Primary Results with Ir-coated Electrodes applied to the Rabbit Heart in modified Langendorff-Experiment

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Introduction

Monitoring of monophasic action potentials was performed for the first time in 1883 by Burdon-Sanderson and Page on frog-myocardium. In the last few decades the technology of measurement of monophasic action potentials was improved to such an extent that clinical application became possible. In 1966 monophasic action potentials were viewed by means of vacuum electrodes by Korsgren et al. during clinical electrophysiological investigation. This technique was improved by Olson and co-workers [5,6]. As a fundamental methodological disadvantage using vacuum electrodes a focal injury of myocardium is caused. Since 1980 the contact electrode technique has been established by Franz and co-workers, in a way that atrial and ventricular action potentials can be measured and recorded by Ag/AgCl-coated electrodes for longer periods of time. Advantages of this technique are, e. g., the possibility of direct monitoring of myocardial repolarization and action potential duration (APD), respectively, detection of ischemic areas, the immediate evidence for the effect of antiarrhythmical drugs with regard to repolarization behaviour, and the display of adaptive processes of myocardial action potential duration during changes in heart frequency [2,3,4]. The purpose of this study was to investigate by means of an animal model if Ir-coated electrodes with three different surface areas (1.3 mm^2, 6 mm^2, and 26 mm^2) are able to detect monophasic action potentials (MAPs) of the same quality as customary Ag/AgCl-electrodes. Advantages of Ir-coated electrodes when compared to Ag/AgCl-electrodes are their biocompatibility and the long-term stability of their electrical properties, by which chronic clinical application of electrodes as pacemaker- and cardioverter-defibrilator-probes is enabled.

Methods

For validation of three different Ir-coated electrodes in comparison with customary Ag/AgCl-electrodes monophasic action potential was measured epicardially at rabbit hearts in a modified Langendorff-experiment. The specific test set-up allowed the measurement of epicardial potentials by up to 12 electrodes simultaneously. Investigations were made on 16 rabbit hearts altogether (breed: New Zealand White; weight 2.5 - 3.0 kg; 6 male, 10 female) with an average heart weight of 10 g. After intravenous anaesthesia with Pentobarbital (Trapanal) and anticoagulation therapy with 1 ml Heparine (= 500 i. U. Liquemine), thoracotomy was performed and the heart was quickly explanted. Then, heart was supplied with tyrode solution (temperature: 37.0° C; perfusate 25 - 40 ml/min; carbogenously saturated) by a perfusion tube in the aorta. Afterwards, ablation of the AV-node was performed by means of forceps-like tongs connected to a power supply unit (Digi 40; Voltcraft), in order to increase the intrinsic cycle length of the heart from about 400 ms to about 1000 ms. After fixation to a holding device different electrodes were positioned by a circular spring suspension epicardially at the heart. Stimulation was performed by an electrode with pulse duration 1 ms at double diastolic threshold (4 - 8 mV) controlled by a stimulating device (Biotronic, UHS 20). MAPs were recorded by a buffer amplifier and an A/D-converter. Data was stored on PC. Regularly, every day of the experiment MAPs were measured simultaneously by four different electrodes placed at left and right ventricle: customary Ag/AgCl-catheter electrodes with distal tip (surface area: 4 mm^2), an Ir-coated large tip electrode (surface area: 26 mm^2), and two fractally

Ir-coated electrodes, one a small tip electrode (surface area: 1.3 mm^2) and one a medium tip electrode (surface area: 6 mm^2). Fractal coating increases electroactive surface area compared to macroscopic surface area by 1000:1.

Electrostimulation

Electrostimulation of the heart was performed at base intervals of 200, 400, and 600 ms. After change of interval there was steady-state pacing for at least 3 minutes at constant interval in order to ensure stabilization of action potentials. The technique of extrastimulus was applied, with an extrastimulus after eight base stimulation intervals at shortening intervals (steps of 5 - 10 ms) until extrastimulus no longer evoked a response, i. e. contraction of the heart. Effective refractory period was determined as the interval of extrastimulus, at which stimulation was no longer followed by a response of the heart: ERP = last responded extrastimulus - 5 ms.

Results

Stimulation at constant interval ('steady-state pacing')

Regarding the morphology of MAPs derived by different electrodes (figures 1 and 2) it is noted, that

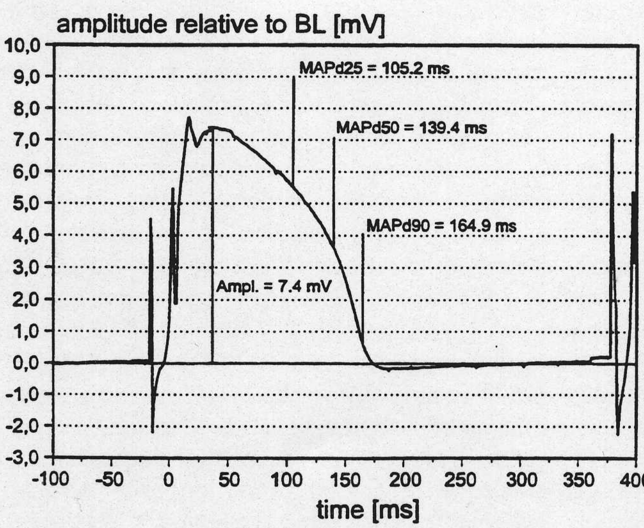

Figure 1. *Epicardial MAP detected by Ag/AgCl-electrode at stimulation interval 400 ms.*

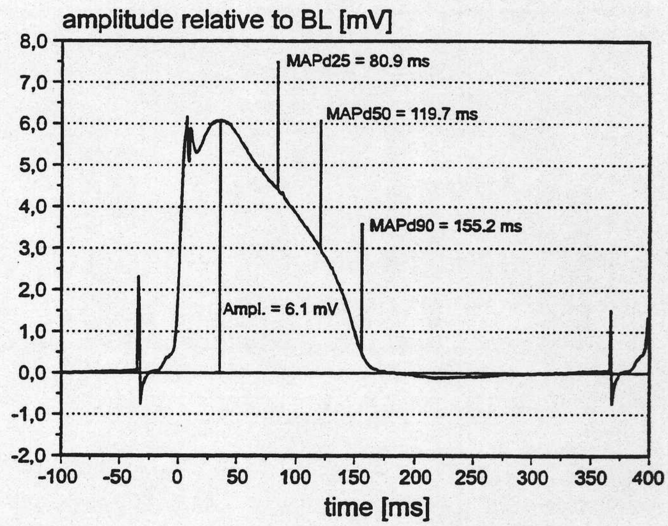

Figure 2. *Epicardial MAP detected by medium tip electrode at stimulation interval 400 ms.*

small tip electrode and medium tip electrode yield the same morphology as the Ag/AgCl-electrode, whereas signal morphology of the large tip electrode differs decisively. We observed a prolonged depolarization (upstroke of MAP = phase 0) for the large tip electrode at all days of the experiment, an essentially lower amplitude and extended MAPd25, MAPd50 and MAPd90 (duration of monophasic action potential at 25%, 50%, and 90% repolarization). For large tip electrodes in the end of repolarization a negative postoscillation was found occasionally. Even for optimized electrode pressure to the epicardium this phenomenon was observable, while lower pressure decreased the amplitude of local MAP but did not reduce the duration of the signal as a whole. Likewise, the measured parameters like amplitude, MAPd25, MAPd50, MAPd90, were almost identical for Ag/AgCl- and both fractally coated electrodes, whereas the large tip electrode resulted in decisively divergent values because of differing morphology. Figure 3 shows mean values of all data for 300 ms base interval at steady-state pacing.

MAPd25, MAPd50, and MAPd90 show an increase for the small tip electrode compared to Ag/AgCl-electrode of 2.6 %, for the medium tip electrode a decrease of 2.1 % and for the large tip electrode an increase of 12.5 %. The average amplitude at all days of the experiment was: Ag/AgCl-electrode 10 mV, small tip electrode 11 mV, medium tip electrode 7 mV and large tip electrode 2 mV.

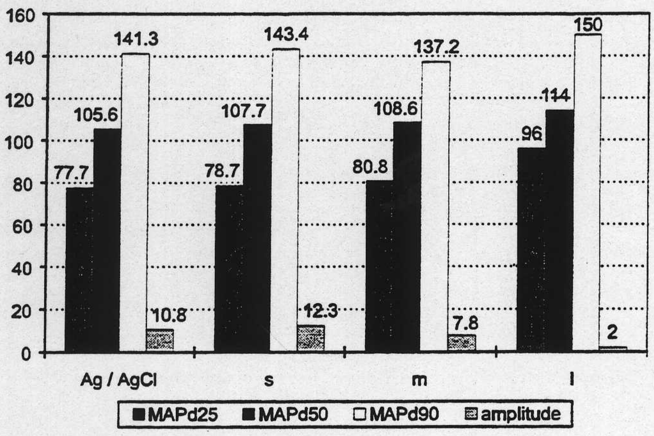

Figure 3. Mean MAPd25, MAPd50, and MAPd90 combined with mean amplitude of MAP at frequency stimulation 300 ms for small (s), medium (m), and large (l) tip electrode.

Extrastimulus technique

By means of the technique of extrastimulus described above it is feasible to discuss the behaviour of the rabbit heart under prematurely encountered pulses and to determine the effective refractory period for any base interval. The so called electrical restitution curve is obtained by drawing up the MAPd50 and MAPd90 values against the interval of extrastimulus (figure 4). It is noticed, that compared values for small tip and medium tip electrode were highly correlated, whereas

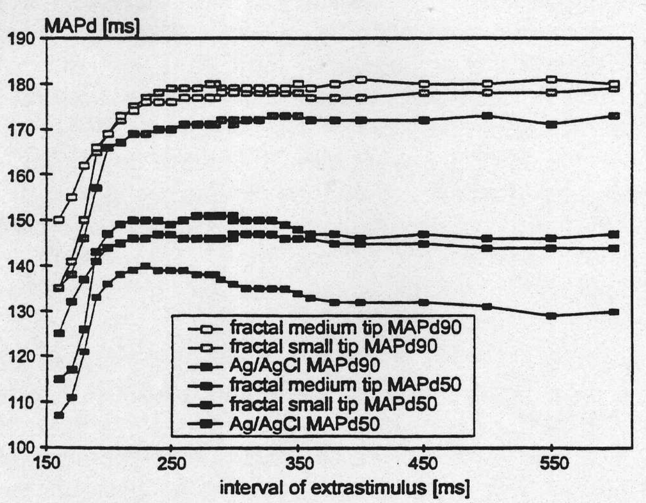

Figure 4. Electrical restitution curve (ERC) at 600 ms compared for Ag/AgCl-electrode, small tip electrode, and medium tip electrode.

the large tip electrode was only moderately correlated (table 1).

	Ag/AgCl vs s	Ag/AgCl vs m	Ag/AgCl vs l
300 ms	r = 0.99	r = 0.97	r = 0.72
400 ms	r = 0.96	t = 0.91	r = 0.87
600 ms	r = 0.98	r = 0.92	r < 0.5

Table 1. Correlation of MAPd90 detected by Ag/AgCl- and three different Ir-coated electrodes for single stimulation at different base intervals (s = small tip electrode; m = medium tip electrode; l = large tip electrode).

Application of antiarrhythmical drugs

The experiment took 7 days, altogether, and every day after base stimulation an antiarrhythmicum was applied (three days Ambasilide and four days Amiodarone). For final statistical evaluation the number of tests was insufficient, but it is possible to demonstrate that fractal Ir-coated electrodes also show detectable changes in repolarization.

Discussion

Measurement of monophasic action potentials of the rabbit heart as in the modified Langendorff test set-up described above is excellently suited to validate different types of electrode, under basic conditions and under pharmaco-therapy as well. Because of uncomplicated application of drugs a wide-range use not only for antiarrhythmica is feasible. Investigation of novel fractally Ir-coated electrodes showed that both with regard to the signal morphology and the characteristics under frequency stimulation or premature stimulation hardly any differences in compare to customary Ag/AgCl-coated electrodes is noted. Morphology of potentials, duration, and reaction to extrastimuli of fractally Ir-coated electrodes with surface areas of 1.2 mm^2 and 6 mm^2 have the same characteristics as customary Ag/AgCl-electrodes. This type of electrode is supposed to supply a valid measurement of MAP. Results for Ir-coated large tip electrode are less promising. Besides decisevely lower amplitudes duration of action potential is increased compared to Ag/AgCl-electrode in particular at longer simulation interval. Yet, it is not sure if this is related to the larger macroscopic surface area of 26 mm^2. With regard to the surface area of 26 mm^2 a considerable part of the distal tip electrode does not immediately contact the myocardium and thus reflects the total repolarization of the heart. Smaller electrodes the tip of which contacts the myocardium extensively in contrary to large surface area electrodes reflect local and thus shorter action potential. Moreover, the influence of the not essentially increased surface area of the electrode can lead to an additional deterioration of MAP-detection. Finally, the question of differences in detection characteristics can only be clarified by further investigations using other types of electrodes.

Although, final conclusions with regard to pharmacological evaluation using fractally coated electrodes might be premature, at present it can be stated that results obtained hitherto show that fractally coated Ir-electrodes are comparable to Ag/AgCl-electrodes.

The results are a prerequisite for use of fractally coated Ir-electrodes in further measurements and provide the possibility to measure repolarization of the human heart chronically. As a restriction must be recognized that results obtained by Langendorff set-up first of all have to be confirmed in clinical measurements at the human heart. Moreover, further types of electrodes have to be investigated in order to find the most favourable electrode design for measurement of monophasic action potentials. If the results described above will be confirmed, new perspectives will open for chronical clinical measurement of monophasic action potentials.

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