Cardiac Pumping and the Function of Ventricular Septum

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Preface

We have made a lot of research and development, based on my thesis. For example, a new type of pump type has been developed: The delta-V pumps. A model that simulates the function of the human body, called "The Circulation Model" has been created. This mode, and comparisons of different types of pumps (and their similarities to the human heart), are described in chapter 10.

Chapter 1

Introduction

A number of questions, intimately related to the way in which the human heart accomplishes its purpose, lack consistent answers. Probably the most important question concerns the general validity of the Frank-Starling relationship for in vivo output and intraventricular output balance regulation. This situation affects a wide range of problems in heart physiology and cardiology. Together with some initial observations with non-invasive heart-imaging techniques, it induced me to reassess the physical action of the heart. This is the main objective of this thesis.

The reader should be aware that such a reassessment must of necessity contain views and interpretations of well-known, or sometimes less well-known, findings by other authors. There is a great complexity of the matter involved, and also an enormous amount of often contradictory evidence gathered up to the present day. Therefore is it extremely difficult to strike a fair balance between what is known, and what is new.

An outline of the historic development of heart physiology is given.

After that an attempt to establish tentative criteria for how to define "current views" on the pumping action and regulating function of the heart is made.

This is followed by an outline of the topographic anatomy of the heart and of some basic physical principles. That is believed to be of particular importance for understanding the pumping action of the heart.

A discussion of the physiology of the working heart in situ links established facts with new ideas. For the sake of clarity, pumping and regulating modes are presented in the form of two basic concepts, which are supported by new experimental evidence:

- Evidence obtained by the study of the beating heart with echocardiography, by analysis of left ventricular cineangiograms, and by TI-201 scintigraphy
- Evidence for the role of the ventricular septum as a physical regulator of the pulmonary and systemic circulation. The role of the ventricular septum was demonstrated by means of an experimental double pump. It made it possible to simulate various types of heart defects, and compare with findings in vivo.

These results allow prediction or explanation of, ventricular septum displacement in a number of volume- or pressure-overload-related heart defects usually not encountered as "pure" defects. The elucidation of the proper working and regulating modes of the heart, and the experimental findings with the double pump was essential; these enabled me to design a new self-regulating single pump. It is described, and its action is explained and compared with the pumping action of the heart.

1.1 Historical Development of Functional Cardiac Anatomy to Heart Physiology of Today

There is a considerable number of monographs in the history of heart physiology and cardiology [165] , as well as chapters in books on the general history of medicine devoted to these topics. But they do not cover development up to the present day. It is thus meaningful to provide the reader with an updated view, which should help in understanding the situation in the field today.

Stenonis [169] was the first to describe the complex anatomy of cardiac muscle 1664.

The 18th century refined the anatomical knowledge of the heart (cf. Haller [64]) but added little to the already established principles. A notable exception is the work of Hales [63] on blood pressure and heart output.

During the last century, interest in this field was revived, first by rapid development of auscultatory techniques and later in a more general way. The concept of active systolic filling of the atria was put forward for the first time in 1843 by Purkinje [137]. His ideas were taken up by Henke [76], Hauffe [71], Böhme [31], Benninghoff [8], Hamilton and Rompf [65] and others.

Another path of investigation was pursued by Starling and his group [129] based on the pioneering work of O. Frank, a pupil of C. F. W. Ludwig (a German scholar, who could be considered as the father of heart physiology of today).

The Second World War changed the scientific scene. The center of gravity shifted in this area (as in many others) to the United States (Berglund, Braunwald, Brecher, Gauer, Hamilton, Opdyke, Sarnoff, Rushmer and others). The post-war period experienced a rapid increase of biomedical knowledge. The Starling tradition, which had the appeal of a well-defined theoretical basis and a repertoire of established experimental models, prevailed [17, 18]. A decisive factor in the success of the Starling school could well have been its elegant explanation of how intraventricular output balance is maintained. Functional heart anatomy in general did not devote any attention to this important problem.

The basic concept of the heart as a double pump with four chambers and four valves goes back to Harvey [70, 180]. He also recognized the consecutive contraction of the atria and ventricles. Harvey [70] and Lower [106] found that by the contraction of the ventricles the AV-plane and apex move nearer to one another. Ventricular filling is affected by an "in-rush" of blood during diastole [106]. Lower gives an explanation for the walls of the right ventricle being thinner than those of the left. He also had quite a clear conception of the lifting of the tricuspid- and mitral cusps as the mechanism for their closure.

The 1970's saw a renewed interest in basic problems of heart physiology - an interest which subsided again in about 1980. Thus, much of the relevant newer work cited in this thesis comes from that period. Access to new non-invasive techniques did not alleviate the fragmented situation. A large number of variables (with combinations), are still used to characterize the state of the heart (normal and diseased) in a wide range of models and experimental conditions (cf. [97]). The prevailing situation is manifest in some of the most influential textbooks and surveys on heart physiology and cardiology [2, 4, 5, 11, 15, 16, 25, 43, 91, 128, 166].

There has been sporadic criticism of the established main line of teaching [101, 120, 124], especially for lack of relevance with respect to pertinent clinical questions in cardiology [37, 88, 146]. This criticism does not encompass the tremendous increase of knowledge about the neural and humoral regulation of the heart;

within the last 25 years, an accumulation which is of great and uncontested clinical and scientific value have been done.

1.2 Current Views on Pumping Action and Regulation Functions

Modern textbooks and surveys in the field differ among themselves about the importance they ascribe to various events. For example events as:

- increase and decrease in the size of the four chambers of the heart
- opening and closing of the heart valves
- blood flow
- microscopic events (that in most cases are the ultimate cause of what is observed at the macroscopic level)

Usually, the physical pumping action of the heart and its topographic anatomy are either treated rather cursorily, or are entirely omitted. The biology, biochemistry and biophysics of the single heart muscle fiber are accorded a central explanatory role. That does not bridge the gap between what is observed at the macroscopic and the microscopic levels, especially regarding the pumping action of the heart as a whole.

The pumping heart may be seen as the solution of two separate bioengineering problems:

- the movement of blood at optimal energetic economy
- the maintenance of the delicate balance between the two circulatory loops

Although these problems are intimately linked, I will refer to them separately when possible.

1.3 Current views on Pumping Action

There is no disagreement about basic anatomical facts, although they are most often treated rather superficially. The heart is a cyclically moving muscle. There is no single configuration that adequately describes the three-dimensional relationship between its parts. Its pumping function is usually characterized by ventricular pressure/volume diagrams [153], ejection fractions [123] and the like. Little attention is paid to changes in its three-dimensional shape over the cardiac cycle.

It is obvious that the heart muscle contracts when pumping and that there is a change of volume in the chamber.

The view that the heart muscle is pumping by contraction with ensuing volume changes of its chambers, is trivial. However, the working mode of the heart is not obvious due to anatomic complexity of the heart muscle syncytium (in fact a pseudo-syncytium [170]); neither due to its interplay with surrounding tissue, nervous and humoral control, the influence of static and dynamic pressure components of the incoming and ejected blood etc.

Many recent texts (e.g. [6, 11, 15, 16, 25, 60, 61, 62, 69, 73, 91, 128, 144, 147, 159, 161, 166, 170]) either describe ventricular systole as a rather uniform contraction, or do not dwell on this matter at all. Other authors [2, 5, 43] give a more complete description i.e., by assigning physiological significance to ventricular contraction in the direction of the major heart axis. Few (e.g. [4, 49]) refer to classic studies [8, 31] in physiological heart anatomy. There is considerable divergence of opinion regarding ventricular diastole - for example, on the role of venous pressure, ventricular compliance, diastolic suction, the role of the pericardium, etc. The function of atrial systole is also a matter of discordance.

The Frank-Starling law1 [129] governing the extension of sarcomeres/contractile force relationship, usually occupies a central place in the interpretation of experimental results, although some authors think its importance is more limited.

For convenience, this term will be used, although it does not give due credit to the discoverers of the relationship between presystolic muscle fibre length and responsiveness (Schlant et al. [159]).

1.4 Current Views on Regulating Function

One should discern between short- and long-term regulations. Long-term regulation is on the whole well understood. The same cannot be said of short-term regulation. The present situation is described by Sokolow and McIlroy (p.19 [166]):

"The circulatory control mechanisms respond to any change in cardiac output within a couple of beats and act to modify cardiac performance and change the hemodynamic state. It is thus difficult to determine the cause of changes in cardiac output on a beat to beat basis, and clear relationships between cardiac filling and stroke volume, which can be seen in isolated heart preparations in the laboratory, tend to be masked in patients. It is possible, however, to recognize the directions of change and, if there is an increase in cardiac output with a decrease in filling pressure, this can be clearly seen to be beneficial whether it results from the Frank-Starling mechanism, from increased intensity of excitation-contraction coupling, or from both".

Chapter 2

Cardiac Pumping and Beat-to-Beat Circulatory Control

2.1 Topographic Anatomy of the Heart

There is no need for an outline of the anatomy of the heart itself (cf. [8, 100, 136, 170]).

The heart is completely embedded in other tissues. This implies in a functional sense, that the walls of the chambers of the heart, atria and ventricles, are not merely myocardium and pericardium. They extend farther and include blood and adjacent tissues of the thoracic cage.

They also constitute the medium, in which the heart has to carry out its work. Physical interaction of this medium with the working heart is different from that of a compressible substance, such as air. The air pressure prevailing in the lungs is approximately 760 mm Hg, whereas atrial pressures are a few mm in excess of that. The atrial pressures effect on adjacent tissues will thus be small. The heart then, should not be thought of as doing its work in physical isolation from the rest of the body [71].

The boundaries of the ventricles may be described as follows:

2.11 Right Ventricle:

Ventrally-medially: muscular wall of right ventricle, pericardium, chest wall

Caudally: muscular wall of right ventricle, pericardium, diaphragm, etc.

Dorsally-superiorly: tricuspid valve, blood in right atrium, etc.

Dorsally-laterally: interventricular septum, blood in left ventricle, etc.

2.12 Left Ventricle:

Ventrally-medially: interventricular septum, blood in right ventricle, etc.

Caudally: muscular wall of left ventricle, pericardium, diaphragm, etc.

Dorsally-superiorly: mitral valve, blood in left atrium, etc.

Dorsally-laterally: muscular wall of left ventricle, pericardium, pleura, etc.

The expansion, or contraction, of the atria will similarly be affected by adjacent tissues. The right atrium and the blood vessels entering the atria are surrounded mainly by pericardium, pleura and the lungs. The left atrium is to a large part squeezed between the spinal column and the rest of the heart. Both atria at their transitional regions near the left and right ventricles have fold-like appendages (the left and right auricles) which have a contour-smoothing function in systole [31].

In contrast to the ventricles, the atria never become separated from the rest of the circulatory system during the cardiac cycle. The tricuspid and mitral valves constitute a border to the ventricles, for the atrial volume. The region of the orifices of vena cava superior and inferior into the right atrium, can be regarded as a part of the atrial volume. The same is valid for the region of the orifices of the pulmonary veins into the left atrium.

2.2 Interaction of the Pumping Heart with Surrounding Tissues

A body immersed in a non-compressible fluid (e.g. a liquid, or liquid-like, matter such as living soft tissue) will displace its own volume of this fluid. An increased change in volume of such a body, will result in displacement of additional fluid equivalent to the volume added. This simple principle applied to the human heart means, that a change in its total volume during the cardiac cycle, must correspondingly affect the tissues surrounding it. That is, no change in total heart volume is possible without a corresponding displacement of adjacent tissues.

Pictorial representation of the heart in cross-sectional view in different phases of the cardiac cycle, is rare in monographs. One opinion is, however, evident from the cross-sectional heart images used, to illustrate the pumping of the heart [2, 4848, 119, 166]; that is, that the heart is looked upon as a displacement pump, changing its atrial and ventricular outer contour rhythmically during atrial and ventricular systole.

Brecher [22], referring to Böhme [31], argues for the importance of the expansion of the atria at ventricular systole, for the venous return.

Rushmer [147, 148, 149], Hawthorne [72] and McDonald [35] propose that the systolic descent of the heart base occurs mainly before ejection. That is a result of early activation and shortening of endocardial layers of myocardium, including the papillary muscles. The mitral valve cusps are thought to be drawn downward, with resulting expansion of the left ventricle ("initial systolic expansion"). Ejection is thought to be accomplished by subsequent circumferential contraction, with little further change in left ventricular length. Arguments for the energetic advantage of this pumping mechanism have been delivered.

Others, Katz [91], Braunwald [16], Brobeck [25], Guyton [60], Gauer [49], Ganong [48] and Kenner [94], do not mention the compensation of ventricular shrinking by atrial expansion and vice versa. This does not mean that these authors are arguing against the course of events, but rather that they do not consider it to be of major relevance.

The discussion of the in vivo situation, regarding volume changes during the cardiac cycle, may be simplified by the construction of appropriate theoretical models.

2.3 Theoretical Models

In one such model, the heart is surrounded by soft tissues, which in turn are confined within rigid walls. The only openings arranged in these walls, are those for the major arteries and veins emanating from the heart. In such conditions the effect of the heart pumping by periodic contraction and expansion is quite obvious:

- The incompressible nature of the tissues between the heart and the rigid walls, will transmit an increase or decrease in volume to the walls
- As the compartment walls are non-yielding, they will resist this force
- The result is plain: in these circumstances a heart, however strong it may be, will not be able to pump any blood by alternatively contracting and expanding

Another model, otherwise identical to the first, can be designed with flexible outer walls. This is approximately the situation we find in the human body. It would certainly allow the heart to exert its pumping function. But the walls would then bulge outward or inward, along with the expansion or contraction of the heart. This implies, that pumping has to be done at the energy cost of moving the mass of tissue between the heart and the compartment walls. Passive diastolic filling would be possible with this model, but its sensitivity to variations in venous pressure will be low. These apparent limitations do not, however, invalidate it.

In the living heart, there are some rigid regions in its confining "walls" (ribs, sternum and spine). There are also parts near the heart that have a flexible outer wall. Furthermore, bordering the pericardium is lung tissue, which is compressible. The transmission of the movements of the heart to adjacent tissues should primarily

affect those complying most easily, i.e. pulmonary tissue. If the heart were pumping in this way, one would thus expect a periodic contraction and expansion of the heart towards the pleura in systole and diastole, respectively. That should approximately correspond to the combined ejection volume of the ventricles. Such a movement, at least to a quantitatively important extent, is not observed. This material is discussed in Chapter 3 and Chapter 4.

Blair and Wedd [13] expressed some of the above views, although they overstressed the importance of intrathoracic pressure changes on venous return. Their idea was corrected by Hamilton and Lombard [67]. Hamilton [66] and Holzlöhner [81] had found earlier, that during the cardiac cycle, intrathoracic blood volume changes by only a small fraction of the stroke volume. This means, a rapid systolic inflow to the chest that nearly equalizes systolic outflow.

2.4 Ventricular Filling

The output of the human heart is amazing. Pumping capacity varies from a few liters per minute, to 15-20 l/minute for healthy adults and up to 35 l/minute for some well-trained athletes.

How important are venous pressure (vis a tergo) and active filling through the movement of the valve plane in systole (vis a fronte) for ventricular filling? How big role plays the contribution of elastic forces (diastolic suction cf. [23])? These questions are still a matter of debate.

There is, however, a consensus of opinion concerning diastolic filling being of paramount importance for cardiac output.

For an authoritative view on the role of atrial contraction (atriums as "booster" or "primer" pumps), see Mitchell et al. [116] and Guyton [60]. This view seems to pervade modern cardiophysiological literature.

2.5 Two Basic Concepts

It is obvious, that current views on the action and control of the human heart need clarification. This can be done by some reconsidering about cardiac pumping, in the context of the specific criteria, described in the first part of this chapter. Our tools for that will be a few basic laws and facts of physics (cf. [29 ,30]) and fresh observations of the living heart, by a number of imaging techniques.

In this analysis, cardiac pumping and physical control functions can be crystallized into two basic concepts.

2.51 Concept 1

The first concept defines the actual mode of pumping:

The heart strives to do its pumping, with a fairly constant total volume and outer contour, in an environment conferring a substantial moment of inertia.

2.52 Concept 2

The second concept identifies the method of control, by which arterial and venous circulation is balanced:

The interventricular septum regulates ventricular stroke volumes, to maintain proper balance between systemic- and pulmonary circulation.

2.6 The "Gripping Heart" Pumping Mode (Concept 1)

The pumping mode according to Concept 1 was, at least in a rudimentary way, envisaged by Harvey [70]. It is related to the operating principle of the well-known garden-pump; it consists of a steel tube surrounding a movable receptacle. Two one-way valves allow water flow in an upward direction only. This pump, has an essentially unidirectional force. In one step, it provides in- and out- flowing water with necessary energy, transmitted through the valve (at the bottom of the receptacle) in a closed position. That valve corresponds to

the valve plane in the heart; it exerts a "gripping" action on the water column, by moving it stepwise towards the outlet.

A similar view has been expressed by Carlsson [32], based on experiments with tantalum-labelled ventricles in dogs. He noticed that "this emptying mechanism is probably more economical from an energy point of view than the generally accepted squeezing mechanism of the ventricles" (author's emphasis).

Further support for this pumping mechanism has been provided by McDonald [35], and by Slager et al. [164], based on endocardially implanted radio-opaque markers and contrast angiograms.

The active phase of the garden-pump is somewhat similar to ventricular systole and the passive phase to ventricular diastole. Water inflow is, however, discontinuous. When the stroke rate increases, the pumping mode becomes continuous, because of the dynamic forces smoothing the movement of the water column over the entire pumping cycle.

In contrast to the receptacle of the garden-pump, the left ventricle has the form of a paraboloid. The right ventricle (with a much smaller work load) is more complex in form; it is attached to the left ventricle, so as to form a new paraboloid in combination.

The paraboloid muscle mass below the valve plane, may be reduced to a cone; it keeps its fundamental geometric properties, when shrinking in the direction of its axis.

Contraction of the muscle fibres of the ventricular wall is arranged in a complex pattern (cf. [9, 170]). It may be represented by two force vectors:

- the first one acting radially inwards from the wall
- the second perpendicularly to the first vector

Their resultant is approximately parallel to the wall, in the direction of the apex. Contraction may result either in the cone base approaching the apex, or vice versa.

The importance of the anatomical setting of the heart, was already obvious to Henke [76] in the end of the 19th century. It is vividly expressed in his criticism, of the determination of outer contour variation on excised hearts by Hesse. Hesse arrived at the result that the ventricles, when shrinking by contraction, definitely do not become shorter, but only more narrow. Henke pointed out that this sort of extension, or contraction, of the heart freely suspended in air or immersed in liquids differ form heart in vivo. It does not prove anything concerning the change in form which it experiences in life.

Henke further stated that "the diastolic form of the ventricles, according to the conclusions of Hesse, would approach the form of a hemisphere. Think of this hemisphere put into the human thorax in the sharp corner between the diaphragm and the anterior thoracical wall. This is the end of all topography".

Henke also clearly conceived the approximately constant volume of the heart, over the cardiac cycle.

It should be noted, that his findings received little attention at that time. The well-known textbook of the physiology of circulation by Tigerstedt [175], published nine years later and otherwise up-to-date, did not mention that work.

Movement of the apex atrially, would necessitate the yielding of the tissues surrounding it, in order to fill the imaginary volume created by its shrinkage. Because of the fixation of the pericardium to the diaphragm, and the rigidity of the thoracic cage, the cone base will approach the apex. A part of the blood volume of the atria, and the great veins, will move apically and fill this imaginary volume.

This mass transfer that occurs in real time, is to a large extent balanced by thoracic systolic blood in- and outflow. The difference will be mainly made up by venous blood, transmitting it's acceleration to the large surface of the major veins. It necessitates a minor acceleration only of their walls, and adjacent tissues in the direction of their lumen.

The pericardium seems to be a stabilizing- and volume-limiting factor [1010, 38, 71, 79, 80, 99, 138, 177], although a different opinion has been expressed recently [111]. Because of its configuration, and the specific properties of the cardiac muscle, the heart thus slides in the pericardial sac. In a similar way the receptacle of the garden -pump slides in its steel tube.

Motion of the ventricular cone apically is preferable to radial contraction, with regard to energy [29].

This pumping mechanism is similar to the valve plane concept by von Spee [167], who 1909 coined the term ventilebene.

He was not aware of the importance of the inertia of tissues, in which the heart is embedded.

Ventricular filling is seen to proceed in two distinct phases at low heart rate: a "fast" and a "slow" phase.

The fast phase is dominated of dynamic forces; the valve plane moving atrially have accelerated the blood in the atrium, under ventricular systole. When the valves into the ventricles opens, the accelerated blood rush into the ventricles.

After a moment the inrush of blood subsides, and the slow phase with low, or no inflow at all, begins (dominance of static forces). During the later stage of the slow phase, influx increases again, due to atrial systole. The contraction of the relatively thin atrial walls does not push blood into the ventricles, by the increase of atrial pressure. The actual role of atrial systole, is instead to move the valve plane further away from the apex, sliding it along the atrial blood mass [4040, 76, 92, 167]. The ventricular volumes increase, by the movement of the valve plane atrially, stretching and thinning the ventricular walls.

At higher heart rates, the fast phase is directly followed by atrial systole, and inflow to the ventricles proceeds at a rapid rate over the entire ventricular diastole.

Experimental proof of this mechanism was provided by Gribbe et al., on anaesthetised intact dogs [57, 58]. Recent non-invasive findings with ventriculography [154, 164], and two-dimensional Doppler echocardiography [46], on the whole agree with this filling sequence. But a substantial part of diastolic filling though, is brought about by the displacement of the ventricular wall relative to the cardiac blood volume, not observable in Doppler echocardography.

The gist of this is that the importance of the atrial contraction is close to zero at higher heart rates.

The pumping action of the heart is primarily designed for the transport of blood mass by intermittent acceleration, and not for the generation of pressure. But the ventricles also have to do their work against aortic and pulmonary pressures (Hauffe [71]; cf. also [94]). The importance of systolic acceleration of blood in the atria and large veins, by the movement of the AV-plane was (as mentioned earlier) first suggested by Purkinje [137].

Epstein [36] 1904, wrote a thorough survey covering the research of the diastolic filling mechanism of the heart. The major concepts for the filling mechanism were static filling pressure (e.g. [75]) and active diastolic suction (e.g. [107]). That survey seems to have prevented the ideas of Purkinje and his followers, from being seriously considered for a long time.

Once blood is circulating, dynamic forces influence the working of the heart (see especially [20, 22]). This is because the blood mass accelerated in systole on both sides of the valve plane is significant, in comparison with the total mass of the heart. The return of the valve plane at the end of ventricular systole and the ventricles diastolic form and volume, has been the subject of many investigations. It has been explained in terms of elastic and hydraulic [110] intramyocardial forces, by arterial blood pressure straightening the aortic arch, and by the action of atrial systole.

The former mechanisms release energy stored in systole (cf. [4]). The role of elastic components in the heart wall has been much debated. Experiments that support elastic recoil (passive elasticity, or operative chamber stiffness [21, 42, 158]), are in contrast to others that disprove it [11]. Brecher [23] states that the vis a fronte is the force which concerns ventricular filling directly. Others [27] argue for relaxation factors, and that the quantitative significance of ventricular wall elasticity for diastolic filling should be smaller, than that of wall viscosity (.f. [1, 47, 173]).

In Chapter 8, another filling mechanism of the ventricles will be described.

In summary, the "gripping" pumping mode of the heart provides effective output, at a relatively constant volume and form. Ventricular filling requires low energy input. Atria and large vessels make the inflow smooth, and the atria also contribute to ventricular filling, by active displacement of the valve plane in atrial systole.

2.7 Circulatory Balance by Ventricular Septum Displacement (Concept 2)

The circulatory system is basically made up of communicating volumes containing moving blood, in which dynamic conditions maintain pressure gradients and thus locally and temporarily varying pressures.

Total blood volume may vary, through water and solute transfer between intravascular and extravascular space, excretion, water intake, etc. These changes are normally rather slow. In a short time perspective i.e., in time periods of seconds (rather than minutes and hours), these control mechanisms are unimportant.

This short term circulatory control ensures the provision of the different parts of the circulatory system. The different parts will have their proper share of total blood volume, and the maintenance or change of this distribution according to metabolic needs.

An important control mode in this respect is generally accepted to be the control of arterial pressure. This is controlled by regulation of heart rate, stroke volume, ventricular contraction (inotrop effect) and arteriolar constriction, mediated by the sympathetic nervous system. The afferent signals come from high pressure baroreceptor areas, in the carotid sinus and arch of aorta. Low pressure baroreceptors in the venous system, indirect affect the high pressure baroreceptors (Lindblad [103103]).

The heart is a double pump:

- one pump which feeds a high resistance system
- another pump which works against comparatively low pressures

Diastolic atrial pressure varies in the normal heart between about 3 and 15 mm Hg on both sides, although the pressure in the left atrium (LA), in general exceeds that prevailing in the right atrium (RA).

Atrial systole raises atrial pressure only slightly, between about 2 and 10 mm Hg.

These low pressures have to be compared with systolic left ventricular pressure, which (during physical exertion of healthy subjects) may exceed 200 mm Hg.

Right ventricular systolic pressure (in the absence of disease) seldom rises above 40 mm Hg (Bevegård [12]).

The pressure in the left ventricle (LV) surpasses that prevailing in the right ventricle (RV) both in diastole and systole. That should result in an essentially circular systolic configuration of the left ventricle (LV), in a plane perpendicular to the major LV axis. If the distribution of pressure were the opposite, the right ventricle would adopt this circular configuration.

Changes in resistive- and elastic properties of the circulatory system due to the effects of control mechanisms, cause a redistribution of intravascular volume. That also causes a varying extent of redistribution between pulmonary circulation and systemic circulation. As the reciprocating rate of the ventricles is by nature the same (even LV and RV end-diastolic volumes and ejection fractions are approximately identical [113]), redistribution must be effected through temporary differences in stroke output between LV and RV. The physical cause for this redistribution, and how it is controlled, is not completely understood.

It is commonly assumed that circulatory balance is maintained by the Starling mechanism1 (e.g. [2, 4, 11, 16, 19, 25, 43, 62, 68, 77, 96, 159, 166]). Experiments were designed to test the hypothesis, that balance in ventricular output is maintained or restored in accordance with the Starling mechanism. Franklin et al. [45] and Le Winter et al. [102] arrived at the conclusion, that the Starling mechanism is not the only mechanism that maintains or restores balance.

In connection with criticism of the hypothesis of the Frank-Starling law [129] i.e., that the impact of venous return governs the output of the normal heart, Hamilton delivered his idea. He stated that he could not think of any other explanation for evolution having preserved the Frank-Starling relationship, if not to maintain the circulatory balance.

In this, Hamilton was supported by some [14, 50, 141, 150], and preceded by Reindell and Delius [140] and others.

At present, there is a prevailing controversy reflected in many research papers and the major monographs cited above.

Braunwald [1717, 18], Sonnenblick [16] and others [34, 157] gives support for a major role of the Frank-Starling law (in the control of cardiac output in the normal heart).

This is at least partially questioned by Noble [120], Bassenge [4] and others [37, 88, 104, 124, 145, 182].

Experimental findings supporting the Frank-Starling relationship have been obtained either on isolated heart-muscle preparations or on open-chest animals. In some cases experimental findings have been obtained on excised and denervated animal hearts, often with their pericardia removed. For early criticism of results obtained from models other than intact animals, see Hamilton [66] and Sjöstrand [163].

Experimental work presented in this thesis aims at demonstrating the following; rigid or semi-rigid environment (and thus the natural setting of the heart) has a profound impact on its working mode and on the regulation of its output.

Considering the pumping mode of Concept 1, it is evident that the predominate mechanism for the ventricles to vary their respective volumes, is by displacement of the ventricular septum (VS). It is the only part of their walls which they have in common (the VS is mainly formed by subendocardial RV and LV fibres, Torrent-Guasp [176]). This volume variation is made possible by the process of ventricular polarization/depolarization. In diastole, ventricular depolarization confers plasticity to the septum. That lets it adopt a position determined by the dynamic and static pressure components, of left and right heart blood volumes during ventricular filling.

At the onset of systole, the AV-plane starts its movement towards the apex, the tricuspid and mitral valves close and after a short interval (the "isovolumetric phase") the aortic and pulmonic valves open.

When the left ventricle is put under excessive pressure, its walls will adopt the most stable configuration, which is the circular one in a transverse plane. That position also predetermines the position of the ventricular septum, as a circular segment of systolic LV wall (cf. [33]). If the configuration of the VS at the onset of systole deviates from the "predetermined" circular segment [3], LV pressure rise will displace it and make it adopt that configuration.

In addition to the pumping action by the valve plane moving apically, the septum itself will exert a membrane pump-like function and thereby affect blood volumes ejected from both ventricles.

Diastolic pressure interdependence of LV and RV [7, 28, 38, 55, 78, 93, 95, 115, 127, 155, 171, 177, 178] under a variety of abnormal or pathological conditions, and a dependence of diastolic pressure-volume relationship of LV on RV filling pressure [1, 7, 74, 127] has been noted. No common explanation for these phenomenons has been given. This may be partly due to different, and sometimes contradictory, findings concerning the interaction of ventricular septum (VS).

Some claim that the deflected VS retain its diastolic position in systole [54, 87, 95, 151]. Others believe that LV compliance [7, 122, 171, 179] and contractility [24] changes, and still others that crista supraventricularis [85] is damaged and that the pericardium interferes [162], etc.

The general importance of the VS for the equilibration of pulmonic- and systemic circulation has therefore been emphasized (cf. [126]). Support for the concept that the VS exerts a balancing influence, is provided by the study of VS displacement by echocardiography in cases of heart disease with atrial pressure overload (Chapter 6). The possibility of maintaining circulatory balance by displacement of the intraventricular septum is also illustrated by experiments with a double pump (Chapter 7).

1 The term "Starling Mechanism" will be used exclusively to differentiate ventricular equilibration from the general application of the Frank-Starling law to venous return. Henderson and Prince [74] had in fact already suggested the controlling influence of the diastolic distending pressures upon stroke volumes.

Chapter 3

Ventricular Dimensions by Coronary Cineangiography: Outer Contour, Wall Thickness, Valve Plane Displacement, Position of Ventricular Septum

3.1 Introduction

The ventricular dimensions of the heart in situ in healthy adults were determined by echocardiography (EC). Such as outer contour, left ventricular posterior wall and ventricular septum thickness, valve plane displacement and the position of ventricular septum (VS) was studied.

3.2 Material and Methods

Heart echocardiograms were obtained from nine healthy adults (of ages between 25 and 35 years) in four steps, using an ATL ultrasound scanner.

M-mode registrations and ECG-triggered mechanical sector scanning registrations were recorded by means of a dry silver recorder (Tektronix).

Measurements were made at midpoint of endocardial, and other lines.

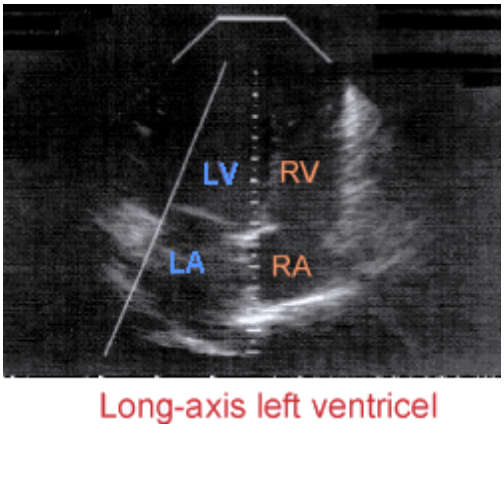
The examinations were also video-recorded, in order to provide for more detailed analysis.

3.3 Ventricular Wall and Septum Movement by M-Mode Scan

An ECG-lead was applied to the person lying on the left side.

A parasternal sector registration in the plane of the long heart axis was recorded.

A M-mode line was, with help of a sector image, positioned as exactly perpendicular as possible to the long heart axis. The line was penetrating at the point at which the cross-section of the left ventricular lumen is at its maximum (Fig 3-1 A, sector image of person No. 2).



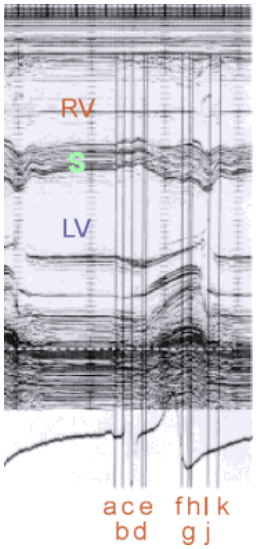


Fig 3-1 A: Echocardiography-sector scans. Orientation of M-mode registration

Fig 3-1 B: M-mode registration no. 1 (M1), person no 2 (M12). Event lines a-k added.

A trace was recorded on paper in the optimally attainable position, at the end of exhalation (Fig. 3-1B, M-mode of person No. 2).

The usual aim of such examinations is to study the variation of ventricular volumes [131], as well as the change in thickness of ventricular walls. In the present case, however, the aim was primarily to study outer contour variation of the left ventricle during the cardiac cycle. This implies that the epicardium and pericardium, as well as the endothelial surface of VS in the right ventricle (RV), were studied.

It is often difficult to assess the variation of wall thickness of the RV in healthy adults. This is due to the right ventricular wall being thin, and to the various sources of error. It was therefore thought to be of no value to assign points of reference and monitor changes in the RV wall.

In instances where it nevertheless was possible to discern the right ventricular wall and its pericardium, no movement at the pericardial-epicardial interface was recorded.

For the sake of easier inter-individual comparison of ventricular interface movement over a full cardiac cycle, nine registrations were analyzed. Maxima, minima and points of inflection was regarded (Fig. 3-1B).

The following EC events were defined by vertical lines a through k ("event lines", same symbols as for the corresponding events):

- a : Commencement of atrial contraction, affecting the ventricular septum and the posterior wall
- b : Point of maximum effect of atrial contraction on the left ventricle (LV)
- c : Closing of the mitral valve
- d : Onset of movement of VS, towards its position in systole
- e : Onset of movement of the posterior wall, towards its systolic position
- f : First systolic maximum of VS, in the direction of LV
- g : Onset of the renewed systolic movement of VS in the direction of LV, which is simultaneous with the closing of the aortic valve
- h : Point of maximal thickness of the posterior ventricular wall
- i :Second systolic maximum of VS, in the direction of LV
- j : End of the fast relaxation (thickness reduction) phase of the lateral posterior wall of LV
- k : End of the fast relaxation (thickness reduction) phase of VS

In addition to these events, some minor septal movements could be seen, that may be interpreted as equilibrating vibration phenomena. They were in most cases indistinct (they could only be identified in two of the volunteers), and have therefore not been given further consideration.

Cartesian coordinates for this M-mode registration were defined in the following way.

One event line a at its intersection with the epicardial - pericardial interface (base), is connected to the next such intersection. This connecting line defines the time axis (abscissa). Time zero is selected at the onset of the P-wave of a simultaneous ECG registration. Regarding events c through k, time zero is selected at the onset of the QRS-complex. P-Q time intervals are recorded individually.

The ordinata is directionally identical with the EC beam, with positive values in the direction of the probe.

Intersections were defined at lines a through k (in the beam direction), with the curves for:

- 1. Epicardium
- 2. Posterior wall endocardium
- 3. Ventricular septum endocardium at LV
- 4. Ventricular septum endocardium at RV

(The curves are labeled {1},{2},{3} and {4} for the individual M-mode registrations. One of those curves is shown in Fig. 3-1C.)

Coordinates for the individual points of intersection were fed to a CAD-system, which reconstructed a M-mode for each of the original M-mode tracing. For one of them (M12), the reconstructed graph is shown in Fig. 3-1C.

The next step was the construction of a M-mode image containing the averaged information of individual registrations. This was done in the following way.

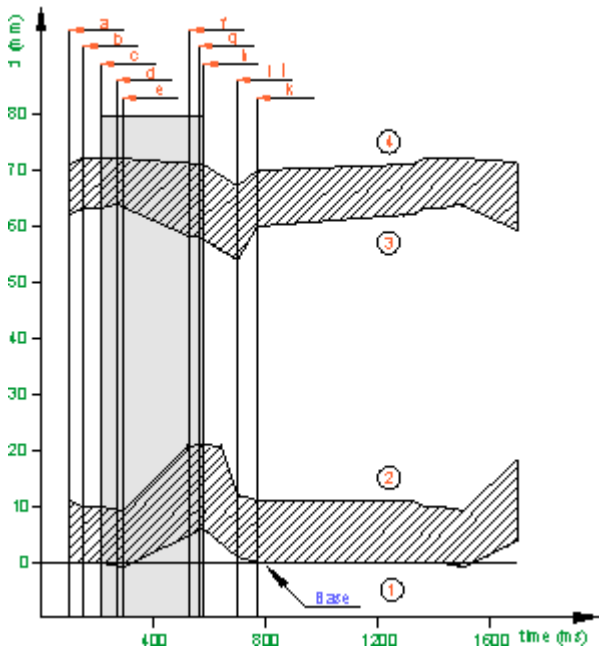


Fig. 3-1C: Reconstructed M-mode (M12). Lines 1 to 4 and event lines a - k also shown. Marks are indicating the time period during which the maximal thickness is within 1 mm of maximum value.

The time relation between events a through k was based on two independent points of reference i.e., atrial and ventricular contraction. The mean of PQ-intervals and RR-intervals was defined where event c and the point of repetition for the reconstituted cardiac cycle, respectively, were to be fixed. In other words, the mean of PQ-intervals was counted on the event c as reference.

Raw data given in Table I, show how often events at the left ventricular posterior wall (e, h or j) coincided with events at VS (d, f, g or i).

A standard LV dimension was obtained by averaging the distance defined by the base line and curve {3}, at event a, 59 mm. The total range at this point is 59 (-5,+3) mm and is indicated in Fig. 3-2 by a dotted line. The confidence intervals, at the other intersections of event lines, were calculated with a t-test on a 0.025 level and are marked with continuous lines.

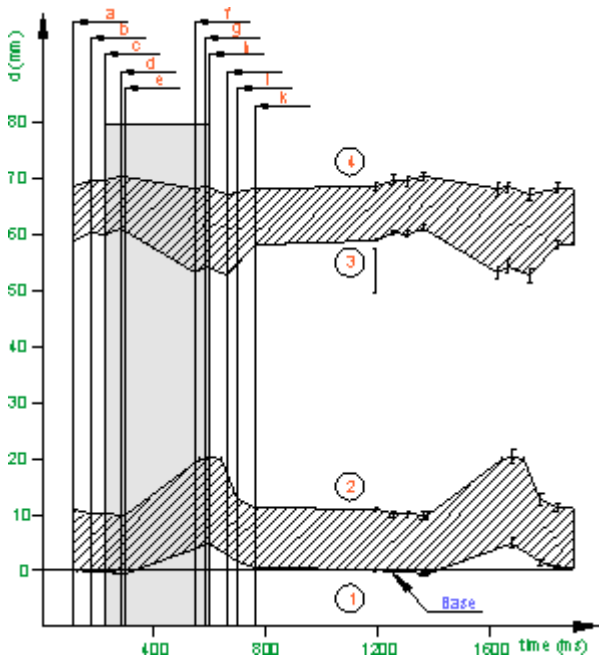


Fig 3-2: Mean of reconstructed mode M1. Registrations M11-M19 is obtained from nine persons, and the confidence interval is calculated with t-test on a 0.025 significance level.The solid vertical line (besides 3) represents range for standard LV-dimension 59 (-5, +3) mm.

The inner contour LV variation is given by curves 2 and 3.

Curve 2 was obtained by averaging the distance between the base line and intersections of event lines a, b, c, e, h, j and k with curve {2}, in the individual M-mode registrations (Table IIa).

Curve 3 was obtained by normalizing the point of intersection of curve {3}, to a value of 59 mm at event a. The other points (b, c, d, f, g, i, k) were then normalized accordingly (Table IIb).

LV outer contour variation is given by curves 1 and 4.

Curve 1 was obtained as the distance mean between the base line and curve {1}, in the individual M-mode registrations at events a, b, c, e, h, j and k.

Curve 4 was obtained by adding to the normalized value of 59 mm, the average for the distance between points of intersection at events a, b, c, d, f , g, i and k, and curves {3} and {4}, respectively (Table IIIa, Table IIIb).

The effects of atrial systole and the early systolic ventricular phase (isovolumetric phase) on the ventricular septum and LV posterior wall are shown in Table IV.

3.4 Atrio-Ventricular Valve Plane Displacement, as Determined by Simultaneous Recording of Three M-Mode Projections in Sector Scan

By means of sector scans along the major heart axis, positions were sought for allowing optimum recording of valve plane motion. M-mode registration was then performed in three positions: M2, M3 and M4.

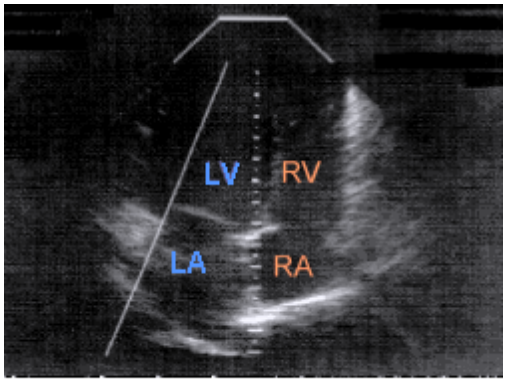
The first position (M2) is given by the attachment of the posterior mitral valve leaf at the anulus fibrosus (Fig 3-3A, authentic sector image 22 from person no. 2).

The second position (M3) is given by the point of attachment of the anterior mitral valve leaf at the anulus fibrosus (Fig 3-4A, authentic sector image 32).

The third (M4) is the point of attachment of the tricuspid valve at the medial part of the anulus fibrosus (Fig 3-5A , sector image 42).

The M-mode images obtained from the nine persons (cf.Fig 3-3B, Fig 3-4B, Fig 3-5B), M21 - M49, were reconstituted (Fig 3-3C, Fig 3-4C, Fig 3-5C). It is explained above in the case of M11 - M19, by definition of the following events:

- a' : Point immediately prior to atrial contraction affecting the valve plane
- b' : Point at maximum displacement of the valve plane by atrial systole
- c': Closing of the mitral valve
- d' : End of the supposed isovolumetric ventricular contraction
- e' : Point at which the valve plane has reached the same position, as prior to atrial systole
- f' : Amplitudinal maximum (closest approach to apex)
- g' : End of rapid return of the valve plane, in atrial direction
- h' : Slight rebound movement, due to overshooting



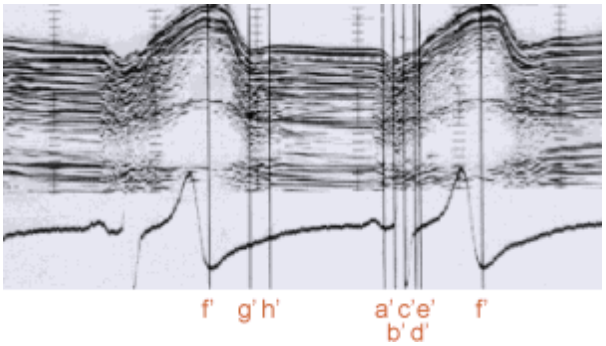


Fig 3-3 A: EC sector scan. Orientation of M-mode registration.

Fig 3-3 B:The movement of the attachment point of the posterior mitral valve at anulus fibrosus, obtained by echocardiography (EC). M-mode registration (M2), person no. 2 (M22). Event lines a'-h' added.

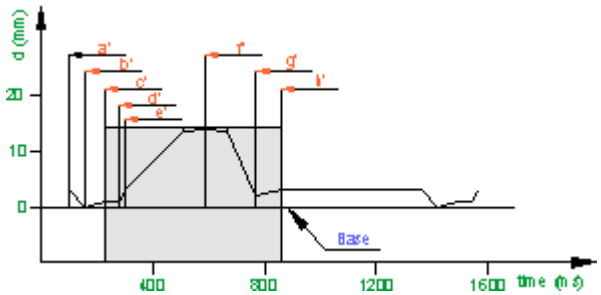


Fig 3-3 C: Reconstructed M-mode (M22) registration. Event lines a'-h' added.

A base line was drawn in M21 - M49 by connecting two intersections of event line b' with the valve plane (Fig 3-3B, Fig 3-4B, Fig 3-5B). This line forms the abscissa (time coordinate).

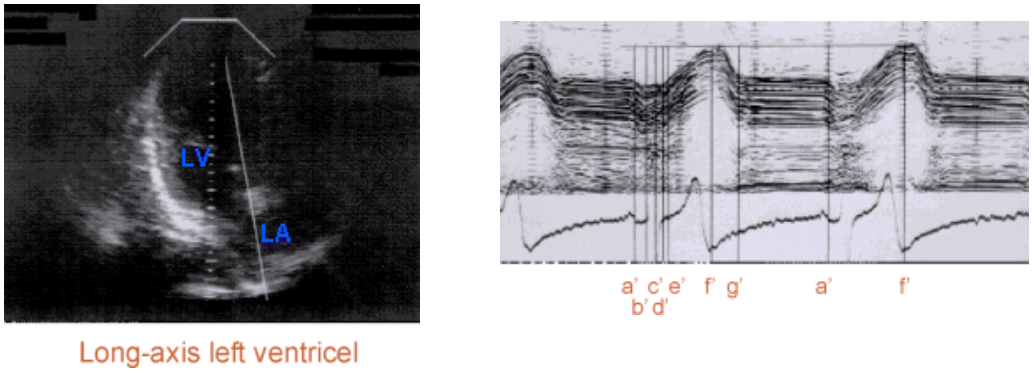


Fig 3-4 A: EC sector scan. Orientation of M-mode registration.

Fig 3-4 B:The movement of the attachment point of the anterior mitral valve at anulus fibrosus obtained by echocardiography (EC) M-mode registration (M3), person no. 2 (M32). Event lines a'-h' added.

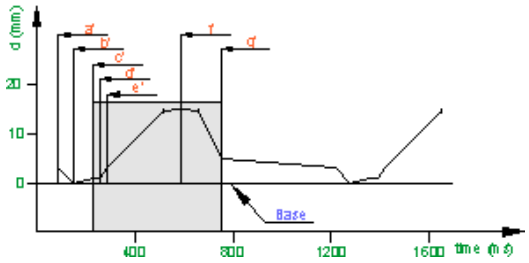


Fig 3-4 C:The movement of the attachment point of the anterior mitral valve at anulus fibrosus obtained by echocardiography (EC). Reconstructed M-mode (M32) registration. Event lines a'-h' added.

Time periods (in milliseconds) (Table Va, Table VIa and Table VIIa), were recorded for events a' through h' with reference to atrial events (starting with the onset of the P wave). Time periods were also recorded with reference to ventricular events (starting with the onset of the QRS complex).

Distances between base line and points of intersection of event lines a' through h' with valve plane, were measured by hand (Table Vb, Table VIb and Table VIIb). They were fed into a CAD-system, with reconstructed M-mode registration (Figures 3-3C, 3-4C, 3-5C).

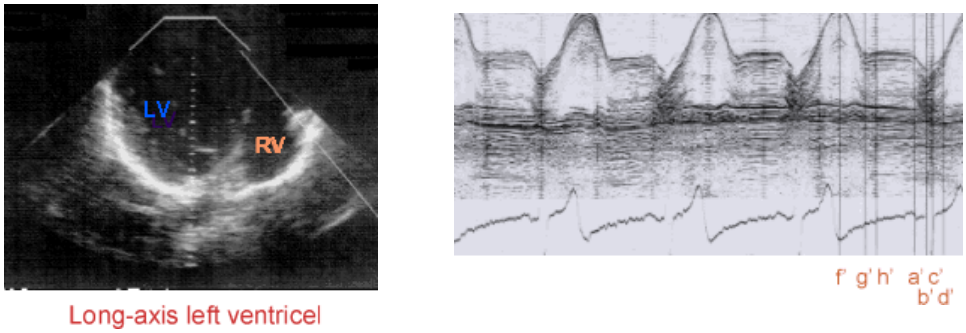


Fig 3-5 A: EC sector scan. Orientation of M-mode registration

Fig 3-5 B: The movement of the attachment point of the tricuspid valve at the medial part of the anulus fibrosus, obtained by echocardiography (EC).M-mode registration (M4), person no. 2 (M42). Event lines a'-h' added.

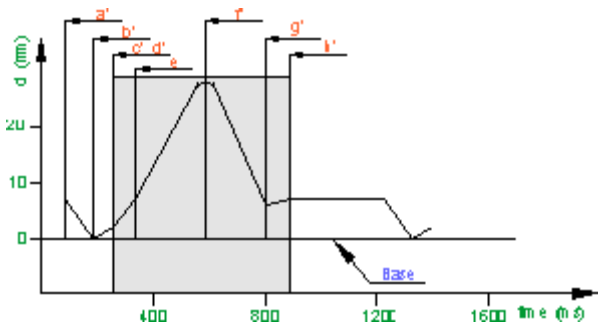


*Fig 3-5 C: The movement of the attachment point of the tricuspid valve at the medial part of the anulus fibrosus, obtained by echocardiography (EC).*Reconstructed M-mode (M42) registration. Event lines a'-h' added.

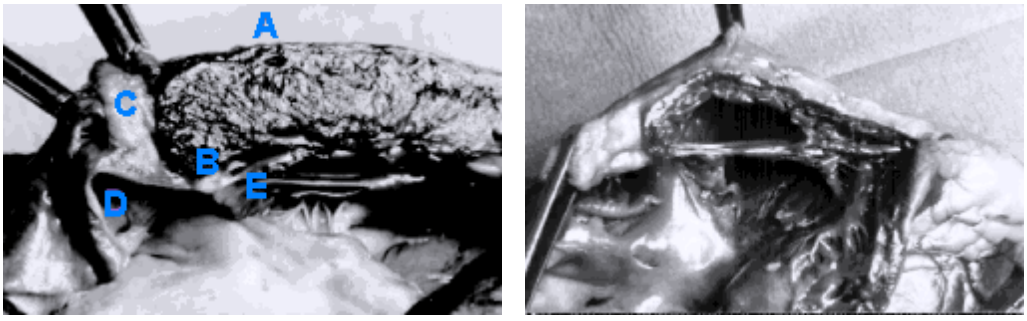
Table VIII has values for the total displacement of the valve plane in M2-M4 (Table VIIIa), and its atrial contribution (Table VIIIb).

3.5 Anatomical Considerations

Because of possible interference with EC measurements, the complex morphology of the region between atria and ventricles was studied, for the purpose of exactly delimiting it.

That was done by dissection of a heart of a recently deceased adult. A triangular formation (in cross-section) of predominantly adipose and connective tissue with blood vessels was conspicuous. It was located in the zone between the posterior wall of LV and the posterior wall of the left atrium. It was in the same place from where the sector EC registrations for identification of valve plane motion were obtained (cf. Böhme [31]).

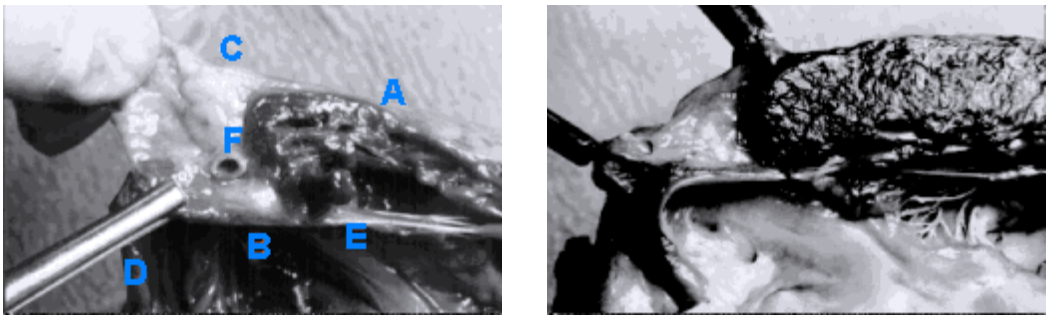
This composite tissue easily complies with elongation stress, and so adds some 10 to 15 mm to the extension of the AV-plane (Fig. 3-7A-B) (cf. [136], Fig. 3-9A-B, Fig. 3-9C).



Non-stretched Stretched in long-axis direction

A: Left Ventricle myocardium, B: Anulus fobrosus, C: Connective/adipose tissue, D: Left Atrial wall, E: Anterior mitral valve

No such region is observed in the corresponding zone between RA and RV. There is a groove though, just below the right auricle in which the right coronary artery is embedded (Fig. 3-8A-B).



Non-stretched Stretched in long-axis direction

A: Left Ventricle myocardium, B: Anulus fobrosus, C: Connective/adipose tissue, D: Left Atrial wall, E: Anterior mitral valve

It can also be seen how the chordae tendineae (with attached papillary muscles), are fixed at the anulus fibrosus. They are forming a bag-like connection, with the right ventricular muscle at the AV-plane. A similar (but less pronounced) form of attachment can also be noticed in LV.

The dimensional changes in anulus fibrosus, effected by atrial and ventricular systole, have been studied by Puff [134].

3.6 Systolic and Diastolic LV Images by Sector Scan. Valve Plane Displacement and Outer Contour Variation

Analysis by "frozen image"-technique of LV outer contour in systole and in diastole, was attempted while simultaneously recording the position of the valve plane.

Sector EC images, triggered on the R-peak of the QRS-complex, were scanned in systole and diastole (Fig. 3-9A-B; authentic images from person no. 2).

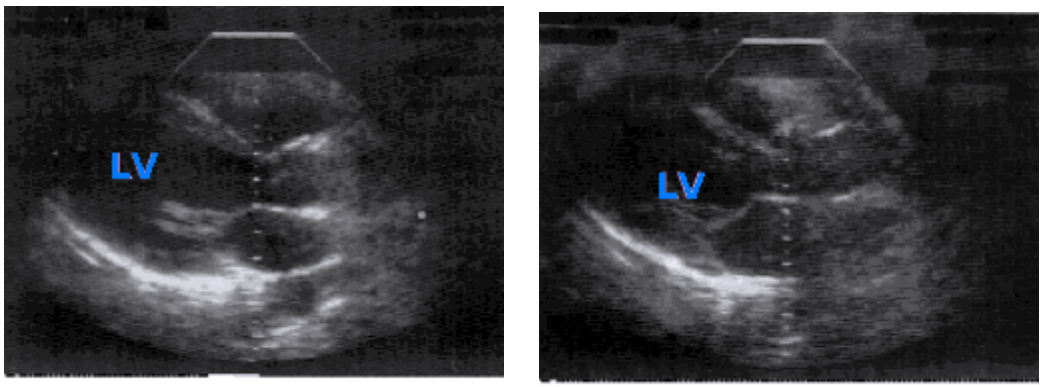


Fig 3-9 A:Systole, Sector image parallel to major heart axis of person no.2.

Fig 3-9 B:Diastole, Sector image parallel to major heart axis of person no.2.

Systolic and diastolic images for each subject were superimposed by using a digitizer tablet, a CAD-system and an x, y-plotter. This was made to visualise the differences with respect to LV and LA outer contour, and with respect to the motion of the valve plane. Fig. 3-9C is the differential image obtained for person no. 2.

Instrumentation allowed the freezing of only one image at a time, which had to be documented before the next could be obtained after repeated gating. This implies that between 10 and 20 seconds elapsed, between

the recording of corresponding systolic and diastolic images. Factors such as changed positioning of probe and/or object, changed respiration period, defective gating etc., may influence the overall result, and necessitate the discarding of pairs of images. Those remaining are thus selected and the result may therefore be biased.

The image pairs were analysed by drawing lines L(s) and L(d) in the systolic and diastolic images respectively (Fig. 3-9C). The lines were drawn from the area adjacent to the ventricular septum where the aorta originates (or alternatively from where the aortic valve is seen). They were drawn to the attachment of the mitral anulus fibrosus at the posterior wall. This latter point is easily identified in systole by the configuration of the afore-mentioned adipose tissue wedge, although in diastole this is not the case.

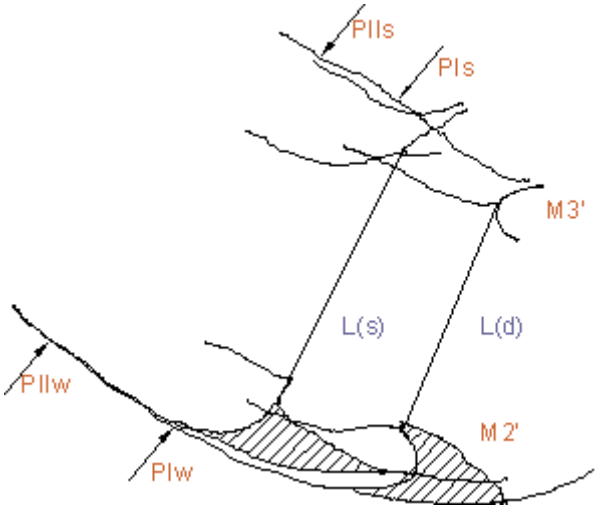


Fig 3-9 C: Reconstructed sector EC image ("frozen image"). Systolic and diastolic frames superimposed. Lines L(s) and L(d) added, defining points M2' and M3'. The dashed areas represent connective/adipose tissues.

It was high reflectivity of the posterior mitral valve leaflet, and the endocardium and pericardium had a curved form in diastole. Therefore it was necessary to assign that point of attachment to a special site. The site was placed, where the distance from the pericardium to the endocardial surface of the adipose wedge corresponds to the thickness of the myocardium in diastole.

In this way, opposite points of attachment were defined (M2' and M3'), comparable with points of attachment of the AV-plane, recorded in mode M2 and M3 (cf.Fig. 3-3A, 3-4A). Movement of the valve plane in M2' and M3' is presented in Table VIIIc under "frozen image".

Outer contour variation of LV was determined in two pairs of intersectional points, designated PI and PII, at VS and LV posterior wall, respectively (Fig. 3-9C). They were defined as the intersection between the outer surface of LV and a line parallel with the EC-beam.

In systole, PIs is situated near the aortic valve and PIw at the posterior wall, where the adipose wedge meets LV muscular tissue.

The second pair, PIIs and PIIw, is positioned at VS and LV posterior wall as near to the apex as possible.

It was provided for, that the outer contour for the area surrounding it can be recorded in both systole and diastole1. The difference between the systolic and diastolic images is given in Table IXa, Table IXb, under "frozen image w" and "frozen image s", respectively.

1 That is, PIIs had to be placed 1-2 cm below the valve plane in systole, which means a distance of 3-4 cm in diastole.

PIIw had to be placed approximately 1 cm apically from PIIs

3.7 Analysis by Video Replay of LV Sector Scan Images of Atrio-Ventricular Valve Plane Displacement and Outer Contour Variation

Analysis by video replay is a repetition of the study described above, but with results analysed in a slightly different way.

Sector images of LV along the major axis of the heart were stored, and later replayed on a video screen. Images from the same respiratory phase representing extremes of ventricular and atrial systolic position of the valve plane were selected. The outer contour of LV and LA was delineated with a felt pen directly on the screen.

The part of the valve plane comprising aortic and mitral valves, was similarly delineated.

Images from a few cardiac cycles were replayed in slow motion, to check that the contours had been correctly traced. Felt pen traces were transferred to transparent sheets and images similar to that in Fig. 3-9C were obtained. Sometimes slight variations were noted despite proper control of respiration phase, probably due to minor movements of the EC probe. In this case several traces were drawn checked and transferred as described above. The images were analysed in a manner analogous to the procedure described earlier.

Results are given in Table VIIId under "video" and in Table IXa, Table IXb under "video w" and "video s", respectively.

3.8 Results and Discussion

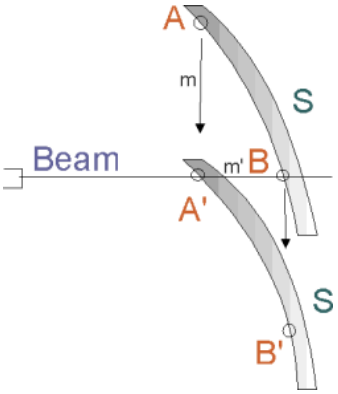
There are several limitations to echocardiography, that should be kept in mind [143, 181].

Bony tissues and air give complete reflection, and thus form barriers from behind which no information can be gathered. In the present case, these barriers are the sternum, the anterior portions of the ribs and the lungs.

Areas that allow the heart to be explored by EC, are therefore rather limited and form "windows". This implies that it is not always possible to get ultrasound images of the heart in the particular projection which is desired. Skew projections have to be used, which may distort information in that muscles for instance will sometimes look much thicker than they actually are. Live registration will also be impaired.

The sonocardiographic images, displaying the intricate system of movement of the different parts of the heart, therefore often demand an interpretation that takes these limitations into account. If technical and operational sources of error are disregarded, three others remain:

- **Low lateral resolution.**
  Although resolution in the direction of beam axis is about 1 to 2 mm, lateral resolution is not so good; it varies from 12 to 30 mm between the near and the far field, because of the finite width of the beam.
- **Defective registration of lateral movements.**
  When, in M-mode registration, the direction of movement at a given point is at variance with the direction of projection, a wrong movement will be recorded. It will be either too small or too large (Fig. 3-10).



- **Distortion of sector images.**
  If the angle of beam incidence is less than 900, reflection is impaired. In the event of the object of investigation having curved surfaces that move and are excessively uneven, the image will become distorted because of the finite width of the beam. This is the case when the heart is the object of observation. Reflection from points in the beam periphery may surpass that from the point produced by the central beam. The reflection from a curved surface will perhaps not be 1800; and will therefore not reach the probe. In that case, distorted information from the periphery of the beam before will dominate that region. In a two-dimensional image, this would result in a banana-shaped configuration of the ventricular septum and the posterior wall (cf. [39]).

3.9 Atrio-Ventricular Valve Plane Displacement

Table VIIIa, Table VIIIb, Table VIIIc, Table VIIId shows the movement of the valve plane visualized by ultrasound. Mean values given under "M-mode", "frozen image" and "video" differ despite the subjects investigated being identical and the close proximity of M2 and M2', and M3 and M3' respectively. The reason for this disparity lies in their sources of error.

EC M-mode registration of the valve plane looks deceptively simple. The transducer cannot, however, be directed at the structural entities in the valve plane easiest to detect i.e., the valves themselves. That is because of their displacement, deviating from the movement of the valve plane itself. They vanish from the image when opening. It would be desirable to direct the beam at points of attachment of the mitral valve in M2, M3 and M4. For anatomic as well as for technical reasons and because of the movement of the valve plane in the direction of the major heart axis, the following happens. M-mode registration does not depict the movement in one point, but rather in a series of points over a curved area.

This implies that for points of definition M2 and M3, the movement recorded will be too small (cf. Fig. 3-10). M4 at the attachment of the tricuspid valve medially at the anulus fibrosus has the proper prerequisites for correct reproduction. It may though nevertheless show a movement that is slightly exaggerated.

The contribution of atrial systole to the movement of the valve plane is approximately 25 % (Table VIIIb). From the movement of the valve plane in M2, M3 and M4 (Fig. 3-6A-E), we can see how the supposed isovolumetric presystolic phase b' through d' affects valve plane motion.

M-mode "frozen image" and "video" are two-dimensional images in the direction of the long heart axis. They allow a reduction of projection errors in the direction of valve plane movement. The figures of the "frozen image" series result from different heart beats, with rather long intervals between the maximum diastolic

(atrial systolic) image and the minimum systolic image. Absolute maxima and minima of the valve plane in these images depend on how they are triggered. This differs from beat to beat, since the timing of sector images is restricted to 30 images per second. Furthermore this differs from beat to beat because diastolic triggering is carried out on the preceding (or actual) R-peak in the QRS-complex.

Therefore, "frozen image" values for valve plane motion would be too small. In addition to this, respiratory variation, changes in heart rate and instability in transducer attachment are to be considered.

In contrast to the "frozen image" technique, "video" recordings (where single beats can be analyzed) do not show these deficiencies to the same extent. There is no triggering problem, but low updating frequency is still problematic. Delimitation of the valve plane in systole and diastole may constitute a source of error in both situations. The highest average values were obtained from "video". They should not, however, be exaggerated since the most common errors of the method (including projection errors) have tendency to reduce displacement values.

Considering the errors of the method, a realistic estimation of the displacement of the valve plane can be achieved. The best approximation to true values for valve plane movement at the side of the LV, is thus given by the displacement mean value recorded in M2 and M3. The result is 22 and 19 mm respectively, as shown under "Video" in Table VIIId.

The motion of the valve plane at the side of the RV could not be analyzed by video-replayed sector scans. The mean from M4 in Table VIIIa under "M-mode"(24.9 mm) is probably slightly exaggerated.

It is uncertain whether the true movement of the valve plane is greater at its periphery, than at the site from which the aorta and pulmonary artery ascend. Experiments show on the whole a larger movement at the right side. This is especially true for M-mode studies, summarized in Fig. 3-6C, which illustrate the combined effect of ventricles and atria on the valve plane. They demonstrate that the movement of the latter ceases almost entirely after the "fast filling phase".

It is furthermore possible to form an opinion about the rest time between events g' and a', and how it is affected by increasing heart rate. It is obvious that g' and a' will coincide at a certain heart rate.

Fig. 3-6C demonstrates the divergence in time of events a' through g' between M2, M3 and M4. By variance analysis it was found that there is no statistically significant difference in event time between M2 and M3. Such a difference was found though, for M4 relative to M2 and M3 regarding events a', b', c' and g' , and relative to M2 alone for e' as well. Event times for d' and f' coincide for all of them. That indicates that the velocity (v) with which point M4 "moves" (in the direction of the apex), is lower at the onset of ventricular systole than at its end. This enables the valve plane to catch up with point M2 (thereby reaching a higher velocity than that by which M2 "moves" apically at the LV valve plane side). This difference in velocity, combined with a possibly greater blood mass above the right valve plane, indicates that generated kinetic energy differ on the right side during the end of systole. It is greater than on the left side. This would also explain the occurrence of event i i.e., the second systolic maximum of VS in the direction of the LV (Fig. 3-2).

3.10 Variation of LV Outer Contour and of VS as Determined by M-mode Recordings

Beam direction of M-mode scans should be as perpendicular as possible to the surfaces of interest. This is difficult, since the working-mode of the heart and its curved geometric form make various parts of the heart wall pass through the beam during the cardiac cycle. That resulting in a constantly changing reflection pattern. Variation of LV and VS outer contour between events a to b (atrial systole), b to h (ventricular systole) and h to a (ventricular diastole) may therefore be exaggerated.

Regarding LV posterior wall, the papillary muscle constitutes a barrier to precise positioning of the EC beam, when trying to avoid thickening artefacts in systole. Positioning the beam closer to the sharply curved posterior wall surface adjacent to the valve plane, will avoid interference of the papillary muscle. There will instead be a disadvantage, with a substantially exaggerated movement of the outer contour of the posterior wall (Fig. 3-9C).

Values for LV posterior wall motion are presented in Table IXc. They have been obtained by subtracting two distances. One is the distance between the base line and the point of intersection for event line h with curve 1. The other is the distance between the base line and the point of intersection for event lines a, b and e with curve 1 (Fig. 3-2).

The values for displacement of VS are shown in Table IXd. They have also been obtained by subtracting two distances; one is the distance between points of intersection formed by event lines a, b and d with the base line and with curve 4 respectively. The corresponding distance is obtained by intersection of event line f with the base line and curve 4 (Fig. 3-2).

Note that the displacement of VS between systole and diastole, provided that atrial contraction and the presystolic phase are disregarded, is close to zero. Neither is VS seen to be thinning from the onset of atrial systole and ventricular presystole.

The LV posterior wall though, is under ventricle systole making some displacement in the direction of VS. Furthermore, the LV posterior wall is seen to be thinning from the onset of atrial systole and ventricular presystole (cf. Table IVa, Table IVb and Fig. 3-2).

If the prevailing view (that the heart is pumping by squeezing motions) is true, the situation is rather peculiar; only one part of the LV is participating in this squeezing motion.

For a long time little interest has been shown [152] in ventricular outer contour variation. Most of it has been concerned with the nature and location of regional variation, as determined by kymographic methods [89]. Interpretation of such measurements usually stresses the importance of any contour variation observed and not the fact that total variation is small per se. In contrast to this, interest has been focused on inner contour variation. LV cine-angiography is now being a routine method for the evaluation of LV function. With this method, the problem is how to view the LV endocardial outline [26]. This, combined with the partial systolic cavity obliteration resulting in a virtual wall thickening near the apex, gives an essentially false idea of ventricular contraction and thus of cardiac pumping (cf. [35, 52, 105, 156, 162]).

3.11 Variation of LV Outer Contour and VS by Sector Scans

As mentioned earlier, observation of a wall moving to the centre of the ventricle, does not necessarily mean that the heart is working in a predominantly squeezing mode. It can also be the result of the ultrasound reflection not occurring at the same site in systole and diastole (Fig. 3-9C). This consideration initiated the two-dimensional EC experiments, reported in Table IXa, Table IXb under "video" and "frozen image". They differ only with respect to sources of error, which are reduced in the "video" experiments.

Measurement of LV outer contour comprised, on one hand, the determination of posterior wall displacement (in positions PIw and PIIw). On the other hand, it comprised displacement of the RV endocardial interface of the VS (in positions PIs and PIIs). (PI = intersectional point one, close to the AV-plane; PII = intersectional point two, away from the AV-plane; w = posterior wall; s = septum, Fig. 3-9C).

Examination of sources of error for "video" and "frozen image" indicate that results from "video" are closest to true displacement values:

- Errors from the difficulty of finding the ultimate systole and diastole in "frozen image" could be eliminated.
- Errors from not holding the EC probe in a fix position, is smaller for "video" than for "frozen image".
- Errors from that persons examined was not lying in the same position under the entire examination, is smaller for "video" ”than for "frozen image".

When "video" values are compared with those from M-mode registration in the short axis direction (reported in Table IXc and Table IXd), VS movement was found to correlate well (Table IXd). But M-mode registration is always preformed with a beam-position more close to the mitral valve, than in "video"-technique; therefore errors from "defective registration of lateral movements" (Fig. 3-10) will be larger for the M-mode registration.

The studies in persons no. 6 and 7 were excluded, because of pulmonary tissue and ribs hindering optimal positioning of the probe, resulting in exaggerated movement of VS. (In contrast, the same persons displayed a rather "normal" outer contour movement of the posterior wall (Table IXc), compared with movement in point PIw under "video w" (Table IXa)).

There is a difference between the movement of VS and the posterior wall in intersectional point pairs close to (PIS/PIw), and not so close to (PIIS/PIIw), anulus fibrosus. It is probably due to the following:

- The pulmonary artery and ascending aorta are attached to the anterior part of the AV-plane, and are relative fix to the surroundings of the heart. That is also true for the apex. The pulmonary artery and ascending aorta forms an angel less than 1800 with VS. When VS during ventricle systole will be shorter, the AV-plane and the parts of VS close to it, moves towards RV.
- The part of VS and and the posterior wall that is close to the AV-plane (PIS/PIw) will thus move towards RV. The part of VS and the posterior wall that is not so close to the AV-plane (PIIS/PIIw) though, will hardly not move at all towards RV.
- As a result,the outer contour variation in PIw will increase, and the motion at PIs will be reduced. In PIIs and PIIw (which are closer to the relatively fix apex), movement of VS and the posterior wall is essentially the same.

The pulmonary artery and ascending aorta are attached to the anterior part of the AV-plane, and are relative fix to the surroundings of the heart. Also the apex is relatively fix to the surroundings. Therefore, when the AV-plane moves in the direction of apex during systole, the posterior part of the AV-plane will move more easily than the anterior part. This creates a momentum that can be felt, which causing the apex to beat against the chest wall.

The "rocking heart" phenomenon seen in pericardial effusion, can be due to the same momentum. It can also be due to the redistribution of fluid around the heart, which is working within the boundaries set by the pericardium and surrounding tissues (constant outer form). A corresponding cyclic redistribution of fluid around the healthy heart is not possible.

3.12 Summary

By digitizing left ventricular wall and septum displacements registered by M-mode in 9 healthy adults, it was possible to get an average of the posterior wall and septal outer contour movement during a heart cycle.

These findings were compared with outer contour variation. This was obtained by comparison of maximal diastolic ventricular sector image in the direction of the long axis (including atrial systole) with the minimum systolic sector image. It was made by frozen image and also by a video replay technique.

It was found that when projection and registration errors were taken into account, the mean value of the outer contour variation close to the AV plane was between 1-2 mm; at apex it was practically reduced to zero.

An analogous registration was performed to investigate the motion of the AV-plane. When the obtained values were compared, and projection and registration errors were taken into account, the motion of the AV-plane was about 21 mm on the left side; on the right side it was 25 mm.

Chapter 4

Ventricular Dimensions by Coronary Cineangiography

Atrio-ventricular valve plane (AV-plane) displacement and left and right ventricular contour variation during the cardiac cycle, were determined by coronary cineangiography. Six patients suffering from coronary artery heart disease was examined.

4.1 Material and methods

Coronary cineangiography (CA) is used as a routine method for the detection of atheromatosis of the coronary arteries.

In our study of six patients examined due to anginal pain (functional group II to III) and because they were all candidates for a coronary by-pass operation, none showed symptoms of heart failure.

Patient no.

- 1: should manifest symptoms of both angina and a slight mitral valve insufficiency.
- 2: showed hypokinesia in the apex area together with an isolated stenosis in the left anterior descending branch of the left coronary artery
- 3, 6 :had anginal pain.
- 4: had healthy coronary arteries, but a very short circumflex artery which hampered registration on the left side.
- 5: had had an infarction more than one year before the examination.

The angiographic reproduction of the left and right coronary arteries, was used to trace the movement of the AV-plane during the cardiac cycle.

The percutaneous femoral approach according to Judkins was used. Cine-images, 30 per second, were recorded on 35 mm film. Two right anterior oblique projections (no tilt crano-caudally) of the left and the right coronary arteries were performed in each patient. The degree of enlargement was adjusted to allow reproduction of the entire heart. Routine doses of contrast fluid were given. Exposure took place at end-expiratory apnea. Angle of projection and distances, are the same for left and right side registration.

One frame in each pair of images was analysed using standard projection equipment, by drawing the atrial contour of the arteries in the atrio-ventricular groove (Fig. 4-1A,Fig. 4-1B). Ossified structures of the spine were used as points of reference. The outer contour of the heart was also drawn. Because of the very slight changes in this contour, only end-systolic and end-diastolic images are shown.

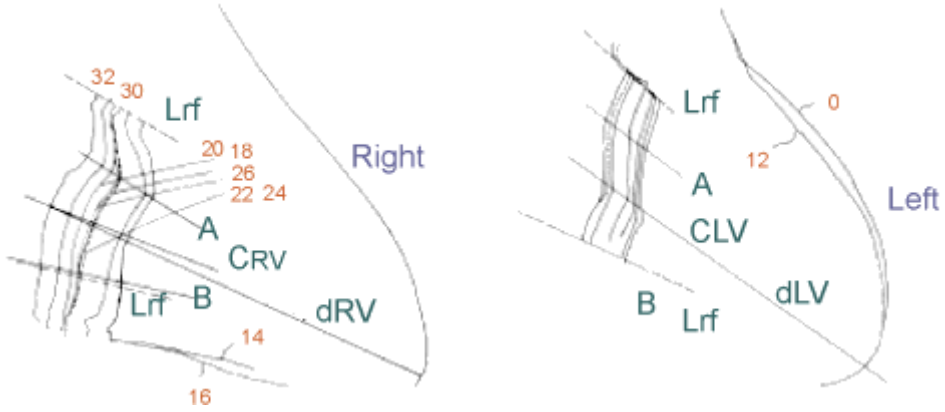


Fig 4-1 A: Coronary cine-angiography, patient no. 2. Frame numbers included.

Fig 4-1 B: Coronary cine-angiography, patient no. 2. Frame numbers included.

Left: Lrf: line of reference CRV: central line, left side dRV: maximal distance apex - valve plane on left side

Right: Lrf: line of reference, CRV: central line, right side dRV: maximal distance apex - valve plane on right side

Lines of reference (Lrf, dashed) (Fig. 4-1A, Fig. 4-1B) were drawn through points in the coronary artery walls, enabling measurement of the movement of the valve plane edge at different positions. The points were selected with respect to ease of identification e.g., at branching or discontinuities. Two central lines (C) were defined:

- one for the left side (CLV) through the point halfway between the left coronary ostium and the crux in the circumflex coronary artery (not shown in the figure).
- one for the right side (CRV) through the point halfway between the right coronary ostium and the inferior part of the right coronary artery.

Directions of lines C were set in accordance with the respective left and right dotted lines of reference adjacent to them. Then distances thus defined were bisected by lines A and B at LV and RV.

At the point of intersection of the valve plane in its extreme diastolic position (after atrial systole) and line C, distances dLV and dRV to apex were determined. They defined the maximal length of the ventricle and were used as reference.

In most cases there was no change in the position of apex relative to reference points in the spine.

Points of intersection of the valve plane with lines A and B, were used to characterise valve plane movement. The distances travelled were measured and calculated as a percentage of the reference distance (dLV, dRV).

Valve plane movement was further visualised in points of intersections for A and B, by plotting their variation against time (Fig. 4-2A, Fig. 4-2B).

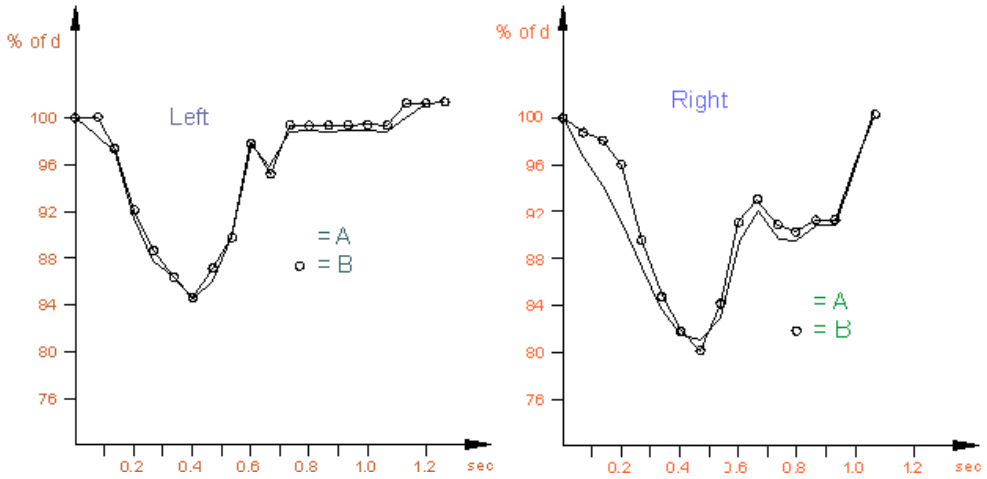


Fig 4-2 A: Movement of valve plane along line A (patient no. 2)as a percentage (%) of maximum distance between valve plane to apex (d). Fig 4-2 B: Movement of valve plane along line B (patient no. 2) as a percentage (%) of maximum distance between valve plane to apex (d).

The mean value of distances travelled by the valve plane in lines A and B (aLV, bLV, aRV, bRV) are given in Table Xa.

Variation of heart outer contour laterally and medially is given in Table Xb.

4.2 Results and Discussion

Observation of valve plane movement by CA, is based on its close morphologic association with the main right coronary artery and the circumflex branch of the left coronary artery. The main stem of the right coronary artery originates from the right sinus of Valsalva, and follows the atrio-ventricular groove. The left circumflex artery leaves the left main coronary artery, and runs in the atrio-ventricular groove in the opposite direction. The arteries are kept in place by adipose and connective tissue, which is in turn connected to the anulus fibrosus (. Fig. 3-7A-B, Fig. 3-8A-B). They may be assumed to move in close association with the valve plane. Their contrast filling is usually excellent.

Valve plane displacement, calculated as a percentage of the reference distance (dLV, dRV) in intersection of A and B (Table Xa), is affected by projection errors and possibly also by different forms of heart diseases.

Patient no. 6 was not considered when calculating the average of the LV values, because of conspicuous deviation from the rest of the group.

In an oblique projection of the long heart axis, distortion will result in reduced valve plane movement (cf. Fig. 5-9). The motion (bRV) of the atrio-ventricular plane on the right side, along line B, can be overestimated. That may be due to the form of attachment of RV at the anulus fibrosus, and the intimate attachment of the right coronary artery to RV (. Fig. 3-7A-B, Fig. 3-8A-B).

Considering the errors of the method, the displacement of the left side AV-plane (which is about 16 % of the reference distance dLV) should be regarded as an underestimated value. Especially magnification and projection errors (Fig. 5-8) and possible effects of heart disease should be considered.

The displacement of the AV-plane at the right side is considerably higher (approximately 21 %) of the reference distance dRV. Whether this value is over- or underestimated is hard to tell, due to the topographic anatomy of right coronary artery (Fig. 3-8A-B).

The effect of atrial systole (Fig. 4-2A,Fig. 4-2B) on the valve plane displacement, was evident in two patients (no. 2 and 5).

The mean value of variation in outer contour is calculated for each patient where variation is at a maximum. Values for laterally-anteriorly LV and medially-diaphragmally RV are given in Table Xb. Variation is expressed as a percentage of the reference distance dLV and dRV.

The recorded movement is the result of tangential beams in both positions. Tangential beams are, however, not parallel. Therefore the contour recorded is an enlarged one. Outer contour variation may therefore be correct, too large, or too small, depending on the positioning of the major heart axis relative to the X-ray source and detector.

In Fig. 5-9 30o oblique long axis projection is shown. This axis will appear longer then it actually is. Outer contour movement related to axis length will therefore be underestimated.

The opposite is true for a 45o oblique projection (Fig. 5-9) giving a reduced axis length.

The studies show that wall motion is greatest near the AV-plane, and that it is the medially and diaphragmatically situated contour that has the greatest variation (cf. [174]).

Movements laterally and medially almost cease near the apex.

Results laterally for patient no. 2 were omitted from Table Xb, due to an inverse movement of about 1.5 mm. The diseases of the other patients did not visibly affect outer contour variation.

If the length of the major heart axis is assumed to be 90 mm, variation of outer ventricular contour is between 1 and 2 mm.

4.3 Summary

By comparing the maximum diastolic image (atrial systole included) with the minimum systolic image, the mean value of the outer contour variation of left and right ventricle obtained. By using coronary cineangiography (in right oblique position), the mean value of the outer contour variation was found to be between 1 and 2 mm at the AV-plane. It was practically reduced to zero at apex.

In the same investigation it was found that the motion of the AV-plane was about 16 mm on the left side, and 21 mm on the right side. At least the value from the left side is underestimated, due to projection errors and underlying heart disease of the investigated group.

Chapter 5

Changes in Distribution of Heart Muscle Mass during the Cardiac Cycle, in Patients with Coronary Artery Diseases, as Visualized by Gated Thallium Scintigraphy[1]

In cooperation with Johan Virgin, M.Sc., Söder Hospital, Stockholm, SWEDEN

Changes in systolic and diastolic distribution of myocardial tissue in five adults with coronary heart disease were determined by gated thallium scintigraphy (GTS). Due to the risk associated with this method, healthy volunteers were not considered.

5.1 Material and Methods

Five patients (of ages between 54 and 64 years) with suspected coronary heart disease were examined by GTS, in conjunction with an ordinary thallium scintigraphy.

Monovalent thallium ion, T1+, can substitute for potassium ions in heart muscle. This property is used with the isotope T1-201 in thallium-201 scintigraphy (for a survey, [83]). The decay of T1-201 is recorded with a gamma camera, and yields a projection of T1-201 activity in volume elements, emanating in a rectangular grid pattern from the detector. The method is used for the detection of potassium uptake deficiency.

Mono- or multigated T1-scintigraphy is known, but has been used sparingly ([125] and lit. cited therein). With this technique we recorded images for specific portions of the heart cycle, and stored them in a data base. Superimposed images from a large number of cardiac cycles for each of the portions were replayed for analysis.

Examinations were carried out with a General Electric 400 T gamma camera and a PDP 11/34 computer, provided with an image analysis system with a Gamma 11 program (Picker Int.). In order to obtain a projection image of the heart in a plane approximately perpendicular to the long axis of the heart, the camera was provided with a slanthole collimator (slit angle 30o). The camera was set up for a modified frontal projection. Slit direction corresponded to the direction of the long heart axis. The cardiac cycle was gated on the ECG R-peak with 18 frames. A deviation of up to 15 % from the predetermined length of the heart cycle was accepted. Registration time was 35 min.

A motion sequence of the human heart obtained in this way gives the impression of a squeeze-like movement of the heart. The impression is in much the same way, as the traditional view of the pumping heart. This is for the following reason; when the heart muscle contracts (and thereby thickens) the isotope level in a dissecting plane perpendicular to the detector, will increase towards the lumen of the ventricles (cf. Fig 5-1). (The dissecting plane is approximately tangential to the ventricular walls of the heart).

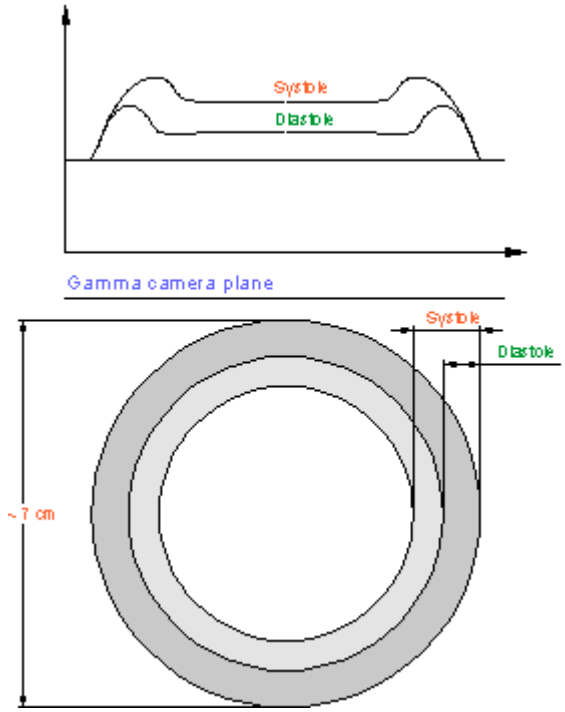


Fig. 5-1 : Theoretical systolic and diastolic gated thallium scintigraphy intensity distribution, from a cylindrical LV segment along its diameter (abscissa). (Attenuation 24 % per cm).

A computer-matched grey scale, with a constant number of grey values are to be distributed over the range zero to max intensity in each of the frames; zero always corresponds to black, and max intensity always corresponds to white. It is therefore impossible to follow variations between images by comparison of grey tones. What will be observed is merely the redistribution of grey values within each frame.

If GTS images are normalised with respect to an absolute colour scale, count density can be displayed in a uniform manner.

Subtraction was done from all frames of the grey value which by visual inspection is judged to correspond to average background and demarcation. With the help of a computer program, that resulted in a motion sequence of areas with remaining activity.

The apex and the lower lateral part of the left ventricle are now projected upon each other both in systole and diastole. The establishment of isocontours at the diaphragmal and medial part of the heart, does not allow delimitation of the outer contour of the RV. That is due to (in spite of a sampling period of 35 min) interference of background radiation from the diaphragm and statistical variation between individual frames.

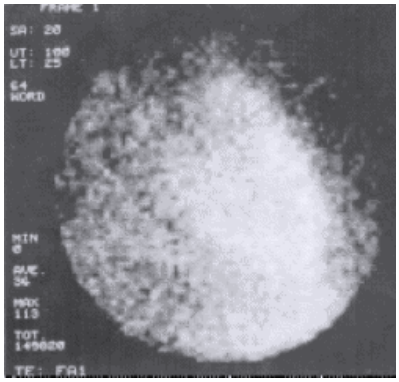
The scintillation image is normally obtained by exposure during a large number of heart beats, and thus contains superimposed information from both systole and diastole. The fact that the heart is not fixed in place over such a long time period, puts a severe limitation on the use of gated thallium scintigraphy.

Movement of the diaphragm also affects the position of the heart. T1-201 scintigraphy has a number of sources of error, the most prominent one being attenuation, which varies according to the absorptivity of the tissues in the radiation path.

Quantification is uncertain as one cannot discern between signals having been produced by strong radiation sources at depth, or by weak ones near the surface.

With the heart as the object of investigation, there may be attenuation variations because of the lungs. In this case it is not even possible to ascertain, whether or not identical radiation sources at the same distance from the detector will give identical signals.

Isocontour setting and image normalization problems could be overcome by storing image sequences tentatively identified as "pure" systolic and diastolic images. This is a way to make exposure time identical for both groups (Fig. 5-2A , Fig. 5-2B).



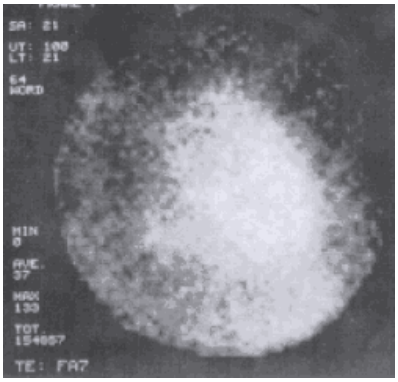


Fig. 5-2 A :Normalized GTS images. Diastolic frame

Fig. 5-2 B : Normalized GTS images. Systolic frame

This was followed by subtraction of both images from each other, without any other manipulation of data. When the diastolic image was subtracted from the systolic image, a differential image (SD) was obtained (Fig. 5-3B). Image areas not having changed their radiation density during the cardiac cycle, should have become extinguished (disregarding statistical variation). Areas with increased isotope density in the systolic image, should be positively manifest in the subtractive image. Areas with decreased isotope density in the systolic image, on the other hand, will not be identified in the SD image, as negative grey values are not permitted.

When the systolic image was subtracted from the diastolic image, another subtraction image (DS) was obtained (Fig. 5-3A). It has positive information in the areas where the SD-image has none, and vice versa.

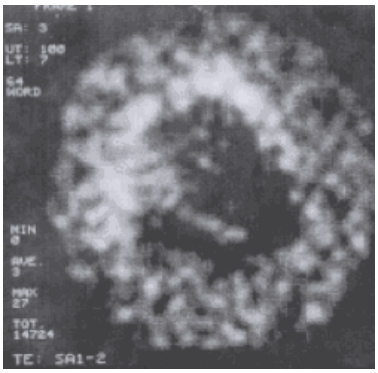


Fig. 5-3 A Subtracted GTS images. (Diastole) - (Systole) = (DS-image)

Both subtraction images demonstrated how the form and thickness of the heart muscle changed during the cardiac cycle.

5.2 Data Treatment

Data manipulation comprised in each individual case the determination of the maximally contracted image (end-systolic image) and of the maximally dilated image (late-diastolic image).

The R-peak triggering restarts the collection of counts; frames 17 and 18 will perhaps not receive counts in every heart cycle. Therefore those frames were consistently discarded.

This implied a decrease in sampling time for these frames, and thus an artificially low count level (to few counts in these frames).

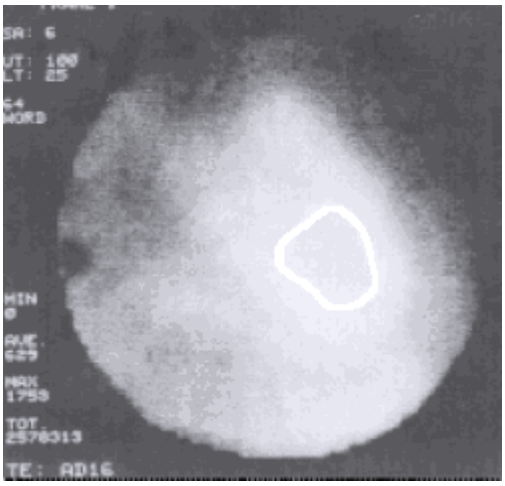
5.21 Step-by-step manipulation was as follows:

1. A supposed diastolic frame was selected (frame 16), and stored in memory 1 (Fig. 5-2A).

2. A supposed systolic frame was selected (frame 6), and stored in memory 2 (Fig. 5-2B).

3. A subtraction image (SD, systole minus diastole), obtained by subtracting the content of memory 1 from that of memory 2, was stored in memory 3.

4. In the SD-image from memory 3, a Region Of Interest (ROI) was delimited in the area corresponding to the left ventricle, ROI-LV, preferably in the apical region. This ROI was transferred to the "total" image i.e., the image obtained by superposition of the content of all 18 frames (Fig. 5-4). The computer then presented the content of each frame with respect to ROI-LV in curve format (Fig. 5-5, memory 4).



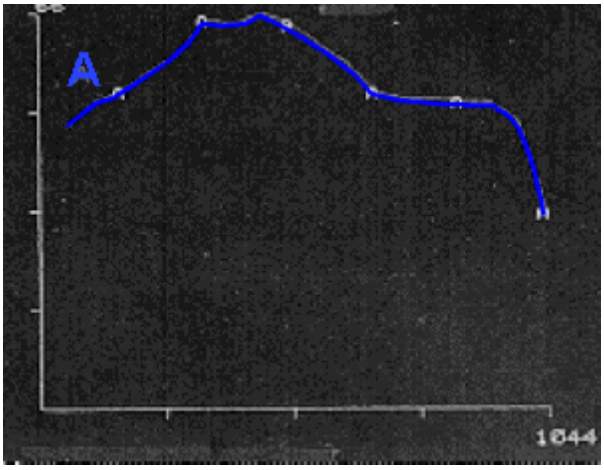


Fig. 5-4 A "total" GTS image Obtained by superposition of all 18 frames, with a transferred ROI-LV

Fig. 5-5 Graphical presentation of the count rate in ROI-LV, frame by frame.

5. Memory 4 content was recalled, and the two frames with the highest number of counts were identified.

Since sampling time for each frame was comparatively long with respect to muscle movement, a new identification was made. These two images, which were alternately subtracted from each other, were recorded. The image that was thereby recognized to have the most concentrated activity distribution within

the ventricular area was chosen as the definitive systolic image. It replaced the supposed systolic image in memory 2.

6. A new operation was aimed at the identification of the frame corresponding to the maximum total volume of the ventricles. Frames 16, 17, 18 and 1 represent the part of the cardiac cycle in which total ventricular volume reaches its maximum.

Frames 17 and 18 had to be discarded, as mentioned. Due to the length of sampling period, Frame 1 may encompass two stages:

- a stage at which ventricular volume has a maximum (due to atrial systole)
- another stage at which it already is decreasing because of the onset of ventricular systole.

In order to decide which of frames 1 and 16 represents the maximum ventricular volume stage, the respective images were compared by alternate subtraction (see above). The image showing maximum distribution of remaining ventricular activity was thereby selected as the definitive diastolic image. It replaced the supposed diastolic image in memory 1.

7. Images in memory 1 and 2 were normalized with respect to an absolute grey scale (Fig. 5-2A , Fig. 5-2B).

8. Definitive diastolic and systolic images were recalled from memory 1 and 2, respectively. The systolic image was subtracted from the diastolic image, and the DS-image obtained (Fig. 5-3A) was stored in memory 5.

9. Definitive systolic and diastolic images were recalled again. The diastolic image was subtracted from the systolic image, and the SD-image obtained (Fig. 5-3B) replaced the supposed SD-image in memory 3.

10. The differential SD-image was recalled. It displayed changes in the position of parts of the heart muscle between systole and diastole. Parts of the ventricles that gain in muscular mass in systole are prominent. They were delimited manually by means of a joystick both from the background and from each other.

Thus an area A corresponding to a part of the left ventricle, and an area B corresponding to a part of the right ventricle were identified. They were called ROI A and B, and together with the SD-image (Fig. 5-6) stored in memory 6.

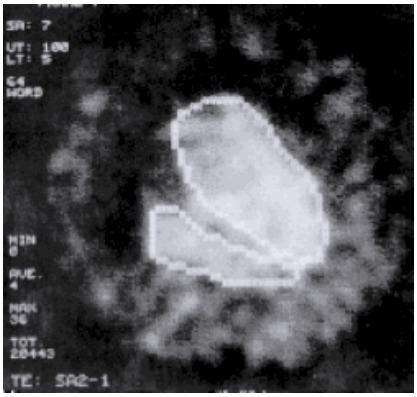


Fig. 5-6 SD-image with ROI A and B delimited.

11. The SD-image was recalled and dark areas (corresponding to lighter toned ones in the DS-image) showing loss of muscular mass in the systolic phase, were delimited as above.

ROI F was delineated on free hand to show the displacement zone of the right part of the AV-plane and ROI C of that of the left.

ROI D and E were delineated on free hand in order to establish zones of outer contour regions A and B.

Furthermore, a typical background area was chosen arbitrarily and designated ROI G.

12. All ROI's were superimposed on the DS-image (Fig. 5-7A) and SD-image (Fig. 5-7B).

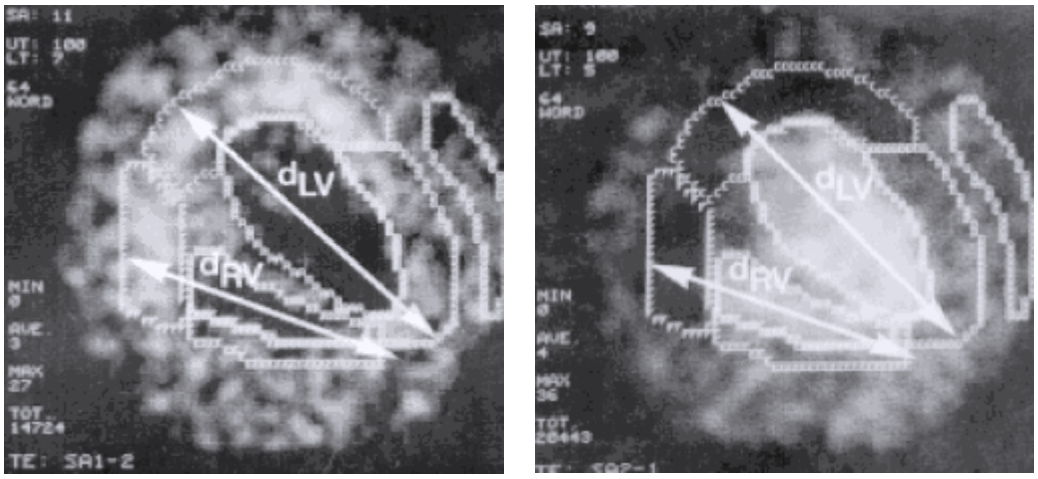


Fig. 5-7A : DS-image All ROI's delimited on the subtracted images, with major heart axis dLV and dRV inserted.

13. All frames were analyzed with respect for total activity for every ROI. Results were given in diagram form (Fig. 5-8) and were stored in memory 7.

5.3 Results and Discussions

A Change in intensity over the entire cardiac cycle for one specific ROI, implies that the muscular mass pertaining to this ROI must have undergone cyclic changes. Another explanation is that the absorptivity of tissues affecting the radiation recorded could have varied.

It is evident from Fig. 5-8 that ROI A and B increase at systole, and that ROI C and F decrease. ROI D and E are rather constant over the entire cardiac cycle as is background ROI G which, however, has a significantly lower intensity.

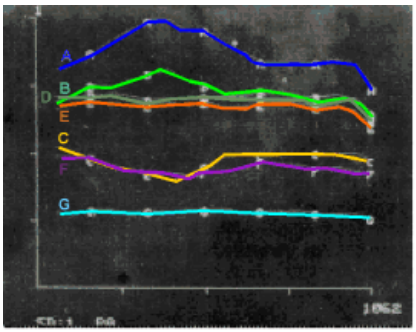


Fig. 5-8 Graphical presentation of the activity in all ROI's frame by frame, delimited in the DS- and SD-images.

The reciprocity of systolic increase of ROI A and B, and of systolic decrease of ROI C and F. That could imply that A and B are approaching the collimator, and that C and F are receding. This possibility is however ruled out by the constancy of ROI D and E. The intensity recorded indicates furthermore the presence of substantial muscular mass.

A better explanation is that the heart is contracting in systole mainly by the AV-plane moving towards the apex. The outer form of the heart is thus essentially unchanged (Fig. 5-7A , Fig. 5-7B). Tissues adjacent to the AV-plane at its atrial side, together with in-flowing blood, fill up the fictive "free volume" generated behind the moving AV-plane. As these areas are rather low in T1-201 content, they will not show up in the GTS images, and thus do not interfere with the present analysis. ROI D and E represent a part of the heart wall, with muscular mass present both in systole and diastole.

The area between ROI A, B, C and F is a region of very complex anatomy. This is due to the base of the pulmonary artery and the base of the aorta joining the heart at this point. The region is being in rocking motion, coupled to the displacement of the AV-plane.

Furthermore, the volume of the right ventricle is superimposed onto the ventricular septum, which is seen in an almost cross-sectional view; for this reason, the radiation emanating from the septum should be substantially attenuated. If these interference's were not present, one might expect to find a ROI for the septal region similar to ROI C and D due to the cylindrical symmetry of the left ventricular septum.

The shapes of region C and of the zone between ROI A, B, C and F is a result of the specific projection of the heart. The AV-plane is perpendicular with respect to the long heart axis and nearly parallel to the left anterior chest wall. Besides, the camera optical axis can only be made to deviate by approximately 30o from the normal right anterior oblique direction. Therefore the movements will appear in shortened perspective, and the AV-plane movement will become distorted in the DS-image (Fig. 5-9). It is the same as outlined in connection with coronary cineangiography (Chapter 4).

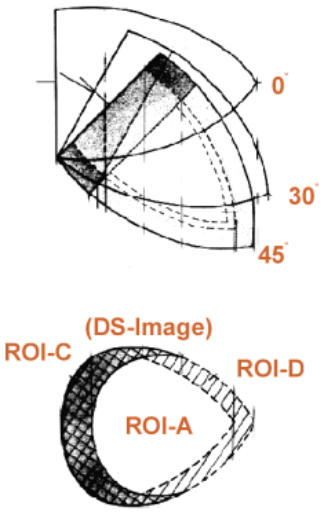


Fig. 5-9 : LV skew projection, 30o and 45o, with respect to major LV axis. Projection distortion in DS-image. ROI-C dimension in long heart axis direction: in 0o is ROI-C uninfluenced, in 30o reduced and in 45o reduced. Long heart axis: in 0o uninfluenced, in 30o enlarged and in 45o reduced.

In a position where the recording area of the gamma camera is parallel to the long axis of the heart, there will be a result of a DS-image and a SD-image (as presented in Fig. 5-10).

Sources of error for GTS are related to projection and to the definition of movement. Errors of projection may vary depending on the position of the heart relative to the gamma camera. The errors will have a tendency to yield values that are to low for AV-plane displacement (Fig. 5-9).

The difficulty in defining the positional extremes, in due to the low number of counts per image (cf. Fig. 5-6, authentic image of Patient no. 3).

Within the scope of GTS precision, the outer heart contour was observed to remain motionless in all patients. A further confirmation is provided by the constancy of ROI's D and E (Fig. 5-7A , Fig. 5-7B).

It was a small number of examined patients and a possible influence of the heart disease. In spite of that, displacement of the AV-plane was calculated as a percentage of the reference distance (major axis) dLV and dRV (Fig. 5-7A , Fig. 5-7B).

The mean values of the AV-plane displacement at RV (22.8 %) and LV (20.1 %) are given in Table XI.

If the major axis length is set to 90 mm (corresponding to a normal heart), AV-plane displacement at LV will be 19 mm and at RV 22 mm. This coincides with the corresponding values 21 mm respectively 25 mm obtained from healthy subjects using echocardiography (Chapter 3), and 16 mm respectively 21 mm in coronary patients using coronary angiography (Chapter 4).

5.4 Summary

Two frames of the heart, obtained by gated thallium scintigraphy, one in diastole and one in systole, were compared. No outer contour variations of the left and right ventricle were detected.

The only detectable changes in the subtraction pictures were the displacement of the AV-plane, about 19 mm on the left side and 22 mm on the right.

Due to projection errors and the underlying heart diseases of the investigated group, these results are considered to be underestimated.

Chapter 6

Echocardiography of Ventricular Septum and Left Ventricular Posterior Wall, in Volume- or Pressure-Overload-Related Heart Defects

A number of patients with manifest heart disease verified by auscultation, phonocardiography, angiography and heart catheterization were examined. The goal was to use echocardiography in order to compare the variation of outer ventricular contour and of endothelial surfaces of the ventricular septum with that in healthy subjects.

6.1 Material and methods

Six patients were selected among a number of patients examined in the Department of Clinical Physiology at Södersjukhuset, Stockholm, Sweden. These patients had extreme volume- or pressure-overload-related heart defects: three had isolated Atrial Septum Defect (ASD), one had Mitral valve Stenosis (MS), one had Mitral valve Insufficiency (MI) and one had Aortic valve Insufficiency (AI). Another patient with ventricular premature beats was also selected.

Echocardiography M-mode registration was carried out, as described in Chapter 3.

The series of events (a-k) was the same as in studies of healthy subjects.

Points of dissection of the corresponding event lines with curve 1 and 4 were also determined. It should be noted that the examination with the diseased patients were carried out in 1981 and 1982. At that time, determination of Atrio Ventricular (AV)-plane movement was not considered to be of major comparative interest, and measurements corresponding to those in points M2, M3 and M4 (Fig. 3-6A-E), were therefore not included.

The M-mode images were recorded and reconstructed in the same way as the M-mode image in Fig. 3-1A , Fig. 3-1B , Fig. 3-1C. Each defect, except for atrial septal defect, is represented by one patient.

6.2 Results and Discussion

6.21 Atrial Septal Defect

Fig. 6-1A , 6-1B depicts one authentic and one reconstructed M-mode registration of an atrial septum defect (ASD).

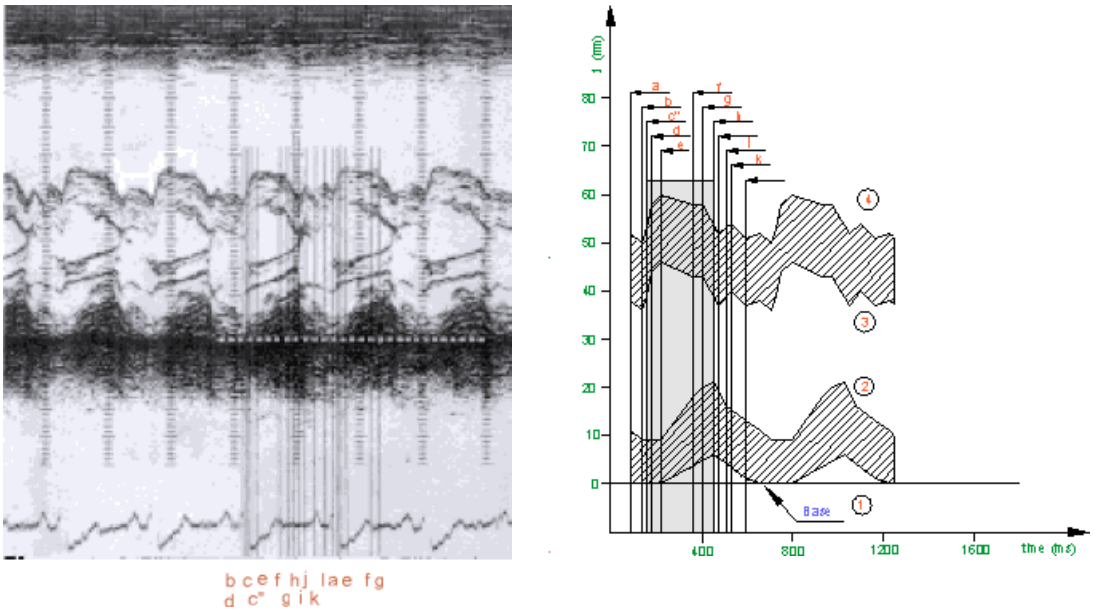


Fig. 6-1A Authentic M-mode EC registration of an atrial-septal defect (ASD), with event lines a to l added.

Fig. 6-1B : Reconstructed M-mode EC registration of an atrial-septal defect (ASD), with event lines a to l added.

Event c was absent at Ventricular Septum (VS). This should be due to that, the VS at the closing of the mitral valve is moving rapidly in the direction of Right Ventricle (RV).

A new event line (c") can be drawn through a point at which septal movement towards RV suddenly ceases, probably due to the closing of the tricuspid valve.

Another new event line, l, which sometimes is also seen in healthy people as a "ringing" phenomenon of the ventricular septum, is marked. It is caused by the dynamic influx forces. It is prominent and was therefore marked as a specific event.

The M-mode images show the VS bulging into Left Ventricle (LV) from event i through b. At the ventricular depolarisation, and even before the closing of the mitral valve, the ventricular septum rapidly adopts its predetermined systolic shape. Fig. 6-2A , Fig. 6-2B displays diastolic and systolic two-dimensional images from the same patient. VS is seen to have lost its convex shape towards RV in diastole (Fig. 6-2A).

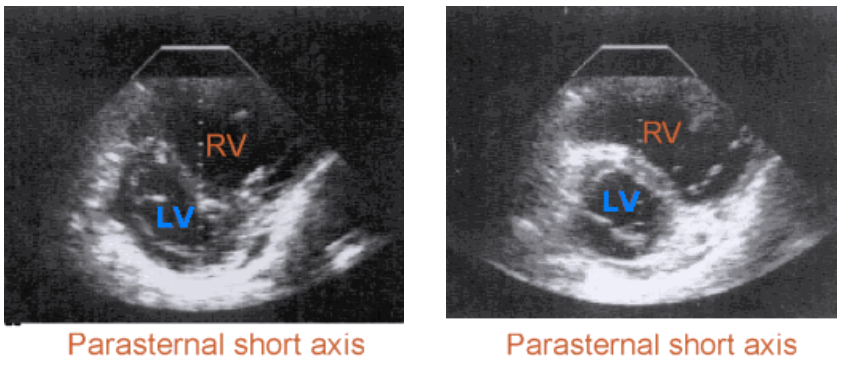


Fig. 6-2A Diastole Two-dimensional image from the same patient as in Fig. 6-1A , Fig. 6-1B (ASD).

Fig. 6-2B Systole Two-dimensional image from the same patient as in Fig. 6-1A , Fig. 6-1B (ASD).

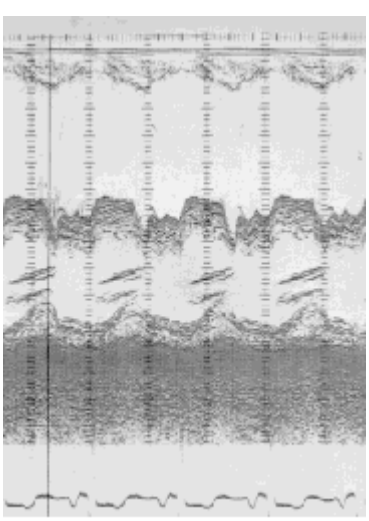
When the AV-plane in the normal heart is drawn towards the apex in ventricular systole, the atriums is filled. Left atrial pressure will normally be somewhat higher than pressure in the right atrium. This makes the VS bulge towards RV also during diastole.

With an ASD, this balance is disturbed. Blood ejected from RV into the pulmonary circulation will pass through LA and the ASD, into the expanding RA. The AV-plane is travelling around 25% further in the RV than in the LV. Therefore the moment of inertia of the blood influx in diastole will be greater at RV than at LV; pressure equilibration between the ventricles will take place by deflection of VS towards LV early on in diastole. Communication between the atria will have a pressure-equalising effect.

In the preceding chapters, it has been shown that the outer heart contour in a healthy person changes very little during the cardiac cycle. ASD and other vitia reported below, display the same kind of LV posterior wall displacement as is seen in healthy subjects. As explained earlier, the observed displacement of 5-6 mm must be exaggerated, due to the curved form of the posterior wall segment in question (Fig. 3-10).

Look at the motion of VS in M-mode registration (Fig. 6-1A , Fig. 6-1B) and the two-dimensional images in Fig. 6-2A , Fig. 6-2B. That demonstrate unambiguously, that there are no substantial elastic forces working in diastole, to keep its form convex with respect to RV.

Increased volume work and, in the present case, also increased pressure work (because of pulmonary hypertension), causes a delay of RV systole. This is reflected in M-mode registration by VS being forced into LV at event i. It causes the mitral valve (which normally opens immediately after the aortic valve closes) to remain closed until RV pressure and volume transmitted by VS is withdrawn. Now the forces affecting the AV-plane of the left atrium, can complete the filling of LV.



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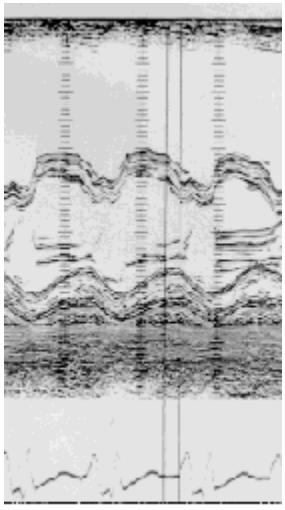


h

A prolonged RV ejection period, coupled with a volume-delimiting VS movement towards LV, causes "excess" muscle length in short and long axis direction. That permitting the part of the AV-plane attached to VS to bulge upwards. This deformation increases the end-systolic residual volumes on both RV and LV.

Before RV pressure has decreased enough to allow the tricuspid valve and the mitral valve to open (by pressure transmission to LV in this situation) something happens; the increase of residual volumes, which for the LV are compensated for by the overriding VS, prevents the myocardium from moving upwards along the pericardial-epicardial interface. That is due to the close connection of LV-wall and VS (V will be affected, see Chapter 11).

The ventricular septum does not show a prominent fast diminution phase in diastole. That must be caused by the absence of a pressure gradient between the right and left side of the heart. The result is excess VS myocardial tissue of high plasticity.

Proof of this high compliance is provided by EC analysis in event l. It is also provided by VS taking up its systolic form already in pre-systole by a rapid movement (even before the closing of the mitral valve).

The above observations demonstrate that the ventricular septum influences the pressure-volume relationship between LV and RV.

The gripping heart pumping mode causes blood to pass via the ASD, as long as the pressure in the pulmonary vein surpasses pressure in the superior and inferior venae cava. Moreover, as long as the LV is working at higher systolic pressures than the RV, a paradoxical movement of VS in systole [179] imparts a greater ejection fraction to RV, and a reduced one to LV.

6.22 Mitral Valve Stenosis

Fig 6-4A , 6-4B shows an authentic and a reconstructed M-mode registration of a severe mitral stenosis (MS).

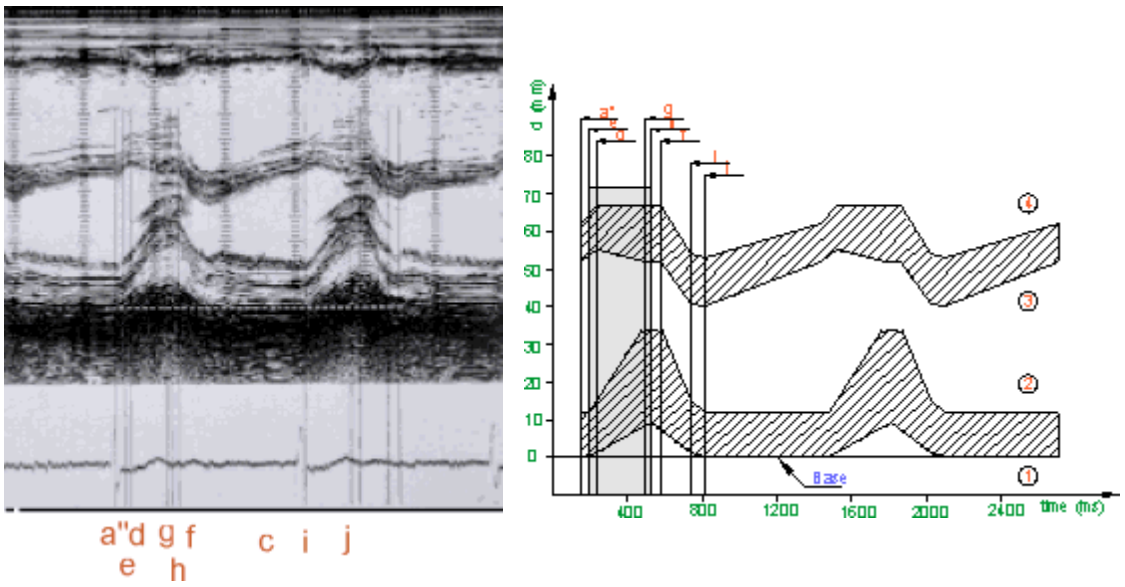


Fig. 6-4A Authentic M-mode EC registration of a mitral stenosis (MS), with lines a to l added.

Fig. 6-4B Reconstructed M-mode EC registration of a mitral stenosis (MS), with lines a to l added.

The patient had a complete atrio-ventricular block. Therefore event a has to be substituted by a ", which dissects VS and the posterior wall just before ventricular depolarisation becomes effective. (In a healthy person this should occur between events b and c.)

In end-systole and at the onset of diastole, the kinetic energy built up during systole begins to push the AV-plane upward and to replace the volume freed by reduction of wall thickness. At RV, the upward forces can act unrestrained. At LV, this upward force is hindered by stenosis of the mitral valve. The sudden restriction to flow is sometimes audible as an opening snap.

MS reduces LV dynamic forces relative to those effective at RV, and forces VS into LV, making event i very distinct.

The bulging of the ventricular septum towards LV also effects blood in LV. In combination with the blood entering through the stenosis, that pushes the left part of the AV-plane upwards, as shown by the area between event h and j. (In this sequence the walls are getting thinner.)

The return of the posterior wall to end-diastolic thickness, begins at the point of intersection for event l.

The pressure of the pulmonary circulation, normally suffices to build up a pressure gradient necessary for the return of VS to its normal pre-systolic form; this is in contrast to the ASD case, and this function depends on the severity of the stenosis and the length of diastole.

Simultaneously, a gradual thinning of the ventricular septum is observed (Fig. 6-4A , Fig. 6-4B) between events l and a", which was not seen in the ASD (Fig. 6-1A , Fig. 6-1B). The posterior wall does not show any movement during these events.

If the length of diastole does not suffice for the return of VS to its normal pre-systolic form (either because of extra-systolic beats or elevated heart rate), following happens; the ventricular septum will act in the manner of a membrane pump driven by the excess pressure in LV, generating an increased stroke volume in RV. The stroke volume of LV will be correspondingly reduced.

By this mechanism, the power resources of LV may drive RV, as long as RV walls and adjacent tissues are coping with the increased strain. Pressure and flow in pulmonary circulation will increase and be transmitted to the mitral stenosis, whereby flow through it will in turn increase, until VS reaches its pre-systolic "neutral" form. It is evident that this action of VS will provide for pulmonary hypertension and pulmonary edema at higher pulse rates.

Detection by echocardiography of paradoxical VS motion in patients with MS has been reported [172, 178].

6.23 Mitral Valve Insufficiency

Fig. 6-5A , 6-5B shows an authentic and a reconstructed M-mode registration of severe mitral insufficiency (MI).

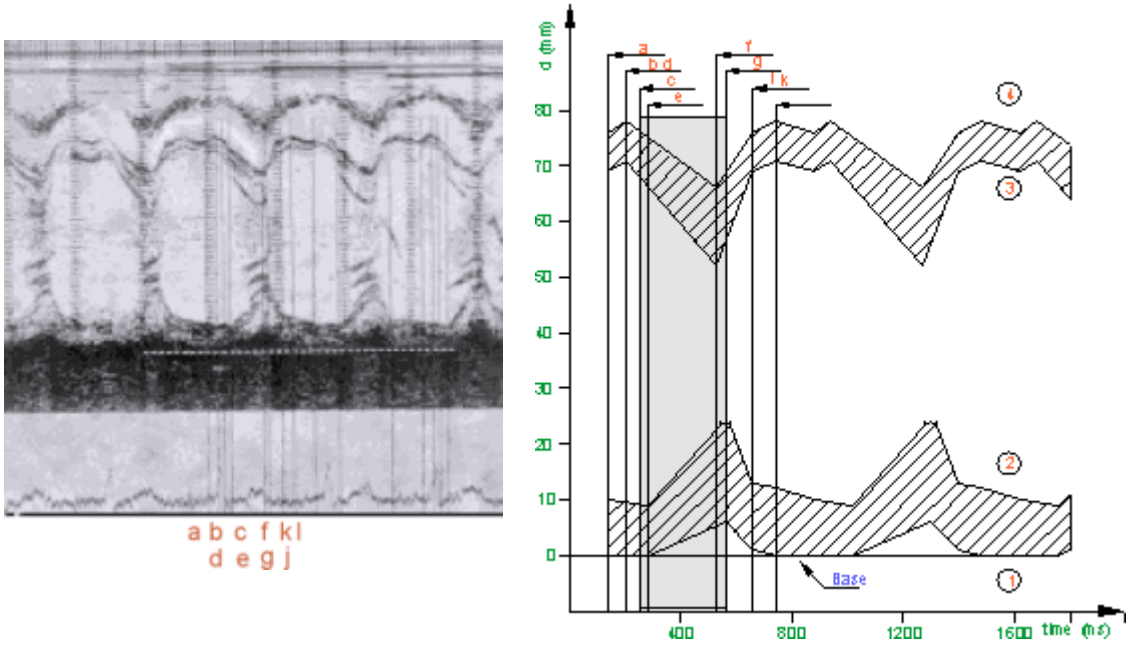


Fig. 6-5A Authentic M-mode EC registration of a mitral insufficiency (MI), with lines a - l added.

Fig. 6-5B Reconstructed M-mode EC registration of a mitral insufficiency (MI), with lines a - l added.

In MI, the left atrium is filled both from the pulmonary veins and through the leaking mitral valve, when the AV-plane moves toward the apex during systole. The need for the flow-levelling effect of the pulmonary veins is thereby reduced. The left atrium and pulmonary veins encounter increased filling pressure, deflecting the inter-atrial septum as observed by oesophageal EC [114]. This static pressure may surpass the dynamic forces generated by the AV-plane in ventricular systole.

The ventricular septum is the part of LV that in the relaxation phase in early diastole has the weakest back-up of all LV wall structures. VS is thus rapidly dilated and pushed towards RV (event k).

With the onset of ventricular systole, LV adopts its circular form (in the plane perpendicular to the major LV axis), as shown by event f in the M-mode image. The result is a contribution to LV stroke volume (and a corresponding decrease in RV stroke volume).

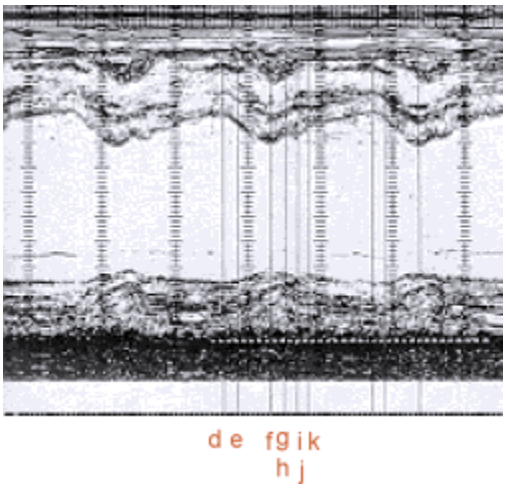
MS entails large variations in filling pressure in LA, depending on heart rate and the movement of the AV-plane in ventricular systole.

MI though, results in a more constant filling pressure, rather independent of heart rate as long as there is no acute heart failure. Atrial contraction, which adds to ventricular filling by raising the AV-plane, may disguise incipient MI until eventually atrial fibrillation sets in.

Echocardiography is not considered particularly useful in the assessment of rheumatic mitral regurgitation [41]. Left atrial overload affecting (among other things) the inter-atrial septum, has caused MI severity-assessment to be concentrated upon deflection of the atrial walls [51].

6.24 Aortic Valve Insufficiency

Fig. 6-6A, 6-6B shows an authentic and reconstituted M-mode registration of a severe aortic insufficiency (AI). The configuration change of VS (from diastole to systole) is best described by sector scans (Fig. 6-7A , Fig. 6-7B).



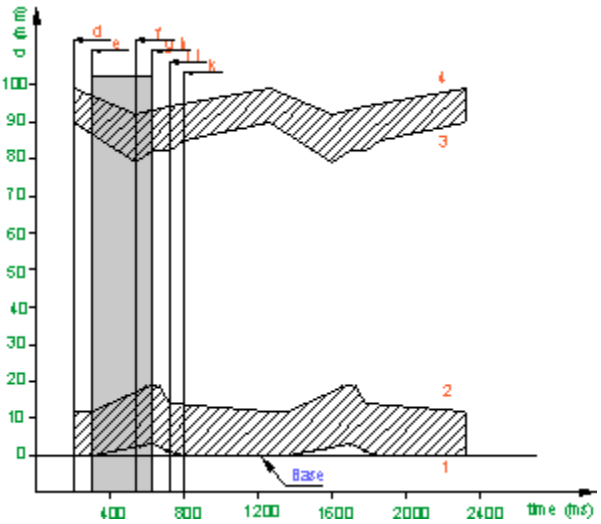


Fig. 6-6A Authentic M-mode EC registration of an aortic insufficiency (AI), with event lines a - l added.

Fig. 6-6B Reconstructed M-mode EC registration of an aortic insufficiency (AI), with event lines a - l added.

When the endothelial surface of the septum at RV was kept under observation from event f onward, it was found that during diastole VS increasingly bulged into RV while simultaneously thinning. No concurrent change of the outer contour of the radially shrinking posterior wall was observed.

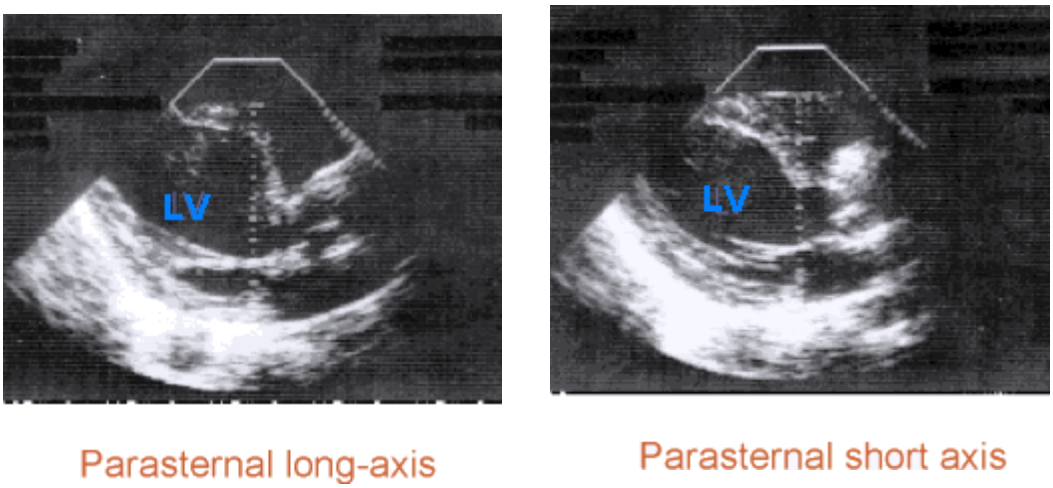


Fig. 6-7A Diastole Two-dimensional images from the same patient as in Fig.6-6A (AI).

Fig. 6-7B Systole Two-dimensional image from the same patient as in Fig.6-6B (AI).

It is apparent from this behavior, that even in a static pressure situation, the valve plane will move away from the apex without the outer contour of the ventricles changing.

But there will nevertheless be a marked change in the shape of VS.

Events a, b and c could not be identified (no ECG was recorded in this case).

A vigorous septal movement began at event d, lasting until event f. This mode of movement in systole, and its attenuation in diastole, must be the result of the aortic insufficiency with its inherent increase in LV diastolic pressure. The septum thereby imparts an extra strike volume increment to LV, and correspondingly reduces systolic output of RV.

An increase in heart rate should not only reduce the effect of this insufficiency, but also increase RV stroke volume.

6.25 Ventricular Premature Beats

The effect on VS of premature beats in an otherwise healthy person, causing considerable distress, is shown in Fig. 6-8.

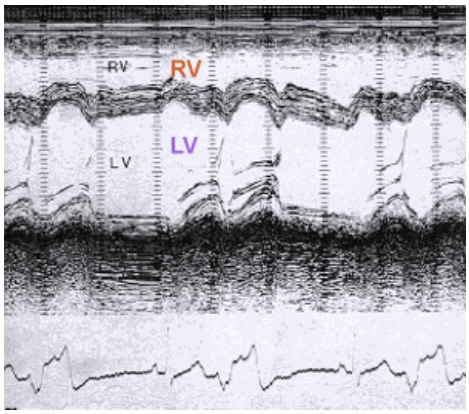


Fig. 6-8 M-mode EC registration showing the displacement of VS of a healthy person experiencing premature beats.

The ventricular septum has not become depolarised i.e., stabilised, before other parts of LV begin to contract. VS moves in the direction of the right ventricle and thins out, while the posterior wall exhibits normal behaviour.

One would expect the movement of the ventricular septum to depend on the site at which the premature beat arises, and on its timing relative to a normal depolarisation [44, 132, 133]. It may therefore have an impact on the stroke volume of both RV and LV.

There are two conceivable situations in the present case. In the first one, deflection of VS into RV transmits force and volume from LV to RV, increasing RV stroke volume. In the other one, a premature ventricular beat causes a sluggish septal movement in apical direction and a poorly stabilised AV-plane, which results in reduced stroke volume.

Possibly it is the sudden perturbation of circulatory equilibrium, that is felt in the form of immediate discomfort.

6.3 Summary

Fig. 6-9 displays a schematic summing-up of the movement of the endothelial septum surface at RV, curve 4, in the heart defects described above. This movement is compared with that of a healthy person (Fig. 3-2), marked in Fig. 6-9 with a dotted line. The cardiac cycle in Fig. 6-9 was divided into five phases:

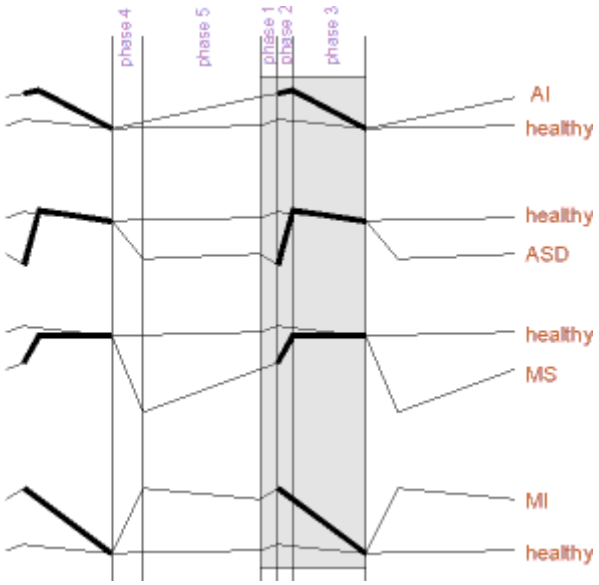


Fig. 6-9 Movement of Ventricular Septum endothelial surface at Right Ventricle in:

Aortic Insufficiency (AI), Atrial Septum Defect (ASD), Mitral Stenosis (MS), Mitral Insufficiency (MI)

Dotted lines show corresponding movement in a healthy person. Phase lines 1-5 added.

- An atrial systolic phase delimited by events a and b (or a'')
- An early-systolic ventricular phase circumscribed by events b (or a'') and d or e, whichever turns out to be the largest
- A late-systolic ventricular phase delimited by events d, e and f
- An early-diastolic phase delimited by events f and i, k or l, whichever is the latest to occur
- A late-diastolic ventricular phase delimited by events i, k, l and a (or b or a'').

No corresponding summing-up for epicardial movement mode (curve 1) in the various defects was made, since it does not deviate from that of a healthy person.

The modes of motion found in the above cases of severe heart defects, are in agreement with the theory; when the ventricles are pumping at essentially constant outer form, VS in diastole adopts the form and position according to the prevailing pressure gradient between the ventricles.

In systole, VS strives to adopt its position as part of the circular LV wall, that is, its predetermined systolic position. If the diastolic and the systolic positions of the septum are not identical, the septum will behave like the membrane in a membrane pump, and add to the stroke volume on the side opposite that to which it had moved in diastole.

Chapter 7

The Self-Regulating Double-Pump: A Working Model of the Human Heart

The findings in chapter 6 initiated the design of a heart model consisting of two pumps in series working with a common displaceable wall (cf. the ventricular septum of the human heart). To demonstrate that a double-pump can work according to the basic balancing principle established for the human heart in situ (Concept 2, see Chapter 2), a self-regulating prototype was built [108]. It had the inlet and outlet of the respective pump halves connected in the same way that the human heart fits into the circulation system.

The pump is shown in Fig. 7-1 and Fig. 7-2, and its design principles in Fig. 7-3. Its working mode will be explained with reference to Fig. 7-3. Numbers in the text (identifying individual pump parts) refer to Fig. 7-2 and/or Fig. 7-3.

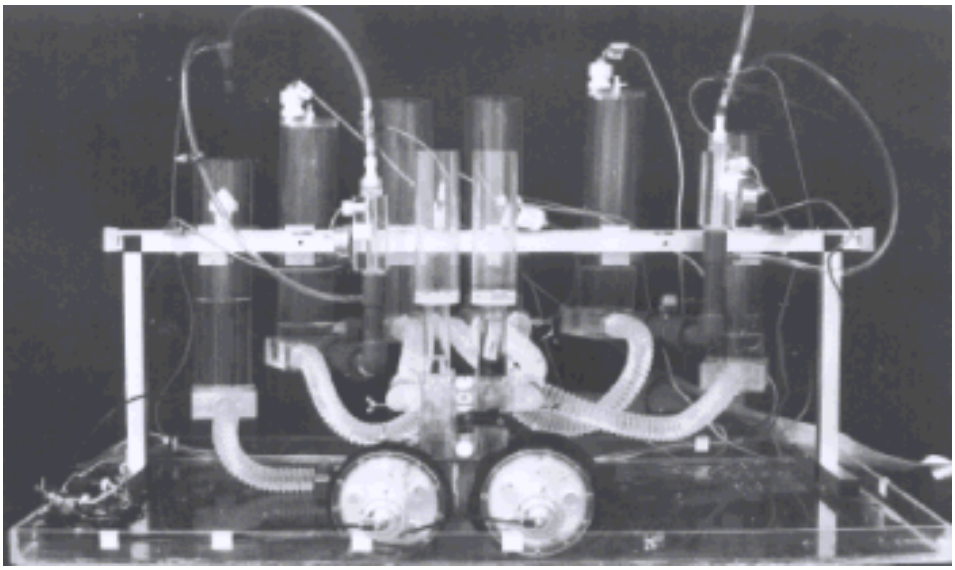


Fig. 7-1: The self-regulating double-pump Prototype for demonstration of effects of different heart defects on circulation

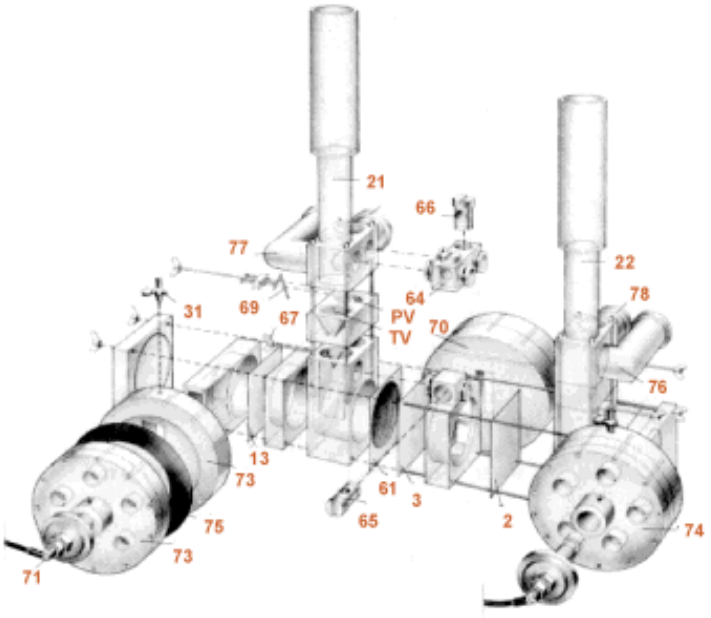


Fig. 7-2 The self-regulating double-pump Identification of parts: point and click on figure or, see text

2 septal membrane at chamber L, 3. septal membrane at chamber R, 13. RV-wall membrane, 21. expansion vessel at right inlet, 22. expansion vessel at left inlet, 31. valve used for water filling and air reducing of the activating volume, LV, 61. septal membrane at chamber R displacement limiting means (Cu-gauze), 64. valve for ASD-simulation ,65. valve for VSD-simulation, 66. valve for DA-simulation, 67. wedge for TI-simulation and V-formed restricting means for TS-simulation, 69. wedge for PI-simulation and V-formed restricting means for PS-simulation ,70. SV activation pressure transducer (PAC-SV), 71. pressurised air cylinder (PAC),73. RV activation pressure transducer (PAC-RV), 74. LV activation pressure transducer (PAC-LV), 75. RV activation pressurised unit transducing membrane ,76. chamber L inlet, 77. chamber R inlet, 78. chamber L outlet, 79 chamber R outlet ,TV "tricuspid valve", one-way valve at inlet of room R , PV "pulmonic valve", one-way valve at outlet of room R

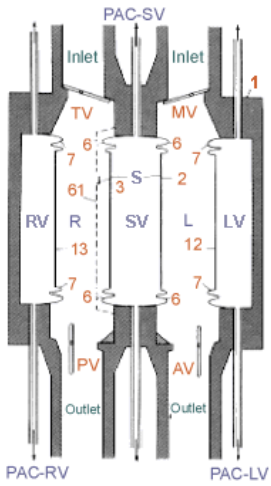


Fig. 7-3: The self-regulating double-pump Identification of parts: point and click on figure or, see text

1. Rigid outer casing, 2. Septal membrane at chamber, 3. Septal membrane at chamber R,6.Highly flexible part of membrane 2 and 3,7. Highly flexible part of membrane 12 and 13,12. Laterally movable wall portion (membrane) in chamber R,13. Laterally movable wall portion (membrane) in chamber L,61. Septal membrane at chamber R displacement limiting means (Cu-gauze),AV. "aortic valve", one-way valve at outlet of room L ,L. Left ventricle,LV. Left volume,MV."mitral valve", one-way valve at inlet of room L,PAC-LV. LV activation pressure transducer, PAC-RV. RV activation pressure transducer,PAC-SV. SV activation pressure transducer ,PV. "pulmonic valve", one-way valve at outlet of room R,R. Right ventricle,RV. Right volume,S.Partioning wall, corresponding to ventricular septum ,SV. Septal volume, TV."tricuspid valve", one-way valve at inlet of room R

7.1 Design and Working Principles

The pump is mounted in a rigid outer casing 1. A partition-wall S (corresponding to the ventricular septum) is arranged in the casing. S has semi-flexible, membrane-like sections 2 and 3. The spacing (septal volume, SV) can be increased with the aid of some external means e.g., by compressed air or in this case by injection of water. Injection of water is effected by a piston driven by pressurized Air Cylinder, PAC (71). The piston, consisting of a membrane with a rigid centre part, has a constant stroke length. It displaces a certain amount of water back and forth between the activation pressure transducer (73) and SV. The total system displace water back and forth to SV (septal volume), RV (right volume) and LV (left volume), is called PAC-SV, PAC-RV and PAC-LV.

The wall structure S divides the space within the casing into two chambers, L and R (corresponding to the left and right ventricles). Each chamber is provided with an inflow flap valve, MV (corresponding to the mitral valve) and TV (corresponding to the tricuspid valve), and an outflow flap valve, AV(corresponding to the aortic valve) and PV (corresponding to the pulmonary valve).

When the pressurized air cylinder PAC-SV connected to the spacing between membranes 2 and 3 is activated, they move apart laterally by the force of the injected water. The rising of pressure in chambers L and R will cause the inflow valves MV and TV to close and the outflow valves AV and PV to open.

If the prevailing external pressures of the outflow valves are different, one outflow valve will open before the other, and the corresponding chamber will begin to empty before the other.

The other chamber will not start emptying until either the outlet pressures become equal, or the respective flexible membrane (6) has been extended to the limit of its movement. (That means e.g., by mechanical restriction between membranes 2 and 3 or externally thereof).

When water in SV is removed, valves AV and PV will close provided there is a generally higher pressure maintained at the outflow side than at the inflow side; valves MV and TV will open, whereupon chambers L and R will take in more fluid.

If the prevailing pressures at the inflow side of the pump are different, membranes 2 and 3 will move towards the chamber with the lower inflow pressure. It will thus decrease in volume.

Provided that the pre-set ranges of movement are the same for both membranes, the membrane at the chamber with the smaller volume will thus be closer to the limit of its movement in the direction of that chamber. At the next activation of PAC-SV, that membrane will be displaced until its expansion limit, provided enough water is injected. Further expansion of volume SV can only be achieved by displacement of the other membrane. In such a situation, more fluid will be expelled from the chamber with the initially larger volume, no matter what the prevailing pressures are at the outlets of chambers R and L.

When the double-pump is connected to a circulatory system in which the same fluid flows in two circuits i.e., a system corresponding to circulation of blood in humans, the filling mechanism will automatically achieve a balance of the volume displacements effected.

For example, should one chamber pump out "too much" fluid, this "surplus" will be returned to the fluid flowing to the other chamber, so in order to compensate. This means that a balance in volume is achieved without any complicated regulating mechanisms.

The pump effect can also be supplemented by providing each of the ventricle-simulating chambers with additional laterally movable wall portions (membranes). These are named 12 and 13, and are arranged by highly flexible membranes 7 attached to the casing 1. Volumes LV and RV between membranes 12 and 13 and

the casing are connected to pressurized air cylinders PAC-LV and PAC-RV. They can be activated individually, to inject a specific volume of water as described for PAC-SV.

The expansion of the volumes delimited by membranes 12 and 13 towards L and R, respectively, will not have any effect on the regulating function of the pump, but will only contribute to its total stroke volume.

In the experimental model, chamber L corresponds to the left ventricle in man, and has thus to work against a higher pressure than chamber R. Copper gauze 61 bulging towards R restricts the movement of membrane 3 towards chamber R.

Membranes 2, 3, 12 and 13 have been made by pouring fast-setting silicone resin into appropriate moulds, in order to obtain the flexible quality of the membrane 6. Each pressure-transmitting chamber, SV, LV and RV, has been arranged to displace 50 cm3 fluids maximally. This means that in a situation where left and right inflow pressures are identical, efflux from each of the chambers L and R will be 75 cm3.

The experimental model has also been provided with a means of preventing the complete closure of each of the valves, for simulation of various types of valve insufficiency. It has also been provided with a means for restriction of the opening of these valves for the purpose of simulating various types of stenosis.

Water was used as circulating fluid in all experiments.

Casing 1 is made from polymethyl methacrylate, which is transparent. It allows the observation of membranes and valves in operation.

7.2 Experimental Limitations

In the first experiments with the double-pump, it has been seen that pulsating inflow into chambers L and R creates two problems. Added to this, is the working mode of the pressurised air cylinders activating the pump. The problems and their solutions are explained below.

Problem 1

Pulsating inflow demands that, each time the chambers are to be filled, the incoming fluid has to be accelerated. In the event of the circulation not being in a state of equilibrium, the fluid that is supposed to fill the larger chamber will need excess force or time for acceleration. The only force affecting the filling of chambers L and R is the static inflow (filling) pressure. Therefore filling time has to be of a maximum length, to secure the filling of the larger volume (in case the pump is not in equilibrium). That means that the pumping rate must not be set too high.

It is important to reduce the mass of fluid which had to be accelerated at the inflow side. Therefore the flexible afferent tubes to the pump chambers were made of equal length, and as short as possible.

But this was not sufficient. Rather high filling pressures were still required. Moreover, the closing of valves MV and TV gave rise to sharp pressure pulses, followed by resonating phenomena. This situation did not allow determination of the regulating function of the pump to be carried out with sufficient precision.

The problem was eliminated by the addition of first expansion vessels 21 and 22 in connection with the inflow tract. The goal was to reduce the need for high filling pressures and, to a large extent, eliminate pressure transients. In the human body, this is naturally provided by the atria and the venous system.

Problem 2

Volume activation by pressurized air from cylinders (PAC) created another problem.

Increased outflow from one of the volumes L or R, can be caused of the regulating function of the intermediate wall. That results in a higher outlet pressure at a given peripheral resistance, which necessitates a higher air pressure, and thus a greater amount of compressed air.

In diastole this compressed air volume must leave the system, to allow fluid to enter LV and RV simultaneously.

If means for controlled recession of the walls are not provided, the regulating function of S will be severely impaired. The incoming fluid will preferably rush into the chamber that dilates most readily. A little later a somewhat higher filling pressure on the opposite side should push the intermediate wall towards the chamber that had accepted the in-flowing fluid most readily; its inflow valve will close, preventing the regulating function of the pump from becoming operative.

This problem was overcome by the addition of restricting means (not shown) to the inlets and outlets of the electromagnetic valves providing PAC-RV, PAC-SV and PAC-LV with pressurized air.

Experiments

The pump was connected to circulatory loops simulating that of man (Fig. 7-1 and Fig. 7-4).

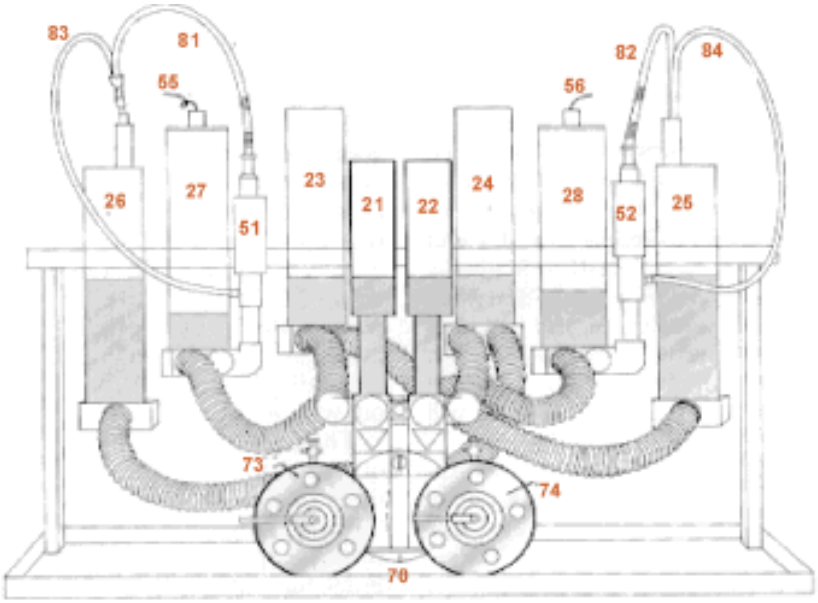


Fig. 7-4: The self-regulating double-pump Expansion vessels and circulation loops. For guidance, uneven numbers are involved with the right circulating system. Identification of parts: point and click on figure or, see text.

21. First expansion vessel, inflow right 22. First expansion vessel, inflow left 23. Second expansion vessel, inflow right 24. Second expansion vessel, inflow left 25. Third expansion vessel, inflow right 26. Third expansion vessel, inflow left 27. Fourth expansion vessel, outflow right 28. Fourth expansion vessel, outflow left 51. Turbo flow meter, right 52. Turbo flow meter, left 55. Pressure Monitor 56.Pressure Monitor 70. SV activation pressure transducer (PAC-SV) 73. RV activation pressure transducer (PAC-RV) 74. LV activation pressure transducer (PAC-LV) 81. "Waterfall" tube, right 82. "Waterfall" tube, left 83. Shunt bypassing right turbo flow meter 84. Shunt bypassing left turbo flow meter.

Air pressure was set at a level sufficient for rapid injection of water, via PAC-SV, PAC-LV and PAC-RV into chambers SV, LV and RV respectively.

The pumping rate was set at about 50 strokes per minute. Activating periods of the air cylinders were adapted to pressures and flows expected in the system. Additional pressure monitors (not shown) were arranged, at the bottom of the second open expansion vessels 23 and 24 for inflow pressure registration.

A Third open expansion vessel 25, was connected to vessel 23 and another third open expansion vessel 26, to vessel 24. These open third expansion vessels 25 and 26 were arranged so as to be easily raised or lowered.

Outflow tubes from chambers R and L were connected to closed fourth expansion vessels 27 and 28. Air enclosed in the fourth expansion vessels 27 and 28 imitated the Windkessel effect of the aorta and the pulmonary artery.

The outlets of the fourth expansion vessels 27 and 28 were provided with two restriction valves (not shown). The action of the restriction valves corresponds to that of the peripheral resistance and of the resistance in the pulmonary circulation respectively.

Pressure monitors 55 and 56 were arranged on top of 27 and 28, for the registration of the pressures at the outflow side.

The outlets of 27 and 28 were provided with turbo flow-rate meters 51 and 52. They had fixed tubes 81 and 82 ending above the respective aforementioned open and movable expansion vessels 25 and 26. This arrangement transforms pulsating into non-pulsating flow i.e., it assumes part of the function of the arteriolar-alveolar system (flow rate independent of pressure drop, the "waterfall" concept [130]).

Inlet-outlet connections of the two pump halves were arranged in a configuration of an eight.

Turbo flow meters 51 and 52 had considerable self-impedance, especially at higher flow rates. There was a sharp increase in flow rate in certain heart defects simulated with this pump arrangement. Giving chamber R a higher outflow than L, flow meter 51 on the right outflow side was shunted (via tube 83) to prevent damage to membranes 2 and 3. The turbo flow meter 51 thus showed reduced flow rates compared with those measured on the left side, 52. This had to be taken into account when analyzing the results given in the diagrams.

A corresponding shunt 84 (to be opened in certain experiments) was provided in the left circulation loop.

Results are presented in the form of eight electrostatic-recorder traces.

The variables recorded are:

- the pressures at the inflow and outflow sides of pumping chambers L and R
- the flow rates at the outflow side of the chambers
- stroke rate (not indicated in the figures)
- event marks

7.3 Demonstration of Regulation Principle, Results and Discussion

SV Activated; LV and RV idle

The regulating action of the pump solely by partition-wall S was tested, with lateral pressurising volumes LV and RV in an idle state. By raising or lowering the open expansion vessels 25 and 26, filling pressures on the right and left side were set.

An increase in filling pressure on the right side, carries with it an incremental increase in volume at the same side. By the balancing action of the wall S, the stroke volume and outflow pressure on the right side was increased (Fig. 7-5).

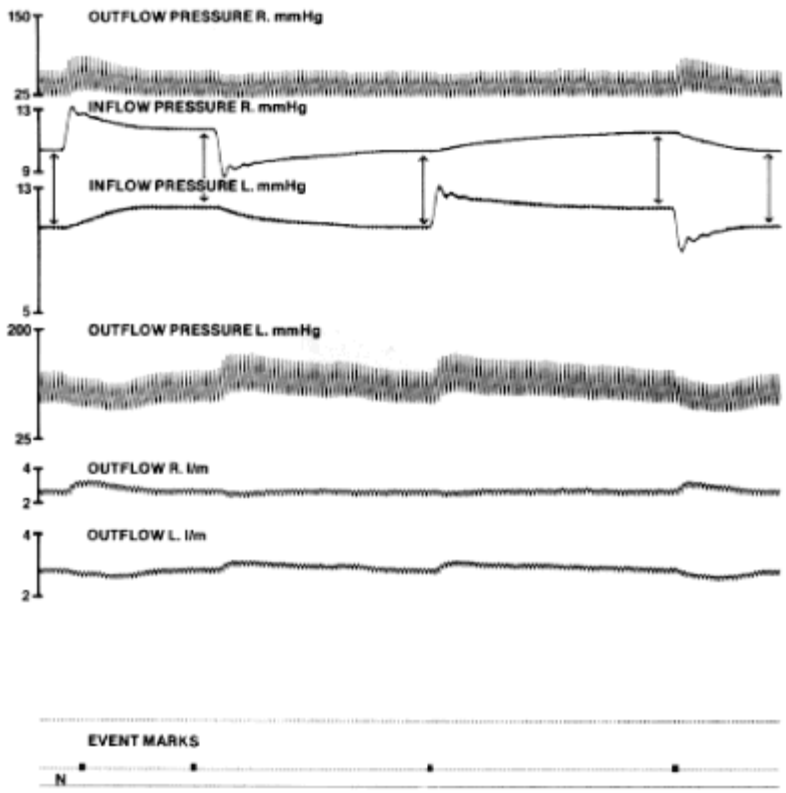


Fig. 7-5 Double-pump Partition-volume (SV) activated. Lateral volumes idle (RV, LV).

N: normal mode (situation at start of experiment).

The stroke volume and outflow pressure on the left side decreased accordingly.

A few strokes later, balance had been attained again and flow rates and flow pressures were the same as before the change in inflow pressure at the right side. Filling pressure coincided, but at a slightly increased level, due to the fluid volume from the expansion vessel 25, which had been added to the system.

Decrease of filling pressure on the right side resulted in an opposite reaction (this is not clearly shown, since flow meter 51 (Fig. 7-4) was by-passed).

Corresponding reactions were elicited by raising and lowering filling pressure on the left side.

SV, LV and RV activated

Experimental procedure was as above, but with lateral pressurising volumes LV and RV in working order.

The results (Fig. 7-6) with respect to balancing are the same, but recorded pressures and flow are consequently higher.

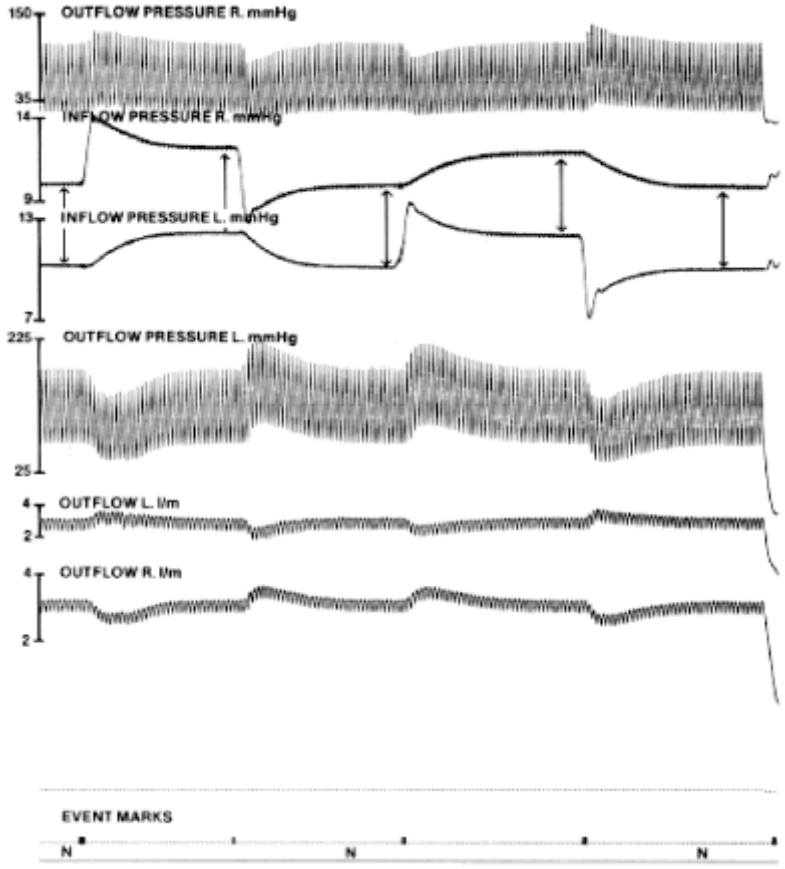


Fig. 7-6 Double-pump . Partitioning volume (SV) Lateral volumes (RV, LV) activated.

N: normal mode (situation at start of experiment).

7.4 Simulation of Various Types of Infarction, Results and discussion

SV and RV Activated; LV Idle

Possible Implications for the Human Heart

Keeping LV idle compares with the situation in a lateral left ventricular infarction.

When starting from the condition in the previous experiment (and by disconnecting LV), the volume was reduced immediately by 50 cm3 (Fig 7-7); it had been 75 cm3 for each of the pump halves in a position of balance. This is seen as a decrease in pressure and flow from chamber L, and an increase of its filling pressure. Partition-wall S deviated towards chamber R already in systole due to this increased filling pressure and thereby lent its total stroke volume, 50 cm3 to the left chamber. Correspondingly, right chamber stroke decreased by 25 cm3. Because of the equilibrating output function of partition-wall S, the system could thus still be kept in balance with an increase in filling pressure on the left side.

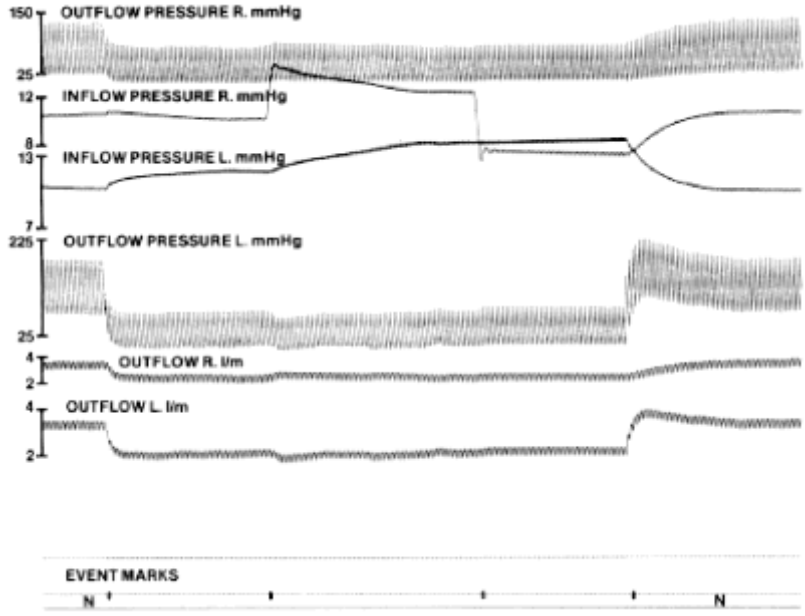


Fig. 7-7 Double-pump Partitioning volume (SV) Lateral volume (RV) activated.Lateral volume (LV) idle. N: normal mode (situation at start of experiment).

Chamber R had its filling pressure somewhat reduced, by transfer of fluid to expansion vessels 22, 24 and 26.

A loss of two thirds of pumping capacity at chamber L, thus resulted in an outflow decrease from that chamber by only one third. The partition-wall was still able to compensate for an increased filling pressure on the right side, but not for a corresponding increase on the left side. The reason for this is, that the maximal regulation capacity of the pump had been fully utilised. The maximal regulation capacity is given by the volume of expansion of the wall S, and the position of copper gauze 61.

Possible Implications for the Human Heart

The human heart stabilises the ventricular septum in systole by its activated network of muscle fibres, which corresponds to the copper gauze in the pump. This means that ventricular septum, in the case of a lateral left ventricular infarction, can bulge over towards the right ventricle in accordance with left-side filling pressure increasing. That activity can thereby raise the left ventricle systolic stroke volume.

Right ventricle stroke volume will be reduced correspondingly.

The net result is a decrease in total pumping capacity for the damaged heart. Balancing capacity will be preserved through a raised left ventricular filling pressure.

SV and LV Activated; RV Idle

Possible Implications for the Human Heart

Keeping the right lateral volume idle, compares with the situation of an anterior right ventricular infarction (Fig. 7-8).

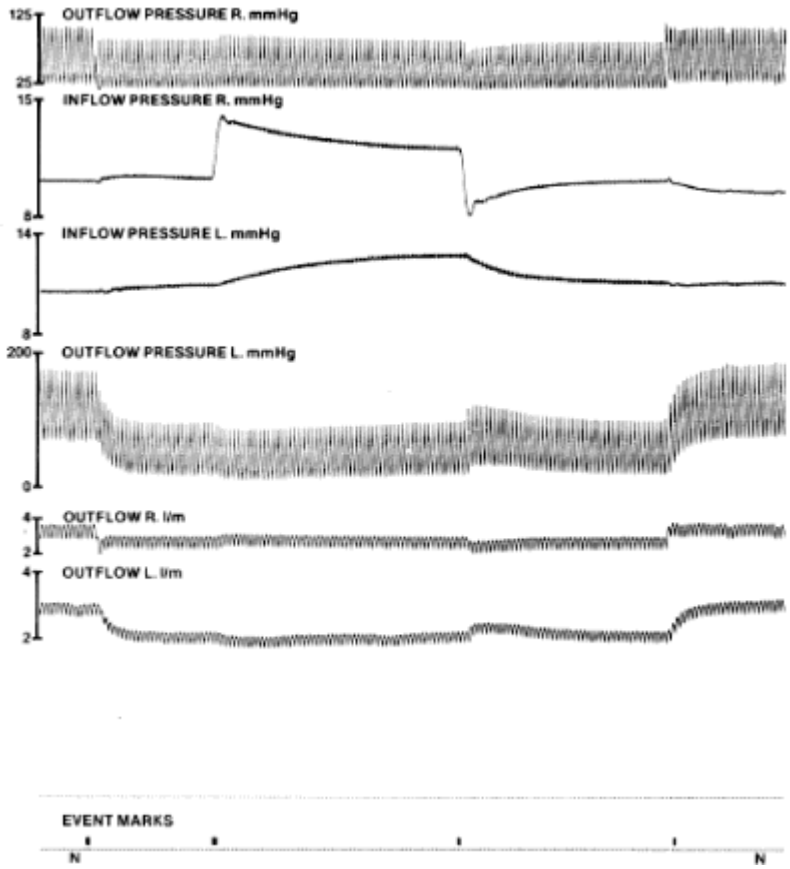


Fig. 7-8 Double-pump Partitioning volume (SV) Lateral volume (LV) activated.Lateral volume (RV) idle.N: normal mode (situation at start of experiment)

The experiment started under "normal" conditions. That is, with the partition-wall and both lateral walls RV and LV activated.

RV was then disconnected. After deactivating RV, flow and pressure at the outflow side corresponded to that in the preceding experiment.

Some consideration had to be given to the less than ideal configuration of silicone membranes 2 and 3, which showed some resistance in flap-over. Increase in filling pressure on the right side caused the intermediate wall S to bulge into chamber L. This caused the membrane pump-like action of S to compensate for the deficit on the right side, to which even the lateral wall LV contributed for a short period. A prerequisite for this compensation of the pumping to be effective is that the pressure at the outlet of L is higher than at the outlet of R.

On increasing filling pressure by raising 25, the regulation by S, brings the pump into balance after a few beats. This can be seen by the fact that flow and outgoing pressure are the same as they were before the raising of 25.

The filling pressure on both sides is high because, of the transfer of fluid to the system.

A relative increase in filling pressure on the left side, achieved by lowering vessel 25, implies that the partition-wall in the passive pumping phase deviates towards R. The stroke volume in R is reduced, until balance is obtained.

Possible Implications for the Human Heart [back]

The experiment shows what happens in a right ventricular infarction without the ventricular septum being damaged; the action of the septum together with the power resources of the rest of the left ventricle wall, can compensate for the loss in pumping capacity of the right ventricle [59, 90, 168].

This is again affected at the cost of total stroke volume.

It is worthy of note that traumatising RV infarction seems to be rare (cf. [84]).

SV Idle; LV and RV Activated

Possible Implications for the Human Heart

Keeping the partitioning wall S volume idle, corresponds to a septal infarction.

In this arrangement, membranes 2 and 3 had only the role of dividing the interior of the pump into chambers L and R. To avoid removing copper gauze 61 (which simulates systolic stabilising properties of VS), flow meter 52 was provided with a shunt 84, identical to that at flow meter 51. That is permitting rapid change in pressure on the flux side.

The pump was started, filling pressures for both pumping chambers were equally set and recorder traces for the starting filling pressures were set to overlap. The experiment is shown in Fig. 7-9.

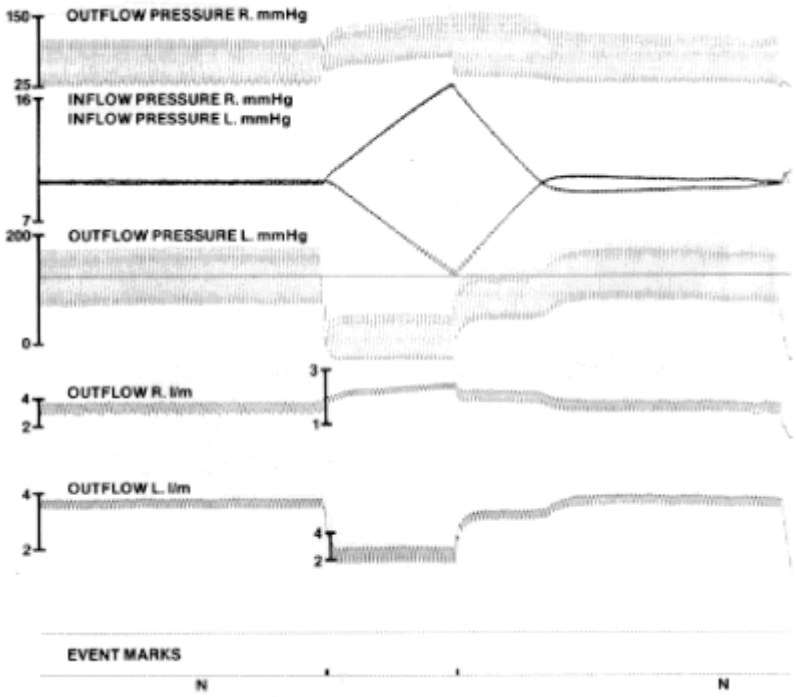


Fig. 7-9 Double-pump Partitioning volumes (SV) idle. Lateral volumes (RV, LV) activated N: normal mode (situation at start of experiment)

Shunt 83 at flow meter 51 was closed and shunt 84 at flow meter 52 opened while partitioning volume SV was simultaneously deactivated. This implies that the right pump half, had to work against a higher pressure than the left, because the flow meters had considerable flow resistance.

It was observed that the filling pressure at chamber R increased whereas it decreased correspondingly at chamber L. This is due to the fact that both expansion volumes RV and LV will through the flexible partition-volume SV expand into the chamber with the lowest output pressure; in this case it is chamber L.

After one or two beats the membranes 2 and 3 bulges over towards chamber L so much, that they will meet with membrane 12. This will result in an outflow even from chamber R.

The elasticity of the membranes 2 and 3 forced them back towards chamber R, though there was a higher filling pressure on that side. In that way chamber L could be filled.

The experiment had to be stopped when the fluid reached the full height of the open expansion vessel 21.

The outflow from chamber R and L is misleading, because of the closing and opening of the shunts 83 and 84.

The constant outflow, though increasing filling pressure at chamber R and decreasing filling pressure at chamber L, indicates that no regulation function is left.

When the experiment was stopped, by opening shunt 83 and closing shunt 84 plus activating PAC-SV, pressures and flow were rapidly normalized.

This experiment had to be repeated several times, since membranes 2 and 3 were damaged as the copper gauze 61 had no effect, when chamber R had to pump against a high pressure.

Possible Implications for the Human Heart

A total septal infarction, where septum does not restrict the systolic pressure of left ventricle in an active way, implies serious damage to the regulation function of the heart. That is the fact, even if a sufficient portion of its pumping capacity is preserved. As long as the pulmonary pressure, together with the passive resistance forces of the damaged muscle, cannot withstand the pressure generated in left ventricle during systole, following happens; a paradoxical movement of ventricular septum will result in an enhanced flow of blood to the pulmonary circuit, with a correspondingly rising pulmonary blood pressure propagated to the left atrium. Pulmonary edema will soon ensue, in combination with a reduced left ventricular output. Molaug et al. [118] found during experiments with intermittent ischemia of ventricular septum in anaesthetised open-chest dogs, paradoxical movement of ventricular septum, contributing to right ventricular ejection. (In these experiments, the heart is allowed to work as a displacement pump).

7.5 Simulation of Valve and other Defects, Results and Discussion

7.51 Mitral Valve Insufficiency

The pump was provided with an arrangement that allowed the insertion of a tiny wedge into the mitral valve, to prevent its complete closure. This corresponds to mitral valve insufficiency.

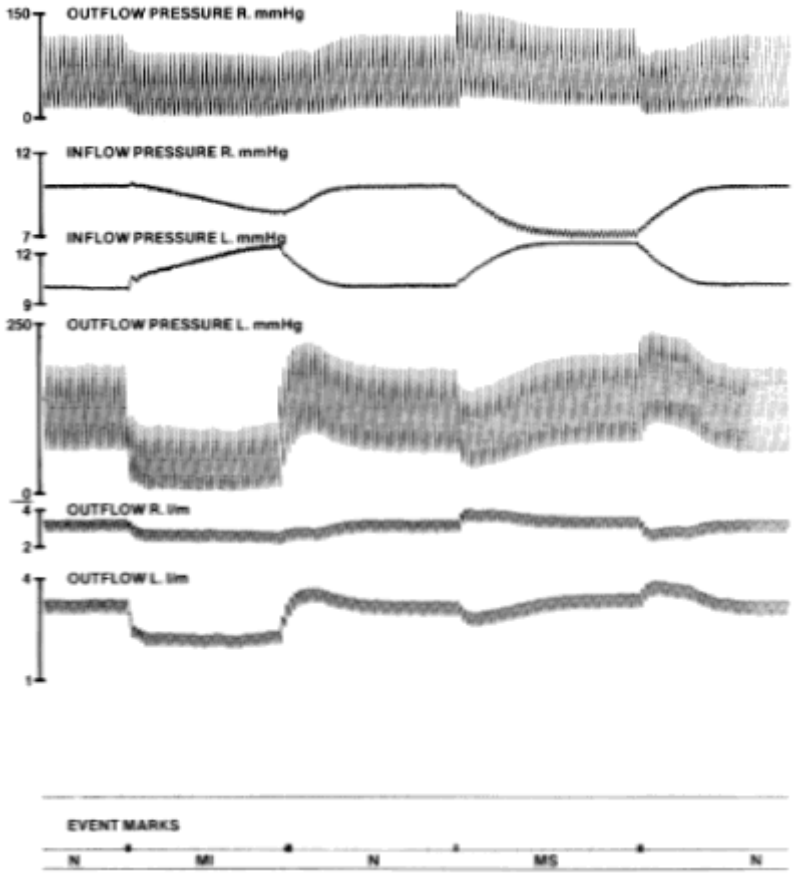


Fig. 7-10 Double-pump Simulation of mitral valve insufficiency (MI) and stenosis (MS) N: normal mode (situation at start of experiment)

In this simulation (Fig. 7-10), flow and pressure at the outflow side of chamber L decreased, and the left filling pressure rose. The increased left filling pressure made the partition-wall deviate in the direction of chamber R, which thereby received a decreased stroke volume. The decreased filling pressure on the right side was partly due to fluid building up in the circulatory loop originating at the outlet of the right chamber. That was effecting the increased filling pressure of the left pump half. The higher left side filling pressure was needed, to provide for its complete filling. This was necessary in order to overcome resistance of the membrane material, due to bulging in the direction of chamber R. The filling pressure at chamber L had a tendency to rise during the simulation. That was due to the experimental insufficiency chosen happened to be a little too large; the expansion range of the volumes of partitioning wall S and the lateral walls could not cope with it. Flow from chambers L and R remained low during the simulation. When the wedge was removed, the system quickly returned to normal.

7.52 Mitral Valve Stenosis

A mitral stenosis (Fig. 7-10) was similarly effected by introducing a V-shaped part, which prevented the mitral valve from fully opening. At first, flow on the left side was reduced, until the filling pressure had risen to a level compensating for the stenosis. Both pressure and flow were thereby restored on the left side. The filling pressure on the right side decreased and the right efflux pressure increased. That implied that the partition-wall effectuated a transmission of this change, in increased flow and pressure on the right side, until the system reached equilibrium again. Mitral stenosis does not reduce pumping capacity, once the pump is in balance. These results can be compared with the echocardiographic registration of a mitral stenosis (Chapter 6).

7.53 Tricuspid Valve Insufficiency

Experimental tricuspid valve insufficiency (Fig. 7-11) was achieved in the same manner as mitral insufficiency. Under these conditions, outflow from R decreased immediately. The filling pressure on the same side increased, pushing the partition-wall in the direction of the left chamber. This also caused a decrease in outflow on the left side. Left filling pressure decreased in proportion to the rising filling pressure on the right side. This means, that there was a redistribution of fluid accumulating in the open expansion vessels 21, 23 and 25. After a time, flow rates reached a new equilibrium. The slow equilibration compared with equilibration in other experiments, is due to the difficulty in producing an insufficiency smaller than membranes 2 and 3 can compensate for (50 cm3). Because of their configuration stiffness, a minimum pressure difference, provided by increasing filling pressure to chamber R, is needed to make them bend over towards chamber L. By removing wedge 67 in the tricuspid valve, the system returned quickly to normal.

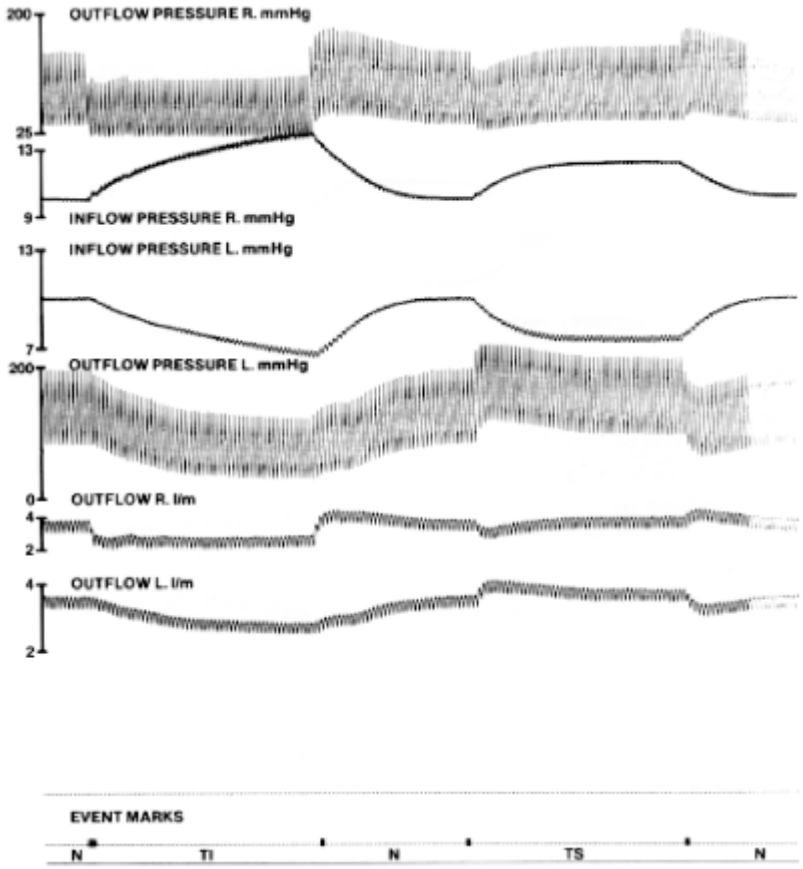


Fig. 7-11 Double-pump Simulation of tricuspid valve insufficiency (TI) and stenosis (TS).N: normal mode (situation at start of experiment).

7.54 Tricuspid Valve Stenosis

An experimental tricuspid valve stenosis (Fig. 7-11) was affected as related for "mitral stenosis"; the V-shaped part is shown in Fig. 7-2. The filling pressure began to rise on the right side and to decrease on the left. The lower pressure in chamber R caused the partition-wall to move over in the direction of chamber R. Outflow from the left side increased initially. Once the pressure gradient in the filling phase had been equalized through the rise of the filling pressure on the right side, the system was in balance again. Pressure and flow on the output side was the same as before the artificial stenosis was induced. Filling pressures, however, stabilized at different levels.

7.55 Aortic Valve Insufficiency

Aortic valve insufficiency (Fig. 7-12) was induced by the insertion of a wedge (as above). Immediately after the experimental insufficiency had been established, forceful pulsations, reduced pressure and flow out from chamber L were observed. With influx pressure building up on the left side, flow and pressure at the left chamber outlet rose slightly. From chamber R, there was a rather fast decrease in both outflow pressure and flow, due to the partition-wall moving toward the right side in the filling phase. The rigid position of gauze 61, and the limit of 50 cm3 for the pumping volume contribution of the partition-wall, sets a limit. It implies that the pump can only compensate for an insufficiency up to that volume. The amount of fluid in the inflow expansion vessels on the left side increased and the amount of fluid decreased in those at the right side. After a short period of time, the system was again in balance, displaying reduced cardiac output because of the compensatory role of the partition-wall. These results should be compared with the authentic M-mode EC image of a patient with an aortic valve insufficiency (Chapter 6). The removal of the wedge resulted in a return to the situation at the start of the experiment.

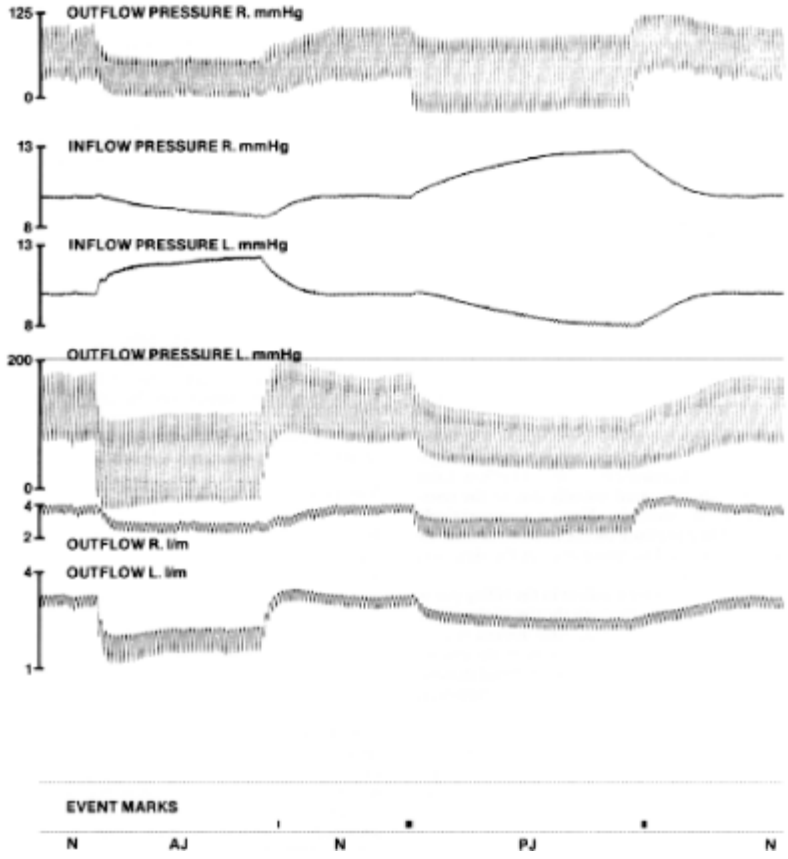


Fig. 7-12 Double-pump Simulation of aortic (AI) and pulmonic (PI) valve insufficiency.N: normal mode (situation at start of experiment).

7.56 Pulmonic Valve Insufficiency

The pulmonic valve insufficiency also resulted in pronounced pulsation's (Fig. 7-12), and in reduced outflow and pressure from chamber R. Filling pressure on the right side increased and made the partition-wall move towards chamber L in the filling phase. This resulted in a reduction in flow and pressure from the left side. The levels of fluid in the inflow expansion vessels on the left and right sides changed accordingly. A new equilibrium was soon established. The removal of the wedge returned those parameters to normality.

7.57 Simulation of Atrial Septum Defect

In order to simulate atrial septum defect (ASD) (Fig. 7-13), the experimental pump had to be provided with an additional valve 64. It connects the inlet tubes just above valves MV and TV.

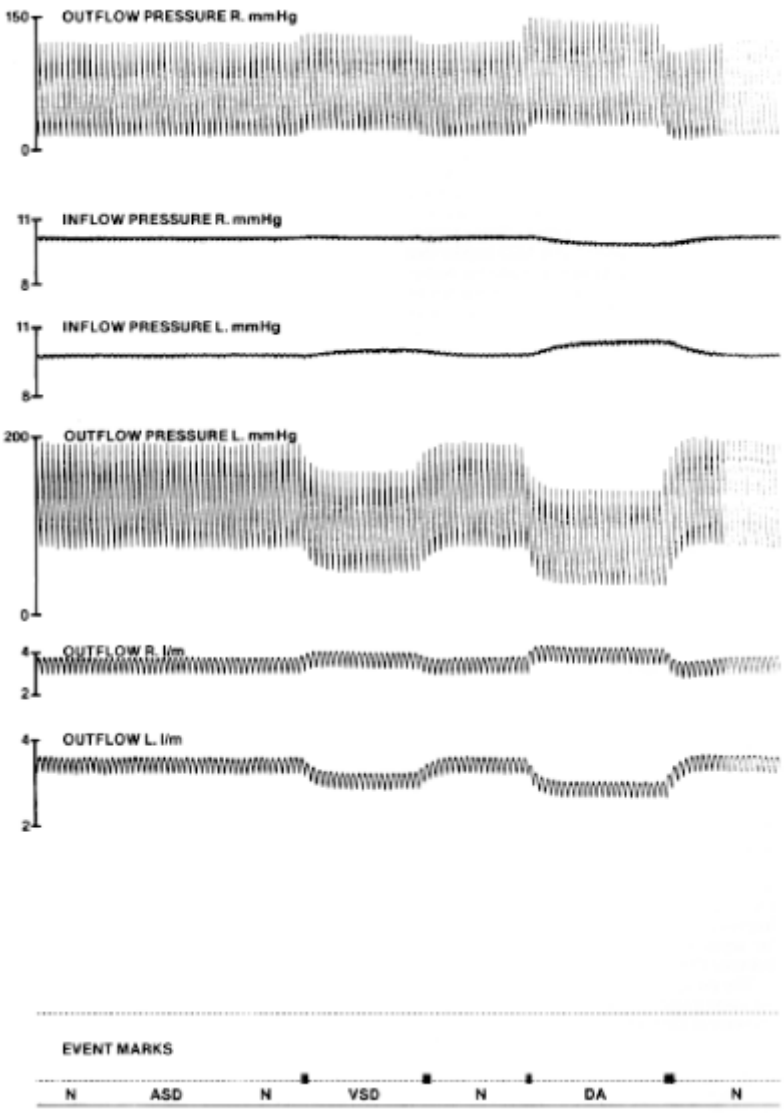


Fig. 7-13 Double-pump Simulation of atrial septum defect (ASD), ventricular septum defect (VSD) and ductus arteriosus (DA).N: normal mode (situation at start of experiment).

By opening valve 64, an atrial septum defect (ASD) was simulated. No change in circulation could, however, be observed. This was due to the system being in a state of equilibrium, in which both chambers experienced the same filling pressure. The partitioning wall thereby assumed a neutral position and no flow through valve 64 ensued.

7.58 Simulation of Ventricular Septum Defect

In order to simulate ventricular septum defect (VSD) (Fig. 7-13), the experimental pump had to be provided with an additional valve 65. It connects chambers R and L.

Opening valve 65 resulted in a ventricular septum defect (VSD). A sudden increase of pressure and flow in the right circulation system was observed. The left side circulation flow and pressure were reduced. Increased left

filling pressure pushed the partition-wall toward chamber R in diastole, and thus changed the stroke volume on the left side, so that a new balance was reached. Closing valve 65 brought the system back to normal.

7.59 Simulation of Ductus Arteriosus

In order to simulate ductus arteriosus (DA) (Fig. 7-13), the experimental pump had to be provided with an additional valve 66. It connects the outlets just below valves AV and PV.

Opening valve 66 simulated an open ductus arteriosus (DA). The observed effect was the same as for a VSD. The response was, however, larger with DA (at same opening degree of the valves), due to a pressure gradient working over the entire diastole.

7.60 Possible Implications for the Human Heart

The healthy heart has its ventricular septum in the same position both in systole and diastole, except when reconstituting equilibrium because of re-partition of blood volumes. The ventricular septum thus has a convex shape against right ventricle also in diastole. In contrast to the experimental pump, the ventricular septum in the healthy human heart, does not normally contribute to the pumping of right ventricle by moving in the direction of right ventricle in systole. To maintain this septal position, a slightly higher filling pressure on the left side is required. An ASD implies that this difference in filling pressure and the pumping action by the Atrio Ventricular-plane is counteracted by flow through the ASD. This causes a paradoxical movement of ventricular septum [179], giving right ventricle a higher stroke volume and left ventricle a lower one.

7.6 Summary

A self-regulating double-pump, operating in accordance with the basic balance principle suggested for the human heart in situ, was constructed[1] (Concept 2). Two circulatory loops, arranged in the same way as the circulation of blood in man, have been shown to be kept in balance by the double pump. The similarity in function between this pump and the human heart goes even further; it allows simulation of a number of in vivo heart defects, including several types of myocardial infarction. It also demonstrates that as long as the partition wall is working properly, it will keep the system in balance as it does in man.

These findings applied to the human heart would suggest that the regulating function of the ventricular septum is similar to that of the common wall in the double pump. That is on the assumption that the human heart pumps with displacement of the Atrio Ventricular-plane at a relatively constant outer contour (Chapter 3, Chapter 4, Chapter 5). This means that different ventricular stroke volumes do not jeopardize the regulation function of the ventricular septum. In fact, in contrast to the double-pump, an increasing stroke volume of the total heart (or a single ventricle) would also improve the regulation capacity of the ventricular septum. That is due to, that the wall between the two ventricles in the heart is more displaceable than the wall in the double-pump.

The pump is inferior to the heart in one major respect, and that is that it requires high filling pressure at high heart rates.

[1]Concept 2

The second concept identifies the method of control, by which arterial and venous circulation is balanced:

The interventricular septum regulates ventricular stroke volumes, to maintain proper balance between systemic- and pulmonary circulation.

Chapter 8

A Single-Pump, with Ability to Control and be Controlled by Filling Pressure

8.1 Introduction

In Chapter 7 it was possible (using the double-pump) to simulate the role of left and right filling pressures in the control of output balance; the balance is mediated by the ventricular septum.

The double-pump does not, however, embrace the other of the two essential working principles of the heart outlined earlier. That is the "gripping" pumping mode, attained by a moving valve plane connecting two chambers. This pumping mode is probably important for several reasons: it saves energy and requires low filling pressure at both low and high stroke rates.

The balancing action of the ventricular septum is activated by force components acting in the direction of the minor heart axis. The "gripping" mode pumping action though, occurs perpendicularly to it. The complex nature of the heart muscle enables it to exert its force in three dimensions.

Moreover, the process of polarization makes it change from a material with high compliance in diastole to material with low compliance in systole.

Timing of the polarization-de-polarization process regionally within the heart is also of major importance. It is, therefore, not surprisingly, that the construction of a single-pump displaying all the attributes of the living heart is hardly feasible.

Left Ventricular Assist Devices, LVAD's, are increasingly gaining acceptance as means of circulatory support, but their clinical use has been delayed by problems. They are related to pumping characteristics (impaired filling at higher stroke rates and with inlet tubes of normal width), control of pumping rate, power supply and to blood compatibility.

There is evidence for the feasibility of artificial maintenance of systemic circulation, by an LVAD without the participation of RV [53, 86, 117, 121, 142].

In the present context, it might be of interest to transfer the "gripping" heart working mode into a mechanical pump [109]. It should be operating at essentially low and constant inflow pressures over a wide range of stroke rates. It should also be giving pulsed outflow pressures, similar to that of the left ventricle of the human heart.

A rather surprising solution for the control problems mentioned above was also found. By incorporating certain features into its design related below, it was possible to achieve stroke and thereby output, control by filling (inflow) pressure.

Its design also incorporates a basic principle for the shape of the inner surfaces of the heart postulated for the first time by Puff [135], implying that the surface area of the endocardium should remain essentially constant over the entire cardiac cycle.

8.2 Pump Design

The pump is shown in Fig. 8-1 and Fig. 8-2.

It is based on a tube with two bulbs made of flexible (but essentially non-extensible) material (e.g., certain types of polyurethane or silicone rubber, possibly reinforced by non-extensible fibres).

The tube with two bulbs, 6, is mounted in a casing 1, composed of parts 1A and 1B. The tube has a smaller bell-shaped bulb 6A and one that is larger, 6V. This can be seen in Fig. 8-1.

It has been produced in the following way: first a paraffin form was turned on a lathe and then polished by heat input; it was coated with several layers of an elastomer (which in this case was silicone rubber) with reinforcing material inlaid (gauze bandage in laboratory device), and finally allowed to set.

In the constriction 9, between the bulbs 6A and 6V, a dish-like rigid drive ring 10, is mounted; for the sake of light weight, it consists of two thin sheet-metal dishes fastened together and provided with holes. The drive ring is mounted in the casing 1 together with valves 4 and 5, in this case heart valves of a well known construction (Björk-Shiley valves).

As is evident from the drawings, the tube with two bulbs is fastened to other parts of the assembly in three places, namely to the valve 5 in the constriction 9 and also at openings 7 and 8 in the casing 1.

The whole arrangement is shown in mounted condition in Fig. 8-1.

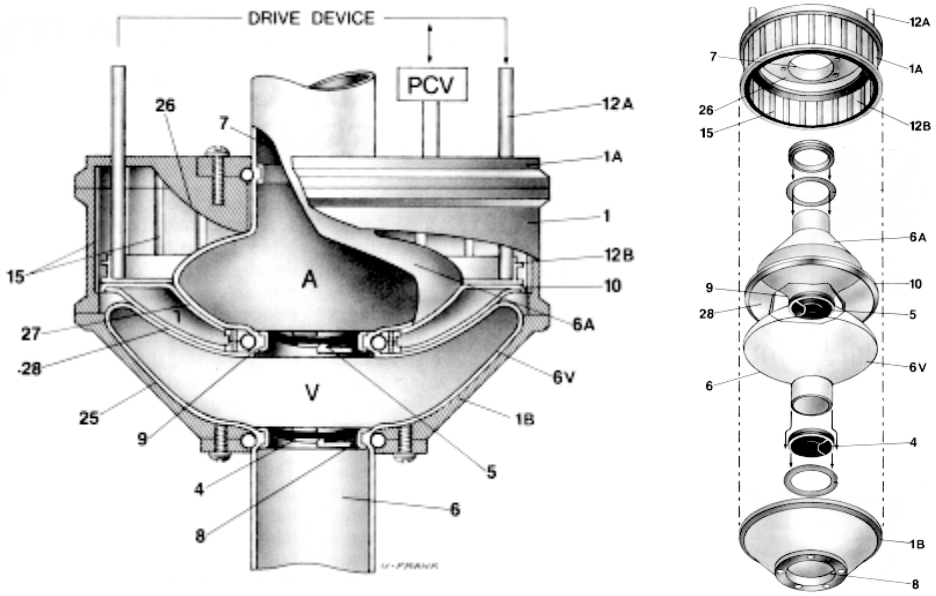


Fig 8-1: Single-pump Side cross-sectional view along axis of symmetry. PCV: pressure control valve

Fig 8-2: Single-pump Exploded

1 Casing,1A Upper part of casing,1B Lower part of casing,4One way valve (Björk-Shiley heart valve), 5 One way valve (Björk-Shiley heart valve), 6 Outlet tube (Aorta),6A Bell shaped bulb,6VBell shaped bulb,7 Opening,8Opening,9 Constriction,10Drive ring,12A Push rods,12B Push ring,15 Grooves,25 Lower wall of casing,26Upper wall of casing,27Upper surface of drive ring,28Lower surface of drive ring, Atrium chamber, PCV Pressure control valve, Ventricle chamber

Drive ring 10 runs freely up and down in the rigid casing 1. It has grooves 15 on its inner surface, so that air can pass freely between the sections of the casing on either side of the drive ring 10.

The smaller bulb 6A defines an atrium chamber (A), and the larger bulb 6V a ventricle chamber (V). The inlet opening to the atrium chamber A is joined to the casing at the opening 7.

The constriction 9 is a passage through which blood can flow only from the atrium chamber A to the ventricle chamber V, through the one-way valve 5.

The opening 8 (containing the one-way valve 4) is the outlet from the pump, through which blood is delivered in pulses under pressure.

Each portion of the bulbs is engaged between complementary, generally dish-shaped, surfaces of the housing and the drive ring. The respective volumes in the atrial and ventricular chambers of the pump are controlled by engagement of bulbs 6A and 6V. They are located between the lower and upper walls 25 and 26 of the casing, and lower and upper surfaces 28 and 27 of the drive ring 10. In particular, the casing surface 25 is concave while surface 28 of the drive ring is convex.

Similarly, the bulb 6A is engaged during a part of each cycle of the pump between convex surface 26 of the casing and concave surface 27 of the drive ring.

8.4 Operation mode

The pump may be driven by any of a variety of electrical or pneumatic drive devices, as represented schematically in Fig. 8-1. It may even be driven by muscular force.

The unilateral driving force is applied to drive ring 10, via push ring 12B attached to a pair of diametrically located push rods 12A. These project out of the casing through openings in the top wall and are sealed by suitable sliding seals (not shown), so that the casing is hermetically sealed. Electric motor acting through the linkage, pushes the push ring 12B down into engagement with the drive ring 10, on the driven stroke of each pump cycle. At the end of the driven stroke, the push rods and push ring disengage from the drive ring and are retracted to the top of the casing by a return spring.

During each down stroke of the push ring and drive ring, the volume of the ventricle chamber is reduced and its pressure is increased. That causing the valve 5 to close and the outlet valve 4 to open, so that blood is ejected from chamber V.

Meanwhile, the volume of chamber A increases, so that blood continues to flow into it during the driving stroke of the pump.

At the end of the down-stroke, push ring 12B is retracted, so that pressure is no longer applied to chamber V.

When the momentum that sustains flow through outlet valve 4 subsides, the valve will close. The pressure of the incoming blood, together with the momentum of blood then passing from A to V through the valve 5, will produce net upward forces. The forces are exerted by the ventricle chamber bulb 6V against the bottom surface 28 of the drive ring 10. One area of engagement is between the bulb 6V and the under surface of the drive ring. It is normalized by projection on an imaginary plane, perpendicular to the directional axis of movement of the drive ring 10. That area is being larger, than the area of engagement (normalized as above) between the bulb 6A and the upper surface 26 of the casing. Hence, the drive ring is lifted upward, and part of the blood in 6A together with incoming blood passes into the ventricle chamber. The volume of V increases as the drive ring rises.

When the normalized areas of engagement between surfaces 26 and 28, and bulbs 6A and 6V respectively become equal, the pump has reached its maximum volume. No more blood can then flow into the pump.

Accordingly, the frequency of the drive pulses of the drive device are established to ensure, that the chambers of the pump do not reach maximum volume between the driving strokes.

Is there something more that decides the extent, to which the chambers of the pump are filled during each operating cycle of the pump? The filling is also influenced by the pressure of the gas within the casing and outside the pump chambers.

During each driving stroke of the pump, the volume occupied by the gas in the casing increases, and the pressure of the gas drops accordingly.

During the return stroke of the pump, the total volume of the chambers increases, the volume of the gas decreases; the pressure of the gas in the casing increases accordingly. As the pressure in the gas approaches the pressure of the incoming blood, the rate of filling of the chambers decreases. It is therefore apparent, that the pressure changes that occur in the gas have a regulating effect on the filling of the pump throughout each cycle.

The gas pressures prevailing in the casing are determined (amongst other things) by the relationship between the displacement volume of the pump, and the volume occupied by the gas at any given point in the operating cycle. This is a matter of the geometric design of the pump.

The amount of the gas in the casing can be regulated by a pressure control valve, composed of two one-way valves, set to provide high and low limits on the gas pressure.

The operating cycle of the pump is schematically shown at four points in Fig. 8-3A-D.

Fig. 8-3A, Fig. 8-3B, Fig. 8-3C and Fig. 8-3D put together as a small animation

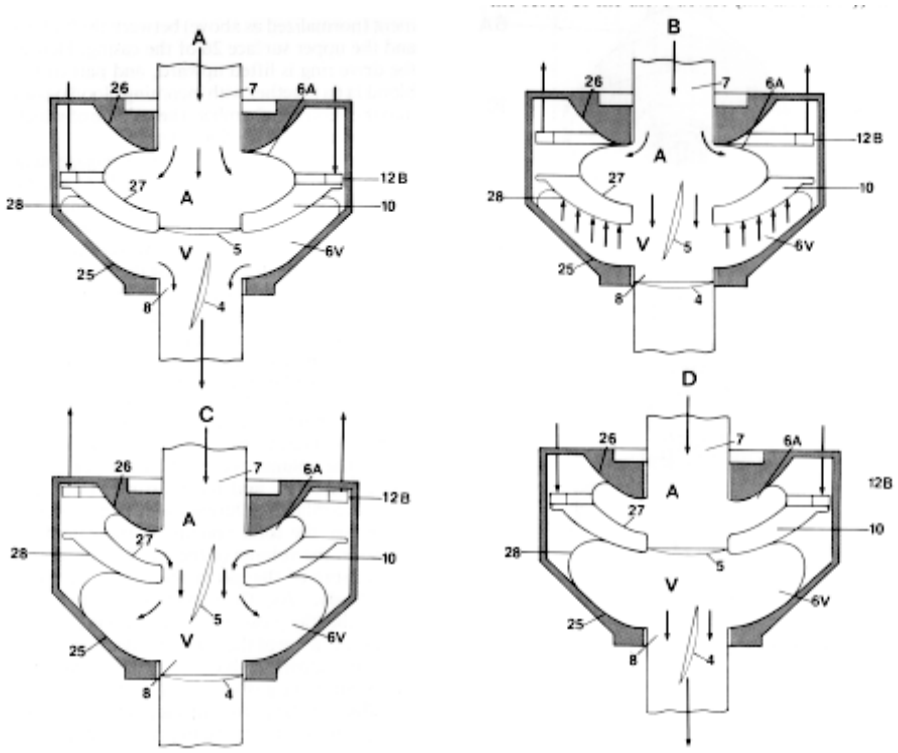


Fig 8-3A Single pump Principle of operating early systole

Fig 8-3B Single pump Principle of operating end systole

Fig 8-3C Single pump Principle of operating early diastole

Fig 8-3D Single pump Principle of operating end diastole

A driving stroke is commenced by a downward movement of the push ring 12B, by the force of the drive device, as shown in Fig. 8-3A.

Fig. 8-3B shows the pump at the end of the driving stroke.

In Fig. 8-3C, the drive device retracts the push ring 12B, at the end of the driving stroke. The hydrostatic pressure in the ventricle chamber will drop abruptly, and valve 5 will open due to both the hydrodynamic and hydrostatic pressures of blood entering the atrium chamber.

From now on (Fig. 8-3D) the two chambers act as a simple unit, confined between two stationary contact surfaces (25, 27) and two variable contact surfaces (26, 28). As long as there is a difference between the areas of the variable surfaces, the combined volume of 6A and 6V increases, when the drive ring moves upwards.

The force acting on the drive ring is equal to the pressure difference multiplied by the differential area. The pressure difference is between inside and outside of the bulb assembly. The differential area is the difference between the variable contact-surface areas 26 and 28. While the push ring 12B is retracted, the force acting on the drive ring is negligible; therefore liquid pressure on the inside must equal gas pressure around the bulbs. The filling thus depends on the difference between liquid pressure outside the inflow opening and gas pressure outside the bulb. A pressure difference of a few mm Hg is sufficient for adequate filling rate.

The single-pump is a new kind of displacement pump, not earlier found to be described.

A suitable name for this kind of pump can be differential-displacement pump (or DeltaV pump).

For in vivo application, the casing and the drive device may be mounted in a bag preferable of silicone rubber. It should be of such a volume, that the whole equipment will reach the same density as the replaced volume in the body.

The pressure control valve e.g., two one-way valves, one in each direction, provides communication between the interior and exterior of the casing 1. They have predetermined opening pressures for pressure regulation. Thereby, gas pressure within casing 1 can be maintained at a predetermined level. If the filling pressure is lower than the predetermined level of the gas pressure in the casing, drive ring 10 will not be displaced. The extent of filling of the ventricle chamber thus depends upon the pressure of the incoming blood.

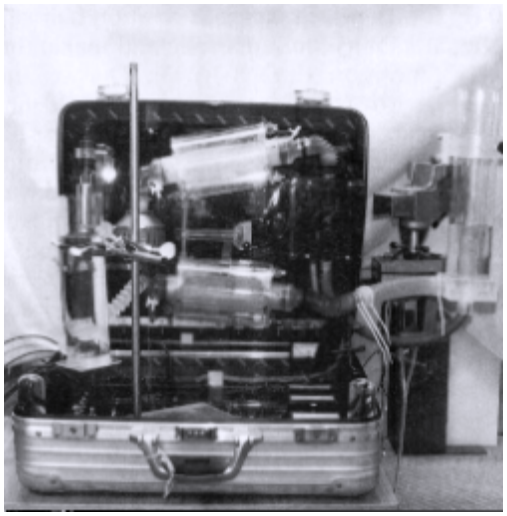
At a certain position, the volumes of chambers A and V become equal. Upward movement of drive ring 10 (and thus the regulating function) then ceases. It does not matter how large the difference in pressure are (between the chambers and that prevailing outside these chambers).

If the pump is working beyond its regulating range, we will have a severe imbalance in the system, and a pulsating inflow to right ventricle. To prevent that, a sensor device may be provided for monitoring the highest position of the drive ring 10 during a cycle.

If the venous return increases, this will become noticeable because the drive ring 10 rises faster, towards the maximum volume. It is then possible to arrange a control circuit, that would increase the stroke frequency of the drive device. That should provide increase in stroke rate (and hence in output) similar to the so-called Bainbridge reflex in man.

8.5 Experimental Pump Model

An experimental model of the pump is shown in Fig. 8-4 and Fig. 8-5.



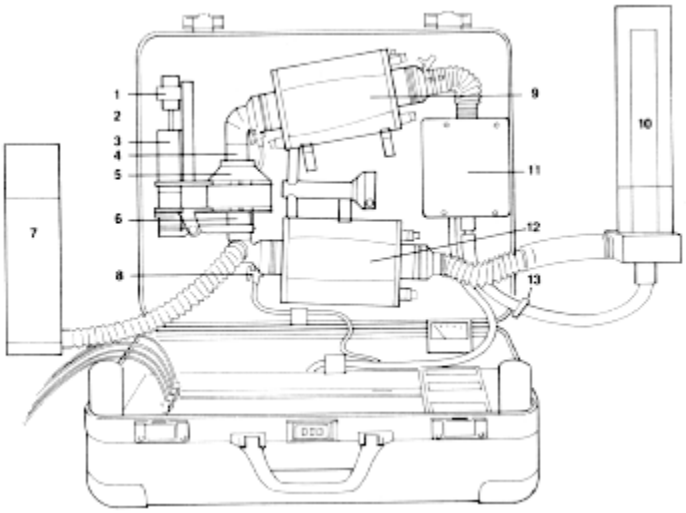


Fig 8-4, 8-5 Single pump Schematized illustration of the circulation loop

1 Tachometer, 2 Outlet pressure monitor, 3 DC-motor, 4 Outlet, 5Pump housing, 6 Inlet, 7 Adjustable expansion vessel, 8Inlet pressure sensor, 9 Windkessel-simulating device, 10 Waterfall vessel, 11Electromagnetic flow meter, 12"negative" Windkessel-simulating device, 13 Flow control valve

It is mounted in an aluminum case, for demonstration purposes.

It is equipped with instruments monitoring inflow and outflow pressure, flow, stroke rate and power consumption.

The pump is driven by a high-efficiency DC motor, provided with a gear box.

A tachometer is attached to the free end of the motor shaft and calibrated to display actual strokes per minute.

The outgoing shaft of the gear box drives a rotor disk, which affects the push rods unilaterally as described above.

The pump outlet is connected to a sealed polymethacrylate container, with silicone rubber bellows. The bellows are connected to the short outlet pipe, as a direct continuation thereof. This container with bellows serves as a capacity load (Windkessel) simulating device [139].

A pressure sensor is also attached between the outlet of the pump and the Windkessel unit.

At the outlet of the Windkessel unit, an electromagnetic type flow meter is arranged. The tube to which this flow meter is attached is flexible and may be constricted e.g., by a clamp to simulate a peripheral-type resistance analogous to in vivo circulation.

From this flexible tubing, the loop goes further to the inlet of a cylindrical container, the "waterfall vessel".

The inlet pipe of the container enters at the bottom, and continues upwards in the inside, concentric to the outer wall. This central pipe is shorter than the cylinder. The fluid flowing through the central pipe falls down

into the space between the pipe and the outer wall. The outlet of the container is at the lower end of the outer wall. This arrangement transforms pulsating into non-pulsating flow i.e., it assumes part of the function of the arteriolar-alveolar system, with an outflow rate independent of inflow rate ("waterfall" concept [130]).

The outlet of the "waterfall vessel" is connected to a third polymethacrylate container, which in turn is joined (by short pieces of flexible tubing) to the inlet of the pump.

The third container is a substitute for the venous system (including atrium and auricle), furnishing the pump with a smoothing means (in a sense, a negative Windkessel type).

A sensor for monitoring inflow pressure is arranged at the inflow.

An open fluid expansion vessel is also connected to the system near the inflow opening. This open expansion vessel may be raised or lowered, in order to increase or decrease the circulating fluid volume. It can also be used to raise or lower fluid pressure at the inlet of the pump. It provides a substitute for the capacity-changing capabilities of the venous system in vivo.

The two Windkessel units are provided with valves enabling their inner air pressure to be changed.

This experimental pump has not been optimised. Its casing has not been sealed against ambient pressure. The model thus does not make full use of the regulation capabilities of the basic pump design, with respect to variable filling pressures (see above). The present pump in all experiments will thus have its regulation level at atmospheric pressure, i.e., a filling pressure of 0 mm Hg.

8.6 Experiments and Results

8.61 Experiment no. 1

The inflow and outflow pressure curves at a low and high frequency (100 and 300 beats/min), were recorded (Fig. 8-6A, Fig. 8-6B).

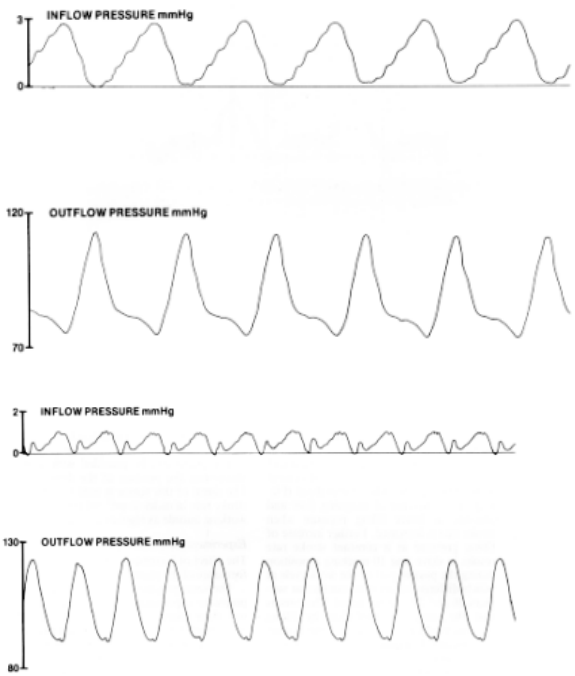


Fig 8-6A Single pump Inflow and outflow at stroke rate: 100 strokes/min

Fig 8-6b Single pump Inflow and outflow at stroke rate: 300 strokes/min

The inflow pressure curves were transferred to an EchoCardiographic (EC) right side registration, of the Atrio Ventricular(AV)-plane of a healthy subject Fig. 8-7. The event marks a'-h' described in Chapter 3 were added.

The EC registration was done with simultaneous ECG and phonocardiogram registrations, together with jugular vein pressure pulse tracing during a slight Valsalva manoeuvre, to raise jugular vein pressure.

At systole, all pressure traces in Fig. 8-7 show a decrease in pressure (x-wave).

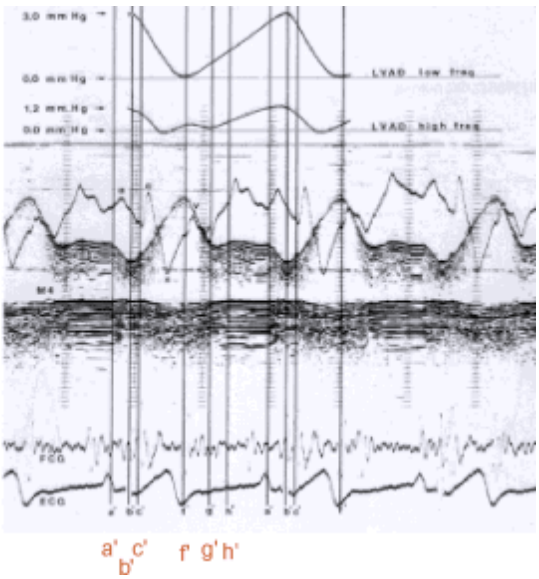


Fig 8-7 Single pump Inflow pressure trace at low frequency (100 beats/min) and high frequency (300 beats/min). It is normalized to the same time scale and compared with M4 study EC registration, jugular vein pulse (JVC), phonocardiogram (FCG) and ECG. Event lines a'-h' added.

a' : Point immediately prior to atrial contraction affecting the valve plane

b' : Point at maximum displacement of the valve plane by atrial systole

c': Closing of the mitral valve

d' : End of the supposed isovolumetric ventricular contraction

e' : Point at which the valve plane has reached the same position, as prior to atrial systole

f' : Amplitudinal maximum (closest approach to apex)

g' : End of rapid return of the valve plane, in atrial direction

h' : Slight rebound movement, due to overshooting

The x-wave is followed by a v-wave in the jugular vein pulse curve, and in the inflow pressure curve of the single-pump at high frequency. There is no v-wave recorded for the single-pump at low stroke rates. The

reason for this is that the profile of the cam disk, transmitting power from the motor to the push rods, determine the slope of the x-wave. Thereby it also determine the size of dynamic forces generated.

In the heart it is the velocity of ventricular muscle contraction that accomplishes that.

The single-pump, in contrast to the heart, has no forced atrial contraction raising the valve plane in further atrially. In other words, it cannot raise the valve plane in the pump in the direction of the inflow. Therefore no extra pressure rise in the form of an a-wave is seen, in the inflow pressure curve for the single-pump.

The major difference at low frequencies between the heart and the single-pump with respect to atrial/inflow pressure, is thus the absence of pressure transients in the latter.

8.62 Experiment no. 2

The effect of the inflow pressure on the minute volume was monitored (Fig. 8-8).

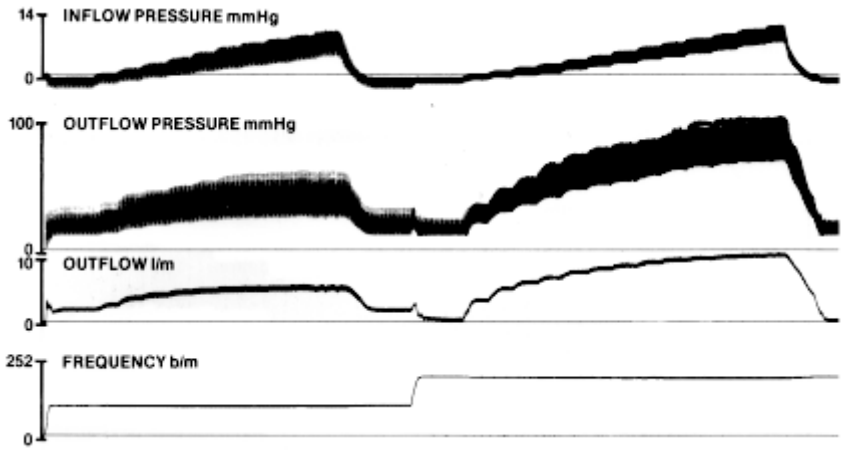


Fig 8-8: Single pump Effect of the inflow pressure on the minute volume at two constant stroke rates, 100 and 200 beats/min.

Before the experiment was started, filling pressure was set to zero. That means, that the fluid level in the adjustable expansion vessel 7 (Fig. 8-5) was placed at the same level as the drive ring 10 (Fig. 8-1). It was in a position halfway between its maximum diastolic and maximum systolic position (Fig. 8-3A, Fig. 8-3B, Fig. 8-3C, Fig. 8-3D).

The stroke length of the drive ring was 18 to 20 mm. This implies, that stroke length due to the influence of gravity deviated up to about 1 mm Hg from the preset value.

The stroke rate was set at 100 beats/min.

Then the experiment was started, and the adjustable expansion vessel was raised step-wise, until pump regulation capacity was fully utilized.

Then, the expansion vessel was again brought back to zero level and stroke rate was increased to 200 beats/min.

The expansion vessel was again raised step-wise.

In connection with this experiment the following observations were made:

Outgoing flow and pressure show a marked increase at the addition of fluid from the expansion vessel, with only a minor increase in filling pressure.

The kinetic energy increases with an increasing stroke rate. Higher kinetic energy of the incoming fluid supersedes the importance of static pressure, for the reverse displacement of the valve plane. This is visualized (Fig. 8-8) by an increase of outgoing flow and pressure, at lower filling pressure when stroke rate is increased. Further increase of filling pressure at a constant stroke rate, results in the following; drive ring 10 reaching a position during the passive part of the work cycle, at which differential areas of contact at surfaces 26 and 28 become equal. This means that the range of regulation by filling pressure has been fully utilized, and further increase of filling pressure does not result in extra output.

Increase of stroke rate at constant filling pressure does not give rise to filling problems. Instead it provides the pump with an extended regulation capacity, resulting in a higher minute volume before the regulation capacity has been fully utilized.

The pump can be provided with a sensor monitoring the position of the drive ring 10. The signal of this sensor is used to control the stroke rate, in order to prevent the pump from working outside its regulating range.

8.63 Experiment no. 3

The effect of increasing stroke rate on the performance of the pump was tested (Fig. 8-9).

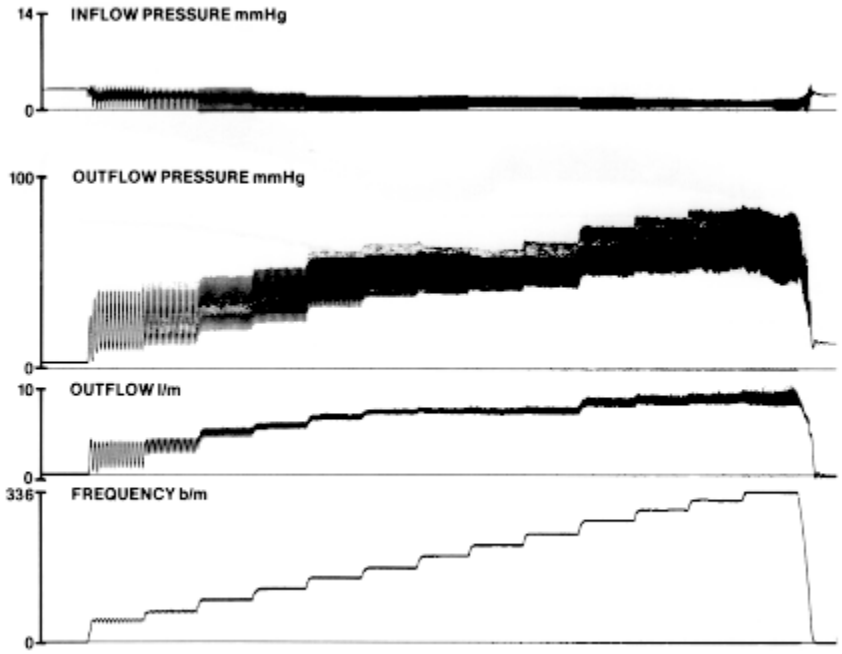


Fig 8-9: Single pump Effect of increasing stroke rate on performance of the pump

The same preparations were made as in the preceding experiment. The expansion cylinder was then raised, so as to achieve an inflow pressure of 3.5 mm Hg.

A constant peripheral resistance was introduced by clamping the outflow tube connecting the electromagnetic flow sensor and the "waterfall" cylinder.

The pump was then started with an initial frequency of 50 beats/min and the stroke rate was increased by increments of 25 beats/min.

The following observations were made:

Filling pressure remains constant up to about 125 beats/min, in spite of increasing minute volume and increasing efflux pressure. As explained above, this implies that the pump is not regulating anymore at higher frequencies than 125 beats/min, and that maximum stroke volume has been reached.

At about 150 beats/min, filling pressure is seen to decrease, which means that stroke rate has risen to a level where regulation by filling pressure again comes into effect. At still higher stroke rates, the output levels off. Filling pressure, however, continues to decrease, because of the dynamic forces now dominating inflow.

At a stroke rate of between 250 and 275 beats/min, a renewed increase of efflux rate and pressure is noticed. Filling pressure then reaches a new constant level, near the extreme systolic position of the drive ring 10. Inflow is almost completely non-pulsating, as can be seen from the very small pressure fluctuations on the inflow side.

A time-expanded recording (Fig. 8-6B) at this frequency range, shows the appearance of a v-wave in the inflow pressure trace. The inflow pressure trace is now almost identical to the jugular vein pulse pressure curve (presented in Fig. 8-7).

Further increase of the stroke rate, raises output due to these dynamic forces, until the decrease of filling pressure exerts a limiting effect on minute volume (Fig. 8-9).

This increased flow at high stroke rates shows that dynamic forces dominate. Outflow through valve 4 (the "aortic" valve) continues even after the drive ring 10 has reached its extreme systolic position. This implies that valve 5 (the "mitral" valve) opens before the closure of valve 4.

The dynamic forces also push back the drive ring. The v-wave in the filling pressure trace of the single-pump, is probably due to these dynamic effects.

The single-pump does not employ any elastic forces, to bring the drive ring 10 to its end diastolic level.

There are two kinds of forces which bring the drive ring back to its end-diastolic level:

- Dynamic forces (vis a fronte), generated by the systolic movement of drive ring 10 (AV-plane). They will on closure of the outlet valve reverse, and exert forces on surface 28. This effect of reversed dynamic forces is described in the literature dealing with (amongst other things) Pelton-turbines (that is used in some hydro-electric generating sets).
- "Passive" feedback forces (vis a tergo). They will move the drive ring, as long as the following conditions prevail:
- pressure outside the pump is still somewhat higher than the air pressure in the pump
- the normalised area between bulb 6V and area 28 is greater than the normalized area between bulb 6A and area 26.

8.7 Comments on the Living Heart

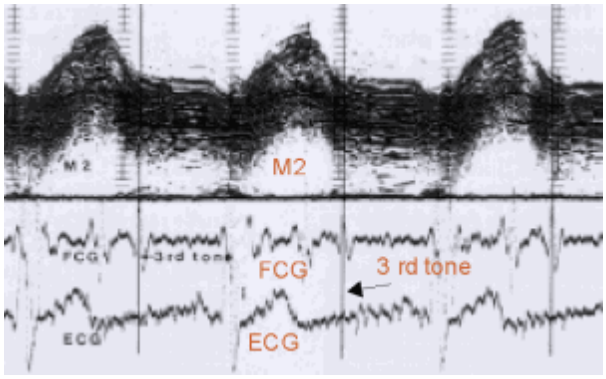
The heart effects the movement of the AV-plane towards apex, by shortening and thickening the muscles within a practically constant outer contour of the ventricles (see Chapter 3, Chapter 4 and Chapter 5).

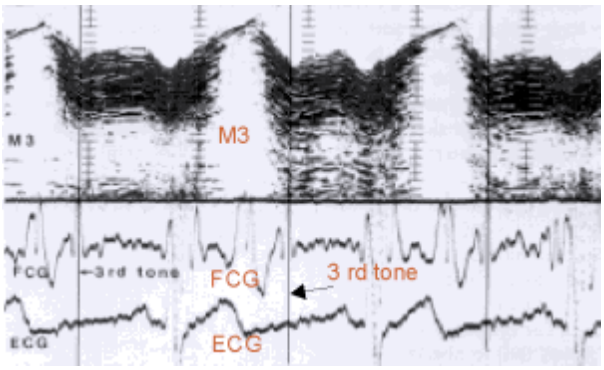
At the end of systole and closure of the aortic- and pulmonic valves, atria and ventricular chambers (as in the single-pump) act as a single unit. They have a common volume that is embedded in the surrounding tissues of the heart (including the pericardium).

The dynamic forces that have been generated by movement of the AV-plane will be directed towards the apex. The ventricular part of the common volume (which is moving in the direction of the dynamic forces) will change direction, due to resistance of the surrounding tissues. As in the single-pump, the dynamic forces will reverse and the AV-plane will be pushed away from the apex.

It is obvious, that if the ventricles at the end of systole were allowed to expand their outer contour, less force would be left to move the AV-plane. Furthermore, the volume expansion of the ventricles would (through the pericardium) reduce the possibility of the atria to expand. This would result in a reduced movement of the AV-plane, and another type of pump (a common displacement pump).

When no more expansion of the total heart volume is possible (due to restriction of the pericardium and the surrounding tissues), the following happens; any remaining dynamic forces will be converted to a pressure gradient (Bernoulli's Theorem, water-hammer effect), and movement of the AV-plane will cease. An example of this is shown in Fig. 8-10A, Fig. 8-10B, Fig. 8-10C, where the third heart sound coincides with the valve plane reaching event g'.





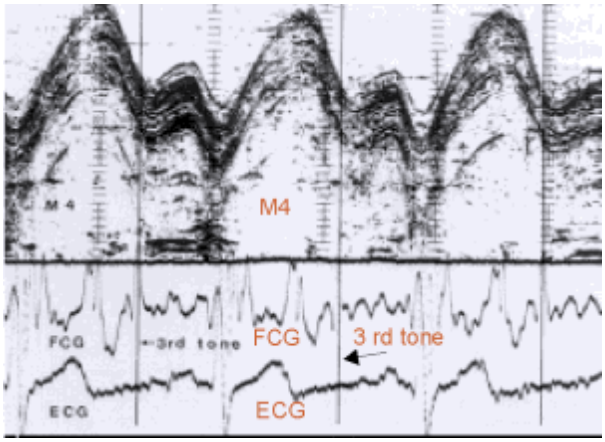


Fig 8-10A Single pump M2 mode EC registrations, phonocardiogram (FCG) and ECG, on a patient with pronounced third heart tone. .The third tone coincides with the level of the AV-plane at event h', before the "overshoot" of the AV-plane towards atria in event g', best seen at M4.

Fig 8-10B Single pump M3 mode EC registrations, phonocardiogram (FCG) and ECG, on a patient with pronounced third heart tone. .The third tone coincides with the level of the AV-plane at event h', before the "overshoot" of the AV-plane towards atria in event g', best seen at M4.

Fig 8-10C Single pump M4 mode EC registrations, phonocardiogram (FCG) and ECG, on a patient with pronounced third heart tone. .The third tone coincides with the level of the AV-plane at event h', before the "overshoot" of the AV-plane towards atria in event g', best seen above

g' : End of rapid return of the valve plane, in atrial direction

h' : Slight rebound movement, due to overshooting

The third sound is thus produced by the sudden retardation of the dynamic forces of diastolic inflow of blood (cf. Ishimitsu et al. [82]).

There are some indications, that larger stroke volumes can be achieved under some conditions, for instance in aortic valve insufficiency (Chapter 6) and at inspiration. The course is, that when the pressure within the thoracic cavity is negative (compared with the pressure within the heart), the following happens; the AV-plane will be pushed further away from the apex, resulting in a thinning of the walls of the ventricles, and thus larger stroke volumes are achieved.

This indicates, that when the heart in diastole expands its total volume by relatively long acting forces (and thus low support by the surrounding tissues), the following happens; the imaginary surface perpendicular to the directional movement of the AV-plane is larger on the ventricular side, than on the atrial side. The net forces are then pushing the AV-plane towards the atria (as in the single-pump).

With rising heart rate, the length of systole increasingly encroaches on ventricular filling.

At a heart rate of 60 beats/min, the length of ventricular diastole is about two-thirds of the cardiac cycle.

At a rate of 180 beats/min, the situation is reversed, with systole now accounting for approximately two-thirds.

It should also be noted that in absolute terms, diastole is reduced in length from about 300 milliseconds to about 100 milliseconds [56]; this is in agreement with earlier observations of intact dogs [57, 58].

It is obvious that with increasing heart rate, dynamic forces must dominate diastolic filling of the heart, in the same way as they do in the single-pump.

It would not be surprising if the same phenomenon that has been observed in the single-pump was found; in the normal heart working at high rates and low peripheral circulatory resistance, the mitral- and tricuspid valves open before the closure of aortic- and pulmonary valves.

8.8 Summary

The "gripping heart" working mode, Concept 1, served as a model for making a mechanical pump operating at essentially low and constant inflow pressures. That was relevant for a wide range of stroke rates, giving pulsed outflow pressure similar to that of the left ventricle of the human heart.

The following conclusions were made, in testing this pump (which can be used e.g., as a Left Ventricular Assist Device, LVAD):

- The single-pump is a new kind of displacement pump, not earlier found to be described. A suitable name for this kind of pump can be differential-displacement pump (or DeltaV pump). The design of the pump provides for smooth inflow and has optimal compliance, which is a major design problem [98] in other types of pumps. An increase in stroke rate adds additional smoothing, and makes the pump work more economically.
- Filling pressure controls stroke volume, as long as the pump is working within its regulation range.
- When filling pressure approaches the preset regulating level of the pump, an increase in stroke rate will not result in increased output. The exception is when the dynamic forces of incoming fluid become dominant, at higher stroke rates.
- This type of LVAD, driven by an electronically controlled motor, is able to limit the systolic pressure of the aorta, while keeping atrial pressure at a preset value.
- The working principle of the single-pump, can easily be transformed to the suggested basic working principle of the human heart[1] (Concept 1).

[1]Concept 1

The first concept defines the actual mode of pumping:

The heart strives to do its pumping, with a fairly constant total volume and outer contour, in an environment conferring a substantial moment of inertia.

Chapter 9

General Summary

The aim of this work has been to reassess the way the human heart regulates the physical pumping and circulation balancing modes. Two concepts have been proposed:

Concept 1

- The heart strives to do its pumping, with a fairly constant total volume and outer contour, in an environment conferring a substantial moment of inertia.

Concept 2

- The interventricular septum regulates ventricular stroke volumes to maintain proper balance between systemic- and pulmonic circulation.

The use of modern techniques, together with a thorough evaluation of ideas and experimental evidence in earlier published research, has provided the basis for this reassessment. The techniques were non-invasive (echocardiography) and invasive (gated thallium scintigraphy and coronary cineangiography).

The proposed pumping mode (the "gripping heart", Concept 1) is primarily characterised by a dominant force vector in the direction of the major heart axis. The old "Ventilebene" mechanism has been revived, and linked to the constancy of the outer heart contour, and thus to the environment in which the heart is working.

In the present study, it was found that the left ventricular wall outer contour displacement, on the average is less than 2 mm near the heart base. The displacement is diminishing in apical direction.

Atrio-ventricular valve plane displacement in the direction of the major heart axis at rest, was observed to be 19-22 mm.

These findings imply that left ventricle shrinks in systole by an approximately cylindrical segment, 19-22 mm in height, and with a radius of 34 mm. (The radius was obtained as a mean value from the left ventricle outer diameter, measured 2 to 3 cm below the atrio-ventricular valve plane.)

The cylindrical segment has a volume of 69-80 cm3, which coincides with the findings in young healthy persons 70-120 cm3, depending on body position [12, 25].

Contribution of atrial systole at rest was found to be about 25 %.

The balancing mode by ventricular interference, Concept 2, is new.

It enables the heart to balance between right- and left ventricle, by a working principle different from that of a displacement pump. It is closely linked to the pumping mode, Concept 1. The comparative rigidity of the outer walls of the heart, makes the ventricular septum to exert a double regulation. This regulating mode ensures a proper working of right- and left ventricle, in case of extensive damage to other parts of the ventricles than the ventricular septum.

The introduction of these two concepts implies a directional reorientation of force vectors for pumping and maintenance of circulatory balance.

The presently accepted concept is contraction/expansion of the ventricles in the direction of their lumen responsible for pumping, and needed for regulation (a common displacement pump), ad modum Starling.

That has been replaced by a new concept:

- a resultant force in the direction of the major ventricular axis (with respect to pumping action)
- a vector perpendicular to the major axis and ventricular septum (with respect to balancing mode).

The unique interplay of myocardial muscle fibres, cannot be reproduced by a single mechanical model.

By separation of the two vectors, it has been possible to design a double- and a single-pump, exhibiting the specific properties of the respective function.

The double-pump model, designed for constant total (left plus right chamber) output, simulates the balancing characteristics of the ventricular septum (Concept 2). It simulates a number of volume- or pressure-overload related heart defects, including different kinds of infarction.

The double-pump is in fact a displacement pump, and shares characteristics with many known artificial heart and left ventricular assist devices; example on characteristics are the quality of pulsating in- and outflow, and that inflow is not assisted by an "a fronte" effect. This is a major disadvantage at low filling pressures and high heart rates.

The single-pump is a new kind of displacement pump, not earlier found to be described.

A suitable name for this kind of pump can be dynamic-displacement pump.

This pump is working with "a fronte" effect (Concept 1), provides for smooth inflow and low filling pressure at high rates.

It also has an ability to control (and be controlled by) the inflow pressure in a closed loop circulation system. By doing this, it accomplishes another essential function of the heart; it is to keep left atrial pressure within a certain range, in order to protect the low pressure system from damage. It should thus be ideal to use, as a heart assist device. Its functional simplicity, and independence of sensor devices, should make it advantageous for safe long-term application.

Chapter 10

Pump- Technology and the Circulation Model Research and development; addendum

10.1 Pump types in comparison with the circulation system

10.11 Introduction

Contents Preface Acknowledgements Chapter 1 Chapter 2 Chapter 3 Chapter 4 Chapter 5 Chapter 6 Chapter 7 Chapter 8 Chapter 9 Circulation Model Function of the heart Tables References

It is important to completely understand how the heart performs its pumping- and regulation-functions, to fully realize the significance of mechanical insufficiency of the heart.

The heart has been placed in the class of displacement pumps. The idea, that the heart should belong to the classes' radial pumps or run through pumps, has been regarded as impossible.

The heart though, has characteristics that are not compatible with the characteristics of the displacement pumps:

- changed (or even lower) filling-pressure for increased frequency and increased minute-volume
- "check valves" that are closing without backflow
- the ability to keep two circulation systems in balance, without control-mechanism

We have been able to prove, that the heart does not belong to any of the previous known types of pumps. The heart has the best of the characteristics from the different types of pumps. These characteristics have been combined to a unique pump, with the following characteristics:

- possibility to have continuous inflow and pulsating outflow
- internal impedance close to zero
- no problems with filling during high frequencies
- increased (instead of decreased) stroke volume during increasing frequency
- the inflow directs the pump
- "the check valves" are closed by inflow (not by back-flow), which do not lead to any losses in stroke volume

Displacement pumps have none of the characteristics mentioned above, but all of them are represented in the heart.

We have developed a new type of pumps, based on the characteristics of the heart. We call them DeltaV pumps

10.12 Radial pumps

Here we have centrifugal pumps and Archimedes screws.

With the circulation system of the human body in mind, the positive characteristics for this type of pumps are:

- continues inflow
- no valves are needed

- can be constructed in miniature, with high rotation speeds and rather large minute volumes
- simple, light and rather inexpensive constructions

With the circulation system of the human body in mind, the negative characteristics for this type of pumps are:

- continues outflow (not good for the vessels in long perspective)
- in- and outflow are always connected, which can produce severe regulation-problems
- problems with bearings and tight joints
- the efficiency do change, if there is changes in pressures and flows

10.13 Displacement pumps

This group includes piston pumps, membrane pumps, hose pumps and gear pumps.

With the circulation system of the human body in mind, the positive characteristics for this type of pumps are:

- pulsating outflow
- the pressures in the inflow-chambers does not affect the inflow
- it is possible for the inflow (to some extent) to direct the pump (passive filling)
- the efficiency do not change, if there is changes in pressures and flows

With the circulation system of the human body in mind, the negative characteristics for this type of pumps are:

- pulsating inflow
- increasing inflow-pressure and problems with filling the pump, if the time period for filling is short
- one or two check valves is essential
- compliance-chamber is in most cases essential, if the pump is going to work in an electro-mechanical way, or is going to be implanted
- complicated technique, with weight- and volume-problem

10.14 Other pump types

Here we have for example run through pumps (ejector pumps or secondary combustion chambers).

The characteristics of the run through pumps are very much alike those for the centrifugal pumps. The run through pumps works with the principle, that one flow give rise to another flow.

With the circulation system of the human body in mind, the positive characteristics for this type of pumps are:

- continues inflow

With the circulation system of the human body in mind, the negative characteristics for this type of pumps are:

- continues outflow

10.15 Delta-V pumps

We have developed a new type of pumps, based on the characteristics of the heart. We call them DeltaV pumps.

With the circulation system of the human body in mind, the positive characteristics for this type of pumps are:

- continuous inflow
- pulsating outflow
- the inflow directs the pump

- can parry changes in outflow pressure, as long as the pump-power is sufficient; if it is not, the pump will stop
- variations in inflow-pressure do not affect the inflow
- internal impedance close to zero, even during high frequency
- no check valves
- the rapid filling make it possible for skeleton-muscles to drive the pump

With the circulation system of the human body in mind, the negative characteristics for this type of pumps are:

- new and untried technique

10.2 The Circulation Model

To improve the understanding of the new knowledge and to facilitate for further research, development and education, Gripping Heart AB is developing a circulation model. It will fulfill all the conditions and the characteristics, that earlier only was possible to measure in the natural circulation system.

In The Circulation Model, a couple of variables could be varied in a randomized- or systematic way:

- peripheral resistance
- compliance
- diastolic pressure
- Bainbridges reflex (heart rate)
- total "blood" volume
- venous volume
- artery volume
- the regulating function of the inter-ventricle septum

A lot of experimental studies, which have direct correspondence to the natural circulation system (and earlier have been difficult to explain), is possible to perform with the parameters above.

In The Circulation Model the cause and result could be exactly presented in tables and in graphic. You learn which of the parameters that is important to control, and how to change the function of the delta-V pumps, inside or outside of a circulation system. You also have the possibility to compare the results, with respective parameters in the natural circulation system. It is an effective and lucid way to discover, how the new knowledge and technology affects the domains of medicine.

In Fig. 10.1 you can see an outline of The Circulation Model.

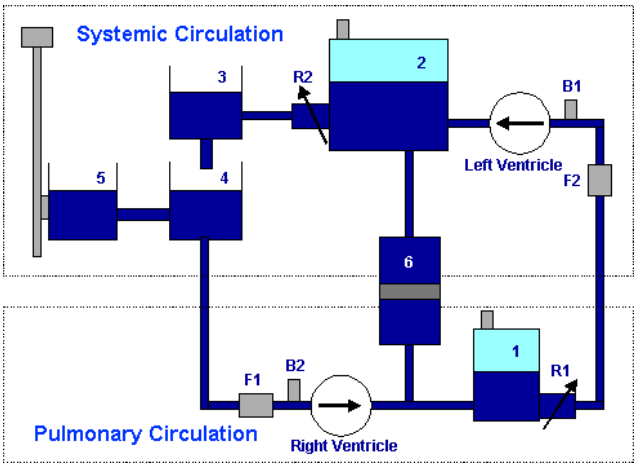


Fig. 10-1: The Circulation Model

The water in the system (which simulate blood in the human body) is pumping into a chamber (1: Lung volume), by a DeltaV pump (Right ventricle) (see Chapter 11).

The flow into the chamber is measured by a flow transmitter (F1: Flow transmitter no. 1).

The chamber is hermetically sealed and contains some air, which simulates the compliance of the pulmonic circulation.

On this chamber there is drainage, with a valve that can be opened to decrease the water volume.

At the outflow part of the chamber is a resistance (R1: Resistance in pulmonic circulation) adapted, which simulates the resistance in the pulmonic circulation.

The water that flows out of the chamber, arrives to another delta-V pump (Left ventricle). It is pumping the water into a chamber (2: Central artery volume).

Between the pump and the chamber a flow transmitter (F2: Flow transmitter no. 2) and a pressure transmitter (B1: baroreceptor no. 1), which simulate the baroreceptors in aortic arch and sinus caroticus, are adapted.

The chamber is hermetically sealed and contains some air, which simulates the compliance of the systemic circulation.

On this chamber there is drainage, with a valve that can be opened to decrease the water volume.

At the outflow part of the chamber is a variable resistance (R2: Resistance in systemic circulation) adapted, which simulates the variable resistance in the systemic circulation.

The next site for the flowing water is a new chamber (3: Periphery artery volume). On this chamber, there is a connection with a water-tap, to make it possible to increase the water volume in the system.

There is also a pipe between Periphery artery volume and another chamber (4: Venous volume), which have a connection with a chamber (5: Regulatory part of venous volume).

Regulatory part of venous volume is possible to increase or decrease, by help of an electric motor. That simulates the possibility for the venous system to vary the pooling of blood.

There is drainage on this chamber, with a valve that can be opened to remove some water from the system.

From Venous volume the water pass into Right ventricle, and between these vessels there is a pressure transmitter (B2: baroreceptor no. 2), which simulate the baroreceptors in the left atrium of the heart.

Both Right ventricle and Left ventricle are connected with a chamber (6: Regulatory function of the inter-ventricular septum), that contains a membrane, which is flexible and separates Right ventricle from Left ventricle.

Gripping Heart AB has today a prototype of The Circulation Model, which do not have the chamber Regulatory function of the inter-ventricular septum. The company has during a long period prosecuted pilot studies according to the prototype model.

A lot of changes must be done in the medicine area, to make it possible to follow and register the function and roll of the heart in the circulation system. Here follows some examples:

- methods and instruments for measurements of static- and dynamic pressure
- methods and calculation models to splitting the total blood volume in central/periphery venous volume and central/periphery artery volume
- methods and instruments for calculation of the tonus in the veins
- new hardware- and software programs is needed in all investigation methods (X-ray, gamma camera, echocardiography and MRI), to measure and register the movements of the AV-plane and inter-ventricular septum. Based on that, it is possible to estimate the condition of the heart.

We are planning to develop new artificial heart- and lung-machines, left- and right assist devices (LVAD and RVAD), plus methods to reconstruct the natural heart. By doing that, we hope that we can contribute to avoid invalidating heart failures in the future.

Chapter 11

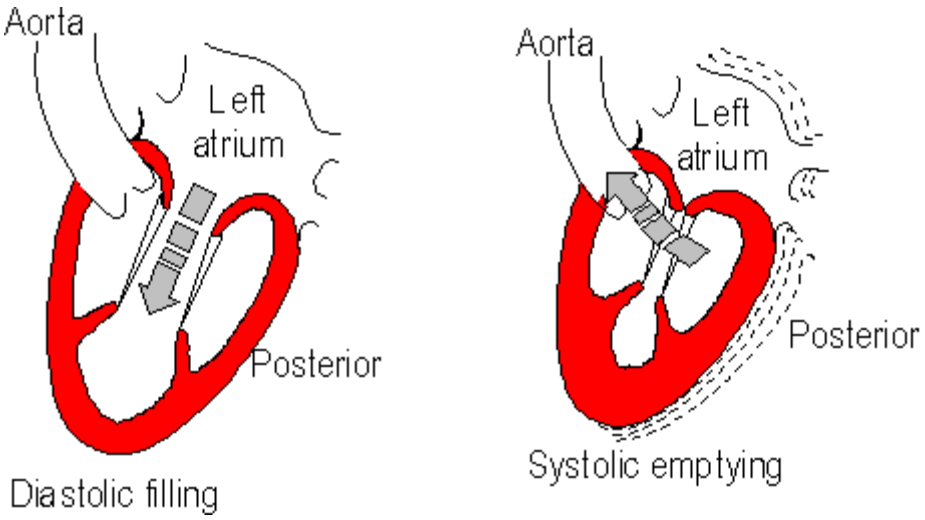
The Heart - the Pumping Function and its Regulation Research and development; addendum

11.1 Part One - The Pumping Function of the Heart

The prevailing view is that the heart is pumping by squeezing motions. This view is relatively new. In fact, for almost 100 years (until the end of the Second World War), the heart was thought to carry out its pumping by a back and forth going motion of the valve plane. For example, this was the view of the German professors Henke and Böhme.

After the Second World War, first X-rays and later gamma camera and ultrasound investigation techniques gave a new interpretation of the pumping of the heart; the pictures was interpreted as if the heart carried out its pumping by squeezing motions.

Fig.11-1 The prevailing view, that the heart is pumping by squeezing motions.



Also, an uncovered heart, surrounded by air, changes its size while pumping. This was seen as another proof of the squeezing pumping motion of the heart.

In the beginning of 1980, M.D. Lundbäck rediscovered the pumping function of the heart. He also made a new discovery; the regulating function of the intra-ventricular septum. The investigations that lead to the discoveries was initiated by three patients with inexplicable and contradictionary observations.

- The first patient was a well known bicyclist. He performed a tremendous high workload in stress tests, although he had a total aortic insufficiency.
- The second patient was a concrete worker. He had a normal workload with no symptoms in stress tests, although he had a huge infarction covering the whole left ventricle, except the intra-ventricular septum.
- The third patient was M.D. Lundbäck's father. He had an infarction in intra-ventricular septum, although the rest of the heart was fully functional, he died in pulmonary oedema.

(Explanations of the observations, see The inexplicable three observations, which led to the discovery of the true pumping and regulating function of the heart)

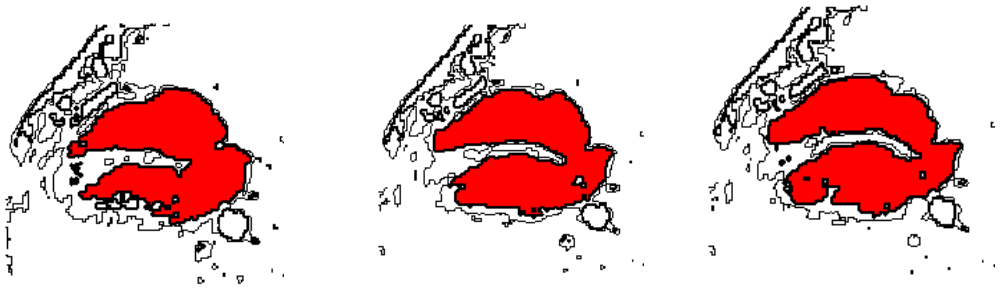
Those observations led to the discovery of the pumping and regulating functions of the heart. presented 1986 in the thesis 'Cardiac Pumping and Function of Ventricular Septum'. The thesis complemented with MRI (Magnet Resonance Imaging) describes why we have the impression/illusion that the heart is carrying out its pumping function with squeezing motions. It also introduce the heart as been a new kind of pump, which couldn't be incorporated into the existing pump-classes. That led to the introduction of a new pump-class we call Dynamic Displacement Pumps (DDP). The thesis also describes the importance of intra-ventricular septum, being the structure that regulate the blood flow through the pulmonary- and systemic- circulation system

There seems to be 5 'illusions' masking the real pumping and regulating function of the heart.

Illusion	Method	Error
1st::	X-ray	Shows the motions of the inner contour
2nd:	Ultra sound:	False reflection of a bent surface
3rd:	Isotope marking:	Errors in the programming of the gamma camera and in treatment of the raw picture
4th:	Open chest:	The heart changes to become a different type of pump
5th:	Magnet Resonance Imaging (MRI):	The power of the heart's way of working generated by shortening and thickening of the muscle. This shows a false picture of a volume displacement

During open chest the heart behaves differently than when it is located in the intact chest. During surgery or in the animal laboratory, the support from the chest is lost, as is the apical fixation. The heart does change its pumping technique; it will transform into a displacement-pump. The displacement of the Atrio Ventricular(AV)-plane is therefore not obvious, and the myocardial contraction appears as a squeezing movement. Given an almost constant volume of the heart within the intact chest though, it is physically impossible for the myocardium to change the intra cavity volume to drive the blood flow.

With Magnet Resonance Imaging (MRI), not available 1986, one gets a different view of the pumping heart. In Fig.11-3A-B, one can easily see that the inner volume of the ventricles change drastically. The squeezing motion has been interpreted as being the mechanism for the pumping function of the heart. However, one can also make the following observations:



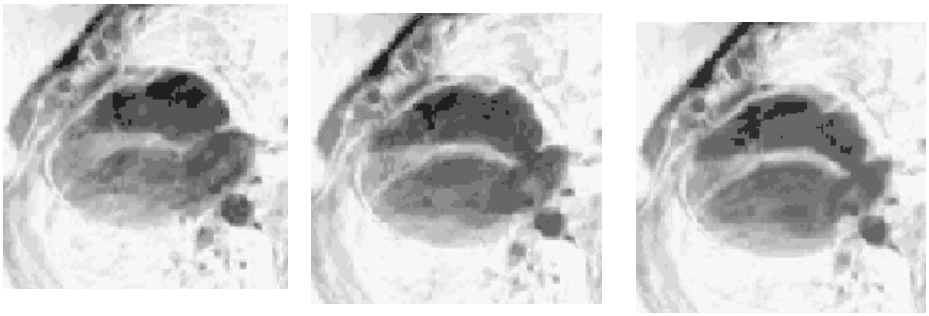


Fig 11-3A-B A: 2 MRI-images (Ventricle-Systole and Ventricle-Diastole) in the parasternal long-axis B: The inner contour of the heart is shown, in synchronization with A, and as can be seen: the inner contour of the ventricles change drastically, but the outer contour are almost constant

- The Atrial Ventricular plane (AV-plane) with its valves is moving back and forth within the pericardium. It is producing a piston-like pumping function, with a (actual) stroke volume determined by the displacement and the area, of the AV-plane.
- When the AV-plane is sliding within the pericardium, the muscle walls are extended and contracted.
- By contracting themselves, the ventricular muscles are bringing the AV-plane towards apex cordis.
- By contracting themselves, the atrial muscles are bringing the AV-plane towards the atria.
- The outer volume change (DeltaV) contributing to the (actual) stroke volume, is small.

20 MRI-images from one heart cycle

These simple observations have strengthened us in our conviction; it is time to return to the earlier ideas of the pumping function being created by the moving valve plane. It is also time for a new way of explaining the regulation of the heart.

Using these new ideas of the function of the heart, hitherto inexplicable observations can be explained. Also, observations with X-ray, gamma camera and ultrasound technique as well as observations of uncovered hearts can be accounted for. This will not be further addressed here though (see Chapter 2 to 9).

Instead, we will present a new mechanical pump designed according to the same principles as we think apply to the heart. Using this mechanical pump as a model of the heart, a number of observations of the behavior of the heart can be accounted for.

11.2 A mechanical pump based on the principles of the heart

In the following description, a distinction is made between two phrases. One is the actual stroke volume of a pump, which can be calculated from the geometry of the pump. The other is the apparent stroke volume, which can be calculated from the flow through the pump and the cycle frequency.

In some cases these phrases are the same, but in others they are not.

In Fig. 11-4, the construction of the mechanical pump is shown. It consists of an inlet and an outlet tube with different diameters, d1 and d2, where d2 > d1. The inlet and outlet tube are joined by a third moving tube, that can move back and forth, sliding against the inlet and outlet tube. The moving tube has an inlet valve, which corresponds to the mitral (or tricuspid) valve of the heart.

Above the inlet valve, there is a volume A and below there is a volume V. The outlet tube has an outlet valve corresponding to the aortic (or pulmonic) valve of the heart.

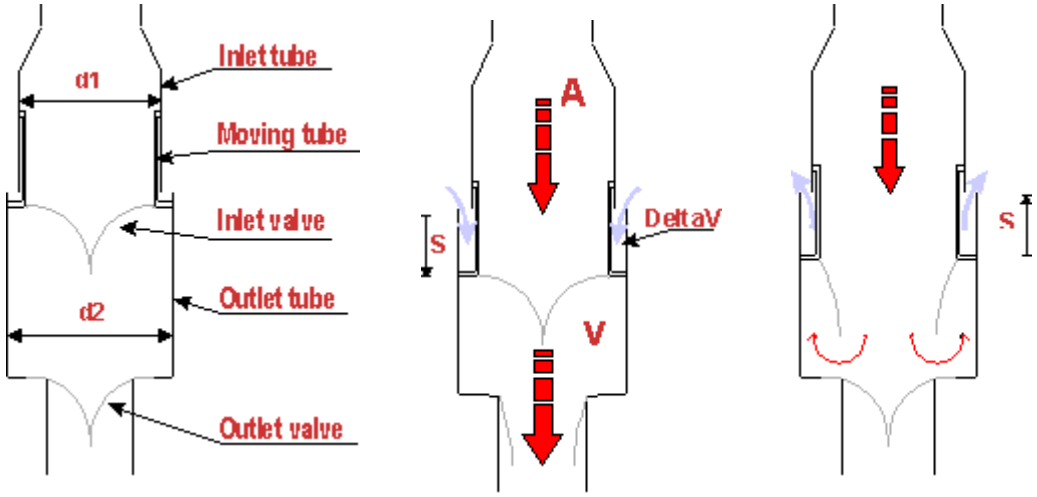


Fig. 11-4 A mechanical pump Based on the principles of the heart. Conditions: d2 > d1, DeltaV > 0 and a freely moving wall

There is a circular space between the outlet- and the inlet tube, that dynamically creates an external volume change DeltaV when the position of the sliding tube varies.

The external volume change DeltaV will affect the surroundings of the pump.

In an ordinary displacement pump (a piston pump), DeltaV is usually equal to the actual stroke volume. It means that the surroundings of the pump have to change its volume to the same extent as the actual stroke volume of the pump. This can cause severe problems when the surroundings of the pump is not air, or if the surrounding air volume is small.

For our pump model, the outer volume change DeltaV is small compared to the actual stroke volume. The latter can be calculated as π x (d2 / 2)^2 x S, where S is the distance between the two end positions of the moving tube.

There is a power source (not shown in the Fig. 11-4) that can move the moving tube a distance S in the direction of the outlet valve. When the moving tube has reached its lower end position (closest to the outlet valve), the power source is disconnected and the moving tube can slide freely.

Fig. 11-5A-D shows the pump cycle at lower frequency. This case is explained first.

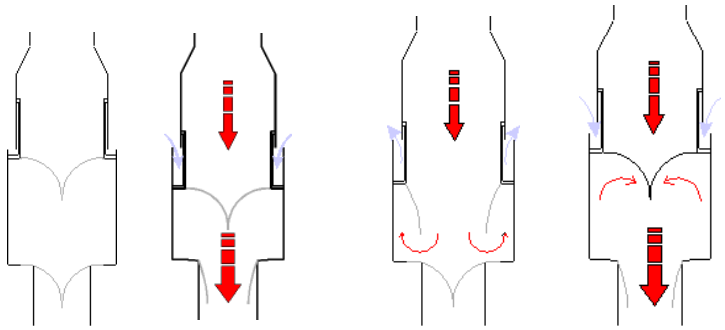


Fig. 11-5A-D Function of the mechanical pump cycle at lower frequency.

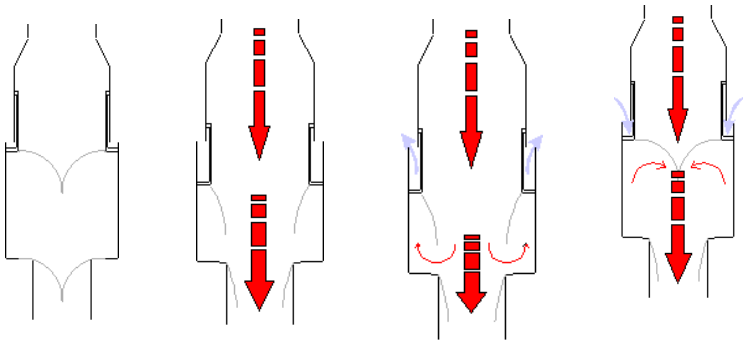


Fig. 11- 6A-D Function of the mechanical pump cycle at higher frequency

Starting from the upper end position (Fig. 11-5A), the moving tube is pulled towards the outlet valve by the power source, with closed inlet valve. This accelerates the fluid column on both sides of the inlet valve.

When the induced pressure exceeds the pressure in the outlet pipe, the outlet valve opens and lets the fluid out of the pump (Fig. 11-5B). When the moving tube has reached its lower end position, the acceleration of the upper and lower fluid column cease and the power source is disconnected.

The upper and lower fluid column has now acquired its maximum kinetic energy (kinetic energy=mv^2/2)

The kinetic energy of the lower fluid column will decrease rapidly because of the resistance in the circulatory system, and the outlet valve will close. (Fig. 11-5C).

The remaining kinetic energy of the incoming fluid column starts to push (when the lower fluid column slows down) the freely sliding moving tube back towards its upper end position. The moving tube will produce an internal redistribution of the fluid inside the pump and a volume increase, corresponding to volume difference DeltaV. The flow behind and through the inlet valve will create the pressure needed to close the inlet valve. The motion of the moving tube occurs because the moving tub has a larger surface, facing volume V, than the surface facing, volume A. When the surfaces are exposed to the same pressure, the force towards the upper end position will be stronger, due to the larger surface, facing volume V . This means that there is still an inflow to the pump, although the outflow has ceased.

If the kinetic energy of the incoming fluid column has not been consumed, by the time the moving tube has reached its upper end position, the following will happen; the kinetic energy will be consumed by an abruptly de-acceleration of the fluid column creating sounds and maybe a small extra output from the pump (compare with the third sound of the heart and the water hammer effect) (Fig. 11-5D).

This can only happen if the moving tube reaches its upper end position before the next pump cycle has been started.

Note: the importance of the difference in volume DeltaV) between the upper and lower end positions of the moving tube. It is this DeltaV that makes it possible to have a continuous inflow although the outflow is pulsating

The pump cycle at higher frequency, as demonstrated by Fig. 11-6A-D, the pump functions a bit differently.

Again starting from the upper end position (Fig. 11-6A), the pull towards the outlet valve of the moving tube, accelerates the fluid columns.

The kinetic energy of the fluid column is now, so large that when the sliding tube reaches its lower end position both valves will be open (Fig. 11-6B).

When the power source is disconnected, the moving tube can move freely. The flow through the outlet valve starts to decrease because of the resistance in the circulatory system but the inflow to the pump doesn't need to slow down. This occurs because of the possibility to fill the volume DeltaV, by pushing the moving tube back against its upper end position, in spite of both valves being open (Fig. 11-6C).

When the new pump cycle begins, the inlet valve will close and again accelerate the fluid column (Fig. 11-6D).

Note: that with higher inflow and thus higher frequencies, the importance of the outlet valve will cease, and the pump will have a continuous inflow and an almost continuous outflow. Also, since both valves are open at the same time, letting fluid pass through the pump, the apparent stroke volume will increase with increasing pump frequency.

11.3 The inflow controls the pump

The stroke length of the moving tube (compare with length S in Fig. 11-4) depends on the inflow to the pump.

With a constant frequency, the stroke length will vary with the inflow. A decrease of inflow gives a decrease in stroke length and an increase of inflow gives an increase in stroke length.

With a constant stroke length, the frequency has to vary with the inflow. A decrease of inflow gives a decrease in frequency and an increase of inflow gives an increase in frequency.

The Dynamic Displacement Pumps, is the only pump-technology where the inflow automatically controls the pump.

11.4 In summary, The new pump-technology (Dynamic Displacement Pumps) has the following characteristics:

- Inflow controls the pump
- Continuous inflow and pulsating outflow, with close to continues outflow if the inflow and frequency is high enough
- The output exceeds the calculated stroke volume with increasing inflow and frequency.
- The closing of the inlet valve is controlled by the inflow, without any back flow losses.
- The dynamic pressure change, but the static pressure can be constant even at at high frequencies.
- No need for an output valve, if DeltaV is small (compared to the actual stroke volume) and the inflow and the frequency is high enough.

11.5 Using the mechanical pump as a model of the heart

What are the similarities between the described mechanical pump and the human heart?

The inlet and outlet tubes of the mechanical model correspond to the pericardium, which with support from the surrounding tissues prevents a change of the outer form of the heart. The shape of the pericardium is such, that the largest diameter is situated approximately 2-3 cm below the AV- plane in diastole; all diameters above this point are smaller. Thus, the prerequisites for a correct movement of the AV-plane exist.

The moving tube corresponds to the atrial- and ventricular muscles which, as observable with MRI, slide back and forth by stretching and shortening themselves inside the pericardium. This moves the AV-plane (with its valves) up and down.

As stated before, the inlet valve corresponds to the mitral (or tricuspid valve) and the outlet valve corresponds to the aortic (or pulmonic) valve.

The volume change DeltaV corresponds to the flexibility of surroundings of the heart (as observable with MRI). That the outer volume change should be small, can be understood by considering the fact that the heart is surrounded by tissues. These have to be moved for each pump cycle. Naturally, this waste of energy should be kept at a minimum.

In the mechanical model, only the movement of the moving tube contributes to the actual stroke volume of the pump. As previously stated, with MRI technique it is easy to see that the ventricular muscles of the heart gets much thicker in systole. Does the thickening of the muscles really contribute to the actual stroke volume of the heart? No, it does not!

In Fig. 11-7A-E, five models of the heart with a moving valve plane are displayed. In Fig. 11-7A and Fig. 11-7C, there is no significant thickening of the muscle walls, while in Fig. 11-7B, Fig. 11-7D and Fig. 11-7E the muscle walls get thicker in systole.

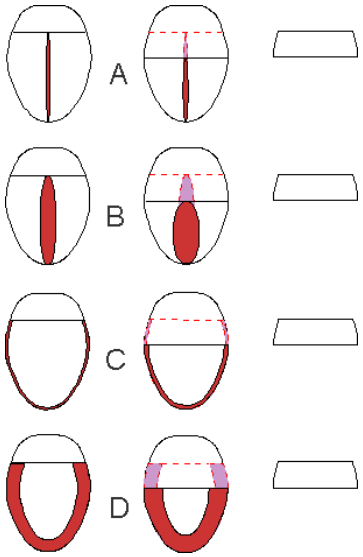


Fig. 11-7A-D

Consider the fact, that the outer contour change is minimal and that the total volume of the muscles does not change. The muscle volume is only distributed in a different way in Fig. 11-7B, Fig. 11-7D and Fig. 11-7E, compared to Fig. 11-7A and Fig. 11-7C.

Also, to make it easier to understand that there is no significant differences between the stroke volume in the five models, assume that the blood enters the heart models from the top and exits in the bottom. With this in mind, looking at Fig. 11-7C, it is fairly easy to realize that the actual stroke volume is determined by the movement of the valve plane, as shown in the third column. However, the same is true for all the models!

As is shown in Fig. 11-7E, DeltaV is divided in to parts, DeltaV1 andDeltaV2.

DeltaV1 is the part of DeltaV that is on the atrial side of the AV-plane, and is essential for the motion of the AV-plane. Even areas of the proximal aorta and pulmonary artery multiplied with the stroke length of the AV-plane gives a contribution to DeltaV1 .

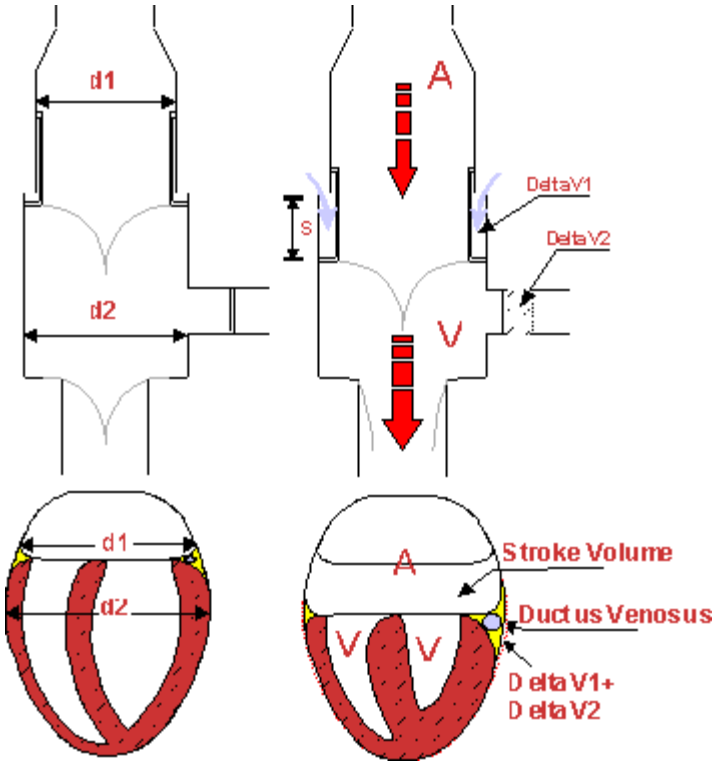
DeltaV2 is the part of DeltaV that is on the ventricular side of the AV-plane. The outer volume change DeltaV2is very small, and do not contribute very little to the (actual) stroke volume. DeltaV2 doesn't contribute to the motion of the AV-plane. It exists due to some compliance in the myocard, pericardia and their surroundings, and is causing loss of energy.

In the mechanical model, there is nothing that corresponds to the atrial contractions of the heart, which contributes to the actual stroke volume. Atrial contractions are important at low frequencies, but the importance decreases with higher frequencies. If desired, this could be added to the mechanical model.

One important difference between the mechanical model and the heart though, is that the power source and the construction material in the heart are the same: the muscle. This is a unique construction, which have varying mechanical qualities depending on the state of muscle activity:

- In an inactive state, the muscle is slack, indulgent and elastic.
- In an active state, the muscle is stiff and resistant.

In conclusion, it seems as if the basic elements of the mechanical pump can be found in the heart. Using the mechanical pump as a model of the heart, a number of questions regarding the function of the heart can be answered. The following are examples of such questions and answers offered by the mechanical model:



11.6 Questions and answers regarding the heart, offered by the mechanical model

How is it possible for the heart to be filled at high frequencies and at large flows?

How can the right ventricle of the heart have a constant filling pressure, regardless of the frequency and the magnitude of the flow through the pump?

Why does not a person normally feel, that the heart is beating?

Why isn't there any back flow losses, when the valves are closing?

How can atrial contractions contribute to the pumping function when they lack inlet valves?

What is the explanation of the auscultatory heart 3rd heart sound?

Why can you sometimes feel palpitations?

How is it possible, that there is an increase of the apparent stroke volume of the heart at high frequencies, although the heart size and the filling pressure to the right ventricle is unchanged ? (The filling pressure and the heart size can even decrease)

Answer 1

The major filling of the heart (except for the minor volume DeltaV) occurs during systole. The prevailing view, that the major filling of the heart occurs during diastole is false.

During systole (when the AV-plan is moving in the direction of apex), the major part of the filling of the heart occurs

Answer 2

The heart is inflow controlled, like the mechanical pump. If the static inflow pressure should rise, baroceptors in the right atrium will immediately tell the heart to increase the frequency. Thus, the static pressure is almost constant, but the dynamic pressure (corresponding to the kinetic energy of the blood that passes through the heart) increases with increasing inflow and frequency. This is not possible to detect with the monitoring technology for medical purpose of today.

Answer 3

The outer volume change of the heart is limited to the very small volume DeltaV. That will not bring enough energy to feel the heart beating.

Answer 4

When the AV-plane has reached its lower end position (closest to the apex), the power from the contracting myocardium is interrupted and the acceleration of the fluid column cease.

The fluid column have now acquired an amount of kinetic energy. When the flow through the proximal aorta and pulmonic artery decreases.

The remaining kinetic energy of the incoming fluid column pushes the AV-plane back towards its upper end position consuming the volume difference DeltaV1. The motion of the blood behind and through the tricuspid- and mitral valves are closing those valves, and thus there will be no back flow losses..

The closing of the aortic- and pulmonic valves, can be achieved by the motion of the AV-plane catching up the speed of the outgoing blood stream, and thus there will be no back flow losses.

Answer 5

Because the force of inertia around and inside the heart. The contracting of the atrial muscles will bring the AV- plane away from apex (cf. Fig. 11-11). The atrial contraction thus contribute to the total stroke length.

Answer 6

3rd heart sound appears, if the kinetic energy of the incoming fluid column has not been consumed by the time the AV-plane has reached its upper end position. The kinetic energy will be consumed by an acceleration

of the entire pump and its surroundings. The sound comes from the pericardium, that suddenly stretches while consuming DeltaV. (It is well-known, that you can never hear a 3rd heart sound on a patient, who do not have a pericardium).

Answer 7

With the prevailing view (that the heart is pumping by squeezing motions), one can never answer this question. How could you feel the apex beating against the chest during systole, with the heart simultaneously getting smaller?

The explanation is, that the pulmonary artery and ascending aorta are attached to the anterior part of the AV-plane, and are relative fix to the surroundings of the heart. Therefore, when the AV-plane moves in the direction of apex during systole, the posterior part of the AV-plane will move more easily than the anterior part. This creates a momentum that can be felt, which causing the apex to beat against the chest wall .

The "rocking heart" phenomenon seen in pericardial effusion, can be due to the same momentum.

Answer 8

At high frequencies, the kinetic energy transferred to the blood by the ventricular muscles, will make both valves open at the same time. That will let more blood flow through the pump in systole, than can be calculated from the actual stroke volume and frequency. Compare the blood flowing through the heart, with a skier moving in a track. The skier continues to slide in the track, some seconds after pushing away with the sticks. In the same way, the blood continues to flow through the heart, some milliseconds after the mitral- and tricuspid valves have opened. Compare the pushing of the sticks, with mitral- and tricuspid valves gripping and moving the column of blood.

11.7 Part Two - The Regulation of the Heart

The nature has, by the motion of the inter-ventricular septum and the pumping function of the heart, created a double auto regulation function, that exactly balance the stroke volumes to the systemic- and pulmonic circulation. This is made by using the passive (non-rigid) and active (rigid) phases of the muscles in the following way.

- In diastole, when septum is in a passive phase, it will be pushed towards the right or left ventricle, depending on the direction of the prevailing pressure gradient between them
- In systole, septum and the rest of the ventricles are in its active phase. Due to a higher resistance in the systemic circulation than in the pulmonic circulation, the pressure is higher in the left ventricle than in the right ventricle. The intra-ventricular septum is a part of the left ventricle. For a homogenous material, the relation between strain and deformation is equal for every point (Hooks law). This means that when the left ventricle during systole is pressurized, intra-ventricular septum will (independent of its shape and position in diastole) form a circular shape in the short axis. A motion of septum increases the stroke volume on one side, and decrease the stroke volume with the same amount on the other side. This double regulating function is a direct result of the almost constant outer volume of the heart.

In order to have a circulatory balance with no regulation, the intra-ventricular septum needs to keep its systolic shape even in diastole. This is why, normally, the left ventricle always has a higher diastolic pressure than the right ventricle. This pressure difference is always generated by the heart itself , because it has to overcome the elastic forces in septum .

11.8 Increased inflow to the heart, Example I

An increased inflow to the right side of the heart will during the first few heartbeats, generate an increased static filling pressure to the right ventricle. By the balancing action of the inter-ventricular septum, the stroke volume from the right ventricle is increased. Accordingly, the stroke volume will decrease during the first few beats from the left ventricle.

An increased inflow to the pulmonic circulation, will soon produce an increase in filling pressure to the left side of heart. An increase in filling pressure on the left side. By the balancing action of the inter-ventricular septum, the stroke volume from the ventricle will increase. The stroke volume from the right ventricle will decrease accordingly and the total static pressure within the heart has increased.

The baroceptors in the right atrium, and to some instant the automation within the muscle itself , will sense the increase in static filling pressure, and increased the heart frequency. Due to the pumping function of the heart, the increase of the heart rate enables the heart, to take care of the increased inflow and convert the increased static pressure to dynamic pressure. Within a few heart beats, balance has been attained again and flow rate has increased and the static flow pressures are the same, as before the change of inflow to the heart

The inter-ventricular regulating function is in fact the key for the transplanted heart, which have to cope with regulation in spite of all external nerves cut off.

11.9 Decrease of inflow of the heart, Example II

A decrease of the inflow to the heart will during the first few heart beats generate a decrease in the static filling pressure to the right side of the heart. Consequently the pressure on the left side, will be relatively higher. This means that intra-ventricular septum during a few beats, will be pushed towards the right ventricle. Compared with Example I, septum now has to be stretched out, which requires extra work-load, this work-load cannot be generated due the fact that the stroke volume from the right side will decrease. This means that the total heart volume will be smaller.

The baroceptors in the right atrium, and to some instants the automation within the muscle itself , will sense the decrease of the filling pressure and decrease the heart rate. The dynamic pressure into the heart will go down, and the static pressure to the right ventricle will go up, and bring back the heart to its 'normal' size. The balancing act of the ventricular septum and the pumping function of the heart, has within a few heart beats adapted to the new inflow. Compare this with the change of stroke volumes and heart size during breathing.

11.10 The combination of construction material and energy source in the same unit is a brilliant but dangerous solution

The pumping function of the heart can roughly be compared with an ordinary garden pump (see Film: Cardiac Pumping and function of ventricular septum). The outer cylinder made of steel or polymeric material can be compared with the pericardial sack. The inner tube, made of the same material, can be compared with the atrial- and ventricular-muscles. The artificial valves can be compared with the valves in the heart. The power needed to create a back and forth movement of the inner cylinder is powered by external forces, like manpower or an electrical motor. In the heart the power is generated by the atrial and ventricular muscles. The produced back and forth movement is gripping/catching the fluid column, when the inner cylinder is reaching its highest position and with the valves closing the inner cylinder will displace the fluid column when going forth again.

If the power supply in the garden pump would change, it wouldn't change the mechanical construction of the garden pump. Instead the change of power supply would alter the capacity of the garden pump.

Example: 50% change of power would result in 50% in capacity.

If the power supply in the heart would change, not only the capacity but also the construction of the heart would be altered. This is due to that the muscle is both the energy source and the construction material, where the construction material varies very much if it is in an active or passive phase. If the part of the heart muscle that is leaning against the pericardial sack for some reason can't stiffen (be rigid), this part of the heart muscle will then be supported (during systole, when high pressure occurs) by the rigid pericardial sack and the surrounding tissues. Other parts e.g. the intra-auricular- and intra-ventricular septum has only its own rigidity in the inactive phase and the difference in blood pressure between the chambers to lean on. This is what the intra-auricular- and intra-ventricular septum has to rely on when it shall withstand the blood pressure that is generated during systole.

The nature has made use of the muscle being a nonrigid material in diastole and a rigid material in systole in the following way: the back going motion of the valve plane in diastole, and the regulating function of the ventricular septum.

The nature has to some instant compensated a malfunction (infarction) of the muscle as construction material (the muscle leaning on the pericardial sack) with the rigidity of the pericardial sack and the surrounding tissues.

However a malfunction (infarction) of the intra-ventricular septum, can bring the mechanical functions of the heart to a lethal outcome, although the power supply is good enough for a healthy normal life. The reason for this is that the inactive parts (infracted area) have not enough support from the surroundings (as is the case with the muscle leaning on the pericardial sack). Its only support is the low pressure in the right ventricle and its own passive rigidity. Therefore the pressure and the pumping function generated by the healthy part of the left ventricle, will create a membrane pump like function of the injured part (that cannot stiffen) of intra-ventricular septum. This membrane pump function together with the healthy part of the right ventricle will pump all blood into the lungs and within seconds kill the patient.

11.11 The inexplicable three observations, which led to the discovery of the true pumping and regulating function of the heart

The first patient was a well known bicyclist. He performed a tremendous high workload in stress tests, although he had a total aortic insufficiency.

The second patient was a concrete worker. He had a normal workload with no symptoms in stress tests, although he had a huge infarction covering the whole left ventricle, except the itra-ventricular septum.

The third patient was M.D. Lundbäck's father. He had an infarction in intra-ventricular septum, although the rest of the heart was fully functional, he died in pulmonary oedema.

Patient 1

As a well-known cyclist, the sportsman came for an investigation of his heart, because he had suddenly had some unspecified, unpleasant feeling in his heart and thorax, especially during rest.

ECG and auscultation of his heart did not show anything unusual. In stress test on a bicycle with 50 W steps every 5 minutes, he went up to 450 W and cycled for 2 minutes with this load.

With ultrasound monitoring, one could see unusually large movements back and forth of the inter-ventricular septum (see Part Two - the regulation of the heart) indicating a large aortic insufficiency.

The cyclist continued to complain. When he was catheterised, it was discovered that he had a complete rupture of two of the three aortic leaflets. It was more or less no pressure gradient over the aortic valve in diastole.

He was operated and got an artificial aortic valve. His career as a cyclist was over.

In those days, the fact that his heart worked so well in spite of the ruptured aortic valve was a mystery.

With the new pump-technology modeling the heart, it is quite obvious that the importance of the aortic valve decreases with inflow and frequency high enough (cf. Fig. 11-6A-D). I.e. when the bicyclist was active the heart didn't need the aortic valves, because the valves never have to close due to the high kinetic energy of the blood. But at rest the aortic valves has time to close, and then it becomes obvious that the aortic insufficiency has a major impact on his well-being.

Patient 2

The concrete worker explained that he one year before the investigation had acquired a heavy flue, during that flue he got severe chest pains but thought this was caused by the flue and never visited a doctor. He went back to his work after two weeks, but felt a little tired for a few months. Later during an ordinary health control they discovered a 'strange ECG'.

The concrete worker had an intact function of the intra-ventricular septum but a total infarction on the rest of the left ventricle. That meant that the infarcted area was about 50% of the left ventricle. The infarcted area had a total support of the pericardial sack and surrounding tissues, and thus had time to stabilize, and the regulating function of intra-ventricular septum was in order and so also the force to bring the Atria Ventricular-plane (AV-plane) towards apex. By a higher frequency and training, the heart could perform an ordinary workload.

Patient 3

Lundbäcks father had four years earlier with good result gone through a coronary bypass operation. Some months before his death, his angina pectoris returned. The angina pectoris this time was also accompanied with the feeling of not having enough air to breathe (dyspnoe). He ended up in the intensive care unit with pre-infarction syndromes. After three weeks at the intensive care unit, and with many attacks of angina pectoris and pulmonary oedema, he was going to a new coronary bypass operation. A few hours before the surgery was due, he died in pulmonary oedema.

During the attacks of angina pectoris and the resulting pulmonary oedemas, one could easily see, with ultrasound registrations, that the intra-ventricular septum couldn't withstand the pressure within the left ventricle when the rest of the healthy heart pulled the AV-plane towards apex.

Septum acting like a diaphragm pump contributed by its pumping function, creating an overflow of blood into the lungs and thereby causing pulmonary oedema and death.

An infarction in septum will not only create a loss of power, but also a loss of the very important regulating function of the heart. If the heart loses its regulating function it more or less doesn't matter how good the pumping function of the heart is.

Tables

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Stockholm, Sweden

1986 Stig S Lundbäck

Preface

I would like to dedicate this thesis to the memory of my father Sune Lundbäck, who died in 1980 of an interventricular septum infarction of the heart.

He lived his life for his family and friends and was prepared to sacrifice everything for his sons; my brother and myself.

He was aware of my theories concerning the regulating mode of the ventricular septum, and encouraged me to study the behavior of his failing heart. During his attacks of severe angina pectoris with pulmonary edema symptoms, I registered the behavior of the ventricular septum by echocardiography. What I saw, convinced me of the importance of the ventricular septums function, in maintaining balance between the right and the left circulatory loops.

Before my father finally died of pulmonary edema and ventricular fibrillation, his last words were "you must do something to prevent this terrible thing". These words still ring in my ears and I hope that this thesis will provoke a discussion of the pumping and the regulating mode of the heart. This discussion could hopefully contribute, to the prevention of unnecessary suffering in heart failure.

Reference

1) Alderman, E L and Glantz S A. Acute hemodynamic interventions shift in the diastolic pressure-volume curve in man. Circulation 54 (1976) 662-671.

2) Antoni, H. Function des Herzens. In: Physiologie des Menschen. R F Schmidt and G Thews, Eds Springer, Berlin 1983.

3) Banka, V S, Agarwal, J B, Bodenheimer, M M and Helfant, R H. Intraventricular septal motion in bi-ventricular angiographic assessment of its relative contribution to left and right ventricular contraction. Circulation 64 (1981) 992-996.

4) Bassenge, E. Mechanik des intakten Herzens. In: Herzkrankheiten. Roskamm, H and Reindell, H, Eds, 2nd Ed Springer, Berlin-Heidelberg 1982.

5) Bauereisen, E. Ed Physiologie des Kreislafs. Springer, Berlin 1971.

6) Bell, G H, Emslie-Smith, D and Peterson, C R. Textbook of physiology. 10th Ed, Churchill & Livingstone, Edinburgh 1980.

7) Bemis, C E, Serur, J R, Borkenhagen, D, Sonnenblick, E H and Urschel, C W. Influence of right ventricular filling pressure on left ventricular pressure and dimension. Circulation Res 34 (1974) 498-504.

8) Benninghof, A. Die Architektur des Herzmuskels. Morphol Jahrb 67 (1931) 262-317.

9) Benninghoff, A. Fortb Lehrg. Bad Neuheim 11 (1935). Quoted by Faller (55).

10) Berglund, E, Sarnoff, S J and Isaacs, J P. Ventricular function. Role of the pericardium in the regulation of cardiovascular hemodynamics. Circulation Res 3 (1955) 133-139.

11) Berne, R M and Levy, M N. Cardiovascular physiology. 2nd Ed. Mosby, C V Co, Saint Louis 1972.

12) Bevegård, S. Studies on the regulation of circulation in man. Acta Phys Scand, Vol 57, suppl 200 (1962).

13) Blair, H A and Wedd, A M. The action of cardiac ejection on venous return. Am J Physiol 145 (1946) 528-537.

14) Brauereisen, E. Die Gesetze der Herzarbeit und ihre Gültigkeit im natuerlichen Kreislaf. Klin Wochenschr 35 (1957) 369-373.

15) Braunwald, E, Ross J Jr, Sonnenblick, E H. Mechanisms of contraction of the normal and failing heart. 2nd Ed Little, Brown and Co, Boston 1976.

16) Braunwald, E, Sonnenblick, E H and Ross J Jr. Contraction of the normal heart. In: Braunwald, E. Heart Disease. 2nd Ed, Vol 1. Saunders, Philadelphia 1984.

17) Braunwald, E and Ross, J Jr. Applicability of the Starling Law of the heart to man. Circulation Res. 15 (1964) 11-169.

18) Braunwald, E. The control of ventricular function in man. BR. Heart J. 27 (1965) 1-16.

19) Braunwald, E and Ross, J Jr. Control of cardiac performance 553-580. Handbook of physiology. Vol 1. The cardiovascular system. Am Physiol Soc, Bethseda, Md 1979.

20) Brecher, G and Galletti, P M. Functional anatomy of cardiac pumping. Handbook of Physiology. Vol II, Hamilton, W F and Dow, P. Eds Am Physiol Soc, Washington D C 1963.

21) Brecher, G E. Experimental evidence of ventricular diastolic suction. Circulation Res 4 (1956) 513-518.

22) Brecher, G A. Cardiac variations in venous return studied with a bristle flowmeter. Am J Physiol 176 (1954) 423-430.

23) Brecher, G E. Critical review of recent work on ventricular suction. Circulation Res 6 (1958) 554-566.

24) Brinker, J A, Wiss, J L, Lapp, D L, Rabson, J L, Summer, W R, Permutt, S and Weisfeldt, M L. Leftward septal displacement during ventricular loading in man. Circulation 61 (1980) 626-633.

25) Brobeck, J. Ed Best & Taylor's Physiological basis of medical practice. Circulation; Ross, J Jr. Section editor. 11th Ed Williams & Wilkins, Baltimore 1985.

26) Brunt, J N H, Love, H G and Rowlands, D J. Objective analysis of left ventricular cineangiograms. In: Recent advances in cardiology. No 9. Rowlands, D J, Ed Churchill & Livingstone, Edinburgh 1984.

27) Brutsaert, D L, De Clerc, N M, Goethals, M A and Housmans, P R. Mechanisms of relaxation in the heart as a muscle and pump. Eur J Cardiol. 7/Suppl (1978) 71-78.

28) Bucher, K, Dettli, L, Weisser, K and von Capeller, D. Über primär kardiale Regulationen bei der gegenseitigen Anpassung von Lungen- und Körperkreislauf. Helv Physiol. Acta 13 (1955) 79-88.

29) Burch, G E, Ray, C T and Cronvich, J A. Certain mechanical peculiarities of the human cardiac pump in normal and diseased states. Circulation 5 (1952) 504-513.

30) Burton, A C. The importance of the shape and size of the heart. Am Heart J 54 (1957) 801-810.

31) Böhme, W. Über den aktiven Anteil des Herzens an der Förderung des Venenblutes. Ergeb Physiologie 38 (1936) 251-338.

32) Carlsson, E. Experimental studies of ventricular mechanisms in dogs using the tantalum-labelled heart. Proc Fed Am Soc Exp Biol 68 (1969) 1324-1329.

33) Cassidy, S S and Ramanathan, M. Dimensional analysis of the left ventricle during PEEP: Relative septal and lateral wall displacements. Am J Physiol 246 (1984) H792-805.

34) Chapman, C B, Baker, O and Mitchell, J H. Left ventricular function at rest and during exercise. J Clin Invest 38 (1959) 1202-1213.

35) McDonald, I G. The shape and movements of the human left ventricle during systole. A study by cineangiography and by cineradiography of epicardial markers. Am J Cardiol 26 (1979) 221-230.

36) Ebstein, E. Die Diastole des Herzens. Ergeb Physiol 3 (1904) 123-194.

37) Elzinga, G and Westerhof, N. How to quantify pump function of the heart. Circulation Res 44 (1979) 303-308.

38) Elzinga, G, van Grondelle, R, Westerhof, N and van den Bos, G C. Ventricular interference. Am J Physiol 226 (1974) 941-947.

39) Erbel, R, Schweizer, P, Lambertz, H, Henn, G, Meyer, J, Krebs, W and Effert, S. Echoventriculography - a simultaneous analysis of two-dimensional echocardiography and cineangiography. Circulation 67 (1983) 205-215.

40) Faller, A. Die fibrillären Strukturen des menschlichen Epikards und ihre Bedeutung für die Performing des Herzens. Cardiologia 9 (1945) 337-372.

41) Feigenbaum, H. Echocardiography. In: Heart Disease. Vol 1. E Braunwald, Ed 2nd Ed W B Saunders, Philadelphia 1984.

42) Fester, A and Samet, P. Passive elasticity of the human left ventricle. The parallel elastic element. Circulation 50 (1974) 609-618.

43) Folkow, B and Neil E. Circulation. Oxford Univ Press 1971.

44) Francis, G S, Theroux, P, O'Rourke, R A, Hagan A D and Johnson, A D. An echocardiographic study of intraventricular septal motion in the Wolff-Parkinson-White Syndrome. Circulation 54 (1978) 174-178.

45) Franklin, D L, Van Gitters, R L and Rushmer, R F. Balance between right and left ventricular output. Circulation Res 10 (1962) 17-26.

46) Fujii, J, Yasaki, Y, Sawada, H. Aizawa, T, Watanabe, H and Kato, K. Non-invasive assessment of left and right ventricular filling in myocardial infarction with a two dimensional Doppler echocardiographic method. J Am Coll Cardiol 5 (1985) 1155-1160.

47) Gaasch, W H, Cole, J S, Quinones, M A and Alexander, J K. Dynamic determinants of left ventricular pressure-volume relations in man. Circulation 51 (1975) 317-323.

48) Ganong, W F. The heart as a pump 451 461. In: Review of medical physiology, 12th Ed, Lange Medical Publ, Los Altos 1985.

49) Gauer, O H. Kreislauf des Blutes. In: Gauer O H et al, Eds Physiologie des Menschen. Vol 3 Urban & Schwarzenberg, Muenchen-Berlin-Wien 1972.

50) Gauer, O. Volume changes of the left ventricle during blood pooling and exercise in the intact animal. Their effects on left ventricular performance. Physiol Rev 35 (1955) 143-155.

51) Gehl, L G, Mintz, G S, Kotler, M N and Segal, B L. Left atrial volume overload in mitral regurgitation: a two-dimensional echocardiographic study. Am J Cardiol 49 (1982) 33-38.

52) Gibson, D G and Brown, D J. Continuous assessment of left ventricular shape in man. Br Heart J 37 (1975) 904-910.

53) Glenn, W W L. Circulatory bypass of the right side of the heart. IV. Shunt between vena cava and distal right pulmonary artery - Report of clinical application. New Engl J Med 259 (1958) 117-120.

54) Goldman, M E. Emerging importance of the right ventricle. J Am Coll Cardiol 5 (1985) 925-927.

55) Gottdiener, J S, Gay, J A, Maron, B J and Fletcher, R D. Increased right ventricular wall thickness in left ventricular pressure overload: Echocardiographic determination of hypertropic response of the "non-stressed" ventricle. J Am Coll Cardiol 6 (1985) 550-555.

56) Gregg, D E. The heart as a pump. In: The physiological basis of medical practice. C H Best and N B Taylor Eds William & Wilkins, Baltimore 1961.

57) Gribbe, P, Hirvonen, L, Lind, J and Wegelius, C. The events of the left side of the normal heart as studied by cineangiography. Cardiologia 33 (1958) 293-204.

58) Gribbe, P, Hirvonen, L, Lind, J and Wegelius, C. Cineangiographic recordings of the cyclic changes in volume of the left ventricle. Cardiologia 34 (1959) 348-366.

59) Guiha, N H, Limas, C J and Cohn, J N. Predominant right ventricular dysfunction after right ventricular destruction in the dog. Am J Cardiol 33 (1974) 254-258.

Reference 60-64

60) Guyton, A C, Taylor, A E and Granger, H J. Circulatory physiology. Vol II. Dynamics and control of the body fluids. W B Saunders, Philadelphia 1975.

61) Guyton, A C and Jones, C E, Eds Cardiovascular physiology. Vol I. University Park Press, Baltimore 1974.

62) Guyton, A C. Physiology of the human body. 6th Ed. Saunders college Publ, Philadelphia 1984.

63) Hales, S. Statical Essays. Vol II. Haemastaticks. Innys and Manby, London 1733.

64) Haller, A. Elementa physiologiae corporis humanis. Vol 1, p 297-459. M M Bousquet et Cie, Lausanne 1757.

65) Hamilton, W F and Rompf, J H. Movements of the base of the ventricle and the relative constancy of the cardiac volume. Am J Physiol 102 (1932) 559-565.

66) Hamilton, W F. Filling of the normal human heart in relation to the cardiopneumogram and abdominal plethysmogram. Am J Physiol 91 (1930) 712-719.

67) Hamilton, W F and Lombard, E A. Intrathoracic volume changes in relation to the cardiopneumogram. Circulation Res. 1 (1953) 76-82.

68) Hamilton, W F. Role of Starling concept in the regulation of the normal circulation. Physiol Rev 35 (1955) 161-168.

69) Hampton, J R, Ed Cardiovascular disease. (Integrated clinical science, McNicol, G P, Ed) William Heinemann Medical Books, London 1983.

70) Harvey, W. An Anatomical Disputation Concerning the Movement of the Heart and Blood in Living Creatures. Translated with introduction and notes by G Whitteridge. Blackwell Scientific Publ, Oxford 1976.

71) Hauffe, G. Das Wirken der Hilfskräfte der als Saug- und Druckpumpe arbeitenden Herzmaschine. Virchows Archiv 266 (1927) 18-50.

72) Hawthorne, E W. Instantaneous dimensional changes of the left ventricle in dogs. Circulation Res 9 (1961) 110-119.

73) Heller, L J and Mohrman, D E. Cardiovascular physiology. McGraw-Hill, New York 1981.

74) Henderson, Y and Prince, A L. The relative systolic discharge of the right and left ventricles and their bearing on pulmonary congestion and depletion. Heart 5 (1914) 217-226.

75) Henderson, Y. The volume curve of the ventricles of the mammalian heart and the significance of this curve in respect to the mechanics of the heart-beat and the filling of the ventricles. Am J Physiol 16 (1906) 325-367.

76) Henke, W. Topographische Anatomie des Menschen. A Hirschwald, Berlin 1884.

77) Hess, O M. Diastolische Funktion des linken Ventrikels (Thieme Copythek). Georg Thieme, Stuttgart-New York 1982.

78) Hishida, H, Sotobata, I, Koike, Y, Okumura, M and Mizuno, Y. Echocardiographic patterns of ventricular contraction in the Wolff-Parkinson-White Syndrome. Circulation 54 (1976) 567-570.

79) Holt, J P, Rhode, E A and Kines, H. Pericardial and ventricular pressure. Circulation Res 8 (1960) 1171-1181.

80) Holt, J. The normal pericardium. Am J Cardiol 26 (1970) 455-465.

81) Holzölhner, E. Die Volumenänderungen im menschlichen Thorax whrend der Herzaktion. Zeitschr Biol 92 (1932) 293-316.

82) Ishimitsu, T, Smith, D, Berko, B, and Craige, E. Origin of the third heart sound: comparison of ventricular wall dynamics in hypodynamic and hypodynamic types. J Am Coll Cardiol 5 (1985) 268-272.

83) Iskandarian, A S, and Hakki, A H. Thallium-201 myocardial scintigraphy. Am Heart J 109 (1985) 113-129.

84) Isner, J M, and Roberts, W C. Right ventricular infarction complicating left ventricular infarction secondary to coronary heart disease. Frequency, location, associated findings and significance from 236 necropsy patients with acute of healed myocardial infarction. Am J Cardiol 42 (1978) 885-894.

85) James, T N. anatomy of the crista supraventricularis: Its importance for understanding right ventricular function, right ventricular infarction and related conditions. J Am Coll Cardiol 6 (1985) 1083-1095.

86) Jamison, W L, Gemeinhardt, W, Jahangar, A, and Bailey, C P. Artificial maintenance of the systemic circulation without participation of right ventricle. Circulation Res 2 (1954) 315-318.

87) Jardin, F, Farcot, J-C, Boisante, L, Curien, N, Margairaz, A, and Bourdarias, J-P. Influence of positive end-expiratory pressure on left ventricular performance. new Engl J Med 304 (1981) 387-392.

88) Jewell, B R. A re-examination of the influence of muscle length on myocardial performance. Circulation Res 40 (1977) 221-230.

89) Jädicke, W, and Reindell, H. Röntgenologische Aufzeichnung der Herzrand- und Gefässpulsation. In: Herzkrankheiten. 2nd Ed H Roskamm and E Reindell, Eds, Springer, Berlin-Heidelberg 1982.

90) Kagan, A. dynamic responses of the right ventricle following extensive damage by cauterisation. Circulation 5 (1952) 816-823.

91) Katz, A M. Physiology of the heart. Raven Press, New York 1977.

92) Keith, A. An account of the structures concerned in the production of the jugular pulse. J Anat Phys 42 (1908) 1-25.

93) Kent, R S, Carew, T E, Le Winter, M W, and Covell, J W. Comparison of left ventricular free wall and septal diastolic compliance in the dog. Am J Physiol 234 (1978) H392-398.

94) Kenner, T. Das Herz als Pumpe. In: Kreislaufphysiologie. R Busse, Ed, Georg Thieme, Stuttgart-New York 1982.

95) Kingma, I, Smiseth, O, Belenkie, I, MacDonald, R P, Knudtson, M L, Tyberg, J V, and Smith, E R. Ventricular septal dynamics in response to altered transseptal pressure in man (Abstr). J Am Coll Cardiol 5 (1985) 511.

96) Kirchheim, H. Kreislaufregulation. In: Kreislaufphysiologie. R Busse, Ed, Georg Thieme, Stuttgart 1982.

97) Kreulen, T H, Bove, A A, McDonough, M T, Sands, M J, and Spann, J D. The evaluation of left ventricular function in man. A comparison of methods. Circulation 51 (1975) 677-688.

98) Lee, S, Rosenberg, G, Donachy, J H, Wisman, C B, and Pierce, W S. The compliance problem: A major obstacle in the development of implantable blood pumps. Artif Organs 8 (1984) 82-90.

99) Lee, M J, and Boughner, D R. Mechanical properties of human pericardium. Differences in viscoelastic response when compared with canine pericardium. Circulation Res 57 (1985) 475-481.

100) Leonhardt, H. Internal organs. In: Colour atlas and textbook of human anatomy. Vol 2, 2nd Ed, W Kahle, H Thieme, Stuttgart-New York 1984.

101) Levy, M N. The cardiac and vascular factors that determine systemic blood flow. Circulation Res 44 (1979) 739-745.

102) LeWinter, M W, Engler, R L, and Karliner, J S. Enhanced left ventricular shortening during chronic volume overload in conscious dogs. Am J Physiol 238 (1980) H126-133.

103) Lindblad, L-E. Baroreflexes in Man. Thesis, Stockholm 1980. ISBN 91-7222-322-7.

104) Ling, D, Rankin, J S, Edwards, C H, McHale, P A, and Anderson, R W. Regional diastolic mechanisms of the left ventricle in the conscious dog. Am J Physiol 236 (1979) H323-330.

105) Lorente, P, Adda, J L, Creplet, J, Masquet, C, Babalis, D, Piekarski, A, N'guyen, A, and Azancot, I. A new computerised segmental area based method to evaluate regional wall motion from cineangiograms and two dimensional echograms. In: Ventricular wall motion. Sigwart, U, and Heintzen, P H, Eds Georg Thieme, Stuttgart-New York 1984.

106) Lower, R. Tractatus de Corde. London 1669. Facsimile edition with an introduction and translation by K J Franklin. Early Science in Oxford. Oxford Univ Press 1932.

107) Luciani, L. Attivit della diastole cardiaca rilevata dai suoi effetti e dalla potenze muscolari e nervose che la promuovono. Riv Clin Bologna 74 (1871) 33-44, 73-131, 201-221.

108) Lundbäck, S (inv). Swedish patent application 8401778-9.

109) Lundbäck, S (inv). Swedish patent application 8401779-7.

110) Lunkenheimer, A. Zum Bewegungsablauf des Herzens. Herz/Kreislauf 15 (1983) 416-424.

111) Mangano, D T, Van Dyke, D C, Hickey, R F, and Ellis, R J. Significance of the pericardium in human subjects: effects on left ventricular volume, pressure and ejection. J Am Coll Cardiol 6 (1985) 290-295.

112) Mann, D L, Foale, R A, Ascah, K J, Newell, J B, Gilliam, L D, and Weyman, A E. Persistence of abnormal wall motion in the canine ventricle after subacute infarction (Abstr). J Am Coll Cardiol 5 (1985) 425.

113) Marving, J, Höilund-Carlsen, P F, Chraemmer-Jörgensen, B, and Gadsböl, N. Are right and left ventricular ejection fractions equal? Ejection fractions in normal subjects and in patients with first acute myocardial infarction. Circulation 72 (1985) 502-514.

114) Matsuzaki, M, Tohma, Y, Anno, Y, Hiroyama, N, Yonezawa, F, Tamitani, M, Maeda, T, Katayama, K, Matsuda, Y, Kumada, T, and Kusukawa, R. Esophageal echocardiographic analysis of atrial dynamics. Am Heart J 109 (1985) 355-362.

115) Maughan, W L, Kallman, C H, and Shoukas, A. The effect of right ventricular filling on the pressure-volume relationship of the ejecting canine left ventricle. Circulation Res 49 (1981) 382-388.

116) Mitchell, J H, Gilmore, J P, and Sarnoff, S J. The transport function of the atrium. Factors influencing the relation between mean left atrial pressure and left ventricular end diastolic pressure. Am J Cardiol 9 (1962) 237-247.

117) Monod-Broca, P. Recherches experimentales sur la circulation pulmonaire aprés du coeur droit. Arch mal coeur. 51 (1958) 841-846.

118) Molaug, M, Geiran, O, and Kil, F. Compensatory cardiac mechanisms evoked by septal ischemia in dogs. Am J Physiol 1983; 51: 201-206.

119) Netter, F D. Heart. The Ciba collection of medical illustrations, Vol 5. Ciba Found USA 1968. 2nd printing 1978.

120) Noble, M I M. The Frank-Starling curve. Clin Sci Mol Med 54 (1978) 1-7.

121) Nuland, S B, Glenn, W W L, and Guilfoil, P H. Circulatory bypass of the right heart. III. Some observations on long-term survivors. Surgery 43 (1958) 184-201.

122) Olsen, C O, Tyson, G S, Maier, G W, Davis, J W, and Rankin, J S. Diminished stroke volume during inspiration: a reverse thoracic pump. Circulation 72 (1985) 668-679.

123) Palacios, I, Powers, E, and Powell, W J. Effect of end-diastolic volume on the canine left ventricular ejection fraction. Am Heart J 109 (1985) 1059-1069.

124) Parker, J O, and Case, R B. Normal left ventricular function. Circulation 60 (1979) 4-12.

125) Parker, J A, Markis, J E, and royal, H D. Assessment of regional wall motion and perfusion by multigated myocardial scintigraphy after intracoronary T1-201. Radiology 1985, 783-786.

126) Parmley, W W, Tyberg, J V, and Glanz, S A. Cardiac dynamics. Ann Rev Physiol 39 (1977) 277-299.

127) Parmley, W W, Chuck, L, Chatterjee, K, Swain, H J C, Klausner, S C, Glantz, S A, and Ratshin, R A. Acute changes in the diastolic pressure-volume relationship of the left ventricle. Eur J Cardiol 4/Suppl (1976) 105-120.

128) Parmley, W W, and Talbot, L. Heart as a pump, p 429-460. Handbook of physiology. Vol 1, 2nd ed. The cardiovascular system. Am Physiol Soc, Bethesda, Md 1979.

129) Parmley, W W, and Talbot, L. Heart as a pump p 429-460. Handbook of physiology. Vol 1, 2nd Ed. The cardiovascular system. Am Physiol Soc, Bethesda, Md 1979.

130) Permutt, S, and Riley, R L. Hemodynamics of collapsible vessels with tone. The vascular waterfall. J Appl Physiol 18 (1963) 924-932.

131) Popp, R L, Wolfe, S B, Hirata, T, and Feigenbaum, H. Estimation of right and left ventricular size by ultrasound: A study of the echoes from the intraventricular septum. Am J Cariol 24 (1969) 523-530.

132) Puff, A. Die Morphologie des Bewegungsablaufs der Herzkammern. Anat Anz 108 (1969) 342-350.

133) Puff, A. Problems concerning the orthopy of ECCG body surface mapping. Adv Cardiol 28 (1989) 9-12.

134) Puff, A. Über das funktionelle Verhalten des Anulus fibrosus bei der Volumenderung der Herzhöhlen und die Konsequenzen für einen Klappenersatz. Thoraxchirurgie 20 (1972) 185-198.

135) Puff, A. Ûber das funktionelle Verhalten des Endokards bei der Volumenveränderung der Ventrikel-binnenräume. Eine Studie zur Problematik des künstlichen Herzens. Thoraxchirurgie 19 (1971) 119-120.

136) Puff, A. Anatomische und physiologische Grundlagen. In: Roskamm, H, and Reindell, H, Eds, Herzkrankheiten, 2nd Ed. Springer, Berlin-Heidelberg 1982.

137) Purkinje, J E. Über die Saugkraft des Herzens. Jber schles Ges vaterländ Kultur. 1843, 157. Cited according to Böhme (8) and Brecher & Galletti (11).

138) Rabkin, S W, and Hsu, P H. Mathematical and mechanical modelling of the stress-strain relationship of the pericardium. Am J Physiol 229 (1975) 896-900.

139) Randall, O S, van den Bos, G C, and Westerhof, N. Systemic compliance: does it play a role in the genesis of essential hypertension? Cardiovascular Res 18 (1984) 453-462.

140) Reindell, H, and Delius, L. Klinische Beobachtungen über die Herz-dynamik beim gesunden Menschen. Dtsch arch klin Med 193 (1942) 639-655.

141) Richards, D W. Discussion of Starling's law of the heart. Physiol Rev 35 (1955) 156-160.

142) Rodbard, S, and Wagner, S. Bypassing the right ventricle. Proc Soc Exp Biol Med 71 (1949) 69-70.

143) Roelandt, J, van Dorp; W G, Bom, N, Laird, J D, and Hugenholtz, P G. Resolution problems in echocardiography: A source of interpretation errors. Am J Cardiol 37 (1976) 256-262.

144) Rosendorff, C. Clinical cardiovascular and pulmonary physiology. Raven Press, New York 1983.

145) Roskamm, H, and Reindell, H. Arbeitsweise des gesunden Herzens. In: Roskamm, H and Reindell, H, Eds Herzkrankheiten. 2nd Ed. Springer Verl, Berlin-Heidelberg 1982.

146) Ross, J, Jr. Afterload mismatch and preload reserve. A conceptual framework for the analysis of ventricular function. Proc Cardiovasc Dis 18 (1976) 255-264.

147) Rushmer, R F. Cardiovascular dynamics, 4th Ed. W B Saunders, Philadelphia 1976.

148) Rushmer, R F, Crystal, D K, and Wagner, G. The functional anatomy of ventricular contraction. Circulation Res 1 (1953) 162-170.

149) Rushmer, R F. Initial phase of ventricular systole: Asynchronous contraction. Am J Physiol 184 (1956) 188-194.

150) Rushmer, R F. Application of Starling's law of the heart to intact, unanaesthesized animals. Physiol Rev 35 (1955) 138-142.

151) Ryan, T, Petrovic, O, Dillon, J C, Feigenbaum, H, Conley, M J, and Armstrong, W F. An echocardiographic index for separation of right ventricular volume and pressure overload. J Am Coll Cardiol 5 (1985) 918-924.

152) Sabbah, H N, Marzilli, M, and Stein, P D. The relative role of subendocardium and subepicardium in left ventricular mechanics. Am J Physiol 240 (1981) H920-926.

153) Sagawa, K. The ventricular pressure-volume diagram revisted. Circulation Res 43 (1978) 677-687.

154) Sandler, H, Meier, G D, and Alderman, E L. Ballistic motion of the heart. In: Ventricular wall motion. Sigwart, U, and Heintzen, P H. Eds Georg Thieme, Stuttgart-New York 1984.

155) Santamore, W P, Meier, G D, and Bowe, A A. Effects of hemodynamic alterations on wall motion in the canine right ventricle. Am J Physiol 236 (1979) H254-262.

156) Sapoznikov, D, Halon, D A, Lewis, B S, Weiss, A T, and Gotsman, M S. Frame by frame analysis of left ventricular function. Quantitative assessment of regional and temporal function. Circulation 70 (1983) 61-72.

157) Sasayama, S, Nonogi, H, Mikazaki, S, Sakurai, T, Kawai, C, Eiho, S, and Kuwahara, M. Changes in diastolic properties of the regional myocardium during pacing-induced ischemia in human subjects. J Am Coll Cardiol 5 (1985) 599-606.

158) Scheu, H, and Hamilton, W F. Evidence for left ventricular diastolic suction on closed-chest dogs. J Am Physiol 197 (1959) 1152-1156.

159) Schlant, R C, Sonnenblick, E H, and Gorlin, R. Normal physiology of the cardiovascular system. In. The heart. Hurst, J W, Ed in chief. McGraw-Hill, New York 1982.

160) Shapiro, J, Boxer, R, and Krongrad, E. Abnormal septal motion in patients with postoperative right bundle branch pattern. Am Heart J 97 (1979) 147-154.

161) Shepard, J T, and Vanhoutte, P M. The human cardiovascular system. Facts and concepts. Raven Press, New York 1979.

162) Sigel, H, Heckenberger, E, Nechwatal, W, and Stauch, M. Significance of different radial axes models to quantify regional wall motion. In: Ventricular wall motion: Sigwart, U, and Heintzen P H. Eds Georg Thieme, Stuttgart-New York 1984.

163) Sjöstrand, T. Volume and distribution of blood and their significance in regulating the circulation. Rev Physiol 33 (1953) 202-228.

164) Slager, C J, Hooghoudt, T E H, Reiber, J H C, Schuurbiers, J H C, Verdouw, P D, and Hugenholtz, P G. Left ventricular wall motion as derived from endocardially implanted radiopague markers and from contrastangiograms. In: Ventricular wall motion. Sigwart, U, and Heintzen, P H, Eds Georg Thieme, Stuttgart-New York 1984.

165) Snellen, H A. History of cardiology. Donker Academic Publ, Rotterdam 1984.

166) Sokolow, M, and McIlroy, M B. Clinical cardiology. Lange Medical Publ, Los Altos 1977.

167) von Spee, F. Bemerkungen betreffend Spannung, Bewegung, Nomenklatur der Brustorgane des Menschens. Verh Anat Ges 1909. Erg H, Anat Anz 34 (1909) 169-180.

168) Starr, I, Jeffers, W A, and Meade, R H, Jr. The absence of venous pressure after severe damage of the right ventricle of the dog, with a discussion of the relation between clinical congestive failure and heart disease. Am Heart J 26 (1943) 291-301.

169) Stenosis, N. De musculis et glandulis observatonium specimen. Matthias Godichenius, Copenhagen 1664.

170) Streeter, D D. Gross morphology and fiber geometry of the heart, p 61-112. Handbook of physiology, vol 1. The cardiovascular system. Am Physiol Soc, Bethesda Md 1979.

171) Stool, E W, Mullings, C B, Leshin, S J, and Mitchell, J H. Dimensional changes of the left ventricle during acute pulmonary arterial hypertension in dogs. Am J Cardiol 33 (1974) 868-875.

172) Tanaka, H, Tei, C, Nako, S, Thara, M, Skurai, S, Kashima, T, and Kanehisa, T. Diastolic bulging of the intraventricular septum toward the left ventricle. An echocardiographic manifestation of negative intraventricular pressure gradient between left and right ventricles during diastole. Circulation 62 (1980) 558-563.

173) Templeton, G H, and Nardizzi, L R. Elastic and viscous stiffness of the canine left ventricle. J Appl Physiol 36 (1974) 123-127.

174) tichonow, K B. Funkzionalnaja rentgenanatiómia serdza, p 116-118. Medizina, Moscow 1978.

175) Tigerstedt, R. Lehrbuch der Physiologie des Kreislaufs. Veit & Co, Leipzig 1893.

176) Torrent-Guasp, F. The cardiac muscle. Fundacion Juan March, Madrid 1973. Cited according to Streeter (103).

177) Tyberg, J, Misbach, G A, Glanz, S A, Moores, W Y, and Parmley, W W. Amechanism for shifts in the diastolic left pressure-volume curve: the role of the pericardium. Eur J Cardiol 7, Suppl (1978) 163-175.

178) Weyman, A E, Heger, J J, Kronik, G, Wann, L S, Dillon, J C, and Feigenbaum, H. Mechanism of paradoxical early diastolic septal motion in patients with mitral stenosis: a cross-sectional echocardiographic study. Am J Cardiol 40 (1977) 691.

179) Wayman, À E, Wann, S, Feigenbaum, H and Dillon, J C. Mechanism of abnormal septal motion in patients with right ventricular overload. Circulation 54 (1976) 179-186.

180) Whitteridge, G. The anatomical lectures of William Harvey. E & S Livingstone, London 1964.

181) Wong, M, Shah, P M, and Taylor, R D. Reproducibility of left ventricular internal dimensions with M mode echocardiography: Effects of heart size, body position and transducer angulation. Am J Cardiol 47 (1981) 1068-1074.

182) Zelis, R, Flaim, S F, Liedtke, A J, and Nellis, S H. Cardiocirculatory dynamics in the normal and failing heart. Ann Rev Physiol 43 (1981) 455-476.