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The Alternative Atrial Pacing Sites

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1. Introduction

A permanent pacemaker implantation changes the electrophysiological and hemodynamic conditions in the heart. The electric system of the pacemaker meets the two main functions of the device, i.e. the stimulation – pacing and sensing of own cardiac rhythm. The possibility of an atrial stimulation sending the electric impulses for the whole heart is the most physiologic pacing mode. The pacing site is no longer determined by the technical and anatomical limitation since the introduction of active fixation leads enables the lead positioning and fixation in almost each place within the heart muscle. Different electrophysiological properties of various parts of the atria influence the pacing and sensing in different ways. The physiologic conduction of an electrical wave front from the sinus node to the atria and then to the atrio-ventricular node and the ventricles favours the optimal hemodynamic function of various parts of the heart muscle, changing additionally with regard to the basic rhythm and metabolic demands during a physical activity.
The physiologic electrical activation of the atria originates within the sinoatrial node, located in front of and medially from the superior vena cava ostium to the right atrium, then spreads ahead and down across the right atrium and to the left atrium throughout the conducive tissue band called Bachmann's bundle. This leads to a rush and efficient activation of the left atrium resulting in single P wave in electrocardiogram, not separating the both atria conduction. The interatrial conduction takes place also within the posterior part of fossa ovalis and coronary sinus. This kind of activation leads to the proper mechanical sequence of contraction covering firstly the free right atrial wall, then interatrial septum and subsequently posterior, anterior and lateral left atrial walls at the same time. The physiologic delay of left atrial contraction in relation to the right atrium amounts to 22+/-11 ms (1-3). The Bachmann's bundle is the fastest way to carry the activation from the right to the left atrium and its dysfunction or a complete block is connected with an unfavourable sequence of electrical and hemodynamic changes. This results in an impaired electrical and mechanical function of the left atrium leading usually to atrial fibrillation. Other causes and diseases such as arterial hypertension, inflammatory process and fibrosis take part in a deterioration of an atrial muscle function favouring the arrhythmia (4, 5).

2. The functions of atrial pacemaker

The ideal atrial stimulation should provide an optimal interplay among the three functions of the device: the pacing of the heart, mechanic or hemodynamic atrial function and antiarrhythmic influences on the atrial muscle. The different locations of the atrial electrode influence these functions in different ways depending on atrial pacing and sensing as well as atrioventricular conduction.

3. The electrical properties of pacemaker-atria unit

The implantation of atrial electrode changes the electrophysiological conditions within the atria. Many studies have shown that the altered electrophysiology could be potentially harmful or beneficial with regard to the hemodynamic and arrhythmogenic properties. The stimulation of coronary sinus was the subject of several studies. Betts et al. assessed the right atrium activation during coronary sinus pacing in experimental conditions in porcine model. They concluded that the site of the earliest activation of the right atrium depends on the part of coronary sinus where the electrode is located, but the main part of the right atrial muscle was activated via posterior wall rather than from the coronary sinus ostium (6). The total atrial activation time was studied by Roithinger et al. (7) in 28 patients without a structural heart disease. The study was performed after catheter ablation of supreventricular arrhythmias. The authors showed that the shortest total activation time could be achieved during Bachmann's bundle pacing in comparison to other stimulation sites such as distal coronary sinus, its ostium as well as high and low right lateral atrium. The influence of different right atrial pacing site on intracardiac signal-averaged electrocardiogram was studied by Kutarski et al. (8) in 24 patients undergoing biatrial pacing system implantation. The authors concluded that right atrial appendage pacing prolongs the duration of atrial potential recorded in external and internal leads. Coronary sinus stimulation is not inferior as compared to sinus rhythm and biatrial pacing carries potential benefits with regard to late potential elimination and arrhythmia protection.

4. The hemodynamic properties of the paced atria in relation to different pacing sites.

Patients with indications to atrial or atrioventricular pacing are not a homogenous group. Both dysfunctions: the impulse generation disturbances or conductive tissue disease as the indications for pacing in general as the patient's co-morbidities as well make the choice of appropriate atrial pacing site difficult. It is even more difficult to prove one of them being superior over the other ones. The important factor influencing the results of the studies and the clinical outcome in a particular patient are the interatrial conduction disturbances resulting in an electrical and hemodynamic deterioration and a subsequent atrial fibrillation. The results of small studies suggest that the interatrial conduction disorders affect approximately 30% of patients with the sick sinus syndrome and up to 12% of patients with atrioventricular conduction disorders (9). The most special group of patients are those subjected to the cardiac resynchronisation, in whom the proper depolarization sequence of atria and ventricles is particularly important and subtle differences in an interatrial and interventricular conduction delay may determine the effectiveness of the whole procedure. As far as the interventricular delay can be the subject of device programming, the differences in the interatrial conduction during pacing and sensing with regard to a different atrial lead position are of a particular interest. The choice of an atrial lead implantation site influences the electrical and mechanical properties of both atria. The time of an electrical activation of both atria and subsequent hemodynamic depends on the location of its origin, so the distance to reach the whole atrial muscle and the conductive properties of the muscle. The artificial pacing resulting in the stimulation of working myocardium leads a priori to the slower conduction of a depolarization wave. The extent of this slowing depends on the muscle properties, the conductive tissue status as well as on the distance of the pacing site to the conductive structures. The dimensions of the atria and the degree of their remodelling – fibrosis or myocytes loss – also play an important role. The duration of both atria activation influences their hemodynamic function. Interatrial and intraatrial conduction disturbances result in a loss of an atrial contraction synchrony, being in particular expressed in the left atrium. The deleterious effects of the interatrial conduction slowing and a non-physiological conduction affect the mechanical and electrical left atrial function. The mechanical results of an improper contraction sequence of the left atrium structures influence its systolic function. The inappropriate time relation of the left atrium and the left ventricle systolic and diastolic function leads to the pressure overload of the left atrium and its remodelling and enlargement (10). The locally activated renin-angiotensin-aldosterone system contributes to the mechanical and electrical remodelling as much as the coexistence of arterial hypertension and myocardial ischemia in some patients. A longer time of the left atrial activation could lead to its contraction during a partial mitral valve closure. Such circumstances contribute to an even more pronounced pressure overload and could be easily detected by the echocardiographic assessment of a mitral diastolic flow, showing sharp A wave cut by ventricular systole. The presence of electrical remodelling resulting from the described pathophysiologic processes ends in conduction and refractoriness dispersion both being substrates for re-entrant arrhythmias maintenance (11, 12). The systolic dysfunction of the left atrium originates in asynchronous contraction of its structures, as the improper timing of its systole with regard to ventricular diastole diminishes the contribution to the left ventricle endsystolic filling. This is particularly important in patients with diastolic dysfunction of the left ventricle, being the other independent factor of an atrium enlargement. All the influences could lead to atrial fibrillation and a complete loss of an active hemodynamic atrial function. Therefore the optimization of atrial pacing site is of a special importance in sicker patients with an initial inter- and intraatrial conduction disturbances, a poorer mechanical function and a greater risk of its further deterioration.

As already mentioned above the population of patients undergoing the permanent pacemaker implantation shows atrial conduction abnormalities as well as the chronotropic dysfunction or atrioventricular block being the primary cause of device implantation. Non-optimal atrial electrode placement in patients with such pre-existing disorders results in its increase and the progression of pathophysiologic process. The prolongation of the interatrial conduction during pacing can be observed in the surface electrocardiogram as the prolonged and deformed P wave. There are many small studies regarding the different atrial pacing sites and the duration of P wave. It was shown that the stimulation of the right atrial appendage results in the longest activation of both atria in comparison to the Bachmann's bundle (13) and interatrial septum pacing site (7, 14-16). The stimulation of septum is considered in many papers to be the best pacing place with regard to the both atria activation time (17-19), which seems to be concordant with a theoretical model. In some papers this kind of atrial stimulation site was also combined with the prevention of paroxysmal atrial fibrillation (20, 21). On the other hand the right atrium appendage pacing provides a better hemodynamic response – better left ventricle filling and a higher cardiac output in comparison to the right atrium free wall stimulation. This last location seems to be the worst pacing site (22). The shortening of the depolarization of both atria and the subsequent shortening of P wave duration related to the optimization of pacing site does not always carry the measurable benefits – both hemodynamic and antiarrhythmic ones. In a number of small studies it was shown that the benefit of such a stimulation was observed only in patients with initially larger interatrial conduction disturbances and/or paroxysmal atrial fibrillation because of the fact that none of the atrial pacing settings will be better than the own physiological conduction in the sinus rhythm and the non-disturbed conductive system (13, 23). In one randomized trial of Hermida et al. the benefits of low septum pacing were shown only in the group of patients with paroxysm of atrial fibrillation during three months before pacemaker implantation (24). A significant shortening of left atrium depolarization requires programming of shorter atrioventricular delays which in turn does not allow to avoid the ventricular stimulation. Moreover the non-physiological spreading of the activation wave front from the mitral annulus because of the proximity of coronary sinus can also be responsible for the limited benefits of this kind of pacing (25, 26). The advantageous hemodynamic response from interatrial septum pacing was observed in the study of Miyazaki et al. (27). They showed that the shortening of atrial depolarization by such pacing mode also shortens the difference in both atria contraction assessed as the time difference between the peak of A wave in mitral and tricuspid diastolic flow. In a 24-month-long follow-up period the mitral diastolic flow improved and the left atrium dimensions decreased. But the patients included in this study already had the documented history of paroxysmal atrial fibrillation and interatrial conduction delay (27). In the study of Di Pede et al. assessing the usefulness of interatrial pacing in patients with cardiac resynchronization there was no superiority in comparison to the right atrium appendage pacing but the patients did not have significant interatrial conduction delay. In patients treated with cardiac resynchronization therapy the increased atrioventricular conduction time results in a greater percentage of a ventricular stimulation which in turn paradoxically could contribute to the better hemodynamic result (28).

In most of the mentioned studies the results of different atrial pacing locations were assessed in acute settings or with a relatively short observation period. It can be assumed that the beneficial effects could only be seen in a longer time or the patients with less pronounced interatrial conduction abnormalities will benefit from such pacing mode later because of the progressive nature of the sick sinus syndrome and paroxysmal atrial fibrillation. On the other hand the development of the deleterious results of non-optimal atrial electrode location resulting in atrial systolic dysfunction can occur in a time period much longer than the follow-up of most studies.

Another factor influencing the described results in patients with resynchronization could be the difference between pacing and sensing of sinus rhythm. In this subgroup of patients the usually observed tachycardia leads mostly to the atrial sensing ventricular pacing mode of a pacemaker action. In this case and normal or nearly normal interatrial conduction the specific location of atrial electrode does not matter at all.

The solution of an increased atrial conduction time and non-physiologic activation pattern could be the biatrial pacing. However the beneficial effects of this kind of atrial pacing were shown only in patients with initially pronounced interatrial conduction disturbances (29-31, 32). The various electrode configuration studied always included the one implanted in the coronary sinus ostium and the other located in the right atrium appendage or Bachmann's bundle. Similarly as in the interatrial septum stimulation it was shown that biatrial stimulation results in shortening of both atria depolarization and shorter P wave duration in surface electrocardiogram. Matsumoto el al. observed a significant improvement of atrial systole synergy using the strain doppler imaging technique to assess the local myocardium movements (33). In the largest study published Dąbrowska-Kugacka et al. assessed the impact of different pacing configuration - single and biatrial - on the electromechanical sequence. They proved that the most beneficial single right atrium pacing location in patients with interatrial conduction disturbances is the Bachmann's bundle region of atrial roof, carrying similar results as biatrial pacing. The right atrium appendage location was related to the latest left atrium walls activation and contraction, whereas the stimulation of coronary sinus admittedly led admittedly to the earliest left atrium activation but resulted also in the significant dyssynchrony within the right atrium (34). These surprising results are difficult to comment because the mechanical function of the right atrium has not been extensively studied. It seems quite probable that the function of low pressure system of right heart does not really benefit or worsen from any kind of optimization of right atrium pacing. In the paper mentioned, in comparison to the work of Wang et al. (1) there was no dyssynchrony within the right atrium observed during the right atrium appendage stimulation. This could be in part the result of different assessment techniques of both studies. Wang et al. used the M-mode view and Dąbrowska-Kugacka et al. studied the atrial synchrony using the tissue doppler imaging. The results of the latter study showed explicitly that the biatrial pacing of both coronary ostium – right atrium appendage and coronary ostium – Bachmann's bundle led to the most physiological effect. Moreover, Stockburger et al. showed that biatrial pacing (coronary ostium – right atrium appendage) contributes to the better left atrium systolic function assessed by the transesophageal echocardiography. Unfortunately they also observed more disturbed diastolic mitral flow. The E wave velocity diminished in comparison to the sinus rhythm, what could be in part the result of the higher pacing frequency (35). The better systolic function of the left atrium appendage can be responsible for lower thrombosis and embolisation rate. Prakash et al. showed that the biatrial stimulation within the right atrium results in a faster activation and a better hemodynamic function of the left atrium, as well as higher A wave velocity in mitral diastolic flow spectrum which could lead to better left ventricle filling and higher cardiac output (36). The observation of Takagi et al. confirmed that biatrial pacing in combination with higher pacing rates promote the sinus rhythm maintenance after direct current cardioversion, prevent atrial fibrillation paroxysms and shorten the atrial stunning period (37).

5. The antiarrhythmic properties of atrial pacing

The atrial stimulation in patients with the sick sinus syndrome eliminates bradycardia as a clinical problem per se and on the other hand prevents bradycardia related dispersion of refractoriness and premature atrial beats eliminating the substrate and triggers for atrial fibrillation. The standard location of an atrial electrode in the right atrium appendage does not fit the physiologic electrical activation direction which occurs normally from the sinus node, so from the rear roof towards the front and lateral wall, to the interventricular septum and left atrium. This is the cause for the lengthening of both atria activation observed as broadening of P wave in the surface electrocardiogram. The optimal positioning of atrial lead or leads can take into account the results of studies examining the electrocardiographic predictors of atrial fibrillation.

The atrial activation parameters were studied by Bennet (14) using an invasive electrophysiological study with single and 2 points stimulation within the right atrium. The studied positions included right atrium appendage, coronary sinus ostium, interatrial septum and simultaneously: right atrium appendage and coronary sinus ostium. The studied parameters were the duration of both atria activation, the atrioventricular conduction time and the synchronous activation of both atria. The total activation of both atria took much longer during right atrium appendage stimulation in comparison to septum, coronary sinus ostium and biatrial stimulation. The right atrium appendage pacing resulted also in a slightly longer atrioventricular conduction. The conclusions from this study taking into account the similar results of septal, coronary sinus and biatrial stimulation strongly suggest the benefits from interatrial septum pacing, keeping in mind the relative simplicity of the implantation procedure in comparison to the cannulation of coronary sinus. These results are also against the biatrial stimulation because of the use of two electrodes and without carrying additional benefits from this pacing mode. The placement of an atrial electrode within the coronary sinus ostium can have another potential disadvantage because of the difficulties or the impossibility to place there another electrode for left ventricle stimulation in order to achieve ventricular resynchronization. The upgrading of pre-existing pacing device in patients suffering from heart failure in such conditions could be particularly difficult or demanding the placement of left ventricle epicardial electrode surgically. In the light of this study and the technical implication the best location of single lead atrial pacing seems to be interventricular septum.

The simplest method of an electrical activity assessment within the atria is the measurement of the duration of P wave in surface electrocardiogram. There is a certain evidence that the prolongation of P wave duration indicates the intra- and interatrial conduction disturbances and is related to more frequent and longer paroxysmal atrial fibrillation occurrence in comparison to patients without this finding. The conduction abnormalities are most probably not uniform, location dependent leading to the differences in P wave duration in different ECG leads. The marker of these differences is the so called P wave dispersion being beside the P wave duration the well established predictor of atrial fibrillation in selected groups of patients. The sole prolongation of the P wave duration was related with a greater risk of paroxysmal atrial fibrillation, a risk of postoperative atrial fibrillation (38-40), and the P wave duration of more than 120 ms with typical inferior leads morphology (notched (+/+) or biphasic (+/-)) is a marker of interatrial conduction block and an increased risk of any atrial tacharrhythmia (38, 41, 42). In the study of Kristensen et al. (43) the described parameters were assessed during the sinus rhythm and 70 bpm and 100 bpm atrial stimulation with the electrode placed on the interatrial septum and the high right atrium. The P wave duration during high right atrium pacing was significantly longer as compared to septal location. During pacing with the higher rate 100 bpm the P wave duration was significantly longer than during pacing 70 bpm in both electrode locations. The main result of the study was that neither P wave duration nor P wave dispersion were the predictors of atrial fibrillation paroxysm in patients with the sick sinus syndrome. De Sisti et al. (44) assessed the influence of the P wave duration on atrial fibrillation burden after a permanent pacemaker implantation. The study group consisted of 140 patients with the sick sinus syndrome with pacing indications and the medical history of at least 2 episodes of atrial fibrillation within the preceding 1 year. The results showed that the prolonged duration of P wave is an independent marker of a risk of atrial fibrillation after implantation. The P wave assessment included not only the duration but also the morphology of P wave. The background for this study were the investigations of Bayes de Luna et al. (38) indicating that the presence of broadened and biphasic P wave is the marker of advanced interatrial conduction disturbances in 4% of the studied population whereas the additional presence of notched P wave in inferior leads considered as less pronounced conduction disorders increased the percentage of patients with interatrial conduction disturbances to 16. In the study of De Sisti et al. the presence of abnormal P wave (notched or biphasic) was a strong predictor of chronic atrial fibrillation after the pacemaker implantation. In a statistical analysis only the left atrial dimensions positively correlated with the P wave duration but in multiregresion Cox hazard ratio neither left atrium dimensions nor the other clinical parameters studied increased an atrial fibrillation risk. The P wave duration was also assessed in the study of Endoh et al. (45). The study was carried out in 57 patients undergoing the pacemaker implantation and aimed to assess the P wave duration in the sinus rhythm and stimulation with the right atrium appendage electrode. The patients were divided into two groups according to the presence of episodes of atrial fibrillation in the medical history (group I and II) and without such events (group III). The group III – without atrial fibrillation - was further divided into patients with the paced P wave duration of less (IIIa) and more (IIIb) than 130 ms. The duration of the P wave during the sinus rhythm in group III was longer than in group I and II, but the paced P wave in group IIIa was similar than in groups I and II. The results indicated the prognostic value of the prolonged P wave duration for atrial fibrillation episodes. Stabile et al. showed the protective value against atrial fibrillation recurrences of single lead atrial pacing in patients with a right atrium conduction delay and an increased dispersion of refractoriness (46).

The duration of the P wave during various site atrial pacing was also assessed in the study of Hung-Fat Tse et al. (47). The electrode was placed in right atrium appendage, high interatrial septum, coronary sinus ostium and distal coronary sinus. In comparison to the duration of the P wave during the sinus rhythm the duration was significantly prolonged during right atrium appendage as well as distal coronary sinus and showed no significant difference during septal, coronary sinus ostium, biatrial: simultaneous right atrium appendage and coronary sinus ostium stimulation. Moreover, the P wave duration was significantly shorter during the stimulation of the septum and both biatrial sites: right atrium appendage and coronary sinus ostium and right atrium appendage and distal coronary sinus in comparison to the right atrium appendage pacing. The results indicate that the septal location or biatrial pacing may reduce or slow down the development of the atrial substrate for fibrillation through the reduction of both atria activation time or make it slower. The results of the studies indicate that the interatrial septum pacing may exert some antiarrhythmic action on the atria, even without any antiarrhythmic pacing algorithms. De Voogt et al. (48) extensively studied the stability of pacing and sensing parameters in relation to the location of atrial electrode – right atrium appendage versus low interatrial septum. Six weeks after the implantation procedure and then after 3 and 6 months the pacing threshold did not differ between the studied groups. After 3 and 6 months the higher voltage of the P wave in the low interatrial septum reached the statistical significance. After 6 weeks the electrodes inserted in the right atrium appendage showed a higher resistance but the difference was no longer statistically significant after 6 months of follow-up. The voltage of the far field R wave during ventricular pacing was higher in right atrium appendage location after 6 weeks but after 3 and 6 months was higher in low interatrial septum site. The far field R wave signals of more than 0,5 mV were observed in both groups/electrode locations (right atrium appendage 88% and low interatrial septum 93%). Even if the far field R wave voltage significantly differed between the groups it had no clinical significance. The interval between the ventricular stimulus and the far field R wave

sensing on the atrial electrode was slightly longer in the right atrium appendage location as compared to the septal location and was probably caused by the depolarization vector direction. Nevertheless the voltage of far field R wave exceeding 0,5 mV in most patients in both studied groups did not allow to set the atrial sensing below 0,5 mV, which seems to be necessary for the confirmation of atrial fibrillation. The results indicate that the long-term pacing of the interatrial septum is a feasible, safe and beneficial alternative of the atrial electrode location. The assessment of the influence of septal pacing was also the purpose of the study of Hakacova et al. (49). Group l (n=22) received atrial pacing using a single-active fixation lead in the atrial septum above the bundle of His near the foramen ovale and group 2 (n=22) received 'standard' right atrium pacing - a single - active fixation lead was placed in the high right atrium. Devices were programmed in a standardized manner. There were 43 patients who completed 6 months of the follow-up and 22 patients who completed 12 months of the follow-up. The important limitation of the study was a relatively small number of patients in both groups. The atrial fibrillation burden was assessed by the number of mode-switch events of the devices and the arrhythmia duration. In the group of right atrium appendage electrode location there was a greater number of mode-switch episodes and a longer total arrhythmia duration in comparison to the group 1 but the difference was pronounced but not statistically significant only after the 12-month-long follow-up. The small number of 12 months observations could be responsible for that finding but the study rather support the concept of an interatrial septum stimulation in patients with atrial fibrillation as the preventive measure.
The location of great expectations regarding the antiarrhythmic influences of atrial pacing is the Bachmann's bundle – the group of muscle fascicles originating from crista terminalis in the proximity of the sinus node and aiming toward the left atrium in the atrial roof above the interatrial septum. The bundle divides into the fascicles going to the anterior and posterior left atrial wall. Some of the fascicles penetrate the left atrium appendage and other ones dissolve among pulmonary veins ostia. The Bachmann's bundle makes the way for impulses to travel between the right and the left atrium. The histological structure of the Bachmann's bundle fascicles resembles more the Purkinje fascicle than the working muscle cells resulting in a faster interatrial conduction and thus shortening the P wave duration (50). The stimulation of the Bachmann's bundle shortens both atria electrical activation, shortens the P wave, improves the symmetry of the left atrial activation, shortens also the sinus node recovery time (18). The long-term electrophysiological properties (sensing, pacing threshold, resistance) of the Bachmann's bundle region in terms of permanent pacing are comparable with that of right atrium appendage. In the study of Bailin et al. (13) the group of 57 patients with the atrial electrode located in the right atrium appendage was compared to the 63 patients with Bachmann's bundle pacing. The paced P wave duration was significantly shorter during the Bachmann's bundle stimulation as compared to the sinus rhythm whereas the right atrium appendage pacing showed a longer P wave. Patients with Bachmann's bundle pacing had longer atrial fibrillation free survival in comparison to the other electrode location. The time of the implantation procedure did not differ significantly between the two approaches indicating the feasibility and safety of the Bachmann's bundle region implantation. There were also no differences with regard to pacing thresholds, sensing parameters and impedance between the studied group during the procedure and after 6 weeks, 6 and 12 months. Nigro et al. (51) studied the stability of sensing and pacing parameters of atrial electrodes implanted in the Bachmann's bundle and right atrium appendage in a group of patients with type I myotonic dystrophy. The point of

interest was raised because of sensing and pacing problems in patients with Steinert disease after right atrium appendage electrode insertion. The same authors already confirmed in another study better sensing and pacing parameters in the region of high interatrial septum and/or the Bachmann's bundle in comparison to the right atrium appendage during the implantation procedure (52). The subsequent study in patients with type I myotonic dystrophy was a prospective one. The initial amplitude of sinus P wave was the same in both groups but after the 12- and 24-month-long follow-up the values increased significantly in the Bachmann's bundle stimulation. The pacing threshold was similar during the implantation and it rose significantly during the follow-up in patients with right atrium appendage electrode location. There were no differences of other parameters such as electrodes impedance, the presence of far field R wave and the frequency of electrodes dislodgement.

In the PASTA study (53) the analysis was performed to assess the influence of alternative pacing sites on the events of atrial fibrillation in patients with the sick sinus syndrome. The study was carried out in 142 patients with atrial electrode located in: right atrium free wall, right atrium appendage, coronary sinus ostium and biatrial pacing in right atrium appendage and coronary sinus ostium. Thus the model included the standard pacing sites and the alternative ones. There was no difference in the burden of atrial fibrillation with regard to different sites of atrial pacing. The prevalence of the ventricular stimulation was about 60% and slightly less but not significant with the right free wall electrode location. The percentage of ventricular pacing was relatively high with recommended parameters of atrioventricular delay of 30 ms more than a spontaneous conduction but as the values were similar in all groups there are no reasons to assume that this could influence the obtained results. The coronary sinus and biatrial location was combined with more dislodgements and a significantly longer implantation procedure time.

Taking into accounts the results of the studies of Saksena et al. (54, 55), Prakash et al. (36), Delfaut et al. (56) and Bailin et al. (57) the alternative atrial pacing sites could be of a possible interest in the secondary prevention of atrial fibrillation and could be beneficial in comparison to standard atrial electrode location. However, the concept of antiarrhythmic properties of interatrial septum or biatrial stimulation has many limitations, some of them mentioned already before. The main limitations in the interpretation of the obtained results are the small number of studied subjects and non-homogenous groups of patients. In the study of Delfaut et al. (56) the patients with symptomatic recurrent atrial fibrillation were included whereas the study of Bailin et al. (57) included patients with paroxysmal atrial fibrillation. In the second study the results showed that the Bachmann's bundle pacing resulted in slowing the progression of paroxysmal atrial fibrillation in its permanent form without pharmacotherapy. In the studies of Delfaut et al. and Saksena et al. (54, 55, 56) the pacing prolonged the time to first atrial fibrillation recurrence in the patients treated with class I and III antiarrhythmic drugs.

In their studies de Voogt et al. (58) and Padeletti et al. (23, 59) have obtained different results in comparison to those previously mentioned. The studied hypothesis was the impact of different atrial pacing sites on the secondary prevention of atrial fibrillation. There were no differences between the stimulation of low interatrial septum and right atrium appendage with respect of arrhythmia recurrences in patients with indications to atrial pacing and paroxysmal atrial fibrillation. The main difference between the discussed studies is a huge difference between the incidence of permanent atrial fibrillation development in PASTA study (53) (3-6%) and Bailin et al. study (57), where in the right atrium appendage group it was as high as 50% and in the Bachmann's bundle group it amounted to 25% during the follow-up. It is possible that the lack of influence of alternative pacing sites on atrial fibrillation depends mainly on this low incidence of arrhythmia recurrence and maintenance. The low incidence of atrial fibrillation paroxysm could indicate that these groups were initially free of arrhythmia, because other studies suggest the strong correlation of previous episodes of the arrhythmia and subsequent episodes following the pacemaker implantation (60, 61). Such a correlation was confirmed in the already mentioned study of Endoh et al. (45). The authors of PASTA study concluded that the small incidence of atrial fibrillation and the lack of differences among various atrial electrode locations could be caused by the beneficial effect of the atrial stimulation per se what could not be confirmed in other sick sinus syndrome patients requiring pacing without the pacemaker implantation. It seems probable that the verification of the concept will need a much more numerous study group in those low atrial fibrillation risk patients.

6. References

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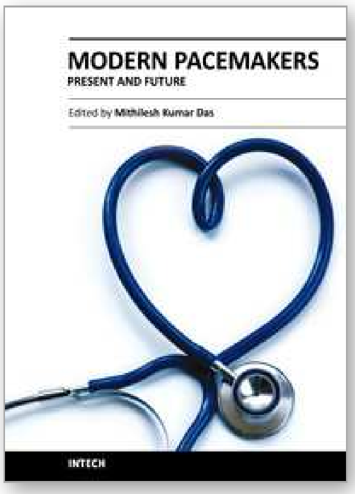

Modern Pacemakers - Present and Future
Edited by Prof. Mithilesh R Das

ISBN 978-953-307-214-2
Hard cover, 610 pages
Publisher InTech
Published online 14, February, 2011
Published in print edition February, 2011

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 conductions 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.