COMPUTER ANALYSIS OF THE VENTRICULAR GRADIENT OF ISOLATED AND PERFUSED MAMMALIAN HEARTS

by

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Introduction

In a British Army Hospital during the latter part of World War I, a young internist - electrocardiographer from the University of Michigan came by coincidence under the command of the renowned cardiologist, Sir Thomas Lewis. Sir Thomas had at this time, gained considerable fame through the clinical application of William Einthoven's recently invented string galvonometer.

Following his return from Europe and his stimulating association with the current leaders in the field this young physician, then 28 years of age, resumed a career in experimental and clinical electrocardiography which even today has yet to see an equal.

In the early years after the war, the writings of this man were primarily concerned with the fundamental phenomena occurring in the heart which gave rise to the electrocardiogram. Interlaced throughout the thoughts which he reported during the early 1920's was the notion that some fundamental invariant relationship existed between the electrical activation and electrical recovery in the heart so long as the metabolic conditions remained unchanged.

By 1931, he and his coworkers were so thoroughly convinced that this relationship was a real,measurable quantity that this as yet unnamed parameter was described. The quantity was found to have the properties of a vector and was called the "ventricular gradient." From that day on, disciples of the concept of the ventricular gradient spent substantial portions

of their lives trying to completely characterize it. Since its introduction well over one hundred papers have been written, either defending, denouncing or describing the concept of the ventricular gradient. That this concept theoretically so simple yet practically so complex has weathered forty years of intensive investigation should be considered an everlasting tribute to the monumental genius of Dr. Frank M. Wilson.

Purpose

The purpose of this thesis is twofold. The first is to describe a method which will make it possible to accomplish ventricular gradient measurements quickly and accurately. The second is to consider the physiological significance of the ventricular gradient armed with the increased confidence gained by employing an improved method in its determination.

The first, by comparison to the second, is quite simple. The method to be described makes use of quite recent improvements in the technic of recording biological signals on magnetic tape and the technic of processing biological data by means of modern electronic computers.

The second primary purpose, hopefully that of shedding light on certain physiological mechanisms in the heart will be approached with the results of previous experiments from this laboratory as well as the experimental results reported in this thesis.

Fundamental Principles of Vectorelectrocardiography

In order to apply the mathematics of vector quantities to cardiac electrical activity, one must demand that the biological electrical generator and the conditions of recording meet the requirements of vector analysis to an appropriate degree of accuracy. In general the requirements for vector representation are met if the system under consideration is a linear system.

The fundamental biological generator results from the flow of ionic current across the membrane of a single myocardial cell during the course of an action potential. The fact that transmembrane current flow in an activated area of a cell is not limited exactly to that site, but declines in current density with distance gives rise to a zone surrounding the stimulated area in which the transmembrane potential is less than normal.

If in this zone the drop in membrane potential reaches a threshold value, this zone will become activated and the activated area will have advanced by an incremental distance. Ordinarily this process advances or spreads in a continuous rather than step-wise fashion, and the overall result is a traveling wave of ionic disturbance. During the transit of such a wave, an electrode stationed at a position just outside of the membrane would see, with respect to zero potential, the approaching relative positivity, followed a short time later by relative negativity.

These zones of positivity and negativity constitute the biological generator

which gives rise to the ionic currents which flow in the vast extracellular fluid. If the magnitudes of the positivity and negativity are equal and if the distance between the peak concentration of charges is several orders of magnitude smaller than the recording electrode separation, this electrical event, with respect to the recording electrodes, can be considered to have the properties of an electrical dipole. The electric field intensity from a dipole generator diminishes inversely as the cube of the distance from the dipole center. The potential, therefore, varies inversely as the square of the distance from the generator since electric field intensity is the first spatial derivative of potential.

Electric field intensity is a vector quantity as is the electric current which is directly proportional to it. The potential differences recorded from two electrodes situated at a distance which is large compared to the distance between the current source (positivity) and the current sink (negativity) of the dipole is proportional to the potential drop as the ionic current flows through the ohmic resistance between the electrodes. The constants of proportionality which allow the scalar quantity, potential, to represent a vector quantity must be linear functions of time and distance in order that the potential record can be used to define the elemental cardiac generator.

These linear functions of time and distance are the simple resistive (non-frequency dependent) character of the fluid volume conductor surrounding the cell, the homogeneity of the volume conductor and the angular relationship between the axis of the dipole and the axis of the recording electrodes.

The "superposition theorem"* is employed to sum the individual cardiac vectors in order to represent the total cardiac vector of the intact heart. Only in a linear homogeneous system will the resultant of n simultaneous vectors regardless of position equal the vector sum of those n vector quantities.

A violation of any one of the above conditions violates to a greater or lesser extent the dipole concept of cardiac electrical activity. It is possible to create experimental conditions which adequately satisfy such requirements as a resistive, homogeneous volume conductor. One cannot guarantee, however, that the apparently well organized wave front of electrical depolarization satisfactorily represents the requirements of a dipole. It is difficult to decide to what extent the depolarization process may vary from moment to moment from one of a true dipole to one of a more complex configuration. In general, the greater the number of poles of different polarity situated in the vacinity of one another, the smaller is the resulting potential in the surrounding field at a given distance. If circumstances were to change from moment to moment going from dipolar to multipolar and back again, the recorded potential with respect to distance would vary in a complex manner. Such a non-linear variation violates the "theorem of superposition" and would prevent the recorded potential from being simply related to the vector sum of all the individual contributing generators.

* For a precise definition of superposition, see:

New Basis of Electrocardiography, Sodi Pallares, D. and Calder, R. P. 674. C. V. Mosby Co., St. Louis, 1957.

History and Review of the Literature

Part I

The Ventricular Gradient

In contrast to many theories in biology whose origins are indistinct, the concept of the ventricular gradient quite clearly originated solely in the mind of one man. Indirect, but quite convincing evidence that this fact is true can be obtained from a review of the literature in electrocardiography between the years 1921 (1) when Dr. Frank N. Wilson began to allude to the gradient in his prolific writings and 1931 (2) when he proposed the name ventricular gradient. In this decade many workers, both in this country and abroad, had put the string galvonometer into service, but no one caught Wilson's hint until after he had made the classic formal announcement in his 1931 paper.

Wilson's ideas of the general nature of the electrical processes in the heart are still accepted today. The need for a quantity, later to be called the ventricular gradient, stemmed from the necessity to account for the magnitude and polarity of the net T wave area of the electrocardiogram in relation to the magnitude of the net QRS area. That this quantity was constant during periods when the metabolic condition of the heart was constant was used as evidence to explain the apparently constant time-voltage relationship between the QRS and T complexes even under quite abnormal conditions of electrical conduction.

Wilson knew from the early work of Burdon-Sanderson (3) and Lucas (4),

as well as his brief experience in Erlanger's laboratory following World War I, that the single cell cardiac electrical activity was predominantly monophasic. Although these recordings were, for the most part, "demarcation potentials" from the injured portion of a large number of cells, it was generally known by 1920 that the electrically active state of cardiac muscle was much greater than for skeletal muscle. Furthermore, it was known that there was a quantitative difference between the speed of the depolarization process and the repolarization process. Wilson realized that if the duration of electrical activity in all cells were uniform and if the conduction pathway and velocity were the same for both depolarization and repolarization, the time-voltage characteristic of the QRS complex would be precisely the negative of the T complex. The obvious fact that this relationship practically never exists led Wilson to postulate the condition of electrical "local variation" distributed throughout the myocardium which was unchanged during normal metabolic conditions and responsible for altering the expected route of repolarization relative to depolarization. A line directed along the maxima of the mean of the local variations from the greatest at the tail to the least at the head produced an arrow (or vector) which pointed from the area of the heart last to repolarize to the area of the heart first to repolarize. This vector was called the "gradient" to emphasize the fact that it lay along the gradient of decreasing repolarization time and was proportional to its magnitude.

Wilson showed that the spatial components of the ventricular gradient vector could be relatively easily derived by finding the vector sum of the