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Adverse Interactions between ICD and Permanent Pacemaker Systems

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1. Introduction

After the introduction of the implantable cardioverter defibrillator (ICD) in clinical practice by Mirowski in 1980 [Mirowski et al., 1980] the first available devices offered only a basic ventricular pacing option. Since approximately 5-20% of patients with an indication for ICD therapy following implantation criteria at that time (secondary prevention) needed antibradycardia pacing as well, the implantation of an additional pacemaker (PM) was often necessary up to the 1990s [Sticherling et al., 1997; Brooks et al, 1995; Geiger et al., 1997]. In contrast, the modern ICD systems offer all forms of antitachycardia and antibradycardia therapy integrated in one device. However in 1997 Sticherling et al. concluded in their review about combined ICD and antibradycardia pacing therapy, that even with the introduction of integrated devices the issue of interactions will stay clinically relevant, as many candidates for ICD implantation present with an already implanted pacemaker system [Sticherling et al., 1997]. In contrast to this prediction, today more than 10 years later, through the tremendous advances in device technology as well as in implantation and revision operation methods, the patients are rare, who are fitted with two separate active cardiac implantable electronic devices (CIED) for antibradycardia and antitachycardia therapy respectively. However these patients require extreme diligence at implantation, testing, programming and follow-up to avoid potentially dangerous interactions between the devices.

„Concomitant implantation of AICD and a permanent pacemaker requires an understanding of the functioning of both devices and their potential interactions“ [Singer et al., 1988]

2. Indications and how to avoid simultaneous use of two active CIEDs

As mentioned above, the CIEDs available today offer all known antibradycardia and antitachycardia therapies including cardiac resynchronization therapy (CRT). Thus it is possible to provide each patient at first implantation with an adequate singular device according to his rhythmological indication. Today there is no indication for the primary simultaneous implantation of two separate CIEDs!

However the situation remains complex in patients, who were already treated with one CIED, but need a system upgrade in the further course due to different reasons. Currently typical clinical indications are the need for antitachycardia and/or cardiac resynchronization therapy in pacemaker patients.

In these particular cases careful preparation and planning of the operative procedure is extremely important. The pulse generator pocket and the scar need to be assessed. Before operation the function and position of old leads are reviewed and a decision is made regarding which leads will be continued to be used, be abandoned or extracted.

An essential requirement for ipsilateral implantation of new leads is an open vascular access route. In 25-33% of patients with an implanted device, a significant stenosis (> 50% stenosis) or even occlusion of the involved axillary, subclavian, brachiocephalic vein or superior vena cava (SVC) is encountered [Minden & Butter, 2008]. Therefore a periphereal phlebography should be performed before an upgrading procedure. Blood flow from the distal periphery, possible access sites, central draining into the SVC, valves and stenosis formation are evaluated. If there is a distal stenosis of the axillary or subclavian vein a more proximal entry into the vessel might be successful, although the long term risk of mechanical lead alteration is increased. If the subclavian vein or SVC show a central stenosis, but a proximal flow can still be seen, it is often possible to pass the stenosis using access to the axillary vein and a hydrophilic wire. A long sheath is introduced over the wire and the lead is positioned with the sheath still in place. Of course the risk of occlusion of the vessel is increased significantly after such a procedure, but the number of intravascular leads is reduced by the usage of old leads compared to performing a complete new implantation on the contralateral side. Leads that are implanted for less than two years can often be extracted by conventional means, thereby further decreasing the number of remaining leads.

In our institution an ipsilateral upgrade is pursued as general rule. Thus the contralateral side remains intact and is accessible for subsequent interventions, if needed, which is especially important for younger patients with expected long duration of implanted devices. If an ipsilateral upgrade is planned, the side of the old pulse generator needs to be taken into account as well. When upgrading a right sided pacemaker to ICD, a high-energy device should be used [Natale et al., 1997]. For upgrading to CRT different guiding catheters are needed for a right sided compared to a left sided approach.

If the patient already has an adequate antibradycardia PM it may seem to be a theoretical option to implant just a new ICD-system on the contralateral side. The pacemaker would keep up the antibradycardia therapy and the new ICD would act as antitachycardia system. The basic advantage would be to make the procedure a simpler one, equivalent in logistics and operation technique to the implantation of an ICD as first device. A right sided pacemaker combined with a new left sided ICD may offer the theoretical benefit of higher shock effectiveness, but that is of limited importance in view of the high energy-ICDs available today. However there is the disadvantage of potentially dangerous interactions. The elimination of these interactions cannot be guaranteed with 100% safety, even after extensive testing and meticulous programming. For this reason considering the up to date device and implantation technology, different solutions should be preferred and, if necessary, the patient should be transferred to a center with experience in this field.

With an ipsilateral occluded vein the following options can be discussed:

1. Preferably the contralateral implantation of a complete new system is done, followed by inactivation of the old device. The old generator is generally explanted and if the risk for lead removal is reasonable, the leads are extracted at the same time. Also functional deactivation of the old generator is possible (e.g. OOO, OVO or ODO mode) and should be made, if explantation is scheduled for a later time (fig. 1a to c). It has to be remembered that not all CIEDs allow complete deactivation (fig. 2). Principally deactivation by programming alone cannot be recommended as a permanent solution.

Firstly, an accidental reprogramming of the generator, e.g. at a later time in ignorance of the specific situation cannot be excluded. Secondly, battery depletion can cause automatic mode changes of the old generator leading to potential interactions [Bastian & Kirste, 2009].

Fig. 1a and 1b. Chest x-ray PA and lateral. Female patient. DDDR-pacemaker on the right side (Affinity®DR 5330, St. Jude Medical, St. Paul, Minnesota, USA, unipolar leads). Implantation in 1994 cause of sick sinus syndrome. In 2008 indication for cardiac resynchronization therapy (chronic heart failure due to dilated cardiomyopathy, left bundle branch block): new implantation of a CRT-D system on the left side (Concerto C 174 AWK, Medtronic Inc., Minneapolis, MN, USA) because of an occluded right subclavian vein.

Standardparameter			
	Initial	=> [Change]	Aktuell
Betriebsart	DDDR	=> [Mode]	ODO
Grundfrequenz	60	[Basic Rate]	60 min ⁻¹
Hysteresefrequenz	Aus		• min ⁻¹
Ruhefrequenz	50		• min ⁻¹
Obere Grenzfrequenz (MTR)	125		• min ⁻¹
2:1-Blockfrequenz	129		• min ⁻¹
AV-Intervall	275		275 ms
PV-Intervall	225		225 ms
Frequenzabhängigkeit (AV-Int.)	Niedrig		•
Kürzestes AV-Intervall	70		• ms
V. Refraktärzeit	250		250 ms
Atriale Refraktärzeit (PVARP)	275		275 ms
Ventrikuläre Werte:			
V. AutoCapture	Aus	[Ventricular]	•
V. Impulsamplitude	2.00	[Pulse Amplitude] • V	
V. Impulsdauer	0.3	[Pulse Width] • ms	
V. Empfindlichkeit	3.0	[Sensitivity] 3.0 mV	
V. Stimulationskonfiguration	Unipolar	=>[Lead configuration] •	
V. Wahrnehmungskonfig. ..Unipolar (Spitze)		Unipolar (Spitze)	
Atriale Werte:			
A. Impulsamplitude	2.00	[Pulse Amplitude] • V	
A. Impulsdauer	0.2	[Pulse Width] • ms	
A. Empfindlichkeit	0.75	[Sensitivity] 0.75 mV	
A. Stimulationskonfiguration	Unipolar	=>[Lead configuration] •	
A. Wahrnehmungskonfig. ..Unipolar (Spitze)		Unipolar (Spitze)	
Magnetreaktion	Batterietest		Batterietest

Fig. 1c. Functional deactivated unipolar dual chamber pacemaker (Affinity® DR 5330, SJM) by programming the device to ODO mode after the CRT-D system has been implanted on the opposite side.

Parameter		
Batterie		OK
ERI, errechnet		5 J. 6 Mo.
Magneteffekt		AUTO -
		Vorher Aktuell
Mode		SSI
Grundfr. Tag/Nacht...	[Lower Rate limit]	30/30 ppm
Frequenzhysteres...		AUS ppm
Repetitiv		-----
Suc		-----
Nachtprogramm		AUS ppm
Nachtbeginn		-----
Nachtende		-----
Sensor		
Max.Sens.Freq		----- ppm
Sensorverstärkung		-----
Autom. Verstärkung		-----
Sensorschwelle		-----
Frequenzanstieg		----- ppm/s
Frequenzabfall		----- ppm/s
Obere Grenzfrequenz		----- ppm
Impulsamplitude	[Pulse Amplitude]	0.1 V
Impulsdauer	[Pulse Width]	0.10 ms
Ven. Empfindl.	[Ventricular Sensitivity]	1.0 mV
Atr. Empfindl.		0.8 mV
Refraktarzeit		300 ms
Polarität Pace		UNIP
Polarität Sense		UNIP
Elektroden-Check		AUS

Fig. 2. Functional deactivation of a unipolar single chamber pacemaker (Philos SR, Biotronik SE & Co. KG, Berlin, Germany). The programming is on SSI (VVI) with a basic rate of 30/min, minimal pacing output (impulse amplitude 0.1 V, pulse width 0.1 ms) and high ventricular sensitivity (1 mV). No interactions were observed until explantation 2 months later (same patient as in fig. 12).

- 2. Contralateral implantation of a functional additive system with continued use of the existing device. The obvious advantage would be the relative simplicity of the procedure. The intervention could be carried out in centers that have less experience with revision procedures. Considering the potential interactions this should be principally avoided.
 - 3. Continued use of old leads with a contralateral new device could be achieved by subcutaneous tunneling over the sternum, but isn't performed at our hospital anymore due to potential long term complications (especially mechanical lead alteration).
 - 4. If the ipsilateral vein is occluded and the contralateral side cannot be used e.g. because of infection or radiation therapy, a remaining option is extraction of the old leads using a sheath, which serves as a tunnel for the new lead.
 - 5. The final option is the implantation of epicardial leads.
- The decision which procedure is finally chosen for a specific patient has to remain an individual one, of course.

3. Interactions

Inappropriate ICD therapy caused by oversensing of pacemaker signals

The problem was first described by Chapman and Troup in 1986 in a patient with recurrent ICD shocks after "double sensing" of bipolar DVI pacemaker actions [Sticherling et al., 1997; Chapman & Troup, 1986].

The underlying mechanism is the erroneous detection of ventricular tachyarrhythmias caused by the ICD oversensing atrial and/or ventricular pacemaker signals, as well as the ventricular response or intrinsic actions (double or triple counting) (fig. 5, 6, 20, 22b). To become an active oversensing problem the timing of the signals has to exceed the

postventricular sense blanking period of the ICD, either due to programming of a long AV-delay or a significant local conduction delay, resulting in a delay between stimulus and locally evoked potential [Singer et al., 1988; Chapman & Troup, 1986; Calkins et al., 1990; Noguera et al., 1997]. The postventricular sense blanking period of an ICD is often around 120-150 ms and usually cannot be programmed. However, some devices allow significantly lower values. The blanking period should not be programmed shorter than 100 ms to avoid double counting (fig. 3 and 4)!

Clinical problem caused by interaction	Pathophysiology	=> Mechanism of interaction
ICD: Inappropriate therapy	PM: Pacing artifacts - unipolar - with high output - ineffective - high rate - asynchronous Noise from lead contact	ICD: Overcounting of PM artifacts + evoked / intrinsic potentials => erroneous VT/VF detection
ICD: Inadequate SVT/VT discrimination	PM: Pacing artifacts	ICD: oversensing of PM artifacts => - artifact as false intrinsic template - stable tachycardia classified as unstable
ICD: Delayed/inhibited VT/VF therapy	PM: VT/VF undersensing => - pacing during VT/VF	ICD: oversensing of PM artifacts => - VT/VF undersensing
ICD: Inhibited post-shock pacing	PM: Post shock ineffective pacing artifacts	ICD: oversensing of PM artifacts
PM: Post-shock dysfunction - device intact	ICD-shock => energy shunted over the PM-lead => thermal damage of endocardial tissue	PM: - increased stimulation threshold with loss of capture - impaired sensing function
PM: Post-shock dysfunction - device affected	ICD-shock - high energy, applicated near the PM	PM: damage or re-programming - e.g. fixed rate back-up-mode
PM: Inhibited pacing	Second CIED: ineffective pacing - Frequency > PM rate	PM: Inhibition by oversensing of artifacts

Table 1. Overview: potential interactions of 2 active implanted CIEDs. PM = pacemaker, ICD = implantable cardioverter defibrillator, VT = ventricular tachycardia, VF = ventricular fibrillation.

Fig. 3. Double counting of wide intrinsic QRS-complexes of an induced fast ventricular tachycardia (VT) due to the manufacturer preset ultra short hardware blanking period of only 8 ms/ noise blanking of 60 ms (ICD Lexos VR-T, Biotronik SE & Co. KG, Berlin, Germany). After extending the blanking period to 100 ms correct sensing was registered (not shown on this stripe).

Fig. 4. Intermittent ineffective ventricular ICD pacing (*) and double counting of intrinsic QRS-complexes (†) after shock delivery. Postventricular sense blanking period (hardware blanking) 8 ms / noise blanking 60 ms (ICD Lexos VR-T, Biotronik SE & Co. KG, Berlin, Germany).

Double detection as cause of inappropriate ICD-therapy has been described also with a biventricular ICD with simultaneous right- and left ventricular sensing [Schrieck et al., 2001]. Additional factors that contribute to the problem of oversensing are leads that are located parallel or very close, unipolar pacer stimulation, high stimulation amplitude of the pacemaker and the use of epicardial or transvenous integrated bipolar ICD leads [Haffajee et al., 1996; Walker et al., 2000]. Inappropriate detection and following therapy are as well more likely to occur with a higher pacer stimulation rate, a lower VT/VF detection rate and shorter detection duration (VT/VF number of intervals to detect) of the ICD. Overall incidence of these interactions is very low. In 1990 a working group from Baltimore reported on a cohort of 30 patients with active pacemaker and ICD-systems with epicardial defibrillation leads [Calkins et al., 1990]. There was one case of double counting, however no inadequate shock was delivered. In another cohort consisting of 9 patients with epicardial ICD-systems, Cohen et al. showed oversensing in 5 cases, 4 patients had unipolar and 1 had bipolar pacemaker stimulation [Cohen et al., 1988]. In later studies with bipolar pacemakers and ICDs with true bipolar sensing no further cases with clinically relevant oversensing were described. [Sticherling et al., 1997]. However even with meticulous implantation, testing and best possible programming and the usage of modern systems, there is no safety guarantee that the interaction doesn't show up in a particular case. In our own cohort we had one patient with implanted bipolar pacemaker (Kappa DR, Medtronic) and transvenous ICD (Marquis VR 7230, Medtronic; lead true bipolar) who had recurrent inadequate ICD-therapies due to double counting of the bipolar ventricular stimulation (fig. 5). Due to an increased stimulation threshold these stimuli were given with high energy after a long

stimulated AV-delay of 240 ms. Many of the sensed pacer spikes were in the refractory period of the ICD, which was documented in the integrity counter of the ICD (fig. 5c). The stored frequent episodes of non sustained VTs were caused by overcounting (fig. 5d). Another example of device interaction is illustrated in fig. 6.

Fig. 5a. Inappropriate shock delivery caused by double counting. V-V interval plot.

Fig. 5b. Inappropriate shock delivery caused by double counting. Intrinsic rhythm: sinus-arrest, considerable prolonged AV-conduction time (560 ms). * = intrinsic QRS-complex. PM rhythm: atrial pace-ventricular pace: † = paced p-Waves, ‡ = ventricular pacing artifact, prior to the shock ineffective due to pacing in the intrinsic ventricular refractory period. § = after shock delivery (CD) effective AV-sequential ventricular pacing by the PM, sensed by the ICD.

Fig. 5c. More than 42,000 ultra short V-V intervals sensed at 120 or 130 ms and some episodes with inadequate therapy delivery caused by double counting. 1581 episodes counted as non sustained VT (see fig. 8).

Fig. 5d. Frequent episodes of non sustained ventricular tachycardia; erroneous detection due to double counting.

Fig. 5e. „Spontaneous termination“ of an inadequate detected non sustained VT episode (monitor zone). Intrinsic rhythm: sinus-arrest, considerable intrinsic AV-conduction delay. * = intrinsic QRS-complex. PM rhythm: atrial pace-ventricular pace: † = paced p-Waves, ‡ = ventricular pacing artifact. Intermittent double counting is caused by the ineffective ventricular pacing artifacts as explained in fig. 5b. Depending on the timing of the p-waves to the intrinsic QRS-complexes safety window pacing occurs without double counting (S). The overcounting is interrupted after the occurrence of a second degree type I AV block (Wenckebach) (#) followed by AV sequential PM pacing with the pacing artifact sensed by the ICD.

Fig. 6a. Detection of a VT in a programmed monitoring zone (marker TD VTM). Initially singular oversensing of a ventricular PM-spike (*). ICD: Marquis VR 7230, Medtronic, dual coil - true bipolar lead. ICD parameter settings for tachycardia detection: VT = Monitor 400-330 ms; FVT = via VF 270 ms; VF = 330 ms. Wavelet = auto. Pacemaker: Kappa DR, Medtronic, bipolar leads.

Fig. 6b. Detection of the VT in the VF-zone (marker FD VF) after spontaneous acceleration with change of morphology and intermitting overcounting (*) of ventricular PM actions (†).

Fig. 6c. Termination of the VT by ICD shock (marker CD) after a second change of cycle length and morphology. The pacemaker artifacts (*) were not double counted.

Other situations where double counting can be encountered are ventricular sensing failure with asynchronous stimulation of the pacemaker in competition with the intrinsic rhythm [Singer et al., 1988], automatic or manual pacing threshold testing (fig. 27), asynchronous magnet testing [Brode et al., 1997; Epstein et al., 1989] as well as - independent of interactions-T-wave oversensing (fig. 7). Multiple counting can be caused by interference signals e.g. with a fractured lead (fig. 8) or mechanical lead-lead contact [Brode et al., 1997]. As a new, currently still experimental technology the combination of a device for cardiac contractility modulation (CCM) with an ICD, pacemaker or CRT-system is possible and useful [Seifert et al., 2008]. Of course it must be ensured that the CCM-signals are not being sensed by the second device.

Fig. 7. Inappropriate ICD-therapy due to T-wave oversensing (*). ICD Atlas®DR V 240, SJM.

Fig. 8. Inappropriate ICD-therapy (30 J, ICD Lexos VR-T, Biotronik) due to ICD lead fracture (Sprint fidelis 6948, dual coil, Medtronic). Multiple artifacts in the pace-sense channel (bottom). The upper far field EGM shows no artifacts. Note that sensing (*) as well as ventricular pacing (†) function is also affected.

Another clinical interaction hasn't been described in the literature so far: modern ICDs have different algorithms for differentiation of supraventricular and ventricular tachyarrhythmias. This includes taking a sample template of the normofrequent intrinsic chamber complex as a reference which is then compared to the morphology of a tachycardia. A match supports more a supraventricular tachyarrhythmia whereas in the case of a mismatch, the algorithm supports more the ventricular origin. Usually this template is automatically updated. With frequent oversensing of pacemaker stimulus artifacts by the ICD, such a stimulus may be erroneously recognized as 'intrinsic QRS complex' and saved as reference (Fig. 9). This could lead to misinterpretation of a supraventricular tachyarrhythmia as VT.

Fig. 9. Ventricular pacing artifact (*) erroneously saved as reference (template) for intrinsic chamber complex during automatic wavelet update (pacemaker Kappa DR, ICD Marquis VR 7230, Medtronic). † = true intrinsic QRS complex

Pro-arrhythmic effects of inadequate ICD-therapies have also been described [Sticherling et al., 1997; Epstein et al., 1989; Pinski & Fahy, 1995] (fig. 10).

Fig. 10. Induction of non sustained VT by inadequate ICD-shock

Undersensing of ventricular tachyarrhythmia by the ICD

This problem is the most serious potential interaction. For safe recognition of VF with a low intrinsic amplitude today’s ICDs have high sensitivity, which adjust automatically to the perceived signal up to a programmed maximum value. The automatic adaptive sensing algorithms of different manufacturers have specific characteristics and are programmable to some extent. If a pacemaker programmed according to normal standards (e.g. with ventricular sensing of 2.5 mV with bipolar systems or less sensitive with an unipolar lead) doesn’t recognize VF because of the low amplitude, the pacemaker will stimulate with its basic rate or sensor rate (fig. 11a). This is also true for AAI-pacemakers, that usually don’t sense any signals from the ventricle, if they are not inhibited by far-field-signals [Singer et al., 1988] These stimulation artifacts can now be sensed by the highly sensitive ICD. Especially with unipolar pacing spikes with high amplitude, the automatic sensing threshold is changed to less sensitive values. The consequence may be undersensing of VF with the worst case scenario of the ICD withholding therapy (fig. 11b).

Fig. 11a. Undersensing of ventricular fibrillation during cardiac catheterization in a patient with unipolar DDD-pacemaker stimulation.

Fig. 11b. Effective ICD shock is delivered after a marked delay of 25 seconds. Subsequent loss of capture (*) and sensing failure of the implanted DDDR-pacemaker (†).

Although some authors think it is in principle possible to use unipolar pacemaker leads when careful implantation and testing are performed [Haffajee et al., 1996], the general opinion states a contraindication for unipolar pacemaker stimulation if there is a second active CIED present [Singer et al., 1988; Epstein et al., 1989; Mattke et al., 1997] (fig. 12). Although for many years there's a predominant use of bipolar leads for conventional pacemakers, unipolar left ventricular leads are still used in implantation of CRT systems because of the venous anatomy. (fig. 13). The unipolar left ventricular stimulation generates a large pacing dipole [Le Franc et al., 1998].

Fig. 12. Chest x-ray PA. Male patient, VVIR-pacemaker on the right side (Philos SR, Biotronik, implantation of unipolar lead 1975 cause of AV-Block III°). In August 2008: new implantation of a singular chamber ICD on the left side (Maximo VR, Medtronic) because of spontaneous VT with syncope, occluded right sided vein and permanent atrial fibrillation. Explantation of the pacemaker in October 2008.

Fig. 13 a and b. Chest x-ray PA and lateral. Implantation of a biventricular pacemaker CRT-P (Insync III 8042, Medtronic) in November 2005 in a patient with dilatated cardiomyopathy. The unipolar LV-lead is positioned in an unfavoured anterolateral way. 2 years later contralateral implantation of a singular chamber ICD (Lexos VR, Biotronik) as bridge to heart transplant. The bipolar right ventricular leads were placed very close together. However, testing showed no inhibition of the ICD detecting induced ventricular fibrillation during pacemaker stimulation.

The problem was already described by Kim et al. in 1986 [Sticherling et al., 1997; Kim et al., 1986]. Among the 30 Baltimore patients inhibition of VF therapy was found in 2 patients with unipolar pacemakers and in one patient with a bipolar pacemaker under testing with high asynchronous output [Calkins et al., 1990]. Van Casteren et al. recently reported a case of temporary VF undersensing by a dual chamber ICD caused by oversensing of unipolar PM artifacts leading to delayed ICD therapy at defibrillation testing [Van Casteren et al., 2009]. So far there hasn't been a description of therapy inhibition of VF by oversensing in the clinical course of patients with bipolar pacemakers with standard programming and true bipolar transvenous ICDs and for example there was no occurrence in the 4 patients observed by Sticherling et al. It has to be pointed out however that there might be the necessity to increase the stimulation energy due to future threshold increases, which will increase the possibility of interactions.

There are 3 further phenomena that were reported by Glikson et al. and resulted from asynchronous pacemaker stimulation during tachyarrhythmias while testing [Glikson et al., 1999]: 1. A fast VT was detected in a slower zone and therefore firstly treated with ATP ineffectively. 2. A VT was detected in the VF-zone due to oversensing of pacemaker-stimuli and VT-complexes (see fig. 6b). 3. A stable VT-cycle length was classified as instable and the VT detection prevented as the stability criterion was activated.

Inhibition of antibradycardia ICD-function

In the presence of 2 active CIEDs the stimulation of the pacemaker at the basic or sensor rate will inhibit the antibradycardia function of the ICD, which will work, as intended, only as the antitachycardia system. If the ventricular stimulation by the pacemaker should be ineffective, the ICD can act as a backup for antibradycardia stimulation with its (usually low) programmed basic rate. However, this ICD stimulation can be inhibited by oversensing of pacemaker stimuli resulting in a loss of the backup function. A clinical example is the

inhibition of antibradycardia ICD back up stimulation by ineffective pacemaker artifacts after shock therapy (fig. 15, 24). The interaction can also be troublesome when e.g. a patient fitted with an AAI-pacemaker for sick sinus syndrome has received a VVI-ICD (fig 14). In case of a new AV-block the ICD could at least maintain ventricular stimulation - of course with loss of AV-synchronicity-, but there is the theoretical possibility of inhibition of ICD-stimulation by oversensing of atrial pacemaker spikes.

Fig. 14. Chest x-ray PA. Male patient, ICD implantation for secondary prevention (Marquis VR 7230, Medtronic, lead dual coil true bipolar). Three years later implantation of a bipolar AAI pacemaker (Insignia I Ultra, Boston Scientific) on the right side because of sinus bradycardia with preserved atrioventricular conduction. The left subclavian vein was found to be occluded.

Shock-induced pacemaker dysfunction

Increase of stimulation and/or sensing threshold of pacemaker

Immediately after shock delivery there may be in rare cases an increase in stimulation threshold with loss of capture and/or impaired sensing function (fig. 11b, 15, 23b, 24).

The mechanism of these phenomena remains unclear. Either a shunting of current to the pacing lead by activation of zener diode and/or capacitive coupling of energy to the lead resulting in a local thermal damage at the electrode-myocardial interface are discussed [Sticherling et al., 1997; Calkins et al., 1990; Levine et al., 1983]. The dysfunction is generally only transient and is more common with external defibrillation than with internal shocks. Shocks with higher energy seem to cause a higher increase in stimulation threshold (compare fig. 22b and 23b) [Sticherling et al., 1997; Brode et al., 1997; Pinski & Fahy, 1995]. Among the 30 patients described by Calkins et al. there was a transient impairment of pacing and/or sensing in 7 cases with a duration of < 10 seconds in 4 patients, < 35 seconds in 2 patients and > 56 seconds in 1 patient. In another case with a unipolar pacemaker the sensing defect lasted > 10 minutes, the lead was changed to a bipolar one. [Calkins et al., 1990]. None of the dysfunctions had a clinical impact on the patients, 5 of the 7 patients had ICD therapies in the follow up without any noticeable adverse interactions. Mattke et al. reported 10 patients, with no one having transient or persisting loss of capture or sensing after ICD-shock delivery [Mattke et al., 1997].

dipoles should be pursued [Geiger et al., 1997; Sheahan et al., 1997]. For this reason it is mandatory to control the positioning of the leads in 2 planes. (fig. 16).

Fig. 16 a and b. Chest x-ray PA and lateral: unfavourable positioning of ventricular electrodes to avoid oversensing: parallel position, very small distance < 1 cm. (Pacemaker/CRT-P: InSync, Medtronic. ICD: Lumax 300 VR-T, Biotronik)

To achieve a long distance e.g. the repositioning of a ventricle lead from the right ventricular apex (RVA) to a new position at the septum respectively in the right ventricular septal outflow tract (RVOT) seems reasonable (fig. 12) [Mattke et al., 1997]. However, an approach that is just guided by the anatomy is not sufficient on its own to prevent interactions [Brooks et al., 1995; Mattke et al., 1997]. Already at leads positioning the far-field-detection of pacemaker-spikes in the EGM and marker-channel of PSA, and after connection with the ICD should be watched. If necessary a different lead position has to be achieved [Cohen et al., 1988; Epstein et al., 1989] (fig. 17).

Fig. 17. EGM during implantation: newly implanted ICD-lead with marker-annotation (Analyser 2290, Medtronic, paper speed 25 mm/s), sensitivity 2.5 mV. The ventricular pacemaker spikes are shown with amplitude between 1 to 5.5 mV. With a QRS amplitude of about 9 mV no double-counting is observed, the stimulation artifacts were not sensed.

3. Leads with active fixation have the advantage of stable positioning in any location and should therefore be preferred [Sticherling et al., 1997].

5. Testing

Extensive testing for interactions is an essential part of the implantation procedure, if two CIEDs are left active [Sticherling et al., 1997; Walker et al., 2000; Cohen et al., 1988; Glikson

et al., 1999; Blanck et al., 1994]. This is also necessary even if the explantation of one device is already planned and the presence of the two devices together is of limited duration. If a CCM device is to be combined with a second active CIED (e.g. CRT-D) testing for interactions is also mandatory [Seifert et al., 2008]. Real time telemetry is particularly helpful with its view of high resolution intracardiac electrogram (EGM) and marker annotations. In practice a structured step by step approach is helpful. An exemplary protocol was evaluated by Glikson et al. and was used by others in a modified form [Sticherling et al., 1997; Walker et al., 2000; Cohen et al., 1988; Glikson et al., 1999; Blanck et al., 1994]:

1. *Assessment of oversensing of pacemaker artifacts:* the predominant criterion to accept a newly positioned ventricular lead is the analysis of pacemaker spikes by the ICD. Therefore, the pacemaker is programmed for stimulation with maximum amplitude and pulse width for all connected leads. With dual or triple chamber leads a long AV delay is selected. Now under stimulation, the EGM of the ICD lead is analyzed using maximum sensitivity and watched for oversensing of pacemaker actions. If there is double or triple sensing it is suggested to first reduce the pulse width and then if necessary the amplitude of the pacemaker until no oversensing is seen any more [Sticherling et al., 1997]. If this setting is not sufficient for effective pacing with enough safety margins, then the lead has to be newly positioned. To avoid oversensing not only the absolute amplitude of the pacemaker – stimulation – artifact is of importance, but also the ratio of signal heights of spikes to the evoked potential respectively the intrinsic chamber complex (fig. 17, 18). The test protocol evaluated by Glikson et al. regarded stimulation artifacts > 2 mV or a ratio of stimulus artifact/evoked QRS $> 1/3$ as insufficient. [Cohen et al., 1988; Glikson et al., 1999]. The authors described a positive predictive value of 18% respective 14.4% for clinical relevant interactions and a negative predictive value of 100% respective 92.3%.

If there is oversensing in the EGM of the ICD, the time interval from ventricular pacemaker spike to evoked QRS complex has to be shorter than the postventricular sense blanking period of the ICD (fig. 22b) [Cohen et al., 1988].

Fig. 18. Oversensing of the high ventricular pacing artifact (amplitude 12.5 mV) by the ICD. The stimulus artifact : evoked QRS ratio was inacceptably high (2.1). The atrial spikes as well as the QRS-complexes were not sensed.

2. *Rule out of VT/NF detection inhibition:* correct ICD-detection of induced VF has to be checked when there is asynchronous pacemaker stimulation. The pacemaker is set to a fixed rate mode (VOO or DOO) with – for each individual patient – the highest stimulation rate, maximum stimulation energy (with just no oversensing) and with 2- or 3-chamber devices with long AV-delay. During induced VF the EGM is analyzed, if ICD -detection and consecutive therapy of ventricular tachyarrhythmia are influenced by the pacemaker stimulation (Fig. 19). It's recommended to test at least twice and with standard clinical as well as maximum ICD sensitivity.

Fig. 19a. ICD testing. The ICD (Marquis VR 7230, Medtronic) was programmed to low sensitivity. The pacemaker (Kappa DR, Medtronic) with bipolar leads stimulates in DDD-mode with high pacing energy. Following induction of VF by t-wave shock (*) intermittend VF-undersensing occurs (†). However VF was detected and terminated by effective defibrillation (**). Before and after the test the ventricular pacing spike (not the QRS-complex) is sensed by the ICD (§). Atrial pacing is to be seen in the EGM, but not sensed by the ICD. Paper speed 12.5 mm/s.

Fig. 19b. The pacemaker was programmed to higher sensitivity and lower pacing energy. Then the ICD was programmed to higher sensitivity and tested again. This time the induced VF showed higher amplitudes and terminated after ATP and organization to monomorphic VT. During the tachyarrhythmia oversensing of the pacing artifact and relevant VF-undersensing occurred only infrequently (†). The ventricular pacing spike was still sensed by the ICD before and after the test (§). Paper speed 12.5 mm/s.

3. *Analysis of VF-detection by the pacemaker:* After completion of steps 1 and 2 testing of effectiveness of defibrillation e.g. as limited safety margin test can follow. The ICD is programmed to clinical sensitivity and e.g. to a shock energy with a safety margin of ≥ 10 J. At the same time the pacemaker is set to clinical parameters (see programming). Shock effectiveness is analyzed as well as the correct detection of induced VF by the pacemaker, to primarily avoid fixed rate pacemaker stimulation during ventricular tachyarrhythmias (Fig. 20 to 24). If there is asynchronous stimulation during VF, the event markers of the pacemaker are examined to distinguish undersensing from „noise reversion“. According to the results, sensitivity and refractory periods of the pacemaker need to be adjusted.

Fig. 20. Proper detection and termination of induced VF by a single chamber ICD (Lexos VR-T, Biotronik) in an patient with a combined CRT-P-system using an unipolar lead for left ventricular pacing (InSync III, Medtronic. Basic rate 60/min, paced AV-delay 170 ms, interventricular delay 4 ms). Only the first beat after the shock shows triple counting (*): the ICD sensed two pacing artifacts and the evoked QRS complex.

Fig. 21. Nearly continuous undersensing of ventricular flutter/fibrillation by an unipolar single chamber VVI pacemaker. (VF induced in the EP-laboratory. HRAp = high right atrium, RV = right ventricle)

Fig. 22a. Correct ventricular sensing (VS) of an induced fast VT (CL 240 ms) by a dual chamber pacemaker (Kappa KDR 700, Medtronic). Paper speed 25 mm/sec.

Fig. 22b. Same episode as fig. 22a. The EGM of the ICD (Ventak Prizm DR HE 1853, Guidant/BSCI) showed no oversensing of PM-actions during the VT, as the PM is inhibited. After correct termination with 21 J there is once double counting immediately after shock (atrial (*) and ventricular (†) pacing artifact). Thereafter the ventricular PM stimulus is detected by the ICD (‡), the evoked chamber complex falls into the blanking period.

Fig. 23a. Complete undersensing of induced VF by the PM in the same patient as in fig. 22. * = t-wave shock for VF induction. Paper speed 25 mm/sec.

Fig. 23b. Intermitting undersensing of induced VF by the ICD resulting from oversensing of ventricular actions of the PM (*). After high energy shock (41 J) transient PM dysfunction († = defect of sensing, ‡ = ineffective pacing).

4. *Assessment of pacemaker function after shock delivery:* After all ICD-therapies sensing and effectiveness of PM stimulation are evaluated. Especially in patients who are permanently dependent on their pacemaker a loss of capture has to be looked out for and the programming of the ICD should include prolonged post-shock stimulation to increase the safety. Proper function of the programmed ICD post shock pacing has to be verified (fig. 4, 15). Finally, reprogramming or damage to the PM need to be excluded. [Pinski & Fahy, 1995].

Fig. 24. Despite unipolar single chamber PM stimulation induced VF is correctly terminated by the ICD. However, after effective defibrillation there is continued ineffective PM stimulation as well as undersensing of intrinsic ventricular actions. (VF induced in the EP-laboratory. HRap = high right atrium, RV = right ventricle)

“An absence of device interaction during implantation and testing procedures does not completely exclude the possibility of this occurring in the clinical setting...” [Blanck et al., 1994]

6. Programming and follow up

There are special points that need to be taken into account for the permanent programming of the two active devices to avoid future interactions.

- 1. As already emphasized, unipolar PM-stimulation has to be absolutely avoided. This also means that the commonly used practice to program bipolar sensing with unipolar stimulation for better visibility of PM-spikes in routine EKGs must not be done. Modern pacemakers have safety algorithms, which will switch permanently to unipolar stimulation, if there is a bipolar lead defect. This feature has to be deactivated (fig. 25).

Fig. 25. Example of PM-programming for combined use together with a separate ICD to avoid interactions with bipolar lead configuration and high ventricular sensitivity.

The safety switch of the PM has to be deactivated to prevent automatic change to unipolar stimulation. In this demonstrated example of BSCI the lead configuration programming window shows the warning: "Safety Switch may result in unipolar pacing, which is contraindicated for ICD patients".

2. Increased sensitivity of the ventricular PM lead is programmed to guarantee pacemaker detection of ventricular tachyarrhythmias with low amplitude and therefore the occurrence of fixed rate stimulation is prevented, especially during VF [Cohen et al., 1988; Blanck et al., 1994]. However it is important to rule out oversensing of myopotentials by provocation testing especially in patients who are permanently dependent on their pacemaker. In our experience programming 1 mV is safe and effective with the modern leads. Automatic adaption of sensitivity should be deactivated (fig. 25).
3. Modern pacemakers feature algorithms to increase the stimulation rate if needed. Examples include sensor response or rate smoothing as well as algorithms for prevention and therapy of atrial tachyarrhythmias. The maximum rate of PM-stimulation must not exceed the detection rate of the ICD, as this could lead to inadequate detection of tachycardias and possible ICD-therapy [Brode et al., 1997; Blanck et al., 1994; Chamberlain-Webber et al., 1994].
4. In the presence of ICD-double counting, the first step is to analyze the EGM and see which signals are being detected by the ICD. Possible sources include atrial and/or ventricular PM-spikes, right- and if applicable left-ventricular evoked or intrinsic potentials, T-waves, and other different artifacts. Then the following questions need to be answered:
 - a. How are the leads of the two devices positioned to each other? What kind of leads are in use?
 - b. Is the PM-stimulation unipolar and/or with too high energy? Are any algorithms for automatic polarity switch or stimulation energy increase or impedance measuring active?
 - c. Is the double-counting caused by too long conduction times, e.g. long AV-delay or long intra- respective interventricular disturbance of conduction or a long QT time? Are the programmed refractory periods too short?

Depending on the cause of oversensing, changing the programming might solve the problem:

- a. Unipolar stimulation with high energy has to be avoided, automatic settings/changes deactivated (if necessary).
- b. It might help to increase the ventricular blanking period of the ICD and to adapt the automatic detection. The reliable detection of VF has to be ensured (fig. 26)!
- c. If there is oversensing of atrial or ventricular signals with long AV-delay of the PM, a shortening of the AV-delay is to be considered. However a short AV-delay may deteriorate the hemodynamic situation and the proportion of ventricular stimulation can be increased, which is usually not desired.
- d. In patients with an implanted 2-chamber PM or singular chamber-ICD and preserved AV-conduction, who have oversensing of ventricular spikes of the PM, the programming of a long AV-delay may be considered to promote intrinsic AV conduction and thereby avoid overcounting of ventricular stimulation artifacts [Sheahan et al., 1997].

Fig. 26. Undersensing of a VT (induced by T-wave-shock) after reduction of ICD-sensitivity (Ventak Prizm 2VR 1860; Guidant) as reaction to overcounting of PM artifacts (Kappa KDR 401; Medtronic, bipolar leads!). The PM artifacts can be seen in the ventricular pace-sense-channel (top) as well as in the ventricular EGM of the defibrillation coils (bottom) and are being detected inconsistently by the ICD.

- e. The reprogramming of a DDD(R)-pacemaker to AAI(R)-mode, if the AV-conduction is intact, was recommended by Brooks et al. and Chapman et al. to avoid interactions caused by oversensing of ventricular pacemaker stimuli [Brooks et al., 1995; Chapman & Troup, 1986].
- f. Another last programming option with double-counting of PM spikes would be - if clinically possible in the individual patient - to limit the upper range of PM stimulation rate to less than half of the detection rate of the ICD [Chapman & Troup, 1986].

However, if oversensing with a clinical relevance can't be avoided by programming, a revision of the system must be pursued.

5. The stimulation output of the PM should be minimized just ensuring an adequate safety margin for effective pacing [Blanck et al, 1994]. Thus the individual stimulation energy has to take the results of the threshold and interaction testing into account. In PM with automatic adaption of stimulation amplitude and pulse width the maximum value of adaptive stimulation energy has to be limited. Attention also needs to be paid to the fact that the automatic measurements of lead impedance are being conducted with higher energy (e.g. 5 volt). If there is oversensing with higher stimulation energies this automatic measurement has to be deactivated.

Caution is warranted in performing the pacemaker threshold testing in the presence of an active ICD. The stimulation with higher rates and energy can lead to inappropriate therapy due to oversensing of stimulation artifacts and of evoked and/or after loss of capture intrinsic QRS complexes [Cohen et al., 1988; Epstein et al., 1989; Azizi & Nägele, 2007]. This is particularly important for CRT-systems with a unipolar left ventricular (LV) lead (fig. 27). Principally the EGM of the ICD has to be watched for oversensing during testing. Some authors even recommend deactivation of the ICD during pacemaker testing [Singer et al., 1988], especially for CRT-PM-systems [Azizi & Nägele, 2007].

Depending on the testing results automatic threshold tests have to be turned off.

6. During programming of the detection criteria of the ICD, the avoidance of inadequate therapy deliveries have to be watched. Therefore - if clinical possible in the individual patient - a high VT/VF-detection rate and long detection durations should be programmed in the respective zones. The morphology as well as the stability criterion

- for discrimination of SVTs should be used only, if an erroneous registration of PM artifacts by the ICD can be surely excluded (fig. 9). It is recommended to check the reference for intrinsic chamber complexes during device control and to deactivate automatic update. In patients with permanent high degree AV-Block the SVT-discrimination can be omitted.
7. In patients who are dependent on their pacemaker, the duration of post-shock pacing by the ICD with high stimulation energy should be extended. This will guarantee effective stimulation, if there is an increase of stimulation threshold of the antibradycardia pacemaker after the ICD shock [Singer et al., 1988; Pinsky & Fahy, 1995].
 8. The specific details of programming have to be mentioned in the report and there must be references in the device card. As the combined use of two active CIEDs is rare, a lot of doctors might not be aware of all the problems and issues involved and therefore might change the programming to a more standard programming in ignorance of the specific situation.

Fig. 27 a and b. Inappropriate shock (CD) due to double counting of stimulation artifacts of the unipolar LV lead (*) and the evoked potentials (†) at LV stimulation for threshold testing (ICD Marquis VR 7230; CRT pacemaker InSync III, Medtronic).

7. Conclusion

As there is no definitive guarantee for long term elimination of interactions and considering the modern technology, the combined use of two separate active CIEDs should be principally avoided. If in an individual case e.g. for a limited time after system upgrade the indication for a dual device therapy is seen, careful implantation, extensive testing and specific programming are essential to minimize the risk of possible dangerous adverse interactions.

There is a possibility that this currently rare problem will regain more clinical impact, when emerging new technologies, such as devices for cardiac contractility modulation, subcutaneous high energy ICDs without antibradycardia therapy or endocardial fixated “leadless pacemakers”, are further developed and are used in clinical routine.

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The book focuses upon clinical as well as engineering aspects of modern cardiac pacemakers. Modern pacemaker functions, implant techniques, various complications related to implant and complications during follow-up are covered. The issue of interaction between magnetic resonance imaging and pacemakers are well discussed. Chapters are also included discussing the role of pacemakers in congenital and acquired conduction disease. Apart from pacing for bradycardia, the role of pacemakers in cardiac resynchronization therapy has been an important aspect of management of advanced heart failure. The book provides an excellent overview of implantation techniques as well as benefits and limitations of cardiac resynchronization therapy. Pacemaker follow-up with remote monitoring is getting more and more acceptance in clinical practice; therefore, chapters related to various aspects of remote monitoring are also incorporated in the book. The current aspect of cardiac pacemaker physiology and role of cardiac ion channels, as well as the present and future of biopacemakers are included to glimpse into the future management of conduction system diseases. We have also included chapters regarding gut pacemakers as well as pacemaker mechanisms of neural networks. Therefore, the book covers the entire spectrum of modern pacemaker therapy including implant techniques, device related complications, interactions, limitations, and benefits (including the role of pacing role in heart failure), as well as future prospects of cardiac pacing.

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