Difference in Cardiac Electrical Vulnerability Between Passive Silicone Steroid Eluting Lead *vs.* Active Screw-in Lead

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Patients with total atrioventricular block are of particular interest and prone to severe prognosis unless treated with emergency cardiac pacing. We evaluated different types of leads and their impact on the myocardium, according to the fixation type and pacing method.. A pacemaker patient has a different depolarization pattern and a single chamber pacemaker, has by definition, an intracardiac desynchronization and a different electro-mechanical coupling activity. The presence of late potentials is an independent prognosis factor for cardiac death and electrical vulnerability, especially after myocardial infarction(MI). Late potentials recorded as magnitude vector are the expresion of late depolarization of the surrounding tissue and represent the morfological substrate for reentry. Thus, the incidence of late potentials after pacemaker implant, represents the expresion of electrical vulnerability of the stimulated right ventricular myocardium. In order to deeply study the parameters of magnitude vectors, we noticed the appearance of late potentials during the transitory stimulation in acute atrioventricular block and a restoration of vector normal parameters, after conduction recovery and sinus rhythm conversion.

Keywords: late potentials, pacemaker implant, active or passive lead

For the past 50 years, we encountered a major development in cardiac pacemakers systems and pacing leads[1]. Epicardial pacing leads, were no more the single option in brady- arrhythmia patients, preventing patients from suffering surgery risks, by replacing those with transvenous electrodes, thus drastically reducing morbi-mortality of pacemaker implantations[1]. The newer coaxial bipolar pacing leads, are silicon-soft, thin and easy insertable systems with upgraded insulation types, and steroid-eluting tips, aimed for better cardiac pacing therapy[1,2]. Also, lead development was seen in the stability of fixation, for ensuring long-term pacing performance[2].

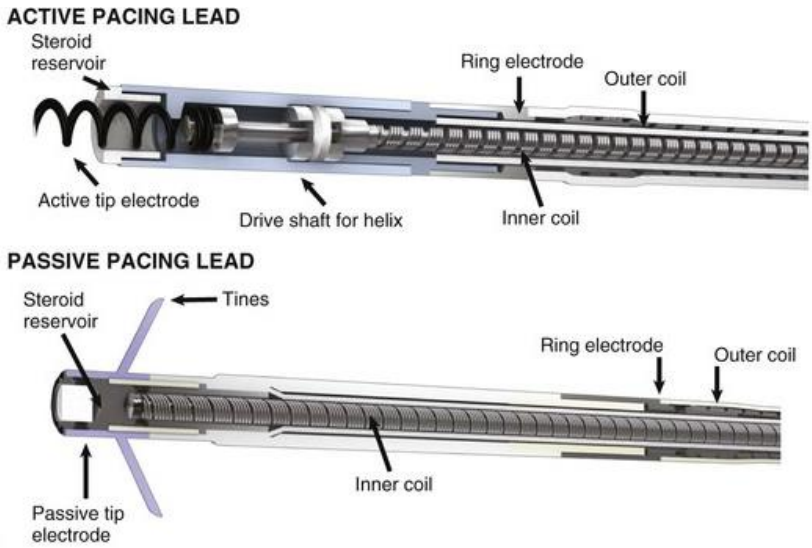

Fig. 1. Active and passive lead design(from thoracickey)

The passive pacing lead(fig 1), was the first introduced with extraordinary results, giving easy passive fixation(tined) in the right ventricular trabeculae of the apex(the most common pacing site) and short implantation time. Active fixation-screw-in(fig1), works by extending the helix (or screw) into the endocardial tissue, ensuring low dislodgement rate and have made them perfect for selecting the convenable pacing site, according to patient cardiac particularities [1].

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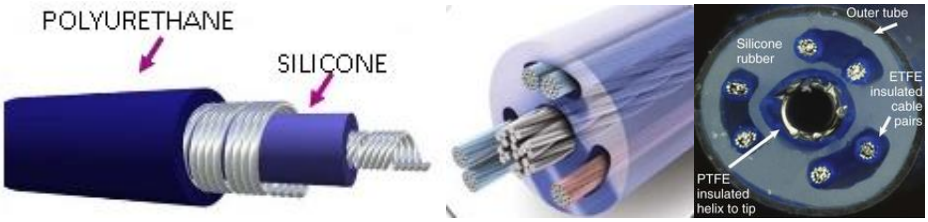

Fig. 2. Bipolar coaxial pacing lead design . ETFE = ethyltetrafluoroethylene; PTFE = polytetrafluoroethylene (from thoracickey and Medtronic)

Silicone and polyurethane insulated leads have smaller diameter , are inert ,biocompatible, biostable with high tear strenght[2], as shown in fig 2.

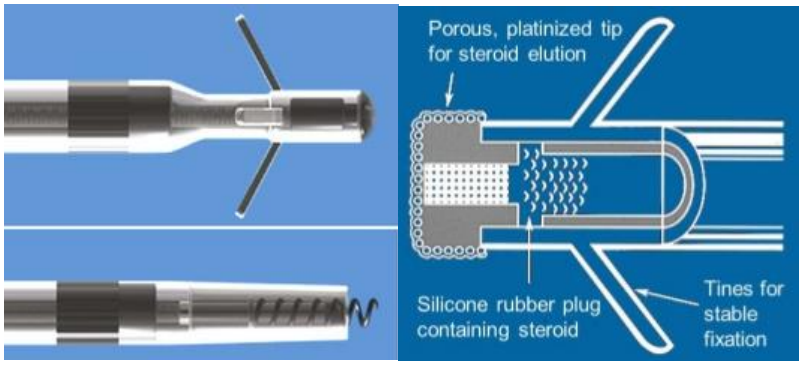

Fig. 3. Steroid eluting leads schematics. (Medtronic)

Steroid eluting leads(fig 3) are designed to reduce inflammatory process in contact with endocardial tissue. Also, it exhibit little acute stimulation threshold peaking and maintain low chronic thresholds .

Studies mentioning long-term evaluation of active vs passive fixation leads and their electrical performances, are limited[2]. The present analysis, retrospectivly evaluates the electrical vulnerability associated with active-fixation compared to passive leads by observing lead characteristics, evaluated through several late potentials parameters.

Experimental part

Material and method

In the first place, we studied the factors that influence the appearance of late potentials and their electrical expresion, using a dedicated Hellige EA RL electrocardiograph with a 40 Hz high-pass cut-off filters, through the mediation of 200 QRS complex, which enabled a noise level bellow 0.7 μV. The process of signal averaging, assumes that the interfering noise is random and that the signal of interest repeats with every beat included in the average. We recorded a magnitudine vector with three parameters – RMS 40 (root mean square voltage in the terminal QRS), LAS (duration of low amplitude signal) and QRS duration –ORS duration at high-pass filtering of 40 Hz.

The pathological values of the magnitude vector used, obtained through the mediation of the stimulated QRS signal were:

- RMS40 < 20μV - the same as in patients with no conduction disturbances
- LAS > 38 ms - the same as in patients with no conduction disturbances
- QRS duration > 180ms - the same as in patients with left bundle branch block, the stimulated complex having this appearance on the surface ECG, according to depolarisation pattern in right ventricle. We established as pathological, the magnitude vector with at least two modified parameters.

We studied 27 patients with acute myocardial infarction with total atrioventricular block who needed urgent transient ventricular pacing, in order to maintain chronotropic competence. We measured magnitude vector parameters at different stimulating rates and we rose the rate with 20 beats per minute starting from 70 b/min, 90, 110, 130 b/min and maintaining it for 15 minutes. We performed signal average ECG without changing the position of leads or any other conditions. These analysis were performed usually after 7 days from the onset of myocardial infarction.

After that, we studied 64 patients with VVIR permanent pacemaker – 27 of them with acute myocardial infarction and total atrioventricular block (those enrolled in the previous part of our study) and 37 patients with chronic total av block and atrial fibrillation with sincope or high grade conduction disorder, following an acute event.

Results and discussions

We found no changes in magnitude vector parameters according to pacing frequency. Late potentials appearance and their expresion were not influenced by heart rate variations and it appears that they are not influenced by vein morpholgy,

patient medication, inflamatory status and other comorbidities [3-8]. In fact, the electrical properties of the myocardium are the source of arrhythmias, but to generate a sustain arrhythmia the entire millieu must be involved and if possible, substantiated by late potentials presence.

Our clinical model was represented by patients with myocardial infarction with total AV block and emergency pacing. Controlled changes in heart rate due to progresive rising of stimulated frequency registered identical magnitude vector, regardless the rate of stimuli. Of course, this controlled rising of heart rate do not corespond to physiologic and pathophysiological conditions of sympathetic stimulation, which has multiple influences on electrical properties of the myocardium at the tisular and celullar membrane level. Cardiac electrical variability plays a role in arrhythmias generation[9], but it does not change late potentials presence.

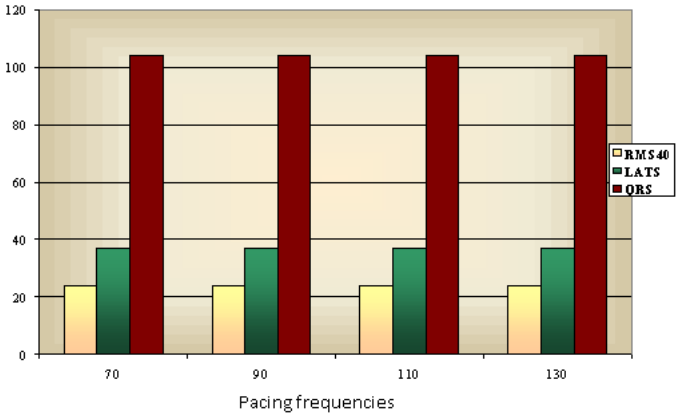

Fig. 4. Magnitude vector parameters at 4 different stimulation frequency

Sympathetic activity is an adaptative response to heart failure and it would be wrong to consider that heart rate variability does not influence late potentials presence and arrythmic substrate[9]. Stimulation with higher rate increases oxigen demand, but changes in autonomic tonus by adrenergic stimulation has other effects than simply tachycardia and autonomic dysfunction is an independent predictor of sudden death. 64 patients needed permanent pacemaker implant, 27 for acute atrioventricular block and 37 for chronic symptomatic disease. The patients were divided into 2 groups:

Group 1 – 30 patients where we used screw-in leads – group A –(active lead);

Group 2 – 34 patients with passive leads – group P – (passive lead).

In fact, we comparatively measured the average values of the magnitude vector parameters in the two groups of patients and their evolution after 6 months.

The option between the two types of leads was random, dictated by availability.

Table 1

THE TWO GROUPS CHARACTERISTICS ARE LISTED IN THE TABEL BELOW

	Group A	Group P	P
Age	68.9±9 years	68.3±7	NS
Diabetus mellitus	11 (36.66%)	12 (35.3%)	NS
Hypertension	14 (46/66%)	16 (47.0%)	NS
Acute myocardial infarction	11 (36.66%)	16 (47.0%)	0.057

There were no significant statistic difference between the two groups in terms of age, comorbidities and medical management. There was, randomly, a slightly larger number of patients with myocardial infarction in group P compared to group A, at the borderline of statistical significance.

Every month we performed clinical evaluation and standard ECG, and every three months signal average ECG was performed. At admission and later on, at 6 month follow up we performed lab test, ecocardiographic evaluation[10] and chest X ray.

The first signal averaged ECG was carried out 24 hours after the implant, when the majority of the patients (63) recorded pathological parameters, most probably due to local edema. The measurement considered as being the "first determination" was carried out 14 days after the implant, when we checked the device, the lead parameters and the threshold value, adjusting the stimulation parameters when required.

Table 2

THE DATA OBTAINED AT THE INCLUSION IN THE STUDY WERE THE FOLLOWING

	A	P	
RMS40	16 ± 3 μV	24 ± 4 μV	p = 0.0034
LAS	37 ± 11 ms	30± 14 ms	p = 0.042
QRSd	188 ± 16 ms	172 ± 11 ms	p = 0.048
RMS40+LAS	63.6%	37.5 %	p = 0.0031
IMA	71.4%	54.54%	p = 0.0067

In Group A -patients with active lead-a severe alteration of the magnitude vector parameters was documented, statistically significant when compared to group P. The amplitude of the signals in the last 40ms (RMS40) was significantly lower in the group of patients with screw-in active leads when compared to the group of patients with passive type: 16 ± 3 μV vs 24 ± 4 μV (p = 0.0034). The duration of the low amplitude signal during the last 40ms of the magnitude vector (LAS) was higher in group A when compared to group P: 37 ± 11 ms vs 30± 14 ms (p=0.042). The QRS duration was higher in patients from group A vs. group P: 188 ± 16 ms vs 172 ± 11 ms (p= 0.048), reaching statistical significance.

The patients with acute myocardial infarction in which an active lead was implanted, presented late potentials in proportion of 71.4% as compared to 54.54% of the patients with acute myocardial infarction on whom a passive lead was placed (p= 0.0067).

The incidence of late potentials in group A is significantly higher when compared to the known incidence in case of inferior myocardial infarction. We know that the incidence of the late potentials post acute inferior wall myocardial infarction is higher, due to delay in the depolarization of the lower areas which are poor in Purkinje fibres and for this reason they have a lower predictive significance . In inferior wall myocardial infarction, the incidence of late potentials ranges between 44 to 57% according to various studies, and acute anterior myocardial infarction patients, the incidence varies arround 24 -39%. Whilst the incidence of the late potentials in the group of patients with a passive lead is similar to the incidence of late potentials in uncomplicated acute myocardial infarction with conduction disorder, according to the literature, in group A these were statistically more frequent.

Of course that the interpretation of these data must be carried out with caution, taking into account that the depolarization in the case of stimulated patients is completely different from the normal way, regardless if we refer to patients suffering from acute myocardial infarction[9], patients who have chronic coronary diseases, diabetes[6] or even those with chronic kidney disease and specific management[10-12]. Moreover, the pathological values of the magnitude vector parameters for the wide QRS are not unanimously accepted, nor standardized[13,2]. However, the observation during recordings makes us draw attention on these differences.

In group A, 7 patients converted to sinus rhythm: 3 did not show positive late potentials during the stimulated rhythm (considering at least 2 pathological parameters) and during the normal rhythm the magnitude vector was normal as well, and 4 showed late potentials during the stimulated rhythm, only 1 patient having normalized the magnitude vector when the normal sinus rhythm and the normal depolarization were restored.

In group P, 9 patients converted to sinus rhythm: 4 without late potentials, with normal parameters and in sinus rhythm, 5 with initially late potentials of which 4 normalized the parameters in sinus rhythm.

It seems that the attachment of an active lead made the restoring of the normal parameters of the magnitude vector in sinus rhythm more difficult. It is possible that an explanation for this behaviour can be also the manner of trigger and propagation of the electrical impulse at the level of the active electrode. The small number of cases prevents us from reaching a statistically valid conclusion.

We recorded 11 deaths: 7 arrhythmic, 3 due to congestive heart failure and 1 due to stroke. The general mortality rate after 6 months for the entire group was 17.18%, and the mortality rate in patients suffering from acute myocardial infarction was 21.8%.

Table 3
THE DISTRIBUTION OF DEATHS ACCORDING TO THE TYPE OF THE ATTACHED ELECTRODE IS SHOWN IN THE TABLE BELOW

	Group A	Group P	
Deaths	23.3% (7)	11.76 % (4)	p = 0.002
Arrhythmia	5	2	p = 0.032
Chronic heart failure	2	1	p = 0.048
Stroke	-	1	p= 0.0031

81.8% of the deceased showed late potentials: those who died from sudden death and 2 of the deceased through heart failure. The patient who died because of neurological complications showed normal parameters of the magnitude vector. 4.34% of those without LP died, 30.43% of those with LP died. Even for a small number of cases, the negative predictive value of the late potentials is imposed. The positive predictive value, verified in case of patients with associated severe pathology - heart failure, conduction disorders, can be applied with reserve in this situation, reserve due mainly to the small number of cases, the predictive positive value depending on the rate of the event to be predicted in the population, as well as due to the lack of standardization of the method for patients with wide QRS complexes.

The high incidence of the late potentials in this category of patients is explained through the significant myocardial injury[9]. The restoring of the sinus rhythm favours the normalization of the parameters of the magnitude vector as an expression of the reduction of the infarcted area, the improvement of the electrophysiological properties, the reduction of the edema and of the fibrous content of the myocardium and the improvement of the cardioelectrical impulse

conduction. Why this improvement is less expressed in the case of patients with active fixation electrode remains to be verified. This clinical observation raises the issue of a possible electric vulnerability induced by the type of electrode used.

References

1.LIU, L., TANG, J., PENG, H. *ET AL*. A long-term, prospective, cohort study on the performance of right ventricular pacing leads: comparison of active-fixation with passive-fixation leads. *Sci Rep* **5,** 7662 (2015)

2.CEVIZ N, CELIKER A, KÜÇÜKOSMANOĞLU O, ALEHAN D, KILIÇ A, UNER A, OZME S. Comparison of mid-term clinical experience with steroid-eluting active and passive fixation ventricular electrodes in children. Pacing Clin Electrophysiol. 2000 Aug;23(8):1245-9.

3.SANTANGELI P, INFUSINO F, SGUEGLIA GA, SESTITO A, LANZA GA.. Ventricular late potentials: a critical overview and current applications. J Electrocardiol 2008 Jul-Aug; 41(4):318-24. Epub 2008 May 1.

5.IOANOVICIU, S,D., IVAN, C., MATUSZ, P., OLARIU, S ; LIGHEZAN, D ., Morphological Variability of the Hepatic Portal Vein Medial Branches Study on corrosion casts, Mat. Plast., **52**, no. 2, 2015, p. 263-265

6.IVAN, M.V., GEORGESCU, M., APOSTOL, A., ALBULESCU, N., SERB, A.F., TATU, C.S., Trimetazidine, a Metabolic Modulator, with Cardioprotective Effects Against Myocardial Ischemia, Rev.Chim. (Bucharest) **69** no 7, 2018, pg:1616.

7.MUNTEANU, M., APOSTOL, A., IVAN, M.V., New Considerations Regarding Chronic Kidney Disease, Cardiovascular Disease and Dyslipidemia in Diabetic Patients, Rev. Chim. (Bucharest), **69** no 8, 2018 pg 2064.

8.IVAN MV, ROGOBETE A, BEDREAG O ET AL., New Molecular and Epigenetic Expressions as Novel Biomarkers in Critically Ill Polytrauma Patients with Acute Kidney Injury (AKI) Clinical Laboratory, volume:64 Issue:5, pg 663-668.

9.ROGOBETE AF, SANDESC D, BEDREAG OH, PAPURICA M, POPOVICI SE, BRATU T, POPOIU CM, NITU R, DRAGOMIR T, AABED HIM, IVAN MV., MicroRNA Expression is Associated with Sepsis Disorders in Critically Ill Polytrauma Patients, Cells. 2018;7(12):271. Published 2018 Dec 13.

9.ALBULESCU, N., IVAN, VS., APOSTOL, A., IOVANESCU, G., IVAN, MV., SCHILLER, A., Cardiac Electrical Vulnerability after Acute Myocardial Infarction Associated with Respiratory Infections , Rev. Chim. (Bucharest), **70** no. 1, 2019, p.. 207-210.

10.IVAN, V.S., ALBULESCU, N., ALBULESCU, I.R., APOSTOL, A., BUZAS, R., SCHILLER, A., TIMAR, R., LIGHEZAN, D., IVAN, M.V., Predictive Value of Several Echo Parameters for Cardiovascular Events in Hemodialysis Patients with Mid-range and Preserved Ejection Fraction Heart Failure. Rev. Chim. (Bucharest), **70**, no. 4, 2019, p.1479-1484

11.ALBULESCU, N., APOSTOL, A., ALBULESCU, I.R., MIHAESCU, A., SCHILLER, A., TIMAR, R., Furosemide Pharmacodynamics and Cardiovascular Effects in Hemodialysis Patients, Rev. Chim. (Bucharest), **70**, no. 3, 2019,p. 973-976.

12.APOSTOL, A., CHISAVU, L., ALBULESCU, N., STOIAN, D., SCHILLER, A., RAS Inhibition in Haemodialysis Patients. Rev. Chim. (Bucharest), **70** no. 2, 2019, p. 442-444.

13.STEINBIGLER P, HABERL R, JELEAZCOV C, KNEZ A, DORWARTH U, MÜLLER D, HOFFMANN E, STEINBECK G. Functional changes of ventricular late potentials by provocation with increase of heart rate. Evaluation during atrial pacing. Europace. 1999 Apr;1(2):103-12.

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