Review

Current status of monophasic action potential recording: theories, measurements and interpretations

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1. Introduction

Monophasic action potentials (MAPs) are extracellularly recorded wave forms that, under optimal conditions, can reproduce the repolarization time course of transmembrane action potentials (TAPs) with high fidelity [1–3]. While TAP recordings require the impalement of an individual cardiac cell by a glass-microelectrode and therefore generally are limited to in vitro preparations, MAPs can be recorded from the endocardium and epicardium of the in situ beating heart, including that of human subjects. MAP recordings therefore are suitable for studying the characteristics of local myocardial electrophysiology, especially of repolarization, in the clinical setting. This has made MAP recordings an important bridge between basic and clinical electrophysiology in multiple areas of arrhythmia research [4].

Despite the growing use of the MAP recording method, there still is surprisingly little hard data on the exact mechanism by which MAPs are created and recorded. New methods for recording MAPs recently have been proposed, and new theories and models have been suggested to explain the mechanisms that underlie the genesis of the MAP signal. There have been attempts to record MAPs from sites within the myocardial wall, an effort spurred on by the discovery that mid-myocardial cells (M-cells) have different repolarization characteristics than either epicardial or endocardial cells [5], and these different characteristics have been found to be important for the development of torsade de pointes arrhythmias [6]. This article attempts to review the available information on the MAP genesis and its particular recording modes. It also highlights some important MAP quality criteria and guidelines for correct interpretation of MAPs and how to avoid artifacts. Last but not least, important differences between unipolar and bipolar recordings of both MAPs and conventional electrograms will be discussed, as they pertain to the fidelity and spatial resolution of these recordings.

2. Brief history of MAP recording techniques

2.1. The ‘injury’ method

The first MAP was recorded in 1882 by Burdon-Sanderson and Page [7] who placed one electrode on the intact epicardial surface and the other on an injured site of a frog heart, and thereby captured the phasic electrical changes of the cardiac cycle on a charcoal-covered recording drum. Burdon-Sanderson and Page produced this injury by cutting into the myocardium, and termed these recordings monophasic action currents (later to be replaced by monophasic action potentials). Until then, electrodes placed on intact heart tissue had been recording multiphasic deflections, similar to those recorded today in the human electrophysiology laboratory by conventional electrode catheters; so the term monophasic was a logical choice. It was believed for several decades that such monophasic action potentials could only be produced by traumatic tissue injury or cellular disruption. Methods such as cutting, stabbing or burning of a myocardial site were invented to produce monophasic ‘injury’ currents [8]. In 1934, Schütz [9] introduced the suction electrode for experimental MAP recording. In 1969, Korsgren et al. [10] used a suction electrode catheter in a patient and recorded, for the first time, MAPs from the in situ ventricular endocardium. This pioneering step subsequently was amplified by the work of Olsson and coworkers [11–13] who...
refined the suction electrode technique and demonstrated the value of MAP recording in exploring human cardiac electrophysiology, mainly of the right atrium. Injury was still deemed necessary and to do this ‘cautiously’ in the human heart by suction technique required the use of three-way stop cocks, bubble filters to prevent air emboli and other precautions [13]. Because this technique was cumbersome and raised patient safety concerns, the suction electrode technique never gained wide acceptance in the clinical electrophysiological laboratory (nor FDA approval).

2.2. The ‘contact’ electrode method

The first nontraumatic method for recording MAPs was published in 1935 by Jochim et al. [14]. These authors demonstrated that MAPs can be obtained by simply pressing an electrode against the epicardium of the toad ventricle while another electrode merely touched the nearby epicardium (Fig. 1). They also showed that the MAP is positive with respect to zero if the pressure electrode is the active electrode (connected to the positive amplifier input). This important observation went largely unnoticed for many years. However, their observation was in both methodology and interpretation surprisingly similar to the current principle of recording MAPs by contact electrode.

The ‘contact electrode technique’ for clinical use was developed between 1980 and 1983 by Franz et al. [15,16]. With the contact electrode technique, MAP recordings can be obtained from the human endocardium or epicardium without suction but rather by pressing a nonpolarizable electrode gently against the endocardium or epicardium. Catheters and probes for endocardial and epicardial MAP recording were developed for clinical studies and for experimental studies [17–19]. Fig. 2 shows the clinically most widely used MAP catheter, which also incorporates pacing electrodes. The ability to record MAPs by the nontraumatic contact electrode technique refuted the previous contention that myocardial injury (or suction) is a prerequisite for MAP recording. Besides being more simple and clinically safe, the contact electrode method provides MAP recordings that, due to lack of myocardial injury, are stable over time. This allows the clinical electrophysiologist to monitor MAPs over periods of several hours from the same endocardial site to assess, for instance, the effects of antiarrhythmic drugs or cycle length changes on local myocardial repolarization [16,20].

2.3. Genesis of the MAP: old and new theories

The MAP is measured with an extracellular electrode that has a diameter of 1 to 2 mm and therefore cannot enter a single cardiac cell. This has given rise to much debate about the genesis of the MAP. The early literature on MAP measurements focussed on the central issue of whether the MAP signal is recorded with the electrode in contact with injured (depolarized) myocardium or with the electrode in contact with uninjured (intact) myocardium. Hans Schaefer, a vehement protagonist of the former assumption, argued that MAPs can only be obtained when injury is present and therefore the electrode in contact with
injured muscle must be the different electrode [21,22]. Others countered that injured cells are electrically inactive and therefore the electromotive force producing the MAP must originate from the uninjured cells [23–25]. As will be explained later, the truth appears to lie in the middle.

2.4. The ‘Schütz-hypothesis’ on injury potentials

Based on experiments in frog hearts, Schütz in 1934–1936 [8,9] promoted the theory that the MAP is the voltage drop that is recorded between the different electrode (in contact with injured myocardium) and the indifferent electrode (in contact with uninjured myocardium). He assumed leak current flow between the injured cells and the uninjured myocardium and explained the MAP by the following simple equation:

\[ E_{\text{map}} = E_m \times (R_e + R_i)/R_i \]

where \( E_{\text{map}} \) is the MAP voltage, \( E_m \) is the transmembrane voltage, \( R_e \) is the extracellular resistance and \( R_i \) is the intercellular resistance. This hypothesis assumes that the MAP is the result of a voltage source, with all electromotive generators in parallel. An increase in extracellular resistance (for instance, by drying the heart’s surface) would result in a greater MAP amplitude (which in fact occurred), and a decrease in extracellular resistance, by wetting the heart’s surface with electrolyte solution, would decrease the MAP amplitude (which also is true for injury potentials in this setting). This hypothesis also assumes that short-circuiting between the injured cells and the extracellular space is minimized by using a tight electrical seal between the MAP recording electrode and the surrounding tissue. The suction electrode method was promoted to some extent because it was believed to provide such a seal. This theory has some semblance to the sucrose-gap technique that is used to record the TAP in vitro without transmembrane impalement [26].

2.5. The ‘volume conductor’ hypothesis

Based on the following observations, Franz [27] concluded that the Schütz hypothesis does not apply to the contact electrode method but that the contact electrode MAP results from a current source and is governed by volume conductor theory. (1) The contact electrode obtains MAPs from the endocardium while surrounded by the blood pool in the ventricular or atrial cavity and has no surrounding seal, suggesting that the extracellular resistance has no influence on the amplitude of the MAP. This was confirmed by experimental studies in small animal hearts [27]. (2) The number of cells (single electromotive generators) contributing to the MAP seems important because greater contact pressure between the tip electrode and myocardium increases the MAP amplitude [16]. Furthermore, MAPs of greater amplitude are recorded from ventricular myocardium than atrial myocardium or from larger hearts (e.g. canine and human hearts) as compared to small hearts (e.g. rabbits), suggesting that wall thickness beneath the MAP tip electrode plays a role in determining the MAP amplitude [27]. This suggests that the MAP amplitude is related to the volume of cells that contribute to the MAP genesis and that the MAP signal results from a current source, with individual electromotive generators more or less in series.

2.6. MAP genesis by the contact electrode method

Fig. 3 schematically depicts the hypothesis by which the contact electrode method produces and records MAPs. Pressure exerted focally against the myocardium depolarizes the group of cells subjacent to the electrode to a level that is estimated at −30 to −20 mV with respect to the diastolic extracellular reference potential. Because sodium channels remain inactivated at these voltage levels, these cells are unexcitable and thus unable to participate in the periodic depolarizations and repolarizations that occur in the adjacent (normal) myocardium. The group of cells depolarized by the contact electrode provide a ‘frozen’ potential, which contrasts with the time-varying potential in the unaffected adjacent cells. Assuming preserved electrical coupling, this causes a time-varying electrical gradient between the depolarized (inexcitable) cells subjacent to the electrode and the adjacent (excitable) cells. This electrical gradient produces current flow across the boundary between these two states. During electrical diastole, this gradient results in a source current emerging from the normal cells and a sink current descending into the depolarized cells subjacent to the MAP electrode. The sink current produces a negative electrical field that is proportional to the strength of current flow, which depends on the potential gradient and the number of cells that contribute to the interface between the subjacent depolarized and the adjacent nondepolarized cells. During electrical systole, the normal cells adjacent to the MAP electrode undergo complete depolarization, which overshoots the zero potential by some 30 mV, whereas the already depolarized and therefore refractory cells subjacent to the MAP electrode cannot further depolarize and maintain their potential at the former reference level. As a result, the former current sink reverses to a current source, producing an electrical field of opposite polarity. According to this hypothesis, the MAP recording reflects the voltage time course of the normal cells that bound the surface of the volume of cells depolarized by the contact pressure. Thus, both the depolarized (‘electrically frozen’) cells and the active cells of the neighboring myocardium contribute to the genesis of the boundary current that produces the MAP field potential; one cannot exist without the other.
Fig. 3. Diagram illustrating the hypothesis underlying the genesis of MAP recording by contact electrode. (A) Late electrical diastole. The myocardial cells are \(-90\) mV negative inside with respect to the outside. The pressure of the tip electrode (black ellipsoid) against the myocardium results in constant depolarization of the subjacent cell volume (shaded hemisphere). A fixed depolarization to \(-20\) mV is assumed but could be slightly larger or smaller. The potential gradient across the boundary between the normal diastolic potential and the fixed depolarization underneath the contact electrode creates current flow (circular lines), which, in the extracellular space, flows from normal to depolarized tissue. Under the present volume conductor conditions, this creates a current sink and a corresponding sink potential at the contact electrode site. The MAP recording (inside in upper right) shows a steady potential negative to zero. An arriving action potential wave, which carries an inside potential of \(+30\) mV near the upstroke, is shown to the right of the contact electrode site. (B) Early electrical systole. The action potential wave arrives at the contact electrode site. The cell volume depolarized by the contact pressure is unexcitable and maintains its potential at \(-20\) mV. Its initial \(+30\) mV inside brings to the contact site a relative positive inside charge and a relative negative outside charge. This leads to a reversal of the boundary current and field potential polarity. The MAP now moves in the positive direction and incribes an upstroke and early phase 1. (C) Mid electrical systole. The propagating action potential wave has completely encompassed the MAP recording site. As the TAP wave gradually repolarizes, the boundary gradients gradually diminish. The MAP undergoes slow repolarization, which nears the isoelectric line as the TAP potential approaches the potential in the pressure-depolarized cell volume. (D) End electrical diastole. The propagating TAP wave recedes from the MAP electrode contact site. Voltage gradients return to their pre-existing (diastolic) state. The cycle is completed and results in a MAP recording that faithfully resembles the original TAP recording. Abbreviations: MAP = monophasic action potential recorded from extracellular space. TAP = transmembrane action potential recorded from intracellular space.

3. Different versus indifferent electrode: which is which and which one records the MAP?

Based on the above model and experimental observations, it has become evident that the MAP originates from cells in the immediate vicinity of the electrode that causes persistent depolarization. It is also evident that, to obtain an upright MAP signal, the MAP-exploring electrode must be connected to the positive input of the amplifier and the reference electrode to the negative input. The following data help to elucidate further the relationship between the active (different) and inactive (indifferent) electrode.

3.1. Unipolar MAP recordings

The name ‘monophasic action potentials’ (MAPs) was introduced at the time of its first discovery in 1882 [7]. Before, only biphasic or multiphasic electrograms had been recorded from the surface of the heart. Later, it became obvious that extracellular monophasic action potentials can only be obtained by using a unipolar recording method. To better understand the conditions giving rise to monophasic action potentials, the following factors need to be emphasized: If both electrodes are placed on intact myocardium, a bipolar signal is obtained. If both electrodes are placed on injured or otherwise depolarized muscle, the monophasic portion of the signal will be canceled out. If one electrode is in contact with depolarized muscle and the other with active tissue, a monophasic signal is recorded. By coupling the active MAP-exploring electrode with a remote electrode, such as a ‘Wilson central terminal’, a monophasic potential is still obtained but will also contain far-field potentials. The extent to which these far-field potentials contribute to the local MAP signal is often unpredictable. If an area of myocardial depolarization caused by ischemia or other causes exists remote from the MAP recording site, the field potential created across its boundaries may contaminate the local
MAP signal to a greater or lesser extent, depending on the particular geometry of the current sources with respect to the position of the two MAP electrodes. This problem is reminiscent of difficulties encountered in interpreting precordial ST segment elevations or depressions when more than one ventricular wall segment is injured by ischemia [28]. Reciprocal changes, cancellations and expansions all may occur, making the precise localization of the primary injury difficult.

3.2. ‘Close-bipolar’ MAP recordings

The problem of MAP contamination by far-field potentials was recognized by Olsson [13], who advocated a ‘close-bipolar’ MAP recording approach. The electrical field potential that is caused by applying suction or contact pressure to the myocardium and that creates the MAP seems to be confined to a finite region that does not extend much beyond the area of depolarization. An electrode placed 5 mm proximal to the depolarizing tip electrode usually is far enough away from the MAP-generating current and therefore can be used as a reference electrode that is indifferent to the monophasic field. This close-bipolar electrode arrangement provides a very small solid angle towards more remote electrical forces and, by using differential amplification, greatly reduces far-field potentials. It is this close-bipolar technique that makes the MAP recording truly local, as the following two examples illustrate:

1. Fig. 4 compares a unipolar MAP, a close-bipolar MAP and a unipolar electrogram, all recorded with the same catheter at the same location, during normal and ectopic ventricular activation. The unipolar MAP shows major differences in morphology during ectopic activation, while the close-bipolar MAP does not. This underscores the fact that, using the close-bipolar technique, the MAP measures only local depolarization and repolarization events. These three signals were recorded by three independent, high-impedance, differential amplifiers. Any two of the three recordings are the sum of the third (similar to the three Einthoven leads). (Further details in the legend to Fig. 4).

2. Fig. 5 shows three types of recordings obtained simultaneously from the anterior left ventricular (LV) epicardium of the in-situ canine heart: the close-bipolar MAP, the unipolar MAP and the unipolar electrogram. Occlusion of the LAD resulted in a decrease in the amplitude of the close-bipolar MAP and a concomitant increase in the ST segment of the unipolar electrogram, with both changes being nearly reciprocal to each other. The unipolar MAP, however, remained almost unchanged. Therefore, it must be concluded that unipolar MAP recordings are not a reliable measure of local electrical activity but are sensitive to influences originating from potential gradients at distant sites. Only close-
boundary currents between the depolarized cells and adjacent normal cells (see above). The spatial resolution cannot be less than the tip electrode diameter (typically 1 to 2 mm). Another determinant is the distance and the solid angle between the tip electrode and the reference electrode with respect to the MAP voltage field source. With our method, the interelectrode distance is commonly 5 mm. When the tip electrode is kept in an ideal position perpendicular to the myocardial surface, the solid angle with respect to areas lateral to the tip electrode is very small, resulting in effective cancellation of remote electromotive sources if differential amplification is used. Franz et al. [2] impaled myocardial cells with microelectrodes in the immediate vicinity of the contact site of the MAP electrode and measured normal transmembrane resting and action potentials as close as 0.1 mm to the MAP tip electrode circumference, suggesting that the area of depolarized tissue which constitutes the MAP boundary is confined to the MAP electrode size. These authors also recorded MAPs across a sharp transmural infarct border [17]. This further supports the view that the MAP signal reflects electrical activity from a very small area, not less than the electrode size and probably not more than 5 mm in diameter. The ‘depth of view’ with which the MAP electrode senses the electrical activity of myocardial tissue beneath the MAP contact electrode has not yet been determined. The fact that MAP recordings from thicker wall segments (left ventricle, large animals) have substantially greater amplitudes than recordings from thin-walled tissue (right atrium, small animals) suggests that tissue at some considerable depth beneath the exploring electrode contributes to the genesis of the MAP signal [27].

3.3. Field of view of MAP recordings

Even with the close-bipolar MAP recording technique, which ascertains that the MAP recording reflects local electrical activity at the recording site, the actual spatial resolution of the MAP has not been determined with accuracy. Levine et al. [29] addressed this issue by analyzing the ‘foot’ of MAP signals recorded from slices of canine myocardium and found that approaching electrical activity may be seen from areas as far as 10 mm from the MAP tip electrode. However, these recordings were done from a tissue preparation that was not perfused but only superfused, and only a unipolar recording technique was applied. Therefore, the foot of the MAP likely included far-field electrical activity.

One obvious determinant for the field of view is the size of the MAP tip electrode that produces and explores the bipolar MAP recordings reflect the local electrophysiological changes during regional ischemia.

4. How accurate are MAP recordings compared to transmembrane action potentials?

The accuracy with which MAP recordings reflect the local cellular depolarization and repolarization was examined in several studies that compared the MAP with the simultaneously recorded transmembrane action potential (TAP) [1–3]. These studies have pointed out a number of similarities and dissimilarities between the MAP and TAP. In general, high-quality MAP recordings should satisfy the criteria listed in Table 1.

Table 1

<table>
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<th>MAP quality criteria</th>
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<tr>
<td>1. MAP amplitude (baseline to plateau crest) not less than 10 mV</td>
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<td>2. Fast, clean upstroke (rise time not longer than 5 ms)</td>
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<td>3. No major contamination by intrinsic deflection or QRS</td>
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<td>4. Smooth, upwardly convex plateau</td>
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<td>5. Horizontal diastolic baseline [no undershoot (‘dip’) during early mechanical diastole, and no upsloping potential for the remainder of diastole]</td>
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<td>6. MAP wave forms closely similar during normal and ectopic activation sequence</td>
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4.1. MAP amplitude and resting potential

Both the diastolic and action potential amplitude are markedly less in the MAP as compared to the TAP. The amplitude of the contact electrode MAP typically ranges between 5 and 50 mV, although values as high as 81 mV have been reported [27]. Despite this variability, which depends on the contact pressure and tissue type (see above), relative changes in the MAP resting and action potential amplitude can be interpreted as long as a stable baseline recording is obtained before and after the intervention [17,30].

4.2. Repolarization time course

The MAP faithfully reflects the duration as well as the configuration of the repolarization phases one through three of the TAP [2,31]. Fig. 6 shows TAP and MAP recordings obtained simultaneously from closely adjacent sites in an isolated perfused rabbit septum preparation during interventions that influence the action potential duration and configuration [31]. Each panel shows TAP and MAP signals superimposed upon each other after they have been rescaled to match in amplitude. With each of the interventions shown, changes in the shape and duration were nearly identical in the TAP and MAP recordings.

4.3. Upstroke velocity

The maximum upstroke velocity ($V_{\text{max}}$) of the MAP is much smaller than that measured with an intracellular electrode. In the canine heart, $V_{\text{max}}$ of the ventricular MAP averages 7 V/s [17], compared to 200 to 300 V/s in the transmembrane record [32]. The smaller rise in velocity of the MAP is in part due to its smaller amplitude and in part to the fact that the MAP electrode records the electrical activity from a group of cells whose depolarizations occur sequentially with time. Despite the marked difference in absolute magnitude of $V_{\text{max}}$ between TAP and MAP recordings, relative changes in $V_{\text{max}}$ may provide important information. Franz et al. [17] demonstrated during acute ischemia that $V_{\text{max}}$ of the MAP decreased by 95% at only 5 min of coronary artery occlusion. This makes the MAP upstroke velocity a highly sensitive marker of myocardial ischemia. Under stable recording conditions, MAPs also provide reliable measures of drug-induced changes in $V_{\text{max}}$, which can help classify use-dependent properties of sodium channel-blocking drugs [30].

4.4. Upstroke and phase 1 morphology

Using high band-width amplification, the upstroke of the MAP contains a rapid deflection, appearing as a biphasic notch within the MAP upstroke or a spike overshooting or undershooting it [2,16]. This notch is the remnant of the ‘intrinsic deflection’ seen in the myocardial surface electrogram prior to applying contact pressure and the development of the MAP. This intrinsic deflection may appear as a positive spike immediately preceding the MAP plateau phase, mimicking an ‘overshoot potential’ or ‘phase 1 repolarization’. This, however, should not be taken as evidence that the MAP reflects recordings from specialized conductive tissue or represents predominant $I_{\text{to}}$ channel activity of epicardial myocardium, as suggested by some investigators [33]. As Fig. 4 shows, during excitations originating from different ectopic ventricular sites, with their attending alterations in activation sequence, the upstroke phase alters its shape and overshoot potential despite the fact that the MAP electrode remains at a constant location.

There currently is no reliable method to eliminate the intrinsic deflection which, in contrast to the remote QRS, originates from myocardium very near the exploring MAP tip electrode. For this reason, we define the MAP amplitude as the distance from the baseline to the crest of its
plateau phase, and not to the peak of the upstroke. It also underscores why the rise velocity of the MAP upstroke cannot be equated with that of the transmembrane action potential.

4.5. Afterdepolarizations

Basic electrophysiologic studies have provided strong evidence that afterdepolarizations play a significant role in the genesis of triggered arrhythmias, such as torsade de pointes. These afterdepolarizations, which can be distinguished between early (EADs) and delayed (DADs) afterdepolarizations, cannot be detected by conventional intracardiac recordings. MAP recordings have been used to detect EADs or DADs during experimental [34–39] and clinical [40–44] electrophysiologic studies and relate them to triggered arrhythmias. However, it is extremely important to apply stringent quality criteria to the MAP recording before interpreting abnormalities in the final repolarization time course as EADs or DADs. ‘Humps’ and ‘wobbles’ in the MAP recording simply may be the result of unstable electrode contact (see Section 5). The following criteria may be helpful in distinguishing true EADs or DADs from movement artifacts: (1) Experimental conditions usually allow the investigator to obtain baseline recordings before beginning interventions. These baseline recordings should be stable with a smooth phase three and a horizontal phase four without appreciable deviations. (2) EADs, when they occur in response to interventions such as application of catecholamines or action potential duration (APD)-prolonging drugs, or short-long pacing sequences, should be critically evaluated to determine if they bear sufficient morphological resemblance, and behavior compliant with, data known from transmembrane recordings. (3) Washout of the inducing agent or cessation of the interventional pacing protocol should result in the disappearance of EADs and return to baseline MAP tracings. Even then, no absolute proof of the validity of the EADs or DADs is obtained. There will always be a degree of uncertainty, which diminishes proportionally with the experience of the investigator and his/her ability to suppress bias. This author believes, after careful inspection of the experimental protocols and figures, that the work presented in references [34–44] is convincing and supports the usefulness of MAP recordings for the purpose of identifying EADs or DADs under the given experimental conditions.

5. Movement artifacts

One of the most important limitations of MAP recordings is that they may be distorted by motion artifacts caused by the beating heart. The MAP amplitude is (within limits) proportional to the contact pressure exerted by the electrode against the myocardium. Unless correct position-
tation coupling [45] or mechanoelectrical feedback [46], can lead to changes in action potential duration [47–49], ‘afterdepolarizations’ [50–52] and even arrhythmias [53] (Fig. 8). The mechanism underlying these electrophysiologic effects is believed to be myocardial stretch [54]. Nonuniformity of ventricular contraction and relaxation [55] creates conditions where some wall segments undergo excessive lengthening during diastole or even late systole, causing regional heterogeneity of load-induced electrophysiologic changes. Some investigators have discarded afterdepolarizations in MAP recordings categorically as movement artifacts because they did not observe the same afterdepolarizations in intracellular microelectrode recordings [56]. However, to ensure stable microelectrode impalements, intracellular recordings are usually obtained from excised, mechanically relatively quiescent, preparations that do not experience physiologic load or length changes. Thus, validation of the MAP by comparing it against the ‘gold standard’ of the transmembrane action potential must fail in this respect. This makes the reliable distinction between ‘true’ and ‘false’ motion-induced MAP changes one of the greatest challenges of the MAP method.

6. Measurement and analysis of MAP recordings

6.1. Determining the MAP duration

Because the asymptotic end of repolarization makes precise measurement of total MAP duration difficult, the MAP duration is usually determined at a repolarization level of 90% (or another fraction) with respect to the MAP amplitude. The MAP amplitude is being defined as the distance from the baseline to the crest of the MAP plateau, not its upstroke peak (Fig. 9) [16]. Others have suggested using the intersection between the diastolic baseline and a tangent placed on phase three repolarization [57], although this may produce more arbitrary results, depending on the slope of final repolarization. We define the beginning of the MAP as the instance of fasted rise time of the MAP upstroke or, if detectable, the notch of the intrinsic deflection, which is superimposed onto the MAP upstroke [16]. Computer algorithms have been developed to automate the analysis of MAP duration at user-specifiable repolarization levels [58,59]. However, due to the complexity of the MAP signal, interactive programs and validation by manual observers are recommended [58].

7. Simultaneous measurement of MAP duration and refractory period at the same site

Conventional electrode catheters used in electrophysiologic studies allow determination of the effective refractory period (ERP) at a given endocardial site but cannot elucidate the relationship between the action potential duration and the ERP. The currently used version of the contact electrode catheter provides both pacing and MAP recording capabilities with a single catheter, thereby allowing easy and accurate measurements of both the ERP and APD simultaneously and at the same site in the human heart [60]. Unlike conventional quadrupolar electrode catheters, the pacing electrodes in this MAP recording–pacing combination catheter are oriented orthogonally halfway between the distal (exploring) and proximal

![Fig. 8. MAP changes caused by abrupt myocardial stretch. Stretch pulses applied to the left ventricle of the isolated rabbit heart via a servo-driven fluid-filled balloon caused transient depolarizations which, when reaching threshold, triggered propagated excitations. LV2-EPI=MAP recording from epicardial site of left ventricle. ΔVOL=left ventricular volume changes. From Franz et al. [49].](image1)

![Fig. 9. Method of analysis of the MAP signal. The amplitude of the MAP is measured as the distance from the diastolic baseline to the crest of the MAP plateau phase, not the peak of the upstroke. The duration of the MAP signal is measured as the interval, along a line horizontal to the diastolic baseline, from the fasted part of the MAP upstroke (or the intrinsic deflection, if discernible) to the desired repolarization level. The example shows evaluation of MAP duration at 30, 60 and 90% repolarization. From Franz [16].](image2)
(reference) MAP electrode (Fig. 2). This electrode configuration provides for extremely low capture thresholds (0.02–0.25 mA, mean 0.09 mA), reducing the interference between the pacing artifact and the MAP signal to a minimum [60]. Pacing artifacts are negligibly small and sometimes hardly discernible despite the fact that the pacing electrodes are very close to the MAP recording electrodes (Fig. 10).

Several factors likely account for the unusually low capture threshold and minimal stimulus artifacts. First, the pacing electrodes used in this catheter have a smaller surface area than conventional ring electrodes and thus produce higher current densities. Second, the electrical field produced by the pacing current is positioned horizontally above the vertical field that produces the MAP, with subsequently less contamination of the latter. Third, the MAP catheter provides and ensures close and stable contact with the endocardium (unstable contact would result in no or unstable MAPs). Fourth, and perhaps most important, only the tip (MAP) electrode is in contact with depolarized myocardium, while the stimulus electrodes usually do not exert pressure against the endocardium. This prevents the pacing site from being depolarized and made relatively more refractory.

Fig. 10 demonstrates how the effective refractory period (ERP) is determined simultaneously with the concomitant MAP duration. In normal ventricular myocardium and in the absence of sodium channel-blocking drugs, the relationship between the MAP duration and the ERP in the canine [19,60] and human [61] heart has been shown to be constant and independent of heart rate. Antiarrhythmic drugs with sodium channel-blocking properties often produce greater increases in refractoriness than in action potential duration; this drug-induced post-repolarization refractoriness progresses with increases in stimulation frequency [62–64]. Simultaneous determinations of MAP durations and ERP therefore are useful in verifying the electrophysiologic profile of antiarrhythmic drugs predicted from in vitro studies for the human heart and may aid in our understanding of the antiarrhythmic mechanisms of such drug effects.

Fig. 10. Simultaneous determination of action potential duration at 90% repolarization (APD90) and effective refractory period (ERP) in vivo using the MAP pacing/recording combination catheter. S1 and S2 denote the basic and the extra stimulus artifacts. The upper tracing shows the shortest S1–S2 coupling interval that elicits a propagated response. The lower tracing shows failure to capture at a 5-ms shorter coupling interval. S1-stimulus artifacts are partially superimposed on the MAP upstroke but do not interfere with the ability to analyze the onset and duration of the MAP signal. S2-stimulus artifacts are superimposed on the repolarization phase but do not distort its time course. From Franz et al. [58].

8. Are intramural MAP recordings possible?

The impetus for recording MAPs intramurally came from the desire to record disparities of the APD across the myocardial wall of the intact heart because it has been shown by microelectrode techniques that such disparity exists and that mid-myocardial cells (M-cells) have longer APDs and are more prone to exhibit EADs at slow rates than epicardial or endocardial cells [65,66]. Thus, the recording of truly local intramyocardial MAP recordings would advance the understanding of the mechanism of many arrhythmias, most notably of the ‘torsade de pointes’ variety. Attempts have been made to obtain MAPs intramyocardially by inserting a multipolar plunge electrode into the myocardial wall and coupling it with a reference electrode placed on a remote (epicardial) site of the ventricle [67]. The initial injury potential resulting from inserting the plunge electrodes into the myocardial wall was allowed to subside until a normal electrogram was obtained. The remote electrode site was then depolarized by KCl. This led to a new monophasic recording. This MAP was of reversed polarity when connected to the amplifier in the conventional manner (see above). To make this MAP upright, the exploring (intramural) electrode was coupled to the negative amplifier input and the KCl electrode to the positive amplifier input. As discussed earlier, this suggests that the monophasic portion of the recording derives from the remote (KCl) electrode and not from the intramural plunge electrode. Because of the wide spacing between the intramyocardial electrode and the remote KCl electrode, these ‘intramural MAP recordings’ by definition represent largely unipolar MAP recordings that are subject to contamination by far-field potentials in much the same way as unipolar electrograms. Superimposition of disparate T wave durations on these MAPs may give the impression that MAPs of different duration are recorded from different intramural sites. Such recordings, while to some degree reflecting intramural differences, are not truly local as obtained by the close-bipolar technique but hybrids of local and far-field potentials.
8.1. Are chronic MAP recordings possible?

Permanent monitoring of local activation and repolarization characteristics would be very desirable. This, if combined with an implantable telemetry device, could be used to monitor the effects of antiarrhythmic drugs on myocardial repolarization at specific intervals, or related to the onset of proarrrhythmic events. Progression of cardiomyopathy and heart transplant rejection are other fields that would benefit from continuously available MAP interrogation. As understanding of the cellular basis of arrhythmias grows, abnormal changes of MAP signals recorded by permanent electrodes and transmitted by telemetry may become predictors and warning signals of life-threatening arrhythmic events.

Unfortunately, this does not seem possible with currently available MAP methods. MAPs have a tendency to decrease their amplitude and change their morphology over time. The MAP signal deterioration is much more rapid (minutes) with techniques that create MAPs by frank cellular injury, such as suction or stapping the tissue with a needle or plunge electrode. It is gradual (several hours) with the contact electrode, especially when only moderate contact pressure is applied. The loss in MAP amplitude over time is associated with two important features. One is that, as the MAP amplitude decreases, the initial spike becomes more prominent. This spike is the remnant of the intrinsic deflection (which becomes unmasked as the MAP plateau amplitude decreases) and should not be confused with a 'spike-and-dome' configuration of TAPs, as was done by Tande et al. [33]. The second feature that accompanies the decrease in the MAP amplitude is that the loss in total (plateau) amplitude is primarily due to a decrease in the diastolic voltage of the MAP. The mechanisms underlying the amplitude decrease of injury potentials was studied extensively by De Mello [68], who concluded that it is promoted by cellular uncoupling between the injured and normal cells. Several experiments led De Mello to believe that this electrical uncoupling takes place at the site of gap junctions and that calcium and proton ion accumulation at these sites plays a pivotal role [69–71].

9. New avenues for MAP recordings

An overview of past and future clinical uses of the MAP technique is given in Table 2. Besides a large number of clinical applications already published, there are newer uses for the MAP recording technique currently undergoing experimental evaluation and clinical validation.

9.1. MAP recordings as a measure of myocardial viability

Mechanical performance of heart muscle decreases very rapidly following coronary artery occlusion and may remain 'stunned' or 'hibernating' and, despite surviving myocardium being present, may require prolonged periods of time for full recovery. Electrical activity may still be preserved due to a lesser metabolic demand for maintaining membrane potential than for the upkeep of mechanical work. Measurements of mechanical activity by echocardiographic or angiographic means may not be able to distinguish between stunned or hibernating (yet still viable) myocardium and myocardium that is jeopardized beyond salvage. This is a potential important application of the MAP recording technique.

It follows from the explanation of the genesis of the MAP (see above) that MAPs can be created only when the electrode is impinging on viable myocardium. In contrast, when the electrode is pushed against nonviable tissue, e.g. a myocardial scar, local depolarization cannot occur and the recording is largely isoelectric [16]. Following coronary artery occlusion, changes in the MAP recording track the progression of myocardial ischemia by exhibiting amplitude and morphology changes [17,72] similar to transmembrane action potentials [73]. Within minutes, the MAP shows a decrease in amplitude and duration, especially of the plateau phase, and a decrease in upstroke

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velocity. The MAP assumes a triangular shape. As ischemia progresses further, the MAP often exhibits an alternans in amplitude and duration. This alternans is very typical of severe ischemia and has been linked to the development of ischemic tachyarrhythmias [72,74,75]. The mechanism of this ischemia-induced action potential alternans has been related to inadequate electrical restitution from one depolarization to the next [76] and, consequently, develops earlier at faster heart rates [77]. Because the close-bipolar MAP recording detects these changes with high sensitivity and local resolution, this technique may help identify areas of ischemic, yet still viable, myocardium.

9.2. MAP recordings for monitoring radiofrequency energy (RF) ablation

Successful RF ablation relies on several objectives. These include (1) identification of the arrhythmia substrate, (2) ascertainrnent of stable contact between the ablation electrode and the target myocardium and (3) successful ablation of the target. Incorporating a MAP electrode into a RF ablation electrode [4] may serve at least two of these three objectives. [1] Because MAPs are obtained only when the catheter tip electrode is in close and stable contact with viable myocardium, a stable MAP recording identifies steady contact between the ablation catheter tip electrode and the endocardial surface [2]. As the myocardium underneath the RF electrode gets destroyed during the process of RF application, the local MAP recording mirrors successful destruction by a rapid loss in MAP amplitude (Fig. 11) [4]. The third objective (identifying the arrhythmia substrate) may also be accomplished in specific cases [4].

9.3. MAP recordings for monitoring myocardial drug absorption

Antiarrhythmic drugs are administered to patients via oral or i.v. routes, based on empiric dosing regimens. Drug blood levels, while easily obtained, are not available at the time of electrophysiological study of the patient; besides, serum drug levels are known to correlate poorly with antiarrhythmic drug efficacy. Furthermore, it is unknown to what extent myocardial drug uptake occurs and whether or not it occurs uniformly within the heart tissue. It would be advantageous to have a method that provides instantaneous feedback on local myocardial drug effect. Because many antiarrhythmic agents have distinct effects on myocardial repolarization (especially class 3 agents), MAP recordings are ideally suited to measure this effect in situ directly at the myocardial surface [78]. Unlike the body surface ECG, which reflects global electrical activity of the heart, MAP recordings can detect repolarization changes at individual areas and thereby determine whether drug uptake is uniform or heterogeneous. This has recently been

![Fig. 11. Effect of radiofrequency energy (RF) on MAP signal recorded with an electrode embedded in the tip of the RF electrode. See text for discussion. From Franz [4].](image-url)
demonstrated for amiodarone and its primary metabolite desethylamiodarone, both of which exhibited heterogeneous myocardial uptake. This heterogeneous uptake was identified reliably by an equally heterogeneous change in MAP duration [79].

9.4. MAP recordings during atrial and ventricular fibrillation

Atrial (AF) and ventricular (VF) fibrillation are characterized by highly irregular patterns of activation and repolarization. A good agreement between TAP and MAP recordings during VF has been shown in the isolated rabbit heart [80]. MAP recordings have an advantage over electrogram recordings in that they allow distinction of activation and repolarization and can visualize the excitable gap even during VF or AF (Fig. 12). This has aided attempts to capture atrial myocardium during AF by overdrive pacing [81].

MAP recordings are useful for monitoring and understanding the induction and termination of VF during defibrillator testing. MAP recordings during induction of VF by T wave shocks have suggested that successful initiation of fibrillation depends on sufficient dispersion of ventricular repolarization immediately following the T wave shock. In concordance with this dispersion mechanism, it has been shown that successful defibrillation depends on sufficient shock-induced resynchronization of repolarization [82–85].

Acute MAP recordings are also useful for the distinction of different types of AF and to better differentiate some forms of atrial flutter from AF. MAP recordings have provided clues to the mechanism of terminating atrial flutter by antiarrhythmic drugs [86]. Recently, MAP recordings have demonstrated the effects of electrical remodeling caused by sustained AF or atrial flutter in patients [87].

A limitation of MAP recordings during AF or VF is that the MAP electrode records the responses of a multitude of cells at the same time, giving rise to summation potentials that may differ from single cell recordings under conditions of extreme local dispersion of activation and repolarization. For instance, the ‘fractionated’ MAP sequence seen in Fig. 12 might very well be the result of multicellular summation. During AF (or VF), multiple wavelets are present simultaneously and one recording site may be influenced by two or three different wavelets travelling in the neighborhood of the MAP electrode.

9.5. MAP recordings as a means of elucidating the mechanism of torsade de pointes arrhythmias

Torsade de pointes arrhythmias occur in a variety of acquired and familial long QT syndromes. The exact electrophysiologic mechanism of torsades de pointes (TdP) is under intense investigation. No isolated animal heart model of this particular arrhythmia exists. A recently developed model uses multiple simultaneous epicardial and endocardial MAPs and a volume-conducted 12-lead ECG in the isolated rabbit heart [39]. Sotalol prolonged repolarization and increased dispersion of ventricular repolarization compared to baseline recordings. With the onset of low potassium and magnesium concentrations, repolarization was further prolonged and dispersion of repolarization was further increased followed by the occurrence of early afterdepolarizations (EADs) in the majority of MAP recordings, i.e., at both endocardial and epicardial locations of both ventricles. Torsade de pointes observed in

Fig. 12. MAP recordings during atrial fibrillation (AF). Two simultaneous MAP recordings are shown, one from the high right atrium (HRA), the other from the low right atrium (LRA). Both recordings show activation and repolarization out-of-sync from one another. There is high frequency AF with intermittent fragmentation of MAPs as well as clearly visible diastolic intervals that are considered to be excitable gaps.
this new isolated heart model was associated with markedly increased dispersion of ventricular repolarization and the occurrence of EADs in multiple locations of the heart.

10. Conclusion

MAP recordings have come a long way and are now an integral part of clinical electrophysiologic studies concerned with understanding basic electrophysiology and arrhythmia mechanisms in the intact heart, including those of patients. MAP recordings in the clinical laboratory have confirmed many basic electrophysiological principles, and observations from human heart MAP recordings have spawned experimental research not previously recognized as being clinically important. However, while the methodology of MAP recording by contact electrode technique is relatively simple, the understanding of the abilities and limitations of the MAP and its proper interpretations are not. Future developments and refinements of the MAP recording technique will undoubtedly advance our possibilities further, including possibly longer-term and simultaneous multiple-site MAP mapping.

References


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