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Vectorcardiographic Ventricular Gradient with Constituents, and Myocardial Action Potential Parameter Distribution

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Theoretical grounds of integral vectors of ventricular depolarization and repolarization and their sum, i.e., the spatial ventricular gradient, have been studied. A systematic description and biophysical interpretation of these parameters are presented based on the distribution of cardiomyocyte action potential parameters in the inhomogeneous bidomain model of the myocardium. Recent medical studies have shown high efficiency and predictive value of the ventricular gradient, its constituents and related parameters, such as the angle between the constituents, the acceleration of repolarization, etc. Simple examples for a myocardial strip clarify the relationship between the action potential parameters and the resulting ventricular gradient. An explanation with graphic illustration is given for the very informative decartogram of repolarization acceleration. The results obtained here are useful in the modeling of vectorcardiograms for various pathological conditions of the heart ventricles and for various characteristics of the cardiomyocyte action potential, which determine its shape.

Keywords: vectorcardiography, dipole electrocardiotopography, ventricular gradient, action potential of cardiomyocytes, bidomain model of the myocardium.

1. Introduction

To date, the parameters defined as areas under the electrocardiogram (ECG) calculated in different phases of the cardiac cycle are becoming increasingly important for diagnostic electrocardiography. These parameters have been introduced in early 1930s by Frank Norman Wilson, an outstanding scientist who contributed greatly to practical and theoretical electrocardiography.

Fig.1. illustrates the genesis of a vectorcardiogram (VCG) during the electrical systole of heart ventricles with a modified figure from classic work of Durrer [1], the action potentials (AP) of the sequentially excited myocardium layers, and the resulting VCG components, and gives electrocardiographic designations used below.

Wilson et al. [2] explained the relationship between the spatial gradient of the transmembrane potential and the observed dipole moment of the electric field using a simple example with the activation of a cylindrical fiber. In their subsequent work [3], the following parameters were determined:

- the *mean electrical axis of QRS* as the direction in which the excitatory process spreads over the average element of the ventricles;
- the *mean electrical axis of T* as the inverse of the direction in which the recovery process spreads over the average element of ventricles;
- the *area of QT* as a measure of the electrical effects produced by local variations in the excitatory process;
- the *mean electrical axis of QT* as the direction of the line along which these local variations are the greatest.

The last two parameters were combined into a single vector named Ventricular Gradient (VG) that turned out to be very important in theoretical and practical terms of theory and practice, especially when moving from the two-dimensional projection in the frontal plane to representation in the three-dimensional space [4].

Some theoretical grounds of VG and, more precisely, of the spatial ventricular gradient as a time integral of the heart vector on the QT interval within one cardiac cycle are given by Burger [5]. In this work, it was also theoretically shown that in simple cases VG is independent of the starting point of the ventricular myocardium excitation (as suggested in [3]) and can be expressed through the gradient of the time interval between depolarization and repolarization or through the gradient of the duration of the AP in the myocardium.

The modern theoretical description of VG is based on the works by Plonsey and Geselowitz (see, in particular, [6]-[8]).

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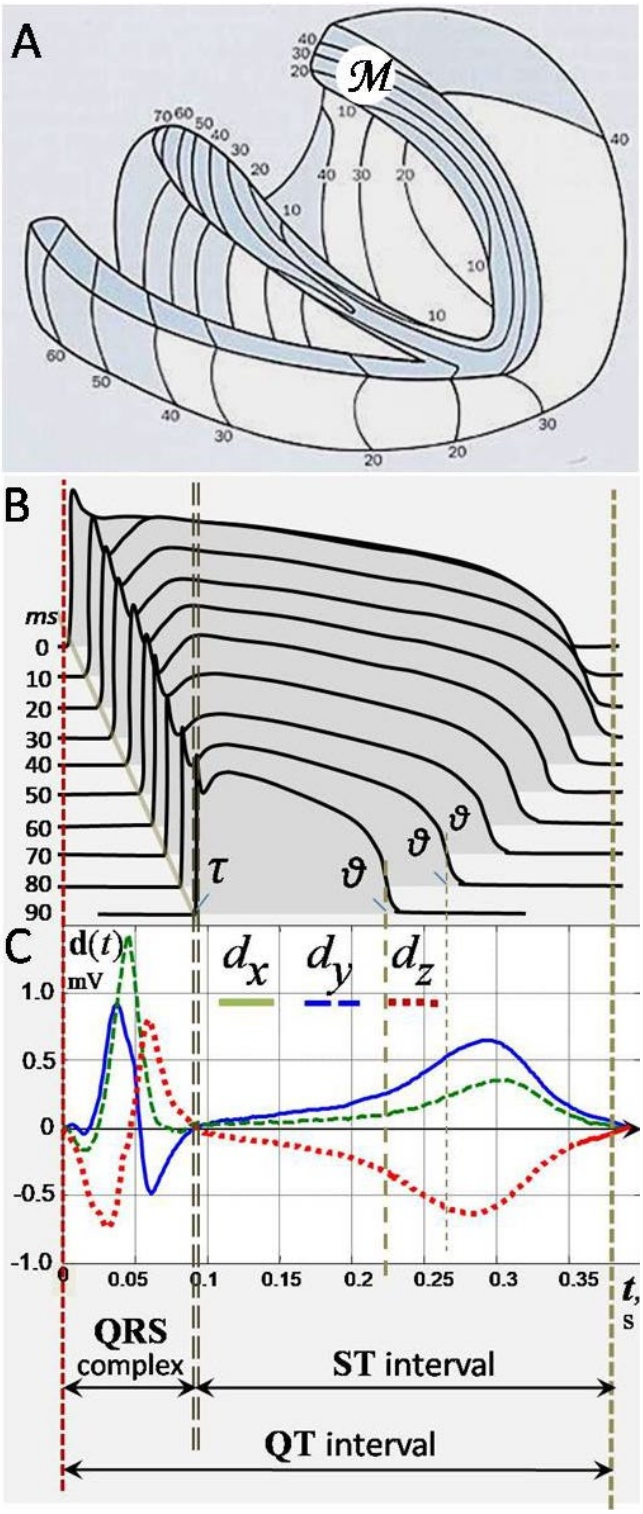

Fig.1. Genesis of VCG during the electrical systole of heart ventricles.

A. The time course of the excitatory process in the ventricles (modified figure from the classic work by Durrer [1]).

B. Action potentials of myocardial layers, which turn on during the QRS interval (ventricular depolarization) and turn off during the ST interval (slow and fast repolarization).

C. Three components of the resultant VCG $\mathbf{d}(t)=[d_x(t), d_y(t), d_z(t)]$ approximating spatial evolution of the heart vector (dipole moment of the electric heart field).

2. SUBJECT & METHODS

Presentation of ECG and VCG in the bidomain myocardial model

ECG in lead L at an instant t can be represented by an integral of current density $\mathbf{J}(t,r)$ over the excitable media region $\mathcal{M}$ (here it is the myocardium, r is a point in it). For the bidomain model, the current density is determined by gradient of the transmembrane potential, and then the result is ([7], [8]):

$$U_{\mathrm{L}}(t) = \int_{\mathcal{M}} \mathbf{J}(t,r)\cdot\nabla Z_{\mathrm{L}}(r)\,\mathrm{d}v_r = -\int_{\mathcal{M}} \boldsymbol{\sigma}_{\mathrm{i}}(r)\cdot\nabla U(t,r)\cdot\nabla Z_{\mathrm{L}}(r)\,\mathrm{d}v_r \tag{1}$$

where $\boldsymbol{\sigma}_{\mathrm{i}}$ is intracellular conductivity tensor; ∇ is the gradient operator; $U(t, r)$ is the action potential (AP), i.e., the time course of transmembrane potential at point r of the myocardium; $Z_{\mathrm{L}}(r)$ is the lead L field; $\nabla Z_{\mathrm{L}}(r)$ is the transfer impedance which relates the current density in the element of the myocardium volume to the ECG value.

If tensors of intracellular $\boldsymbol{\sigma}_{\mathrm{i}}$ and extracellular $\boldsymbol{\sigma}_{\mathrm{o}}$ conductivities are proportional ($\boldsymbol{\sigma}_{\mathrm{i}} = c\,\boldsymbol{\sigma}_{\mathrm{o}}$), the ECG can also be expressed through AP distribution, but over the entire surface of the myocardium $\partial\mathcal{M}$ ([7], [8]):

$$U_{\mathrm{L}}(t) = -\int_{\partial\mathcal{M}} \boldsymbol{\sigma}_{\mathrm{i}}(r)\cdot U(t,r)\cdot\nabla Z_{\mathrm{L}}(r)\,\mathrm{d}s_r \tag{2}$$

The expressions that are analogous to the above would be also true for the heart vector (summary dipole moment of current sources in the myocardium) and thus to VCG $\mathbf{d}(t) = [d_x(t), d_y(t), d_z(t)]$ which is the result of measuring the spatial components of the heart vector:

$$\mathbf{d}(t) = \int_{\mathcal{M}} \mathbf{J}(t,r)\,\mathrm{d}v_r = -\int_{\mathcal{M}} \boldsymbol{\sigma}_i(r)\cdot\nabla U(t,r)\,\mathrm{d}v_r;$$

and if $\boldsymbol{\sigma}_{\mathrm{i}} = c\,\boldsymbol{\sigma}_{\mathrm{o}}$, (3)

$$\mathbf{d}(t) = -\int_{\partial\mathcal{M}} \boldsymbol{\sigma}_{\mathrm{i}}(r)\cdot U(t,r)\,\mathrm{d}s_r.$$

Presentation of VCG through the distribution of AP characteristics of cardiomyocytes

Transmembrane potential distribution over the myocardium and its changes during the systole are determined by AP of individual cardiomyocytes which turn on during ventricular depolarization and turn off during slow and fast repolarization:

$$U(t,r) = a(r)\cdot\Lambda(t,\,\tau(r),\,\theta(r),\,\kappa(r)), \tag{4}$$

where $a(r)$ is the myocyte AP amplitude at point r; Λ is a normalized AP as a function of the onset time $\tau(r)$; the completion time $\theta(r)$, and other parameters $\kappa(r)$ that determine the shape of the AP at point r; $t\in\mathfrak{I}_{\mathrm{QT}}$; $\mathfrak{I}_{\mathrm{QT}}$ is the time interval

from depolarization beginning to the end of repolarization; on VCG – from the beginning of the QRS complex to the end of the T-wave (QT interval, Fig.1.).

It is convenient to represent the normalized action potential Λ as a sum of two functions, that is, an ascending function $\Lambda_\uparrow$ for the depolarization process, increasing from zero to one with the onset at instant τ, and a descending function $\Lambda_\downarrow$ for the repolarization process, decreasing from one to zero, conventionally ending at instant θ (Fig.2.):

$$\Lambda(t,\,\tau,\,\theta,\,\kappa) = \Lambda_\uparrow(t-\tau,\kappa_\uparrow) + \Lambda_\downarrow(t-\theta,\kappa_\downarrow) - 1. \qquad (5)$$

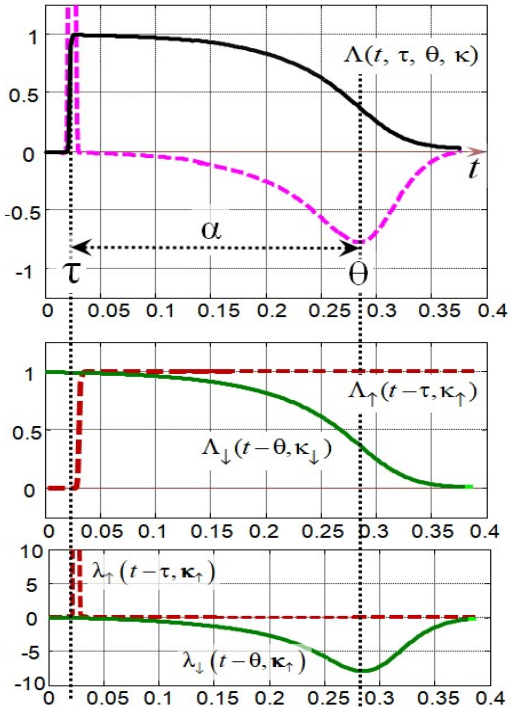

Fig.2. A simplified representation of the cardiomyocyte AP and its derivative as the sum of the ascending and descending functions, representing cardiomyocyte depolarization and repolarization, respectively, at one point of the myocardium.

Then the VCG is the sum of three components, which are the result of depolarization and repolarization, respectively, as well as a constant component characterizing myocardial inhomogeneity in the AP amplitude:

$$\mathbf{d}(t) = \mathbf{d}_\uparrow(t) + \mathbf{d}_\downarrow(t) + \mathbf{d}_-,$$
$$\mathbf{d}_\uparrow(t) = -\int_{\mathcal{M}} \boldsymbol{\sigma}_i(r)\cdot\nabla\Big(a(r)\cdot\Lambda_\uparrow\big(t-\tau(r),\kappa_\uparrow(r)\big)\Big)\,dv_r;$$
$$\mathbf{d}_\downarrow(t) = -\int_{\mathcal{M}} \boldsymbol{\sigma}_i(r)\cdot\nabla\Big(a(r)\cdot\Lambda_\downarrow\big(t-\theta(r),\kappa_\downarrow(r)\big)\Big)\,dv_r; \qquad (6)$$
$$\mathbf{d}_- = \int_{\mathcal{M}} \boldsymbol{\sigma}_i(r)\cdot\nabla a(r)\; dv_r\,.$$

It is worth to introduce the notation for the derivatives of functions $\Lambda_\uparrow(t,\kappa_\uparrow)$ and $\Lambda_\downarrow(t,\kappa_\uparrow)$ with respect to time t:

$$\frac{d\Lambda_\uparrow(t,\kappa_\downarrow)}{dt} = \lambda_\uparrow(t,\kappa_\uparrow);\quad \frac{d\Lambda_\downarrow(t,\kappa_\downarrow)}{dt} = \lambda_\downarrow(t,\kappa_\downarrow). \qquad (7)$$

For any point of the myocardium $r \in \mathcal{M}$, the following equalities are fulfilled:

$$\int_{\mathfrak{I}_{QT}} \lambda_\uparrow\big(t-\tau(r)\big)\,dt = 1;\quad \int_{\mathfrak{I}_{QT}} \lambda_\downarrow\big(t-\theta(r)\big)\,dt = -1; \qquad (8)$$

3. Results

Formulas for integral VCG parameters

Formulas for integral parameters are derived from the above expressions. Assuming that the AP amplitude is constant a, and the shape of the ascending and descending parts of AP is invariable all over the myocardium, simple expressions are obtained:

$$\mathbf{D}_\uparrow = \int_{\mathfrak{I}_{QRS}} \mathbf{d}_\uparrow(t)\,dt = a\int_{\mathcal{M}} \boldsymbol{\sigma}_i(r)\;\nabla\tau(r)\,dv_r.$$
$$\mathbf{D}_\downarrow = \int_{\mathfrak{I}_{ST}} \mathbf{d}_\downarrow(t)\,dt = -a\int_{\mathcal{M}} \boldsymbol{\sigma}_i(r)\;\nabla\theta(r)\,dv_r. \qquad (9)$$
$$\mathbf{D}_V = \mathbf{D}_\uparrow + \mathbf{D}_\downarrow = \int_{\mathfrak{I}_{QT}} \mathbf{d}(t)\,dt = -a\int_{\mathcal{M}} \boldsymbol{\sigma}_i(r)\;\nabla\alpha(r)\,dv_r.$$

where $\mathbf{D}\uparrow$, $\mathbf{D}_\downarrow$, $\mathbf{D}v$ (it is just VG) are integrals of the VCG $\mathbf{d}(t)$ on the intervals QRS, ST, and QT, respectively, and they are determined by the gradient distributions of the AP onset time $\tau(r)$, AP completion time $\theta(r)$, and AP duration $\alpha(r) = \theta(r) - \tau(r)$ in the heart ventricles.

Under the additional assumption of $\boldsymbol{\sigma}_i = c\,\boldsymbol{\sigma}_o$:

$$\mathbf{D}_\uparrow = a\int_{\partial\mathcal{M}} \boldsymbol{\sigma}_i(r)\;\tau(r)\,d\mathbf{s}_r;$$
$$\mathbf{D}_\downarrow = -a\int_{\partial\mathcal{M}} \boldsymbol{\sigma}_i(r)\;\theta(r)\,d\mathbf{s}_r; \qquad (10)$$
$$\mathbf{D}_V = -a\int_{\partial\mathcal{M}} \boldsymbol{\sigma}_i(r)\;\alpha(r)\,d\mathbf{s}_r.$$

Illustrative examples

Simple formulas are obtained using (10) for integral VCG parameters of activation of a small transmural section of the myocardium from endocardium to epicardium with $\boldsymbol{\sigma}_i(r) = \sigma_i = const$ over this section surface (Fig.3.):

$$\mathbf{D}^s_\uparrow = a\sigma_i\left(\tau_{Epi} - \tau_{En}\right)\vec{S}_{Epi};$$
$$\mathbf{D}^s_\downarrow = a\sigma_i\left(\theta_{En} - \theta_{Epi}\right)\vec{S}_{Epi}; \qquad (11)$$
$$\mathbf{D}^s_V = a\sigma_i\left(\alpha_{En} - \alpha_{Epi}\right)\vec{S}_{Epi};$$

where τ, θ, α denote the time of AP onset, completion, and duration; En, Epi indices indicate the surface to which these parameters relate; $\vec{S}_{Epi}$ is the vector area of the epicardial surface of the section; $\vec{S}_{Epi} = -\vec{S}_{En}$.

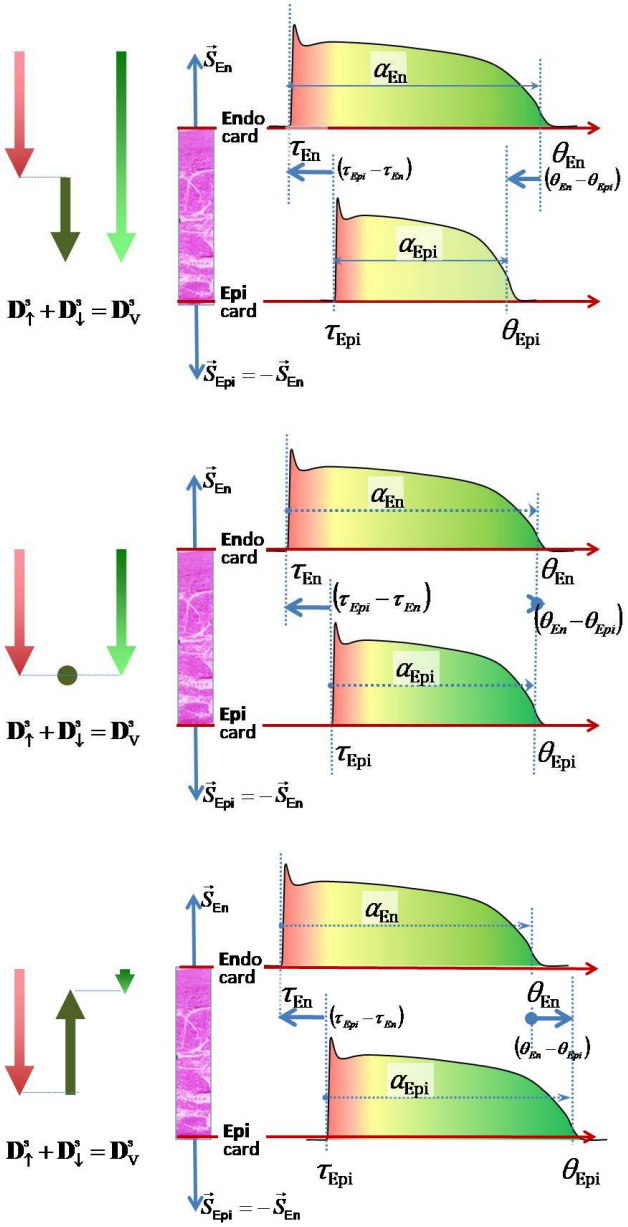

Fig.3. Three examples of integral VCG parameters of activation for a small transmural section of the myocardium from endocardium to epicardium (in the center). VG as sum of de- and re-polarization vector integrals (left). Endocardial and epicardial AP curves (right).

There are three different cases in Fig.3.:

1. duration of endocardial AP is longer than that of epicardial AP; in this case, the directions of the integral QRS and ST vectors coincide and the VG magnitude is large;
2. endocardial and epicardial AP are completed simultaneously; in this case, the integral ST vector magnitude equals zero, and the VG magnitude equals the integral QRS vector magnitude.
3. duration of endocardial AP is shorter than that of epicardial AP, meaning that the repolarization process on the endocardium is completed earlier than on the epicardium; the integral vectors QRS and ST are directed in opposite directions, and the VG magnitude will be small. In this case, there is a vulnerability of the myocardium to arrhythmias. The myocardial cells that accomplish the repolarization too early may be activated again leading to early reactivation and reentry.

4. DISCUSSION

All three integrals defined above are closely related to practical electrocardiographic parameters. Let us consider these interrelations and their biophysical meaning and make some terminological clarifications. It is helpful to remember that the gradient is in the direction of the greatest growth; $\|\mathbf{a}\|$ denotes the magnitude of the vector **a**.

Characterization of integral VCG parameters

Juxtaposing (9)-(10) with (3), one can see that the distribution of the AP onset time $\tau(r)$ plays here the role of a negative potential, but the distributions of the AP completion time $\theta(r)$ and AP duration $\alpha(r)$ – are a positive potential.

- $\mathbf{D}\uparrow$, an integral vector of the ventricular depolarization (*integral QRS vector*), is directed towards increasing the activation time, i.e., it indicates the general direction of the ventricle activation spread and is, on average, proportional to the difference between the time of depolarization beginning and end.

  The **related** parameters include:

  - *mean vector of ventricular depolarization* ($\mathbf{D}\uparrow$ / "QRS duration");
  - *mean electrical axis of QRS* = $\mathbf{D}_{\uparrow} / \|\mathbf{D}_{\uparrow}\|$, a unit vector in the direction defined by the *integral QRS vector*. Its projection onto the frontal plane, named *mean frontal QRS axis*, *electrical heart axis* or *cardiac axis*, is considered in standard electrocardiography. It is determined by the angle relative to the coordinate axis in this plane.

- $\mathbf{D}_{\downarrow}$, an integral vector of the ventricular repolarization (*integral ST vector*), is directed towards decreasing the repolarization completion time, opposite to the propagation of the heart ventricle repolarization, and is, on average, proportional to the difference between the time of repolarization beginning and end.

  The related parameters include:

  - *mean vector of ventricular repolarization* ($\mathbf{D}_{\downarrow}$ / "ST duration");
  - *mean electrical axis of ST* . = $\mathbf{D}_{\uparrow} / \|\mathbf{D}_{\uparrow}\|$, a unit vector in the direction defined by the *Integral ST vector.*

- $\mathbf{D}_V$, a spatial ventricular gradient (*integral QT vector*) directed towards a decrease in the AP duration; its magnitude is the rate of decrease.

  The related parameters include:

  - *spatial QRST-T angle*, the angle between the integral vectors of ventricle depolarization and repolarization, or, which is the same, between the electric axes of the QRS and ST.
  - *repolarization acceleration* $\mathbf{D}_V / \max_{t\in QRS}\left(\|\mathbf{d}(t)\|\right)$ [9], it is VG normalized to the maximal heart vector magnitude during the QRS interval. The dimension is "second", so it is just proportional to the gradient of the AP duration. It is

used in Dipole ElectroCARdioTOpography (DECARTO, [9],[10]; Fig.4. illustrates the basic principle of the DECARTO methodology). Fig.5. demonstrates a decartogram of the repolarization acceleration that graphically displays the magnitude and the direction of AP duration change. Acceleration of repolarization is equivalent to shortening the AP.

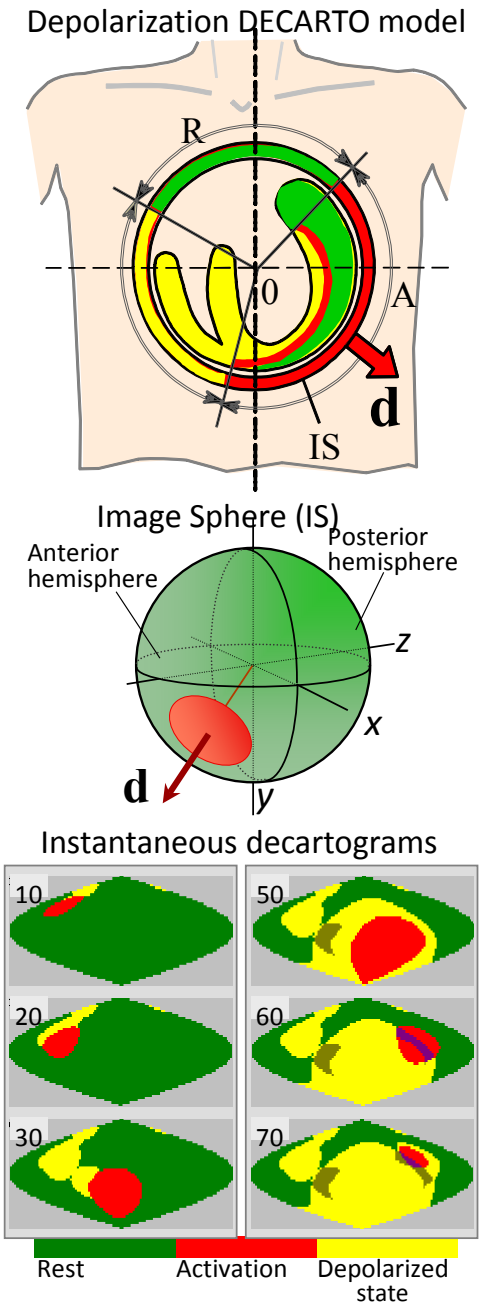

Fig.4. Dipole ElectroCARdioTOpography. DECARTO model of ventricular depolarization (above), image sphere (IS), and instantaneous decartograms of ventricles for typical normal case (below). The image sphere is cut along the meridian facing the right side of the patient's chest, unrolled, and projected onto a plane in the isoareal format. **d** is a heart vector. States of the myocardium: Rest, resting state; Act, activation state; Dep, completely depolarized state.

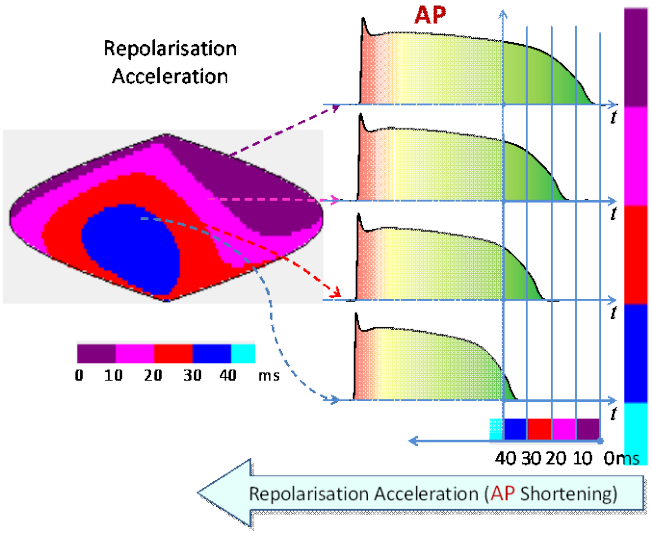

Fig.5. Decartogram of the repolarization acceleration for a healthy subject (left); on the right, AP in the corresponding areas of the decartogram with decreasing values of the AP duration.

7. Conclusion

Synchronous measurements of standard ECGs that have become routine nowadays allow for approximate calculation of the VCG using standard ECGs [11]-[12], thereby providing additional advantages of vectorcardiography, decartography, and, in particular, integral VCG parameters.

Theoretical analysis presented here somehow elucidates the concept of VG and gives a certain insight about why VG and various options arising from this concept are so important for diagnostic ECG analysis.

Recent medical research has demonstrated high efficiency and predictive value of integral VCG parameters [13], [14]. Also noteworthy are the works [15], [16], where, along with the components of the VG vector and the angle between its constituents, the decartogram of the repolarization acceleration is successfully used for diagnostic analysis.

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