallel to the left parasternal margin (Figure 2.1).

The second study on acute cases compared the effectiveness of this configuration with that of a conventional T-ICD shock in 48 patients: the induced ventricular fibrillation was efficiently interrupted in all cases except for one, with a mean DFT of 37 J for S-ICD, versus 11 J for T-ICD, with no correlation between the DFT of the S-ICD and no clinical or anthropometric parameters.

Subsequently two studies were carried out in chronic patients. The first, on six patients who underwent complete subcutaneous device implantation with shocks in two possible polarities, with a fixed energy of 80 J, showed feasibility of the intervention, of the tests (at least two) of acute defibrillation, and in almost 1.5 years of follow up there were no problems related to the device, with no intervention on tachyarrhythmia of any kind. The second study, which represents the first multicentre trial on the use of S-ICDs performed in Europe and New Zealand between 2008 and 2009, included 55 patients with normal indications for ICD and without any signs of any form of pacing (anti-bradycardia or anti-tachycardia). Among these, 52 patients were eligible for permanent implants after at least two acute defibrillation tests with 65 J of energy used. The

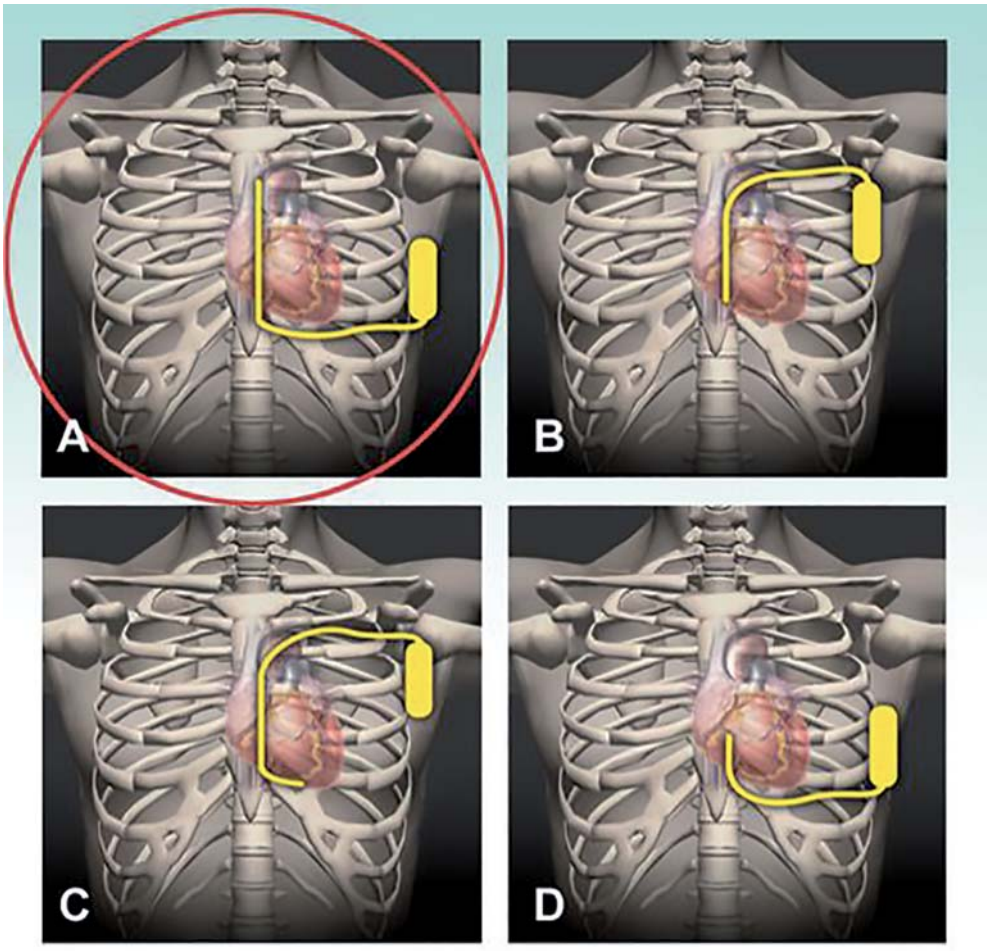

FIGURE 2.1

Four configurations of a subcutaneous implantable defibrillator. The most effective of the four configurations tested to select the best position for S-ICD components was the one with the pulse generator placed in the left lateral side with 8 cm lead positioned on the left parasternal margin (A).

tests require at least one shock with standard polarity plus one with reversed polarity. The detection of VF was correct in all cases; among the three patients excluded, only one showed ineffective defibrillation, but in a single configuration. After a follow-up of an average of 10-months, there was one death due to a non-cardiac disease and four patients had sensing problems, all corrected non-invasively. Twelve episodes of ventricular tachyarrhythmia were identified and properly treated, and there were no episodes of untimely shocks[19].

These studies confirmed S-ICD as a valid therapeutic option due to the optimal positioning of its elements outside the thorax. This mechanical and electronic model has also been significantly defined, after minor changes to the case, and greater ones to the algorithms. The model used today has a ca. 70 mL generator and weighs 145 g. As already mentioned, the electrode/catheter has a single high voltage coil with low impedance and two low voltage and low impedance sensing electrodes capable of making three sensing configurations and two shock polarities; 80 J fixed nominal shock.

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Chapter 3

The Subcutaneous Defibrillator: from the Laboratory to Clinical Evidence

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Four fundamental biophysical and technological problems were tackled during the development of the subcutaneous defibrillator (S-ICD). The first one concerned hardware (materials and battery). The second was the choice of the site, practicability and safety of the surgical insertion in a large number of individual somatic and biophysical configurations. The third identified the defibrillation threshold and effectiveness of the interruptive shock (shock Delivery) and, lastly, the appropriateness of ventricular signal detection. This Chapter focuses on the results of the clinical use of S-ICD, with particular reference to evidence regarding efficacy and safety that has emerged from use in patients over the years, from preliminary studies and 'authorisation' for full availability in routine daily practice (Figure 3.1).

With reference to S-ICD, **efficacy** indicates the capacity to interrupt VF/VT, from the time of implant onward and, therefore, indefinitely maintained over time. The interruption must be considered both at the first discharge and at the end, after the entire sequence of shocks of the treatment cycle (currently 5 consecutive shocks), in terms of the amount of energy necessary for cardioversion. Moreover, considering the high energy delivered by the device between 65 and 80 J, today this index is only evaluated during implantation.

Safety, in addition to the success of the implantation and the short and long-term complications, is above all the ability to accurately distinguish ventricular tachyarrhythmia from other different electrical situations that can mimic it. Most of all, the T-wave count as R waves, the relief of muscular electrical activity and the detection of supraventricular

arrhythmia. All inaccuracies in recognition result in the risk of providing inappropriate shocks. The surface ECG screening test was introduced to reduce this risk, and has been used in all studies performed with S-ICD. This test externally reproduces the sensing vectors used by the S-ICD to obtain a quantitative measurement of the 'Suitability' for recognition of the QRS[1,2].

The evidence of efficacy and safety of the use of S-ICD is still based on cohort registries and studies, whereas comparison with transvenous ICD (T-ICD) has been carried out only indirectly so far. A large, multicentre randomised trial is underway, PRAETORIAN[3] (Prospective, RAndomizEd comparison of subcuTaneOus and tRansvenous ImplANtable cardioverter-defibrillator therapy) designed for direct comparison between S-ICD and T-ICD, with primary focus on safety (inappropriate interventions and complications) and secondarily on the effectiveness of shock and mortality, which will provide answers not only on survival but also on the quality of life in patients with S-ICD (Figure 3.1).

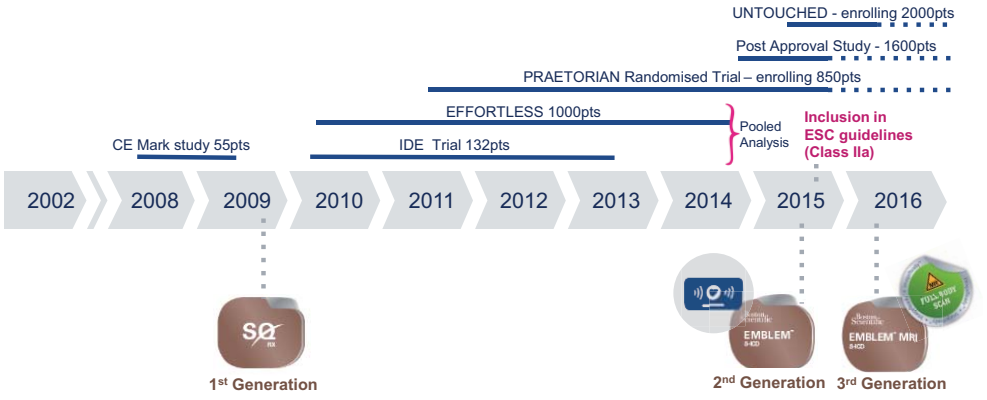

FIGURE 3.1

Evolution of therapy with S-ICD.

Initial Clinical Studies

In the early 2000s, there were already some reports of isolated cases on the use of subcutaneous defibrillation in children, but these were adaptations of the already existing technology and detailed to particular anatomical situations[4,5]. The paper that provided a crucial contribution to introduce the S-ICD procedure in clinical practice was published by Bardy et al. in 2010[6]. The authors compared four different possible configurations of the device (positioning of the generator and electrode) in order to obtain effective defibrillation thresholds in 78 patients.

The best configuration was the one consisting of a parasternal electrode and the generator in the left lateral thoracic position with an average DFT of about 32 J. Subsequently, the S-ICD was implanted and compared in 48 patients in which a traditional ICD was also implanted, to verify its reliability. After these two pilot studies, the subcutaneous ICD was then implanted in another 55 patients. The results were very favourable, with equal efficacy between the S-ICD and T-ICD in the interruption of ventricular tachyarrhythmia, and a predictable greater need for energy for S-ICD (36 J), compared to T-ICD (19 J). There was a 100% correct detection of VF induced by implantation, with a 98% interruption with 65 J shock in two consecutive induction tests, and a 100% correct detection and effective correct treatment of spontaneous VT/VF occurred in the follow-up of almost a year[6].

Following reports published between 2011–2012 regarding the use of the subcutaneous device in clinical practice as we know it today in its technological evolution, and in a limited number of cases[7–9], shed light on some good effects and, not surprisingly, also on some bad ones. Two single centre studies[7,8], with a total of 47 patients predominantly with genetic arrhythmic syndromes from canalopathies, showed the safety of the intervention, with low complication levels, and in an average follow-up of around nine months, the effectiveness of the treatment, with conversion at the first shock in all patients with the occurrence of VT-VF. However, there were significant problems in terms of function. There were inappropriate shocks in 16% to 25% of patients, mostly related to over-sensing of the T wave and only to a lesser extent to myopotentials; recognition delay in three cases of bi-directional catecholaminergic VT leading to a delay in the initiation of treatment. Problems concerning wounds (an infection, three reopening-dehiscence sutures) were, instead, treated conventionally.

A third, multicentre work[9] in 40 patients, more than half of whom were in secondary prevention, showed that out of 28 shocks in 4 patients, only 4 were inappropriate (8%), but the effectiveness at the first

shock was only 57%, while the overall effectiveness of the defibrillation sequence was achieved in 96% of cases. Altogether these initial experiences identified 'shadows' concerning the high incidence of inappropriate shocks, the delayed recognition of ventricular tachyarrhythmia and the interruptive efficacy of the first shock. Moreover, the studies in question were certainly revolutionary but with limited horizons, and some cases studied exhibited particularly unfavourable aspects, as in the case of catecholaminergic VT characterised by spontaneous wide T wave and R wave variations. The observations made in these studies generated a profound technological revision based on which improvements were made to the recognition of algorithms and the general software, and to the implantation technique. The effectiveness of these revisions was ascertained 'in progress' when conducting the research, sometimes in the same patients in which the problem had previously been detected. Some examples of this are both the double area of intervention and the algorithm discrimination of the morphology associated with it. The double intervention area provides for frequency values that can be programmed in a possible zone in which shock delivery is based on the heart rate alone, and in another zone, defined as conditional, in which morphological discrimination algorithms are applied to refine the device's distinction between ventricular and supraventricular tachycardia. The appropriateness of the most advanced version of the discrimination algorithm, which combines frequency, morphology of single beats and their sequences and extent of QRS, was specifically evaluated in a multicentre comparative study, START (Subcutaneous versus Transvenous Arrhythmia Recognition Testing) in an original setting[10]. During T-ICD implantation with atrial electrode, transvenous endocavity signals and signals of the skin (obtained with electrodes placed on the skin) were simultaneously acquired during VT/VF and supraventricular tachyarrhythmia, and then inserted offline into the sensing channels of T-ICD and S-ICD. The S-ICD showed some sensitivity, that is to say 100% appropriateness of the VT/VF recognition, and specificity, 98% adequacy of the recognition of supraventricular tachycardia; the results of the latter were better than those calculated on T-ICD[10].

The discrimination algorithm was introduced in clinical routine in 2013, and the first results of its large scale use were published in 2014 (IDE study), where, as described below, it produced significant improvements in signal analysis sensitivity and specificity.

Two observational multicentre studies, one Dutch, Nordkamp et al., and the other British, Jarman et al.[11,12], were published in 2012–2013. The studies included a total number of 229 young patients (mean age 50 and 33 years, respectively) with a follow up of 18 and 12 months. They

detected 98% efficacy of the first appropriate shock and 100% efficacy in a total of 45, with 28 treatments provided appropriately. They also found an occurrence of inappropriate shocks in 13% and 15% of patients, mainly due to oversensing of the T wave. A shock in the Nordkamp study and no shock in the Jarman study were delivered on supraventricular tachycardia that fell within the 'conditional' intervention zone, where the morphology discriminators were active. There were no cases of sudden death and only one patient died of repeatedly treated and recurrent ventricular tachycardia. Other additional aspects that seemed to be important were the discrete incidence of surgical problems of the subcutaneous chamber (about 8% in the Nordkamp study), which were resolved conservatively or with local revision for the most part; among these, chamber infection prevailed in 5.5% and in 10% of the cases in the two studies, respectively, in which ICD system explantation was carried out in only one third of the cases, with subsequent complete resolution of the case[11,12]. Finally, in the phase of large scale implementation of S-ICD, a significant piece of information intensifies the importance of the rapid improvement of technology and technique induced by the observations made during clinical practice. In the Nordkamp study, both the detection algorithm that governs sensing, and the electrode fixing technique were modified during the course of the study, determining a significant advantage for subsequent research[11].

The IDE and EFFORTLESS Studies

The most significant historical studies, which supported the approval and clinical diffusion of the use of S-ICD as standard treatment, were the IDE study, carried out under the auspices of the US Food and Drug Administration, and the EFFORTLESS S-ICD postmarket register sponsored by the S-ICD producer, Boston Scientific, both of which started in 2009[13,14].

The IDE (S-ICD System IDE Clinical Investigation) study examined the performance of S-ICD for FDA approval for marketing in the US[13]. The prospective observational study evaluated the safety and efficacy of S-ICD, both in the acute defibrillation test phase, with a 6-month repeat in a subset of patients, and during an average follow-up of 11 months. The population consisted of 330 patients with an average age of 51 who showed, among other basic characteristics, an average EF equal to 39%. The indication was for primary prevention in 79% of cases. In the 304 cases of which data were available, S-ICD effectively stopped all VFs induced in the implant with an energy shock of 65 J; each defibrillation test was repeated a second time, and if the first or second attempt was ineffective,

up to four attempts were made at cardioversion of VF with the same polarity. The induction test did not cause any complications. The follow-up recorded 119 episodes of VF/VT, out of which only 38 were isolated cases and the remaining 81 as part of an arrhythmic storm, in 21 patients (6.7%). The shocks were effective at the first attempt in 92%, including those under arrhythmic storm. Total mortality was 2.5%, with no arrhythmic deaths, although interrogation of the device was not available in two deaths due to indeterminate causes. Inappropriate shocks occurred in 13% of the patients, caused by supraventricular arrhythmia and T-wave oversensing. The treatment applied was conservative, reprogramming of the device or drug therapy in 78% of cases, invasive procedures in a minority of 22%, including the four cases in which the device was either removed or switched off. It is important to note that all inappropriate shocks occurred in the 'unconditional' zone where the intervention algorithm solely relies on the detected heart rate. It follows that no discrimination error was involved for supraventricular tachycardia. The morphological discrimination algorithm was introduced and tested during the IDE study. The results are that, in the 226 patients with dual programming of intervention and algorithm activated in the first zone, the one with lower frequency, compared to 88 patients with single zone of intervention only, resulted in a 60% reduction of inappropriate shocks, decreasing from an incidence of 24% to 10%. The infection rate was 5.6%, treated for the most part by conservative therapy, and the system was explanted in 4 patients (1.2%).

The results of the IDE demonstrated for the first time significantly higher levels of safety and efficacy of S-ICD, compared to those known up to that point (studies by Nordkamp and Jarman).

Even more relevant is the fact that the other multicentre study, EFFORTLESS S-ICD, quite independently confirmed these results in a short period of time.

The EFFORTLESS S-ICD study (Evaluation oF FactORs ImpacTing CLinical Outcome and Cost EffectiveneSS of the S-ICD) is a non-randomised registry on the standard of care, which has enrolled over 1,000 patients in in various European countries and in New Zealand[14]. In 2014, the results of the ad interim analysis were presented for 472 cases evaluated at 6 and 12 months from the implant, half of which were prospective and half retrospective. The population, with an average age of 49, included about one third of subjects with ionic channel or hereditary diseases, idiopathic ventricular fibrillation and congenital heart disease. It was obligatory to perform a defibrillation test on each implant, verifying the efficacy of the external CV with an energy equal to or less than 80 J to interrupt the VF. The device was then programmed with maximum output (80 J).

The double zone of detection was present in 82% of cases. The published results showed 169 S-ICD interventions in 59 patients, equal to 13% of the population; 55% of these interventions were appropriate, 45% were not appropriate, but the inappropriate interventions were concentrated in only 7% of cases; therefore, few subjects had to have more inappropriate interventions. The appropriate interventions were highly effective, meaning that with any of the five possible and foreseen shocks, all VT/VFs were interrupted (100% effectiveness).

Effectiveness at the first shock was 88%. Inappropriate S-ICD interventions were predominantly caused by oversensing on the T-wave in 84% of cases, and only 8% were caused by high frequency supraventricular tachyarrhythmia. A proportion of these inappropriate interventions were corrected with reprogramming and/or pharmacological treatment, but in 2% of the patients the inappropriate shocks persisted even after the attempt to correct it. In three patients the device had to be either removed or switched off due to discomfort or dejection. Dual zone programming was associated with a reduced incidence of inappropriate interventions, compared to that in a single zone (that is, with only a high frequency criterion) (Figures 3.2, 3.3).

Complications, defined in rather rigid terms as the events that involved a new invasive procedure, occurred in 7% of patients. There was no elec-

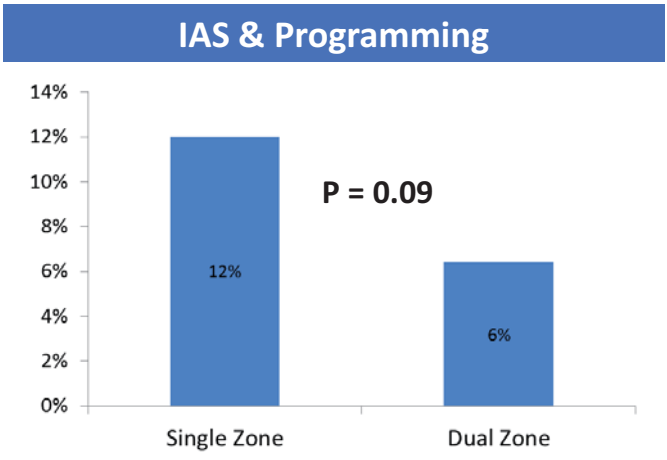

FIGURE 3.2

Dual zone programming is associated with a reduced incidence of inappropriate shocks, compared to that in a single zone. The 82% of cases programmed with dual zone showed a reduction of inappropriate therapy.

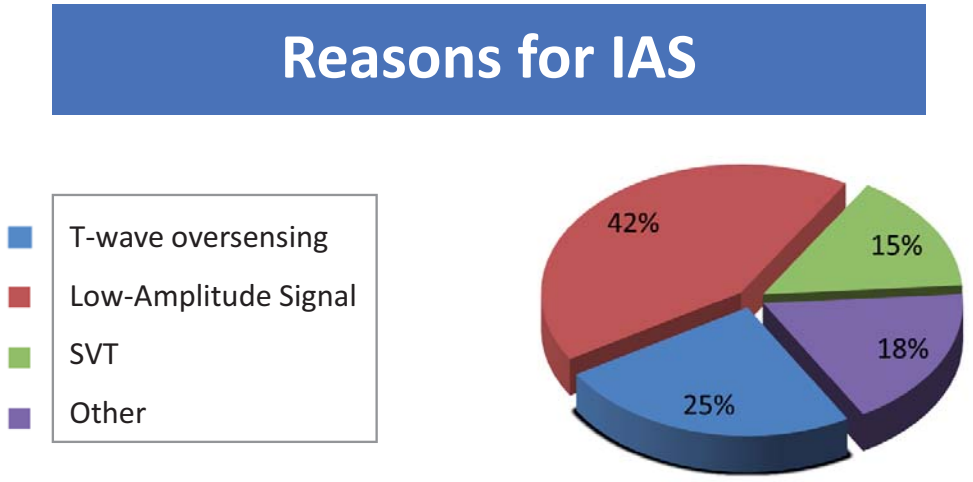

FIGURE 3.3
The figure highlights the main causes of inappropriate shocks.

trode breakage among these. The temporal distribution of complications was 3% at 30 days, 6% at 6 months and at 12 months. The incidence of total infections was 4%, but the serious infections that required removal of the system were 2.2%.

The two IDE and EFFORTLESS studies highlighted overlapping profiles of S-ICD efficacy and safety; the minor differences in the percentage of infections seem to be justified by the differences in the definition of criteria adopted, and do not affect the substantial homogeneity of the results that are most relevant. The data of the inappropriate complications and shocks reported in both studies are much more favourable than the few antecedent Dutch and British registers but this result was, somehow, expected. In fact, the analysis of the results of the two previous studies led to the revision and correction of programming, with subsequent rapid implementation in the major studies that were in progress. These corrections were applied to the algorithms, the implantation technique and the positioning modalities, and also for surgical precautions[15,16].

The main conclusions of the two studies were confirmed along with other important findings by the cumulative analysis of the results of IDE and EFFORTLESS, and published by Burke et al. in 2014[17]. Moreover, the results of EFFORTLESS with a three-year follow-up, that were released in 2016, have not been published as yet[18].

The collective analysis of IDE and EFFORTLESS, which incorporated data relating to a portion of the EFFORTLESS patients that were

enrolled later in the study (the study continued enrolment), comprised 889 patients with a mean age of 50 years and an average follow-up of 22 months, 70% of which were primary prevention[17]. The EFFORTLESS study presented long-term data regarding 985 patients who underwent implantation in 42 centres worldwide, with an average age of 48 years, and an average follow-up of 3.1 years, including 65% in primary prevention[18].

In both studies, cumulative and with long-term follow-up, the favourable outcomes of the use of S-ICD detected at the follow-up of about 1 year were maintained, with a decrease in the rate of overall complications and inappropriate shocks, thanks to the new highly technological improved implants. The most consistent results were as follows: from Burke's work, with actuarial evaluation, the incidence of the first therapy was 5.3% at one year, 7.9% at two years and 10.5% at three years; effectiveness at the first shock was 90%, with total 98% for each shock, while in the long-term EFFORTLESS study the corresponding values were 88% and 97%. The incidence of inappropriate shocks was 13% at three years in the collective analysis, with a clear difference between the frequency associated with a single intervention zone, equal to 20.5%, and that with a double zone, equal to 11.7%. In the long-term follow-up EFFORTLESS study the incidence of inappropriate shocks was 8.1% in the first year, predominantly of cardiac origin, 1.5% of which due to atrial tachyarrhythmia[17,18]. In the long term there were no events of electrode malfunction or systemic infections or endovascular complications related to the device. The cumulative analysis showed that, in the more recent period of the study, there was a 34% decrease in inappropriate shocks (in the last quartile of patients enrolled, compared to the first quartile) as a consequence of reprogramming in two intervention areas[17] (Figure 3.4).

T wave oversensing, thanks to corrections implemented to the patient selection and detection method, accounted for less than 40% of the causes of inappropriate therapy and, in any case, this number remained lower than the one reported in several preliminary studies. The total overall complication rate was 9.6%, mainly consisting of wound obstructions (about 5%) of which, however, infections involving reoperation or explantation were scarce (1.7%). A further interesting finding was that, patients who had been submitted to explantation of a previous transvenous ICD due to system infection and who presented a more unfavourable general morbidity profile, no difference in the incidence of new S-ICD infections was observed, compared to the other subgroups with lower theoretical risk of infections[19].

The minimum percentages of explants for the necessity of bradycardia pacing and recurrence of VT treatable with antitachycardia pacing could

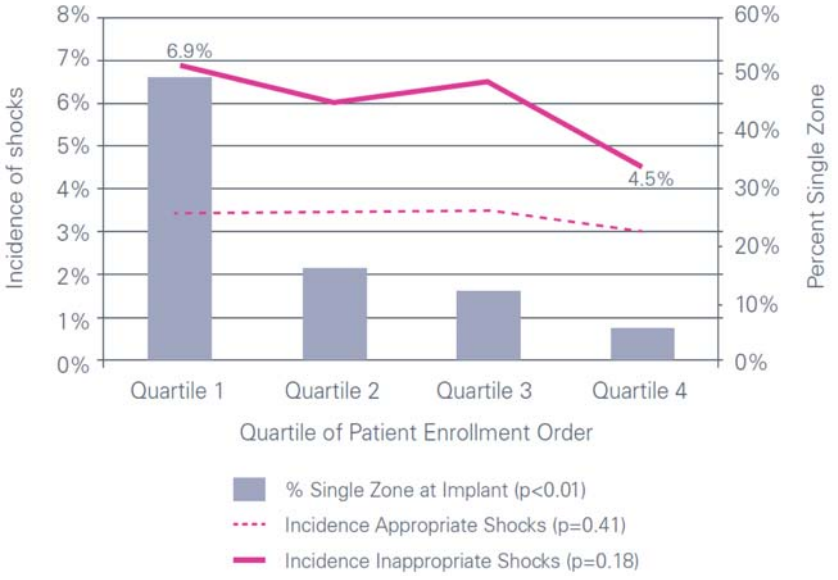

FIGURE 3.4

The graph highlights the reduced incidence of inappropriate shocks with dual zone programming.

be attributed to the accuracy of the selection criteria and preliminary evaluation: 3 patients and 1 patient, respectively, in the cumulative database, and 1 and 5 patients in the long-term EFFORTLESS study. Regarding this aspect, the remaining 1.4% of patients with more than one single documented VT subjected to cardioversion should also be considered, which corresponds to an annualized incidence of 0.8% of recurrence treated VT. In Burke's study, the authors hypothesise, based on the analysis of the literature on antitachycardia pacing in T-ICD carriers, that the additional benefit of this therapeutic option would be between 0.3% and 1% per year and, therefore, have limited influence in the selected S-ICD population[17]. Another important finding was that, in the long-term EFFORTLESS study, compared to 2.2% of patients with at least one monomorphic VT, there was no correlation with the underlying ischaemic heart disease, thus contradicting the opinion that antitachycardic pacing would be usually needed in ischaemic substrate. Finally, after observing patients for a longer period of time, while keeping in mind that the IDE and EFFORTLESS studies were not designed to evaluate mortality, the mortality rate is also significant, equalling 1.6% the first year, with a total of 3.2 % at two years.

The indirect comparison presented in the same study with the mortality values observed in more recent trials with T-ICD[23] seems to favour S-ICD: in MADIT-RIT (primary prevention only) and in SIMPLE (30% of cases in secondary prevention), the two-year mortality rate was 5% and 11%, respectively[20,21].

Some comparisons between the two ICD systems, S-ICD and T-ICD, were finally performed in an indirect way, using the methodology of the 'propensity-matched' analysis among patients selected from large multicentric registers. Accepting the limitations of this approach, the results are rather interesting and can at least 'generate working hypotheses': in Brouwer's study[22], with a population of over 1,100 ICD implanted subjects over a period of ten years, 140 S-ICD were selected retrospectively, and the same number of T-ICDs with paired features; a 5-year follow-up study revealed an identical effectiveness of interrupted therapy and the incidence of inappropriate shocks; the complications were globally superimposable, but the typology differed sharply between T-ICD and S-ICD: electrode-related complications were 11.5% versus 0.8%; infections were 3.6% vs 4.1%; non-electrode or infectious complications were 2.2% vs 9.9%. Similar results on efficacy and inappropriate shocks came from a second similar analysis in a smaller sample[23].

Clinical Evidence in Specific Subgroups

All the data published so far has revealed that, beyond widespread use in all arrhythmic diseases and in all the morbid conditions, there are less prevalent categories of patients that have a great clinical impact, categories in which S-ICD has been either considered or proposed as a first choice alternative: paediatric or very young patients with cardiac channelopathies-cardiomyopathies-congenital heart disease and subjects with hypertrophic cardiomyopathy. In these types of patients, in addition to the duration of time, the application of S-ICD poses additional problems related to the thoracic conformation, lower weight, distortions caused by possible anatomic anomalies and the high incidence of atrial tachyarrhythmia, which present a high frequency. Maximum levels of interrupt efficacy and operating complication rates that are similar to those of the other age groups emerge from the evaluation of clinical data obtained both by isolating the subgroups within compound populations and from some small studies on homogeneous cohorts, while the most variegated was the verification of inappropriate interventions[24–28]. In smaller or less recent cohorts, inappropriateness appeared greater and was mostly related to oversensing of the T wave[8], while in more recent cases the improve-

ments in signal detection seem to have limited the problem and there are assumptions for further improvement of the discrimination of supraventricular tachycardia[24,25]. The risk of inadequate T-wave detection seems particularly high in patients with hypertrophic cardiomyopathy where wave anomalies are common and impair proper signal identification. In addition to improvements in detection, it has been shown that stress assessment of repolarisation can unmask incorrect sensing conditions[29]. Furthermore, it has not been confirmed that the incidence of electrode malfunction would be high in young patients with cardiomyopathies and cardiac channelopathies[28]: the significant complications related to electrode malfunction were null and void in the subgroup with hypertrophic cardiomyopathy in the IDE and EFFORTLESS studies[30].

The Basu-Ray Meta-Analysis

Interesting results were highlighted by the meta-analysis of case-control studies conducted by Basu-Ray[31] that analyzed five case-control studies for a total of 6400 patients by directly comparing S-ICD and TV-ICD for device-related complications, inappropriate shocks and infections. The S-ICD reduced lead-related complications but was similar to the TV-ICD with regard to non-lead related complications, including inappropriate shocks and infections (Figure 3.5).

These results support the concept that the S-ICD is a safe and effective alternative to TV-ICD in appropriate patients.

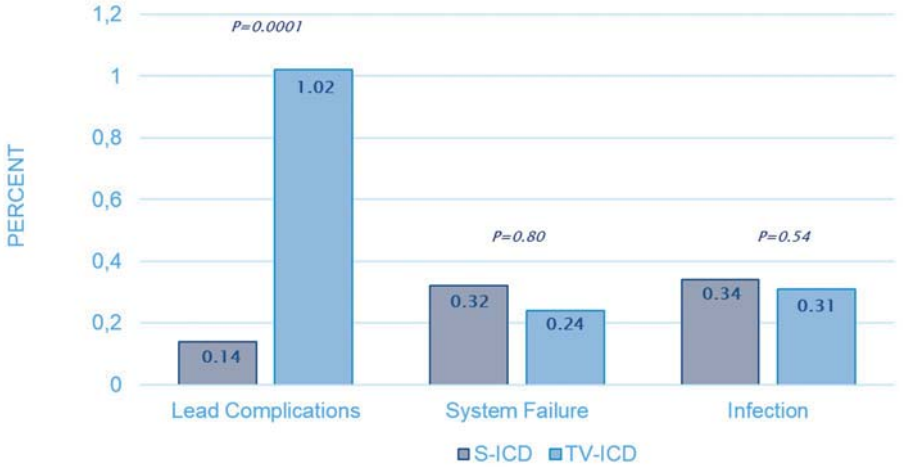

FIGURE 3.5

Lead complications were significantly less in S-ICD group compared to TV-ICD group, while no significant differences were found in system/device failure or rate of infection.

The PRAETORIAN Trial

The PRAETORIAN trial (A PRospective, rAndomizEd Comparison of subcuTaneOus and tRansvenous ImplANtable Cardioverter Defibrillator Therapy) aimed to make a direct comparison to demonstrate non-inferiority between S-ICD and TV-ICD evaluating as primary end-point, the composite of device-related complications and inappropriate shocks[32,33]. The exclusion criteria were the indication for anti-bradycardia pacing, anti-tachycardia pacing or cardiac resynchronization, previous ICD implantation and unsuitability for S-ICD according to pre-implant screening.

A total of 849 patients, 426 in the S-ICD group and 423 in the VT-ICD group were included in the study. At a median follow-up of 49.1 months, a primary endpoint event occurred in 68 patients in the subcutaneous ICD group and in 68 patients in the transvenous ICD group (Figure 3.6).

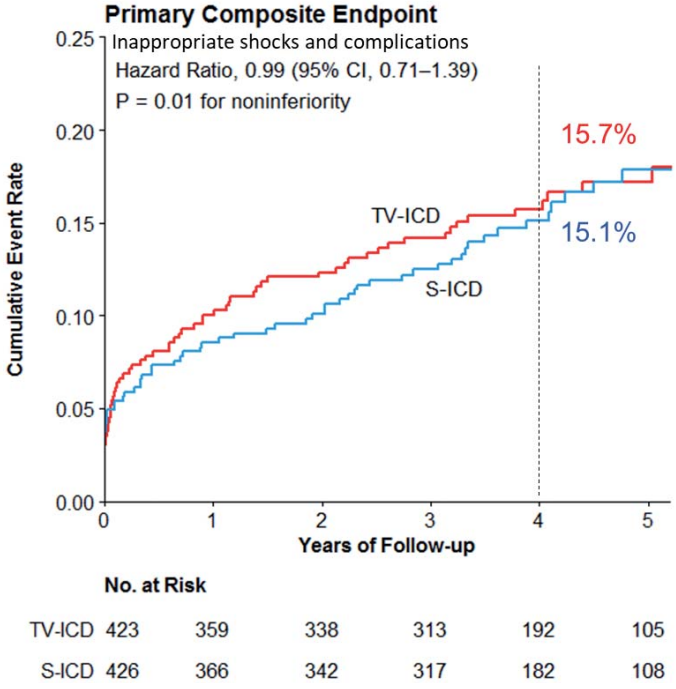

FIGURE 3.6

The graph shows 48-month Kaplan–Meier estimated cumulative incidence, 15.1% in the subcutaneous ICD group and 15.7% in the transvenous ICD group. The hazard ratio for the primary end point was 0.99 (95% confidence interval [CI], 0.71 to 1.39; noninferiority margin, 1.45; P=0.01 for noninferiority; P=0.95 for superiority).

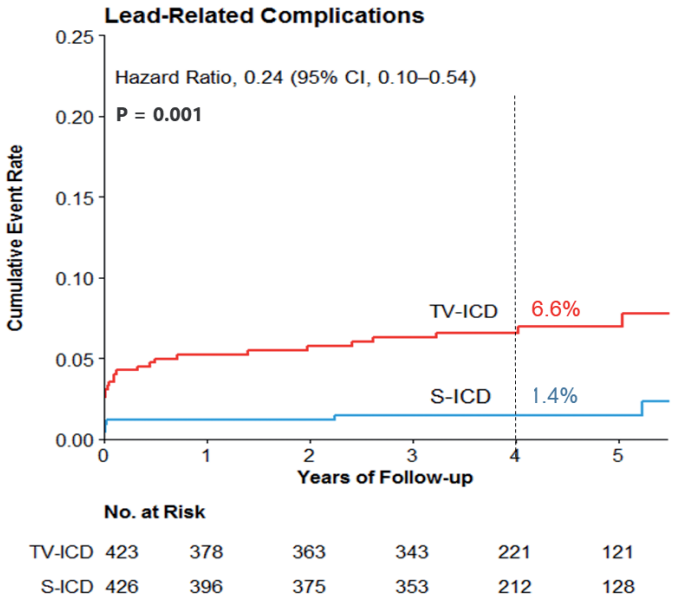

FIGURE 3.7

The S-ICD group had significantly fewer lead-related complications.

Device-related complications occurred in 31 patients in the S-ICD group and in 44 in the TV-ICD group (Figure 3.7).

Death occurred in 83 patients in the S-ICD group and 68 in the TV-ICD group; Appropriate shocks occurred in 83 and 57 patients, respectively.

Inappropriate shocks occurred in 41 patients undergoing subcutaneous defibrillator implantation and 29 patients undergoing transvenous defibrillator implantation. However, it should be emphasized that 58.5% of the first inappropriate shocks occurred in the S-ICD group were associated with cardiac oversensing (mainly T wave oversensing), a figure that may not reflect the current incidence of these events because 78% of S-ICD patients had not available the SMARTPASS filter, that has already been shown to reduce inappropriate shocks caused by T wave oversensing.

Lastly, no significant differences emerged between the two groups in terms of all-cause mortality and the number of sudden cardiac deaths, while only one patient required the switch from S-ICD to TV-ICD due to the need for antitachycardia pacing.

The results of the Praetorian showed that the S-ICD, for patients who do not require pacing, was non-inferior to the transvenous ICD with re-

spect to cumulative incidence of device-related complications and inappropriate shocks.

The PRAETORIAN Score

Quast et al. have developed a non-invasive scoring system, the PRAETORIAN score, which uses routine postoperative chest radiographs to evaluate implant position and identify those at risk for unsuccessful conversion[34] (Figure 3.8).

The score consists of three steps:

1. Assessment of the amount of adipose tissue insulating the shock coil
2. Assessment of the generator position to ensure that the electric field is directed towards the critical mass of the heart
3. Measurement of the amount of adipose tissue between the generator and the thorax

Step 1)

Determine the amount of subcoil fat by assessing the thickness of the adipose tissue between the coil and the sternum or ribs by using the coil width as a reference by evaluating the number of coil widths of fat tissue between the nearest half of the S-ICD coil and the sternum or ribs.

Number of coil width	score
≤ 1 coil-width	30
> 1 ≤ 2 coil-widths	60
> 2 ≤ 3 coil-widths	90
> 3 coil-widths	150

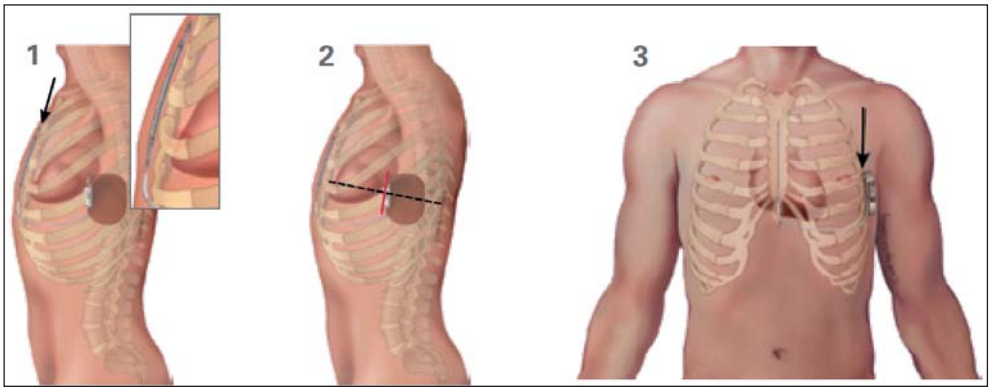

FIGURE 3.8
The PRAETORIAN score steps.

Step 2)

Determine the position of the S-ICD generator in relation to the mid-line and whether is positioned on, or posterior to the midline (red line).

Position	multiplier
Generator is on or posterior of the mid-line	x1
Entire generator is anterior of the mid-line	x2
Entire generator is > 1/2 length anterior	x4

Step 3)

Determine the amount of fat tissue between the nearest point of the generator and the thoracic wall by using the generator width as a reference, and in case one generator width of adipose tissue is present between the generator and the thorax, the score is multiplied by 1.5.

Generator-width	multiplier
<1 generator-width	x1
≥1 generator-width	x1.5

Step 4)

Patients with a BMI of ≤25 kg/m2 are rewarded by subtracting 40 points in the case of a score of ≥90.

PRAETORIAN score ≥90:
BMI ≤ 25 kg/m2 – 40
BMI ≥ 25 kg/m2 = Final score

The individual components are multiplied to give the final PRAETORIAN score. The minimum score is 30 (≤1 coil width of adipose tissue [30 points], generator positioned on the midline [x1] and <1 generator width of fat between generator and thorax [x1]). The maximum score is 900.

Final PRAETORIAN score:

< 90	Low risk of conversion failure
90 < 150	Intermediate risk of conversion failure
≥ 150	High risk of conversion failure

The authors retrospectively validated the PRAETORIAN score: The positive predictive value (the percentage of patients with a high PRAETORIAN score who fail conversion testing) was 51.0%. The negative predictive value (the percentage of patients with a low PRAETORIAN score who have a successful conversion test) was 99.8%.

This means that the PRAETORIAN score is effective in identifying

those patients whose device positioning means they are at higher risk of unsuccessful defibrillation. The sensitivity and specificity for the PRAETORIAN score are 95% and 95%, respectively.

The PRAETORIAN score gives feedback on device position to implanters and identifies patients with high defibrillation thresholds[34,35].

The UNTOUCHED Study

The UNTOUCHED (Understanding Outcomes With the S-ICD in Primary Prevention Patients with Low Ejection Fraction) study was designed to assess the inappropriate shock rate (IAS) in a more typical ICD patient population (EF ≤ 35% and no indication pacing) implanted with the S-ICD using standardized programming and advanced discrimination algorithms[36]. The main objective of the UNTOUCHED study was to better understand the inappropriate shock rate with S-ICD in the more traditional (low EF) and optimally programmed cohort of patients compared to TV-ICD in the same population analyzed in the MADIT RIT.

Primary effectiveness endpoint was freedom from inappropriate shocks at 18 months compared to a performance goal of 91.6%. The primary safety endpoint of the study was freedom from system and procedure complications at 30 days compared to a performance goal of 93.8%.

A total of 1111 patients were included in the post-implant follow-up analysis with a mean age of 55.8 ± 12.4 years, 25.6% were female, 23.4%

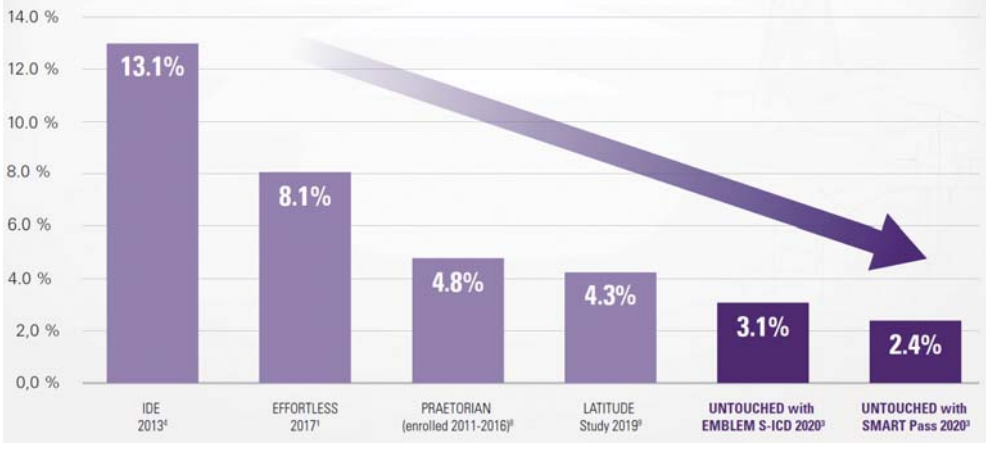

FIGURE 3.9

The image shows how improvements in technology, including implementation of software upgrades and algorithms, such as SMART Pass, as well as improvements in implant technique, have significantly reduced rates of IAS over time.

were black, 53.5% had ischemic heart disease, 87.7% had symptomatic heart failure, and mean left ventricular ejection fraction was 26.4 ± 5.8%.

This study shows high S-ICD efficacy and safety with contemporary devices and programming despite the "sickest" cohort studied to date. The inappropriate shock rate (3.1% at one year) is the lowest reported for the S-ICD and lower than many TV-ICD device studies using contemporary programming to reduce inappropriate shocks (Figure 3.9).

Conclusions

Clinical data of several thousand patient from comparison studies and experience gained on the field indicate that the effectiveness of S-ICD is very high and completely superimposable to that of T-ICD; The latest studies, showing that the subcutaneous defibrillator is not inferior to the transvenous, open up new scenarios that place the S-ICD as an appropriate and potentially desirable alternative for patients who are candidates for ICD and who do not require pacing.

The subcutaneous defibrillator should be considered as the first choice over the traditional defibrillator in those patients who do not require pacing or resynchronization therapy. The limited use of S-ICD deriving from the lack of anti-tachycardia and anti-bradycardia pacing (other than immediate post-shock pacing) is not relevant if patient selection preliminary requirements are satisfied.

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CHAPTER

4

Technical Characteristics, Algorithms and Programming

G. Bisignani, S. De Bonis, A. Bisignani

Technological and scientific development has led to the introduction of the subcutaneous implantable defibrillator (S-ICD, subcutaneous implantable-cardioverter-defibrillator).

In the course of time the system has undergone many important changes as shown in Figure 4.1, which compares the second generation of the device against the original produced by Cameron Health.

A new generation of the S-ICD device, EMBLEM, has been developed and marketed by Boston Scientific since March 2015. EMBLEM S-ICD has several positive features (see Figure 4.1), compared to the first S-ICD generation (SQ-RX 1010, Cameron Health):

- smaller case dimensions: with a substantial reduction in volume, thickness and weight;
- shape of the device: the edges of the new Pulse Generator (PG) are more rounded and softer to make positioning in the pocket easier and more comfortable;
- moreover, the head of the device is centred to facilitate the insertion of the subcutaneous electrode.

These new physical features of the second generation are important for the patient since they reduce discomfort and especially mechanical stress/skin erosion, with less complications, such as haematoma and infections of the pocket.

Another important trait of EMBLEM S-ICD is the longevity of the battery (from 5.1 to 7.3 years), a decisive factor in reducing the number of replacement interventions associated with significantly high costs and risk of infection.

FIGURE 4.1

The second generation of S-ICD (EMBLEM), compared to the first generation (SQ-RX 1010).

The new generation of devices are compatible with remote monitoring (LATITUDE).

Despite the remarkable progress achieved in almost 15 years, future improvements in research and design are still needed to address various aspects. For example, a paediatric model of S-ICD for use in young children (e.g., <8 years, <30 kg) could be an alternative option in the future. At least theoretically, subcutaneous defibrillation would require lower amounts of energy for these subjects due to their small cardiac mass and transthoracic impedance.

There is also a need for continuous improvements in detection algorithms in order to reduce inappropriate problems. The possibility of simultaneously analysing three, rather than one, available detection vectors to define the state of the rhythm could be an advantageous feature to consider and develop in the future. Finally, the integration of the S-ICD system with a wireless stimulation system could play an important role in defibrillation technology, and allow wider access to less invasive therapy with S-ICD to a larger cohort of ICD population.

The technical evolution (Figure 4.2) has, however, affected not only the dimensions but also other features that improve its performance.

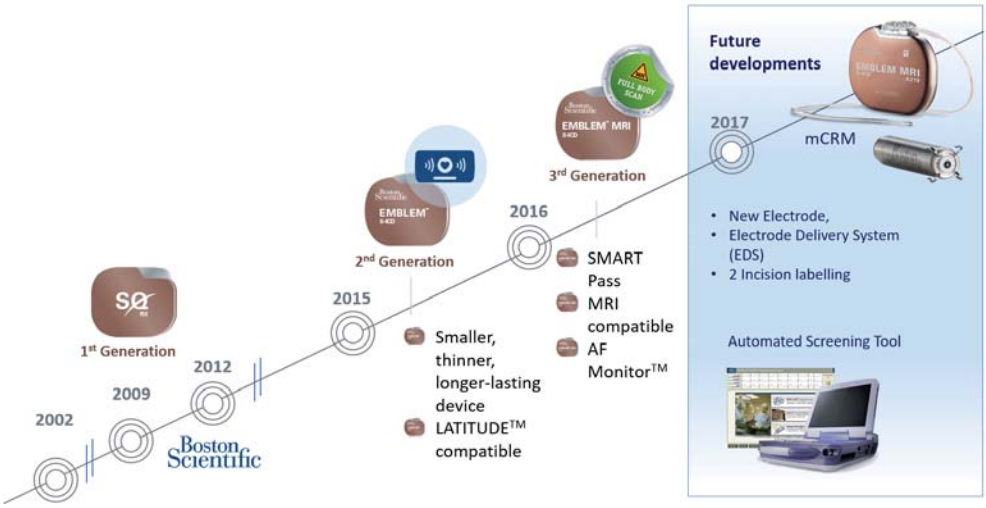

FIGURE 4.2
Evolution of therapy with S-ICD.

The 3rd generation EMBLEM MRI S-ICD devices have been tested and approved for use in the MRI* environment (**Image Ready**™) and include a dedicated MRI mode with a timer that automatically restores the programmed settings. This device allows total body scans, compatible with MRI for 1.5 T systems. Moreover, the **AF Monitor**™ function has been added, an instrument designed to facilitate detection of new onset or progressing silent AF by analysing the RR variable. Instead, the **IN-SIGHT**™ algorithm allows to obtain better discrimination between AF and SVT, while the **SMART Pass** filter reduces cardiac oversensing (experimental tests have shown a reduction of more than 40% in inappropriate therapies).

This modern device recognises and treats ventricular arrhythmia by shock using a single electro-catheter implanted subcutaneously. It does not require access to the cardiac chambers and blood vessels to insert the intracavitary electrodes (Figure 4.3).

The Boston Scientific S-ICD system consists of:

- Pulse generator
- Subcutaneous electrode
- Electrode insertion tool
- Programmer

The **pulse generator**, already described in the first part of this chapter, is a battery-powered device controlled by a computer and inserted

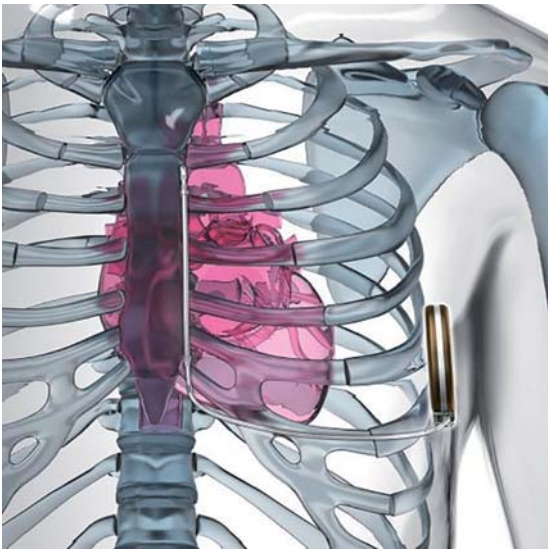

FIGURE 4.3
S-ICD system with subcutaneous approach. No lead inside the heart.

in a metal case. It is generally implanted on the left wall of the chest, and allows to program settings and parameters through wireless communications with an external programmer.

Table 4.1 reports the mechanical specifications.

While the specifications of the materials used are the following:

- case: titanium hermetical seal, titanium nitride coating;
- head: polymer suitable for the implant;
- battery pack: lithium manganese dioxide cell; Boston Scientific; 400,530.

The **subcutaneous electrode** consists of a partially coated metal wire surgically implanted just under the skin, parallel to the sternum. The integrated suture sleeve allows easy and fast fixation in the incision site.

TABLE 4.1
Mechanical Specifications of the Pulse Generator

Model	Size L×H×P (mm)	Mass (g)	Volume (cm^3)	Type of connector
A209, A219	83.1×69.1×12.7	130	59.5	Connector SQ-1 S-ICD (non standard)

FIGURE 4.4
Third generation of S-ICD.

The lead has two sensing points placed along the parasternal line, and a shock coil. The resulting sensing vector is selected among three different vectors that include the generator. The cardiac rhythm is analysed by acquiring a high resolution signal, similar to the surface ECG, selecting the sensing vector among the three available with the best ratio between R wave and T wave to avoid oversensing of the T wave.

It includes a coil for high voltage shock electrode; this electrode consists of several portions of metal wire shaped into an 8 cm long defibrillation coil. Sensing electrodes are also present.

The parasternal electrode of the subcutaneous system is without light, not needing a guide for intracavitary positioning, and has a higher voltage capacity than conventional intracavity electrodes. This feature and its subcutaneous position causes less torsional stress and guarantees a long-lasting product, as indicated by the absence of any type of electrode rupture in the records published so far.

Table 4.2 provides the electrode specifications.

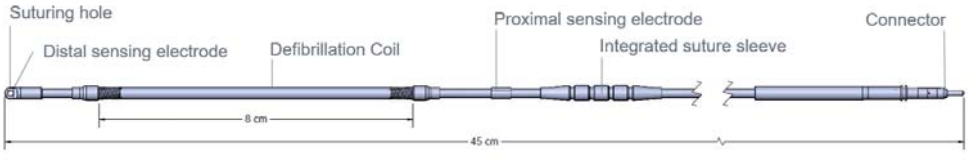

FIGURE 4.5
Subcutaneous electrode.

TABLE 4.2

Electrode Specifications

Component	Specifications
Connector	Connector SQ-1 S-ICD (non standard)
Length	45 cm
Size of distal tip	12 FR
Size of coil	9 FR
Size of electrode stem	7 FR
Area of the surface of the distal electrode	36 mm^2
Area of the proximal electrode surface	46 mm^2
Positioning of sensing	Electrode distal to the tip Proximal electrode 120 mm from the tip
Defibrillation surface area	750 mm^2
Defibrillation position	20 mm from the tip
Insulation material	Polyurethane
Electrode material, sensing leads, connector pins	MP35N

The **Electrode Delivery System** (EDS) is used for implanting the S-ICD subcutaneous electrode. The EDS consists of a lateral (long) and superior (short) tunnelling tool. Each tunnelling tool is pre-loaded with an 11 French sheath which is secured with a locking collar. The EDS is optimised to facilitate the 2-incision technique, which eliminates the superior

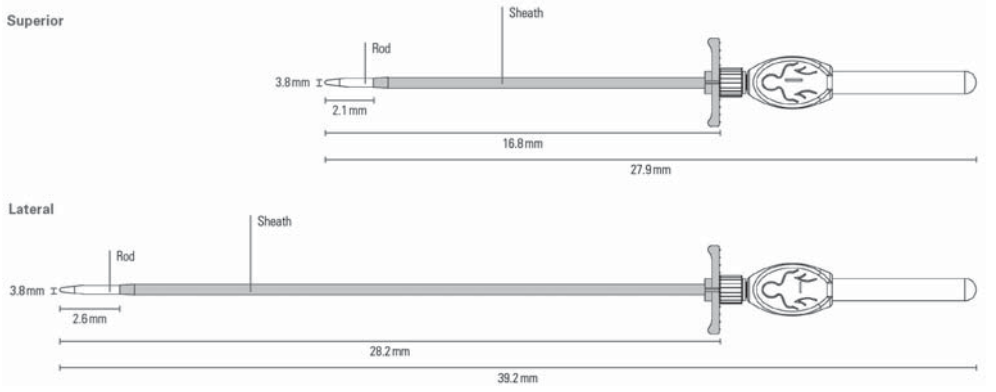

FIGURE 4.6

EMBLEM S-ICD Electrode Delivery System

FIGURE 4.7
S-ICD programmer.

sternal incision during implantation of the S-ICD. The longer tunnelling tool can also be used to perform the 3-incision technique. The EDS provides physicians with the appropriate tools to efficiently and consistently implant the S-ICD electrode (Figure 4.6).

Lastly, the **programmer** is a non-sterile and non-im- plantable computer tablet controlled by a graphical user interface (GUI) displayed on a touch screen. An AC power line or an internal lithium ion battery pack powers the programmer. The programmer uses a connected RF telemetry head to communicate in wireless mode with the S-ICD pulse generator in order to adjust program settings and collect patient data (Figure 4.7).

Algorithms and Programming

Introduction

S-ICD programming is a very important process to ensure treatment adequacy and to minimise the risks. It needs to be periodically re-evaluated particularly in the first post-implantation period, when patients resume their daily routine activities, and when therapy is delivered.

This complex management is not associated with a high number of programmable parameters and their possible interference. The S-ICD was conceived and developed to ensure easy control and verification of the parameters, and is characterised by a high degree of automaticity; there are less than 10 parameters to choose from, compared to the approximately 100 of the T-ICD. Therefore, difficulties in managing the S-ICD system are associated both with the system being relatively new and with

the expectations that it will be able to solve well-known and non-reducible T-ICD problems.

The S-ICD alone can cause a high risk of inappropriate shocks unless very strict behaviours are not adopted and repeated over time to prevent it from happening. This includes verifying the programming of the main parameters. The most important parameters to be verified and/ or programmed in the individual patient are the sensing vector and the various aspects of electrical therapy, areas of intervention, intervention frequencies and post-shock pace. There is a margin of programmability also for the polarity of a subsequent shock or late shock, even if the device readjusts it automatically.

Sensing

The sensing vector is automatically chosen from three possible options by the 'Vector Select' algorithm. The algorithm balances the qualities of sense, in particular with reference to the width or amplitude of the QRS and the relationship between the QRS and T wave.

The three possible configurations are: the primary one (*ring to can*), secondary (*tip to can*) and alternate (*tip to ring*). The primary configuration is usually the best one as it is located along the main electrical axis of the left ventricle.

However, the automatic selection can be changed programmatically. The choice of device made automatically at the time of implantation should be verified before the patient is discharged, in different postures and during physical activity, and must certainly be re-evaluated when a shock is applied. If the shock is inappropriate, the mechanism must be examined; the process could be difficult outside the dynamic situation during which the shock occurred[1,2]. Hence, evaluation during physical exercise is recommended, along with an attempt to reproduce the situation in which the shock occurred, e.g., rapid postural changes or in particular physical dispositions. The evaluation of stress sensing is also recommended in patients who are most vulnerable to oversensing of the T wave and, therefore, to inappropriate shocks, such as young subjects performing intense physical activity, those with genetic channelopathies, with hypertrophic cardiomyopathy or complex congenital heart disease[3,4]. It should be noted that, if patients have conductive disorders related to increased heart rates within the physiological range, or important alterations in repolarisation due to stress/tachycardia, sensing must be verified during the reproduction of such alterations, and not only in their absence.

Likewise, it is appropriate to subject the patient to a complete revaluation of the sensing process when there are variations in his 'biologi-

cal' state: introduction of new drugs capable of modifying surface ECG complexes, relevant morbid states, interventions in particular on thoracic organs or on the chest walls. It has been elegantly demonstrated that inappropriate shocks can be adequately limited through optimisation of the sensing vector and acquisition of a template of the ECG complexes during physical exercise as a basis for the automatic discriminations performed by the 'Insight' algorithm[5].

A new 'high-pass' filter called 'Smart Pass' was introduced quite recently, specifically designed to reduce oversensing, and active in reducing oversensing of both T-waves and QRS-T anomalies. Its use has been studied on models by processing data previously acquired without the 'Smart Pass' function. The results are still presented at symposiums today but have not been published as yet. They infer a pronounced reduction in oversensing, estimated between -71% and -82% in the various simulated comparisons[6].

When and How to Change the Sensing Vector

One of the non-invasive options to manage situations of incorrect detection by the system, for example in cases of detection of a double count of the T wave or, in general, of inappropriate sensing, is to modify the sensing vector through a variation in software programming.

To manually change the selected sensing vector of the S-ICD system, from the device's initial interrogation screen, press the **arrow** (**blue**) in the top right corner, proceed to the following screen and select **Manual setting** and then select **Utilities**.

At this point a screen will appear on the part of the device where the evaluation of the impedance value of the lead is shown, and a message will confirm that the measured impedance value is within the allowed operating range. Once this is done, continue by selecting the **Continue** button to open the selection screen of the sensing vector.

At this point, all you have to do is choose the vector you want, and the device will perform an evaluation/validation of the vector in question. You will be able to understand and evaluate the quality of the signal soon after validation by the device by looking at the lower part of the screen that displays the cardiac signal heard by the S-ICD system.

Shock Interventions

S-ICD interventions can be programmed according to two treatment areas for heart rates between 170 and 250 beats per minute: in the first area, tachycardia with lower frequencies are analysed by dedicated algorithms and can be treated in a 'conditioned' manner, i.e., only if other criteria,

in addition to the frequency, are satisfied, in order to better discriminate supraventricular tachyarrhythmia and avoid inappropriate shocks; on the other hand, in the higher frequency area, the treatment mode can only be 'non-conditional' and the heart rate is the only intervention criterion.

Data available undoubtedly support programming in dual zones[7,8]. The conditional zone can be programmed with lower and upper cut-off frequencies, in relation to various strictly individual factors: young age, routinely high frequencies and previous supraventricular tachyarrhythmia all suggest higher conditional zone frequencies (type 200–220). Conversely, reduced circadian frequencies, poor tolerance for non-fast ventricular tachyarrhythmia, may suggest lower limit values of the conditional zone. The 'automatic discriminators' introduced for years act in the conditional zone and prove to be very effective in distinguishing ventricular and supraventricular tachyarrhythmia[9]. The Insight algorithm, which is automatically activated when programming the conditional zone, analyses the rhythm when the rate is within the programmed rate window: the algorithm compares QRS morphology against the templates stored in the memory, and does not deliver therapy for the rhythms that show a good match with the stored QRS morphologies. In the second case, if there is a poor match, the algorithm compares each beat with the previous one to detect uniformity. The intervention is activated if this is missing, that is, if there is polymorphism along with non-concordance with the 'normal' memorised QRS template: the therapy is dispensed once the capacitor has been charged and a new rhythm detection is completed.

Instead, if monomorphism is detected, combined with non-concordance of the QRS, a further analysis of the duration of QRS complexes during tachyarrhythmia is undertaken, compared with the standard stored QRS template.

If the difference is greater than 20ms, the therapy is delivered. The episode documented in the conditional zone is considered finished when there are 24 consecutive beats at a frequency lower than the detection limit.

The shock is delivered with two possible configurations (coil-generator and generator-coil), thus foreseeing the inversion of polarity if the first shock is ineffective. The shock delivered by S-ICD is different from that of T-ICD, as its vector is horizontal and placed between the generator, and the parasternal electrode, facing the apex of the left ventricle. Clinical studies on defibrillation energy have shown that the average defibrillation threshold is about 37 Joules (J), which infers that the maximum capacity of 80 J deliverable by S-ICD allows for a wide margin of safety. A defibrillation test for the effectiveness of 65 J is recommended for each implant.

Since inappropriate shocks represent an independent negative prognostic factor, it is advisable to use high levels of recognition, close to 200 bpm, even for the conditional zone, unless there are clinical findings that account for minor intervention frequencies.

The duration of the recognition and the repeated recognition (detection and re-detection) is fixed in all zones as 18 fast beats out of 24, and it cannot be further modified, except to indirectly obtain a longer time with the 'Smart Charge' function. This option may be useful in patients with a history of well tolerated VT.

The shock zone is programmable for the detection frequency. The shock energy, outside the implant defibrillation test, is fixed at 80 J, with automatic polarity (standard: coil-case-coil to can; inverted: case- coil-can to coil), partly modifiable but subjected to an automatic revision by the device, which automatically applies the polarity of effective shock in the last intervention. The immediate polarity change after an ineffective shock is also automatic.

Post-shock pacing has a standard duration of 30 seconds, and programmability depends on whether to activate it or not.

Other Characteristics

Other functions of the device's latest version, some of which have been upgraded, while others are completely new, include the ability to record 40 episodes of arrhythmic events, 7 episodes of atrial fibrillation; memorisation of electrode impedance trends, battery status and alerts, acoustic warning signals for the time remaining to replace the battery, for variations outside the tolerance range of the electrode, for the extension of the charging time and for alterations in the reliability of the device. The MRI-conditional and remote monitoring functions have also been added to the latest version of the device.

In summary, the S-ICD has essentially four main algorithms to which the remote control (LATITUDE™ NXT) has been added.

1. The INSIGHT™ Algorithm, to Classify and Recognise the Different Cardiac Rhythms

The INSIGHT™ algorithm has three operating phases (Figure 4.8). In the **detection phase** it filters the subcutaneous signal (S-ECG) and generates, using a series of profiles, useful data for subsequent analysis. In the **certification phase** the algorithm analyses the detected signals and classifies them as cardiac events or as noise murmurs. Four functions are used to identify oversensing and to ensure accurate heart rate: static template

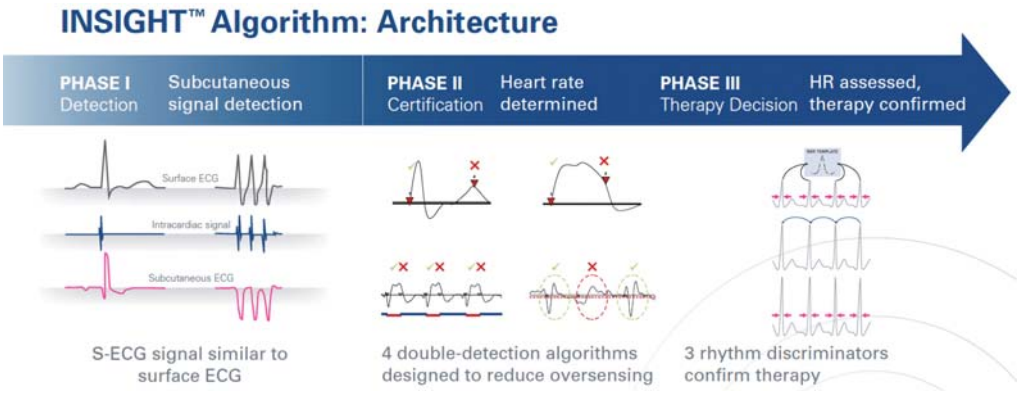

FIGURE 4.8
INSIGHT™ algorithm.

analysis, wide complex analysis, interval analysis and alternate morphology analysis.

Finally, in the third phase of therapy, namely **decision-making**, the INSIGHT™ algorithm distinguishes between treatable events and other events characterised by a high rate, such as atrial fibrillation, sinus tachycardia and other forms of supraventricular tachycardia, in order to avoid the administration of inappropriate shocks.

It does this by using three simultaneous rhythm analyses: the analysis of static morphology, which identifies non-shockable rhythms using the normal sinus rhythm (NSR) model; dynamic morphology analysis, which identifies the shockable polymorphic rhythms by comparing each complex with the previous ones; QRS width analysis, which compares the width of the QRS with that of the QRS of the normal sinus rhythm.

In the therapy **decision-making phase**, the algorithm also uses useful functions to confirm that therapy delivery is actually necessary. These include SMART Charge, Charge Confirmation and Shock Confirmation. The SMART Charge function, in particular, improves the system's ability to prevent charging in the event of suspicion of unsupported events, and to automatically extend the initial detection time to allow spontaneous interruption.

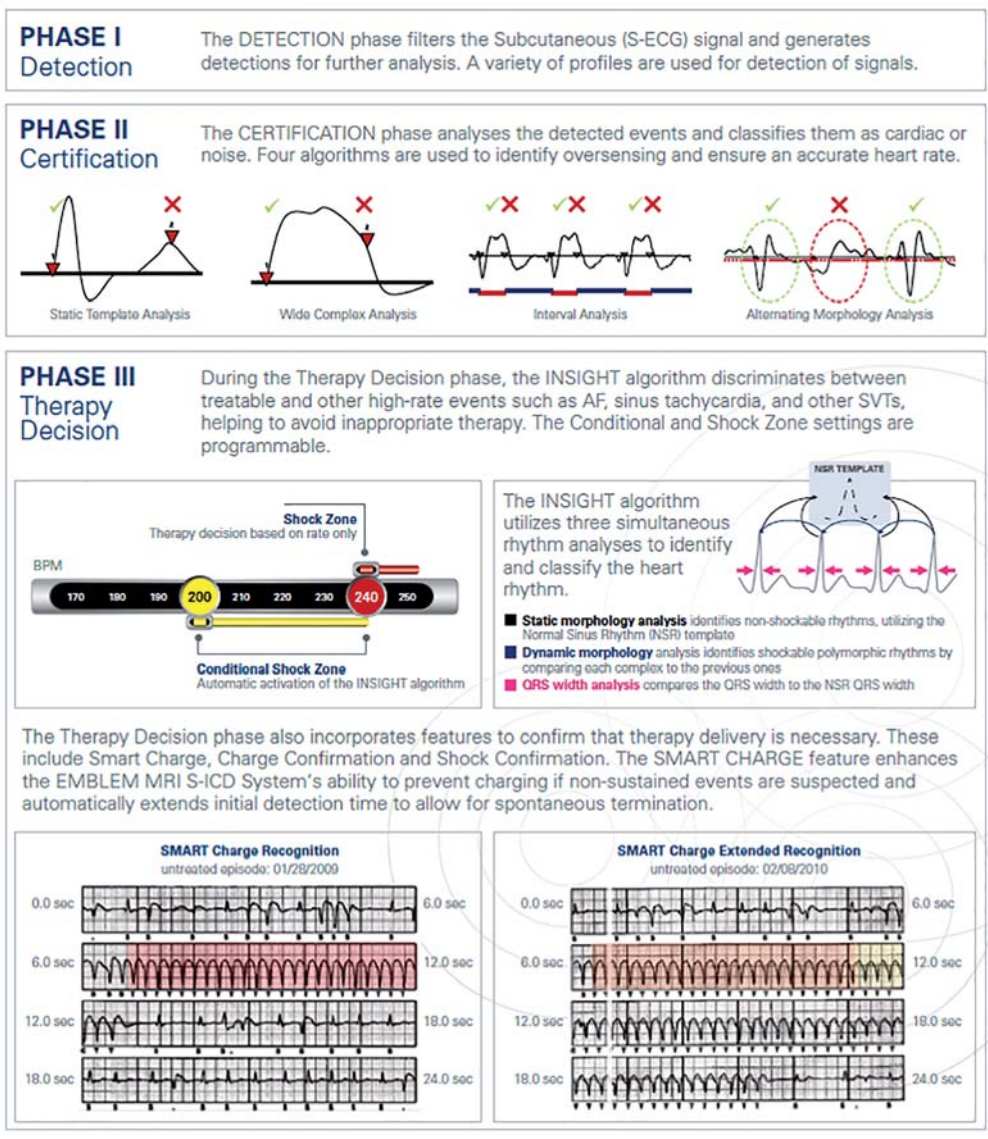

FIGURE 4.9

An outline of INSIGHT™ algorithm functions.

2. SMART Pass, to Reduce Inappropriate Shocks

The new SMART Pass algorithm reinforces the existing INSIGHT™ algorithm.

SMART Pass reduces the amplitude of signals with lower frequencies, such as T waves, by applying an **additional high pass filter** (which allows higher frequencies to pass). The detection of signals with higher frequencies remains unchanged.

SMART Pass technology has reduced the overshoot of the T wave by 82% compared to the 1st generation S-ICD system, and by 71% compared to the EMBLEM S-ICD system.

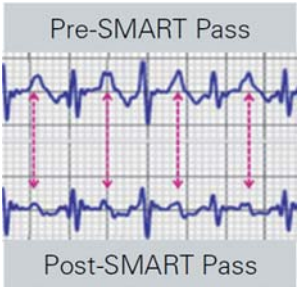

FIGURE 4.10
SMART Pass: T wave discrimination.

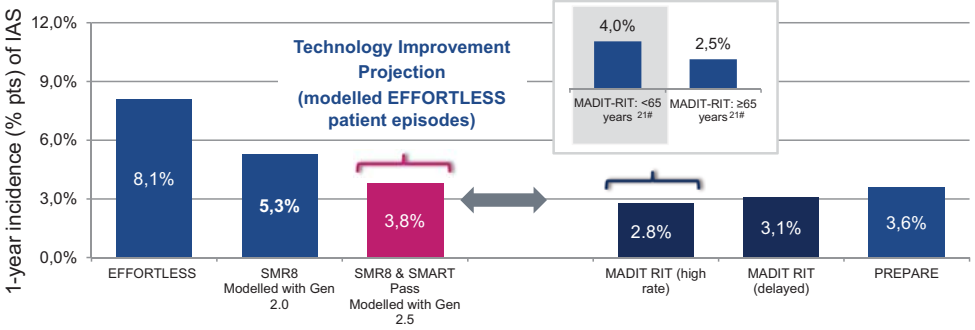

FIGURE 4.11
Reported percentages of inappropriate shocks and future of the impact of new technology.

3. ImageReady™, for MRI Compatibility

The EMBLEM™ MRI S-ICD system offers ImageReady™ technology for compatibility with magnetic resonance scans performed using 1.5T systems. This allows the patient to undergo total body MRI examinations without any time limit for scanning or other restrictions. ImageReady™ can be used through a simple and intuitive programming interface and provides a dedicated MRI report for clinical documentation. Furthermore, this mode is also compatible with previous technologies of EMBLEM™ S-ICD systems and viewable on LATITUDE™.

4. AF MONITOR™

AF MONITOR™ is an algorithm designed to facilitate detection of silent, new onset or progression AF.

Ventricular dispersion and heart rate index (HRDI) functions are used to identify and classify the rhythm. In order for the rhythm to be classified as AF, the evaluation of both these parameters must be fulfilled in a window of 192 beats (Figure 4.12).

5. LATITUDE™ NXT for Remote Patient Management

LATITUDE™ NXT technology, compatible with the EMBLEM™ MRI S-ICD system, allows to view the trends of the AF detected in the last 100 days (AF minutes/day) and to program and perform efficient remote follow-up.

There will be a later Chapter specifically dedicated to this function.

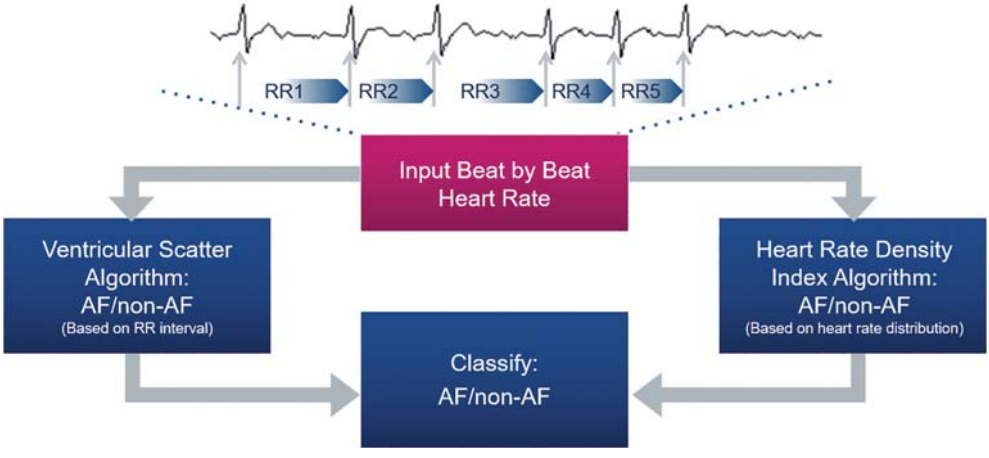

FIGURE 4.12

Diagram of the AF detection algorithm.

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CHAPTER 5

Recommendations and Guidelines for the S-ICD

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Recommendations and Guidelines for the use of the S-ICD are constantly changing due to the new knowledge gained from the increasing number of implants performed each year all over the world, and the considerable amount of follow-up data that exists now after almost 10 years since it was first released on the market. Based on data from the registers and cumulative analyses, and also on pending results from ongoing multicentre randomised trials[1], the quantitative comparison with T-ICD has to date shown an equal efficacy and global functional safety profile[2,3], besides the many advantages associated with the fact of not having electrodes in the venous circulation and in the heart. It goes to say that when choosing patients for an S-ICD, an accurate examination of the advantages and disadvantages demonstrated by the device is essential for each specific clinical case and for arrhythmic risk, and not only in comparison to the similarly definable profile of the use of T-ICD. It was to be expected that the new guidelines for clinical practice would lean towards a tendency to a variation in the role of the S-ICD on the basis of new technology and the increasingly extensive and prolonged studies on S-ICD. Recommendations are changing from that of a 'second choice' if the T-ICD implant is not technically feasible or exposes high risks, to that of an alternative to T-ICD in which the selection of the patient primarily and 'positively' depends on patient characteristics[4,5].

Advantages and Disadvantages of S-ICD

The main advantages of S-ICD have already been categorised with the preliminary experience of implantations performed between 2008 and 2012, before the completion of official scientific guidelines, and can be summarised as follows:

- absence of vascular access;
- absence of intracardiac intravascular electrode;
- relatively simple extraction/explant, even years after the implantation;
- minimum or zero use of ionising radiation during the implant procedure, potentially unnecessary altogether;
- no need of a lead coat for doctors or technicians;
- lower risk of fracture of the subcutaneous electrode;
- no risk of post-implantation displacement;
- in case of infection of the pocket, 'local' management is possible with no risk of endocarditis;
- better capacity to distinguish supraventricular tachycardia when adopting the double sensing zone.

With these specific characteristics of the implantation along with S-ICD performance over time, arrhythmogenic cardiopathies of the young and congenital heart defects are 'natural' candidates for S-ICD, since the first studies[6,7], when one or both of these two essential conditions that represent a problem and/or high risk for T-ICD is present:

1. technical difficulty or greater risk of complications of vascular access and of positioning in the right ventricle due to structural problems of the venous system (small, abnormal, with shunts in the large vessels) or due to the complexity of the passage within the cardiac cavities (innate or corrected malformations);
2. young or very young age, which involves a significantly high risk of long-term complications with T-ICD, due to the longer period 'at risk': in fact, the long life expectancy due to age determines an increased possibility of transvenous electrode problems with the need for replanting or extraction, in the medium-long term, when compared with the average expected rate of battery replacement and electrode wear/malfunction.

This preferential option of use in young patients and/or with congenital heart disease was then confirmed by subsequent studies, including EFFORTLESS S-ICD, and by the cumulative analysis of the IDE and EFFORTLESS S-ICD studies in which over a third of 472 patients with a mean age of 49 and 14.9% out of 882 patients with an average age of 50,

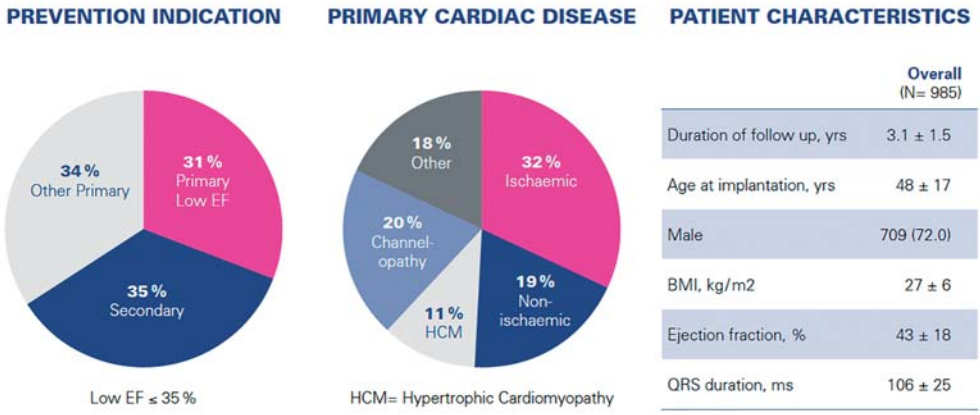


FIGURE 5.1

The EFFORTLESS study: the characteristics of enrolled patients.

respectively, presented combinations of ionic/inherited diseases, idiopathic ventricular fibrillation and congenital heart disease[8,9] (Figure 5.1). These pathologies are represented in 14% of 5,380 patients with a mean age range of 33–56 years analysed in the recent cumulative evaluation of Chue[3].

The other type of clinical condition that has prematurely outlined the evidence of an advantage of S-ICD is also related to the absence of endovascular electrodes, namely the high risk of infection. Indeed, the lack of vascular invasiveness of S-ICD determines minimal or zero centripetal diffusion of local infections, and S-ICD has been proposed as an elective option both for patients already subjected to T-ICD removal for infection, and for those who present major predisposing factors to infection (diabetes, states or therapy associated with immunodepression, chronic renal failure). The clinical evidence has fully satisfied expectations, whereas leading multicentre registries and the most recent cumulative analyses of more than 5,000 patients reported infection rates of 4-2.7%, among which, however, only 1.7–1.8% required reoperation or explantation[2,3,8–10]. The finding that, in patients previously subjected to transvenous ICD removal due to system infection and, therefore, with a more consistent infection risk profile and general morbidity, was very significant. There was no greater incidence of new S-ICD infections compared to other patients with no history of infections, even in the presence of severe kinetic impairment of the left ventricle and of a younger age. The same results in terms of safety from infections were detected in adults and in paediatric

patients[9,10]. The finding of the extension of the advantages of S-ICD also to primary prevention of infections in higher risk categories, such as immunocompromised patients or patients with advanced renal insufficiency or diabetes, is more recent[11].

These pillars of evidence in favour of S-ICD relative to the risk of infection are, therefore, summarised below:

- total absence of endocarditis correlated to the device and to the implant;
- efficacy of conservative treatment of S-ICD infection, without relapses or systemic diffusion in case of failure in local conservative treatment;
- complete eradication of the infection by explantation, in the minority of cases, when required.

Having a clear picture of the structural and functional characteristics of S-ICD makes it easy to define the disadvantages of its use:

- lack of ability to deliver some type of sustained bradycardia pacing, i.e., outside 30 seconds of pacing in emergency;
- correlated to the previous one, lack of ability of an antitachycardiac function for ventricular tachycardia;
- lack of resynchronisation capacity.

Other disadvantages are much less limiting, and will soon be corrected by research and technological improvements:

- possible shorter battery life, even if the data acquired so far seems to show a life of at least 7 years easily with average use;
- the risk of T wave oversensing, which is reduced over the years with the refinement of the algorithms;
- the larger size of the generator;
- the shape of the chest that allows for the device to be implanted, even if the increasing reduction of the dimension of the device will soon eliminate this limitation.

Although it is an 'operating mode', the need for pre-implantation screening, possibly supplemented by a stress test, can also be included among the limiting characteristics.

Finally, it should be noted that some previous limitations have been recently overcome with new technology. In fact, the possibility of carrying out MRI (Magnetic Resonance Imaging) examinations under certain conditions (MRI conditional) and the option of remote monitoring of the device, which will be discussed in other chapters, are now conceivable.

Scientific Guidelines

The definition of evidence-based recommendations for the clinical use of S-ICD dates back to 2015, with the publication of indication classes within the guidelines (GL) of the European Society of Cardiology (ESC), which were also adopted in Italy[4]. These identified S-ICD as an 'alternative' in one case, and as a 'useful alternative' in another, compared to T-ICD, placing the indication in class IIa and in class IIb, respectively, with the same level of evidence C (Table 5.1).

The two cases were attributed accordingly: the more generic 'alternative' for the higher class, without further specifications, while the weaker reference was made to the clinical situations of complex/difficult vascular access, of young age and of the high post-explant infection risk of an infected T-ICD system. Hence, this approach led to three specific clinical conditions associated with a lower strength of the indication[4]. The doubts underlying this particular approach were also expressed in detail, and were linked to the absence of long-term randomised studies and to certain discrepancies between the results of the studies produced up to now (for example, concerning reporting of a high inappropriate shock rate in the paediatric patient)[7].

Two years later the American guidelines, under the sponsorship of the Heart Rhythm Society, took a decisive step towards a stricter class of indication, attributing class I with evidence B to the high risks of conditions for 'problematic' vascular abscess or infectious diseases[5]. As a result, the approach proposed previously by the European GLs, based on evidence that was less complete at the time (2014–2015), was substantially modified. The American GLs first refer to 'primary' infection risk caused

TABLE 5.1

ESC Guidelines 2015: S-ICD vs. T-ICD

Recommendations	Class	Level
Subcutaneous defibrillators should be considered an alternative to transvenous defibrillators in patients with an indication for an ICD when pacing therapy for bradycardia support, cardiac resynchronisation, or antitachycardia pacing is not needed.	IIa	C
Subcutaneous ICD may be considered a useful alternative to the transvenous ICD system when venous access is difficult, after the removal of a transvenous ICD for infections or in young patients with a long-term need for ICD therapy.	IIb	C

TABLE 5.2

AHA/ACC/HRS Guidelines 2017: indications and contraindications for S-ICD

Class	Level	Recommendations
I	B-NR	1. Implantation of a subcutaneous defibrillator is recommended: in patients who meet the criteria for ICD, that have inadequate vascular access or high risk of infection, and in those with stimulation for bradycardia, for VT interruption or for resynchronisation therapy that is not necessary or predictable[1-5]
IIa	B-NR	2. The implantation of a subcutaneous defibrillator is reasonable in patients who meet the criteria for ICD, if the stimulation for bradycardia, VT interruption or resynchronisation therapy is not necessary or forseeable[1-4]
III:Harm	B-NR	3. A subcutaneous defibrillator should not be implanted in patients who require stimulation for bradycardia or resynchronisation therapy or ATP to interrupt VTs

by important systemic pathologies, but without an infection, such as advanced renal failure and diabetes mellitus. The indication for class IIa in which the S-ICD is an alternative to the T-ICD remains unchanged (Table 5.2).

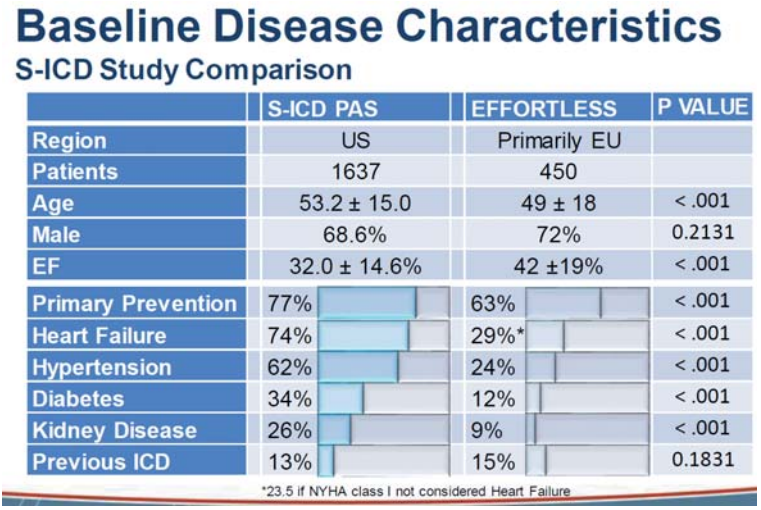


FIGURE 5.2

The S-ICD PAS study cohort represented a 'sicker' population with more comorbidities.

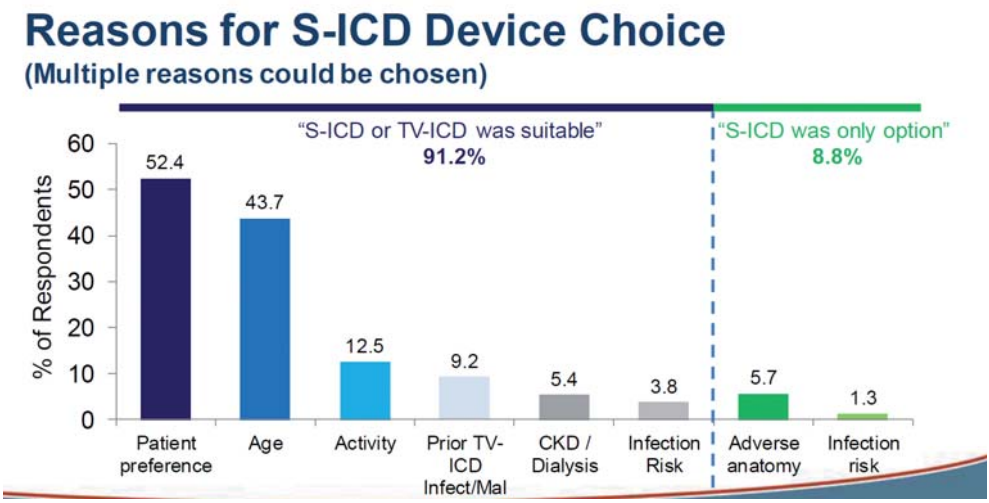


FIGURE 5.3

The image demonstrates the different reasons for choosing S-ICD. It shows that 52% of patients although eligible for T-ICD preferred S-ICD implantation, and 43% chose S-ICD due to their young age.

Both guidelines very clearly state that the indication applies only if there is no concurrent or foreseeable indication, in the subsequent period, for bradycardia pacing, antitachycardia pacing or cardiac resynchronisation therapy, for which it is still necessary to use T-ICD. The PAS study (Post-market Approval Study) is very interesting[11], conducted on 1,637 patients who underwent S-ICD implantation in a real world context and, therefore, in patients with comorbidities. It showed how S-ICD is stepping out of the niche, and that the indications have been accepted for a larger ICD population. S-ICD was the only reasonable option for 8.8% of patients. 52.4% were eligible for T-ICD, but the patients preferred S-ICD and 43.7% opted for S-ICD due to their young age. The absence of implant complications in S-ICD at 30 days was 99%. The authors conclude that even in real-world patients with comorbidities, implant success is high and complication rates are acceptable.

Instructions for Use

Taking into consideration all aspects, both favourable and unfavourable, and knowledge gathered so far by leading studies, the subjects for whom the implantation of S-ICD is conceivable must first present a favourable possibility of discrimination between the R wave and the T wave

at the preliminary screening.Moreover, their chest and integumental configuration must allow the device to be safely implanted without any problems. Once these prerequisites are satisfied, S-ICD seems feasible for the following patient groups:

- patients with venous system anomalies and/or with complex congenital heart defects that can either prevent or render a transvenous approach risky;
- young patients with hereditary arrhythmic syndromes, such as channelopathies or hypertrophic cardiomyopathy, in whom, during the patient's life time, there will be several future generator replacements associated with incremental risks of infection, erosion, dysmorphic outcomes of the pocket, and the possibility of one or more malfunctions of the transvenous electrode, leading to possible surgical procedures for of extraction;
- young patients with left ventricular dysfunction and defibrillator indications;
- subjects with a greater risk of infection, or immunocompromised subjects, or those who have suffered a cardiac device infection treated with extraction and explantation; of these, dialysis patients and patients with valvular prostheses, at high risk of local and systemic infections/endocarditis could be of particular interest;
- subjects with electrodes left inside the heart, that can interfere with the effectiveness of the intracavitary shock;
- in general, subjects in primary prevention, in which pure shock is reasonably sufficient for events of low probability.

A particular group of patients that have not yet been the subject of clinical studies, but that could benefit from the use of the SICD:

a. patients already wearing pacemakers who need to upgrade to an ICD due to the appearance of left ventricular dysfunction. There are no controlled studies in this regard, but only experiences in single Centres. When the conditions of the veins do not allow the introduction of another electrocatheter or as an alternative to extraction implantation of an S-ICD can be chosen leaving the pacemaker for stimulation. In such a patient, careful screening is essential both in stimulated rhythm and in spontaneous rhythm to avoid false recognition by the subcutaneous system (Figure 5.4);
b. patients with potentially reversible ventricular dysfunction but who need protection from an SCD.

There are reports of S-ICD implantation as a bridge to normalisation of left ventricular function. In patients exposed to potentially reversible

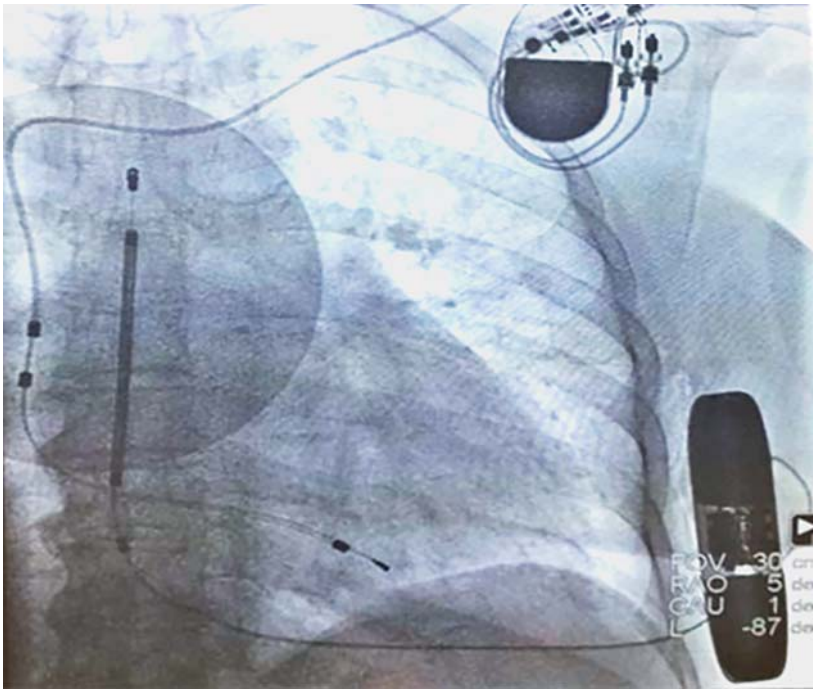


FIGURE 5.4

Patient with PM implanted for 10 years, who needed upgrading to an ICD for left ventricular dysfunction, had an S-ICD implanted.

pathogenic noxa (drugs, alcohol, etc.), but with the need to protect the arrhythmic risk[13].

Clinical case study

A 35-year-old young man, a habitual consumer of cocaine and alcoholic beverages, was brought to our notice due to dyspnea and a syncopal episode. The echocardiogram showed dilated myocardiopathy with EF <15%, negative coronary angiography and absence of scar in cardiac MRI. We hypothesised potentially reversible heart failure due to exposure to toxic damage, or myocarditis; therefore, an S-ICD was implanted.

After adequate therapeutic and psychological support, the patient stopped using cocaine and alcohol, and his EF became normal over time. After about 2 years, during sports activities the patient suffered a thoracic trauma with erosion of the pocket and exposure of the device, which subsequently became infected.

We re-evaluated the patient with echocardiography, stress test and 24 to 48-hour Holter monitoring ECG, observing normal ventricular function and full recovery from any use of alcohol or drugs.

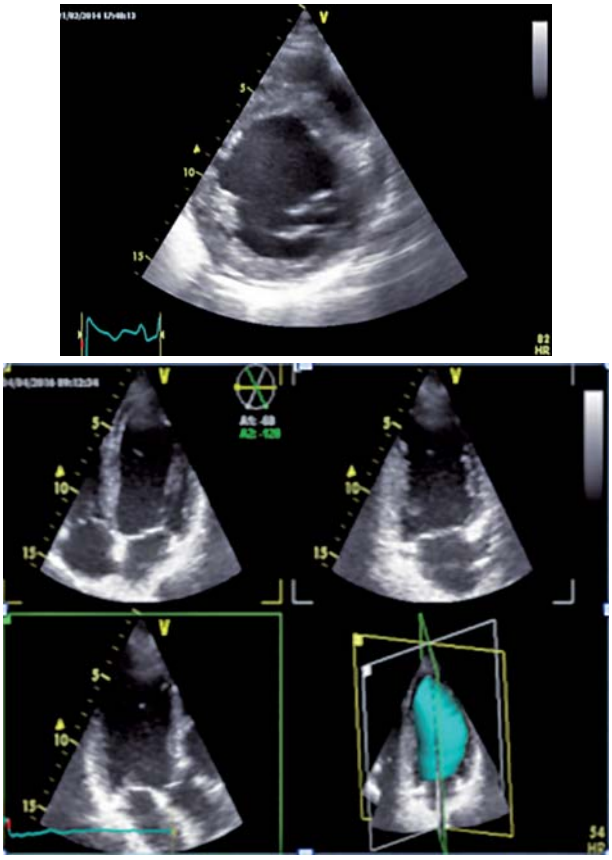


FIGURE 5.5

Echocardiographic examination before and after implantation of S-ICD.

Considering the normalisation of ventricular function and the absence of arrhythmic episodes, we decided, in agreement with the patient, to explant the device without re-implantation. The procedure was easily performed without complications. Two years after explantation the patient has recovered with normal ventricular function, and has no further ICD indications[13] (Figure 5.5–5.7).

Current ESC guidelines suggest that this category of patients could be potential candidates for a wearable cardioverter defibrillator (WCD)[14]. The WCD could be an appropriate 'therapeutic bridge' for primary prevention of SCD in patients with newly diagnosed cardiomyopathy that is potentially reversible during the early period after the initial diagnosis, but the question of how long the patient has to wait to be free of arrhythmic risk still remains unanswered.

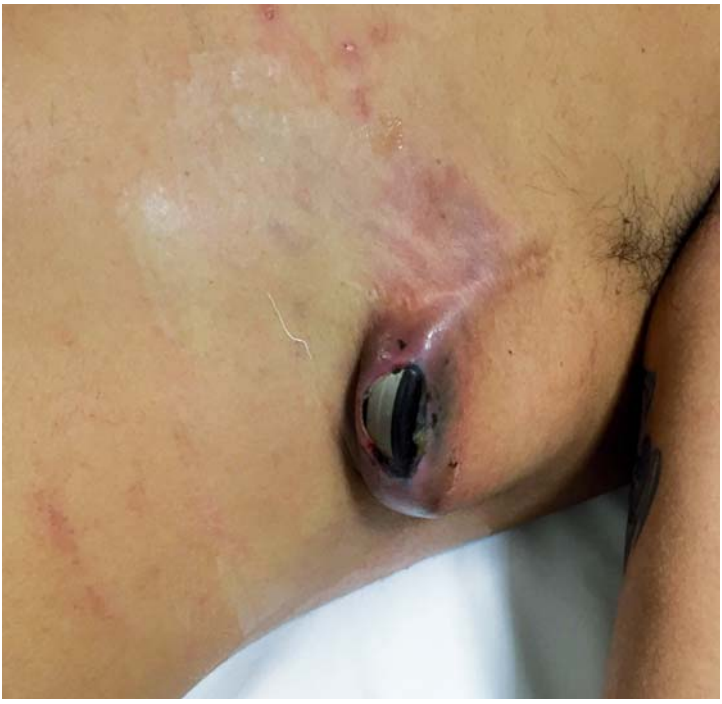


FIGURE 5.6
Erosion of the pocket with exposition of the device.

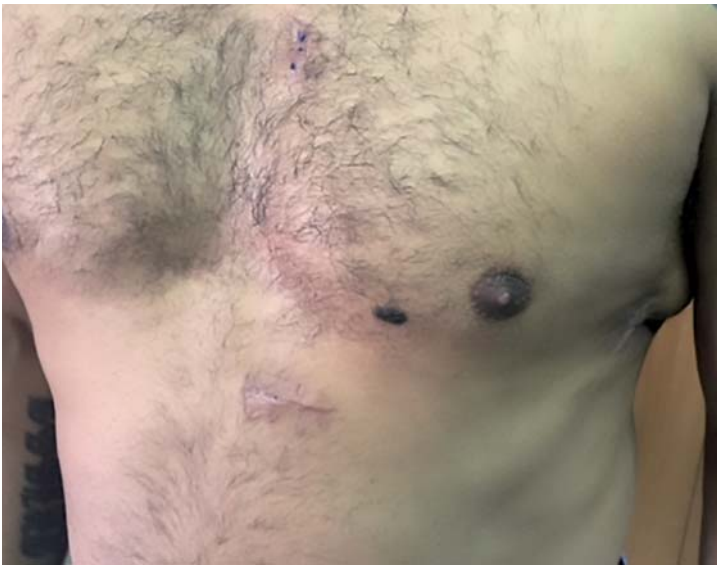


FIGURE 5.7
Post S-ICD explantation.

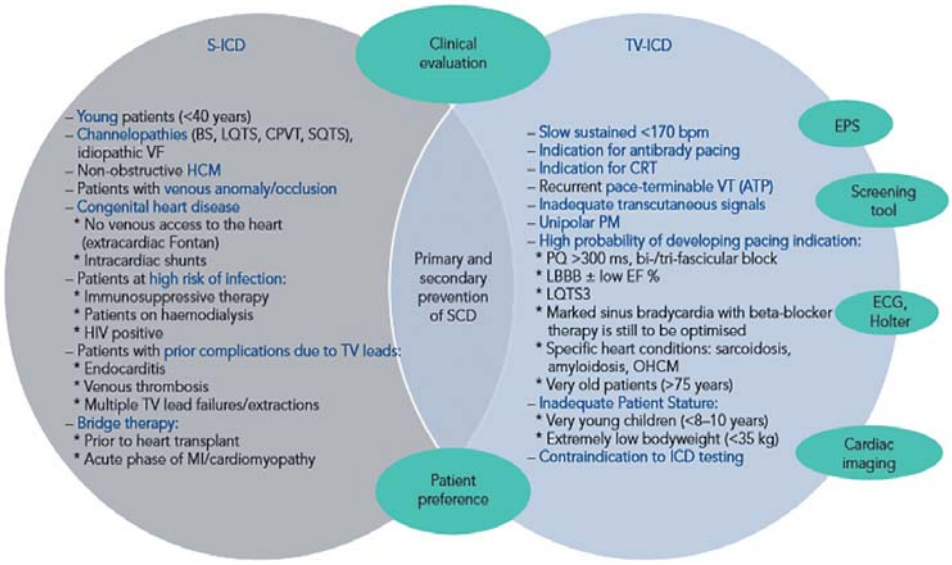
This is particularly important when we are unable to fully determine the cause of heart failure.

In particular, the first major obstacle to the use of WCD is the very high cost[14], in particular when the device remains in use for a long period of time. Furthermore, a study conducted by Opreanu et al.[16] reported that only 17% had experienced an improvement in EF; the rest of the patients who had used a WCD had to have an ICD implanted. This leads to an additional non-refundable cost of this therapy, besides poor compliance and the patient's discomfort[15].

In our case, we were unable to diagnose the actual cause of heart failure at the time of implantation. Patient compliance was uncertain and the time needed for ventricular function to improve was undefined.

We, therefore, chose a less invasive final solution. The less invasiveness of S-ICD ensures easy removal of the entire system, compared to an intravascular ICD, and could also be helpful for patients who need temporary-permanent protection from SCD. Exclusion criteria of candidates for S-ICD must be carefully assessed:

- the need for bradycardia pacing, which is the main impediment; subjects with only intraventricular or minor conduction disorders are difficult to evaluate;



TP = antitachycardia pacing; BS= Brugada syndrome; CPVT = cathecolaminergic polymorphic ventricular tachycardia (VT); ECG = electrocardiogram; EF = ejection fraction; PS = electrophysiology study; HCM = hypertrophic cardiomyopathy; LBBB = left bundle branch block; LQTS and SQTS = long and short QT syndromes, respectively; MI = myocardial infarction HCM = obstructive HCM.

FIGURE 5.8

Clinical characteristics and data in favour of subcutaneous ICD or transvenous ICD.

- the presence of VT that can primarily benefit by stimulation with antitachycardia pacing, a treatment that avoids shock;
- indication for cardiac resynchronisation therapy.

The following image shows a series of clinical and instrumental elements that can help to make the decision to implant the device or not (Figure 5.8).

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Chapter 6

Pre-Implantation Assessment

S. De Bonis, G. Bisignani, A. Bisignani

Pre-implantation assessment is an important step in the decision-making process for the use of the subcutaneous defibrillator. The clinical indications for the implantation of S-ICDs are now widely classified[1,2], but the track leading to the procedure requires the completion of a series of preliminary 'empirical' assessments. The positive outcome of these assessments constitute the opinion of suitability that either confirms the indication or blocks the operation. The following indications, stated in the guidelines[1,2], may be considered implicit: the absence of conditions of current or likely need for pacing therapy for antibradyarrhythmic purposes, for ATP treatment of ventricular tachycardia, and for cardiac resynchronisation therapy. Based on this premise, preliminary empirical assessments are measurements and non-invasive tests that explore the risk/benefit of S-ICD implantation considering three aspects: 1) anatomical compatibility; 2) sensing congruity; 3) coexistence of other necessary or non-removable electrical devices. The positive outcome of these evaluations can confirm the indication to use S-ICD for the prevention of sudden arrhythmic death and for the treatment of malignant ventricular tachycardia.

Evaluation of Anatomical Compatibility

After meeting the criteria indicated by the above guidelines, visual evaluation of the shape and size of the chest is the first step to be taken when deciding to implant the subcutaneous device.

S-ICD is a bit bulky, with a volume of 59.5 cc, and a weight of 130 g. The electrode (lead) is entirely subcutaneous with two separate sensing

points (electrodes) and separated by an 8 cm shock coil. It requires an inevitable minimum distance from the case. Usually the device/generator and the electrode must be placed in the left hemithorax, the case at armpit level, and the electrode along the edge of the sternum, except in cases of dextrocardia and congenital cardiopathy, such as Fallot. Where indicated, the electrode can be placed along the right edge of the sternum, but this depends on the 'screening' illustrated below. There is currently no smaller device available to meet the needs of patients who are smaller in size or younger in age: this one model must, therefore, be adapted to very different anatomical situations. An initial assessment of suitability should, therefore, aim at measuring the size of the chest. There are no reported problems for large thoraxes; the problem is the very small or very malformed thorax. The small thorax is generally encountered in children under a certain weight and/or age. The current consensus, based on the prac-

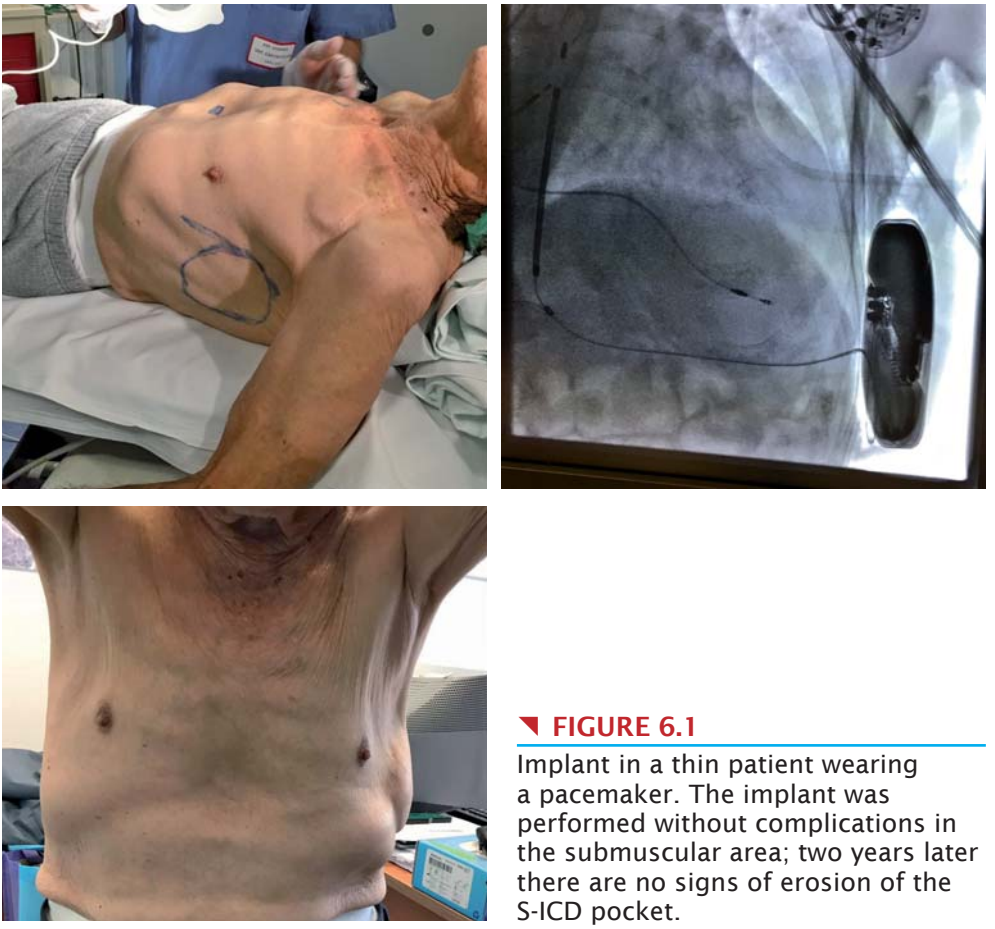


FIGURE 6.1
Implant in a thin patient wearing a pacemaker. The implant was performed without complications in the submuscular area; two years later there are no signs of erosion of the S-ICD pocket.

tical experience of the major centres, is to consider a weight of 25 kg and 8–9 years as cut-off parameters, evaluating feasibility in the range of 25-35 kg, depending on the anatomy of each individual[3,4]. It should also be noted that there are reports of implantations performed with parameters well below those indicated, and the devices functioned quite well, at the inevitable cost of subsequent re-implantation of the electrode due to body growth, and using abdominal placement. The second problem is more commonly related to the presence of a very pronounced pectus excavatum, which leads to difficulties in placing the S-ICD electrode and greater risks of its superficialisation and skin erosion[5,6]. Moreover, in extreme situations, their might also be the problem of dislocation of the heart-left ventricle into the mediastinum, which requires accurate screening to verify the sensing vectors and the suitable positions for the electrode and the case[6]. However, low weight patients should not be discouraged but, instead, very carefully evaluated in order to determine other implantation options, for example intermuscularly or submuscularly (Figure 6.1).

The Analysis of Possible Sensing

The distinction of rhythm disturbances carried out by S-ICD is based on an electrical body surface map, constructed from electrical signals recorded on the chest, such as an ECG plot: in the absence of intracardiac electrodes, there is no contribution of the endocavitary signal. Hence, unlike the T-ICD signal acquired with tightly spaced endocavitary electrodes, the tracks recorded by S-ICD have a lower amplitude and frequency and are more sensitive to postural variations. In S-ICD, the sensing vectors are formed between the two sensing points (electrodes) and the S-ICD case, which acts as a third electrode, determining three sensing vectors through which the P and T waves are discriminated and measured. The QRS complexes and QT intervals, which resemble complex analogues recorded with surface ECGs at the level of precordial derivations and R/T and R/P ratios are also measured. The S-ICD software and algorithms analyse the signal that is produced to distinguish the ventricular complexes from the atrial ones, from the T waves and from the ventricular far-fields. A screening system developed by the manufacturer, Boston Scientific, is a well constructed simulation scenario of S-ICD sensing modes, reproducing the limitations that could be encountered, based on numerical cut-off values (Figure 6.2) [7,8]. The test is carried out using modified surface derivations, which mimic the three sensing vectors of S-ICD, and a measuring instrument supplied by the manufacturer. The ECG plots are recorded after having been modified according to a specific pattern in the main postures, in other different

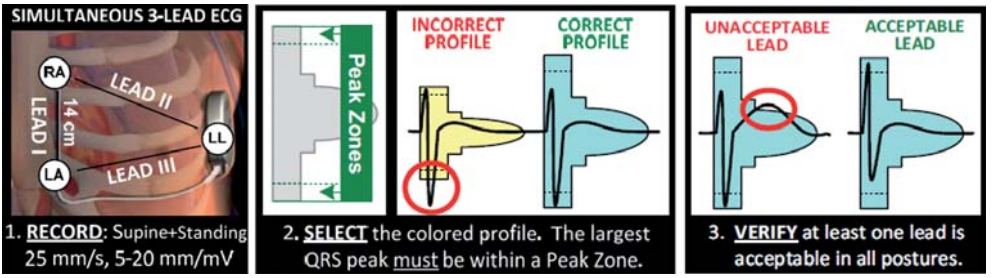


FIGURE 6.2

The screening TOOL, with two correct/incorrect examples.

positions and possibly also during physical exercise. The QRS complexes are then evaluated with the instrument (Figure 6.2). Eligibility is given when the standards are satisfied in at least one of the simulated carriers. It is also possible to evaluate the modified right derivations, since it is possible to place the S-ICD electrode along the right marginal-sternal line.

Moreover, S-ICD algorithms, although possessing a high ability to discriminate supraventricular tachyarrhythmia from ventricular ones, higher than those of intracavitary detection, encounter greater problems for the discrimination of QRS and above all of T waves, particularly if these are prominent, double or associated with a very wide QRS. Not all the P-QRS-T ECG complexes have characteristics suitable for effective identification as they are surface complexes and it is intuitive that there are innumerable causes for ECG morphology variation that can be reflected on the S-ICD recorded leads.

The first cause of inadequate discrimination is the simplest: variation of the position of the heart and between the heart and electrodes due to postural dissimilarities. This is true beginning with the simple changes between a lying position and orthostatism, and even more so during physical activity in which the diaphragm and rib cage excursions are wide and fast, and most of all in young subjects in whom occurrence and intensity of the effort is usually greater. This seems to be a crucial factor in T-wave oversensing, which has been shown to be mainly affected during exercise/exertion[9].

Screening remains crucial, and if the results of the screening are negative, then the patient should not be implanted due to the risk of inappropriate shocks. A negative test result was described in 7–10% of patients, and associated with the presence of congenital heart disease and hypertrophic cardiomyopathy[7,10,11]. In this pathology, in particular, a recent survey has shown a 38% incidence of ineligibility for manual screening[11],

and a correlation between unfavourable outcome and clinical characteristics of patients presenting a higher risk. Even when eligibility criteria are met, a suboptimal negative predictive ability is found, demonstrated by the incidence of inappropriate shocks that are not entirely insignificant even in those eligible for the test. To improve prediction, the use of a concurrent stress assessment was proposed, and seems to be more sensitive to situations of potential difficulty in detecting ECG signals related to high heart rates, to polarity variation of ECG complexes, to the presence of myopotentials, and to the variation of the anatomical correspondence detection of the sensing vectors[10]. The results have been reassuring, so the repetition of screening during exercise is recommended in patients belonging to groups at high risk of T wave oversensing, as well as in the presence of right branch bundle block, and extensive repolarisation anomalies. Stress assessment was also proposed in combination with less stringent selection criteria to improve eligibility for S-ICD[12].

The manufacturer, Boston Scientific, has made an automatic screening test performed by a specific algorithm available for some time now. The method, which was originally proposed in a study[9] that evaluated manual screening versus the direct use of S-ICD sense vectors correlating to the surface ECG, appears to increase eligibility rates, eliminating at the same time the manual difficulties sometimes encountered in the execution of the test[13].

Automatic Screening

EMBLEM S-ICD Model 2889 Automated Screening Tool (AST) is a software used on the ZOOM LATITUDE model 3120 programmer for patient screening with the aim of assessing their suitability for the EMBLEM S-ICD system.

The Automated Screening Tool application is exclusively intended for the screening of EMBLEM S-ICD implant candidates and should not be used to diagnose heart disease. The Automated Screening Tool is an alternative to the Manual Patient Screening Tool, model 4744. These two screening tools have the same function and can be used either together or independently (Figure 6.3).

The **equipment** needed to carry out the screening consists of:

- Programmer 3120 with Automated Screening Tool software application;
- external ECG cables compatible with the model 3120 programmer and associated accessories (for example electrodes and materials for skin preparation);

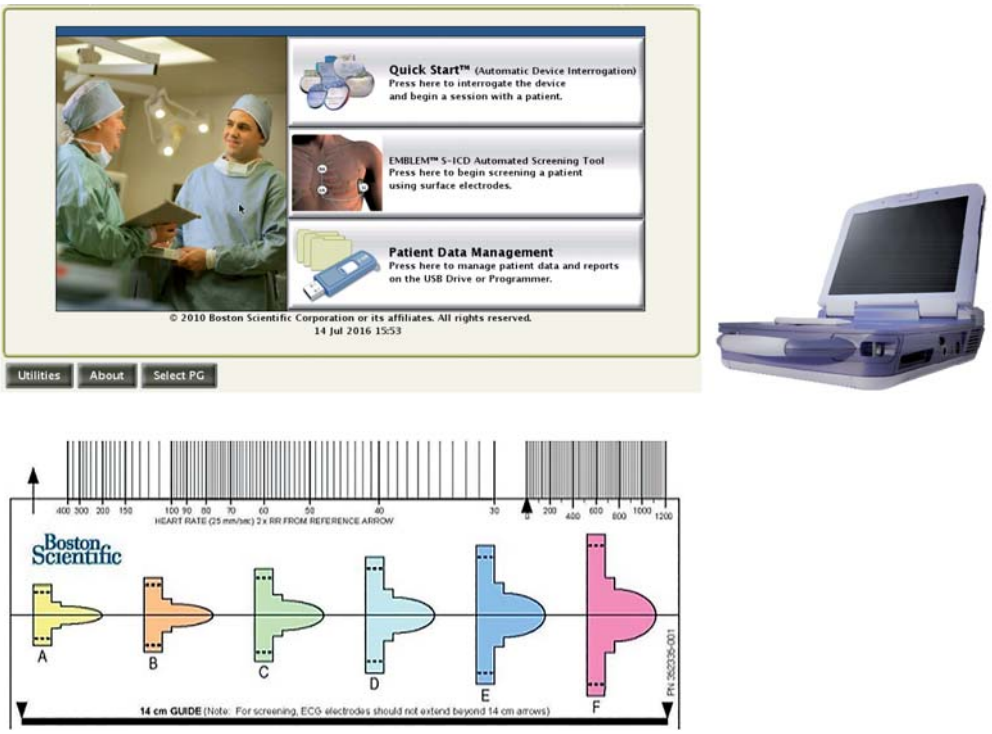


FIGURE 6.3
Automated Screening Tool and Manual Patient Screening Tool.

- measuring instrument to measure 14 cm (the Manual Patient Screening Tool model 4744 can be used);
- external printer or storage unit connected to the model 3120 programmer.

The Automated Screening Tool report cannot be printed using the model 3120 programmer's internal tape printer.

To perform the patient screening process it is necessary to obtain a surface equivalent of the subcutaneous sensing vectors used by the implanted EMBLEM S-ICD system. The model 3120 programmer is used to collect the surface ECG, and the Automated Screening Tool software application evaluates the QRS complexes for each patient's posture examined.

Use of the Automated Screening Tool Application

1. Turn on the model 3120 S-ICD programmer
2. Click **EMBLEM S-ICD Automated Screening Tool** from the Home screen (Figure 6.4).

FIGURE 6.4
Home screen.

Implementation of the ECG Connection

Preparation of the Skin before Placing the Surface Electrodes

1. Shave the area
2. Clean the skin using a cloth moistened with non-alcoholic liquid or with skin preparation gel.

Placement of Surface ECG Electrodes

It is important to record the surface ECG in the exact point where the S-ICD system will be implanted. During the positioning of the S-ICD system in the standard implantation point, it is necessary to position the ECG electrodes as described below (Figure 6.5). If a pulse generator or a subcutaneous electrode of the non-standard S-ICD system is requested, the positions of the ECG electrode can be modified accordingly.

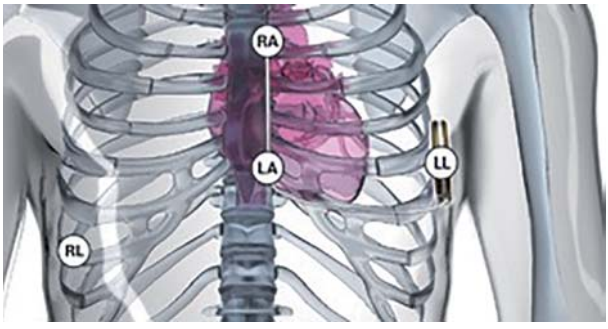


FIGURE 6.5
Standard positions of the surface ECG electrodes for patient screening. RA: right arm, LA: left arm, LL: left leg, RL: right leg.

For a Standard Installation:

- The **LA ECG electrode** must be placed 1 cm lateral to the xyphoid midline to represent the desired position of the proximal sensing ring of the implanted subcutaneous electrode
- The **RA ECG electrode** must be placed at 14 cm above the LA ECG electrode, to represent the desired position of the distal sensing tip of the implanted subcutaneous electrode. Measure 14 cm using the Model 4744 Patient Screening Tool or another measurement tool
- The **LL ECG electrode** must be placed in a lateral position, near the 5th intercostal space along the mid-axillary line to represent the desired position of the implanted pulse generator
- The **RL ECG electrode** is positioned to serve as the patient's reference electrode.

To obtain an ECG with a stable baseline, free of noise and motion artifacts:

- Make sure the surface electrodes are new. Avoid using previously opened package electrodes. The electrodes dry up quickly after opening the package
- Make sure that there is enough electrode gel on the electrode contact point.

Check that the ECG monitor is clean (Figure 6.6).

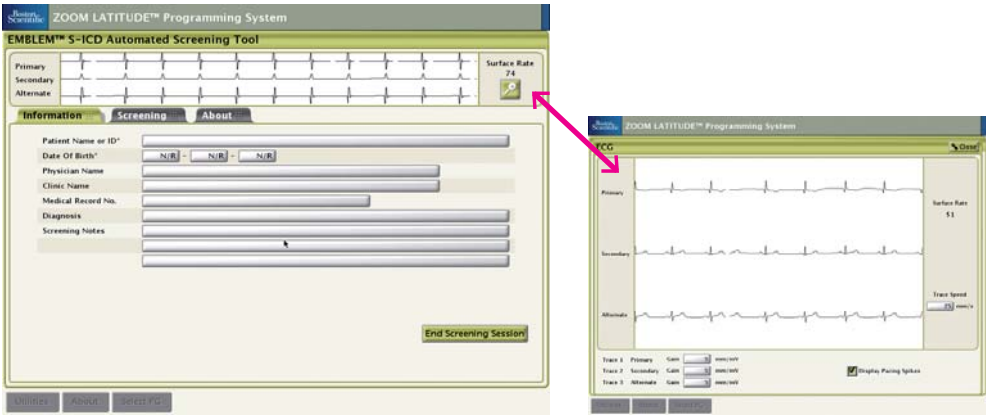


FIGURE 6.6
Verify ECG on the screen.

Observe the ECG on the Screen:

1. Observe the ECG signal on the model 3120 programmer screen. Each ECG signal must have a **stable baseline** and be free of noise and **motion artifacts**
2. Enter the full screen view to enlarge the signal by clicking on the magnifying glass button in the upper right corner. The gain can be adjusted to improve the display. Manual gain adjustments do not affect the results of the Automated Screening Tool or printed reports.

Use the following suggestions to resolve any problems you may have with noise or an unstable baseline:

- Replace the ECG cables used to collect surface ECGs
- In particularly difficult cases, prepare the skin again using for example, a gauze to thoroughly clean the electrode placement site
- Ask the patient inhale, exhale and hold his breath for 10 seconds to manage respiratory artifacts.

The application of the Automated Screening Tool consists of data cards. Complete each card when performing screening tests (Figure 6.7).

Information card: enter the patient information (it is necessary to fill in the fields for the **Name** or **ID of the patient** and **Date of birth**).

NOTE. This information can be changed at any point of the screening process.

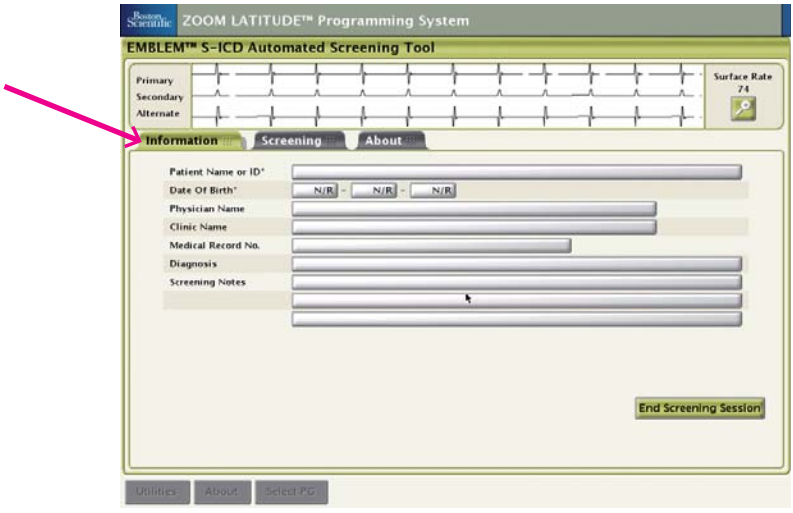


FIGURE 6.7

Filling out card details.

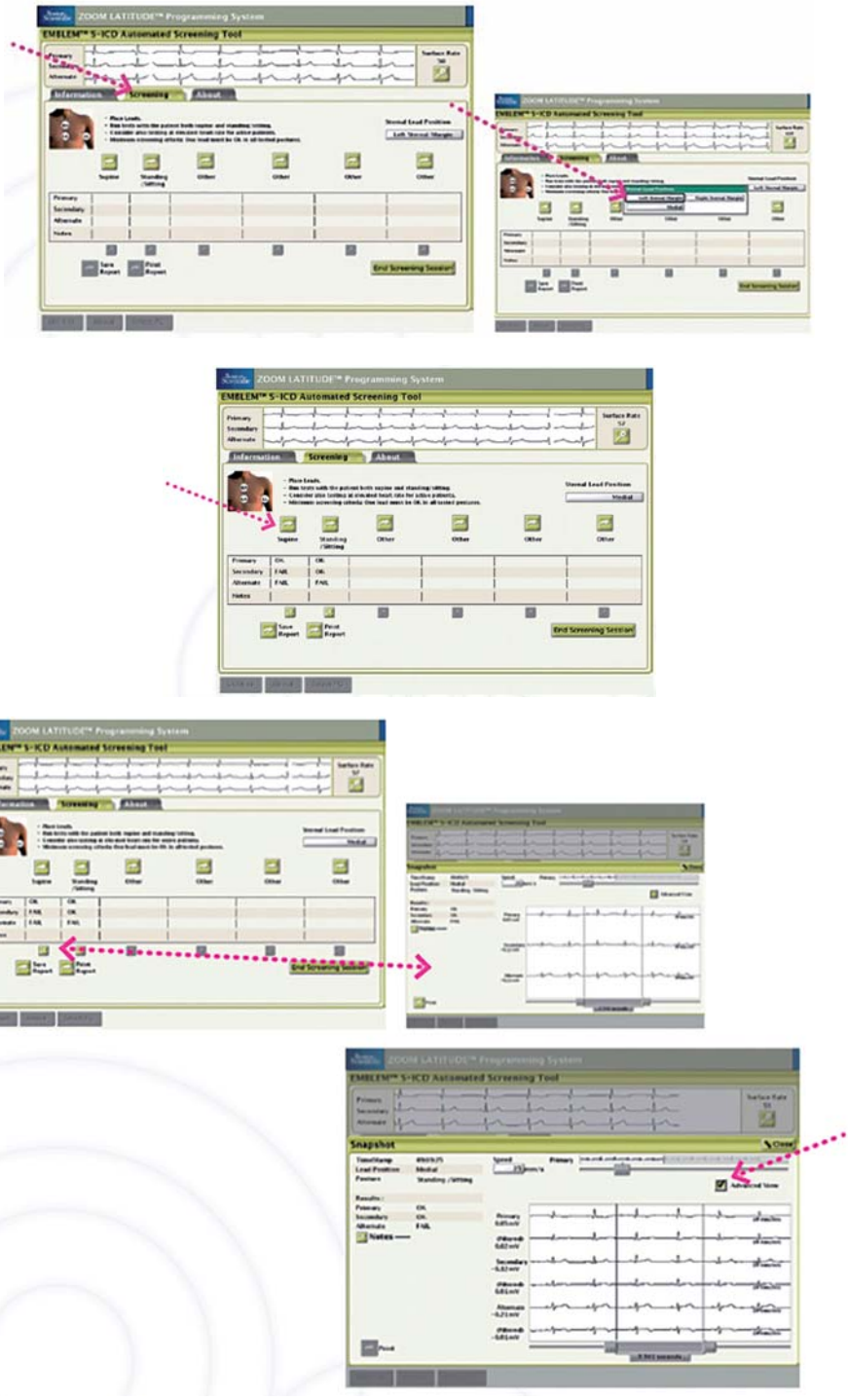


FIGURE 6.8

Screening screen.

Screening Card: run the ECG screening test on the **Screening** card.

1. Select the **sternal position for the lead** by clicking on the drop-down menu (default setting for most positions - **Left sternal margin**; the other options are **Right sternal margin** and **Medial**). The **sternal position for the lead** represents the predicted position of the vertical part of the implanted S-ICD electrode (Figure 6.8).
2. Perform the **Supine** posture (required) - Place the patient in the supine position, then click on the corresponding **Execute** button to perform the ECG screening test. The results are displayed when the test is finished.
3. Perform the posture **Standing/sitting** (required) - Have the patient stand or sit, then click on the corresponding **Run** button to perform the ECG screening test.
4. Perform postures or **other** conditions (optional) - Click the button associated with the **Others** column to add specific patient postures or conditions as needed. Click on the text field to add descriptions for these postures or conditions.
5. Click the **magnifying glass** button below each column to review the details of each test. Each ECG signal must have a **stable baseline** and be free of noise and **motion artifacts**.

NOTE. It may happen that the test result is *Fail* and the physician would like to repeat it, but revising an ECG reveals a signal **disturbance** caused by some kind of noise, patient movement or intermittent connection to surface electrodes. To repeat a test, simply click the *Execute* button again for the desired posture, then observe the results. If you run a test for more than 6 postures or conditions, you will need to save the report and start a new session. The user interface provides only 6 columns for postures or conditions for a single session.

Use of the Screening Report to Determine an Acceptable Sensing Vector

Report Saving, Printing and Exporting

1. To save the report, click the **Save report** button. In the lower left corner of the **Screening** card - a PDF file of the report is saved to the model 3120 programmer disk (Figure 6.9).

NOTE. It takes only a few minutes to produce the PDF report, depending on the number of postures or conditions performed.

NOTE. A maximum of 100 reports can be saved on the hard disk. When the maximum capacity is reached, a warning is displayed. The operator has the option to delete the oldest session or to end the session.

FIGURE 6.9

Saving screening data.

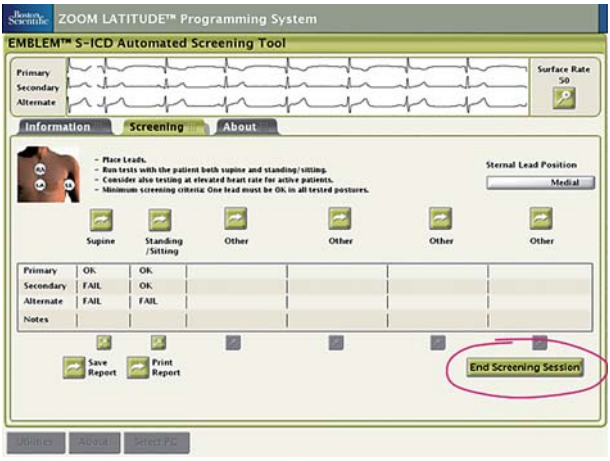
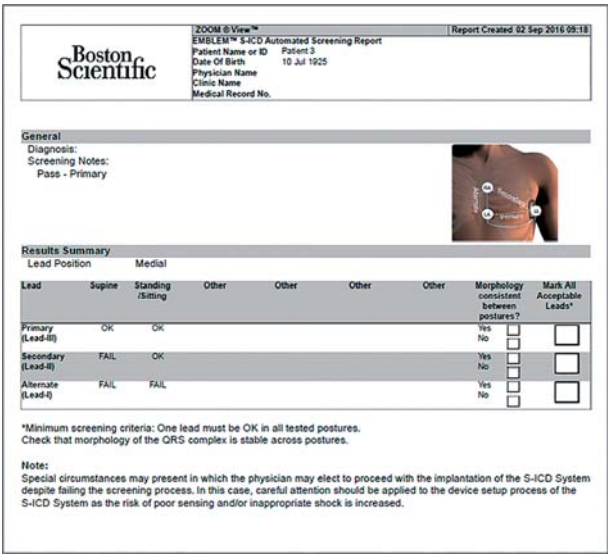
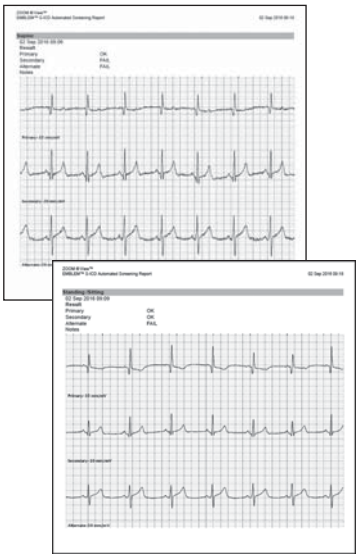


FIGURE 6.10

Print report.





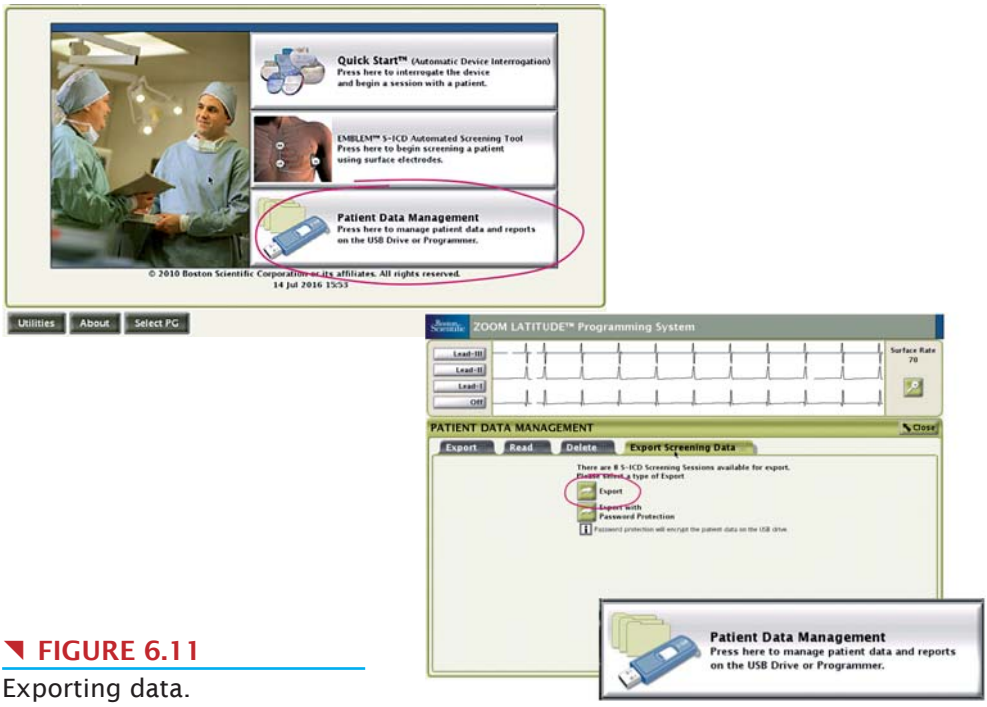


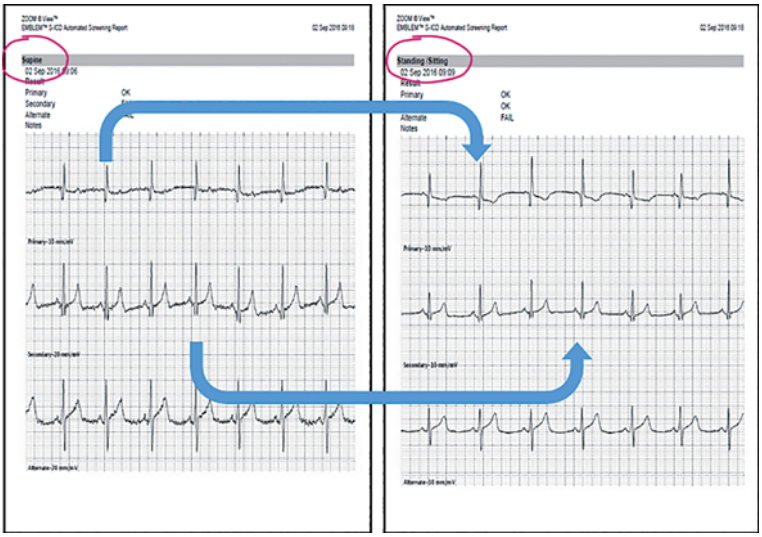
FIGURE 6.11
Exporting data.

2. To print the report, click the **Print Report** button to send the report to the connected external printer (Figure 6.10).
3. To export data to a storage unit:
   - Click on **End screening session** to return to the main screen of the programmer
   - Insert the storage unit in the USB port of the 3120 programmer
   - Click on **Patient data management**, then select the **Export screening data** tab;
   - Click **Export** or **Export with password protected** and follow the instructions (all saved reports will be exported) (Figure 6.11).

How to Determine an Acceptable Sensing Vector

The doctor must analyse the report to determine if the patient is suitable for implantation of the S-ICD system and confirm that the following conditions are met:

- At least one common ECG derivation must be considered acceptable for all tested postures, and the postures of supine and sitting/standing and **Supine** and **Standing/Sitting** should be tested;
- The morphology of the intrinsic/stimulated QRS complex is stable in the different postures (similar to the positive/negative amplitudes of



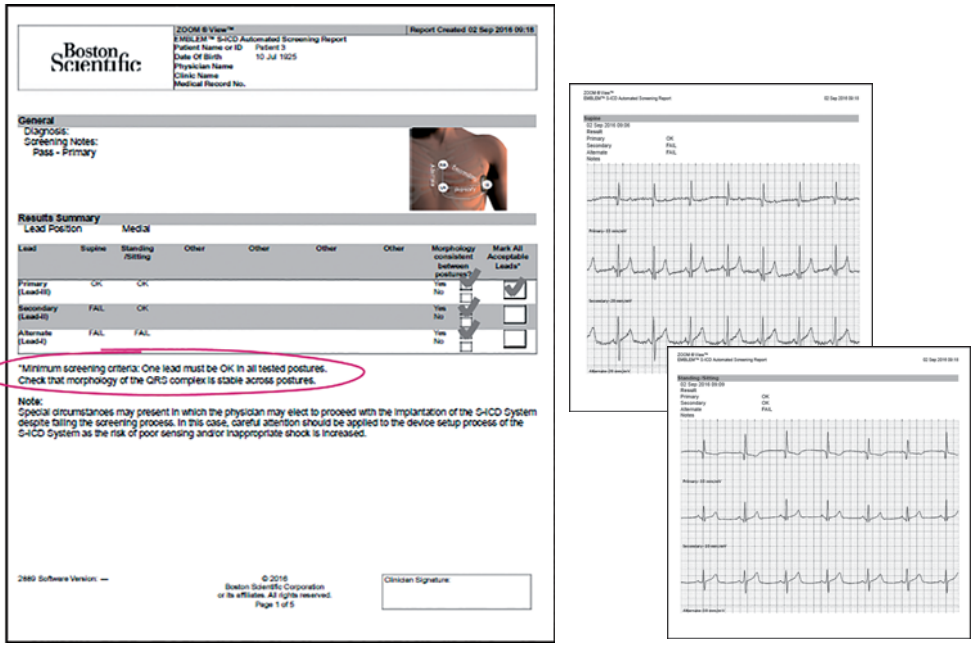


FIGURE 6.12

ECG assessment.

the peak and to the widths of the QRS). A significant change in the QRS complex is not valued as a result of postural modification. For multi-peak signals, make sure that the position of the largest peak is consistent with the lowest peak (Figure 6.12).

NOTE. Special circumstances may arise in which the doctor chooses to proceed with the implantation of the S-ICD system despite failure of the screening process. In this case, special attention must be paid to the S-ICD system device setup process as the risk of poor sensing and/or inappropriate shock is greater.

Combination of Electric Thoracic Devices

Often there are already implanted cardiac electrical devices in the S-ICD candidate. The basic and intuitive caution, adopted from the beginning of the S-ICD experience, was not to leave any other electrode or, obviously, generator in order to prevent interference between the systems, or even possible effects of disturbance on the sensing process and/or on cardioversion. This concept has been rigidly maintained as regards to the presence of T-ICD: the transvenous system was and still is needed to be removed before implantation of S-ICD. Instead, sometimes, when it is unavoidable in extreme cases, S-ICD and the traditional transvenous pacemaker are combined, using the utmost precaution to avoid unipolar electrodes. The results have been published by various authors and, although in very small series or single cases, they have shown 'compatibility' between the systems. Especially in patients with extreme situations of impossibility to implant T-ICD and/or with the concomitant presence of indications, as for anti-bradycardia pacing and for S-ICD, the two devices were used, both concurrent and simultaneously active, with adequate programming of both (for example: maximum frequency of pacing not exceeding half of the minimum recognition value)[14,15].

If another device, such as a PM, is present, the assessment must be performed both with spontaneous rhythm and with a stimulated rhythm, verifying that the screening is positive for at least one derivation in two postures and is in both spontaneous and stimulated rhythm.

Compatibility between the two systems cannot exist with the use of monopolar electrode catheters.

Beyond the 'frontier' experience, the coexistence faced between the two systems undoubtedly offers very interesting research perspectives.

Synopsis of Practical Guidelines

- Assessment of the anatomical condition: S-ICDs can be proposed in many paediatric patients weighing more than 25 kg.
- Screening with programmer and automatic algorithm in two positions in all patients.
- Patients with a high physical activity, congenital heart disease, hypertrophic cardiomyopathy, right bundle branch block and extensive repolarisation abnormalities should repeat their ECG screening during a stress test.
- An accurate assessment of the medical history of previous cardiac device implantation and any of their parts that might have been retained.

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CHAPTER 7

Becoming Familiar with the Implantation Site: Useful Tips on Anatomy for the Implantation Technique

A. Bisignani, G. Bisignani, S. De Bonis

The thorax can be divided into four parietal regions: sternal, costal, mammary, dorsal.

Some *vertical* and some *horizontal* lines have been designed to facilitate semiotics.

Vertical lines are illustrated in Figure 7.1.

The *horizontal lines* are:

- the horizontal mammary line
- the bi-spino-scapular line
- the bi-angle-scapular line

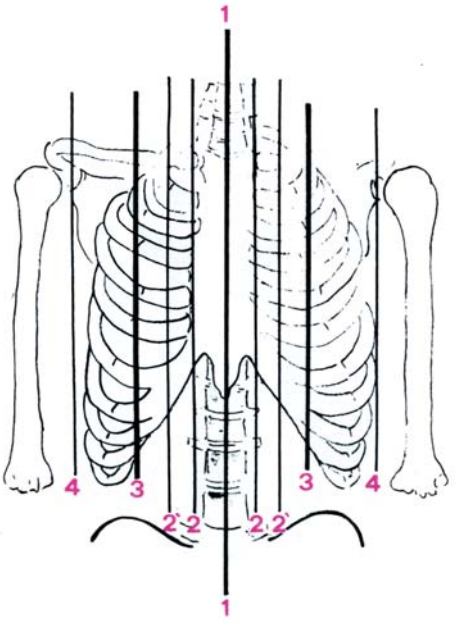
To better describe the implantation site, it is useful to remember that:

- the anterior axillary line passes perpendicularly to the lateral margin of the pectoral muscle
- the middle axillary line runs on the lateral wall of the thorax and passes through the apex of the axilla
- the posterior axillary line passes through the large dorsal lateral margin.

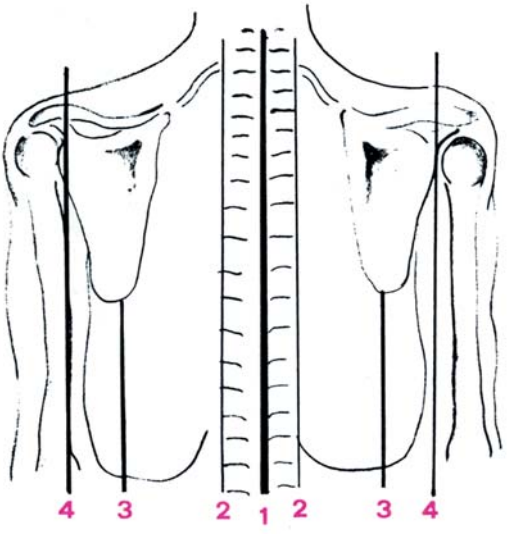
Axillary reference lines are used to position the pulse generator.

The correct position of the S-ICD generator straddles the mid-axillary line.

This position ensures that there is sufficient cardiac tissue between the generator and the electrode (not too much up front, or not too much in the rear) (Figure 7.2).



1 = mid-sternal line
2-2 = marginal-sternal lines
2'-2' = parasternal lines
3-3 = hemiclavear lines
4-4 = anterior axillary lines



1 = supraspinous line
2-2 = paravertebral lines
3-3 = angle of the scapular lines
4-4 = posterior axillary lines

FIGURE 7.1

The vertical reference lines on the chest wall: A) anterior; B) posterior.
[From De Caro R, Anatomia Topografica di Munari, Piccin Nuova Libraria, 2016]

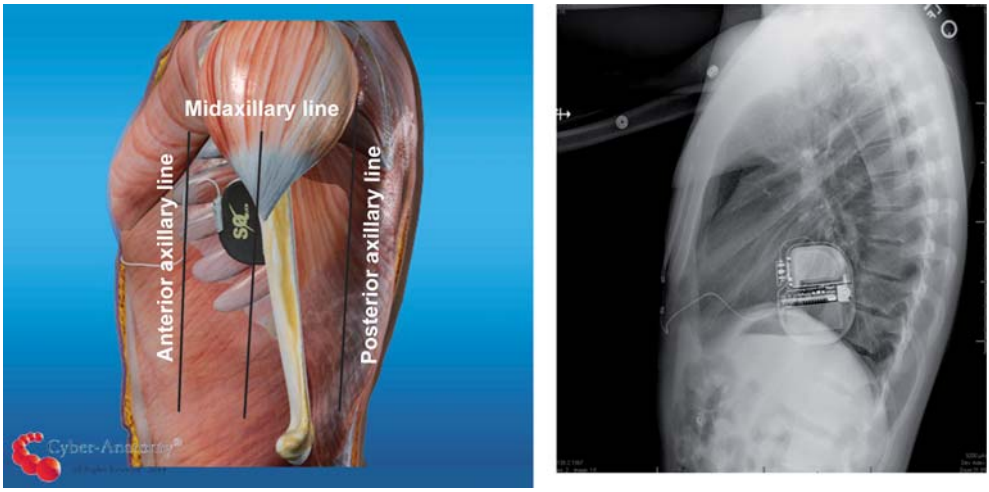


FIGURE 7.2

Axillary reference lines are used to position the pulse generator. The correct position of the S-ICD generator is to straddle the mid-axillary line.

Muscles

The chest muscles are divided into two separate groups: a) chest muscles that extend up into the upper limb and are innervated by the brachial plexus, b) the group of muscles that form the chest wall.

The first group is made up of four muscles: pectoralis major muscle, pectoralis minor, subclavius, serratus anterior or 'big swing muscle'.

The *serratus anterior* or *'big swing muscle'* located in the lateral thoracic region originates with fleshy slips from the first to the ninth rib and is divided into three parts: superior, intermediate and inferior.

The intermediate part is the weakest; the inferior, the most powerful, originates from the fifth to the ninth rib and inserts at the lower corner of the scapula on the anterior border of the latissimus dorsi or grand dorsal muscle to then reach its insertion in the scapular angle placing itself between the costal surface of the scapula and its musculature and the lateral wall of the thoracic cage.

The *pectoralis major* muscle is superficial and covers the *pectoralis minor* muscle and the *serratus anterior* or 'big swing', whose inferior tract, located in the lateral region of the thorax, is uncovered and, therefore, in a superficial position like the pectoralis major.

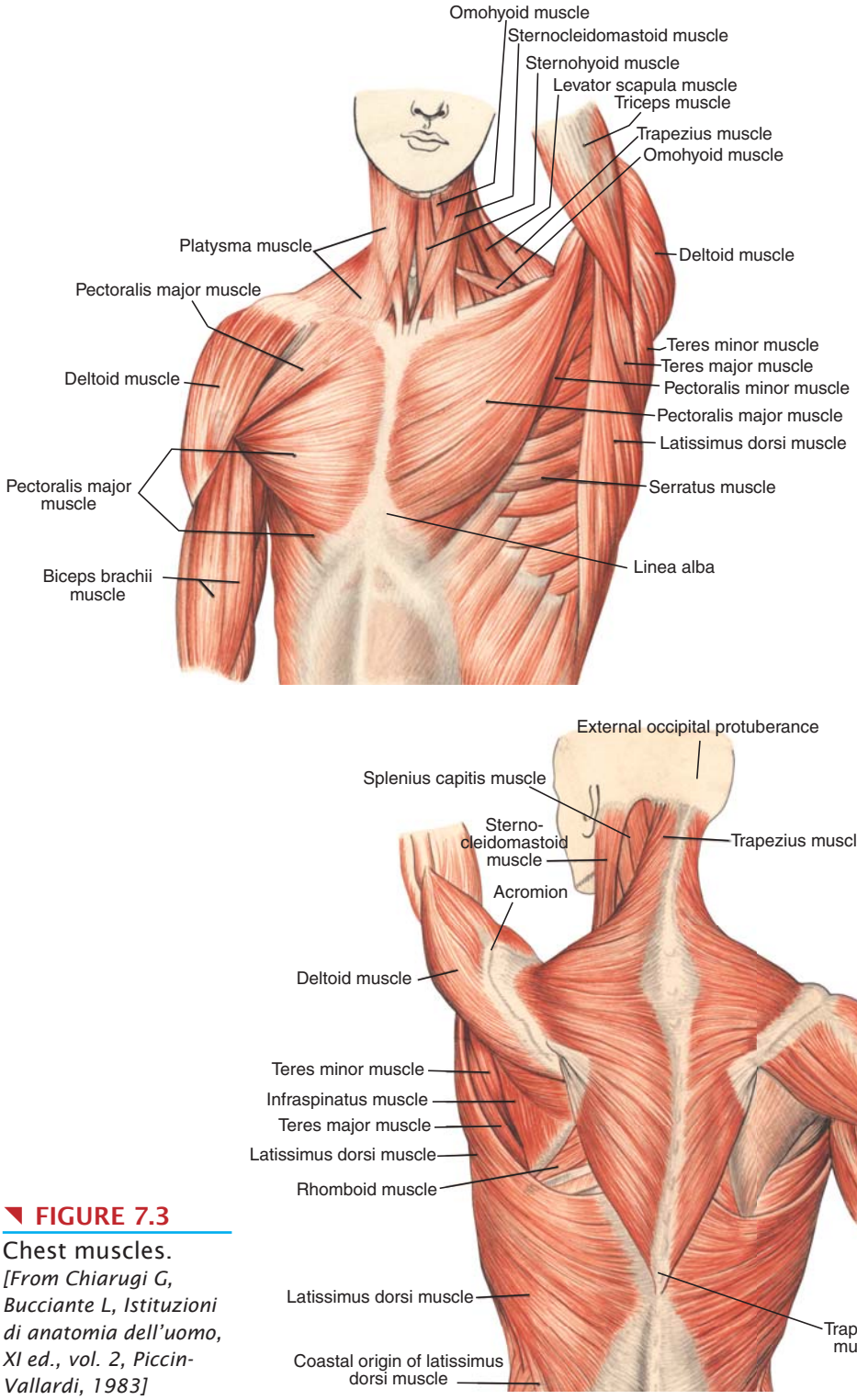


FIGURE 7.3

Chest muscles.
[From Chiarugi G, Bucciante L, Istituzioni di anatomia dell'uomo, XI ed., vol. 2, Piccin-Vallardi, 1983]

The serratus is innervated by the long thoracic nerve of the brachial plexus and the function of the muscle is to fasten the scapula to the trunk (Figure 7.3).

Thorax Region

The chest or thorax region covers the entire anterolateral-posterior wall of the two hemithoraxes, with the only exception of the two middle areas, one anterior (sternal region) and one posterior (dorsal region) (Figures 7.4, 7.5).

Layer Sequence

Skin

The skin is thin on the front, but gradually thickens on the sides, becoming thick on the rear wall. It is smooth on the underlying layers.

Subcutaneous Layer

This layer is thick and dense; more or less rich in fat, it contains the vessels and superficial nerves.

It increases in thickness in the back and this is particularly useful for S-ICD implantation.

Aponeurosis Layer

The anterior muscles are made up of the large pectoralis, the small pectoralis and the subclavius.

Laterally we observe the digitations of the serratus muscle or serratus anterior (Gerdy line), which originates from the outer face of the first nine ribs and is inserted into the medial margin of the scapula. Depending on the fixed point it takes each time, it acts as a motor muscle of the scapula or as an inspiratory muscle.

At the back we find the *posterior axioappendicular muscles*: the trapezius and the latissimus dorsi are situated the most superficially, with the trapezius covering the rhomboids (minor and major) and the levator scapulae, which are placed deeper.

Then we find the *spinocostal muscles*; *serratus superior* and *serratus inferior*. These two posterior muscles are attached to the *serratus fascia*.

Skeletal Plane

It consists of 12 ribs, the internal and external intercostal muscles, the arteries, the veins and the intercostal nerves.

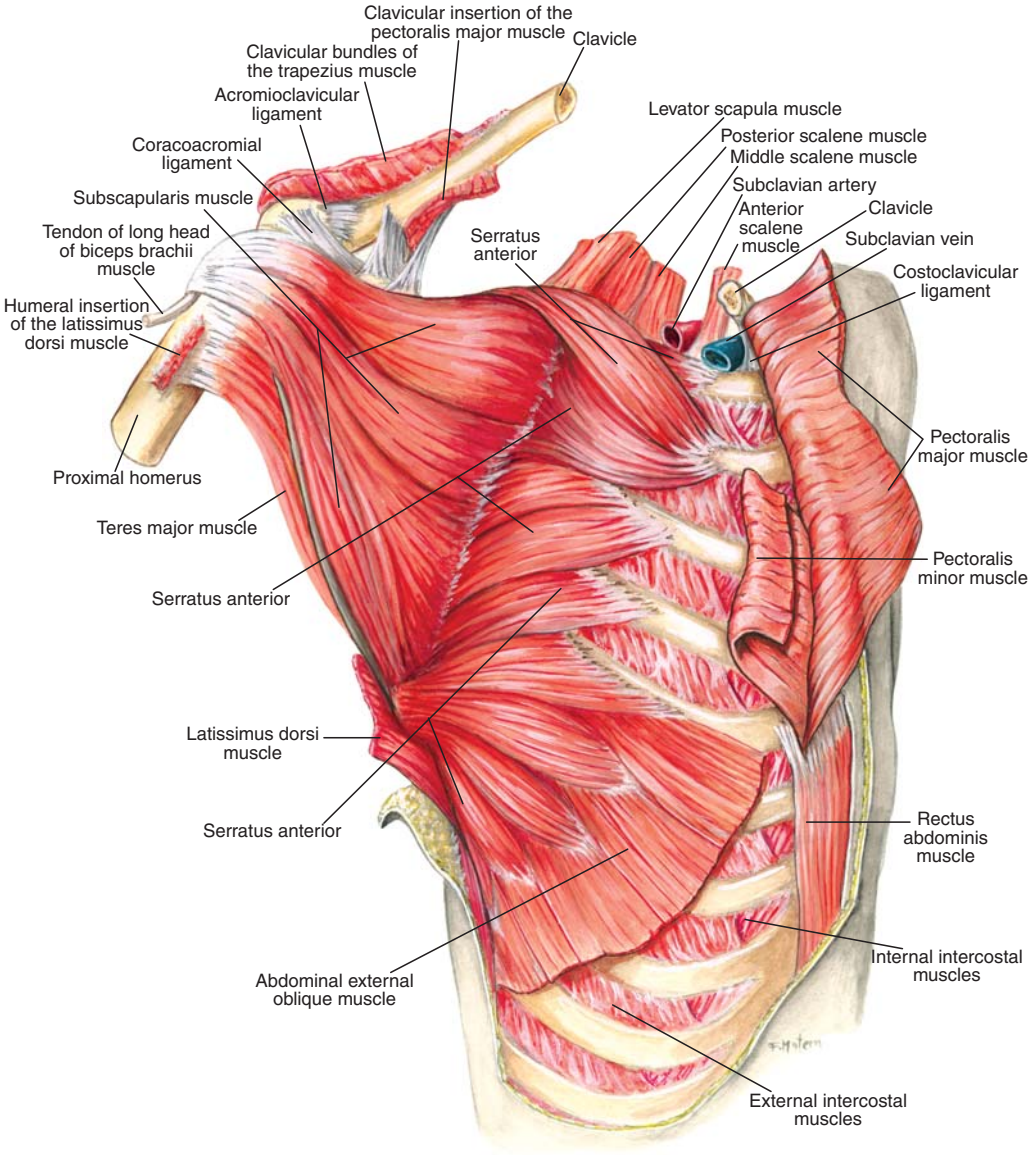


FIGURE 7.4

The serratus anterior muscle and other muscles related to it. The lateral margin of the scapula is delineated between the outer margin of the subscapular muscle and the large round muscle. *[From Chiarugi G, Bucciante L, op. cit.]*

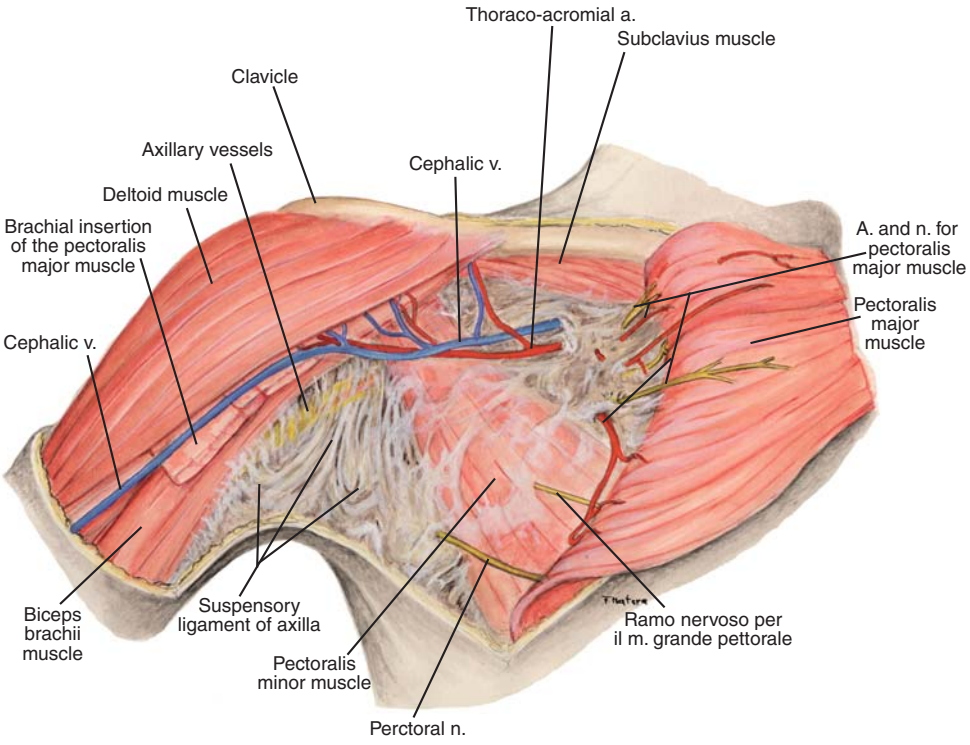


FIGURE 7.5

Muscles of the axillary area and cleido-axillary fascia. *[From Chiarugi G, Bucciante L, op. cit.]*

Internal Layer

It is made up of the *transverse thorax* muscle, the *subcostal* muscles, the *endothoracic fascia* and the parietal *pleura*, which is the deepest layer of the chest wall.

Vessels and Nerves

The anterior arteries include the *internal thoracic artery* or *internal mammary* artery originating from the subclavian artery, lateral branches from the *lateral thoracic artery*, which originates from the axillary artery and irrigate the pectoral muscles, the mammary gland, the serratus anterior, the gran dorsal and the integuments of the region; and, finally, the twelve *intercostal arteries*.

The superficial veins create a sub-superficial venous network, which is also an important anastomotic pathway between the subclavian vein system and that of the femoral vein.

The *thoracoepigastric* vein runs along the lateral aspect of the trunk between the superficial epigastric vein below and the lateral thoracic vein above, and establishes an important communication between the great saphenous tributary femoral and axillary veins, finally reaching the *intercostal* veins and *internal mammary* veins.

The *nerves* come from the brachial plexus, from the cervical plexus and from the intercostal nerves, which are responsible for all the innervation of the chest wall.

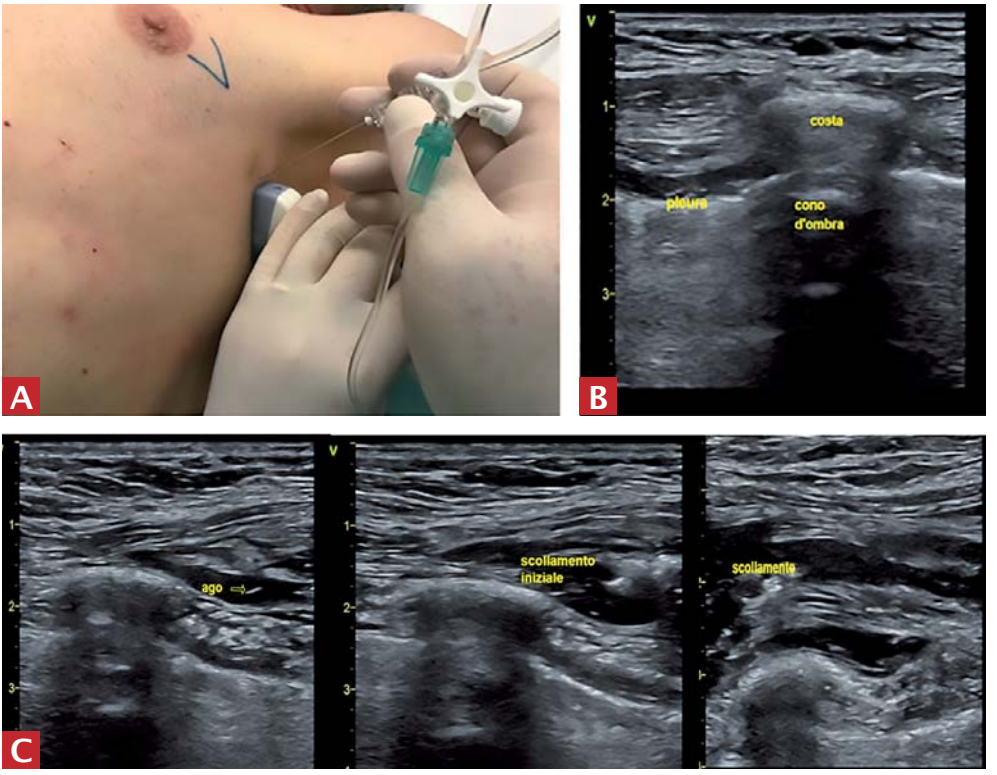


FIGURE 7.6

The anaesthetic technique used for the serratus will be discussed further in more detail in another chapter. From the anatomical point of view note that both the long thoracic nerve and the lateral thoracic artery run on the surface of the serratus. The latter could also be used as a marker. In the figure, the echo probe placed at the level of the V intercostal space identifies the structures highlighted in figure B. In the basic echo images, it is important to have the rib as a landmark, easily recognisable by the cone of shadow and the pleural plane. Once these structures are highlighted, the anaesthetic, injected slowly with ultrasound control, will cause the muscular planes to become detached.

In particular, the *long thoracic nerve* (Bell nerve), which is of interest in regional anaesthesia of the serratus, stems from the brachial plexus, runs, along with the *lateral thoracic* artery, along the lateral surface of the thorax into the large serratus muscle.

When performing regional anaesthesia of the serratus, it is important to remember that the serrated or serratus anterior muscle is covered by the pectoral fascia. Above the serratus anterior, the two layers of the pectoral fascia adhere to form a single fascial lamina. The injection of local anaesthetic must be made in the fascial plane of the serratus anterior muscle because it provides repeatable and effective anaesthesia of the anterolateral chest wall. Injected at this level, the anaesthetic in addition to numbing helps to detach the plane between the two muscles; latissimus dorsi and serratus anterior (Figure 7.6).

The following images (Figures 7.7–7.10) are particularly useful because they outline the anatomical references of the thoracic area that is affected by the implant. It shows a virtual pocket that is useful to house the device that lies between the large dorsal muscle or latissimus dorsi and the serratus anterior or 'big swing'. The course of the long thoracic nerve is also illustrated.

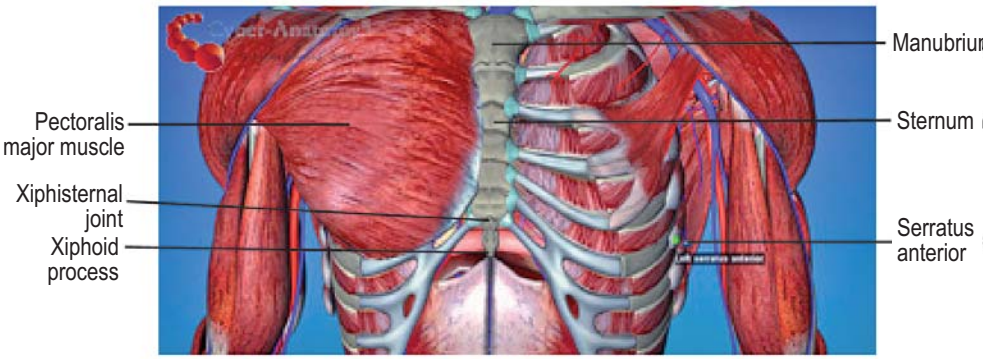


FIGURE 7.7

The xiphoid process is the main point of reference for S-ICD positioning. Lines of skin tension (Langer lines) correspond to the direction of collagen fibres in the dermis. Surgical incisions made parallel to the lines of skin tension may heal better and produce less scarring because the lines of force pull in such a way that the scar heals faster.

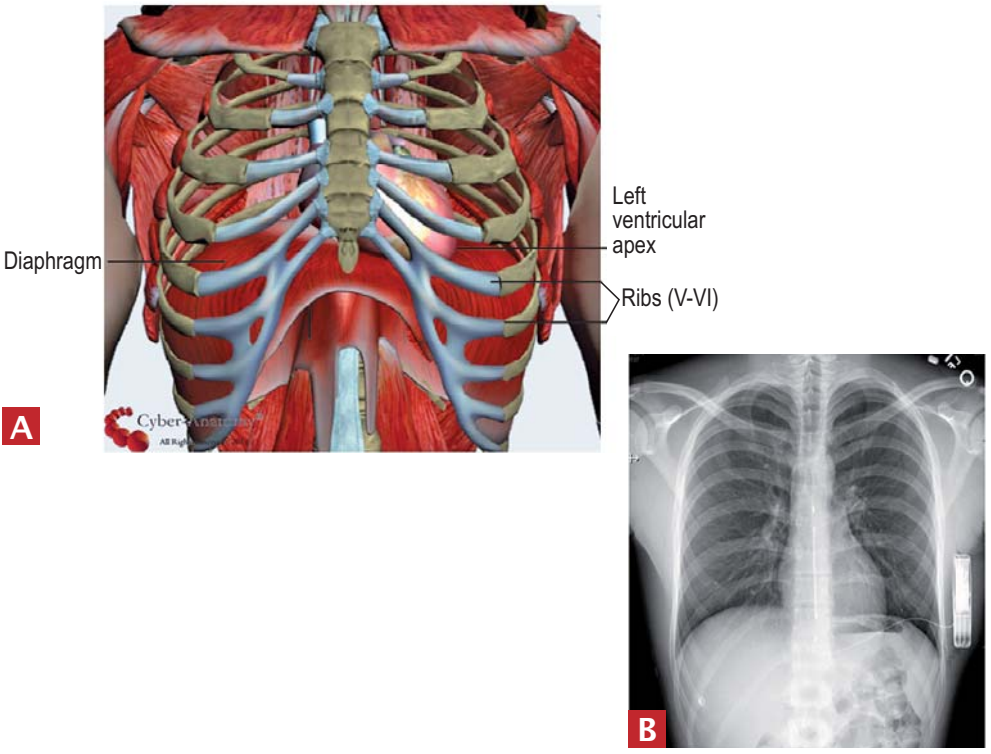
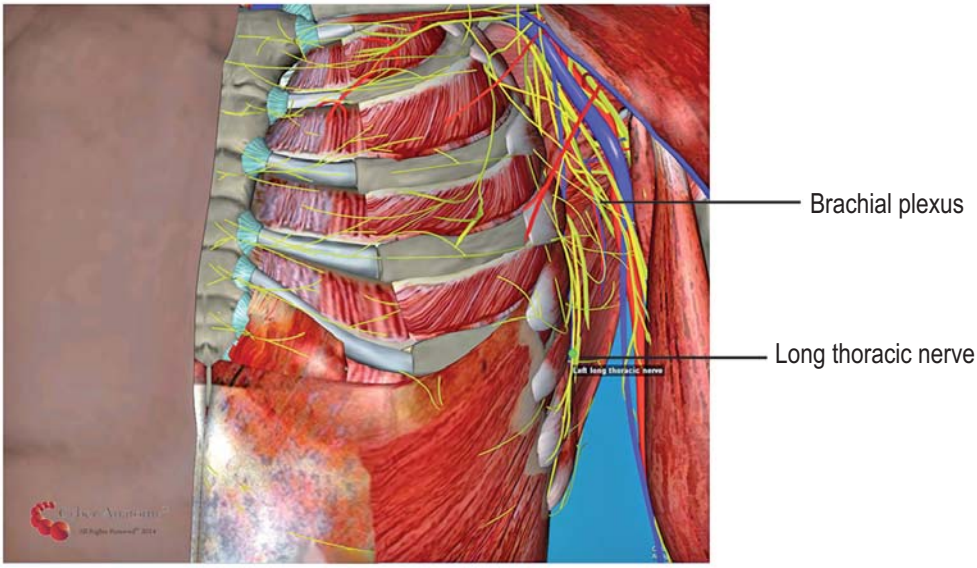


FIGURE 7.8

The images illustrate the normal position of the heart in the thoracic cavity and anatomical reference points used to position the S-ICD system.

- The heart is located between the right and left lungs, posterior to the sternum. About 2/3 of its mass is to the left of the midline. The right side of the heart projects towards the sternum (anterior position); the left side towards the spine (posterior position).
- The apex of the left ventricle (LV) rests on the thoracic diaphragm, higher than the xiphoid process. It is posterior to the fifth intercostal space, about 9 cm from the median plane.
- The diaphragm is the muscle that separates the chest cavity from the abdominal cavity. Because of its size, shape and position, it serves as an important anatomical landmark.
- The S-ICD system is placed above the xiphoid process and diaphragm (Figure B).
  - The pulse generator is positioned between the 5th and 6th intercostal space on the left medial-axillary line.
  - The proximal electrode is on the same plane as the pulse generator. The detection ring is 1 cm to the left of the xiphisternal joint.
  - The distal electrode is positioned along the sternum, one centimetre to the left of the median line.
  - The placement of the S-ICD system depends on the position of the heart in the chest. The object is to make sure that there is enough ventricular mass between the generator and the electrode.



Axillary vessels and nerves

FIGURE 7.9

The long thoracic nerve runs along the outer surface of the serratus anterior muscle. The patient needs to be prepared very carefully in order to protect the brachial plexus. Pay close attention to the long thoracic nerve when placing the pulse generator.

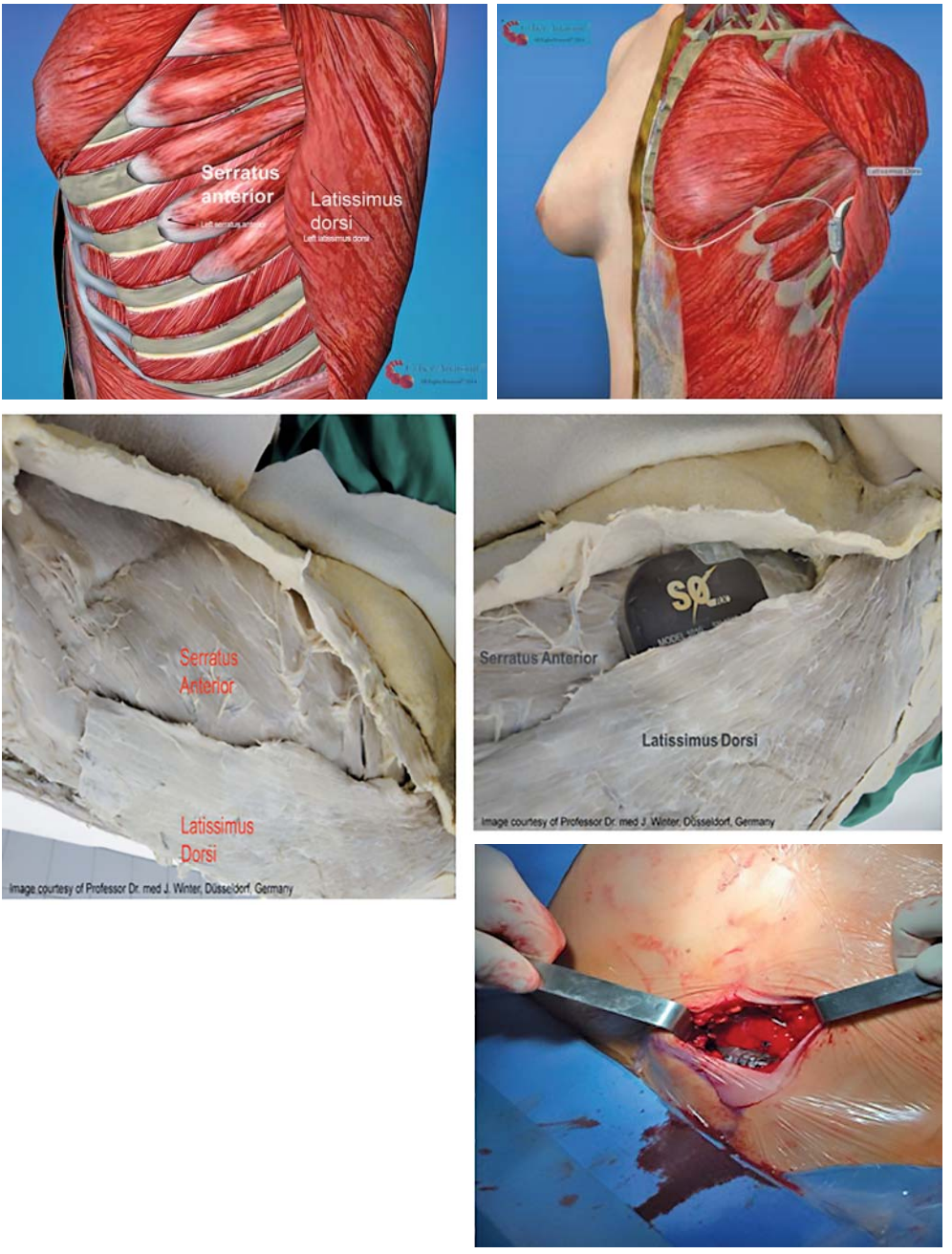


FIGURE 7.10

The different orientation of the fibres between the latissimus dorsi muscle and the serratus anterior is clearly evident. And the 'natural' pocket between the two muscles is obvious. This is the point where the device is going to be implanted. The initial incision of the generator pocket is made near the front axle line. Remember that a vertical alignment of the generator is usually more comfortable for the patient.

Knowledge of anatomy and keeping in mind the anatomical indications along with careful patient preparation allow for safe and technically feasible implantation in most patients.

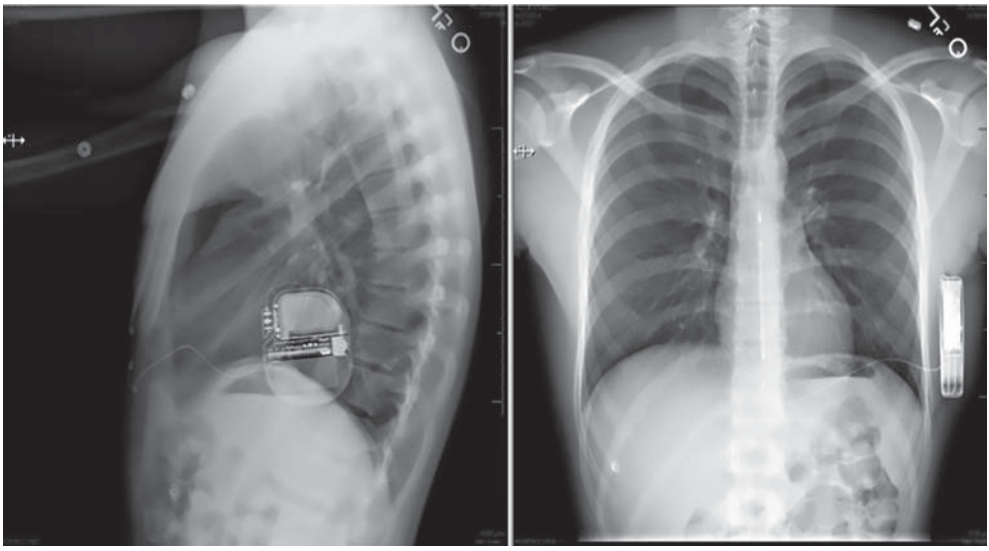


FIGURE 7.11

These radiological images report the successful results of an implantation showing an optimal position. This is thanks to a good knowledge of anatomy and the technique (left lateral projection, right in AP).

The following are some illustrations of anatomical variants that, if not recognised and carefully evaluated, could make the implantation of the S-ICD difficult (Figures 7.12–7.14).

These variants are:

- Pectus carinatum
- Pectus excavatum
- Dextrocardia

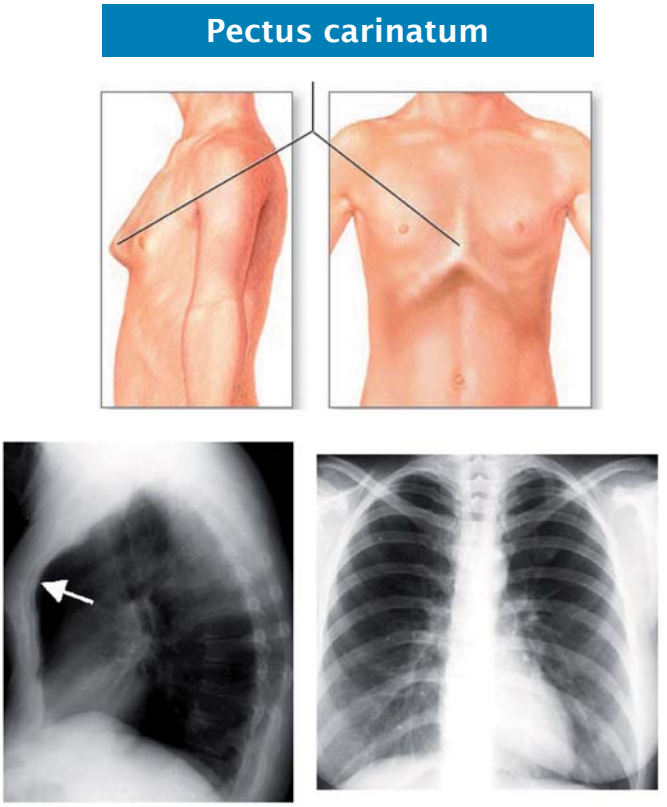


FIGURE 7.12

The pectus carinatum is a congenital anomaly that causes forward progression of the sternum, giving the chest a birdlike appearance. The pectus carinatum can be asymmetrical, with one side of the chest more pronounced than the other. In some cases, you may find pectus carinatum on one side of the chest and pectus excavatum on the other. Pre-implant radiographic images help to identify the anatomy and the reference points and positioning of the plane of the S-ICD system. Fluoroscopy helps to ensure good visualisation when tunneling along the fascial plane.

Pectus excavatum

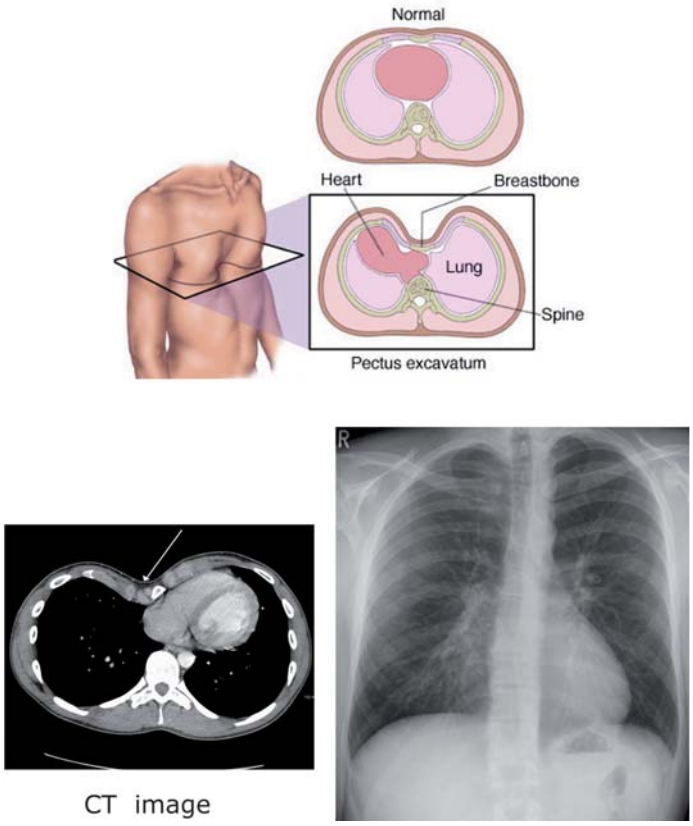


FIGURE 7.13

Pectus excavatum is a congenital anomaly caused by excessive growth of connective tissue between the ribs and the sternum, which causes the sternum and the anterior ribs to move inwards. The diagram shows how the pectus excavatum moves the heart inside the thoracic cavity from its original position. The X-ray image shows an obliterated right edge, an indication of pectus excavatum. The degree of deformity in pectus excavatum varies from person to person. A pre-implant CT scan and chest X-ray help identify anatomical landmarks and to better plan the placement of the S-ICD generator and electrode. Fluoroscopy ensures good visualisation during tunneling along the fascial plane.

Dextrocardia

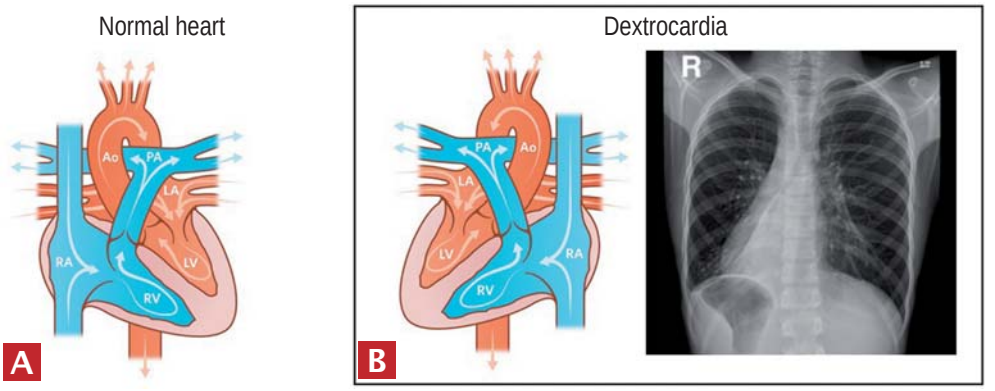


FIGURE 7.14

Dextrocardia is a congenital condition in which the apex of the heart is located on the right side of the body and, therefore, the heart points to the left side instead of the right. Even the large vessels are inverted. Isolated dextrocardia is the inverted positioning of the heart and large vessels (Figure B). Dextrocardia with situs inversus is the inverted position of the thoracic and abdominal organs. Other defects may be present. Dextrocardia requires reverse positioning of the S-ICD system. The distal electrode is placed 1 cm to the right of the median of the sternum and the generator to the right medial-axillary line. A pre-implant MRI with clear labeling of the right and left sides helps to identify anatomical landmarks. The pre-implant X-ray helps to better plan the placement of the generator and of the electrodes.

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Chiarugi G, Bucciante L. Istituzioni di anatomia dell'uomo, XI ed. Piccin-Vallardi, 1983.

De Caro R. Anatomia Topografica di Munari. Piccin Nuova Libraria, 2016.

Chapter 8

Anaesthesiological Management and Thoracic Loco-Regional Blocking Procedures for S-ICD Implantation

A. Droghetti, P. Scimia, E. Basso Ricci, F. Harizaj, O. Putina, V.Y. Njike

In recent years, thanks to the use of ultrasonography in clinical practice there has been an important development in regional anaesthesia. This progress has brought about the use of various novel nerve blocking procedures, which are more efficient and safer to use than traditional techniques in various surgical fields. Droghetti and colleagues describe Ultrasound-guided Serratus Anterior Plane Blockings (US-SAPB) and Ultrasound-guided Parasternal Blockings (US-PSB), recent loco-regional blockings that have been introduced into clinical practice[1,2]. The use of the US-SAPB allows us to have anaesthesia/analgesia of the antero-lateral thoracic wall that can be extended to the dermatome region between T2 and T9 through the blockage of anterior and lateral branches of the intercostal thoracic nerves. As a result of these characteristics, this technique is a suitable method for anaesthesia and post-operative analgesia for many thoracic and mammary surgery procedures, and also for the implantation of a defibrillator (S-ICD).

To perform these blockings, a preoperative anaesthesioligcal routine examination is performed to the patient and the patient is handed the informed consent form. The patient is informed that sensitivity to pain will only be eliminated in the thoracic area, at the implantation site during the procedure. This procedure is not performed in patients presenting with contraindications that are stated in the Italian and European guidelines for safety during regional anaesthesia[3,4].

The loco-regional blockings are performed at least 40-60 minutes prior to S-ICD implantation. Since anesthetic procedures are relatively easy

and quick to perform, they can be performed either on the ward at the patient's bedside, or in an outpatient clinic, or directly in the preoperative room. The patient might be sedated only during the implantation procedure.

The implantation of a subcutaneous implantable S-ICD represents one of the most important life-saving therapeutic strategies as it prevents sudden cardiac death in patients at risk of lethal cardiac arrhythmias[1]. The standard procedure described by Knops and colleagues provides an intermuscular two-incision technique; with the positioning of the device generator in an intermuscular pocket between the serratus anterior muscle and the grand dorsal muscle, and the subsequent tunneling of the defibrillator lead through a left parasternal incision[2]. This chapter describes the US-SAPB and the US-PSB, loco-regional blocking techniques, which can be used as an alternative approach to anaesthetic-analgesic management of S-ICD implantation.

Neuroanatomy of the Chest Wall

The lateral cutaneous branches of the intercostal nerves innervate the anterolateral-posterior thoracic wall. The same nerves give rise to anterior branches that, completing their course towards the parasternal region, and are responsible for the innervation of the medial region of the chest wall. The serratus anterior muscle originates from the surface of the first eight ribs and inserts along the entire anterior length of the medial border of the scapula. This muscle is divided into three main parts. The upper portion is cylindrical in shape, originating from the first and second ribs and, after a slight ascending trajectory, is inserted into the upper medial border of the scapula. The middle portion is very thin and comes from the lateral and anterior surface of the second, third and fourth ribs. Its muscle fibres have a divergent route and have a transverse arrangement, so they are inserted into the medial border of the scapula. The lower part is the widest and longest, going from the third to the eighth rib. Its muscle fibres form a convergent trajectory at the lower scapular angle (Figure 8.1).

The pectoral fascia covers the serratus anterior muscle[5], which originates from the clavicle and then divides into two layers to include the pectoralis major muscle. Above the anterior serratus, the two layers of the pectoral fascia adhere to form a single fascial lamina. At the back, this single layer divides again to enclose the grand dorsal muscle or latissimus dorsi in the same way as the pectoral fascia and the pectoralis major muscle. In the middle, the deep layer of the pectoral fascia is inserted into the

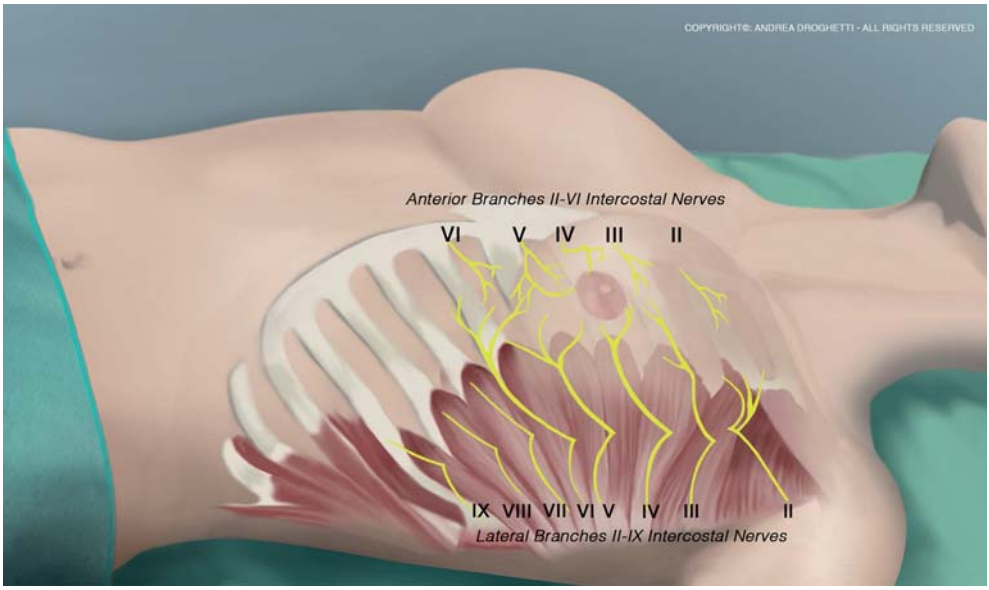


FIGURE 8.1
Neuroanatomy of the chest: serratus anterior muscle and intercostal nerves.

sternum, while the superficial layer extends beyond the sternum with the pectoral fascia on the other side[6].

The US-SAPB, described by Blanco and colleagues, allows us to obtain a multi-dermatomal anaesthesia and analgesia of the anterolateral thoracic wall with extension from T2 to T9, thanks to the blockage of the lateral cutaneous branches of the intercostal nerves[7]. In the original description of the technique, the authors reported the possibility of a double injection: at the level of the fascial plane between the serratus and latissimus dorsi muscles at the level of the fifth rib (superficial US-SAPB) or between the serratus muscle and costal plane (deep US-SAPB). Although the initial results suggested superiority in terms of metameric extension and duration of action of the blocking in favour of the superficial approach, recent literature seems to highlight a substantial analgesic equivalence between the two approaches[8]. This technique, associated with US-PSB, that enables us to obtain anaesthesia of parasternal region from T2 to T6 with an adequate intraoperative sedation, is considered a suitable method for the implantation of the S-ICD device and reduces pain during the creation of the intermuscular pocket and parasternal tunneling of the lead.

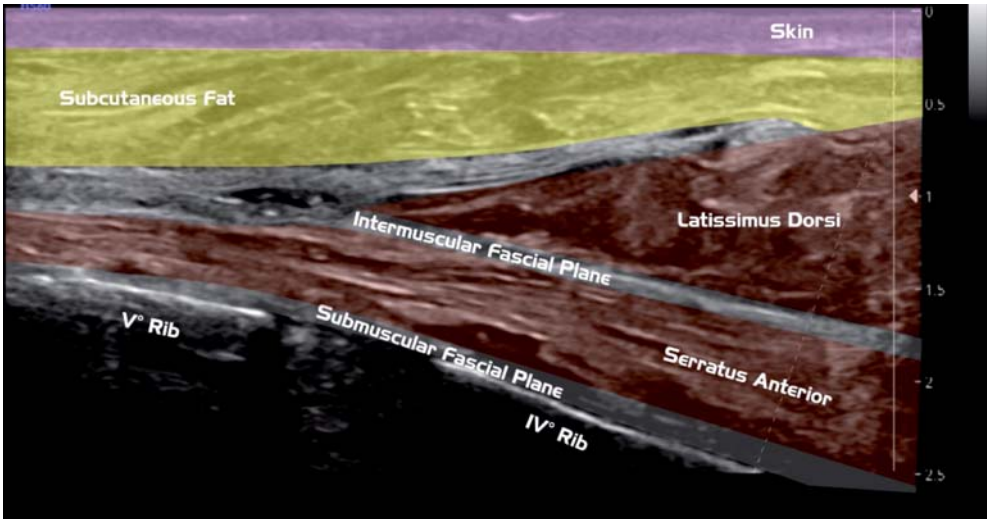
Anaesthesiological Management

After obtaining a peripheral venous access and vital signs are monitored, the loco-regional blocks should be performed at least 40-60 minutes before implantation in an adequately prepared preoperative room, carefully checking the dermatomal level of the block using the ice test or pin prick test. Despite the relative simplicity and speed of execution in the hands of an expert, it is the anaesthesiologist's duty to always guarantee the patient adequate analgesic sedation before blocking. An antalgic effect is normally obtained by combining benzodiazepines and opioids to tranquillise the patient both psychologically and emotionally in order to adapt to the invasive procedure of administering a regional anaesthetic and to the environment in the operating room. There is also the option of an analgo-sedation scheme that allows execution of the blocks in a sedated but collaborative patient; it involves intravenous administration of Midazolam (0.02 mg/kg-1) that can be associated with Fentanyl (1–2 μg/kg-1) or Sufentanil (0.1–0.15 μg/kg-1). During implantation of the S-ICD, continuous intravenous infusion of hypnotic drugs, such as Propofol, in order to reduce the patient's discomfort and make the procedure easier can only be used when necessary.

Ultrasound-Guided Serratus Anterior Plane Block – US-SAPB

The patient is in a supine position with the left upper limb abducted at 90 degrees. The costal arches are counted starting from the XII, moving upwards towards the head, using a dermographic pen to mark the V arch in the point where it crosses the anterior edge of the latissimus dorsi muscle. Surgical disinfection of the pectoral region, axillary cavity and lateral chest wall is also performed. 22G echogenic needles (SonoTap, Pajunk, Geisingen, Germany) of variable lengths ranging from 50 to 120 mm are prepared, depending on each patient's conformation, along with a high frequency linear ultrasound probe (US) (7.5–12 MHz).

Another possible approach to identify the V costal arch, consists of positioning the probe on the angle of Louis well-known anatomical landmark, formed by the junction between the manubrium and sternal body, moving the probe laterally you will find the second rib, shifting in caudal direction obliquely towards the axilla, where the pectoralis major muscle, the minor pectoralis and the underlying axillary vessels are identified. We count the ribs and reach the V rib, above which the target fascial plane is identified. At this level, the thoracic-dorsal artery is a useful anatomical



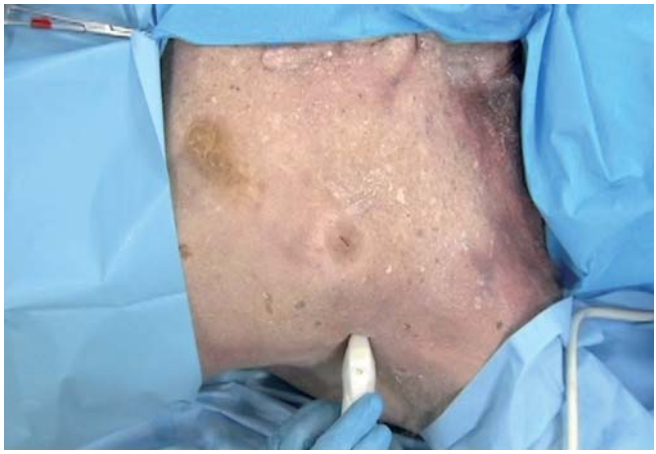


FIGURE 8.2
Ultrasound anatomy of lateral chest wall over the V rib.

landmark. It can sometimes be visible with Color Doppler ultrasonography. The linear probe is positioned parallel to the 5th costal arch, anteriorly to the latissimus dorsi muscle. The probe is slowly shifted dorsally to reach the latissimus dorsi, which is identified by ultrasound together with the serratus anterior (Figure 8.2).

Before starting the procedure, the site is infiltrated with 2 mL of lidocaine 1%, although most of the time this infiltration is not necessary. Then the catheter-needle 'priming' system is filled with physiological solution to avoid introducing hyper-echogenic air spots. The echogenic needle is

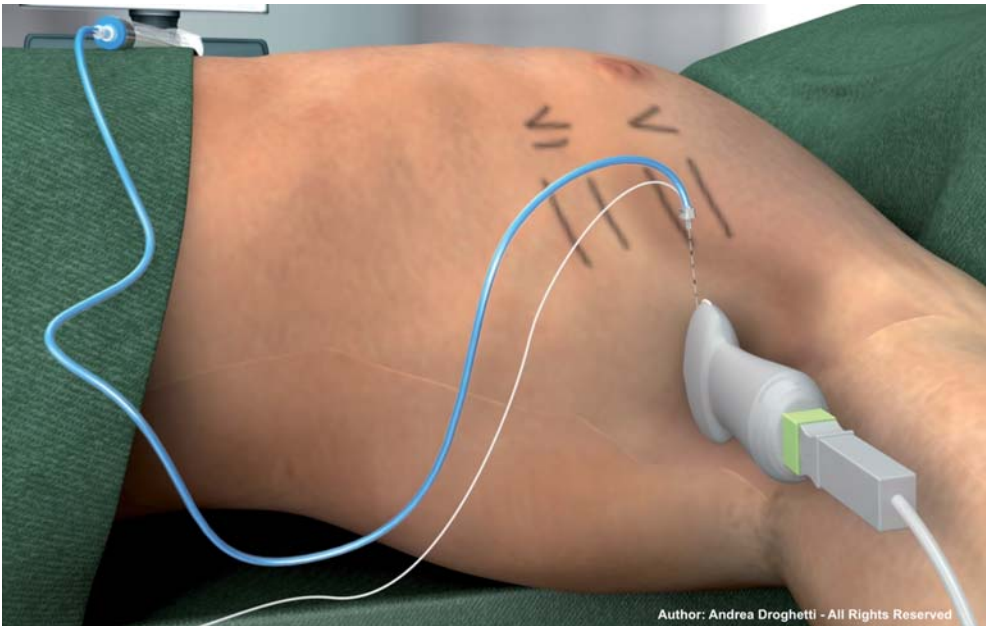


FIGURE 8.3
Needle and ultrasound probe 'In Line' on the V costal arch.

inserted at a distance of about 1 cm from the probe 'in plane' in an antero-posterior direction (Figure 8.3).

The US-SAPB can be performed with two different approaches, either superficial or deep. In the former, the anaesthetic is injected into the anatomical section between the serratus anterior muscle and the grand dorsal muscle. Instead, in the latter, it is injected into the area between the serratus anterior muscle and the plane of the costal arches and intercostal muscles, but always in level with T4 and T5

After the interfascial plane between the 2 muscles has been identified and a 1–2 mL test bolus of saline solution is injected showing a small anechogenic 'hydro localisation' pocket, it is necessary to find the tip of the needle which, if correctly positioned, will lead to dissection of the plane itself. At this point, 30 mL of a long acting local anaesthetic (Ropivacaine 0.75% or Levobupivacaine 0.5%, max 3 mg/kg) solution is injected in increments of 5 mL, ensuring appropriate aspiration to prevent intravascular injection. The purpose of this technique is to provide adequate anaesthesia and analgesia to the thoracic region where the implant is located, covering most of the patient's anterolateral hemithorax at a dermatomal level from T2 to T9 (Figures 8.4 and 8.5).

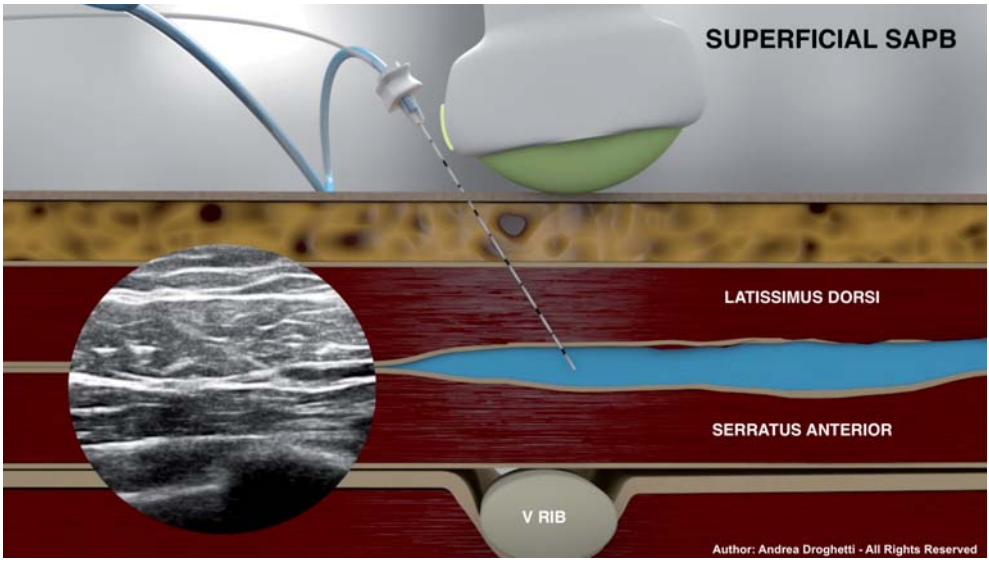


FIGURE 8.4
Superficial US-SAPB.

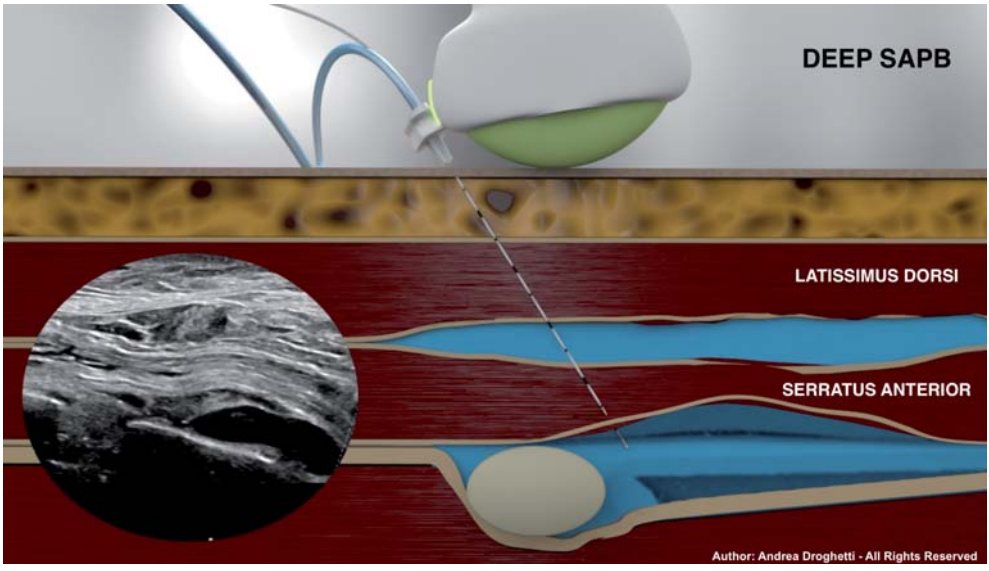
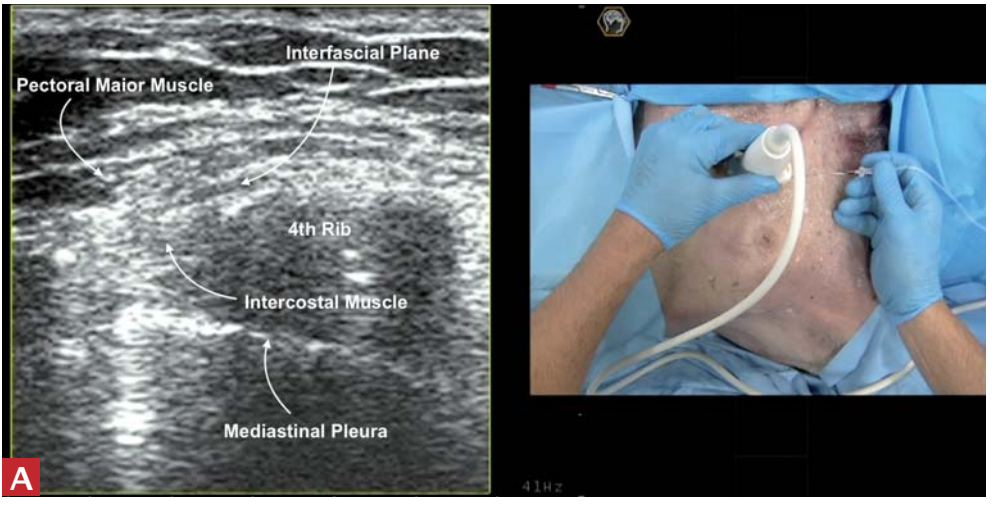


FIGURE 8.5
Deep US-SAPB.

Ultrasound-Guided Parasternal Block – US-PSB

Although the preliminary results related to the use of US-SAPB are extremely satisfactory, our experience has shown that some patients might experience intraoperative pain at the time of parasternal tunneling of the device[2]. This problem could be explained by the fact that the US-SAPB does not block the anterior branches of the intercostal nerves, which provide innervation of the parasternal area and do not communicate with the lateral branches of the same nerves[9]. The US-PSB, recently described by Droghetti and colleagues mainly applied to S-ICD implant[10] to ensure blockage of the anterior branches of the intercostal nerves. This is necessary to provide adequate coverage of the parasternal region from T2 to T6 during S-ICD implantation. The combination of this technique with US-SAPB thus ensures complete anaesthesia and analgesia of the anterolateral chest wall.



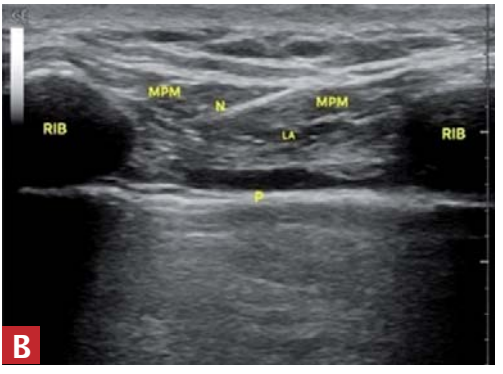


FIGURE 8.6

A) Ultrasound-guided Parasternal Anatomy and block. B) Ultrasound-guided Parasternal block.

When the patient is in the supine position, a linear high frequency probe (7.5-12 MHz) is placed over the angle of Louis in a longitudinal position, recognizing the junction between the manubrium and sternal body, moving the probe laterally we find the second rib, and shifting in caudal direction we count the ribs and reach the IV rib. The short axis view of the IV rib is taken with the corresponding posterior cone of shadow, the pectoralis major muscle over, the intercostal muscles and pleural sliding due to slipping of the mediastinal pleural leaflet over the parietal one. The target fascial between pectoral major and intercostal muscles or rib plane is identified.

A 22 G, 50 mm echogenic needle is inserted 'in-plane' to the ultrasound beam in a cranio-caudal direction, following the direction of the upper margin of the IV rib. This avoids the intercostal vascular nerves and protects the tip of the needle from a possible pleural puncture. US-PSB needs two separate injections, namely 5 mL of Levobupivacaine 7.5% at the level of the IV and VI intercostal space, targeting the interfascial compartment between the pectoralis major muscle and the intercostal muscles at the level of the external intercostal membrane (Figure 8.6).

Intraoperative Sedation

In the operating room, after obtaining venous access, it is essential to ensure adequate monitoring of the patient's vital parameters, making sure that there are always drugs for cardio-pulmonary resuscitation available and a 20% lipid emulsion (Intralipid®) in the event of systemic toxicity from local anaesthetics (LAST). When it is time to make the skin incision, the operator can still perform, if necessary, an infiltration of skin and subcutaneous tissue with a rapid onset local anaesthetic drug (e.g., Lidocaine or Mepivacaine). Adequate procedural sedation should be guaranteed both during the implantation procedure and before inducing ventricular fibrillation. It is important to underscore the fact that the main cause of morbidity and mortality associated with sedoanalgesia is drug-induced respiratory depression and subsequent obstruction of the airways with a risk ratio that is directly proportional to the level of sedation and its duration. Hence, it is recommended to consider the evaluation criteria of the level of sedation and to check the availability of all necessary aids to cope with any complications. The level of sedation can be clinically evaluated by using different scales, such as the Ramsay scale, in combination with instrumental monitoring, such as the Bispectral Index (BIS).

During the S-ICD implantation procedure, the goal is to have the patient capable of responding to verbal commands while maintaining spon-

taneous breathing and airway patency (Ramsay sedation score <4, with BIS target values between 60 and 80)[11]. Procedural sedation can be obtained by continuous infusion of Propofol at a dosage of 2–3 mg/kg/h, in combination with the administration of supplemental oxygen (4–6 L/min, 35–50% FiO_2-inspired oxygen fraction), using a Venturi mask to keep the end-expiratory CO_2 ($EtCO_2$) level under control and to guarantee an oxygen saturation percentage (SaO_2%) higher than 90%. The heart rate, ECG, blood pressure and SaO_2% are constantly monitored during the implantation process.

Alternatively, a drug that can be used successfully is Dexmetomidine, alpha 2 agonist that is administered as a loading dose of 0.8–1 mcg/kg in about 15 minutes and then reduced to continuous intravenous infusion at a dosage of 0.2–0.4 mcg/kg/h, which enables the patient to be capable of responding to commands and protective airway reflexes[12]. The only side effects of this drug are bradycardia and hypotension that can be avoided by properly titrating the drug.

Conclusions

US-SAPB and US-PDB can be the loco-regional anaesthesiological/analgesic approaches utilized during surgical procedures involving the incisions on the anterolateral thoracic wall, such as in the case of S-ICD implantation. These techniques offer several advantages, compared to traditional techniques. There are relatively simple to perform, have a high success rate and few complications. These blockings, when performed by experienced operators, have shown a good efficacy and safety profile. In addition, the targeted anatomical structures are rather superficial and, therefore, posing minimal risk to internal structures of the thoracic cavity such as blood vessels and pleura membrane.

The risk of LAST after the execution of US-SAPB and US-PSB can be linked to the large volumes (i.e., max 3 mg/kg) of anaesthetic management employed. However, this risk is limited because the injection of the anaesthetic solution is always carried out under ultrasound guidance and in an area fewer blood vessels. In addition, US-SAPB and US-PSB can be executed from 40-60 minutes up to a few hours before implantation, thus facilitating the preparation of the procedure and ensuring optimal coverage of intra and post-implantation pain with a subsequent reduction of patient discomfort after the procedures. Based on our experience, the possible inadequate coverage of the medial region during the tunneling of the device through the parasternal incision can be overcome by performing an US-PSB in association with the US-SAPB.

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CHAPTER 9

S-ICD Implantation: Two-Incision Technique with Creation of an Intermuscular Pocket

A. Droghetti, V.Y. Njike

Three incisions were previously used to create a subcutaneous pocket on the lateral chest wall to install an implantable cardioverter defibrillator (S-ICD). This chapter describes an alternative novel technique that requires only two incisions to create a deeper pocket (i.e., between two muscles of the chest wall) to install the S-ICD. This two-incision procedure which eliminates the upper parasternal incision was initially described by Knops and colleagues. They introduced the use of a peel-away for parasternal tunneling of S-ICD device, thus avoiding a possible site for dehiscence, infection, decubitus and an unsightly scar[1]. We want to describe further the evolution of the implant technique, now widespread in Italy and across Europe, which substitute the usual subcutaneous allocation of S-ICD device into a deeper virtual and natural pocket, which is present in the human body between the latissimus dorsi and the serratus anterior muscles. Hence, it is called 'intermuscular' implantation technique[2]. This approach helps to reduce patient discomfort, ensure better aesthetic results and reduce pocket-related complications that were observed in the three incisions subcutaneous technique (Figure 9.1).

Anatomical Details

The intermuscular technique emerged from thoroughly understanding in detail of the anatomy of the chest wall and the muscular planes that cover it. The S-ICD finds its ideal location in a natural pocket of the human body formed by the latissimus dorsi or grand dorsal and serratus anterior muscles.

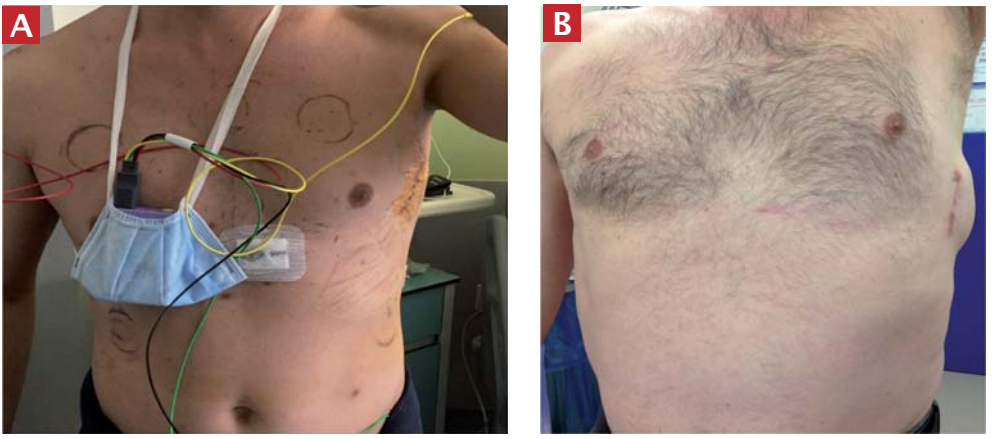

FIGURE 9.1

Aesthetich results of two incision intermuscular technique (A) and three incision subcutaneous technique (B).

Latissimus dorsi is the largest muscle in the human body and covers the posterolateral part of the chest. It is subtended between the small tuberosity of the humerus and the medial third of the iliac crest, dorsally reaching the thoracic and lumbar vertebrae; hence, it was called by the Latins 'Musculus tersor seu scalptor ani'. The serratus anterior muscle originates from the medial margin of the scapula and is inserted in front of the first 10 ribs.

The S-ICD device is usually placed between the left VI rib and the VII ribs to optimise the defibrillation vector. In this site, the grand dorsal muscle in its thoracic path forms the posterior wall of the axillary cavity and runs towards the iliac crest. Deep inside the grand dorsal muscle is the serratus anterior muscle. The two muscles are easily recognisable due to the different orientation of their muscle fibres, the former being cranio-ocaudal and the latter being oblique (Figure 9.2). In this area there is the Charles Bell nerve or long thoracic nerve, which descends posteriorly to the roots of the brachial plexus and anteriorly to the scalenus posterior muscle, and runs along the chest wall in the mid-axillary line and lie on the superficial surface of the serratus anterior muscle (Figure 9.3). This nerve is responsible for the innervation of the serratus anterior muscle; due to its length and its relatively superficial course. The long thoracic nerve is susceptible to damage during the implantation of an S-ICD from either by risk of direct trauma or stretching. When the long thoracic nerve is injured, a phenomenon known as winging of the scapula results.

The virtual space without blood supply located between the fasciae of

these two muscles is the ideal site to position the S-ICD. Therefore, it would be more appropriate to refer to the procedure as an 'intermuscular' implantation of an S-ICD device (Figure 9.4)

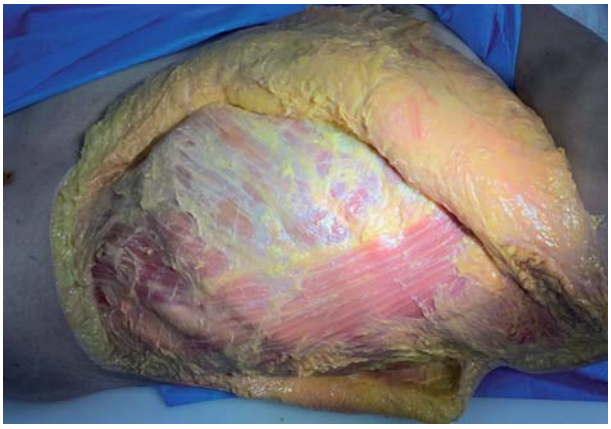

FIGURE 9.2
Chest wall anatomy: different orientation muscles fibres.

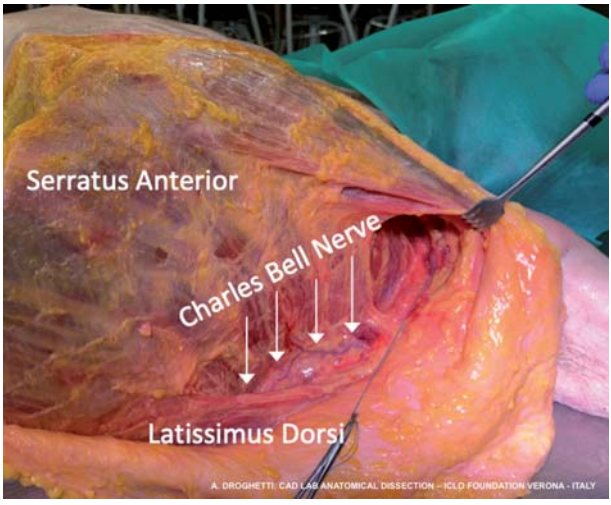

FIGURE 9.3
Chest wall anatomy: Charles Bell nerve or long thoracic nerve.

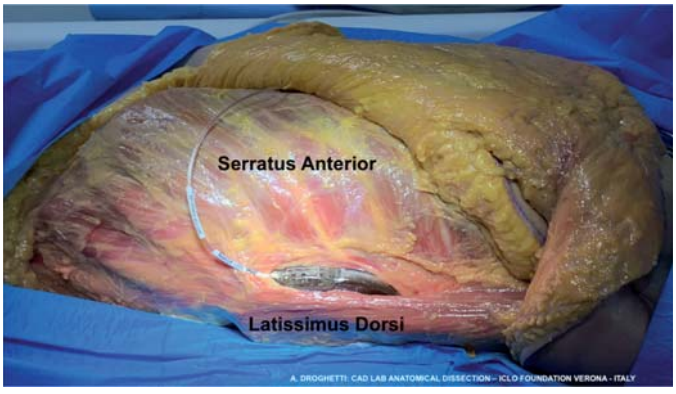

FIGURE 9.4
Avascular planes and intermuscular pocket.

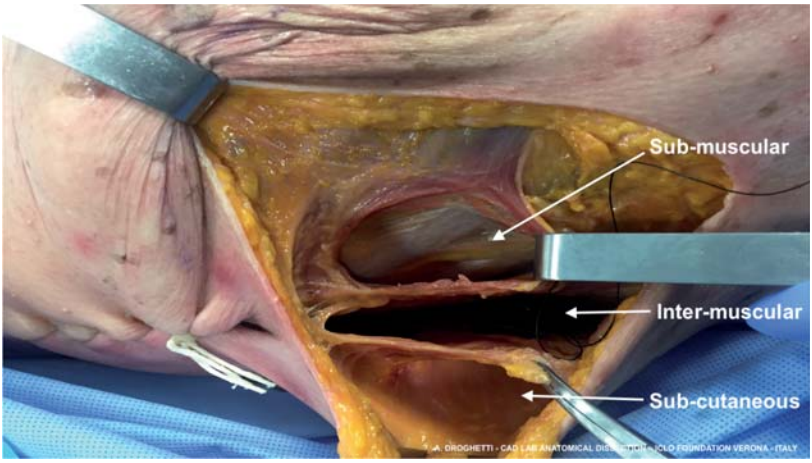

FIGURE 9.5
Three different pockets for S-ICD.

There are three possible pockets to create in the lateral chest wall:. the-first is the old standard in subcutaneous fat thickness; the second is the sub-muscular, which is created directly on the ribs plane under the serratus anterior muscle; and the third is the gold standard intermusclar pocket, which is created between latissimus dorsi and serratus anterior muscles (Figure 9.5).

Enrolment Screening

Before implantation, each patient undergoes the recommended automatic screening test. The screening test is a modified 3-channel surface electrocardiogram (ECG), which mimics the sensing vectors of the S-ICD system to exclude patients with an unfavourable R/T wave ratio[3]. Once the 3 ECG vectors have been obtained, the appropriate instrument is used to evaluate the R/T wave ratio and selects the best corresponding vector. The device will use only 1 of the 3 detection vectors, selected based on the result of the screening test[4–6].

How to Do It: the Two-Incision Technique with Intermuscular Pocket

Patient Positioning

The patient is placed in a supine position; some operators prefer the left hemithorax to be slightly raised from the operating table at an angle of

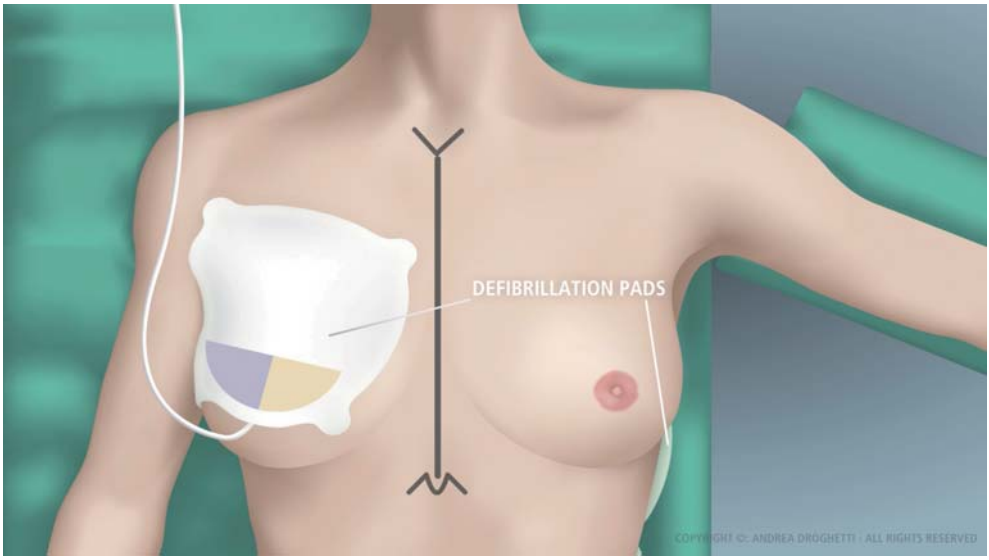

FIGURE 9.6
Patient position.

35°. This position can be obtained by placing a support, such as a 'squeezer bag', under the shoulder blade of the patient. The bag can be inflated and deflated during the different implantation phases. Both upper limbs are abducted at 90° to expose the thoracic wall to the left and give easy venous access to the right. The paddles for external defibrillation are then positioned in the right pectoral area and the left dorsal chest wall (Figure 9.6).

Pre-Implantation Vector Optimisation

There is no difference in performing the pre-implantation vector optimisation procedure either in an electrophysiological laboratory or in an operating room in accordance with the standard sterilization guidelines[7]. A dermographic pen is used to draw the anatomical references that are useful for temporary positioning of the demo system. These landmarks are the median longitudinal sternal line from the jugular process to the ensiform appendage, the V and VI ribs, and the anterior margin of the grand dorsal muscle, identified by asking the patient to push up the arm along the side as the operator pushes down (Figure 9.7).

The catheter is fixed along the parasternal line with the proximal ring approximately 1 cm upwards, compared to the xiphoid appendix. The generator is positioned on the left lateral thoracic wall with the upper edge aligned at the VI rib and the ventral one along the anterior margin of the grand dorsal muscle. Both are held in place by adhesive bandages that se-

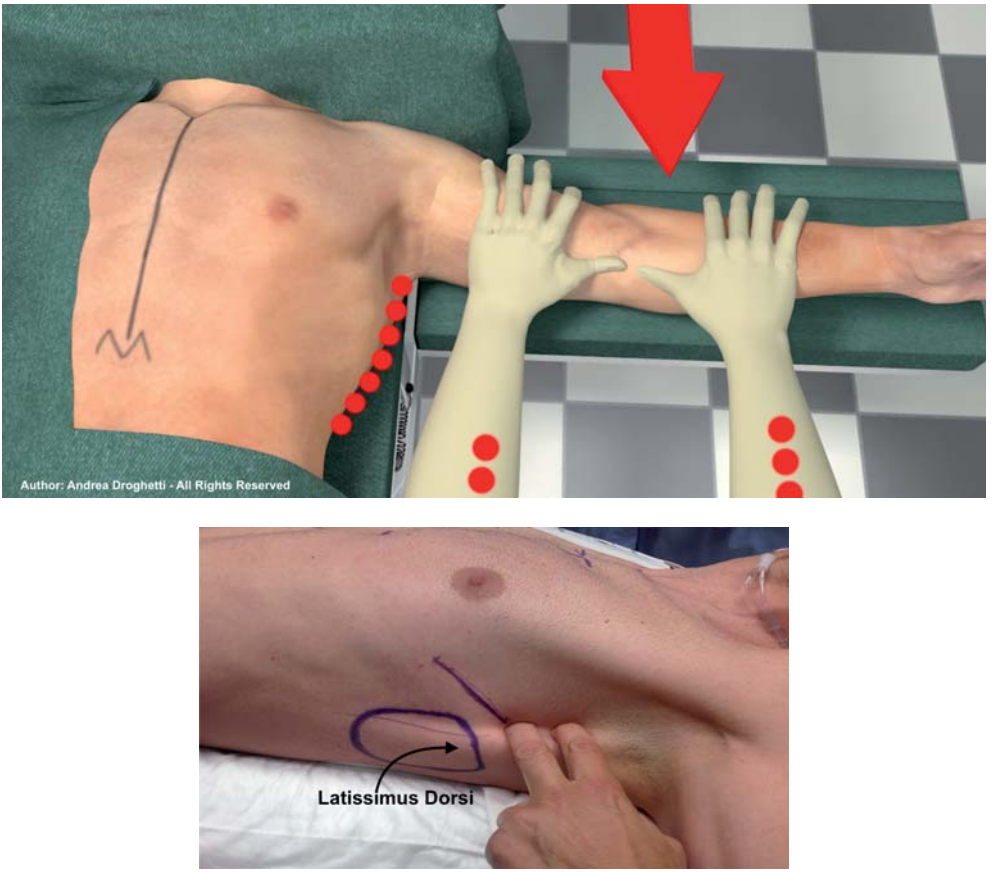

FIGURE 9.7
Anatomical references: latissimus dorsi contraction.

cure them to the patient's skin to perform a standard anterior-posterior chest X-ray. The chest X-ray allows for the confirmation of the defibrillation vector or, when necessary, to make small craniocaudal corrections to optimise the vector, including the largest possible mass of the left heart (Figure 9.8).

Once the vector optimisation has been found, the parasternal incision line is drawn using a dermographic pen along the sleeve, with the medial limit reaching the longitudinal parasternal tunneling line.

The second surgical incision, the one to cover the intermuscular pocket, is drawn making sure there is a distance of about two inches from the cranio-ventral edge of the defibrillator, following the 'Langer lines', which are parallel to the line of the ribs in the lateral thoracic surface. The mark

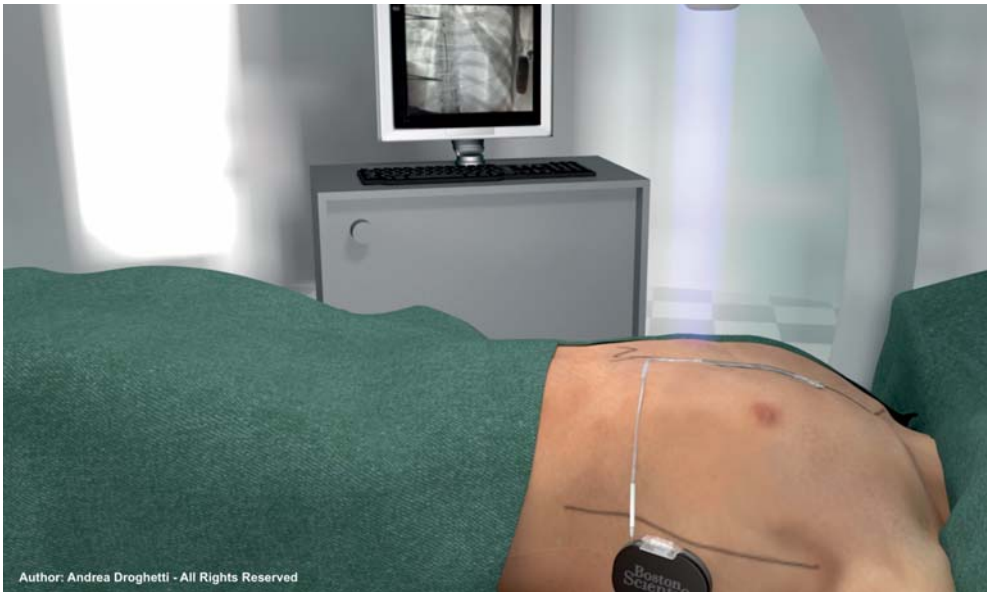

FIGURE 9.8
Vector optimisation using chest X-ray.

will be pushed back until it overlaps the grand dorsal muscle for about 1 cm (Figure 9.9).

Lastly, the path of the catheter is drawn as a reference to the direction that needs to be followed during tunneling (Figure 9.10).

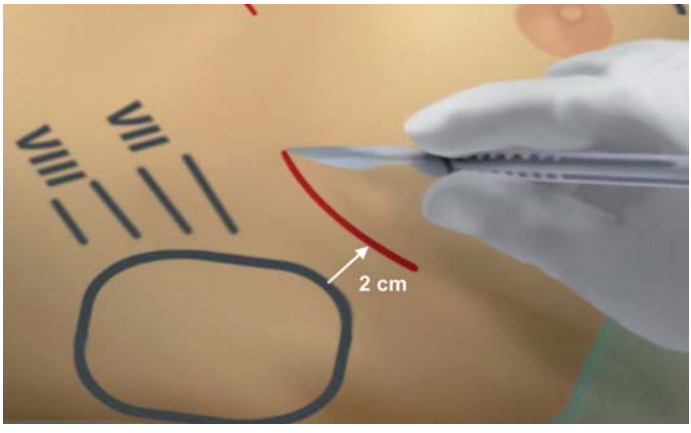

FIGURE 9.9
Correct pocket skin incisions following Langer's lines.

Operating Field

Disinfection concerns the entire surface of the left hemithorax, extending to the contralateral anterior wall, cranially reaching the jugular process and caudally the transverse umbilical line. We prefer to use an alcohol-free antiseptic solution based on Iodopovidone, which is active against both Gram positive and negative bacteria, fungi, protozoa, yeasts and some viruses, with the advantage of not altering the dermographic lines. This approach is better tolerated by the skin and mucous membranes with less irritation.

A polyethylene transparent film Steri-Drape™ (3M, St. Paul, MN, USA) with appropriate size is applied after the surface has been disinfected but before delimiting the surgical field with sterile sheets. It is also important to include the posterior axillary line, the jugular process, the counterlateral parasternal area and the ensiform appendix in the operating field (Figure 9.10).

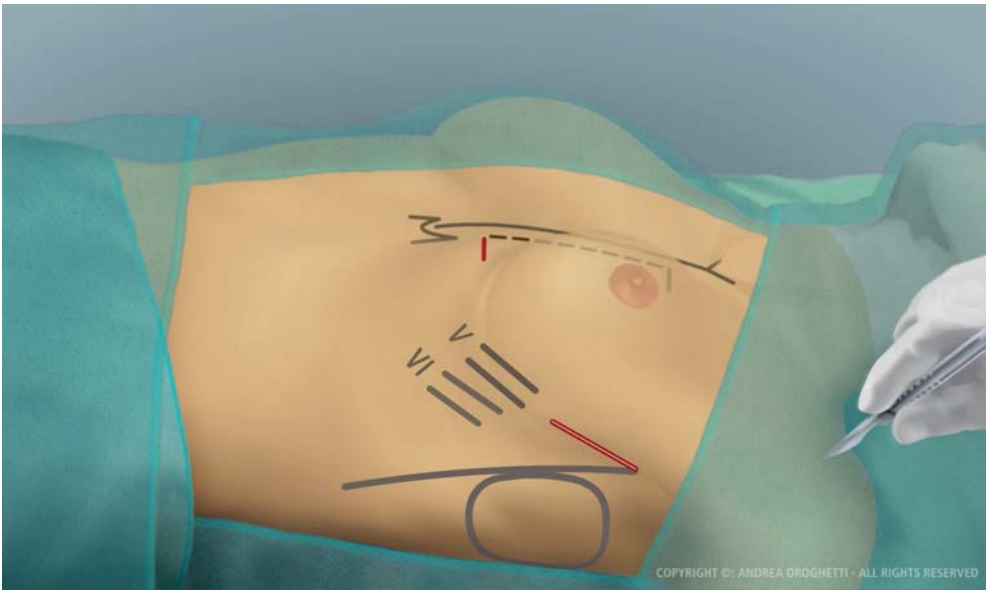

FIGURE 9.10

Operating field: skin landmarks using a dermographic pen, in red skin incisions.

No Blood Implantation Technique: Two-Incision Intermuscular S-ICD

Before performing the surgical incisions, a local anaesthetic is delivered to the surface area corresponding to the lines that have been drawn. These local anaesthetics with 2% Lidocaine have a rapid and long lasting action.

First Incision and Enclosing of the Intermuscular Pocket

The first skin incision performed is the lateral thoracic incision needed to create the defibrillator pocket. We use the No. 11 cold blade scalpel to precisely incise only the 'dermis' without touching the subcutaneous tissue to avoid unnecessary bleeding. It follows the dermographic design perfectly, performed during the vector optimisation phase, resulting oblique, like the Langer lines, which in this area are parallel to the ribs, and keeping a distance of at least 2 cm from the cranial-ventral edge of the device to avoid direct pressure of the incision and to minimise surface contact with the generator. For aesthetic and practical reasons, in women, this incision is made along the inframammary fold (Figure 9.11A).

The dissection of the subcutaneous tissue and the deeper tissues is, instead, performed using electro-cauterisation in coagulation mode at a 'forced' power of 60–80 W. Depending on the different subjective conformations, pre-muscular fat must be sectioned to full thickness, parallel to the skin incision and perpendicularly to the thoracic wall (Figure 9.11B).

All the adipose tissue must be sectioned gradually and in thin layers until a translucent and pearl-like plane is reached, represented by the muscu-

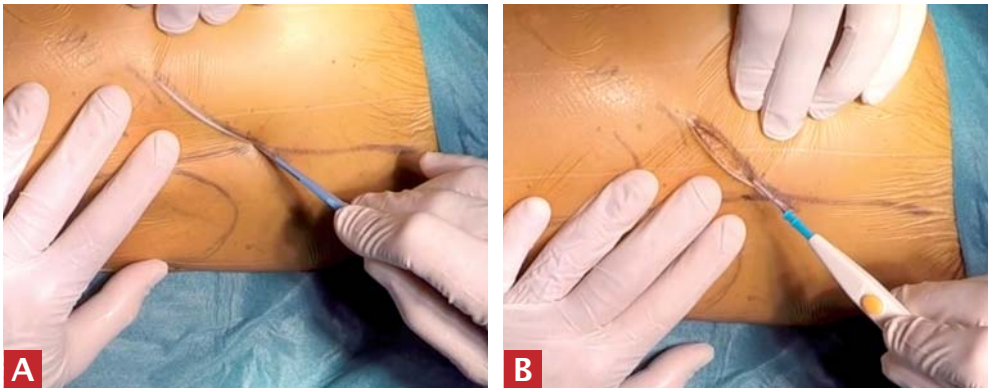

FIGURE 9.11

A) Langer's line skin incision, only dermis. B) Subcutaneous fat with electrocautery.

lar fascia, which must be preserved as much as possible to avoid damaging the underlying muscle and the Charles Bell nerve (long thoracic nerve). In the anterior 2/3 of the incision the prepared fascia will overlook the serratus anterior muscle, which is easily recognisable by the oblique direction of its fibres. Conversely, the dissection of the third dorsal exposes a band of muscle fibres in a longitudinal craniocaudal direction, which comprises the anterior margin of the latissimus dorsi muscle. The intermuscular connective tissue that joins the two muscles together must be dissected using the electrosurgical unit once again. This incision must be carried out parallel to the ventral margin of the latissimus dorsi muscle for a length that is more or less superimposable to that of the short side of the defibrillator. Gripping the edge of the latissimus dorsi muscle, with a Farabeuf retractor, it is then detached from the serratus anterior muscle (Figure 9.12). This leads to an exposure of an avascular plane, where the two muscle bands or fasciae can be easily separated in a non-traumatic way using two fingers, with a manoeuvre referred to as 'digitoclasia' in surgery (Figure 9.13).

The pocket is modelled following, as much as possible, the craniocaudal lines drawn on the skin before implantation procedure, during the vector optimisation phase and according to the sufficient dimensions needed

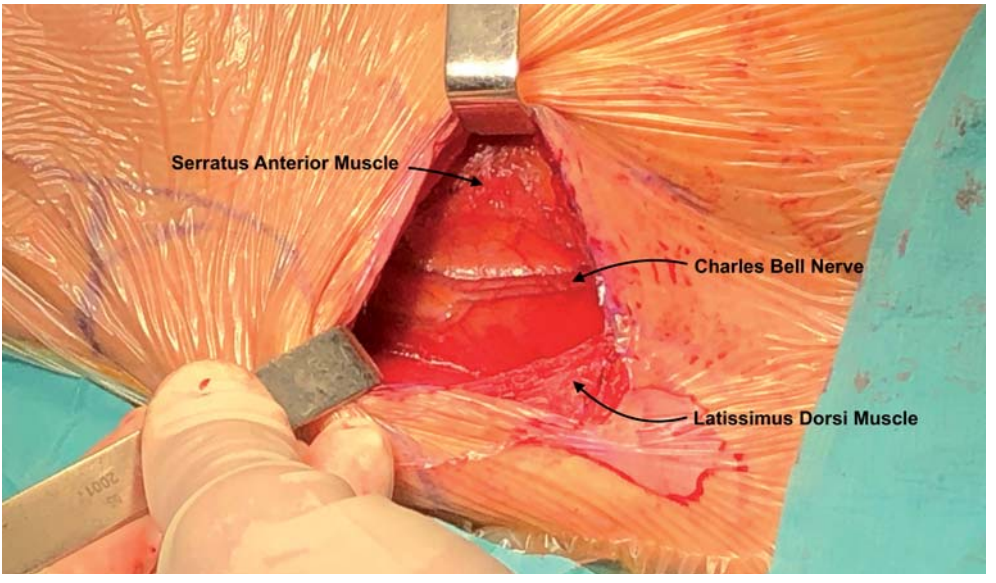

FIGURE 9.12

Intermuscular pocket and Charles Bell nerve, latissimus dorsi retraction with a Farabeouf.

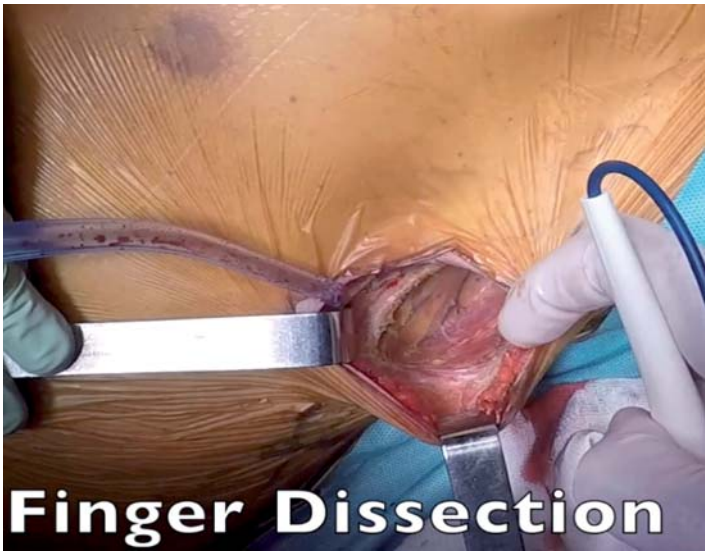

FIGURE 9.13
Digitoclasia.

to place the generator case, ensuring a tension-free pocket. This space is deeply enclosed underneath by the serratus anterior muscle and is externally enclosed by the latissimus dorsi muscle; hence it is called an 'intermuscular pocket' (Figure 9.14).

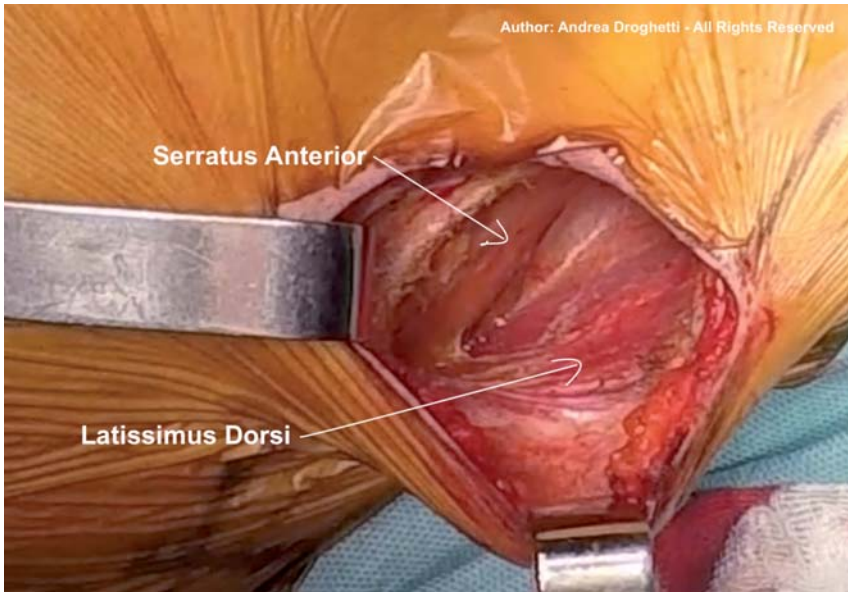

FIGURE 9.14
Intermuscular pocket, avascular plane between fasciae.

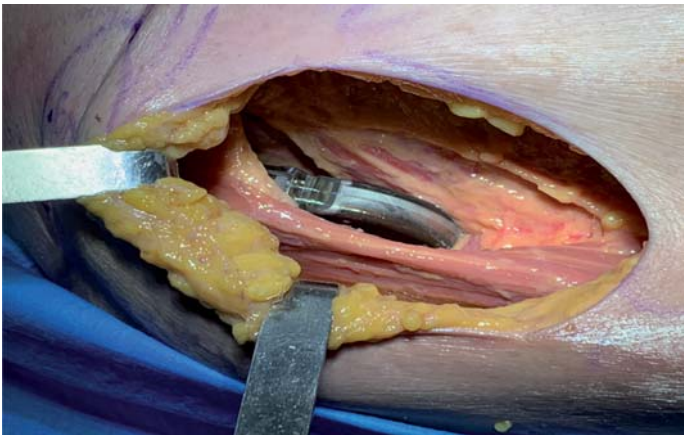

FIGURE 9.15
Intermuscular S-ICD.

It is essential for the S-ICD device to be completely covered by the latissimus dorsi muscle in the anteroposterior axis (Figure 9.15). The caudal limit of the pocket was previously marked with a dermographic pen approximately 1 cm cranially from the cutaneous limit because adduction of the left arm causes physiological caudalisation of the defibrillator.

Parasternal Incision

The second incision is left parasternal - it is hardly ever on the right - in a transverse direction and about 20 mm in length. Here too, subcutaneous fat must be dissected in all its thickness to reach the translucent muscular fascial plane (Figure 9.16). In this area, depending on its craniocaudal position, compared to the ensiform appendix, it will be possible to identify the pectoralis major with its lateromedial fibres near its sternal insertion, or the craniocaudal fibres going towards the rectus abdominus muscle at its insertion point to the V-VI and VII costal cartilages, as well as to the ensiform appendix itself. Once again an electrosurgical unit is used to create two small 'slits' by dissecting the fascial plane from the adipose tissue above the two extremities of the skin incision to correctly insert the tunnellisers.

Two non-absorbable sutures, interlaced with a 5/8 needle are placed passing the fascia in a craniocaudal direction, at a distance of about 1 cm from each other, and suitable for subsequent fixing of the catheter sleeve (Figure 9.16). After executing three knots, the two ends of the thread or wires are separated, one towards the jugular and the other towards the abdomen, and they are hung by two Klemmer clamps. This technical detail allows the instrument to penetrate, with less resistance, easily and safely,

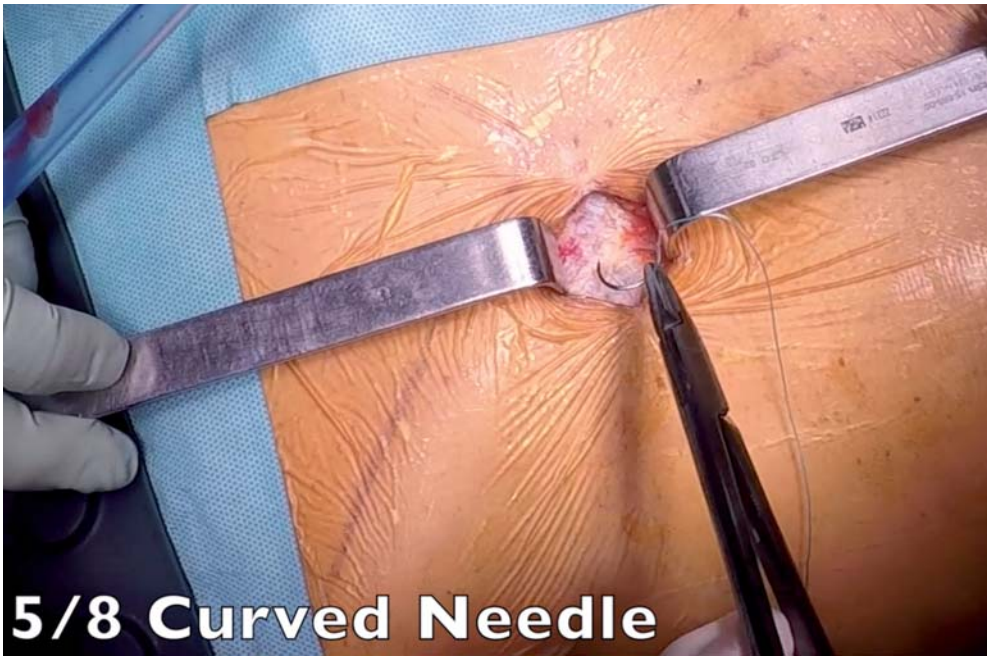

FIGURE 9.16
Parasternal pocket for the sleeve of the lead.

reducing the risk of bleeding or of too shallow positioning of the electrode.

Tunneling Technique

Now the two devices of the Electrode Delivery System (EDS) kit are inserted. The kit consists of 2 rigid and metallic tunnelers, each covered by a pre-assembled peel-away sheath. The two tunneling tools of the new electrode positioning system have different lengths, one for the longer lateral tunneling and one for the parasternal tunneling. The first tunneler is inserted into the side incision, pushing with the necessary force towards the side pocket. It is good practice to lift the tip of the tunneler every few centimetres to be sure that the iron has not gone too far into the intercostal muscles (Figure 9.17). Tunneling must be carried out on the fascial plane, not inside the thickness of the adipose tissue, and towards caudal extreme of the pocket. It is necessary to avoid tunneling directly towards the lateral skin incision, in order to prevent the catheter from passing along the incision line with the risk of being damaged during the procedure to reopen

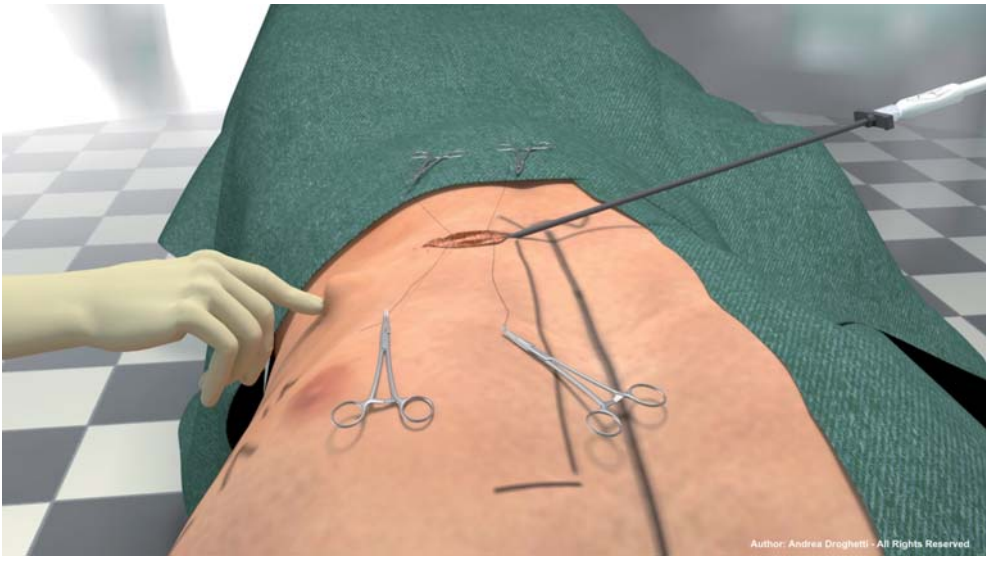

FIGURE 9.17
Lateral or side tunneling.

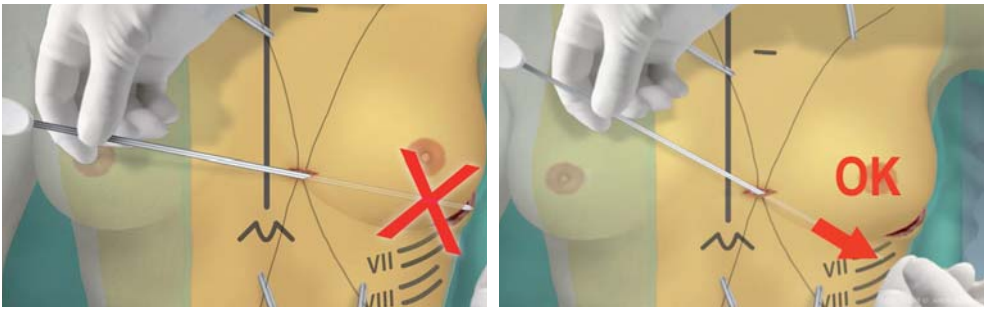

FIGURE 9.18
Lateral tunnelization.

the pocket to replace the generator (Figure 9.18). Once the end of the tool has protruded from the pocket, the metal tunneler is retracted, leaving the peel-away where the catheter is inserted, so that the connector for the generator remains towards the pocket. The catheter must be guided into the white sleeve and slid until it is placed along the parasternal incision. The peel-away sheath must then be removed.

The second parasternal tunneler is inserted into the medial end of the parasternal incision and pushed along the fascial plane parallel to the sternum along its entire length. In this manoeuvre it is fundamentally im-

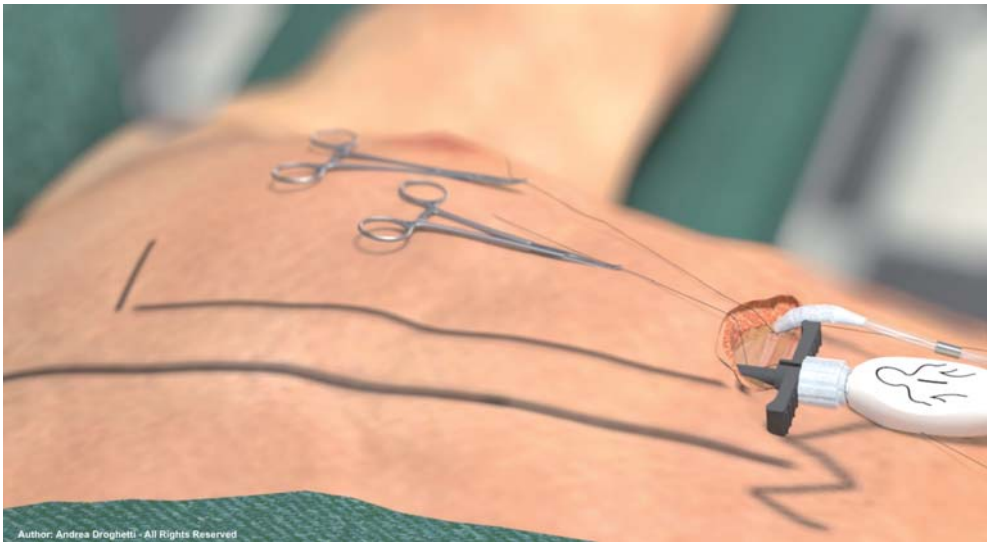

FIGURE 9.19
Parasternal tunneling.

portant to start tunneling on the muscular fascial plane and try to keep it there along the entire route, gradually raising the handle to allow the tip of the instrument to excavate in depth to follow the physiological deflection of the sternum towards the jugular vein (Figure 9.19). The metal part is removed leaving the peel-away in place and the tip of the catheter is introduced, taking care to have it straddling the wires hung by the Klemmer clamps. Once the entire length of the catheter is inserted, the peel-away is removed by opening it according to the traditional technique, taking care to keep the catheter sleeve in place using anatomical forceps in order to avoid retraction. The catheter is now in the desired parasternal subcutaneous position (Figure 9.20A). The 'sleeve' is secured to the muscular

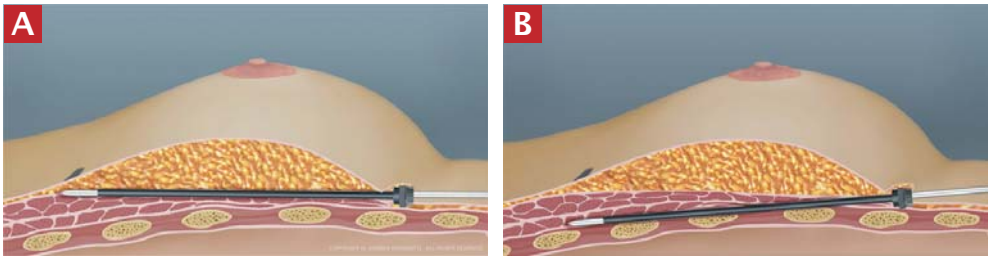

FIGURE 9.20
A) Subcutaneous tunneling. B) Submuscular tunneling.

FIGURE 9.21
Removing air bubbles.

fascia using the two previously fixed sutures. This is a critical step that requires maximum accuracy, as it prevents the displacement of the catheter, ensuring that the system functions correctly. A traction test is also run to ensure that the parasternal fascia is fastened properly. A craniocaudal massage of the parasternal electric catheter removes the small air bubbles that may be formed during tunneling procedure (Figure 9.21).

The proximal end of the catheter that comes out of the side pocket must be inserted into the appropriate orifice of the S-ICD device and screwed in. In this case, too, a traction test is performed to ensure the correct positioning. Further confirmation is given by closure of the circuit detected by the device through automatic control of system integrity. A non-absorbable and braided suture with calibre 0 or 1 must be passed over the serratus anterior muscle band and knotted without tightening too much to avoid the risk of ischaemia of the muscle fibres. When the device is housed in the pocket, the same needle will pass the suture through the appropriate channel of the device, in an internal-external direction, and knot it in order to hang it and keep it from sliding downwards. This step must be repeated in the second channel (Figure 9.22). The remote device will indicate system suitability by evaluating the impedance in the appropriate range.

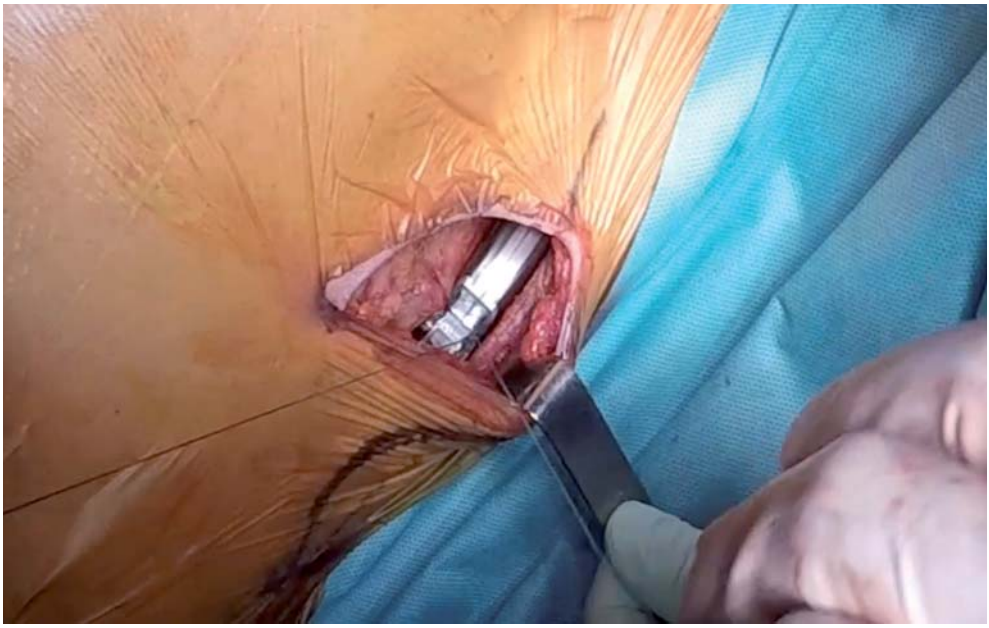

FIGURE 9.22
S-ICD fixation in the pocket.

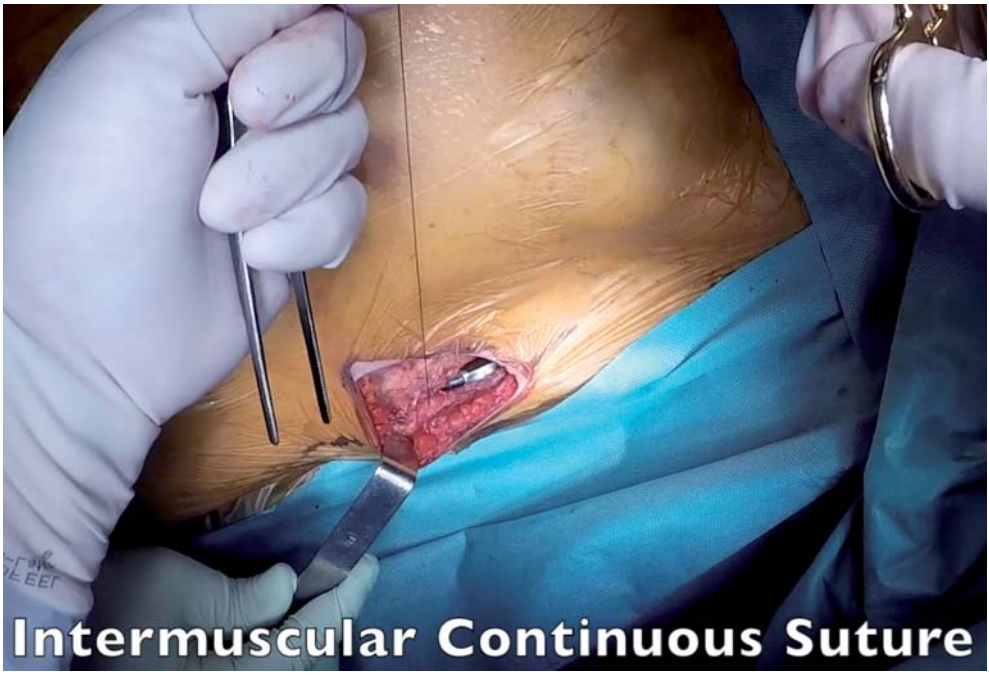

FIGURE 9.23
Continues suture closing intermuscular pocket.

Pocket closing is a very important step and the method must be carried out precisely in order to guarantee maximum protection, better aesthetic results and less complications. It begins with a continuous suture performed with an absorbable 0 calibre braided suture using a non-traumatic needle. The bands of the latissimus dorsi and serratus muscles must be sutured to restore their continuity, thus completely separating the placement pocket of the defibrillator from the subcutaneous planes (Figure 9.23).

Another continuous suture in reabsorbable 2/0 thread must be performed to close the subcutaneous tissue, which, in some cases, can be double-layered. The skin is closed with 3/0 or 4/0 suture thread or wire with rapid reabsorption in intradermal modality. The same method of closure must be performed for the subcutaneous tissue and the skin of the parasternal incision.

Tip and Tricks

The intermuscular pocket is easy to achieve because it uses an anatomical pocket that is already present in the lateral chest wall, the one formed by the latissimus dorsi muscle. This pocket, which is deeper than the subcutaneous one, provides excellent housing for the S-ICD device, which is almost imperceptible reducing aesthetic impact in particular in young patient and women (Figure 9.24). In fact, the S-ICD is covered by the latissimus dorsi muscle, which is an excellent protector. It proves to be a very valid technique, even if superficial infection caused by wound dehiscence could be a risk for device sterilization. It is protected by the

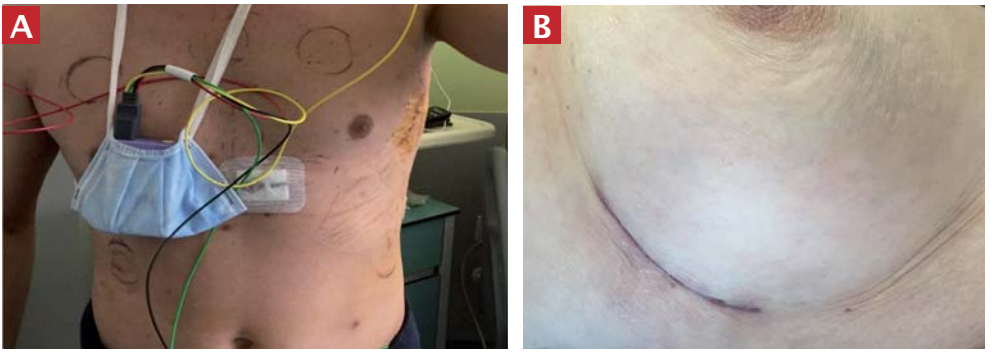

FIGURE 9.24

A) Aesthetich results of intermuscular technique. B) Submammary fold incision in women.

muscular barrier, and there is no harm. Furthermore, young and athletic patients benefit from being able to perform extreme movements without discomfort.

Obesity

The intermuscular technique is very useful in overweight or obese patients because the deeper positioning of the defibrillator, compared to a subcutaneous implant, reduces the thickness of adipose tissue that the energy from the implanted device must pass through and also reduces the distance to travel between the catheter and the defibrillator. Hence, it allows to us obtain an effective implantation even in these patients who would, otherwise, be unable to pass the defibrillation test with the standard technique. When a patient with class II or greater obesity is not converted to sinus rhythm at the first attempt due to a high impedance >130 Ohm, it is absolutely necessary to think about using the intermuscular technique.

When the intermuscular pocket is not sufficient in size, the other solution to avoid explanting the system is to reduce the thickness of the tissue between the catheter and the heart through subpectoral repositioning of the catheter. Once the parasternal fascia is attained, it is incised, causing the fibres of the underlying pectoralis major muscle to spread, reaching the cartilaginous costal surface of the sternochondral joints and making it possible to perform submuscular tunneling (Figure 9.20B). In the cases performed, the low energy 10 J test detected a significant reduction in the impedance value, and the subsequent defibrillation test was effective[8].

Decubitus and Subcutaneous Pocket Infection

The intermuscular technique is also used in cases in which complications such as device decubitus, skin perforation extrusion, pocket infection or simply aesthetically unacceptable results occurred after implantation with the subcutaneous technique. After the removal of the old implanted device, the old infected subcutaneous pocket is drained and cleaned. The deeper intermuscular pocket completely separated from the previous one and closed between two muscle walls, allows the implantation of the new S-ICD system to be completed while preserving the sterilization of the device. Many implants have been saved thanks to this method and these patients have not been explanted and they keep their lifesaving defibrillator in place. This aspect is a big advantage of the S-ICD system compared to traditional transvenous implants in which an explantation is required in the event of an endocardial infection to save the patient's life: a procedure

not without risk of major complications. Therefore, this great advantage of the S-ICD system necessitates a 'Mind-Shift' on the part of operators who must change the management approach to infections of a subcutaneous implant (Figures 9.25 and 9.26).

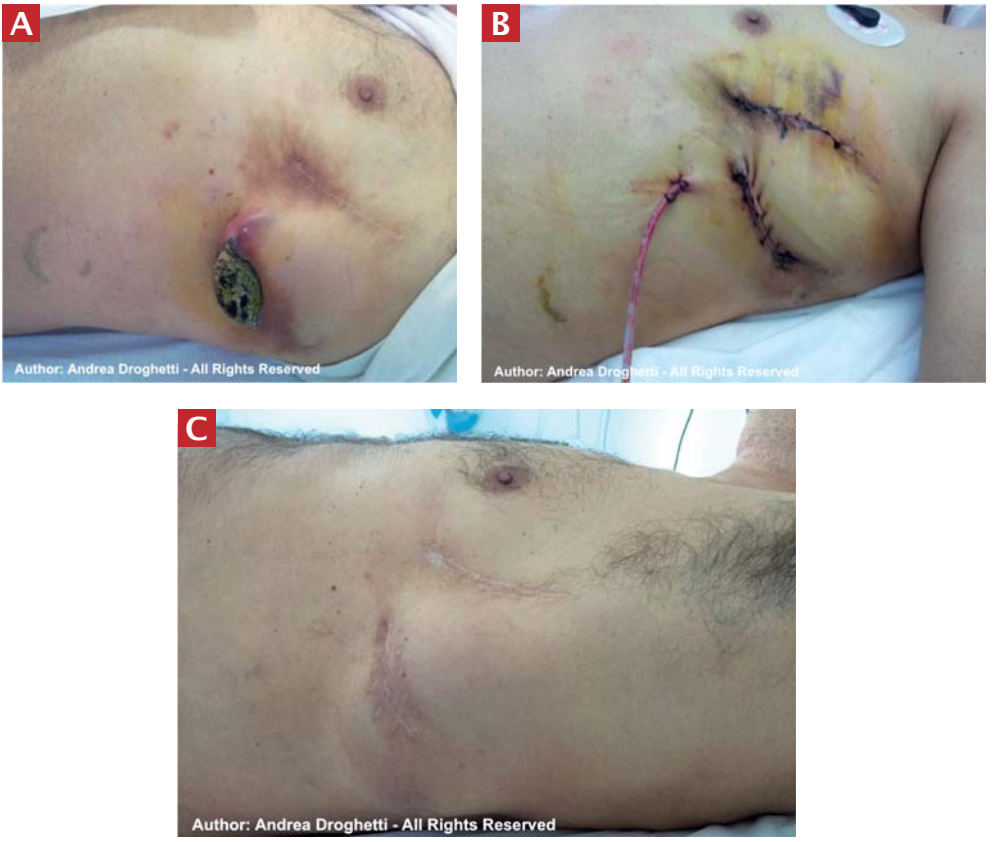

FIGURE 9.25

A) Decubitus. B) Explantation, subcutaneous pocket drainage and intermuscular reimplantation. C) 1 year follow-up.

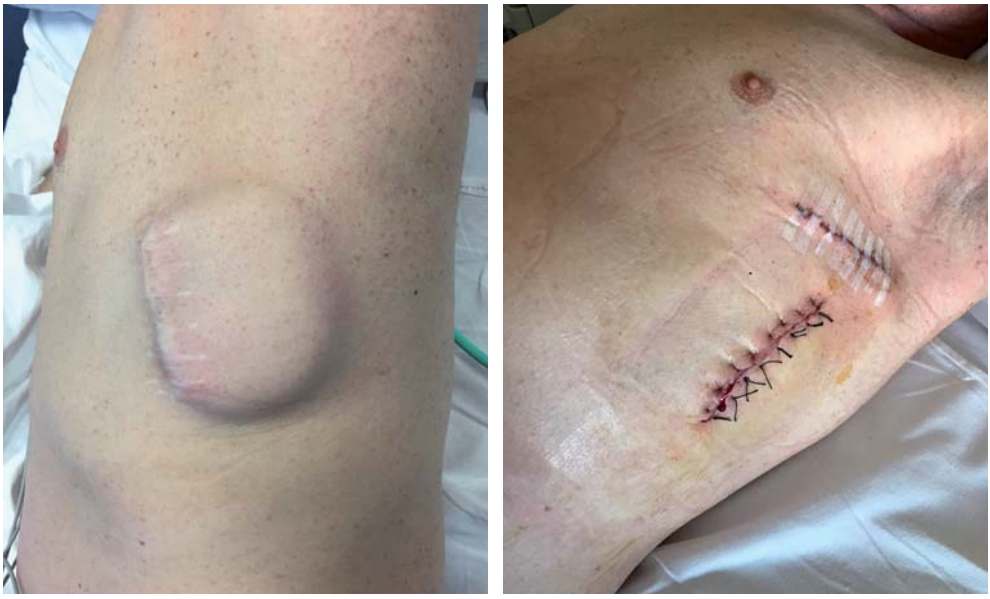

FIGURE 9.26
Upgrade from subcutaneous to intermuscular pocket.

Protocol Procedure

Two-Incision Intermuscular S-ICD Implant

Patient

- *On the Ward*
  - Patient preparation - day 1:
    Thorax and left armpit trichotomy
    Chlorhexidine shower
    Fasting from midnight
  - Preoperative routine (blood tests, blood coagulation)
- *Operating Room/Cath lab*
  - Patient positioning
  - Plates for external defibrillator
  - Right thigh electrosurgical plate
  - Anaesthesiological management: loco-regional SAPB blockade and sedation
  - Pressure and ECG monitoring by polygraph or defibrillator (12 derivations)
  - Team position: 2 operators, 1 operator on the left, help on the right

Instruments

- *In the Operating Room*:
  - Dermographic pen
  - Standard chest X-ray or X-ray image intensifier
  - External biphasic defibrillator
  - Electric scalpel (setting: coagulation 60-80W forced mode)
  - S-ICD Tablet programmer with relative printer
- *Operating Table*:
  - Surgical drapes: 2 large (head and feet) and 2 small (lateral)
  - Steri-Drape large
  - Farabeuf: 2 small or medium
  - Surgical Scalpel Blade No. 11
  - 2 surgical clamps
  - 2 anatomical forceps
  - 1 pair of suture scissors
  - 4/6 Klemmer clamps
  - 1/2 needle holders
  - 2 Klemmer pliers
  - *Suture threads:* 2 threads 0, NON absorbable, braided, with needle 5/8; 1 wire 0 or 1 NON-absorbable, braided for defibrillator fixing; 2 wires with rapid 3/0 or 4/0 absorption for intradermal
  - S-ICD-Emblem
  - SQ-Track electric catheter
  - Kit for tunneling
  - Screwdriver

Operation Time Schedule

- Preparation, patient positioning, anatomical landmarks drawing (latissimus dorsi and median sternal line)
- Positioning simulation with Demo S-ICD and Coil with chest X-ray
- Pocket design and skin incisions
- Prepare sterile field
- Local anaesthesia and sedation of the patient
- Intermuscular pocket enclosure according to the routine technique
- Second left parasternal caudal incision
- Tunneling of the catheter in the pocket
- Coil tunneling in left parasternal
- Electrode connection to the S-ICD generator
- S-ICD in pocket and fixing
- Suture for faciae planes
- VF induction and conversion test (protocol foresees testing 65 J on the induced event)

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Chapter 10

Early and Late Complications of S-ICD Implantation

G. Bisignani, S. De Bonis, A. Bisignani

The evaluation of possible complications of the implantation of an S-ICD is a very interesting concept because, since it is a device that does not touch the heart, it should theoretically have fewer adverse events than T-ICD.

Practicability and safety studies have been characterised and, subsequently, research registers, thanks to the accurate and extensive documents regarding S-ICD function, effectiveness and complications. The use of S-ICD has been strictly verified and continuous data acquisition has produced perspective documentation, updated in real time, of the activity of each single device.

The adverse event verification process has progressed somewhat differently from the one carried out for a long time with transvenous ICD. In T-ICD, the acknowledgment of a higher complication rate in clinical practice than in the results of randomised trials and long-term occurrence are essentially attributed to the large prospective registers starting from the 2000s, that is over 10 years after the transvenous device was introduced into clinical practice (Figure 10.1).

Despite a certain heterogeneity of the classification criteria of adverse events, the various registers and case studies on S-ICD have given us a continuous and updated surveillance of every problem related to the device. The use of a census and classification modelling approach of the complications, with peculiarities specific to each study, generated a greater decomposition of events within specific study categories, without affecting either the documentary precision of each event or easy description and grouping of the most significant complications.

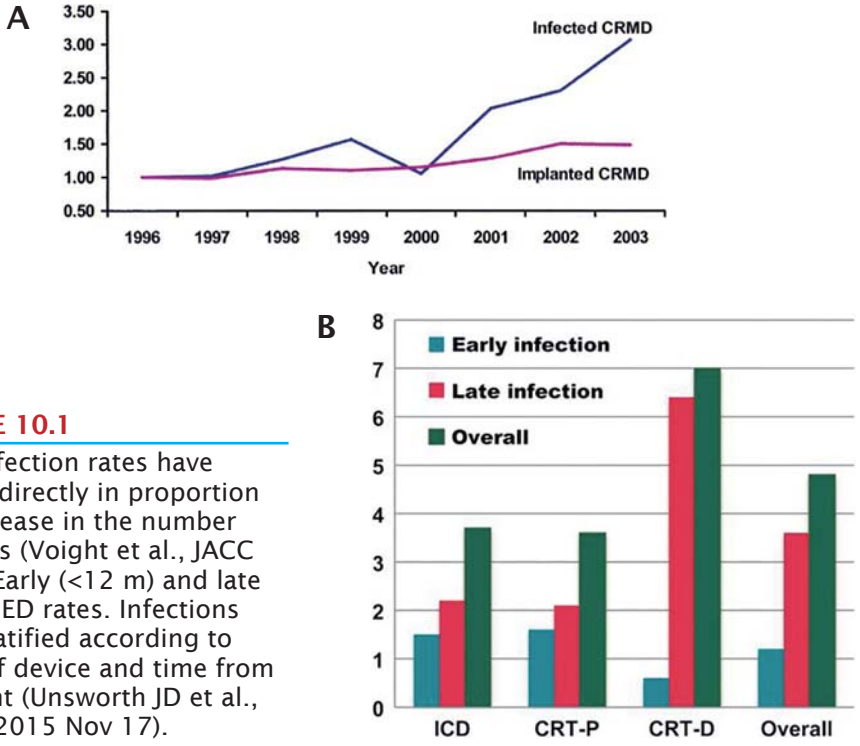

FIGURE 10.1

A) CIED infection rates have increased directly in proportion to the increase in the number of implants (Voight et al., JACC 2006). B) Early (<12 m) and late (>12 m) CIED rates. Infections (%) are stratified according to the type of device and time from the implant (Unsworth JD et al., Europace 2015 Nov 17).

For the purposes of this review, and in light of the above, an analytical grouping of complications made up of three categories can be adopted:

1. Complications related to the implant procedure, mostly early appearance
2. Device-related complications and early and late infectious complications
3. Complications from impaired detection of tachyarrhythmia, mainly represented by inappropriate shocks, considered at different times (usually: at 1 month, at 1 year, for each year, after long-term follow-up).

Preliminary Data

Preliminary cases, limited to a total number of 87 patients published between 2011 and 2012[1–3] with a prevalent indication of arrhythmic syndromes showed a low percentage rate of surgical complications of the implantation. Such complications were mostly treated with a conservative intervention, safely and with relatively easy explantation of the system, with a discreet amount of inappropriate shocks (8–25%) mainly due to oversensing of the T wave.

Larger multicentre studies published later reported, in a total number of 229 patients, a higher percentage rate of consistent surgical problems. In 7–8% of cases the problems were confined to the subcutaneous location and treated conservatively, with a lower incidence of inappropriate shocks, around 14%[4,5], because of improvements in the recognition algorithms and the reduction of oversensing from myopotentials[1].

Registry Studies

The most important source of data on early complications, intrahospital and periimplantation of S-ICD, is the National Cardiovascular Registry of the USA (National Cardiovascular Data Registry–ICD Registry), which has reviewed almost all the implants since September 2012[6]. The data published in 2016 relating to 3,717 S-ICDs showed a 1.2% rate of early total complications including death, of which the total mortality rate was 0.3%, haematoma 0.3%, and revision surgery of the implant 0.1%. Evaluating the characteristics of S-ICD implants with those of T-ICD implants in the same cohort by means of 'propensity matching' analysis, it was found that the risk profile of S-ICD patients was more severe, but the incidence of early complications was low and comparable to that of T-ICD patients[6].

The two most important sources of documentation of medium and long-term adverse events that can be correlated to the device are represented by the registry studies, mainly prospective, IDE (S-ICD System IDE Clinical Investigation), and EFFORTLESS S-ICD (Evaluation oF FactORs ImpacTing CLinical Outcome and Cost EffectiveneSS of the S-ICD)[7,8].

The IDE study was the first of the two studies to be published in 2012. It included 330 patients with an average age of 51 years. This study demonstrated a total mortality rate of 2.5% at a follow-up of 11 months, with no sudden arrhythmic deaths, although there were two deaths with unknown causes. The rate of infection was 5.6%, of which explantation was necessary in 1.2% of patients. Inappropriate shocks were found in 13% of patients due to supraventricular arrhythmia and oversensing of the T wave. 78% of these cases were treated without intervention using device reprogramming or drug therapy, and 22% invasively. In four cases the device was either removed or switched off[7]. In the first phase of the study, 26% of patients had inappropriate shocks, which were related to a single programming zone, the so-called non-conditioned, that is, only influenced by the heart rate, thus excluding discrimination for supraventricular tachyarrhythmia. In the second part of the study, after the dual area of intervention for tachyarrhyth-

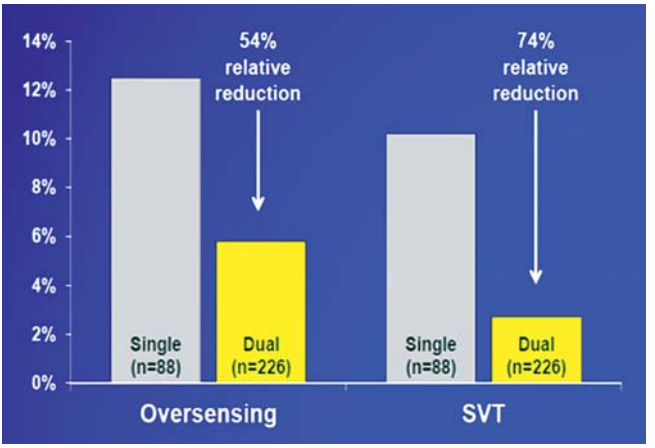

FIGURE 10.2

Reduction of the percentage of inappropriate shocks in patients with a double area of intervention compared to patients with a single area of intervention.

mia was introduced, inappropriate shocks of supraventricular arrhythmia were drastically reduced, lowering the two-year incidence to 10% (Figure 10.2).

The EFFORTLESS S-ICD study[20] has, to date, enrolled over 1,000 patients in various European countries and in New Zealand. It is continuously updated over the years through the follow-up. The first publication[8], which dates back to 2014, presented the results of the ad interim analysis relating to 472 patients with an average age of 49 years, evaluated at 6 and 12 months after implantation. Complications, defined in net terms as the events that involved a new invasive procedure, occurred in 7% of patients, with a temporal distribution of 3% at 30 days, and 6% at 6 months and 12 months. The incidence of total infections was 4%, of which 2.2% caused a removal of the system. The inappropriate interventions of the S-ICD were caused mainly by oversensing on the T wave (84% of cases) and only 8% by high frequency supraventricular tachyarrhythmia. A proportion of these inappropriate interventions were corrected with reprogramming and/or drug treatment, but in 2% of patients inappropriate shocks persisted after attempted correction: 3 patients were subjected to removal or turning off of the device. Dual-zone programming was associated with a reduced incidence of inappropriate interventions, compared to single-zone interventions (i.e., with only high frequency criteria).

The two studies IDE and EFFORTLESS showed the same results in the context of complications and inappropriate shocks, both generally more favourable than in previous studies. This was further confirmed by the cumulative analysis prepared thereafter. In this analysis, in addition to the number of patients of the first publications, other EFFORTLESS patients enrolled in the meantime were included, reaching the results for 882 patients, with an average age of 50 and an average follow-up of 22 months[9]. The total complication rate, all included, was 9.6%, and that of inappropriate shocks was 13% at three years; in both types of events there proved to be an improvement trend.

Wound healing problems were found in about 5% of patients; in these, infections caused by reoperation or explantation amounted to 1.7%. The distribution of inappropriate shocks clearly confirmed the difference between the incidence associated with a single area of intervention, equal to 20.5%, and with a double zone, equal to 11.7%. Consequently, inappropriate shocks were reduced by 34% in the most recent period of the study, which was associated with reprogramming in two interventional areas[9] and adjustment of the programming modalities. In this phase, T-wave oversensing accounted for less than 40% of the causes of inappropriate therapy. As already reported in a previous chapter, but worthy of mentioning again, is the fact that, in patients with previous transvenous ICD explantation for system infection, the incidence of new S-ICD infections did not differ, compared to patients with no history of previous infections[10]. The raw data of mortality derived from accumulative analysis of the average follow-up showed values of 1.6% yearly, and a two-year total of 3.2%, which can be compared with the mortality values found in the most recent trials with T-ICD[23], equal to 5% and 11% at two years in the MADIT-RIT (primary prevention only) and in the SIMPLE study, respectively[11,12].

The EFFORTLESS study, with its advanced registry model designed to report 'real world' patient outcome, has continued to provide fundamental analyses over time[13]. The recent update published in 2017, involving 985 patients with an average age of 47, 72% of whom were male, with primary prevention in 64%, channelopathies in 20% and ischaemic heart disease in 28%, showed three fundamental findings over an average follow-up of 3.1 years: absence of electrode malfunction, absence of systemic infections related to an implant site infection, in particular, complete absence of endocarditis and, finally, an extremely low incidence of post-implantation of an S-ICD, indications for some form of transvenous electrode implant (substantially from: need for anti-bradyrhythmic pacing; need for anti.tachycardia pacing or cardiac resynchronisation therapy)[13].

A fourth concept, mortality, is very interesting, but it must be substantiated by studies that are not designed for a specific evaluation. There were 4.8% deaths on the average follow-up, none of which were related to the procedure; 98% occurred more than 30 days after implantation during the perioperative treatment window, and 1 death was due to arrhythmia only.

In terms of definition adopted by the protocol, for which a complication was every adverse event involving an invasive intervention, the details of the events are as follows: 4.1% complications of the system and of the intervention at 30 days, and 8.4% of the cases at 1 year, with an improving temporal trend from the first quartile of patients enrolled to the last, which corresponded to complication rates of 11.3% and 7.4%, respectively (reduction of ca. 30%); for an average follow-up of 3.1 years, complications were found in 11.7% of the cases, among which the single most frequent system defect was oversensing, which caused inappropriate shocks. This was followed by premature depletion of the battery (0.5%) and other minor disabilities of the programmer, without no technical problems of the electrode. Infections involving removal of the device were 2.4% at 3.1 years, while local surgical-pocket problems were another 4.5% overall. Inappropriate shocks occurred in 8.1% of cases at one year, and in 11.7% at about three years, against scheduled double area interventions already established in 86% of cases at the time of implantation. The cause of inappropriate shock was 7.7% of cases of cardiac oversensing, predominantly of the T wave, and in 2.2% of oversensing of non-cardiac 'noise', mainly from electromagnetic interference. The cases of transition to a transvenous system due to the need for some form of pacing occurred in 1.3% of cases with a follow-up of 3.1 years, of which over a third due to the onset of treatable VTs with anti-tachycardia pacing. The study also assessed the association between clinical variables and risk of complications, noting that non-ischaemic heart disease, the presence of a previous defibrillator (any type), the width of the QRS and the body mass index were independent predictive factors.

The EFFORTLESS registry data gives substantial evidence to an extensive meta-analysis, particularly with regards to the three fundamental data described above: non-electrode malfunction, no systemic or endocardial infections, and low explant rate for pacing or CRT indications. The cumulative analysis study published in 2017 by author Chue[14], involved 16 studies, including the EFFORTLESS, IDE and National Cardiova-Scholar registries of the US, with a total of 5,380 patients having the following characteristics: 33-64 years average age, 62–92% males, primary prevention in 68% of cases, ischaemic heart disease in 42%, congenital heart disease and channellopathy in 14%. The results were: 3.4% total mortality,

2.1% mortality per person/year, and 0.1% arrhythmic. The major complications were thus distributed: 2.7% total infections, 1.7% infections per person/year, less than 2% other surgical problems of the implant, 1.5% device complications (premature battery depletion, communication deficit). The explants were 3.8% of the cases, with an incidence of 2.2% per person/year, mostly due to infection. Minimum device explantation rates confirmed for pacing needs equalled 0.6%. Inappropriate shocks occurred in 4.3% of patients, mostly due to oversensing of the T wave, while the causes attributable to myopotentials and supraventricular arrhythmia were very rare. Even on very large and varied series the favourable impact of the double recognition zone and of the new sensing algorithms was highlighted in terms of a temporal trend. Finally, while awaiting the results of ongoing randomised trials comparing the efficacy and safety of S-ICDs and T-ICDs, we must report the results of single or double high volume studies, comparing the adverse events of S -ICD and T-ICD in cohorts of patients according to the 'propensity-matching' analysis (15,16). The authors retrospectively analysed 1,160 patients undergoing S-ICD or T-ICD implantation in two major Dutch hospitals. In order to make the comparative populations homogeneous, the authors applied propensity score matching, using two matched cohorts of 140 patients subjected to T-ICD implantation and 140 patients subjected to S-ICD implantation. The clinical outcomes analysed were device-related complications that required surgery and appropriate or inappropriate device interventions. An estimate of clinical events involving re-operation in 140 S-ICD implants and in equal numbers of T-ICD implants at 5 years were investigated in the two Dutch hospitals, reporting values of 13.7% versus 18% in the two groups respectively.

The difference was largely attributable to the marked asymmetry of electrode-related complications (0.8% vs. 11.5%) only partially offset by the prevalence of complications unrelated to the electrode in S-ICDs. The estimates of infections (4.1% vs. 3.6%) and inappropriate shocks (15) are superimposable. In conclusion, the study compared two homogeneous populations subjected to T-ICD or S-ICD implantation, showing that the rate of complications between the two groups is similar but that their nature is different.

This result is compatible with the different designs of the two devices. The weak point of the T-ICD is the electric catheter; instead, that of S-ICD is inappropriate sensing.

Hence, S-ICD has a significant advantage over T-ICDs in terms of lead-related complications, and this advantage could become even more evident after a longer follow-up.

In the other single centre study, Honarbakhsh (16) compared the safety and efficacy of S-ICD and T-ICD, and performed the first analysis of the cost-effectiveness of S-ICD, compared to T-ICD. Sixty-four cases of S-ICD showed, compared to the matched T-ICD cohort, a real incidence of device-related complications of 9%, versus an incidence of 29% in the VT-ICD group. The relative risk of device-associated complications was reduced by 70% in the S-ICD group, compared to the T-ICD patient group. Initial implantation costs (device and procedure costs, including general anaesthesia) were higher for the S-ICD patient group than for the T-ICD patient group (total $ 1,166,082 compared to $ 741,749), but the costs of device-related complications, including hospital stay, procedure-related costs, and generator costs and/or lead replacement costs, were significantly lower in the S-ICD patient group than in the patient group T-ICD (total $ 23,784 compared to $ 199,251). Finally, if the complication rate remains stable in the next 5 years, there will be no difference in costs between the S-ICD group and the T-ICD.

Another meta-analysis on five studies (17) performed a comparative analysis between efficacy and safety between the subcutaneous implantable cardioverter defibrillator (S-ICD) and the implantable cardioverter transvenous defibrillator (T-ICD). The basic characteristics were similar between the S-ICD and T-ICD groups. In particular, the study analysed the complications of the electrocatheter, the efficiency of the system, inappropriate therapies, T-wave oversensing, and the recognition of supraventricular arrhythmia. Fewer lead complications occurred in the S-ICD group than in the T-ICD group (OR: 0.13, 95% CI: 0.05–0.38). The infection rate was similar between the S-ICD and T-ICD groups (OR: 0.75; 95% CI: 0.30 to 1.89). There were no differences in system or device failure between groups (OR: 1.13; 95% CI: 0.43 to 3.02). Overall,

TABLE 10.1

Difference of Clinical Events in Groups of Patients with S-ICD and T-ICD

Clinical events	S-ICD	T-ICD	OR (95% CI)
Lead complications	0.14	1.02	0.13 (0.05–0.38)
System failure	0.32	0.24	1.13 (0.43–3.02)
Infections	0.34	0.31	0.75 (0.30–1.89)
Inappropriate therapies	8.30	9.46	0.87 (0.51–1.49)
T-wave oversensing, episodes of oversensing	8.99	0.72	9.81 (2.60–37.05)
SVT Supraventricular Tachycardia	1.08	10.43	0.12 (0.0–0.35)

inappropriate therapy (T-wave oversensing, supraventricular tachycardia, inappropriate sensing episodes) was similar between the two groups (OR: 0.87; 95% CI: 0.51–1.49). However, the nature of inappropriate therapy was different between the S-ICD and T-ICD groups. Regarding appropriate shocks both devices seem to work well (Table 10.1).

Outcomes in Patient Subgroups

Considering the indications for S-ICD, first oriented empirically and then clinically indicated in classes that favour groups of patients with a more severe clinical profile or of patients who are more at risk, such as patients with congenital heart disease, channellopathy arrhythmia, end-stage renal disease or hypertrophic caromycosis. The practical experiences of adverse events related to S-ICD in these categories of patients are of particular interest. The first findings in a small series of medical records put forth the question of the high incidence of inappropriate shocks in channellopathy congenital arrhythmia, but only the single detection zone was in use[18]. Subsequent experiences in studies mostly on paediatric patients of a single centre showed that the complications of the implant and the device were substantially superimposable to those of the other age groups, while the correction of inappropriate therapies remains more challenging[19]. The vulnerability is related to the higher basic frequencies and to the higher incidence of high frequency supraventricular tachyarrhythmia: the dual area of intervention, individualised reprogramming and careful use of preimplant selection criteria seem to be able to control the problem[20].

Even in patients with hypertrophic cardiomyopathy, the major problem seems to be related to inappropriate shocks, resulting in complications of the implant and the device that are the same as in other groups of cardiopathies/arrhythmic abnormalities in patients having the same age[21,22]. The presence of large T-wave anomalies and increased QRS-T voltages in these patients accounts for the oversensing of the T-wave detected in 18% of patients with a long follow-up, and for the incidence of inappropriate shocks reported at 15%.

The evaluation of complications, in this category of patients, is of particular relevance because they are young, have a longer life expectancy, and include subjects presenting hereditary cardiomyopathies.

One study analysed 62 young patients[23] with hereditary cardiopathies and with no indication for stimulation who underwent implantation of an S-ICD.

The complication rate was found to be very low, with no infection of

the pocket or revision of the device needed, and there were only two cases of inappropriate shock.

In conclusion, these data show that, in young patients with hereditary arrhythmic syndromes, the S-ICD system is associated with a lower incidence of complications and a lower rate of inappropriate shocks.

In dialysis the rate of complications seems particularly favourable: in a total of 120 patients rates of infections are reported to be lower than those of non-dialysed patients (note, compared to a high infection risk with the use of T-ICD), with percentages of similar inappropriate shocks between the two subgroups[24,25].

Myocardial Consequences of the Shock Delivered by S-ICD

The exact consequences that S-ICD shock has on the myocardium have not been clearly identified as yet, taking into the fact that the electric catheter is not in contact with the myocardium. It is well known that the shock delivered by the T-ICD causes myocardial microlesions and could be associated with a higher mortality rate.

One study[26] showed that, unlike T-ICDs, shocks delivered by S-ICDs do not cause injuries to the heart muscle.

The study evaluated the blood levels of high-sensitivity cardiac troponin (hs-CTnl) and creatine kinase-MB (CK-MB), before and after a shock delivered during an intraoperative defibrillation test (DFT), and the variable of N-terminal fragment serum levels of natriuretic propeptide type B (NT-proBNP) and copeptin (CP).

There were no differences in results regarding the levels of hs-CTnl and CK-MB and NT-proBNP immediately after or long after DFT. Instead, serum copeptin levels were higher one hour after shock delivery, but this alteration disapeared at 6 and 24-hour evaluations.

The authors of the study conclude that the delivery of shocks by an S-ICD does not cause myocardial lesions.

Management of Complications

A single centre study[27] evaluated 123 patients over a 2-year follow-up period: 10 patients (9.4%) suffered from implant-related complications. There were 5 infections, 3 erosions and 2 implant failures, and 21 surgical procedures were required. In 9 out of 10 patients, S-ICD therapy was continued after surgery. In 6 patients, the period between extraction and re-implantation of the S-ICD system was filled with a wearable cardioverter defibrillator (WCD). In five patients the pulse generator was reimplanted in the original site, and in three, below the serratus anterior

muscle. One patient did not undergo reimplantation after extraction due to recurrent infections.

The author concludes that in the majority of patients presenting a complication, S-ICD therapy can be continued after surgery, avoiding the need to convert to a transvenous system.

In cases of less serious infections or wounds, such as a simple haematoma or simple erosion, the infection can be managed locally and the generator can be placed in a deeper layer or moved to a more posterior and slightly more lateral position.

The system must be extracted in cases of major infection or erosion with exposure of the device.

The period between extraction and re-implantation of the S-ICD may vary, as this study also states, between 6 weeks to 3 months. To protect the patient from prolonged hospitalisation, a wearable cardioverter defibrillator (WCD) is provided along with antibiotics that can be controlled by the tissue culture results. The duration of therapy depends on the clinical and laboratory tests for infection or on the state of the wound.

During re-implantation, the S-ICD case can be positioned at the same point in an intermuscular position or in a submuscular position, un- der the serratus anterior. In this case, it is important to maintain the integrity of the long thoracic nerve to avoid functional impairment of the shoulder that could lead to scapula winging.

In this implantation technique, the pulse generator is positioned under the muscle and the muscle slips are sutured from lateral to medial.

The use of a WCD for a period of 6 weeks to 3 months leaves enough time for the skin and subcutaneous tissue to heal in cases of erosion or infection.

In this study all three cases of pocket erosion were initially managed by repositioning the generator deeper into the subcutaneous layer and with no transition period using a WCD. Nevertheless, this strategy proved to be effective only in 1 case. As cutaneous erosion often occurs in the presence of low grade infection, extraction of the S-ICD system followed by a transition period with a WCD seems to be more appropriate in these cases.

No case, however, has shown signs or symptoms of systemic infection in this reported study or in our experience.

In this regard, a case report (24) showed that S-ICD pocket infections can advance, although not often, towards a systemic infection. In this report, both patients presented risk factors for haematoma of the pocket, and factors inclined to infections because of renal insufficiency, diabetes mellitus and double antiplatelet therapy that coexisted in each patient.

Moreover, in these patients the implant had been placed under the serratus muscle, and this caused late recognition of the haematoma due to the deep positioning of the device. The authors conclude by highlighting the importance of vigilance for pocket complications immediately after the implantation of the S-ICD. Early intervention for haematomas and pocket infections can prevent the progression of systemic infection.

In conclusion, in most patients with a pocket complication, ICD therapy can be continued after surgery, avoiding the need to convert to a transvenous system.

The complication rate in this cohort is similar to what has been reported for T-ICD, although this complication rate in this cohort may be overestimated due to a learning curve. A wearable defibrillator is a viable option while awaiting the re-implantation procedure.

In our experience, as in that of other centres, the learning curve has improved. The complications of the pocket become less and less frequent, so much so that now we no longer need to suspend dual antiplatelet therapy or oral anticoagulants.

The few complications that occurred during our experience (Figure 10.3) were all handled locally; only one case required device removal. The patient was obese, diabetic, dialysed and receiving dual antiplatelet therapy (Figure 10.4).

One month later the wound was perfectly healed and a new S-ICD implantation could be performed.

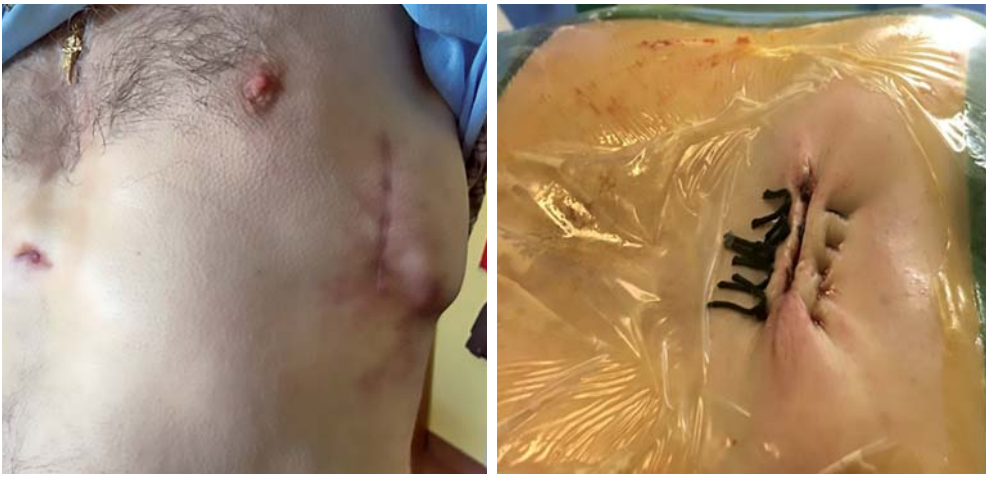

FIGURE 10.3

Patient with infection at the site of the sternal cut. Revision of the wound allowed full recovery.

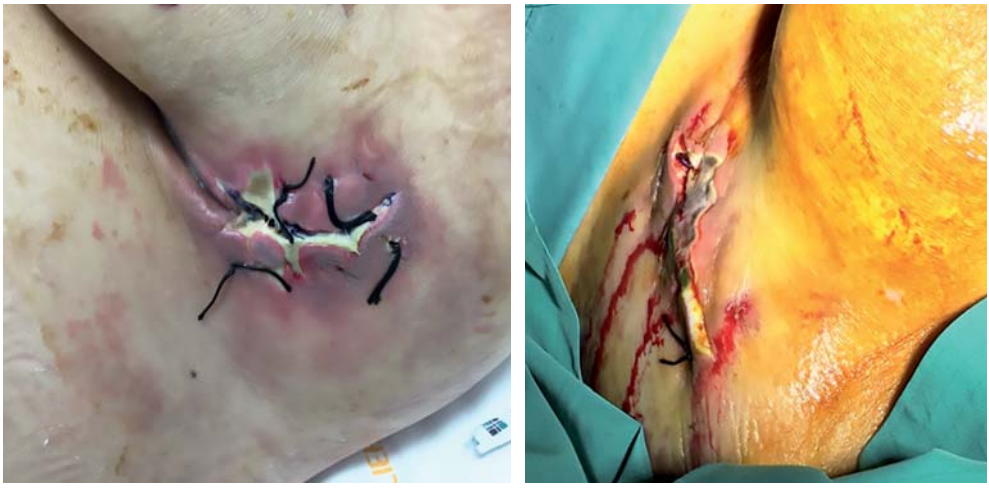

FIGURE 10.4

Obese woman, diabetic, with dual antiplatelet therapy. *Proteus mirabilis* infection. The infection was resolved by removing the ICD, targeted antibiotic therapy and drainage placement. One month later it was reimplanted in the submuscular area.

In most cases, after removing the previous S-ICD, washing and draining the infected subcutaneous pocket and then creating a new and deeper pocket under the latissimus dorsi muscle, keeping it completely separated from the previous one, and, finally, implanting a new defibrillator in an intermuscular or submuscular position has shown to preserve system sterility (Figure 10.5). Patients were able to keep their implant in place.

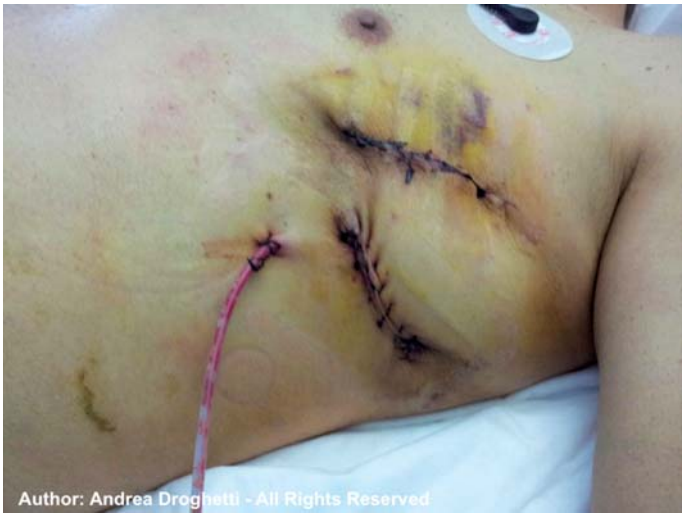

FIGURE 10.5

Patient with pocket infection of an S-ICD and drainage.

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CHAPTER 11

Remote Monitoring: LATITUDE™ NXT for Remote Patient Management

S. De Bonis, A. Bisignani, G. Bisignani

Remote Monitoring (RM) is the automated transmission of data based on scheduled alerts related to device function and clinical events, rapidly identifying the possibility of both technical device anomalies and early diagnosis of arrhythmic events. It also gives us a continuous collection of information related to the patient's clinical status.

The remote evaluation of implantable cardiac devices started with Trans Telephonic Monitoring (TTM) for pacemakers, introduced in 1971. This technology gave us limited data on the function of pacemakers through analogue transmission on a landline; the information included data on battery life, sensing and capture, the same as a real-time n electrocardiogram.

Late in 1990, a radiofrequency transmission system was introduced, capable of transferring data from the patient's device to a transceiver. The remote interrogation procedure is similar to that performed in a typical outpatient check-up. Once the head of the transmitter is positioned above the device, data programmed, stored and measured are sent by radiofrequency transmissions in real time from the patient's device to a transceiver from home. The patient receives feedback regarding the success or failure of the transmission. The data is then sent from the transceiver to a central server where it is securely stored and processed.

The first fully automatic platform for the RM was introduced in 2001. Nowadays there are quite a few platforms for the RM available. There are very few differences between the methods of these various RM systems. Basically, the implanted device can be programmed to download or transmit data at specific dates and times. Symptomatic patients can also transmit additional information. Transmissions are sent wirelessly to a

transceiver or base unit located near the patient. Using either analog lines or wireless data networks, the transmitted data is sent to the central server of the manufacturer for storage and retrieval. Doctors can access patient data by accessing a dedicated and secure website.

Today, this technology is also present in S-ICDs with the LATITUDE™ NXT system.

LATITUDE™ NXT for Remote Patient Management

There is evidence that remote management of the patient with heart rhythm pathologies is associated with a reduction in mortality, hospital admissions and outpatient controls, as well as allowing early detection of events. The LATITUDE™ NXT technology, compatible with the EMBLEM™ MRI S-ICD system, views the trends of the AF detected over the last 100 days (AF minutes/day), and programs and performs efficient remote follow-ups (Figure 11.1).

The LATITUDE™ NXT system uses a transmitter capable of communicating in radio frequency with compatible implanted automatic cardiac defibrillators (with a range of up to a few metres). It collects the information sent by the device and transfers it encrypted via a telecommunications network (mobile or mobile telephone with roaming between operators or through the patient's Internet network) to a central server that collects the data. The data transferred are then made accessible online at any time to authorised users for consultation on a dedicated and secure Web interface (Figure 11.2).

The LATITUDE™ NXT system associated with the EMBLEM S-ICD allows to perform:

- event-based remote monitoring, with weekly requests sent manually by the patient with an event, including the report of completed transmission;

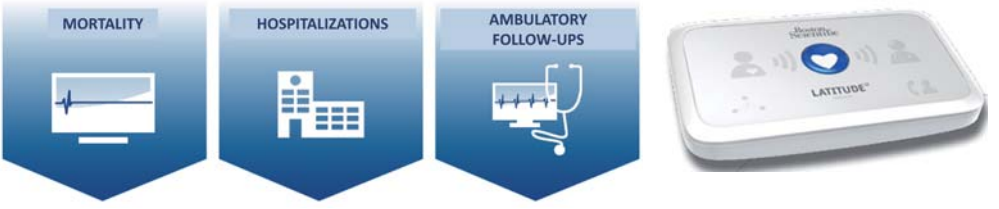


FIGURE 11.1
LATITUDE™ NXT system.

FIGURE 11.2

The LATITUDE™ NXT system allows to receive data sent from the device and transfer it encrypted via a telecommunications network to a central server that collects the data.

- remote monitoring from a schedule calendar, with programmed remote transmissions periodicaly sent manually by the patient, including the report of a completed transmission;
- monitoring on request, sent manually by the patient with a report of completed transmission.

Unlike remote monitoring with the LATITUDE™ NXT system associated with the T-ICD, which can be done automatically, the LATITUDE™ NXT system associated with the EMBLEM S-ICD does not allow automatic transmission without patient intervention. Transmission must be started manually by the patient. A flashing button is activated on the transmitter to alert the patient to perform a transmission (Figure 11.3).

The interrogation frequency of the S-ICD is weekly, while it is daily with T-ICD.

Events that can trigger an alert can be set by the clinician using the dedicated website and concern:

- the entirety and function of the device and the lead,
- rhythm disturbances and their treatment.

FIGURE 11.3

A flashing button is activated on the transmitter to alert the patient to perform a transmission.

You can define different priority levels:

- **Red alarms** (urgent):
  - Device battery has reached the end of life (EOL)
  - High electrode impedance
  - OFF therapy
  - Possible device malfunction
- **Yellow alarms** (optional):
  - Device battery has reached ERI
  - Shock therapy delivered to convert arrhythmia
  - Untreated episode
  - Sensing not fully optimised
  - AF measured within a 24-hour period (above the limit selectable by the user)

The data available on the site are identical to those obtained through the programmer during a check-up at the clinic.

Figures 11.4–11.7 show examples of LATITUDE™ NXT transmissions of patients with an S-ICD.

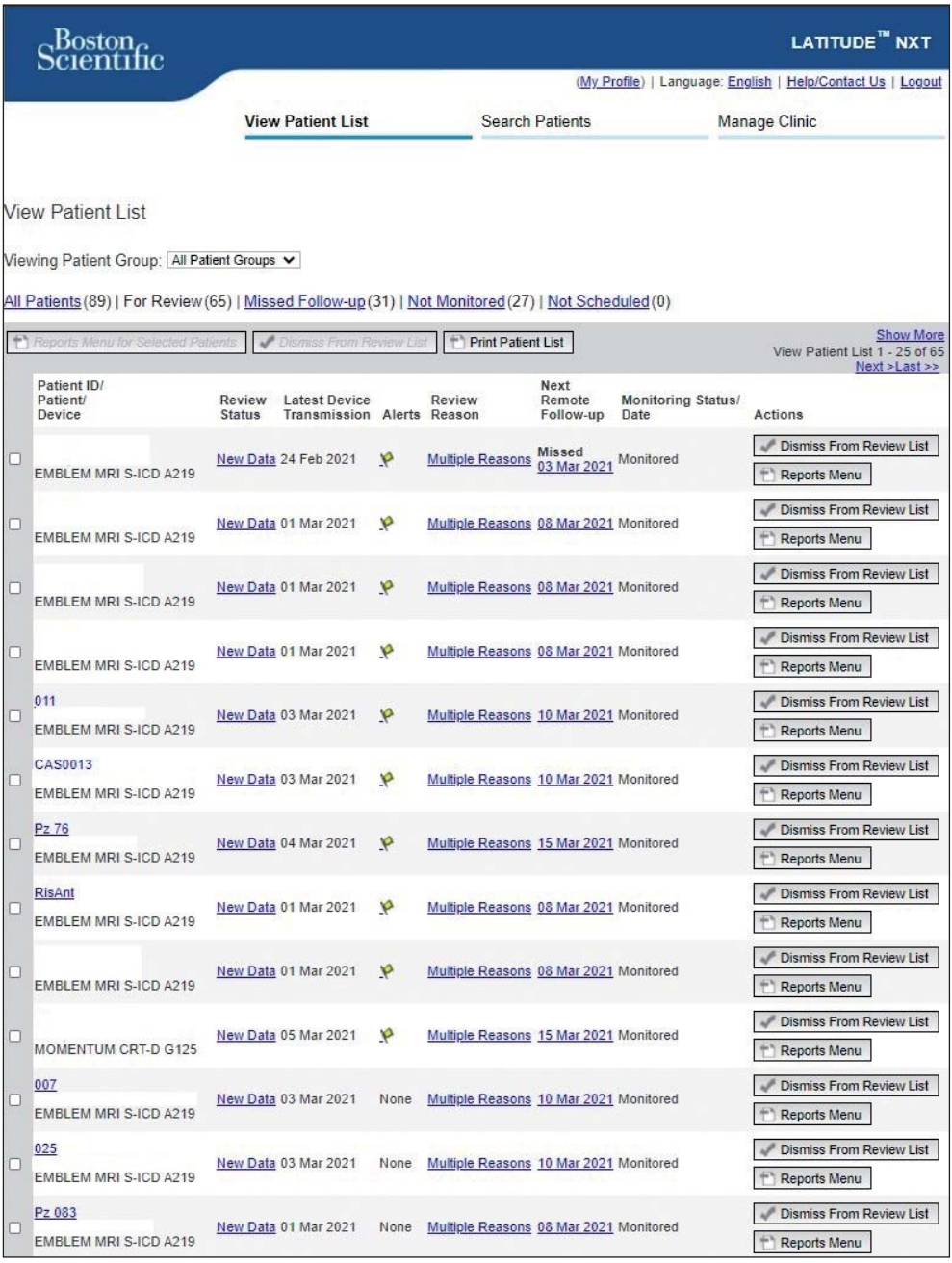


FIGURE 11.4

LATITUDE™ NXT home screen view: patient list.

LATITUDE™ Patient Management - Summary Report | **Report Created: 01 Mar 2021**

Boston Scientific

Date of Birth:
Device: **EMBLEM MRI S-ICD A219**
Clinic: **P.O.FERRARI -CS**
Search Tags:
Therapy: **ON**

Latest Device Transmission: **30 Oct 2020 06:41 CET**
Last Office Interrogation: **14 Jul 2020**
Implant Date: **2019**
Patient Group: **P.O.FERRARI -CS (Primary)**

My Alerts

There are no alerts to display.

Device Status

Last MRI Protection Mode	N/R

Events Since Last Reset (14 Jul 2020)

29 Oct 2020 12:16 CET AF
28 Oct 2020 20:21 CET AF
See last page for full list of Events Since Last Reset.

AF Monitor (01 Aug 2020 - 29 Oct 2020)

Days with measured AF	24 day(s)
Estimate of measured AF	1 %

Battery

Remaining Battery Life to ERI	85 %

System Detail

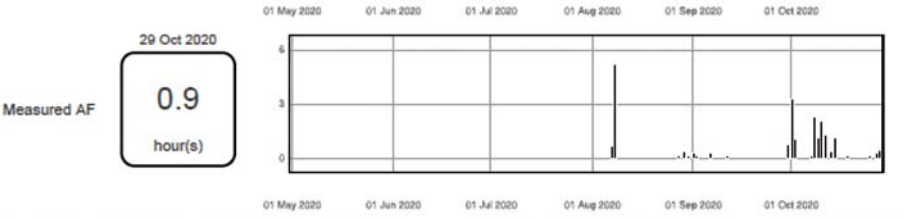
Electrode Impedance Status	OK	Electrode Model #	3501
		Electrode Serial #	160107

Settings

Tachy Therapy Settings		Additional Device Settings	
Therapy	ON	Post Shock Pacing	OFF
Shock Zone	220 min^{-1}	Gain Setting	1X
Conditional Shock Zone	200 min^{-1}	Sensing Configuration	Primary
		Shock Polarity	STD
		SMART Charge	1.83 s (8 intervals)
		SMART Pass	OFF
		AF Monitor	ON

Event Counts	Since Last Reset 14 Jul 2020	Since Implant 10 Sep 2019
⚠ Untreated Episodes	2	2
⚠ Treated Episodes	1	2
# of Shocks Delivered	1	2
MRI Protection Mode		0

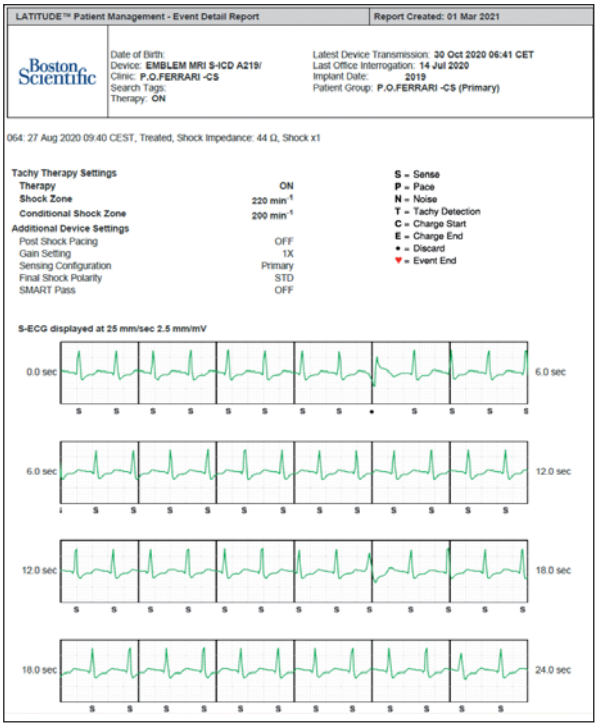
Trend Graphs



Note: Measured AF trend data is available for up to 100 days. The patient's implanted device is limited to 100 days of measured AF.

FIGURE 11.5

LATITUDE™ NXT follow-up summary page.



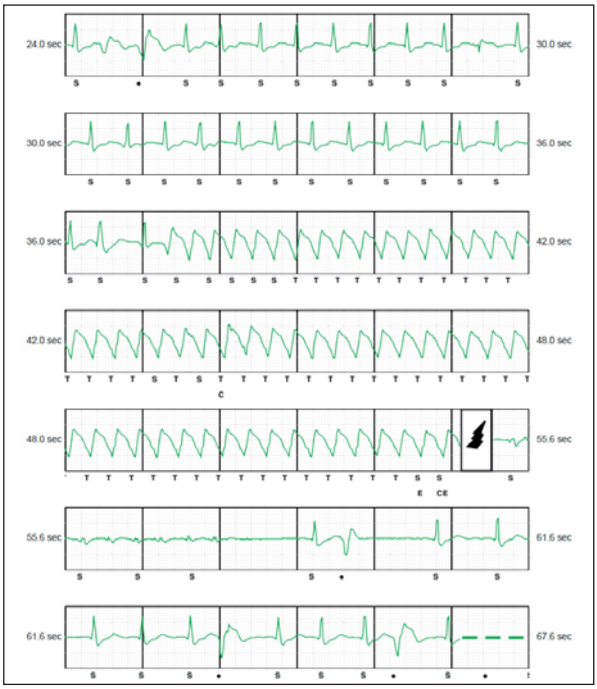


FIGURE 11.6

Event report of appropriate sensing and shock delivered on VT.

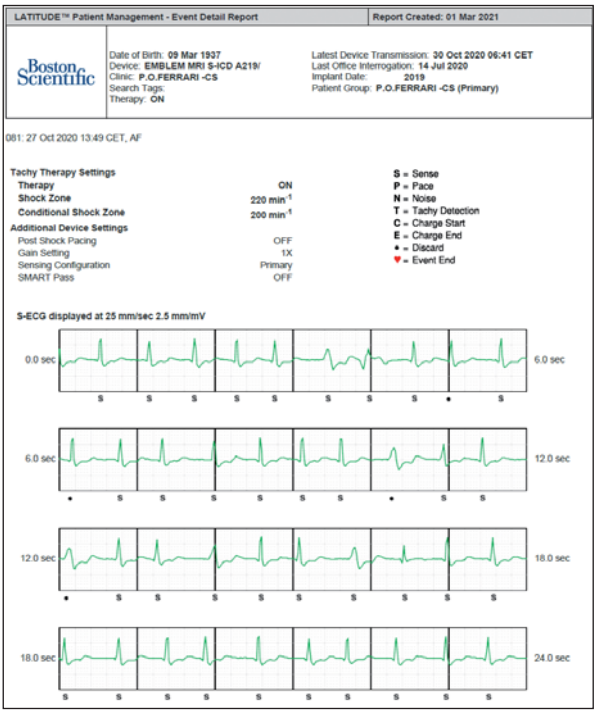


FIGURE 11.7
Event report with episode of AF.

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CHAPTER 12

Subcutaneous Defibrillator and Magnetic Resonance

G. Bisignani, S. De Bonis, A. Bisignani, R. Vico, L. Perretti

EMBLEM S-ICD devices are considered MRI-conditional. The EMBLEM MRI S-ICD system offers ImageReady MRI technology for compatibility with Magnetic Resonance (MRI) scans.

The programmer is MRI Unsafe, that is, it is a device that is not safe for use with MRI equipment and must be positioned outside the MRI area.

The nomenclature of medical devices in MRI in European standards refers to the ASTM F2503-05 standard, which has now become the IEC 62570: 2014 standard.

The device can be classified regarding the risks connected to Magnetic Resonance (1) as follows:

- **MRI Safe**: the device does not involve any type of risk in any possible MRI setting;
- **MRI Conditional**: the device does not present any real risks in a specific MRI environment, under specific conditions of use. There are parameter values to define the specific MRI conditions that need to be met, including the static magnetic field strength, gradient limitations (slew rate or dB/dt) and the SAR value (energy absorbed per unit mass). In addition there may be further requirements, such as a particular configuration of the device;
- **MRI Unsafe**: there are risks, which have been proven with the device under all MRI conditions.

These three categories determine that the exact classification for the S-ICD is MRI Conditional as it reaffirms the concept that the examination is safe only if carried out under certain conditions.

TABLE 12.1

S-ICD MRI Conditional Models

Name of Device	Model Number
EMBLEM MRI S-ICD	A219
EMBLEM S-ICD	A209
S-ICD Electrode	3010, 3400, 3401, 3501

EMBLEM MRI S-ICD is Image Ready and total body scans can be performed, compatible with MR for 1.5 T systems, with no exclusion zone and no limit for scan time. It has an automatic MRI timer mode. It is compatible with 1.5 T MR (SAR <=2.0 W/kg whole body averaged, SAR<=3.2 head W/kg).

S-ICD MRI Conditional models are listed in Table 12.1.

Before giving a patient an MRI scan, it is necessary to program the ImageReady S-ICD system in MRI Protection Mode using the programmer (2). The **MRI Protection Mode** modifies certain functions of the pulse generator to reduce the risks associated with exposing the pacing system to the MRI. Choosing the MRI protection mode starts a sequence of dialogue boxes needed to evaluate the suitability and adequacy of the patient and the patient's pacing system for scanning in MR Conditional.

How to change the device in MRI Protection Mode:

- **Anti-tachycardia therapy is suspended.** The MRI protection mode disables anti-tachycardia therapy. Ventricular arrhythmia will not be detected and the patient will not receive defibrillation therapy with shock until the pulse generator resumes its normal function. System diagnostics (electrode impedance, battery performance monitoring, AF Monitor) and magnet detection are suspended;
- **The Time-out function** is set nominally to 6 hours, with programmable values of 6, 9, 12 and 24 hours;
- **The acoustic signal is disabled** and may no longer be usable after an MRI scan. Contact with the strong magnetic field of an MRI scanner can cause permanent loss of the volume of the acoustic signal, which cannot be restored, even after leaving the MRI environment and exiting the MRI protection mode. Before an MRI procedure, the doctor and the patient must evaluate the advantages of the examination with regard to the risk of losing the acoustic signal. It is strongly advised to follow on LATITUDE NXT, if this is not already the case, for patients who have undergone an MRI scan or to increase the frequency of follow-up visits. Otherwise we recommend scheduling a quarterly follow-up visit to monitor device performance.

The following are situations that will no longer trigger the acoustic signal with the emission of tones that can be heard after exiting MRI Protection Mode (if the acoustic signal is not re-enabled):

- Elective replacement indicators (ERI) and end of life (EOL)
- Electrode impedance outside the permitted range
- Prolonged charging times
- Irregular battery discharge.

MRI Scan after ERI Status

The MRI scan after reaching the ERI state can cause premature battery depletion, a shorter device replacement time window or sudden interruption of therapy. After performing an MRI scan on a device that has reached the ERI status, check the pulse generator and plan replacement of the device.

When the Possibility of Performing MRI is Precluded

The following device conditions preclude the possibility for the user to enter MRI Protection Mode:

- The presence of a magnet is detected by the magnet sensor;
- A Tachy episode is ongoing;
- The setting process has not been completed;
- The battery capacity status is End of Life (EOL).

WARNING. After reaching the ERI status, the MRI scan may result in premature battery depletion, less time for device replacement or sudden termination of therapy. After performing an MRI scan on a device that has the same ERI problem, verify pulse operation and schedule device replacement.

The MRI Protection Mode is interrupted with the manual output or with the setting of a time-out period programmed by the user. Emergency Shock stops the MRI Protection Mode. When exiting the MRI Protection Mode, all the parameters (except the Acoustic Signal) return to the previously programmed settings.

The system proactively activates the acoustic signal when the MRI protection mode is programmed. The acoustic signal remains off when exiting the MRI protection mode. The acoustic signal can be re-enabled with the option *'Control acoustic signals'*.

Six hours in MRI Protection Mode *can reduce the longevity* of the pulse generator by about 2 days.

MRI - Conditions of Use

The following MRI conditions of use must be met in order for a patient with an ImageReady S-ICD defibrillation system to undergo an MRI scan.

Compliance with the conditions of use must be verified before each scan to ensure that the most up-to-date information is used and to assess the patient's suitability and preparation for a Conditional MRI scan.

Cardiology

1. The patient was implanted with an S-ICD ImageReady MRI Conditional system.
2. Absence of other devices, components or accessories implanted, active or abandoned, such as adapters for leads, extensions, electric catheters or pulse generators.
3. The pulse generator is in MRI Protection Mode during the scan.
4. As soon as the MRI Protection Mode is programmed, the patient needs to be monitored continuously with pulse oximetry and electrocardiography (ECG). Also, make sure that the backup therapy is available (external resuscitation).
5. The patient was judged clinically able to tolerate the absence of antitachycardia protection for the entire period in which the pulse generator is in MRI Protection Mode.
6. At the time of the scan, the patient's temperature is not high and the thermoregulation is not compromised.
7. At least six (6) weeks have passed since the implantation of the device and/or any electrode revision or surgical modification of the ImageReady S-ICD system.
8. There is no evidence of fractured electrode or impaired integrity of the electrode-pulse generator system.

Radiology

1. Magnet MRI power only 1.5 T, RF field approx. 64 MHz, Maximum spatial gradient 30 T/m (3,000 G/cm), Closed, horizontal MRI equipment only with 1H proton therapy.
2. Specific absorption rate (SAR) limits for the entire active scan. Normal operating mode at:
   - the whole body on average, ≤2.0 Watts/kilogram (W/kg);
   - head, ≤3.2 W/kg.
3. Maximum specified rate of change of the gradient ≤ 200 T/m/s per axis.

4. There are no limits on the use of local receive-only coils. The local transmission-only coils or the local transmission/reception coils can be used, but they must not be placed directly on the ImageReady S-ICD system.
5. The patient must be in the supine or prone position.
6. The patient must be continuously monitored by pulse oxymetry and electrocardiography for the entire period during which the pulse generator is in MRI Protection Mode. Backup therapy (external resuscitation) must be available.

S-ICD Programming for a Scan

Use the programmer to program the input of the S-ICD device in MRI Protection Mode.

NOTE. Print or save (with End Session) the desired data from the current session before programming the device in MRI Protection Mode.

From the main menu screen, select the MRI Protection Mode button '*Main Menu*'.

Certain conditions in the pulse generator and/or in the system result in the rejection of the user's request to access the MRI Protection Mode. These conditions include:

- an ongoing ventricular episode detected and recognised by the pulse generator;
- the presence of a magnet is detected by the magnet sensor.

If one or more of these conditions are present, a dialogue box will appear describing the condition and the MRI Protection Mode as not accessible.

After selecting the *MRI Protection Mode* button, the *MRI Protection Checklist* screen is displayed. The Checklist summarises the conditions that must be fulfilled at the time of the scan for a patient to be eligible for a Conditional MRI scan. Further verification is required before each scan to prevent the possibility of changes occurring in the system or patient after the original pulse generator/system installation.

In case of any doubts, or for further help and confirmation of the MRI conditions of use, refer to the Boston Scientific website *https://www.bostonscientific.com/imageready/en-EU/emblem-mri-sicd.html*. After you enter the device number, it will give you the correct behaviour to be followed in case of an MRI examination (Figure 12.2).

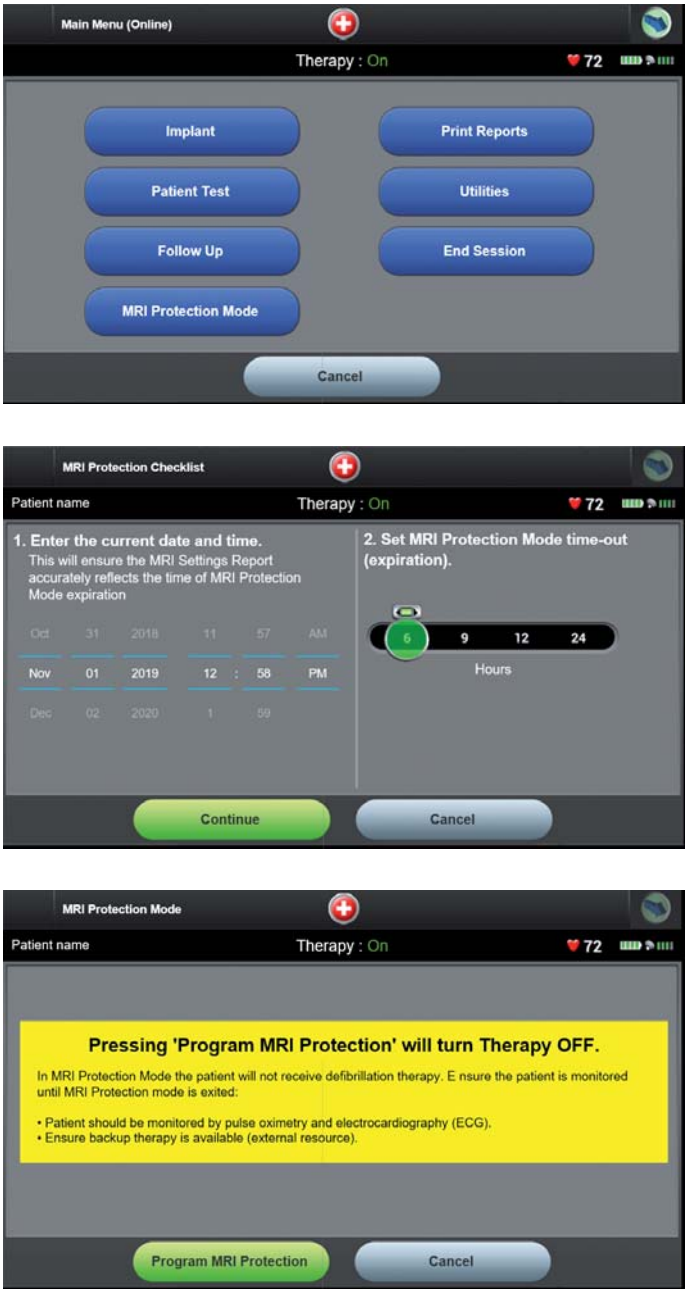


FIGURE 12.1

An S-ICD programmer screen with MRI mode programming. *Top figure:* the main screen when starting MRI mode. *Centre figure:* Use of Time-out function to program the request to check date and time (time in which the device will remain in MRI mode). Nominally set at 6 hours but programmable also at 9, 12 and 24 hours. *Bottom figure:* request for confirmation of programming in MRI mode with antitachycardia therapy in the OFF position.

TABLE 12.2

Summary Table on the Conditions of Use of the S-ICD in MRI Mode

Conditions of Use – Cardiology
Pre-Scan
1. Check the patient's suitability for scans according to the Cardiological MRI conditions of use.
2. As close as possible to the start of the scan, the patient's pulse generator is reprogrammed to MRI Protection Mode and continuous patient monitoring begins.
3. Refer to the MRI Protection Settings Report to confirm that the patient's device is in MRI Protection Mode. The report includes the exact time and date in which the MRI Protection Mode expires via the Time-out function. Check that there is enough time to complete the scan.
During the Scan
4. Ensure that the patient is continuously monitored by pulse oximetry and electrocardiography, with the backup therapy (external resuscitation) available, while the device is in MRI Protection Mode.
After the Scan
5. Verify that the pulse generator is returned to pre-MRI function, automatically via the Time-out function, or manually if the programmer is used. Continue patient monitoring until the pulse generator returns to pre-MRI function. A follow-up test of the S-ICD system can be performed after exiting the MRI Protection Mode.
Conditions of Use – Radiology
In order for a patient with an ImageReady S-ICD system to undergo an MRI scan, the following conditions of use must be met.
• PMRI magnet power = only 1.5 T.
• RF range = about 64 MHz.
• Maximum gradient strength = 30 T/m (3,000 G/cm).
• Equipment Specification MRI = 1H horizontal proton closed scanners only.
• Specific absorption rate (SAR) limits for the entire active scan (normal operating mode): - the whole body on average, ≤2.0 Watts/kilogram (W/kg); - head, ≤3.2 W/kg.
• Maximum rate of change of the gradient ≤200 T/m/s for each axis.
• The use of receiving coils is unlimited. The local single transmission coils or the local transmission/reception coils can be used, but they must not be placed directly on the S-ICD ImageReady system.
• Patient only in supine or prone position.
• The patient should be monitored continuously by pulse oximetry and electrocardiography for the entire period in which the pulse generator is in MRI Protection Mode. Make sure backup therapy is available (external resuscitation).

http://www.bostonscientific.com/imageready/en-EU/home.html

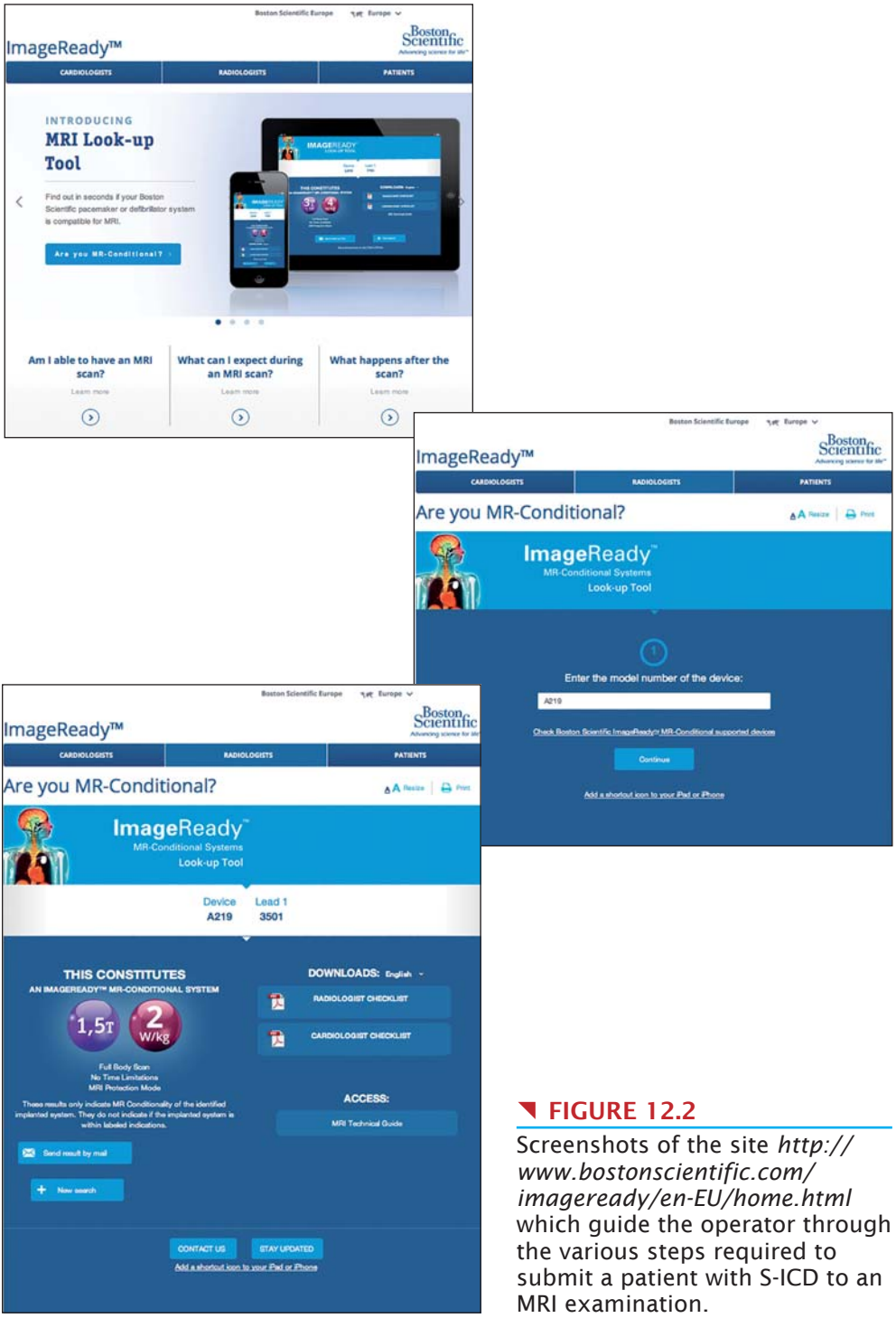


FIGURE 12.2

Screenshots of the site *http://www.bostonscientific.com/imageready/en-EU/home.html* which guide the operator through the various steps required to submit a patient with S-ICD to an MRI examination.

Cardiac Magnetic Resonance

Cardiac MRI in recent times has forcefully entered the clinical practice of cardiology because of the information that this method can give, the study of vitality, quantification and localisation of scar, arrhythmias, myocarditis, etc. Patients with cardiac electrical devices (DEC) may also need to undergo cardiac MRI.

However, stimulation systems containing ferromagnetic material can hinder the diagnostic quality of MRI images. In fact, to date, most of the papers published so far are focused on aspects linked to the risks for the patient, while the impact on image quality and on diagnostic value of implantable devices has been given much less attention. The metal components of implantable cardiac stimulators have a magnetic susceptibility that differs considerably from that of tissues. These differences lead to a distortion of the local magnetic field and, therefore, can produce artifacts. The extension and direction of the artifacts depends not only on the susceptibility of the PM/ICD/S-ICD and the related catheters but also on the direction of the magnetic field and on the type of sequence used. In general, the most significant artifacts are located in the area where the stimulator is present and, to a lesser extent, along the electrocatheter. For this reason, the evaluation of the quality of imaging is particularly important in cardiac MRI. The image is, however, influenced by the number and size of the leads, and its quality decreases as you go from the study of a patient with a pacemaker to one with an ICD and, finally, to the CRT-D. Figures 12.3–12.5 show a cardiac MRI in a patient with a single chamber PM (Figure 12.3), in a patient with a dual-chamber ICD (Figure 12.4) and in a patient with CRTD (Figure 12.5).

It is well known that artifacts increase as the number of leads increase. In an S-ICD, unlike transvenous systems, heating near or around the electrode in contact with the myocardium is absent and, therefore, there is no danger of myocardial damage.

In theory, in view of the lower number of leads, among other things not in contact with the myocardium, the MRI test in patients with an S-ICD should generate less interference and therefore higher image quality.

However, no studies have evaluated safety and feasibility, as far as the quality of images are concerned, and, therefore, how useful cardiac MRI can be for diagnosis in patients with an S-ICD.

There are still no clinical cases reported in the literature on the use of cardiac MRI in carriers of an S-ICD, only one study[3] reports the data of three patients who, among other things, did not perform sequences for enhancement. In our clinical experience, cardiac MRI was performed on

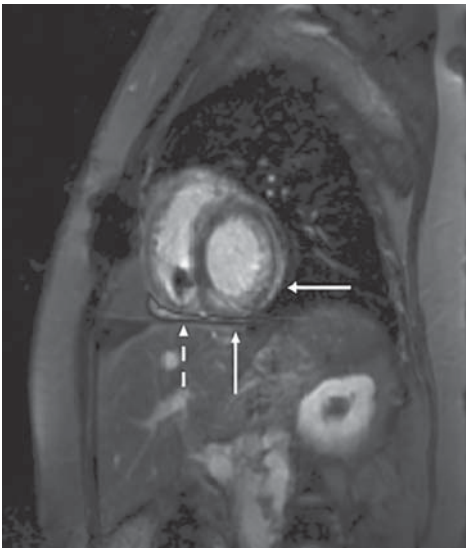
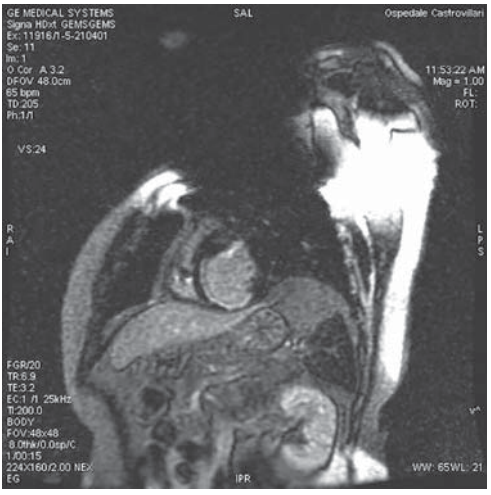


FIGURE 12.3

Cardiac MRI in a patient with single chamber PM. The electrocatheter in the right ventricle and the perfusion defect in the perfusion sequence are highlighted.



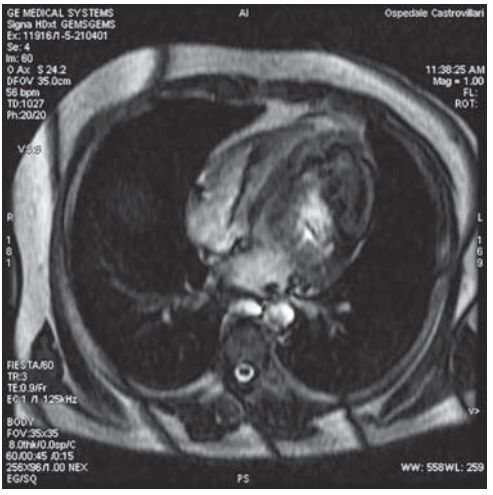


FIGURE 12.4

Cardiac MRI in a patient with a dual chamber ICD. Electrocatheter is evidenced in the right ventricle and the enhancement study is poor due to the presence of artifacts.

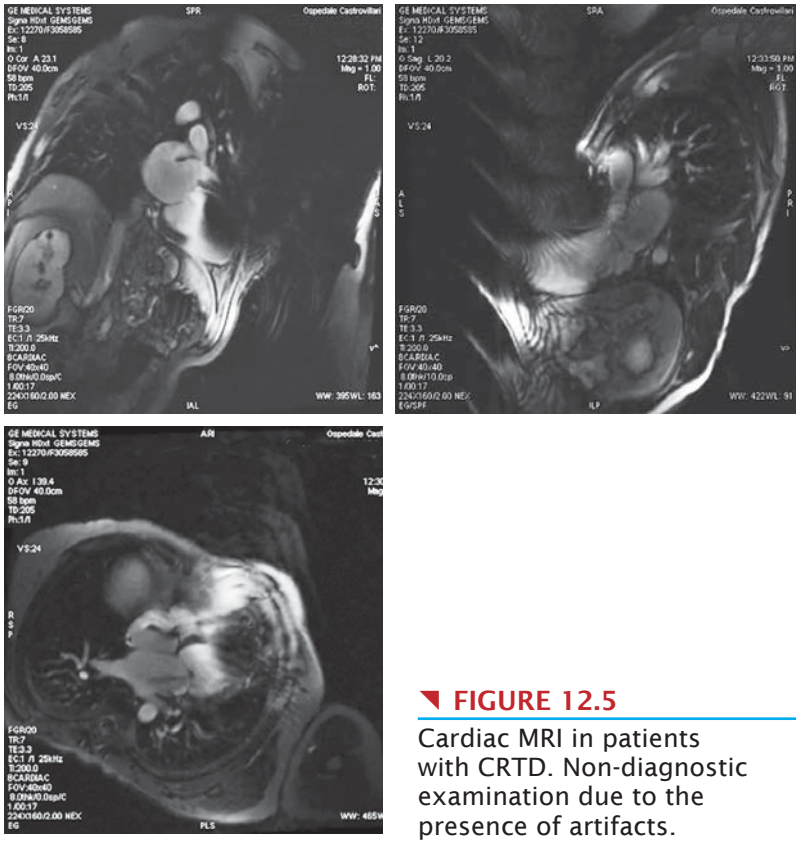


FIGURE 12.5
Cardiac MRI in patients with CRTD. Non-diagnostic examination due to the presence of artifacts.

12 patients, conducted in the absence of complications and without subsequent damage to the device, except for 4 patients who had an irreversible loss of the acoustic alarm signal. The test was safe, although in a good percentage of patients the image was disturbed by the artifact due to the device case rather than the lead, particularly in gradient-echo sequences.

Better image quality is obtained after gadolinium administration both to assess perfusion and delayed enhancement. Unfortunately, in many patients the visualisation of the lateral wall may not be clearly visible due to the artifacts in the proximity of the case. However, in most patients the analysis of delayed enhancement can give the clinical information needed (Figures 12.6–12.9).

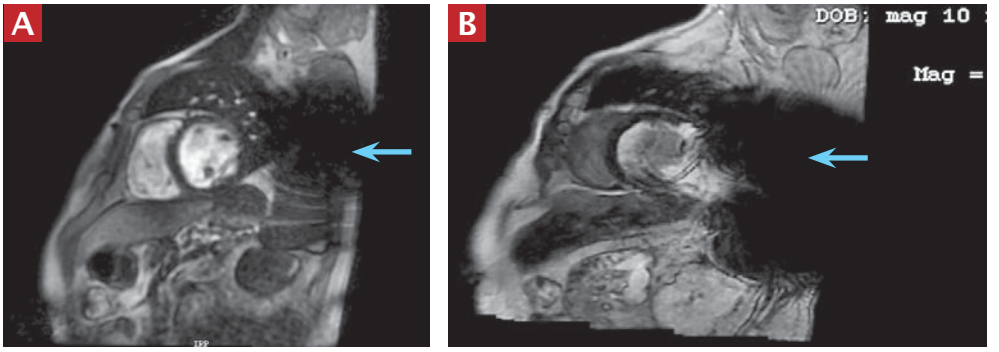


FIGURE 12.6

Cardiac MRI in a 50-year-old patient with an S-ICD. Perfusion (A) shows a high quality image, enhancement (B) loses quality in the evaluation of the lateral wall of the left ventricle. The right ventricle is well evaluated. The arrow indicates the 'black hole' made by the device.

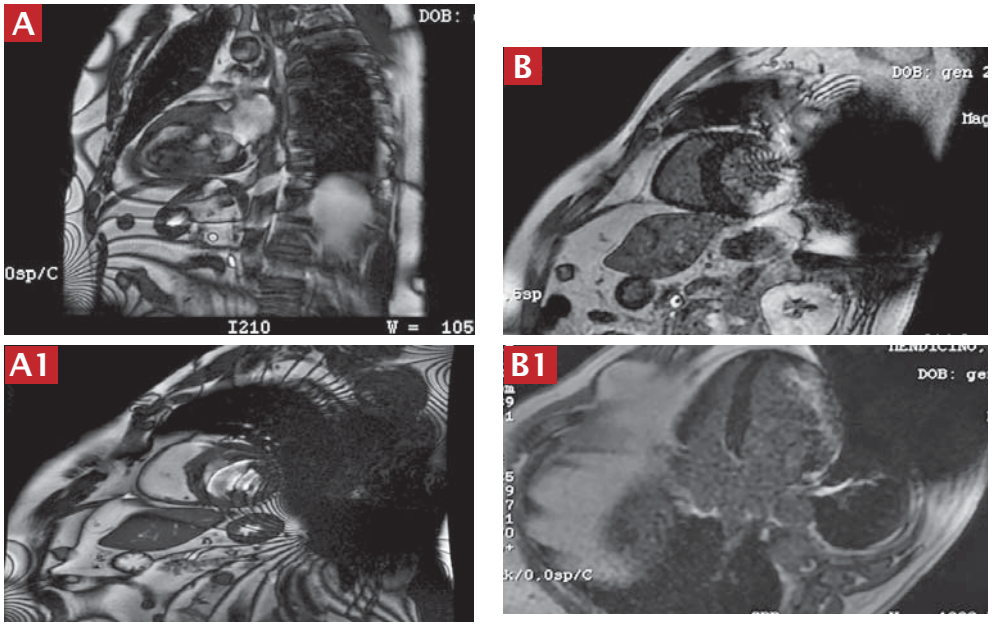


FIGURE 12.7

Cardiac MRI in a 45-year-old patient with an S-ICD. In images in gradient echo artifacts are highlighted (A-A1); in the enhancement sequences (B-B1) artifacts appear on the lateral wall of the left ventricle.

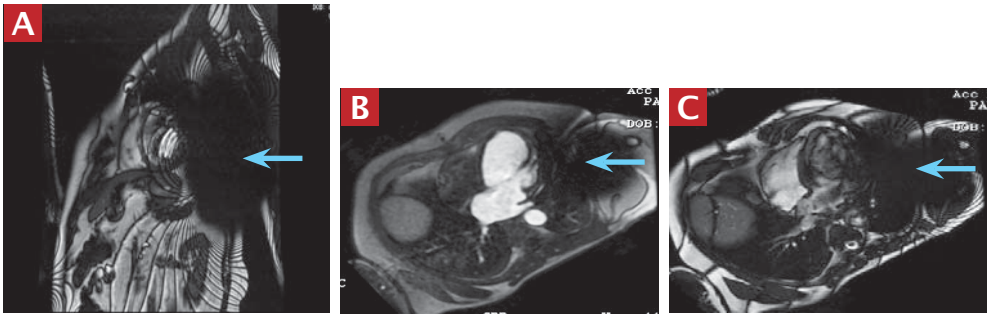


FIGURE 12.8

Cardiac MRI in a 58-year-old patient with an S-ICD. Poor quality image in gradient echo (A) due to interference from the case of the S-ICD (arrow). The image improves with the perfusion sequence (B); with the enhancement loss of definition in the lateral wall of the left ventricle (C).

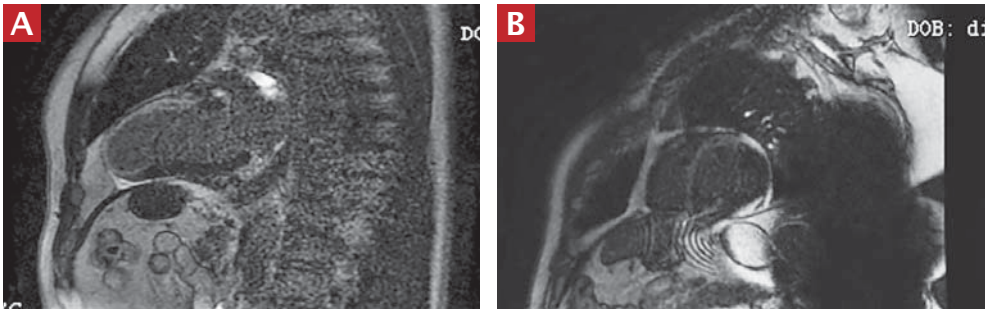


FIGURE 12.9

Cardiac MRI in a 50-year-old patient with an S-ICD. A good quality of the enhancement is highlighted (A,B).

Conclusions

The MRI test in patients with an S-ICD is feasible and safe when compliance with the conditions of use is ensured.

However, when a patient with an S-ICD is subjected to a resonance examination, the decision should always be balanced with respect to the potential risks and the possibility, in some parts of the body, of a non-optimal image.

With regard to cardiac MRI, a study on the most appropriate sequences to be used, and more experience, will certainly make the examination safe, feasible and of good quality in most patients.

Possible interference with the acoustic alarm must also be considered.

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CHAPTER

13

A Look into the Future: Modular Management of Cardiac Rhythm

L. Auricchio, G. Bisignani

S-ICD seems to have the prerequisites to become not only an alternative to the transvenous defibrillator, to be used in cases in which ICD implantation could be difficult or the risks high, but also as a 'first choice' therapeutic tool in all patients. When selecting patients for S-ICD, it is essential to have an accurate analysis of both favourable and unfavorable characteristics that the device can have for the patients. One of the limitations in opting for an S-ICD is due to its lack of ability to deliver anti-bradycardic and anti-tachycardia pacing for ventricular tachycardia. The presumed future need for patient stimulation is the most common reason to choose a traditional transvenous device over an S-ICD, despite the minimum number of patients who meet the conditions for a Class I recommendation for permanent stimulation[1].

An alternative approach, foreseen in the immediate future, is to use a combination of technologies in order to treat the patient's pathology according to their present and future needs. The **Leadless Pacemaker Empower™ by Boston Scientific** in combination with the S-ICD is able to do this.

Boston Scientific's Leadless Empower™ pacemaker stands out from the others in one crucial aspect. The current leadless pacemakers are designed only to be simple single-chamber pacemakers, while the real truth of leadless pacemakers is the development of a modular technology in which, in addition to serving as a single-chamber pacemaker, it is also able to coordinate therapy with an S-ICD and to offer patients the possibility of having a complete leadless system[2].

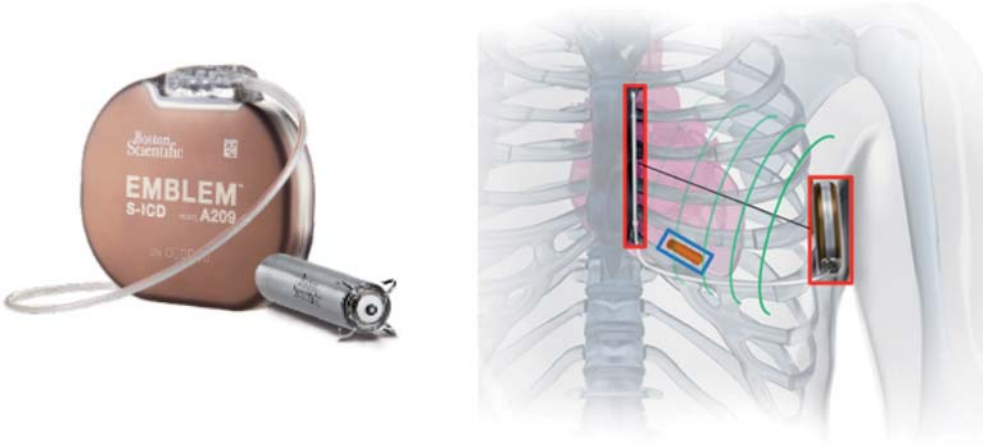


FIGURE 13.1
Schematic representation of the modular CRM system.

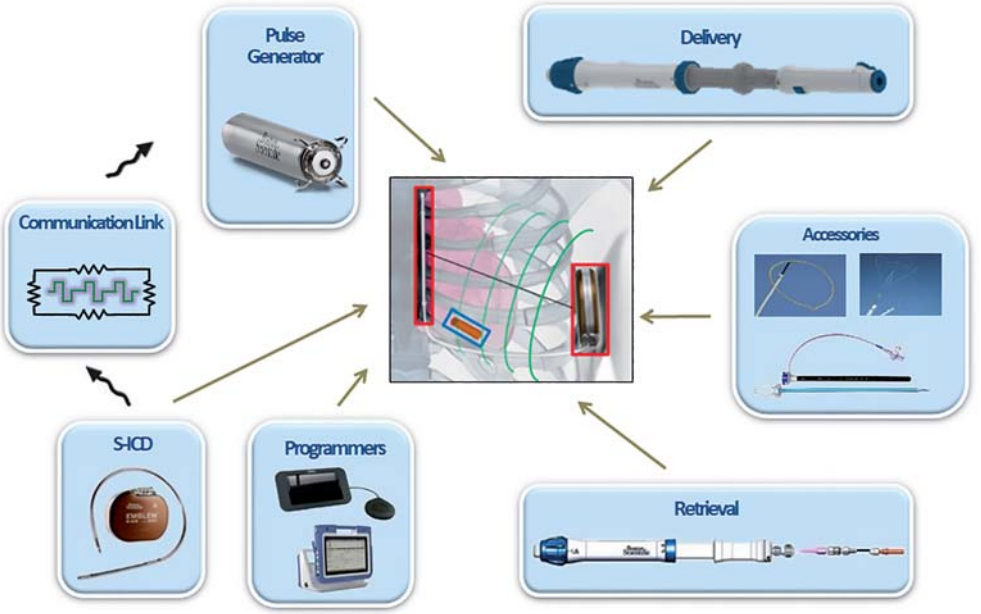


FIGURE 13.2
The figure illustrates all the components necessary for implantation and function of the modular CRM system.

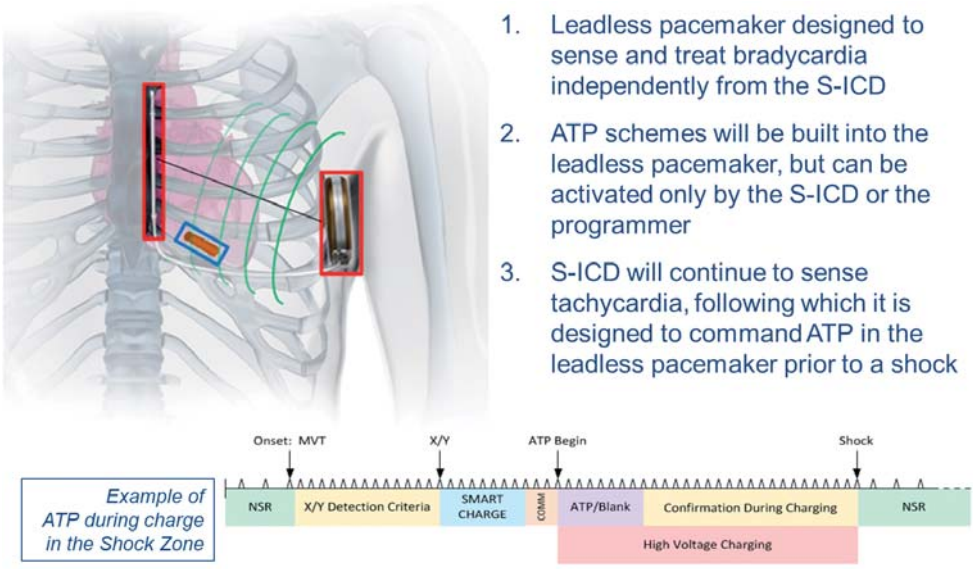


FIGURE 13.3

Operating steps of the modular CRM system.

The intended use of this combination of technologies, called mCRM or modular cardiac rhythm management, can be two-fold.

The two devices can be implanted together, simultaneously, to offer the patient a complete cardiac rhythm management, if necessary, or they can be used to provide upgrading over time during patient follow-up. If a

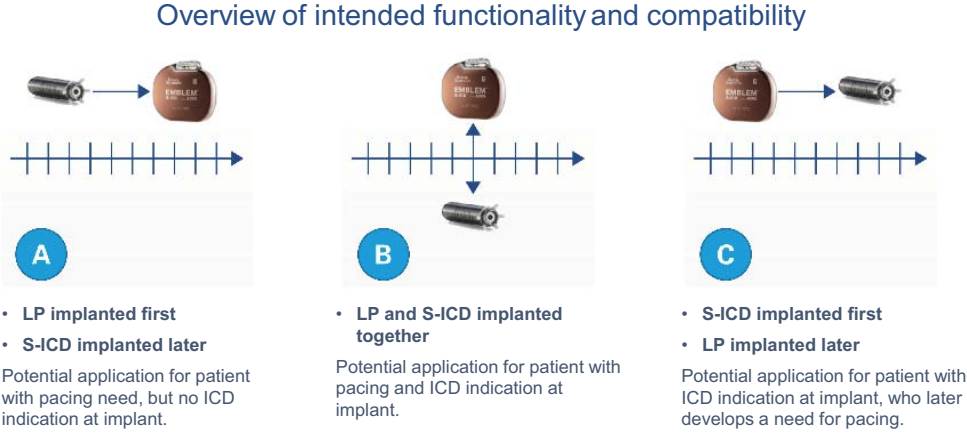
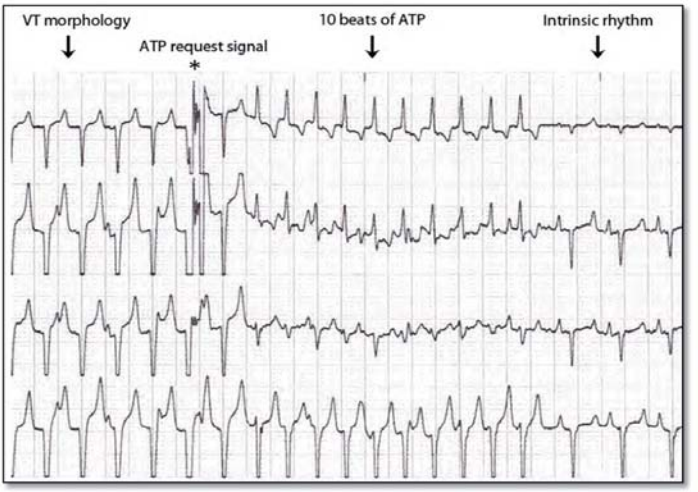


FIGURE 13.4

Use of mCRM.

The First Report on Communicating Leadless Anti-Tachycardia Pacemaker and Subcutaneous Implantable Defibrillator: The Next Step in Cardiac Rhythm Management [3,4] (Preclinical Study)



An episode of simulated VT (LV Pacing) followed by manually triggered S-ICD ATP command resulting in successful ATP-delivery by the LCP (10 beats, at 81% of coupling interval)

FIGURE 13.5

Example of intervention with ATP of the modular CRM system[4].

patient already has a device and later needs a modular system, this mCRM system is currently the most suitable once, as long as each device can function independently, because it is able to give each patient the therapy he or she needs when needed, unlike the current 'one size fits all' approaches.

Feasibility studies of stimulation with an mCRM system prototype consisting of a leadless pacemaker (LP), wirelessly controlled by an S-ICD, with intracorporeal communication between devices have already been carried out[3]. Currently the prototype envisages communication between an S-ICD and LP in unidirectional mode, through a series of short electrical pulses from S-ICD to LP produce effective pacing (ATP).

In these studies S-ICD and the LP were successfully implanted in 39 animals, 23 of which were monitored for 90 days. Performance of the LP was adequate and showed ventricular inhibition behaviour (VVI) in all the tested animals, with correct ATP delivery, defined as an ATP supply following an ATP request signal from the S-ICD[4].

Unidirectional communication between the S-ICD and the LP was effective in all attempts, and ATP was delivered in all 306 ATP requests

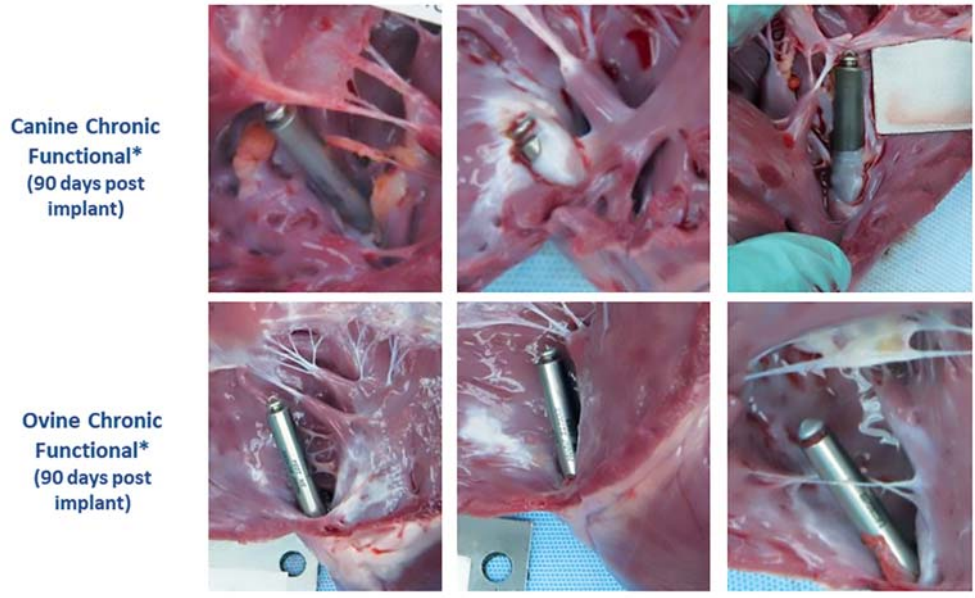


FIGURE 13.6

Anatomical findings in animals implanted with a leadless pacemaker at 30 days after implantation.

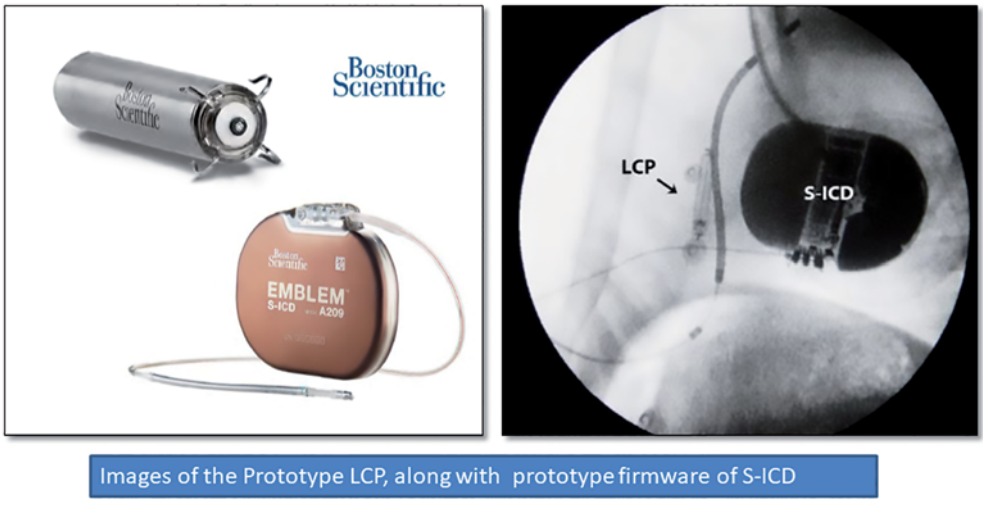


FIGURE 13.7

Preclinical study images with combined S-ICD implant and leadless pacemaker[3,4].

activated by S-ICD and received by LP. The first trials in humans have been planned and, if they are successful, the mCRM system could offer new opportunities in personalising the patient's treatment, becoming the future of device-based anti-arrhythmic therapy[4].

Our perception is that in the future the treatment of patients with cardiac arrhythmia based on device implantation will become completely leadless and minimally invasive.

Disclaimer

Concept device or technology. Not available for sale.

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