FROM: MEDICAL DEPARTMENT, SECTION OF CARDIOLOGY, REGIONAL HOSPITAL, TRONDHEIM, NORWAY, HEAD: PROFESSOR ROLF ROKSETH, M: D.

METHODS FOR STUDYING FLOW DYNAMICS IN THE LEFT VENTRICLE AND THE AORTA IN MAN

USE OF A SIMULATION MODEL AND ULTRASOUND

ALF O. BRUBAKK

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TRONDHEIM 1978

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Contents

Foreword

This thesis is based on work performed from 1970—1977 at the Section of Cardiology, Department of Medicine. Regional Hospital, Trondheim and the Division of Engeneering Cybernetics, the Norwegian Institute of Technology, University of Trondheim. The work is part of a collaborative study by civ.eng. Rune Aaslid, Ph. D., civ.eng. Bjørn Angelsen, Dr.techn. and myself.

Trondheim, December 1977

Alf O. Brubakk

General Summary

In this thesis two methods for measuring flow and flow velocity in the aorta and in the left ventricle is presented. One is based on the use of a simulation model of the cardiovascular system, the other is based on the use of doppler ultrasound.

The thesis is based on the following papers:

I. Brubakk, A. O. and Angelsen, B. A. J. Measurement of blood flow and flow velocity in the thorax using pulsed ultrasound.
in Taylor, D. E. M. and Whamond, J. W. (eds.): Non-invasive clinical measurement, Pitman Medical, U. K. 19—31, 1977.

II. Angelsen, B. A. J. and Brubakk, A. O. Transcutanous measurement of blood flow velocity in the human aorta. Cardiovascular Research, 10, 368—379, 1976.

III. Brubakk, A. O., Angelsen, B. A. J. and Hatle, L. Diagnosis of valvular heart disease using transcutanous doppler ultrasound. Cardiovascular Research, 11, 461—469, 1977.

IV. Brubakk, A. O. and Aaslid, R. A model approach to studying cardiovascular function in man.
in Perkins, W. J. (ed). Biomedical Computing, Pitman Medical U. K., 269—279, 1977.

V. Brubakk, A. O. and Aaslid, R. Use of a model for simulating individual aortic dynamics in man. Medical and Biological Engineering & Computing. In press.

VI. Brubakk, A. O. Use of a simulation model for estimating cardiac output from aortic pressure curves. Medical and Biological Engineering & Computing. In press.

In Paper I, the problem associated with measuring blood flow and flow velocity in the thorax using ultrasound, is discussed. It is pointed out that the instantanous mean velocity is of importance for measuring changes in blood flow and that the maximum blood velocity must be measured if the pressure drop across a heat valve is to be calculated.

In Paper II, a method for calculating the mean velocity of the blood stream from the reflected ultrasonic spectrum is presented and its capabilities tested both in vitro and in the human aorta. It is shown that the estimator is able of measuring mean velocity with acceptable accuracy. When measuring blood flow velocity in the aorta, the angle between the ultrasonic beam and the blood stream is unknown, and this technique will give a considerable underestimation of true blood velocity.

In Paper III, a maximum frequency estimator is presented and its capabilities demonstrated. A technique for measuring flow velocity in different valve areas of the heart is shown.

In Paper IV, the general theory behind the use of a model for studying cardiovascular function is discussed. The model is presented, and examples of its application are demonstrated.

In Paper V, the model is employed for simulating the aortic dynamics in 29 partients. The ability to simulate the pressure transmission properties of the aorta is shown, and the aortic compliance calculated.

In Paper IV, the use of the model for calculating cardiac output from aortic pressure curves in 39 patients is demonstrated. The ability of the model to follow changes in the cardiovascular state is emphasized.

Acknowledgements

During the course of this study I have received assistance, encuragement and advice from many sources. I am particulary indebted to.

Civ.eng. *Rune Aaslid* and civ.eng. *Bjørn Angelsen,* Division of Engineering Cybernetics, Norwegian Institute of Technology, Trondheim, without whose help and collaboration this study would not have been possible.

Nurse *Elin Amundsen* who assisted with all the measurement procedures and who was an invaluable help during all these years.

Professor *Kristen B. Eik-Nes,* Institute of Biophysics, Norwegian Institute of Technology, Trondheim, who devoted so much time to reading manuscripts and giving scientific advice.

Professor *Rolf Rokseth,* Section of Cardiology, Medical Department, Regional Hospital, Trondheim, who gave me an opportunity to work at his department and who taught me

the procedures needed to perform the measurements.

Professor *Jens G. Balchen,* Division of Engineering Cybernetics, Norwegian Institute of Technology, Trondheim, for providing encouragement and working space at his department.

Jørn Bathen, M. D. and *Liv Hatle,* M. D., Section of Cardiology, Medical Department, Regional Hospital, Trondheim, for collaboration during part of this study.

Ron Bradley, M. D., St. Thomas Hospital, London, for his hospitality and his willingness to share his large experience in haemodynamic investigations of the seriously ill.

Marit Knudsen, for typing and retyping the various manuscripts, eng. *Thor Stuedal,* for preparing the figures and *Bjørn Tonning* for photographing them.

I also wish to express my graditude to the staff at the Section of Cardiology and the A8, Medical Department, Regional Hospital, Trondheim, for the patience when the hospital rooms looked like an elecronics department.

Finally, a special thank is due to professor *Jon Lamvik* for his unfailing enthusiasm and the assurance that all would turn out well.

During the main part of this study, I was a research fellow paid by the *County of Sør-Trøndelag.* The most important financial contribution to this work has come from *Forenede Liv A/S,* Trondheim, without whose help this study would not have been possible. The study has further been supported by the *Norweigan Council on Cardiovascular Disease,* the *Royal Norweigan Council for Scientific and Industrial Research, SINTEF, AUTRONICA A/S,* Trondheim, the *University of Trondheim* and *«Gammeldansforeningen Tempo 1964»,* Trondheim.

Introduction

The left ventricle is the main energy source for circulation of blood and the main criterion for its overall function is its ability to deliver sufficient blood flow for the peripheral demand. To pump the required amount of blood, the left ventricle must generate enough pressure to overcome the resistance to flow in the peripheral vessels. The interaction between the heart and the peripheral circulation is regulated, so that when the heart is functioning normally, the demands of the periphery for blood supply will determine the amount of blood pumped (1).

The ability of the left ventricle to pump blood can be impaired in many ways. The function of the left ventricle depends on the performance of the heart muscle fibres, the geometrical confirguration of the ventricle and the condition of the valvular apparatus. These factors interact in a complex way to generate a certain pressure and a certain flow of blood out of the heart. Pressure and flow in the ascending aorta therefore describe only the overall behaviour of the left ventricle in the circulation, and will give little information about the kind of impairment present.

In valvular heart disease, changes in the flow pattern inside and outside the heart will occur. Such abnormal flow patterns can usually be detected by auscultation. However, Measurement of the actual flow patterns can make a more accurate and quantitative evaluation of the disease state possible.

Purpose of the study

This study is concerned with methods for studying flow dynamics of the left ventricle and the aorta in man. For studying flow dynamics, blood pressure, volumetric flow or the time dependent velocity of flow represent the variables★) of main interest (2).

The hemodynamic state can change rapidly. Therefore, methods that permit measurement of pressure and flow continunously are preferable. Furthermore, the time variable pressure and flow curves contain information both about the state of the left ventricle and the aorta (3,4).

★) The term variable is defined as pulsatory quantities with regard to time.

Of the above-mentioned variables, only blood pressure can be measured in a clinical situation by simple means. The purpose of the present work was therefore to develope methods capable of measuring flow and flow velocity inside and near the heart, to describe the theoretical and practical problems connected with the use of these methods, and to demonstrate their clinical application. The statistical confirmation of their clinical usefulness is beyond the scope of this study.

Pressure measurement.

Noninvasive pressure measurement, using the Riva-Rocci method and the inflatable pressure cuff, can only determine the absolute values of systolic and diastolic blood pressure. This method gives no information about the shape of the pressure curve and can not be used for a detailed study of circulatory flow dynamics. Furthermore, when the circulation is impaired, the values obtained with this method can vastly underestimate the real pressure in the vessel (5).

The methods use for invasive pressure measurements are well known (6), and only some points about their use will be made here. Pressure is usually measured by a fluid filled catheeter-manometer system, where the pressure transducer is placed outside the patients body. This method has the drawback that the pressure wave is distorted through filtering introduced by the fluid filled system. The dynamic characteristics of the system can be described by the resonant frequency and the dampening factor of the system (6). For accurate determination of the pressure curve form, particularly at high heart rates or when the rate of the rise of the pressure curve (dp/dt) is to be determined, resonant frequencies between 20 and 25 Hz are necessary, as the pressure pulses contain up to 14 harmonics (7,8). This is a frequency response that is difficult to achieve in a clinical situation. Frequency responses can be tested by suddenly changing the pressure at the tip of the catheter-manometer system and studying the pressure oscillations in the system following this change. *Fig. 1* shows results from an experiment testing frequency response by this technique. In Fig. 1a, the transducer is connected to a catheter and carefully filled with fluid. obtaining a frepuency response of 6 Hz. After flushing the system with CO_2 for 3 minutes, a method advocated for increasing frequency response, the response increase to 20 Hz (Fig. 1b). Subsequent to the passage of a guide wire through the catheter, the frequency response is decreased to 5 Hz (Fig. 1c). This experiment demonstrates that testing frequency response before and after the actual catheterisation procedure is of little value. Methods based on compensation during the actual measurement procedure have to be used to retrieve the original signal (9). The dampening factor is also of importance. It has been shown that errors ut på + 100% can be made when calculating dp/dt from underdamped catheter-manometer systems (10). The detailed analysis of pressure curves measured with fluid filled catheter-manometer systems must therefore be viewed with some caution unless adequate corrections are incorporated.

These problems can be overcome by the use of catheter trip manometers. These are still expensive and because of catheter stiffness, not easy to use.

Flow measurement

The methods for flow measurement can be devided into methods that measure the mean flow over a certain period of time and methods that measure the instantaneous flow and flow velocity.

The two methods most commonly used for measuring mean blood flow are the one based on the Fick principle and the Stewart-Hamilton indicator dilution method.

The Fick principle

This method is basen on the concept of mass balance and was first described by Fick in 1870 (11). In clinical medicine this principle has mostly been applied to measuring cardiac output by using O_2 as the indicator. Cardiac output is calculatet from the equation:

$$\text{Cardiac output (l/min)} = \frac{\text{O}_2 \text{ consumption (ml/min)}}{\text{arterial-venous O}_2 \text{ content (ml/l)}} \qquad (1)$$

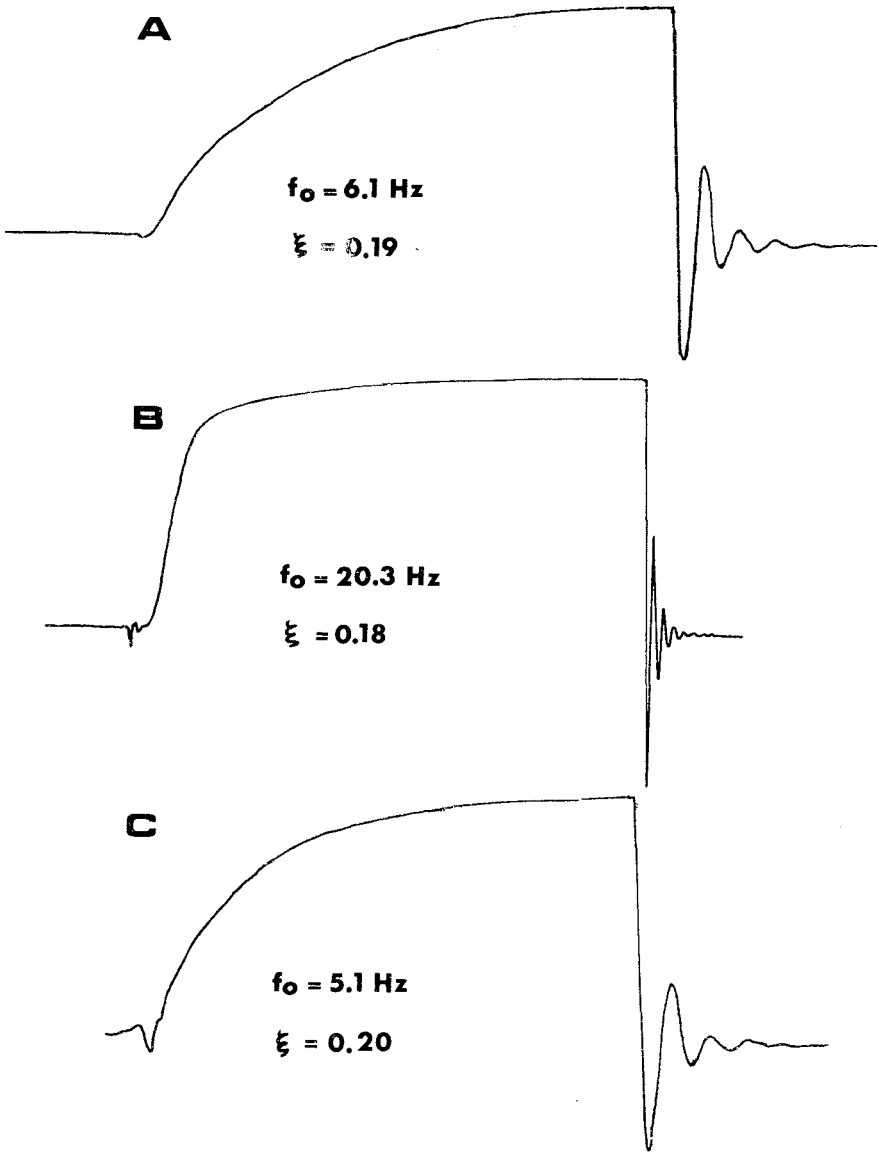

FIG. 1. The frequency response and dampening of a catheter-manometer system tested with the pop method (11). The frequency response and dampenings are calculated according to Gabe (11).
Transducer: Statham P23Db.
Catheter: Polyethylene, length: 60 cm, inner diam.: 2,5 mm.
Fluid: 9% NaCI at room temperature.
In A the response is shown after the catheter is connected to the transducer and carefully filled with saline. No visible air bubbles were present. In B the response after CO_2 has been passed through the system for three minutes is recorded. In C the response after a quide wire has been passed througt the catheter is shown.

In order to get a mixed venous sample of blood, the blood must be sampled in the pulmonary artery, since thorough mixing of blood from the upper and lower caval vein takes place in the right ventricle (12). Thus, right heart catheterization is necessary in order to determine the oxygen concentration of the mixed venous blood. Arterial oxygen concentration can be determined in any arterial sample provided mixing in the left heart chamber has been adequate. The need for right heart catheterization obviously limits the use of this method for determining mean flow through the heart, althougt the use of Swan-Ganz balloon catheters had made pumonary artery catheterization much simpler (13).

Furthermore, several sources of error must be considered in using this method. Warren et al. (12) pointed out that the right ventricular oxygen content can change rapidly. Thus blood must be withdrawn slowly in order to obtain an average sample for oxygen measurement. Apart from the more obvious errors in analyzing and collecting the expired air, changes in barometric pressure of enviromental air must be kept in mind, since the oxygen concentration in the inspired air can change considerably (14).

One of the conditions for using the Fick principle is steady state, i. e. that the cardiac output does not change during the procedure. Thus, the method is not well suited for studying rapid changes in cardiac output. Guyton et al. (15) have devised a continuous cardiac output recorder based on the Fick prinsiple, that permits measurement of cardiac output about 45 sec. after a change in steady state. During steady state and with proper precautions regarding sources for error, the Fick method is considered very accurate, and is widely used as reference for other methods.

The Stuart-Hamilton method

The Stuart-Hamilton method bears the name of the two investigators most closely linked with its development (16,17). Both a continuous and a single injection method have been described, but only the latter will be considered here, since it is the one most widely used. This method should perhaps more adequately be named the Henriques-Hamilton method, since the single injection principle was first published by Henriques (18) while Stewart (16) described a continuous injection method.

After a single injection of an indicator, the cardiac output is calculated from the equation.

$$\text{Cardiac output (l/min)} = \frac{\text{m (mg)}}{\int c \cdot dt \text{ (mg/l/min)}} \quad (2)$$

where m is the amount of indicator injected, and c is the concentration of indicator at the sampling site.

When used in man, the two most commonly employed indicators are indocyanine green and cold saline.

Indocyanine green is a green dye with an absorption maximum at 805 nm. this is the wavelength representing the so called isobestic point for haemoglobin, i. e. the wavelength where reduced and oxygenated haemoglobin have the same absorption coefficient for light. This is of practical importance since oxygen concentration in blood can change considerably during short periods of time (12).

Indocyaninge green is bound to blood plasma proteins. Unbound indocyanine green has a higher optical density than protein bound indicator. This might cause considerable overestimation of flow, if the transit time between injection and sampling site is too short (19). Once indocyanine is bound to plasma proteins it is stable and disappears from blood at an exponential rate of about 20% per minute (20).

Cold saline is used as indicator by injecting the solution at room temperature or colder into the circulation, and measuring variation in the temperature of blood at the sampling site. Due to the problems associated with temperature change along the catheters used for injection and between the blood stream and the tissue, the catheters used and the distance between injection and sampling site must be kept as short as possible.

For measuring cardiac output, indocyanine green might be injected into any vein and can be sampled in any artery. However, to ensure injection of the dye as a pulse, injection into the right atrium is preferred. Cold saline is usually injected into the right atrium and sampled in the pulmonary artery. Since indocyanine green stays in the circulation, recirculation of the dye is often a problem, particularly

in states of low flow. Errors due to recirculation are therefore usually corrected by plotting the data on indicator concentrations in the blood on semilog paper and extrapolating this curve towards zero along a straight line, as first proposed by Kinsman et al. (21). Recirulation is no problem using cold saline as indicator, making this method superior at low flow states or when rapid, repeat measurements are needed.

As for the Fick method, one of the basic assumptions made in using the Stewart-Hamilton method is the presence of steady state during the measurement procedure. Thus, the method is not accurated when rapid changes in cardiac output occur.

Instantaneous flow and flow velocity.

For studying rapid changes in the cardiovascular state and to permit more detailed knowledge about the relationship between pressure and flow in the circulation, the flow out of the heart following each heart beat must be kown. This can be measured in several ways.

From measurement of heart volume using angiocardiography (22,23) or isotopes and γ - cameras (24), the stroke volume can be calculated. Employing echocardiography, the diameter of the left ventricle can be measured and the volume calculated (25,26). This last method is only accurate as long as the ventricle is contracting uniformly, since local changes in left ventricular wall movement influence the calculations to a considerable degree (27).

The above mentioned methods are usually employed to determine the mean flow during each heart beat. In principle, the instantaneous flow curve can be calculated from the rate of change in volume, as demonstrated by Hammermeister et al. (28). This method is however complex, and therefore some sort of flowmeter is usually used for measurement of instantaneous flow out of the heart.

All flowmeters are based on the measurement of mean velocity of blood flow through a cross section of the vessel. Several methods can be used for measuring this velocity (29). However, only the two methods most commonly used in man will be discussed here, namely the one based on the electromagnetic principle and the one using ultrasound.

The oldest method is the one based on magnetic induction, i. e. when a conducting fluid is moving through a magnetic field, the potential across the fluid channel will change proportional to the flow velocity of that fluid. If the artery is exposed, circular probes fitted around the vessel can be used (30) and the flow through the cross sectional area of the exposed artery can be determined. Using transducers mounted on catheters, the velocity of flow can be measured inside the vessel (31). One of the problems connected with measurement of blood flow velocity using catheter tip probes, is that only the velocity at the catheter tip is measured and not the mean velocity over the cross-section. This is no serious problem in the aorta, since the cross-sectional velocity profile in this vessel is rather flat (32). Measurement of velocity and flow of blood using the electromagnetic principle, has many theoretical and practical problems, mainly concerned with baseline stability and calibration (33).

In using the ultrasonic technique, the blood vessel of interest is located in the path of an ultrasonic beam using frequencies from 2—10 MHz. Two principles have been used for measuring velocity of flow with this method, a transit time method and the doppler principle. In the first method, the difference in transit time between the upstream and the downstream direction of an ultrasonic pulse, transmitted througt the blood stream, is measured. This method, as first proposed by Franklin et al. (34) has found little use, mainly because it requires exposure of the vessel, and has to a great extent been replaced by the doppler method. The latter is based on measuring the frequency shift, f_d, of an ultrasonic beam reflected from the red blood cells in the moving blood,

$$f_d = 2 \cdot f_o \cdot \frac{v}{c} \cos \Theta \qquad (3)$$

where f_o is the emitted frequency, v is the velocity of blood, c is the velocity of sound and Θ is the angle between the beam and the blood stream.

The instruments used for doppler measurements are essentially of two types, the continuous wave meter and the pulsed meter. In the continuous wave meter, the ultrasound is emitted continuously and all velocities inside

he beam are measured. The pulsed meter emits short pulses of ultrasound. By receiving he signal at certain time intervals after pulse emission (timegating) the velocity at a certain distance from the transducer can be determined.

A difficulty in using the continuous wave meter is that all velocities inside has beam are measured, and blood flow inside a particular vessel can not be identified. The limitation of he pulsed meter is that only velocities up to a certain value can be detected at a certain depth, as defined by the limit of the range velocity product $v \cdot R$.

$$v \cdot R < \frac{c^2}{8f_o}$$

where v is velocity, R is distance from transducer, c is velocity of sound and f_o is emitted frequency (35).

Ultrasound can be transmitted through body tissues, and thus this method offers the possibility of measuring velocities noninvasively. For measuring blood velocities inside the thorax, both continuous and pulsed meters have been used. Huntsman et al. (36) and Light (37) have recorded velocities in the aortic arch using a continuous wave meter. Johnson et al. (38) used a pulsed meter for localization of cardiac murmurs. Using catheter-tip probes, velocities have been measured in the aorta (39) and in the left ventricle (40).

Calculation of flow from pressure curves

Many attempts have been made at calculating aortic blood flow from aortic pressure. Mainly three methods have been used.

Since the pressure gradient along the artery will determine pulsatile flow (41), the difference in pressure at two points along the blood stream can be used to determine blood flow (42). The main practical problem involved in using this method is that the pressure gradient is minute, thus accuracy of the manometer system used for pressure measurements is a limitation.

The second method is based on the fact that pressure difference will be found if the blood pressure is measured simultanously in the longitudinal and transverse direction of the vessel lumen (Pitot principle). This pressure difference is proportional to the square of the velocity of blood flow. This method is again difficult to use in practice, mainly due to the inaccuracies of the pressure-manometer systems.

While the first two methods measure instantanous flow, the third method measures stroke volume. This third method is based on the fact that there is a relationship between the aortic pulse pressure during systole and the stroke volume. At a constant mean pressure, this relationship is determined by the elasticity of the vessel wall. When the patient is in steady state, the results obtained with this method (43,44) agree well with those of independent techniques. This correlation is, however, low when the peripheral resistance, mean pressure and vessel wall elasticity are changing during measurements.

Methods used in this work.

In our study, a model of the aorta has been employed for estimating mean blood flow out of the heart from the aortic pressure curve. the instantaneous flow velocity in the aorta and inside the heart has been measured by a pulsed doppler velocity meter.

Althougt these methods are based on well known principles, the way these principles have been applied in the current work represents a novel approach. Using the model and the method developed for adapting it to individual patients, mean blood flow can be calculated continuously even when the state of the circulation is changing. The doppler meter enables calculation of flow velocity at selected points in the aorta and inside the heart. Recorded velocities are presented as analogue curves, making recording and further data analysis simple.

Since use of models of the type presented in this study is not very common in medicine, some general comments about models will be made.

A model can be regarded as a hypothesis. In clinical medicine most of the models used are of the verbal, descriptive type and not suited for quantitative analysis. However, exact formulation of hypothesis or a model will make testing of the validity of the hypothesis easier.

In Fig. 2, the basic requirements for formu-

lating and testing a model are described. As can be seen, testing of the model is an essential part of any model building activity. the aim of such testing is, as has been strongly pointed out by Eccles (45) and Popper (46), not primarily to affirm that the hypothesis is correct, but to try to disprove it, so that it can be replaced by «new» models with greater explanatory power.

Any model is a simplification of reality. This is at the time the greatest asset and the greatest limitation of using models. It is therefore essential that the use of a model is clearly defined before the model is constructed. In this study the primary aim was to develop a method that predicted the relationship between mean blood flow in the aorta and blood pressure in this vessel with reasonalble accuracy. Thus, the model employed is not suited for a detailed study of the flow dynamics.

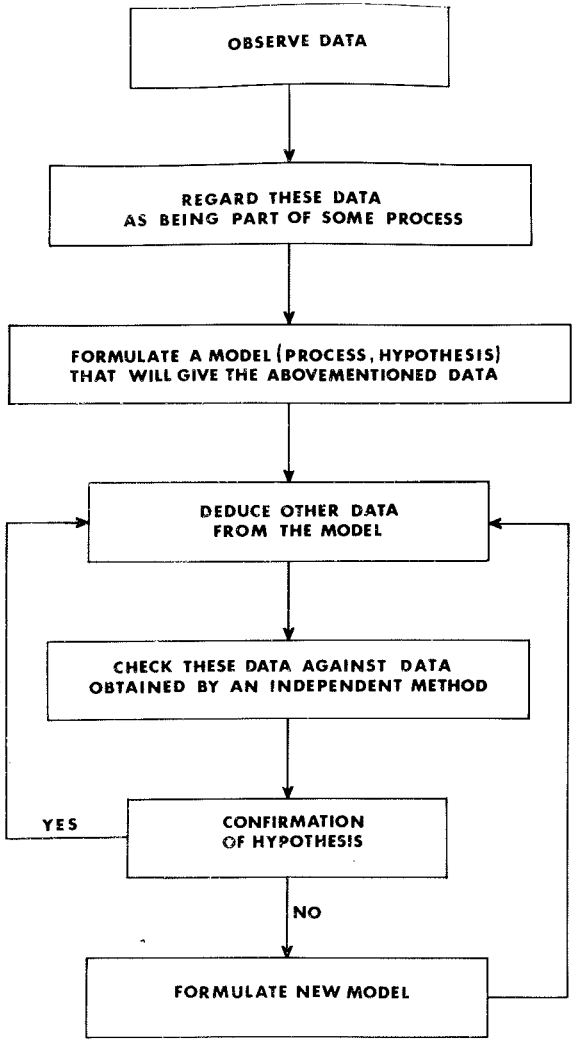

FIG. 2 Principles for developing and testing models.

CHAPTER TWO

Measurement of blood flow and flow velocity in the thorax using pulsed ultrasound

Alf O. Brubakk and Bjørn A. J. Angelsen

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imitations of present ıethods

AT PRESENT NO SIMPLE method exists for measuring blood flow and blood flow velocity in the thorax. The methods currently being used (Fick principle, indicator dilution, electromagnetic and ultrasonic probes) require the introduction of catheters into arteries and veins. This limits their use, and makes frequent repetition of the measurements difficult.

Some of the proposed 'non-invasive' methods have disadvantages—as for instance the impedance method[1], which only measures changes in thoracic fluid volume, or the echocardiographic method[2], which gives only indirect information about flow. Thus information about blood flow is used much less widely in clinical practice than is information about blood pressure, and consequently we know comparatively little about the behaviour of blood flow in health and disease. As cell nutrition is dependent on blood flow rather than on blood pressure it is highly desirable that some simple and reliable method of estimating blood flow is available for clinical use.

trasonic techniques

By means of ultrasound and the doppler effect it is possible to observe blood velocity transcutaneously[3]. From the skin ultrasound is transmitted towards the vessel and is scattered by the fluctuation in the red blood cell concentration. The backscattered wave is picked up by a receiving transducer. The

ultrasound may be transmitted continuously or pulsed. Using a continuous wave, all blood flow along the path of the ultrasound beam is observed, while it is possible to study the blood flow at a certain depth beneath the skin with a pulsed wave[4,5]. The received signal from a small portion of blood moving with velocity, $\vec{v}$, will undergo a change in frequency described by the doppler equation:

$$f_d = -f_0 \frac{\vec{v}}{c}(\vec{n}_t + \vec{n}_R) \tag{1}$$

where f_0 is transmitted frequency, c is the velocity of sound, and $\vec{n}_t$ and $\vec{n}_R$ are the unit normal vectors of the transmitting and receiving transducer faces. The region of observation will not contain a single velocity, but a distribution of velocities. Thus the received signal will contain a spectrum of doppler-shifted frequencies.

In this chapter we shall consider the problems associated with using ultrasound for measuring blood flow. We shall demonstrate the use of a pulsed ultrasonic doppler instrument, and shall show the capabilities and the shortcomings of the mean frequency estimator with reference to full spectral analysis. We shall also describe a scanning method for calculating velocity profile and absolute values of flow.

Pulsed ultrasonic doppler technique

The instrument is described in detail elsewhere[6] and thus we shall confine ourselves here to its main features. It emits coherent pulses of 2 MHz frequency with a duration of 10 μsec at a repetition rate of 6·50 and 9·75 kHz. These pulses are transmitted by a lead–zirconate–titanate transducer 2 cm in diameter which acts alternately as a transmitter and a receiver. For focusing the beam, transducers in the form of a spherical shell with a curvature radius of 10 cm and a diameter of 24 mm are used. This gives a focal diameter of the beam of 5–6 mm extending from 6 to 11 cm. Lenses made of plastic can also be used for focusing. In the continuous mode a double transducer is used. The backscattered signal is sampled for 1 μsec at a certain time after the transmission of the pulse, thus enabling measurement at a depth determined by the sample position control. The received signal is led through a quadrature demodulator and is fed to a velocity estimator which converts this signal into an analogue voltage proportional to the mean frequency shift and thus the mean velocity in the region of observation. High-pass filters with selectable cut-off frequencies are used for filtering signals from slowly moving tissues.

The mean frequency estimator is described by the equation:

$$\bar{\omega} = \frac{E\{e_2(t)\ sgn\ e_1(t)\}}{E\{|e_1(t)|\}} \qquad (2)$$

where $e_1(t)$ and $e_2(t)$ are the quadrature components of the doppler signals, *sgn* denotes the sign (+1 or −1) of the signal, and $e_1(t)$ denotes the absolute value. $E\{|\cdot|\}$ denotes the mean over a sufficiently long period of time, and $\bar{\omega}$ is an estimate of the mean angular frequency shift in the spectrum. The theoretical basis of this estimator is published elsewhere[7].

To aid in the flow detection, the doppler-shifted frequency is led to an audio output. Due to the limitation of the range-velocity product[8], only velocities up to 1·7 m/sec can be measured in depths down to 6·5 cm below the skin, while the limit is 1 m/sec between 6·5 and 10 cm. The instruments can also be used in a continuous mode, when higher velocities are encountered. Using a simple integrator circuit triggered either by the ECG or the flank of the velocity signal, the area under the velocity curve is calculated.

By testing our instrument in laboratory conditions, we have been able to show that it can be used to measure flow velocity and changes in flow. By positioning the transducer in the suprasternal notch, velocities in the ascending aorta as well as in the aortic arch can be measured. Placing the transducer in the intercostal spaces near the sternum, blood flow velocity can be determined in the aorta as well as in the different valve areas. The different valves may be identified, using anatomical knowledge about the relative positions of the valves and the form of the velocity curves[9].

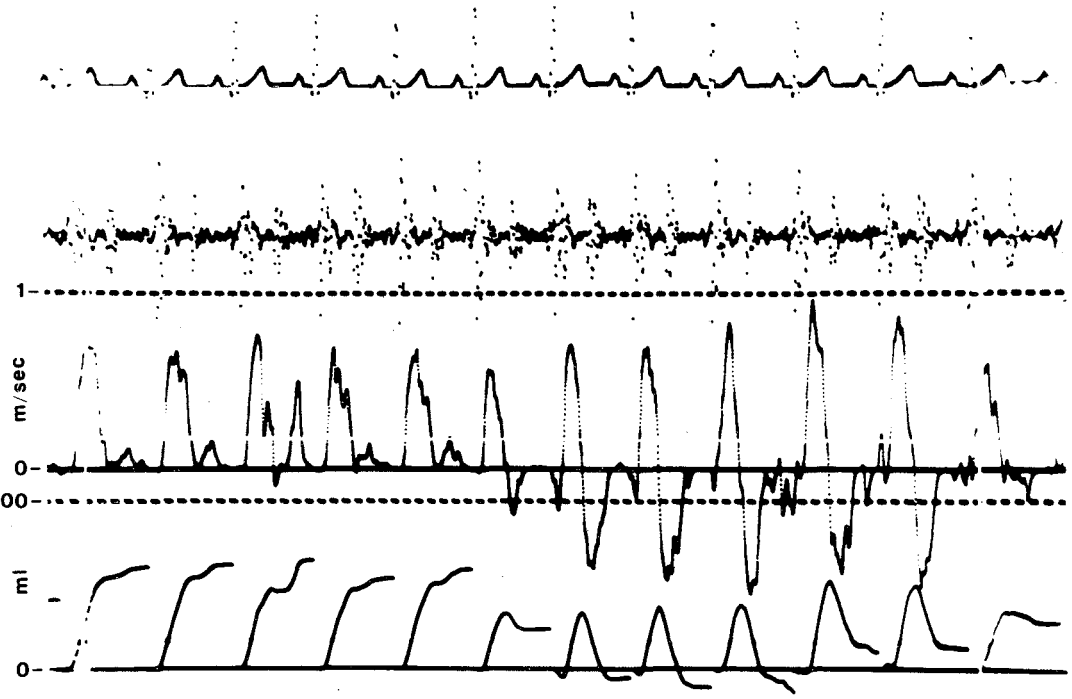
scending aorta

Figure 2.1 shows the measured blood velocity in the ascending aorta in a normal person. The sample position is moved so that the figure shows velocities at depths from 2 to 10 cm below the suprasternal notch. Note that the velocities increase, while the integrals are reduced, indicating regions of high velocity just outside the valves. In this region an increased backflow is also observed.

Measuring flow velocity in the ascending aorta in 18 normal persons, where the aortic diameter was measured by an ultrasound echotechnique, showed that the calculated cardiac output was between 30 and 70 per cent of normal values[6]. The reason for this discrepancy was probably the unknown angle between the blood flow and the ultrasonic beam. Even if absolute values of blood cannot be measured, flow changes can

ig. 2.1 Blood flow velocity in the scending aorta measured from the uprasternal notch in a normal per-on. From top to bottom can be seen CG, phonocardiogram, velocity, and ntegral under the velocity curve. At ne left side of the picture the velocity measured in a depth of 2 cm and the ange-cell is moved successively ownwards so that the measurements re performed at 10 cm depth on the ght side of the picture.

be recorded. Fig. 2.2*A* and *B* show changes in flow and flow velocity as a normal person moves from the supine to the upright position.



Mitral valve

By positioning the transducer in the intercostal spaces, blood flow velocities inside the heart can be measured. Fig. 2.3 demonstrates a measurement of mitral valve flow velocity in a normal person.

Aortic insufficiency

In aortic insufficiency a certain amount of blood is regurgitated with each heart-beat. There is at present no practical and easy method for calculating the amount of regurgitation in this disease state. Fig. 2.4*A* and *B* show an example of a measurement of velocity in the ascending aorta in a person with severe regurgitation. Fig. 2.4*A* shows a spectral analysis of this signal.

Figs. 2.2 *A* and *B* Measurement of ascending aortic flow from the suprasternal notch in a normal person. In *A* the person is in a supine position, in *B* the velocities are measured immediately after standing up.

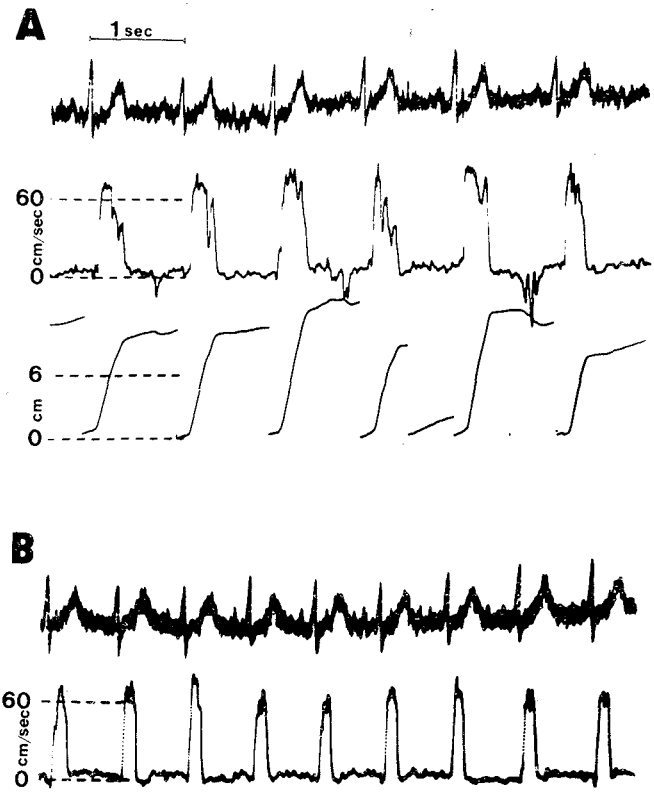
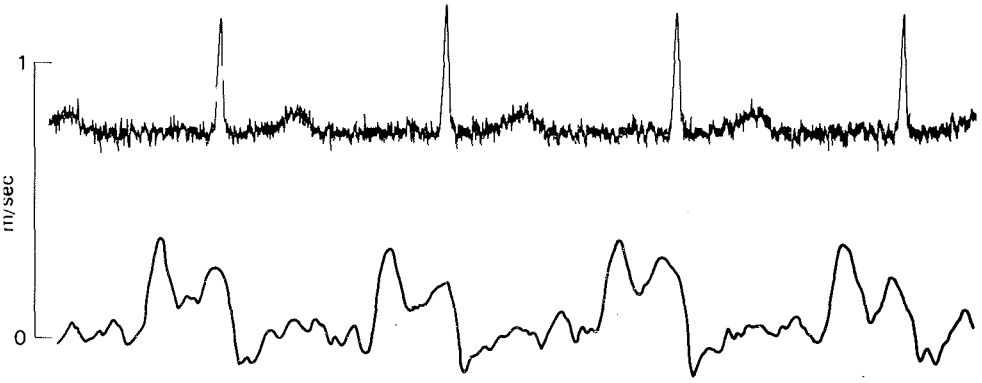
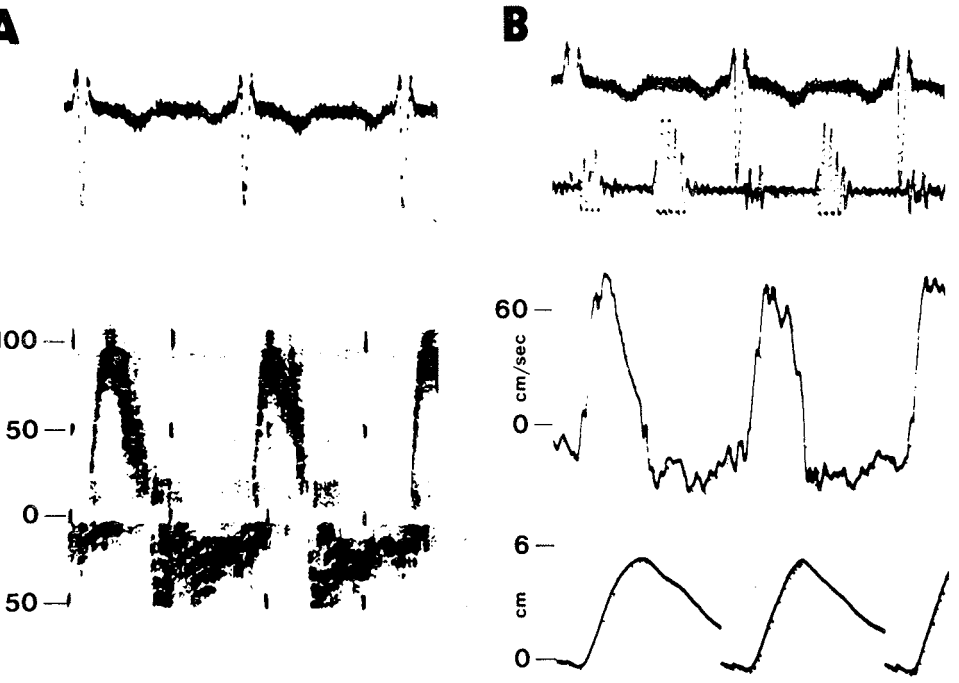


Fig. 2.3 Measurement of mitral flow velocity in a normal person. Measurement performed from the 4th intercostal space near the left sternal border.



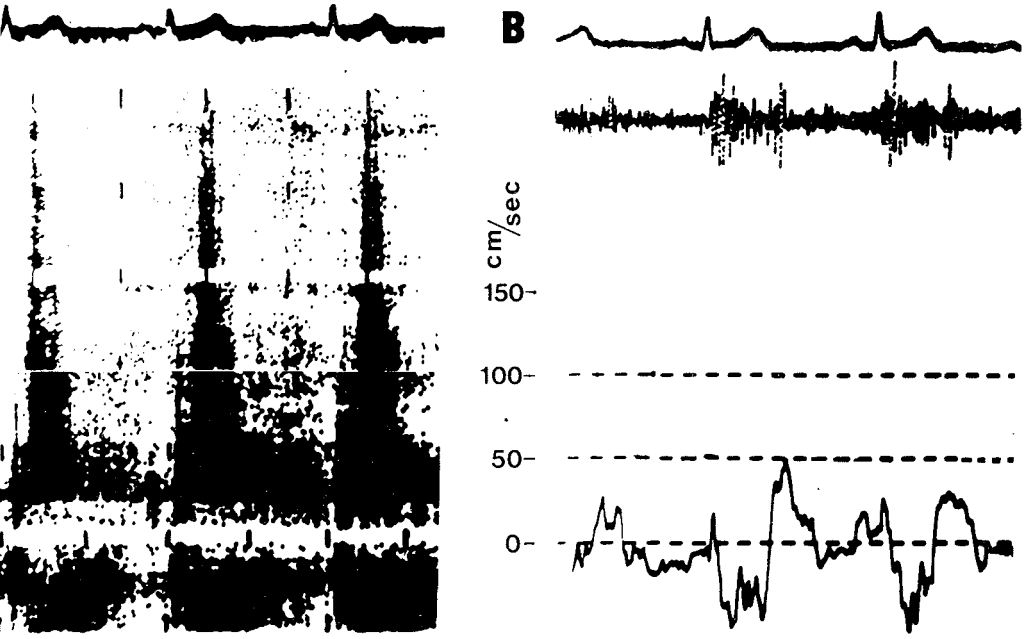
s. 2.4 *A* and *B* Measurement of ending aortic flow velocity from the rasternal notch in a person ering from aortic insufficiency. In spectral analysis of the signal is wn. In *B* the mean velocity is wn together with the integral un- the velocity curve. The integrator eset by the ECG. The relative in- iciency can be calculated from the tive height of the rising to the ng curve.

The darkening of the display indicates the intensity of the frequencies present in the signal. It can be seen that in systole only a small number of frequencies are present, while in diastole many frequencies are represented. In Fig. 2.4*B* the mean velocity in this signal is shown. The lower trace is the integral of the mean velocity curve. The ratio of the ascending to the descending part of the integral represents the relative amount of regurgitated flow.

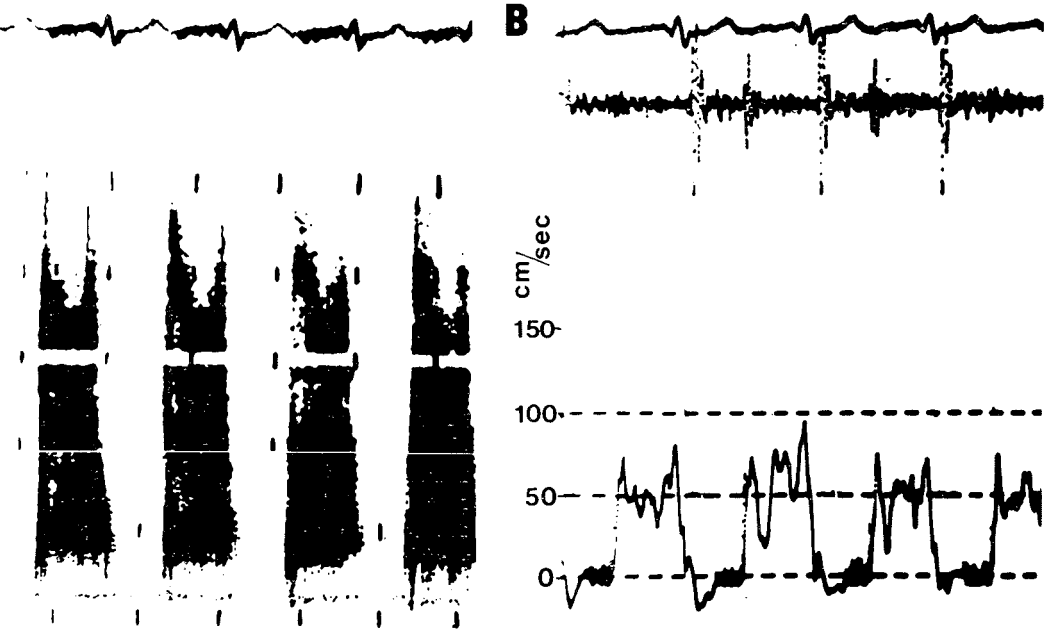


rtic stenosis

Fig. 2.5*A* and *B* is obtained by directing the transducer from the suprasternal notch towards the ascending aorta in a patient suffering from aortic stenosis. The instrument is used in the continuous mode so that velocities above the limit set by the range velocity product may be recorded. In Fig. 2.5*A* a spectral analysis of the signal is shown, while Fig. 2.5*B* shows the mean velocity. In the continuous mode, the instrument observes all velocities present in the beam. This accounts for the negative doppler shifts which stem from blood moving away from the transducer. The intensity of the negative frequencies is so strong that the mean frequency estimator gives a negative output in the systole although the aortic flow is towards the transducer.



. 2.5 *A* and *B* Flow velocity measured from the suprasternal notch in the direction of the ascending aorta in a patient ering from aortic stenosis. In *A* the spectral analysis is shown. In *B* the mean velocity is displayed. Note that the mean city goes away from the transducer although the velocity is up to 250 cm per second in the ascending aorta.



2.6 *A* and *B* Mitral flow velocity measured from the thorax in a patient suffering from mitral stenosis. In *A* the spectral ysis of the signal is shown. In *B* the mean velocity is displayed. Note the large difference in velocities found.

Mitral stenosis

Fig. 2.6*A* and *B* show the mitral flow velocity in a patient suffering from mitral stenosis, where Fig. 2.6*A* shows the spectrum and Fig. 2.6*B* shows the mean velocity present. The large difference in mean and maximum velocity can clearly be seen.

The spectrum of the received signal will contain information about the velocity profile in the region of observation. When all parts of the vessel are uniformly illuminated, a parabolic velocity profile will give an approximately rectangular power spectrum. The spectrum is not fully rectangular due to the finite transit time of blood through the observation region, which smoothens the fall-off of the spectrum at the upper end[7]. A profile flatter than a parabola will give an increase in the intensity of the frequency components near the maximum doppler shift present.

Nature of the signal

The received signal is the sum of independent stochastic contributions from different parts of the vessel. The signal can thus be modelled by a gaussian stochastic process, and all obtainable information of the velocity field in the region of observation is contained in the stochastic properties of this process. Since the signal is gaussian, its stochastic properties are contained in second moments, ie its correlation function or power spectrum. Thus the spectrum incorporates all information in the signal. The spectrum is strictly defined for stationary processes only, which requires time steady velocity fields. When the velocity field is time varying as in the arteries, the spectrum has to be estimated over so short a time (5 msec) that the velocity field may be considered constant. The finite estimation time introduces a stochastic error in the estimate.

Complications

For a given profile and illumination of the vessel a unique power spectrum is obtained. In deducing the form of the velocity profile from the spectrum, two problems arise. One is the illumination of the artery, which is difficult to check transcutaneously. Even if this illumination is known, the deduction of the velocity profile is not unique, but as only one class of profiles is expected in the thorax (parabola, flat profile) this is not a serious problem. A third effect can also be of importance. Our experiences indicates that the scattering cross-section of blood will depend on the state of flow. Turbulence in stenoses has been shown to give high intensity of the back-scattered signal. This probably arises from an increased fluctuation in the red cell concentration, caused by the unsteady flow. One could also expect high shear velocities in laminar flow to increase the fluctuation in the red cell concentration and thus the scattering cross-section. This would increase the intensity of the low-frequency components in the spectrum, as these originate from the blood near the vessel wall where the

shear gradients are highest. This effect probably does not introduce large errors in the laminar flow situation.

dvantage of pulsing e beam

By pulsing the beam, the range-cell can be made so small that the velocity field is practically constant inside the cell. The velocity profile across the vessel can be observed by moving the cell across the vessel or by multi-range gating[4,10]. Thus the velocity profile can be obtained without the problems mentioned above. Due to the wave nature of the ultrasound and the limited bandwidth of the transducers, a minimum size of the range-cell is given. This introduces a special low-pass filtering effect, making the measured profile a convolution between the range-cell and the actual profile. By deconvolution the original profile can be obtained[11].

ectral analysis

Although spectral analysis displays all information in the backscattered signal, it is costly in terms of equipment. If a full spectral analysis is not necessary, simpler methods for information retrieval would be preferable. One of the main uses of the ultrasound doppler method would be to get information about the flow or changes in flow. In this case the mean velocity across the vessel will be the interesting quantity. The volume flow of blood will be the product of this velocity and the vessel area, the latter may be obtained by, for instance, echo-techniques. With a uniform illumination of the artery, the mean velocity is obtained from the mean frequency shift in the backscattered signal and thus the simple mean frequency estimator may be used instead of complete spectral analysis.

nitations

When measuring in the thorax, the angle between the beam and the bloodstream is unknown, and therefore the measured velocity will deviate from the real one by an unknown factor (equal to the cosine of the angle). However, relative changes in flow can be recorded from the mean velocity changes, without knowing the angle and the cross-sectional area of the vessel. Another difficulty in applying the ultrasonic doppler method in the thorax, is to achieve a uniform illumination of the vessel without interference from neighbouring arteries and veins. This is not possible by a continuous wave method because all blood flow along the beam will be recorded. By using a pulsed system and a wide beam an approximate uniform illumination can be achieved in most cases. Interference from other arteries when measuring in the ascending aorta is sometimes a problem.

tral valve

Holen *et al.*[12] have presented a method for calculating the pressure drop across the mitral valve using the ultrasonic doppler method. A fluid element starting at zero velocity in the atrium will obtain a velocity v in the mitral orifice due to the

pressure drop Δp (Bernoulli equation):

$$\Delta p = \tfrac{1}{2}\rho v^2 + R \qquad (3)$$

where ρ is the density of blood and R is viscous losses. For fluid elements in the middle of the orifice the viscous losses will be so low that they can be neglected. Thus the pressure drop can be calculated from the maximum velocity present in the mitral jet. The mitral valve is located so that flow is directed towards the thoracic wall and the angle between beam and bloodstream is practically zero. Thus the maximum velocity can be calculated from the maximum doppler frequency present. For this application a mean velocity estimator can clearly not be used.

Aortic valve

In this and in a previous paper[6], we have been able to show that our instrument is able to measure flow velocity at selected regions in the thorax. Fig. 2.2 shows that the changes in aortic flow can be recorded. The reduced stroke volume in Fig. 2.2*B* is probably due to a reduced venous return to the heart as the subject rapidly stands up from a supine position.

If changes of blood flow velocity are to be recorded, the measurements in the aorta must always be performed at the same depth below the skin. Fig. 2.1 shows that near the aortic valve, areas with high velocities at the beginning of systole may be found. These high velocities are not representative of the mean velocities over the cross-section of the aorta, but probably represents jets of blood around and behind the aortic valve. The large backflow may be caused by a lowering of the base of the heart as the left ventricle is emptying.

Mitral valve

The normal mitral valve flow velocities shown in Fig. 2.3 demonstrate the typical double-peak of this flow curve, where the second peak is caused by the atrial contraction. As the mean velocity is proportional to the mean flow across the valve, the relative height of the two peaks may be used to determine the relative contribution of the atrium to ventricular filling.

Mean velocity

The mean velocity is the important quantity for determining flow changes. This is demonstrated in Fig. 2.4. The spectral analysis shown in Fig. 2.4*A* demonstrates that in systole only a narrow band of frequencies is found, indicating a rather flat velocity profile. In the diastolic part of the curve all frequencies are present, indicating that in this case the velocity profile is more parabolic. One method that has been proposed for simplifying the recording of the curves is to display an envelope around the spectrum only[13,14]. By using this method, the curves can be displayed on a simple chart recorder. Using

the envelope method, two different curves can be compared only if they have approximately the same velocity profile. Fig. 2.4*A* and *B* clearly demonstrate that the amount of regurgitation will be overestimated if an envelope is placed around the spectrum (Fig. 2.4*A*) compared with the mean values measured in Fig. 2.4*B*. Thus in this case, the mean velocity estimator is preferable to spectral analysis as it measures only the quantity of interest. Fig. 2.5, however, shows that the use of a mean velocity estimator may introduce errors if used with a continuous wave meter. As all velocities inside the beam are recorded, the estimator output may not coincide with the mean velocity inside the artery of interest. In this case a mean velocity away from the transducer is recorded, although velocities up to 250 cm/sec towards the transducer can be recorded in the ascending aorta.

laximum velocity

In the mitral valve, the pressure drop between atrium and left ventricle determines the velocity of flow. There may, however, be large differences between the mean and the maximum velocity as Fig. 2.6 clearly shows. In this case, the maximum velocity is the one that is of interest as discussed previously.

The example in Fig. 2.4 demonstrates that the envelope around the spectrum may actually be misleading. On the other hand a mean velocity estimator will not give the information necessary to calculate the pressure drop over the mitral valve.

An instrument capable of measuring both mean and maximum velocity would therefore be desirable, and for most practical purposes obviate the need for full spectral analysis. Furthermore, knowing the mean and the maximum velocity would enable us to get an impression about the velocity profile present. For a flat profile, the mean velocity will be only slightly smaller than the maximum velocity, while for a parabolic profile the mean velocity is half the maximum velocity.

roblem of beam angle

Due to the unknown angle between the beam and the blood stream, only relative values of blood flow and blood flow velocity can be measured in the thorax with the possible exception of flow through the mitral valve, where the ultrasonic beam in most cases may be directed along the flow[12]. There is at present no practical way of solving this problem. Although changes in blood flow can give information about the effect of drugs, for instance, the absolute flow values are of interest in many instances.

canning method

This problem can be solved by a scanning method. Using a focused transducer a small sample volume can be obtained inside which the velocity is approximately constant. The

instrument output is the component of the velocity along the beam. By sector scanning the transducer, the range-cell may be moved across the vessel cross section. The flow $q(t)$ through the vessel is given by the following equation:

$$q(t) = \int \int_S dA \cdot \vec{n} \cdot \vec{v}(\vec{r}, t) \quad (4)$$

where S is an arbitrary surface crossing the artery, $\vec{n}$ is the unit normal vector to this surface, $\vec{v}(\vec{r},t)$ is the velocity field as a function of space, $\vec{r}$, and time t. $\vec{n} \cdot \vec{v}$ is the quantity measured at each position of the range-cell. By summing the contribution from different parts of the artery, an approximation to the integral is obtained without knowing the actual cross-section of the artery or the angle between the beam and the artery. The surface S will then be the part of the sphere across which the range-cell moves in the sector scan.

In our experience it is only possible to scan in the aortic arch from the suprasternal notch. The flow measured here will be about 20 per cent lower than the cardiac output, due to the fraction going to the head and arms. Apart from giving the flow values, this method makes it possible to estimate the velocity profile across the vessel. Finally, it also offers the possibility of measuring the regurgitation of blood through the mitral valve. The mean velocity cannot be used for this, as the area of the valve is not the same in systole as in diastole. By scanning over the jet, these areas can be calculated and the amount of regurgitated blood determined. However, one problem in applying this method is that the orifice during systole is of the same size as the range-cell. Therefore, deconvolution must be performed to get correct results.

egurgitated blood etermination

CKNOWLEDGEMENT

This work was supported by the Norwegian Council for Scientific and Industrial Research and the Life Insurance Company Forenede Liv A/S, Trondheim, Norway. We gratefully acknowledge also the assistance of Liv Hatle, M.D., in performing the measurements.

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RANSCUTANEOUS MEASUREMENT OF BLOOD FLOW VELOCITY IN THE HUMAN AORTA

BY

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Reprinted from Cardiovascular Research
Volume X, *No.* 3, *pages* 368–379, May, 1976

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, LONDON WC1

ovascular Research, 1976, **10**, 368–379.

anscutaneous measurement of blood flow ocity in the human aorta[1]

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the Division of Engineering Cybernetics, Norwegian Institute of Technology, rsity of Trondheim, and the Section of Cardiology, Department of Medicine, nal Hospital, Trondheim, Norway

IORS' SYNOPSIS A Doppler velocity meter for measuring blood flow velocity in the human is described. Using pulsed ultrasound, this instrument allows the velocity to be measured at ed depths. The instrument has been tested in laboratory experiments, and appears to give ate estimates of mean flow velocity for both steady and pulsatile flows. Flow velocities and ates of stroke volume have been obtained from the ascending aorta in 18 patients. It is suggest- iat at present only relative values for flow and flow velocity can be measured. A method for ning absolute values for these parameters, based on scanning in the aortic arch, is proposed.

ng the past few years, there has been con- able interest in using ultrasound for uring blood flow and blood flow velocity in uman aorta. In theory, ultrasound offers ossibility of measuring these parameters nvasively. In practice, however, several ems exist involving mainly the angle een the ultrasonic beam and the flow of l and the heterogenety of the ultrasonic

anscutaneous measurement of aortic blood velocity has been reported by MacKay), Light and Cross (1972), Light (1974); both s used a continuous wave method. The ducer is placed in the suprasternal notch and locity signal is recorded from the aortic arch. system using continuous ultrasound has no ition along the beam (depth resolution), herefore all bloodflow in the path of the beam is measured. Light and Cross (1972) claim that this problem can be solved by spectral analysis of the received signal. This argument is based on the fact that flow in vessels outside the aorta all have a greater inclination to the beam than flow in the aortic arch itself. Thus the largest frequency shift will be from the aortic flow velocity.

The inability to resolve depth, however, is a practical limitation. Depth resolution enables the operator to control what region of flow is actually under investigation. This removes false information from the received signal and simple mean velocity estimation may be used instead of spectral analysis. By focusing the beam, the velocity profile across the vessel lumen may be obtained either by scanning the beam or by 'multiple-gating' of the received signal (Haase *et al,* 1973).

The present study was undertaken to construct a pulsed Doppler meter for measuring blood flow velocity in deep arteries such as the aorta. The instrument has been tested in vascular

ork was supported by the Norwegian Council for Scientific ustrial Research and the Life Insurance Company Forenede , Trondheim.

nt requests to A.O.B., Section of Cardiology, Medical Depart- egional Hospital, 7000 Trondheim, Norway.

to determine its ability to measure both and pulsatile flow velocity. The field of asonic transducer has been studied with to inhomogeneities. The instrument has ed clinically to demonstrate its ability to velocity signals from the ascending aorta e aortic arch. Measuring the aortic dia- with an echo-technique, the data have ed to give estimates of volume flow and volume. Using a scanning technique, profiles across the aortic lumen could tructed.

Methods

entation principle

am of the instrument is shown in Fig. 1. A or emits coherent rf-pulses of 2 MHz cy with a duration of 20 periods (10 μs) at a n rate of 6.5 or 9.75 kHz. The pulses are d in a power amplifier and then transformed rasonic energy by a transducer. The trans- connected to the power amplifier during the ssion (10 μs) only. Until the next pulse is trans- the transducer is connected to a receiving r and acts as a pick-up for back-scattered ic waves. The signal is split into two channels in a quadrature demodulator. A sample gate closes for 1 μs at a fixed time after the transmission of the pulse. This time is set by the sample position control. By these devices the signal from a small volume of 7.5 mm length and a certain width (determined by the width of the beam at the depth given by the sample delay), is led through the two channels.

To remove signals from the slowly moving tissues in the path of the beam, highpass filters with selectable cut-off frequencies are inserted (see discussion). A low pass filter removes the high-frequency components introduced in the sampling. A cut-off frequency of 4.2 kHz is used for the 9.75 kHz repetition rate, while 2.8 kHz is used for the 6.5 kHz repetition rate.

The signals are fed to a velocity estimator which converts them into an analogue voltage proportional to the mean frequency shift. This frequency shift is proportional to the mean velocity in the region of observation.

As an aid for directing the transducer, one of the signals is fed to an audio amplifier.

The ultrasound is scattered from inhomogeneities in the tissue and the blood. The scattered wave received at the transducer will observe a change in frequency (Doppler effect) proportional to the velocity of the scattering centre along the beam,

$$f_d = 2\, f_0 \cos\theta \, \frac{v}{c} \qquad (1)$$

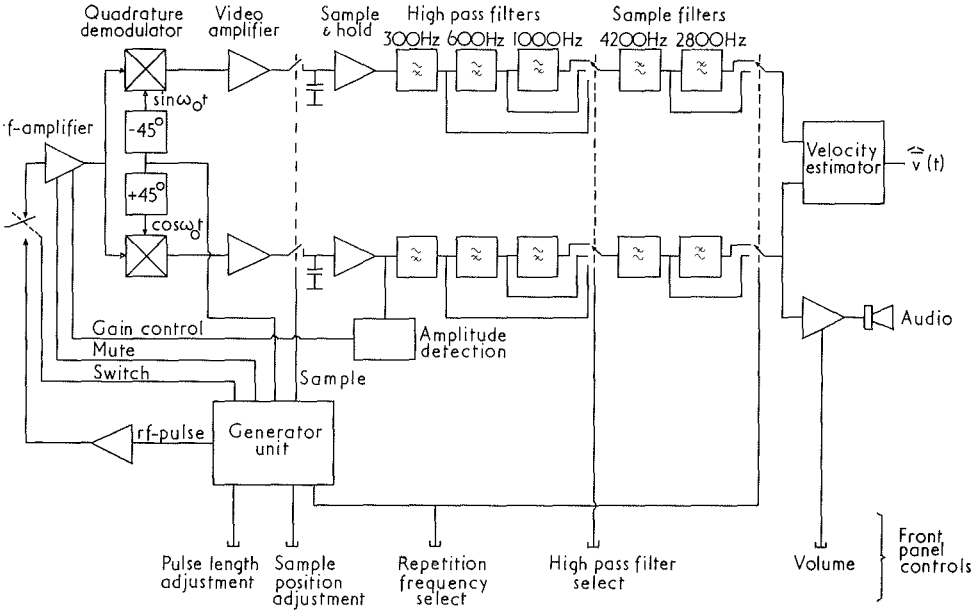


Diagram of the pulsed Doppler velocity meter.

/here f_d is the Doppler shift in frequency, f_0 is the mitted frequency, c is the velocity of sound, v is ıe velocity of the scatterer, and θ is the angle etween the direction of the velocity vector and the eam.

Since many scatterers are present, a spectrum of Doppler-shifted frequencies near f_0 is received. By emodulation the spectrum is displaced so that f_0 s changed to zero frequency. Thus only the Doppler-hifted frequencies are heard in the audio output, he highest frequencies corresponding to the highest elocities.

The velocity estimator used is described by the ollowing equation:

$$\bar{\omega} = \frac{E[\acute{e}_2(t)\cdot \operatorname{sgn} e_1(t)]}{E(\,|\,e_1(t)\,|\,)} \qquad (2)$$

/here $e_1(t)$ and $e_2(t)$ are the signals in the two hannels, sgn denotes the sign (+1 or −1) of the ignal and $|\,e_1(t)\,|$ denotes the absolute value. $E[\cdot]$ denotes the mean over a sufficiently long period f time and $\bar{\omega}$ is an estimate of the mean angular requency shift in the spectrum. The theoretical asis of this estimation is given elsewhere (Angelsen, 975).

To avoid ambiguity in depth, the echo from one ulse has to be received before the next pulse is ransmitted. In order to study deep arteries, a low ulse repetition frequency is required. On the other and, the sampling frequency must be at least twice he Doppler frequency (Shannon samplings theorem). Thus, in order to measure high velocity, a high epetition frequency is needed.

The deeper the artery the lower is the maximum elocity that can be measured by a pulsed meter. This is expressed by the limit of the product between he velocity v at the depth R (Newhouse and Bendick, 1973).

$$v\cdot R < \frac{c^2}{8f_0} \qquad (3)$$

/here c is the velocity of sound and f_0 is the emitted requency.

With the lower repetition frequency velocities up o 1 m/s may be measured at depths up to 10.5 cm, while at the higher repetition frequency, these alues are 1.7 m/s and 6.5 cm, respectively. In the commercial version of the instrument, the repetition requency is automatically selected by the depth control device[1].

The transducers are made of lead-zirconate-itanate (Trade-Mark PZT-5A Brush-Clevite). The liameter is 2 cm. For scanning, a transducer formed as a spherical shell with a curvature radius of 10 cm and a diameter of 24 mm is employed. This gives a focal diameter of the beam of 5–6 mm extending from 6–11 cm.

[1] Manufactured by SINTEF, Trondheim, Norway.

Laboratory testing

In order to test the accuracy of the instrument fo measuring pulsatile flow, a model of the aorta anc the left ventricle was constructed from plexiglass (Fig. 2).

The 'heart' delivers a flow into the 'aorta'. The stroke volume of the pump is constant, but the pulse-rate can be varied. A mixture of oil and glycerine was used to simulate blood.

The experimental conditions used for testing the ability of the instrument for measuring steady-flow velocities can be seen from Fig. 3., From a reservoir, ox blood is driven through a pipe. The time of volume flow is measured and compared with the output from the instrument. By changing the direction of the ultrasonic beam relative to the flowing blood, the flow velocity towards as well as away from the transducer can be measured.

The field of the transducers were tested by scanning a small pick-up transducer ($0.5\times0.5\times1$ mm) across the field of the radiating transducer.

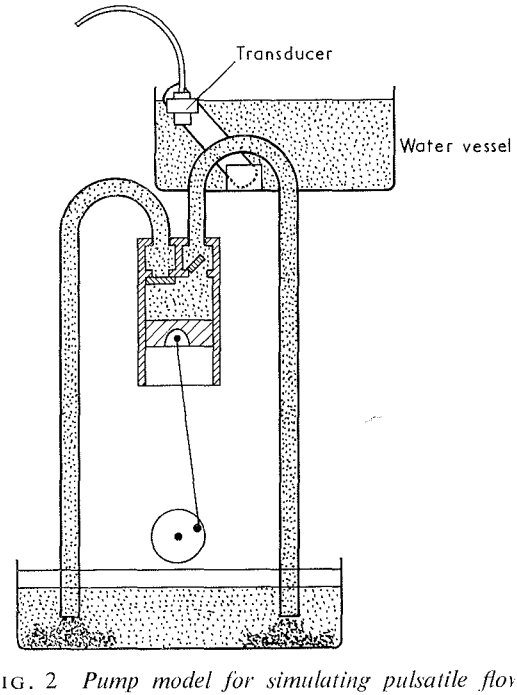
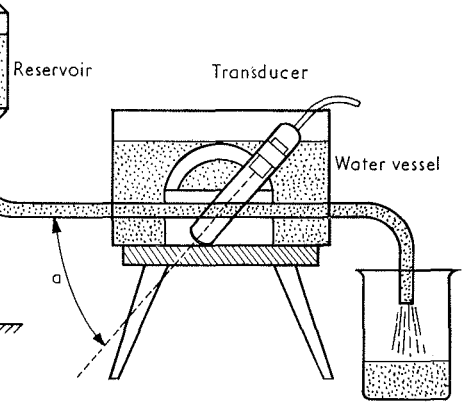


FIG. 2 *Pump model for simulating pulsatile flov The pump gives a constant stroke output, but strok rate can be varied.*



Experimental setup for testing the accuracy city measurement. The reservoir is kept at a t level from the ground by means of a spring. gle between the transducer and the pipe (a) *varied.*

testing

itioning the transducer in the suprasternal flow velocity in the ascending as well as the arch can be recorded, as demonstrated in By angling the transducer until no velocity s recorded, one can assume that the angle the beam and the bloodstream is approxi-90° (position B in Fig. 4). In this position the r of the vessel can be calculated from the between the echos from the posterior and vessel walls.

lood flow velocity and aortic diameters have easured in 18 subjects with normal aortic Four subjects had angina pectoris, the rest signs of cardiovascular disease. The velocie measured in depths 6–10 cm below the of the skin, in a position giving the maximum der the velocity curve. The subjects were d in the supine position in a semi-darkened

er to evaluate if these velocities and diameter ments could be used to obtain volume flow ke volume, the following calculations were ed:

$$F = \frac{\pi \cdot D^2}{4} v \qquad (4)$$

is the volume flow estimate, D is measured

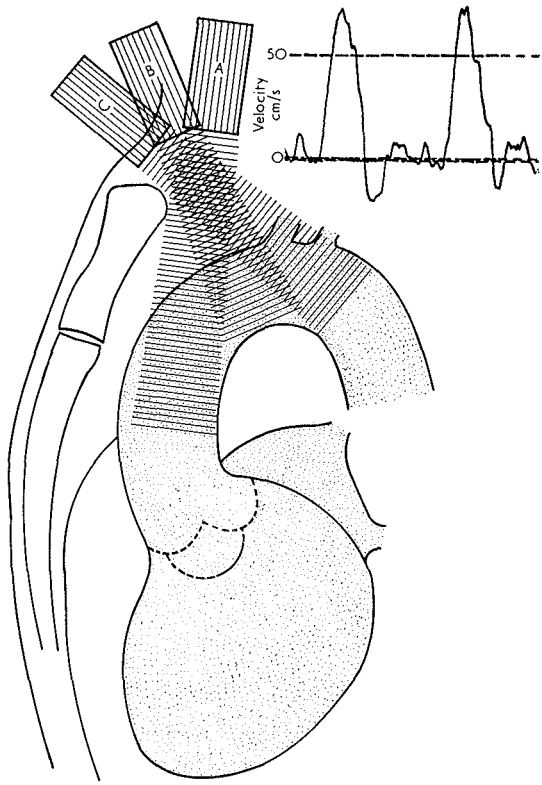


FIG. 4 *Transducer positions for measuring aortic blood flow velocity in the aorta (lateral view). In position* A *and* C, *the velocities are measured in the ascending aorta and the aortic arch, respectively. In position* B, *the beam is normal to the blood stream, this position is used for measuring aortic diameter. The velocity in position* A *is shown on the right.*

diameter, and v is measured velocity.

$$SV = \int F(t)dt \qquad (5)$$

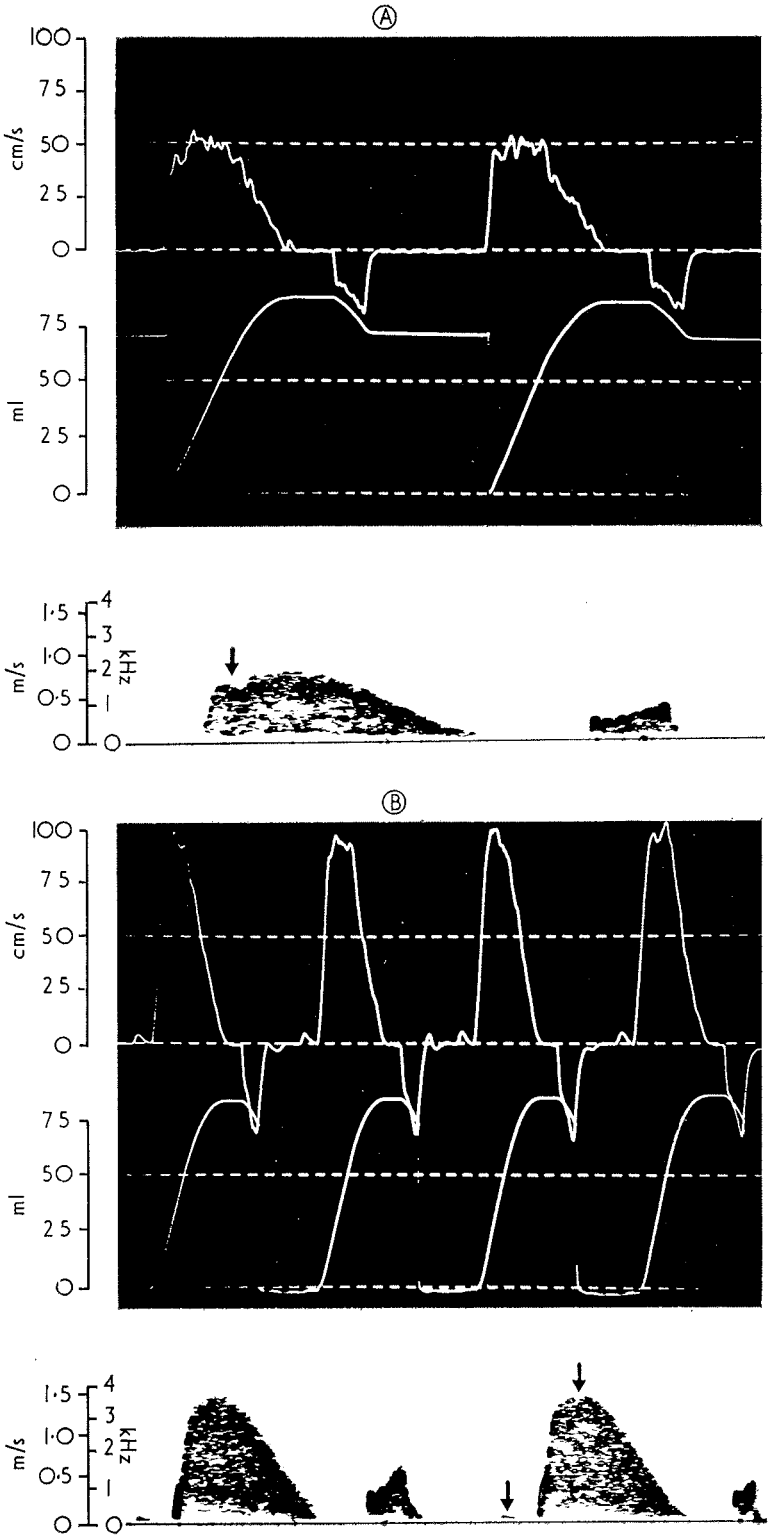
where SV is the stroke volume estimate.

$$CO = SV \cdot HR \qquad (6)$$

where CO is estimated cardiac output and HR is heart rate as calculated from the ECG.

Ascending aortic flow velocity has also been measured in a patient with aortic insufficiency.

Aiming the transducer towards the aortic arch and using lenses for focusing the beam, the velocities inside a cylinder of approximately 7.5 mm length and 5 mm diameter can be determined. The transducer is connected to potentiometers which will



FIGS. 5a and b *Measurements from the pump model (Fig. 2), showing velocity, stroke volume, and spectral analysis of the last beat (Fig. 5a) and the two last beats (Fig. 5b). In Fig. 5a the pump rate is 30 beats/min, in Fig. 5b it is 60 beats/min.*

be the angular direction of the transducer and the position of the focal point. Using a e oscilloscope, a system was constructed made the oscilloscope beam light up in the on determined by the output from the potentio- every time the velocity exceeded a preset By progressively lowering the velocity thresh- nd mechanically scanning over the vessel er, areas with velocities above a certain could be registered on the screen. Approxi- 15–20 min were needed to complete these

ng the radii of the areas developed in this r, the velocity profile across the lumen may nstructed by plotting the radii against the old velocities.

Results

es 5 a and b show measurements on the model. The measurements are performed e straight part of the 'ascending aorta', pper curve being the velocity and the lower the integral of this velocity multiplied by rea of the tube. The lower curve gives an ate of the pump stroke volume of 84 ml, alue calculated from construction data 87 ml. Compared with Fig. 5a, the pulse s increased in Fig. 5b and an increase in nal velocity with no significant change in ted stroke volume is noted. Similar s, showing a proportional increase in ty and constant stroke volumes with increas- lse rate, were obtained when changing the rate from 10 to 60 pulses/min.

eath the curves are shown a spectral is of the last pulse in Fig. 5a and the two ulses in Fig. 5b. Due to the dynamics of w system, a velocity overshoot appears at ading edge of the flow pulse at low pump s can be seen from the spectral analysis . 5a. This is reproduced by the velocity tor, which also reproduces the random ons in the spectrum indicated by the at the top of the last pulse in Figure 5b.

ure 6 shows a comparison between the y measured by the instrument and the ies calculated from time of volume flow, the model described in Fig. 3. A close tion was found between the values both sitive and negative flows. The zero-offset, an absolute error of 4 cm/s in the velocity

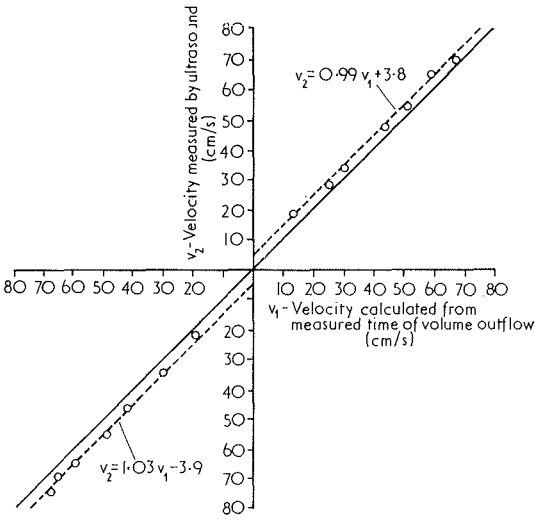


FIG. 6 *Relation between velocities measured by ultrasound and calculated from measured time of volume outflow, using the experimental setup shown in Fig. 3. The line of identity is drawn. The high pass filter cutoff frequency is 200 Hz.*

measurement, is caused by the high pass filters of the ultrasonic instrument, which for this experiment were 200 Hz.

In Fig. 7 the intensity of the ultrasonic field is represented at different distances from the transducer. The inhomogeneities of this field,

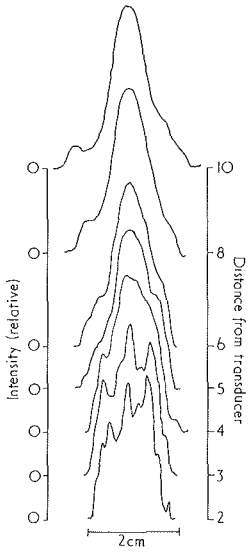
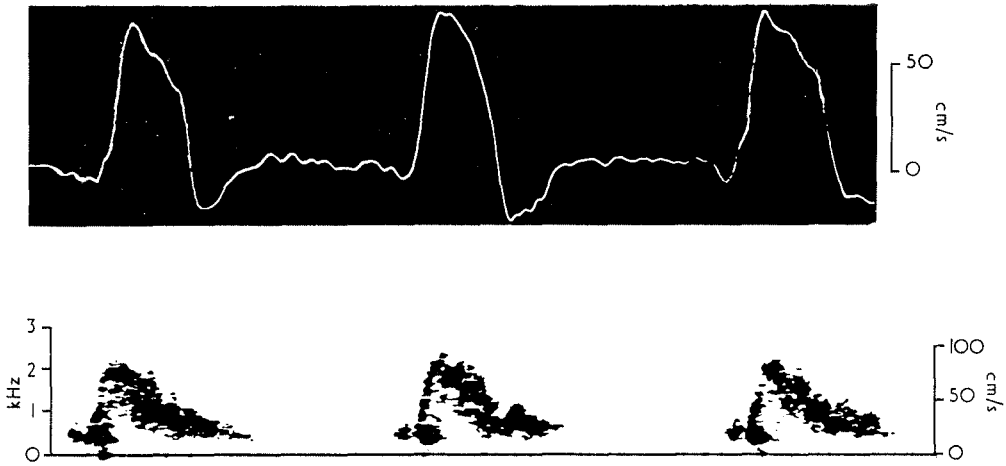


FIG. 7 *Ultrasonic field intensity (relative) measured at different distances from an unfocused circular transducer of 18 mm diameter. Ultrasonic frequency is 2 MHz.*

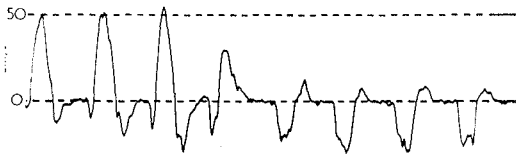


IG. 8 *Blood flow velocity in the ascending aorta in a normal person. The lower curve shows the spectral nalysis of the received signal.*

/hich are caused by the finite extent of the ransducer disc (Zemanek, 1971), can be clearly een.

Figure 8 demonstrates a typical curve from the scending aorta in a person with a normal ortic valve. A spectral analysis of this signal hows correlation between the mean frequency nd the mean velocity signal, indicating that the stimator output is representative for the mean elocity component along the ultrasonic beam. 'he small irregularities in the frequency spectrum re also seen in the velocity curve.

From the suprasternal notch it is possible to ieasure velocity both in the ascending aorta and he aortic arch. In Fig. 9, the velocity signals re-orded when the transducer is moved from osition A to position C in Fig. 4 are shown. 'he velocity changes from being positive (to-



G. 9 *Velocity signals recorded from the ascend-g aorta and the aortic arch in a normal subject. The ansducer is moved from position* A *to position* C *ee Fig. 4).*

wards the transducer) in the ascending aorta to being negative (away from the transducer) in the aortic arch.

Table 1 compares the velocities in the ascending aorta and aortic diameters from the 18 subjects investigated. A maximum signal could only be obtained in a certain depth and with a certain transducer angle in each patient. Repeating the measurements did not change either the maximum velocity or the curve shape significantly, provided the measurements were performed in the same depth.

From these data estimates of aortic flow, stroke volume and cardiac output were calculated as described in the methods.

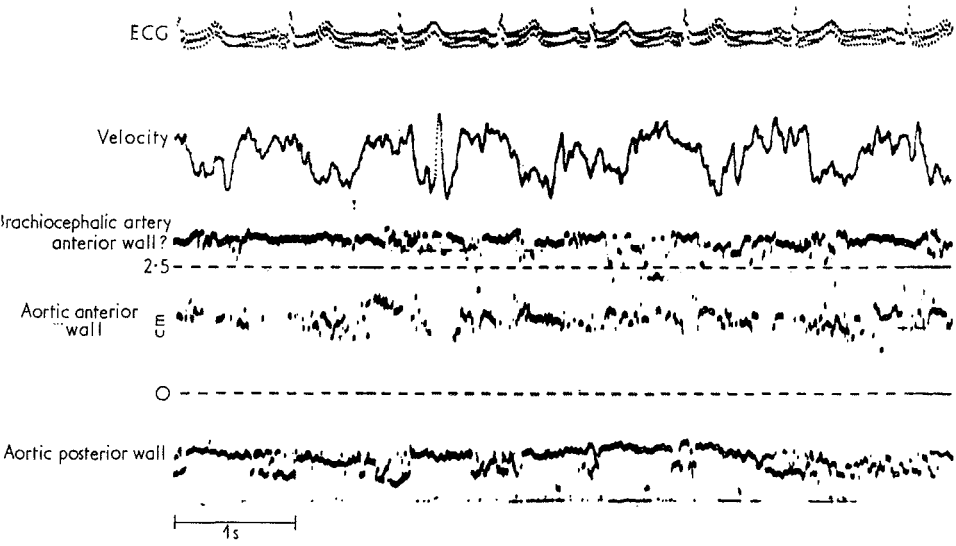
Figure 10 shows an example of the aortic diameter measurement. Above (nearer the transducer) the aorta, another vessel lumen can be seen. This is smaller than the aorta and inside its lumen flow towards the transducer could be measured. This vessel is probably the brachocephalic artery.

Figure 11 demonstrates the ability of the instrument to measure changes in flow and flow velocity. The patient exhibited a paired cardiac rhythm, with unequal cycle length. It can be seen that the peak velocities and estimated stroke volumes are lower in those beats which have the shortest cycle lengths.

In patients with aortic insufficiency, the backflow during the diastole will be greatly increased.

TABLE 1

Patient	*Aortic diameter (cm)*	*Heart rate (beats/min)*	*Aortic flow velocity (cm/s)*	*Aortic flow (ml/s)*	*Stroke volume (ml)*	*Cardiac output (litres/min)*
1	2.2	88	50	206	28	2.5
2	2.4	84	55	250	40	3.4
3	2.2	60	68	280	41	2.7
4	2.5	72	44	226	39	2.8
5	2.4	52	39	200	33	1.7
6	2.7	60	52	294	53	3.2
7	2.4	64	55	257	39	2.5
8	3.3	76	55	278	34	2.6
9	2.9	84	42	280	38	3.2
10	2.4	48	64	288	47	2.3
11	2.9	60	55	363	53	3.2
12	2.9	66	42	275	41	2.7
13	2.8	96	36	220	22	2.1
14	2.6	60	43	227	59	3.5
15	2.7	72	40	227	43	3.1
16	2.4	72	46	208	32	2.3
17	2.5	80	34	166	28	2.3
18	2.1	75	64	309	22	1.7



M-scan of the aortic diameter measurement, using position B *in Fig. 4. From top to bottom: velocity signal, and echoes from arterial walls; the upper echo is nearest to the transducer. The lower lines represent the aorta, while the upper two lines represent an artery where the bloodstream was towards the transducer, probably the right brachiocephalic artery.*

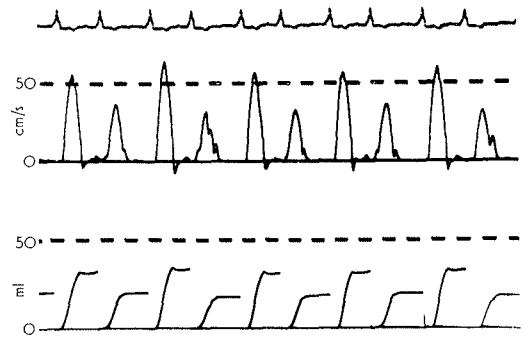


FIG. 11 *Registrations in a patient with bigeminal rhythm. From top to bottom: ECG, velocity, and stroke volume. Note that the beats with the shortest cycle length have the lowest velocities and smallest stroke volumes.*

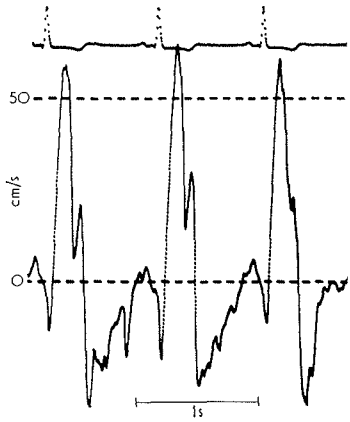


FIG. 12 *Measurement of velocity in the ascending aorta in a patient with aortic insufficiency. Note the large backflow. The sharp, negative deflection at the beginning of systole is probably due to the movement of the aorta during the isovolumic period of heart contraction.*

In Fig. 12 a velocity curve from such a patient is shown, demonstrating this feature.

Using the scanning procedure described in the methods, areas with different velocities were developed (Fig. 13). It can be seen that the areas increase as the velocity threshold is lowered. At low velocities, an area below the aorta appears. This is probably velocity signals from the pulmonary artery, having a greater angle to the ultrasonic beam and consequently lower velocity components along the beam.

Discussion

Pulsed ultrasonic blood velocity meters were first developed by Peronneau *et al* (1969) and

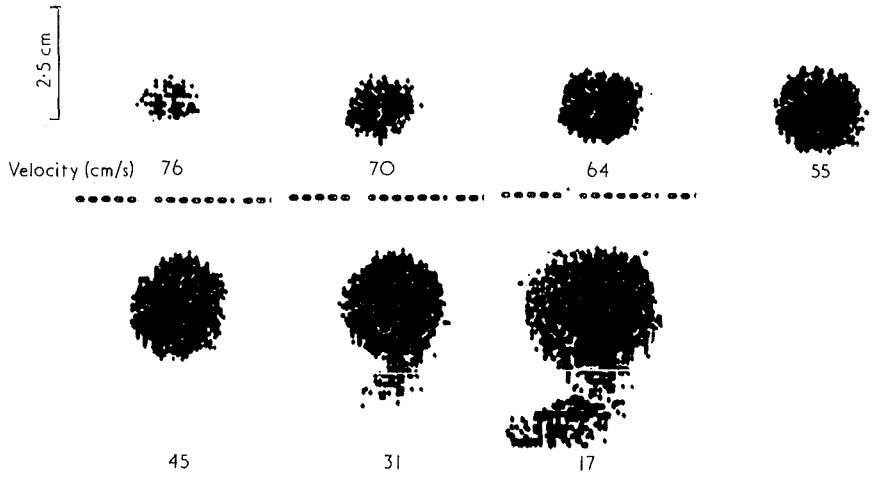


FIG. 13 *Scans from the aortic arch in a normal person.*

(1970), using ultrasonic frequencies from 4 pwards. Due to absorption in the tissue, it ssary to reduce the ultrasonic frequency easuring in deep arteries such as the aorta. er, the scattering intensity from blood is tional to the frequency to the fourth power. t a given depth, there exists a frequency an optimum signal-to-noise ratio. These ments are valid both for continuous and systems. In addition, when using pulsed und, low frequencies have to be employed asuring high velocities in deep arteries, due limitation in the range-velocity product on 3).

e requirements led us to choose an ultra requency of 2 MHz. The use of a quadra- thod for determining direction of velocity than the zero-offset method used by eau *et al* (1969), enables measurements of Doppler shifts at the same repetition ncy. Thus, with the repetition frequencies n this study, maximal velocities from m/s can be measured, depending on the e from the transducer. This seems to be te for most uses, except in patients with stenosis.

the earliest experiments of Satomura there has been no solution to the problem to estimate blood flow velocity from the d ultrasonic signal. The zero-crossing has been widely used because of its ity. However, the theoretical work of *al* (1970) has shown that the estimator will give the mean squared velocity in the observed, making the calibration depend- the actual form of the velocity profile In addition, the estimator is very e to noise. These limitations have also erified by the experimental work of an *et al* (1973).

problems associated with zero-crossing have led many workers to use a full analysis of the received signal (MacKay, Light and Cross, 1972; Johnson *et al,* This, however, requires complex instru- on and gives information which in most ions are not necessary, since only the elocity across the vessel lumen is of A spectral analysis can, however, be or revealing the laminar, turbulent or pes of flow.

Brody (1971) suggested an estimator which calculates the mean frequency shift of the Doppler spectrum. When the artery is uniformly illuminated, this is proportional to the mean velocity component along the beam in the region observed, regardless of the form of the velocity profile. This principle has also been used by Reid *et al* (1974). A simplified version of this method has been suggested by Arts and Roevros (1972). Since this method is based on analogue multiplication stability for a sufficient length of time is difficult to achieve. The estimator described in this paper, has the same capabilities as those mentioned above without using ordinary multiplication. Thus, adequate long term stability is obtained, making frequent calibration unnecessary.

As can be seen from Figs. 5 and 6, the velocity and change of velocity can be measured with sufficient accuracy under ideal conditions. In applying this principle to velocity measurement in the human aorta, several practical problems arise.

The orientation of the beam relative to the artery is critical, as illumination of only parts of the artery will not give the mean velocity across the lumen. In addition, the ultrasonic field is inhomogeneous (Fig. 7). If the beam therefore is aimed towards the centre of the artery, the central region will be more strongly illuminated than the periphery and false high mean velocity values will result. Uniform illumination of the vessel lumen and hence correct values of the mean velocity are therefore difficult to obtain, even if the angle between the ultrasonic beam and the flow velocity is known.

Near the heart, all tissues will be moving with each heart beat, giving strong reflections at Doppler shifts up to 400 Hz in the resting subject. During physical work, these Doppler shifts can approach 1 KHz. High-pass filters with selectable cut-off frequencies are inserted to remove these signals. As these filters also remove the signals from slowly moving blood, too high mean velocity estimates result, as can be seen from the zero-offset in Fig. 6. In this experiment the velocity profile was parabolic as deduced from a rectangular frequency spectrum (Roevros, 1974). As the relative magnitude of the low frequencies will decrease when the velocity profile goes from parabolic to rectangular, the zero-

offset in Fig. 6 represents an upper limit of this error at 200 Hz cut-off frequency. With increasing cut-off frequencies, this limit will increase proportionally.

As can be seen from Table 1, the values for volume flow and stroke volume are low. Assuming the values for aortic diameter to be approximately correct (they are in close correlation with values obtained by angiography [Benninghoff-Goertler, 1960]), the flow estimates in our work are between 30–70 % of those expected in normal, resting subjects.

As non-uniform illumination and high-pass filters will give overestimation of velocity, the reason for the low values is probably the angle between the blood stream and the ultrasonic beam.

Although absolute values of flow and flow velocity is not achieved, the curve form is faithfully reproduced, making measurement of relative values possible with this instrument. From Fig. 11 it appears that changes can be recorded in one position in the ascending aorta. For the method to be of value for recording changes, the problem of reproducibility is important. This problem has no definite solution at the present time. Our experience, measuring in the ascending aorta, indicates that in the same depth from the skin, only one transducer angle will give a maximum integral of the velocity curve. This angle does not always coincide with the angle giving the maximum peak velocity, since the integral is determined by the total velocity curve. Transducer angles giving large peak velocities with small integrals have frequently been observed, especially at depths approaching that of the aortic valve. This is probably due to rotational flow in this region

Changing the transducer angle or the depth of observation will give different curves, but it was always possible to reproduce the original curve if the transducer position was returned to the original one. Measurements made before and after giving a drug known to increase flow, has demonstrated that the expected flow increase could be recorded (Angelsen *et al,* 1975).

Obviously, only experience will show if the results obtained to date can be reproduced in a large group of patients. At present, it seems reasonable that changes of flow and flow velocity can be recorded in the ascending aorta and that the results are reproducible if the measurements are preformed in the same depth and with the patient in the same position.

The inability to measure absolute values of flow and flow velocity is a limitation of the method. However, in order to measure volume flow, it is only necessary to know the cross-sectional area of the artery normal to the beam and the mean velocity across this area. The reason for this is that with increasing angle, θ, between the beam and bloodstream, the area will increase while the velocity decreases proportionally, keeping the product constant.

To obtain correct mean velocity, a uniform illumination of the artery is necessary. Sufficient uniformity is difficult to achieve as has been previously pointed out due to the large area under observation, especially when there is an angle between the beam and the artery. This problem can be solved by using a focused transducer and scanning over the vessel lumen for several heart cycles. By integrating the velocity over the area, volume flow is obtained. In our experience, it is only possible to scan in the aortic arch, and unknown flow of blood to the head and arms would still introduce an error, as would rapid changes in the state of circulation.

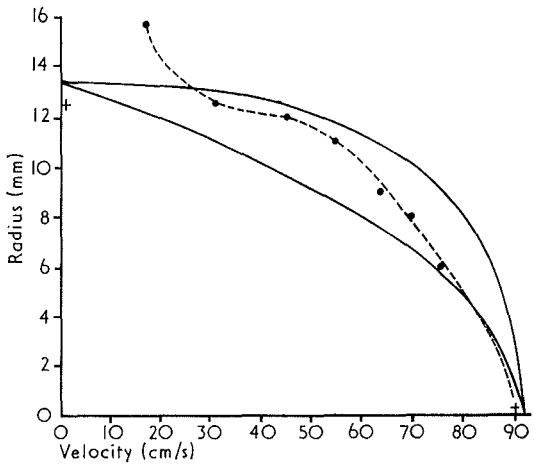


FIG. 14 *The relation between the radii of the scans in Fig. 13 and the threshold velocities. The + on the velocity axis represent the maximal velocity measured and that on the radius axis represent the radius measured by the echo-method. The velocity profile is constructed by deconvulution as described by Angelsen (1975). A parabola is drawn for comparison.*

he sample-volume of the focused transducer te and not a point, errors will be introduced mean velocity estimates. It can be shown lsen, 1975), that the velocities will be -estimated as long as the observation n is fully inside the artery and overesti- l in regions near the vessel wall. The data a scan (Fig. 13) giving a nearly circular is plotted in Fig. 14. In this case, it can be ned that the ultrasonic beam is nearly ntial to the blood stream. The 'real' ty profile has been constructed by de- olution and is found to be rather flat. this profile, the cardiac output can be ated to 4 litre/min, which accounts for ximately 20% flow to head and arms, can nsidered a reasonable value for resting

e deconvolution necessary to calculate the profile is time consuming and sensitive to Methods based on models and parameter- ation seem more promising in this respect are currently under investigation in our atory.

en with its present limitations, the method ntated in this paper offers possibilities udying the behaviour of the cardiovascular n. Using Doppler flow measurements, es from beat to beat can be recorded as as changes over longer periods of time. uring blood pressure simultaneously, e in total peripheral resistance can be ated.

demonstrated in Fig. 12, the backflow in insufficiency can be recorded. One prob- ssociated with this use of the instrument is he flow velocities are very small at the end astole making accurate measurements lt, due to the cutoff frequency of the high- ilter.

asurements of the transducer field were performed by Fensli (technical student), whose help we gratefully ledge. The valuable suggestion and advice of Rune are gratefully acknowledged.

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DIAGNOSIS OF VALVULAR HEART DISEASE USING TRANSCUTANEOUS DOPPLER ULTRASOUND

BY

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Reprinted from Cardiovascular Research
Volume XI, *No.* 5, *pages* 461–469, September 1977

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, LONDON WC1

Cardiovascular Research, 1977, **11**, 461–469

gnosis of valvular heart disease using nscutaneous Doppler ultrasound[1]

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RY An ultrasonic Doppler instrument capable of measuring mean and maximum velocities a small sample volume is presented. The instrument has been used for determining velocities mal and diseased heart valves. A method is described for identifying the different heart based on their relation to one another as well as the form of the velocity curve. The pressure cross the mitral valve can be determined from the maximum velocity and the mean velocity used to determine the degree of aortic insufficiency. Recordings of mean and maximum ies can give an indication of the form of the whole spectrum, thus making complete frequency s unnecessary for most purposes.

und Doppler methods offer the possibility asuring blood flow velocity noninvasively ted points inside the thorax (Johnson *et al.*, Angelsen and Brubakk, 1976; Brubakk and en, 1976). Valvular heart disease affects blood through the diseased valve. In valvular ency, leakage velocities will be found in the of the heart cycle when the valve is normally Stenosis of a valve will give increased forward es because of the reduction in orifice area.

ler measurements also offer the possibility titating some of the lesions. A small volume d starting at zero velocity in the atrium or e will accelerate to a velocity v by the e drop across the valve, Δp, according to lis equation

$$\Delta p = \tfrac{1}{2}\rho v^2 + R \qquad (1)$$

blood density (1.06 g·cm^{-3}) and R the viscous For volume elements passing through the f the valve, viscous losses can be neglected s the pressure drop may be calculated from ximum blood velocity through the valve *et al.*, 1976).

ow of blood in a tube is the product of tube d the mean velocity across this area. If the tube area is timeconstant, flow of blood is proportional to this mean velocity. Thus, in this case, relative changes in flow can be measured from the mean velocity.

The mean and maximum velocities of the blood in the observation region is proportional to the mean and maximum frequencies present in the Doppler signal. In a previous paper, a pulsed ultrasound Doppler instrument using a mean frequency estimator was described (Angelsen and Brubakk, 1976). This instrument has in addition been equipped with an estimator giving the maximum frequency of the Doppler signal. The instrument can also transmit continuous wave ultrasound, to observe velocities exceeding the limit given by the range velocity product for pulsed meters (Newhouse and Bendick, 1973). In this paper, a method for measuring blood flow velocity through heart valves is described. Examples of velocity curves from normal and diseased states are shown.

Instrumentation

The ultrasonic Doppler velocity meter used has been described in detail elsewhere (Angelsen and Brubakk, 1976) and only its main features will be given here. The ultrasonic frequency used is 2 MHz and the repetition frequency 6.7, and 9.8 kHz. With this instrument, velocities up to 1.7 m/s can be measured in depths down to 7 cm below the skin, and velocities up to 1 m/s down to 10 cm depth.

dy was supported by the Insurance Company Liv A/S, Trondheim, Norway, and the Norwegian for Scientific and Industrial Research.

for correspondence: Dr Alf O. Brubakk, Section ology, Medical Department, Regional Hospital, ndheim, Norway.

The instrument can be used as a continuous wave meter, with no limitations on measurable velocities, but with loss of range resolution.

The sample volume has a width of approximately 20 mm and a length of 7.5 mm. The mean frequencies in the sample are established by a mean frequency estimator described in detail previously (Angelsen, 1975). A description of the maximum frequency estimator has also been published elsewhere (Angelsen, 1976). The maximum frequency estimator tracks the envelope around the frequency spectrum.

The sign of the Doppler shift is determined by the direction of the flow. Flow towards the probe gives a positive Doppler shift, while flow away from the probe gives a negative Doppler shift. The mean frequency estimator is directional, *ie* the polarity of the output gives the sign of the Doppler shift. The maximum frequency estimator is nondirectional. To give a directional display, the polarity of the output may be determined by that of the mean frequency estimator. This is useful when the mean and maximum frequency shift are of the same sign, as often occurs. In some cases, when measuring in the continuous mode, the mean and maximum frequency shift can be of the opposite sign, and such control of the polarity will introduce an error. The control of polarity of the maximum frequency estimator is therefore selected by a front panel switch.

Fig. 1a and b show measurements of flow velocities in a pump system described earlier (Angelsen and Brubakk, 1976). A pump discharges a mixture of oil and glycerine into a plastic tube. Fig. 1a shows the spectrum of the Doppler signal. The darkening of the figure is given by the intensity of the frequency components at each interval of time. The positive Doppler shifts are caused by the ejection of the pump, and the negative shifts are caused by the backflow as the outlet valve closes.

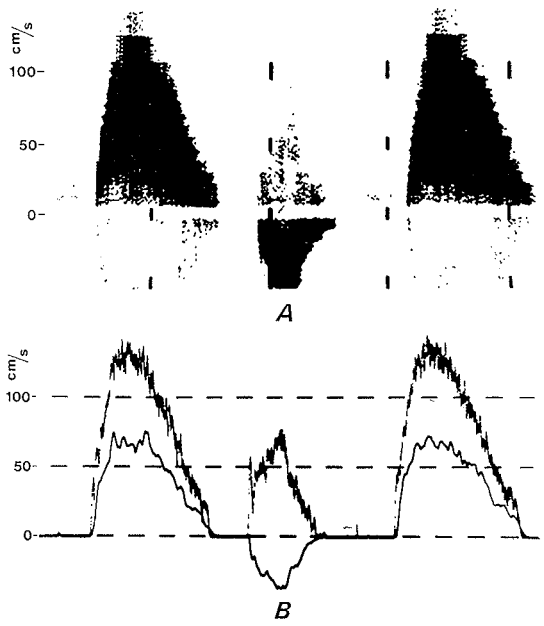


Fig. 1a and b *Measurements performed on the* in vitro *flow system described in a previous paper (Angelsen and Brubakk, 1976). (a) The spectral analysis of the Doppler signal. (b) The same signal is analysed with the mean and maximum frequency estimator. Note that the maximum velocity estimator is nondirectional.*

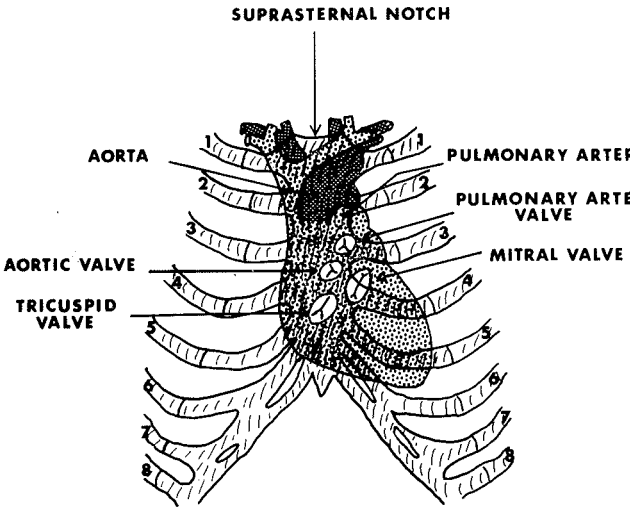


Fig. 2 *Relative position of the heart valves. (Redrawn from Sobotta-Becher, 1962).*

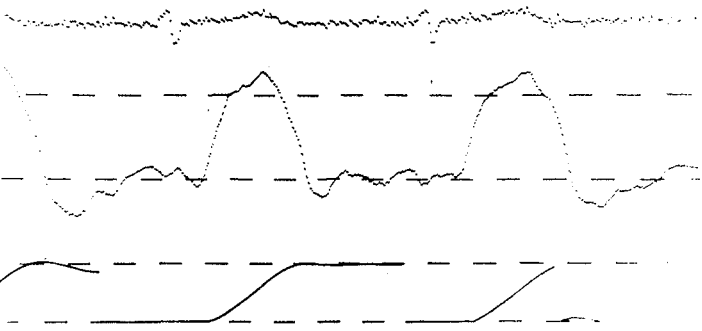


Fig. 3 *Mean ascending aortic flow velocity measured from the suprasternal notch in a normal person. From top to bottom: ECG, velocity signal, and integral under the velocity curve.*

spectral analyser does not show negative ncies exceeding −1250 Hz, corresponding to m/s. Fig. 1b shows the output of the mean naximum frequency estimator. It can be seen the maximum frequency estimator closely the maximum frequency of the spectrum. ne maximum frequency estimator is non- ional, the maximum velocity during closure of lve is displayed as a positive signal.

urement method and results

ities inside the heart have been measured in al subjects and in subjects with different kinds art disease.

the aim of this study was to demonstrate the odology for measuring velocities in normal diseased valves, only patients with verified ar heart disease were selected for investiga- The subjects were studied in the supine or clining position. ECG and phonocardiogram neasured simultaneously and in some cases the d pulse was recorded.

horough knowledge of normal cardiac ana- is needed to measure velocities inside the Fig. 2 shows the different valve areas and elationship to the anterior thoracic surface. different valves all have a fixed relationship another, the method described is based on he aortic valve as reference and to determine ier positions relative to this. Access to the is through the same 'window' as is used in rd echocardiography (Feigenbaum, 1972).

transducer is first placed in the suprasternal and aimed downwards. In this position the ies in the ascending aorta can be recorded in from 4 to 7 cm below the skin. Fig. 3 shows itput of the mean velocity estimator when ing in the ascending aorta of a normal

4 shows measurements of flow velocity in a with aortic insufficiency. Fig. 4a shows the

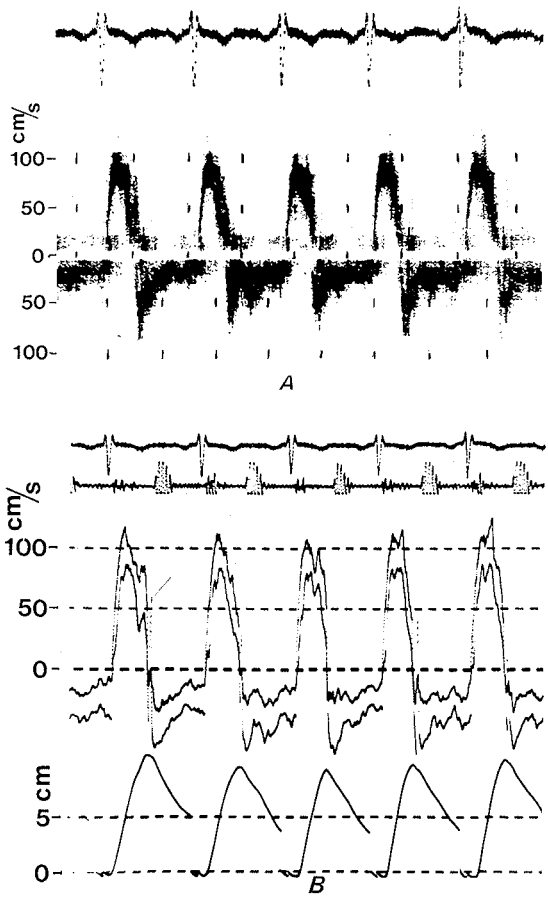


Fig. 4a and b *Ascending aortic blood flow velocity measured from the suprasternal notch in a patient suffering from aortic insufficiency. (a) The spectral analysis of the Doppler signal. (b) The mean and maximum velocity present in the signal. From top to bottom: ECG, phonocardiogram, maximum velocity, mean velocity, and integral under the mean velocity curve.*

spectral analysis of the signal and Fig. 4b the maximum and mean velocities measured as well as the integral under the mean velocity curve. The negative velocity in diastole is caused by the regurgitation of blood.

Fig. 5 records the signal in the direction of the ascending aorta in a person suffering from aortic stenosis. The instrument is used in the continuous mode. Fig. 5a demonstrates the spectrum of the Doppler signal, while Fig. 5b shows the mean and maximum frequency estimates. The spectrum analyser does not show negative frequency components greater than –1250 Hz (–50 cm/s). The velocity in the aorta is towards the transducer in systole, giving positive Doppler shifts. The negative mean velocity in this period must therefore be caused by blood flowing away from the transducer in other arteries. To control the polarity of the maximum velocity estimator by that of the mean velocity estimator would give erroneous results in this case. The polarity of the frequency components present is shown in the spectral analysis.

The remaining measurements are performed from the chest. First of all, the location and orientation of the heart relative to the intercostal spaces is determined. As the movement of blood and vessels walls can be heard in the instrument's audio output as whistling sounds and low frequency clicks respectively, it is possible to identify the surface area from which measurements can be performed. The lowest value of instrument high pass filter must be used. The uppermost intercostal space where Doppler shifts from blood flow and vessel walls occur is located. This is usually the first to the third intercostal space at the left sternal border. In occasional cases blood flow can be recorded from the right sternal border. The lowest point to the left where heart wall motion can be heard is then found. In this way, the approximate orientation of the heart's long axis is determined.

To identify the individual valves, the form as well as the direction of the velocity signal is used. Furthermore, ECG is used for identifying in which part of the cardiac cycle the movement of blood is observed. Phonocardiography can be used for additional time reference.

We have found the following procedure useful in identifying the valves:

The transducer is first placed in the third or fourth intercostal space and aimed cranially and a little medially. In this position, aortic flow velocity can be recorded, usually in depths of 4 to 7 cm below the skin, and its form can be compared with that recorded from the suprasternal notch. Keeping the transducer in the same position and aiming the beam downwards and to the left, the mitral valve can be located (Fig. 2). The mitral valve is found a little deeper below the skin than the aortic valve, the difference in distance from the skin being determined by the degree of rotation of the heart. Fig. 6 shows the mean velocity as the transducer is moved from the mitral to the aortic orifice.

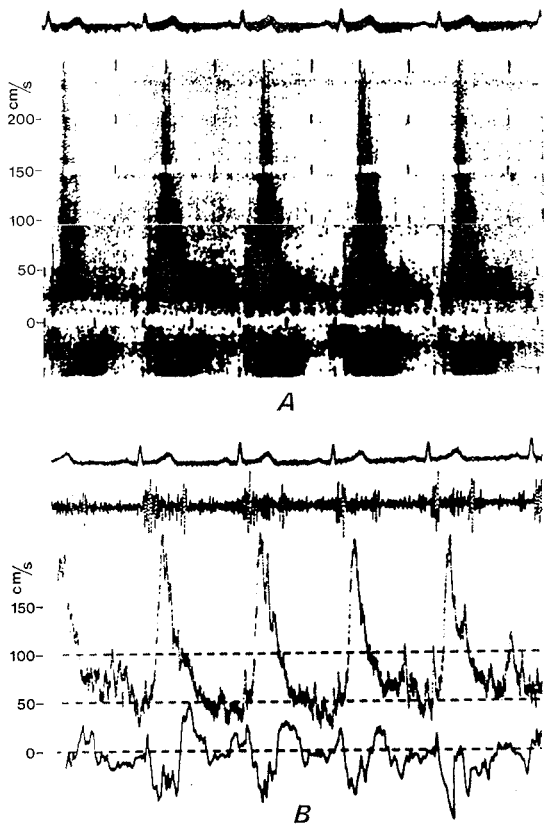


Fig. 5a and b *Blood flow velocity measured from the suprasternal notch in the direction of the ascending aorta, the instrument is used in the continuous mode. (a) The spectral analysis of the signal. (b) The mean and maximum velocity shown together. From top to bottom: ECG, phonocardiogram, and maximum and mean velocity.*

On the left side of the figure, the flow velocity in the mitral orifice is recorded. Keeping the transducer in the same position, but aiming more medially, the velocity changes from going towards the transducer to going away from the transducer in the aortic valve. The mitral flow velocity shows a characteristic double peak. The first peak is caused by the rapid inflow of blood into the ventricle when the valve opens, the second by atrial contraction.

Fig. 6 *Mean flow velocity through the mitral and aortic valve. On the left hand side the blood flow velocity in the mitral valve is recorded. Keeping the transducer in the same position, the beam is swept medially and velocities going away from the transducer in the aortic valve area is recorded (right hand side of picture).*

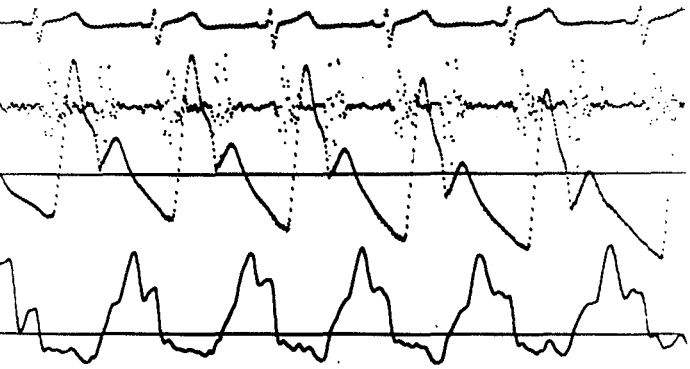


Fig. 7 *Mean velocity recorded just below the mitral valve area in the left ventricular inflow tract in a person without mitral valve disease. From top to bottom: ECG, phonocardiogram, carotid pulse, and mean velocity. Note the flow away from the transducer during systole.*

ough a normal mitral valve, no flow is to be ed during systole. Flow away from the trans- can, however, be recorded in normal persons systole, if the sample volume is positioned the left ventricle, instead of exactly in the area. This is demonstrated in Fig. 7 and is ortance as this situation must be differenti- om the backflow recorded in patients with insufficiency. Fig. 8 shows the mean velocity ed in a patient suffering from mitral stenosis sufficiency. Mitral insufficiency causes large e velocities during systole, while the stenosis exceptionally high velocities towards the icer in diastole.

9 shows examples of the mean and maximum ies measured in 2 patients with stenotic valves. The maximum velocity in Fig. 9a has racteristic double peak seen in sinus rhythm, he second peak is missing in Fig. 9b. This tient is suffering from atrial fibrillation. It so be seen that there is a large difference n the mean and maximum velocity estimator

10a and b shows the spectral analysis of the ignals demonstrating the tracking capability naximum frequency estimator.

To determine maximum velocity through the mitral valve, the transducer must often be positioned further to the left and 1 or 2 intercostal spaces lower than described above. This is particularly the case with patients having enlarged right ventricles.

The pulmonary artery may be found by using the aortic flow signal measured from the left sternal border as reference. Starting with this signal, the probe is turned more medially and downwards. In this position, closer to the surface than the aortic signal, a flow signal towards the transducer can be observed. This is flow in the right ventricular out-

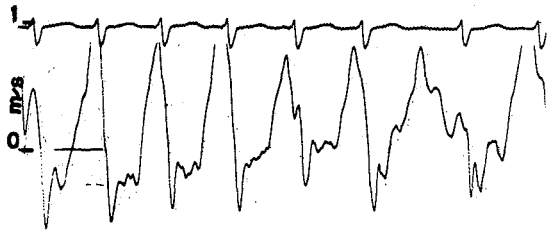


Fig. 8 *Mean mitral blood flow velocity in a patient with mitral valve insufficiency, mitral stenosis, and atrial fibrillation. Note the large backflow during systole.*

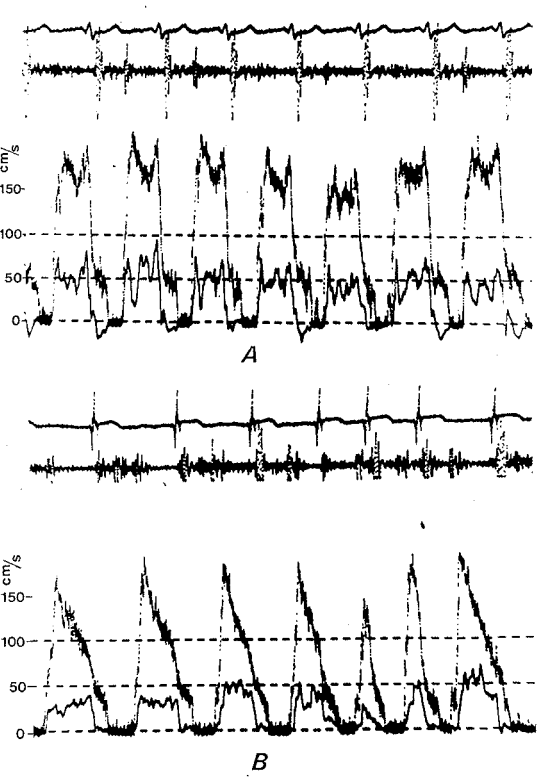


Fig. 9a and b *Mean and maximum mitral blood flow velocity in 2 patients suffering from mitral stenosis. (a) A patient in sinus rhythm. (b) The same measurements in a patient with atrial fibrillation. From top to bottom: ECG, phonocardiogram, maximum, and mean velocity.*

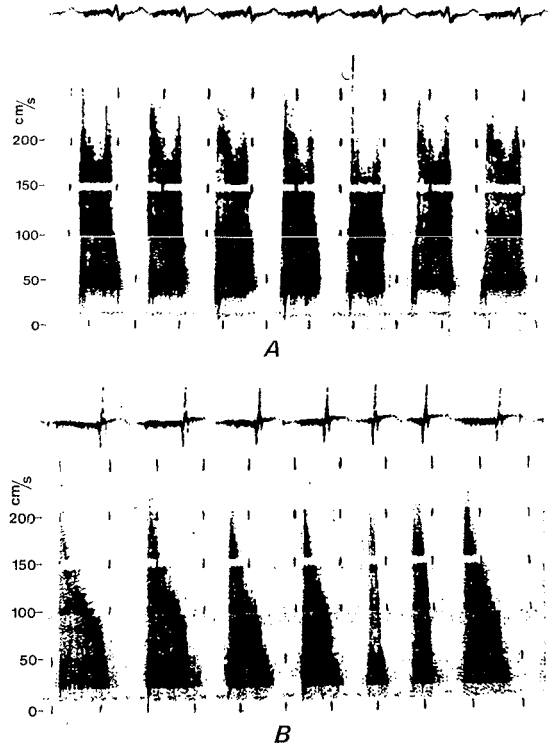


Fig. 10a and b *Spectral analysis of the signals shown in Fig. 9. (a) and (b) correspond to Figs. 9a and b respectively.*

flow tract or the pulmonary artery. Fig. 11 gives an example of this in a normal person. The systolic part of the curve is more rounded than its aortic counterpart, and a large positive flow in diastole is frequently seen.

The flow in the tricuspid valve is most easily found by placing the transducer at the left sternal border in the intercostal space just below the one used for recording aortic flow and aiming the beam medially and cranially. As can be seen from Fig. 12, this signal is quite similar to the one recorded from the mitral valve.

In patients with tricuspid insufficiency, a large backflow during systole can be seen, as demonstrated in Fig. 13.

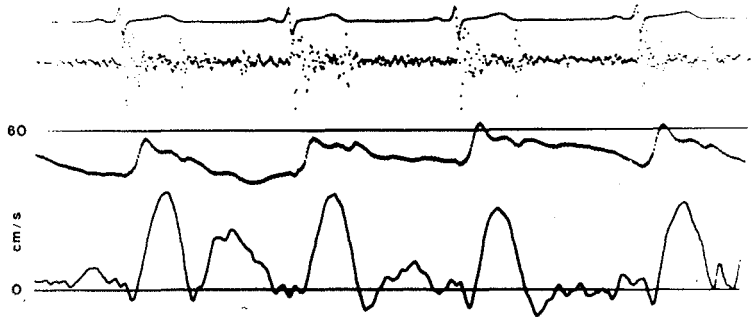


Fig. 11 *Mean pulmonary artery flow velocity in a normal person. From top to bottom: ECG, phonocardiogram, carotid pulse, and mean velocity.*

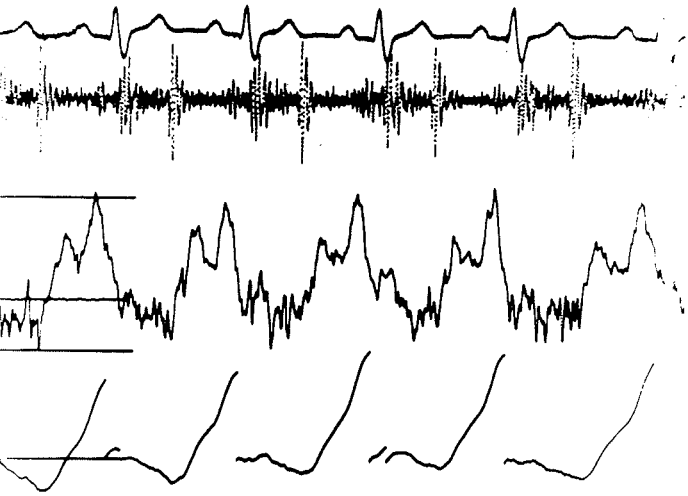


Fig. 12 *Mean velocity measured in the tricuspid valve. From top to bottom: ECG, phonocardiogram, mean velocity, and integral under the velocity curve.*

sion

the development of ultrasonic Doppler ds, the noninvasive observation of bloodflow the heart was not possible. The velocity of is proportional to the frequency of the back-ed ultrasound according to the equation

$$V = 2 \cdot f_0(f_d/c) \cdot \cos\alpha \qquad (2)$$

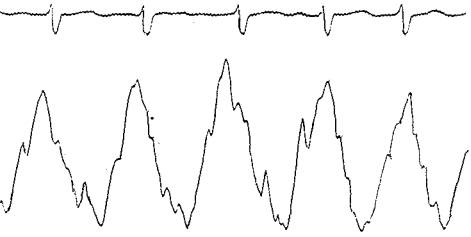
V is the velocity of blood, f_0 is the emitted ncy, f_d is the Doppler shift in frequency, c is ocity of sound and α is the angle between the and the blood stream.

s, in order to measure absolute values of y, this angle must be known.

e a profile of velocities is observed, a spectrum quencies will be present in the reflected signal us spectral analysis will display all information signal, as described elsewhere (Brubakk and en, 1976). Spectral analysis is, however, in terms of equipment and will in many cases give redundant information. As has been pointed out earlier, the mean and maximum frequencies (velocities) are the quantities of interest in medical diagnosis.

The performance of the maximum frequency estimator is demonstrated in Figs. 1, 4, 5, and 10, while the capabilities of the mean frequency estimator have been shown in a previous paper (Angelsen and Brubakk, 1976). A combination of mean and maximum frequency estimation will give an indication of the form of the whole spectrum. In Fig. 4b it can be seen that during systole, the mean frequency is only slightly smaller than the maximum frequency, indicating a narrow band of frequencies and hence a flat velocity profile (Angelsen and Brubakk, 1976). In diastole, the mean frequency is half the maximum frequency, indicating a more rectangular form of frequency spectrum and hence a more pointed profile than in systole (near parabolic). A large difference in mean and maximum velocity can also be seen in Figs. 9a and b. This is caused by the pointed velocity profile and a large volume of observation caused by the width of the ultrasonic beam (approximately 20 mm). The pointed profile is probably caused by a divergent flow jet in front of the mitral orifice.

Using this instrument and the methods described in this paper, it is possible to determine the form of the velocity curve in all valvular areas inside the heart. It must be kept in mind that the sample volume has a constant placement with respect to the chest wall and not necessarily with respect to a particular heart structure. This is probably no serious problem because of the relatively large size of the sample volume (20 mm × 7.5 mm). The



Mean velocity in tricuspid valve insufficiency ial fibrillation.

form of the normal velocity curves demonstrated in this paper are similar to those recorded previously, using velocity probes placed inside the heart (Benchimol *et al.*, 1972; Kalmanson *et al.*, 1972). The backflow in the mitral valve demonstrated in Fig. 7b, clearly stems from the left ventricular inflow tract as the curve is quite similar to the one displayed in Fig. 1 (Benchimol *et al.*, 1972) and in Fig. 9 (Kalmanson *et al.*, 1972). The reason for this negative flow during systole is most likely to be that it represents flow towards the aortic valve as the ventricles are emptying (Kalmanson *et al.*, 1972).

Even if the form of the velocity curve can give information about the disease state present, for instance the change in the curve form of mitral valve flow occurring with atrial fibrillation (Fig. 9b), the possibility of quantifying the degree of valvular diseases is of greater importance. Quantification of valvular insufficiency is only possible if the flow cross-section does not change from systole to diastole. This is true for a first approximation of the case in the aorta or the pulmonary artery, as the arterial diameter shows small changes during the heart cycle. In insufficient mitral or tricuspid valves, the valve area is different in systole and diastole. This makes quantitative measurement of the ratio of regurgitated to forward volume from the velocity curve difficult. But as can be seen from Figs. 8 and 13, the method may be used to indicate the presence of such a valvular lesion. As previously mentioned, one must, however, be careful to measure in or above the mitral valve, as negative flow during systole occurs in the left ventricular inflow tract (Fig. 7). A qualitative estimate of the degree of insufficiency may, however, be obtained.

As the flow is given by the product of the mean velocity and the flow cross-section, it is the mean velocity that is of interest for determining the degree of regurgitation. Assuming uniform illumination of the artery, the mean velocity will be proportional to the mean Doppler frequency. The degree of regurgitation may, therefore, be obtained from the mean frequency estimate if the cross-section is considered constant from systole to diastole. The lowest curve in Fig. 4b is the integral of the mean velocity estimate. The degree of regurgitation can be calculated as the ratio of the descending and the ascending part of the curve. The integrator is reset to zero by the ECG.

The uniform illumination of the artery is difficult to check. It would, therefore, be desirable to base the estimate on quantities that are less sensitive to the illumination such as, for instance, the maximum frequency. However, as already pointed out, Fig. 4 indicates that the flow profile in the aorta changes from a flat form in systole to a more parabolic form in the diastole. This means that the difference between mean and maximum velocity will be much larger in diastole than systole and estimates of regurgitation based on the maximum velocity must therefore be corrected according to the velocity profile present. A direct integration of the maximum velocity curve (Fig. 4b) will give a regurgitation volume of about 1.5 times greater than the actual one.

The high pass filters used to remove signals from slowly moving tissue will also introduce errors when using the mean frequency estimator. Since this filter also removes signals from slowly moving blood, an overestimation of the mean velocity will be obtained. In systole the intensity of low frequency components is small and the error can be neglected. In diastole, a uniform distribution of frequencies is found. An overestimation of mean velocity by half the value corresponding to the cut-off frequency of the high pass filters is obtained. In studying small degrees of valvular insufficiencies this overestimation must be taken into consideration.

To calculate the pressure drop across a valve from the maximum velocity of the midstream jet of blood, the angle between the ultrasonic beam and the blood stream must be known. In normal mitral valves, the blood stream is directed towards the anterior thoracic wall, making it possible to obtain an angle between the beam and the blood stream of nearly zero. Thus maximum velocity can be measured. Assuming that the normal pressure drop across the valve is not more than 0.2 to 0.3 kPa (1.5 to 2.5 mmHg) at rest, this will indicate that the maximum velocity that can be measured in a normal valve is 60 to 80 cm/s (Equation 1). Thus, velocities higher than this will indicate a flow obstruction.

In severe mitral stenosis, enlargement of the right heart is usually found, This will cause the heart to be rotated towards the left and thus the flow jet through the valve may be directed away from the anterior thoracic wall. In these cases, the maximum velocity measured will be less than the maximum velocity present and the pressure drop will be underestimated accordingly. It is therefore of importance that the probe is placed as laterally on the thorax as possible in these patients.

Even if absolute values of pressure drop cannot be estimated, as is the case in the aortic and the pulmonary valves, repeated measurements can easily be performed. Thus, the development of a stenosis may be followed and the effect of treatment may be judged.

The help of Ms Elin Amundsen in preparing the figures and Ms Marit Knudsen in typing the manuscript is greatly appreciated.

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PRINTED IN GREAT BRITAIN
BY F. J. PARSONS (WESTMINSTER PRESS LIMITED)
LONDON AND HASTINGS

CHAPTER THIRTY

A Model Approach to Studying Cardiovascular Function in Man

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Clinical practice is in great need of simple methods for evaluating the state of the cardiovascular system. Most methods that we have to-day give only indirect information about the variables of interest. Quantitive data about the parameters of heart function and blood flow are important both for diagnostic use and for evaluating the effects of treatment. Usually, such data can only be obtained by complex techniques. Frequently these techniques have to be performed in the catheterisation laboratory and measurements can be taken over only relatively short periods. Data analysis is further complicated by the continually changing cardiovascular state. We concluded from such considerations that there is a need for methods giving quantitative information about the changing state of the cardiovascular system, based on less elaborate measurement techniques.

iovascular model

We decided to tackle the problem by constructing a model of the human cardiovascular system, based on physiological data and physical principles, making simulation of the system possible. In order to simulate individual patients, we devised a method permitting adaptation of the model to the individual cardiovascular system. This we have now used for estimating cardiac output from the aortic pressure curve and the aortic pulse transmission time. The model is able to follow rapid changes in the cardiovascular state. The contractile state of the ventricular muscles can be estimated from the pressure curves.

Because our main interest has been the function of the left ventricle and the aorta, we constructed these parts of the system in greatest detail. The model is, however, a closed loop model, describing also the venous circulation and the right heart. The model is discussed in detail elsewhere,[1] so it is our intention here only to describe its main features.

Aorta model

A model of the aorta must describe the volume storage effect ('Windkessel function') as well as the transmission properties of the system. One way of doing this is to describe the aorta as a series of elastic reservoirs, joined by rigid tubes. This lumped description allows the pressures and flows to be computed only at selected points. Each segment is decribed by two differential equations. The pressure in a segment is considered to be a linear function of the volume.[2] The motion of fluid between two segments is determined by the pressure gradient, and the volume of each segment is determined by integrating the difference between flow into and out of the segment.[3]

In our model the aorta consists of six segments, each with a length proportional to the pulse wave velocity in the corresponding part of the aorta. As the wave velocity increases towards the periphery, a model segment also represents a longer portion of the artery. The iliac artery, the femoral artery and the carotid artery are modelled as individual segments, as they represent aortic branches where pressure and flow pulses can be easily measured. Likewise the arteries to the head and arms, to the legs, and to the viscera are modelled as individual segments. The vessels beyond these locations are described as impedance approximations. The peripheral resistance is represented as a linear pressure flow relation.

The parameters used in the arterial model can be seen in Table 30.1. The aortic inertia, L_i, resistance, R_i, and viscous damping, D_i, for each segment are assumed to be constant, the numerical values being based on the study of de Pater[2] and our own experience with the model. The compliance of each segment is a fraction of the total aortic compliance, which can be varied. Elastic tapering is assumed. The damping, Tp, controls the oscillatory input behaviour of the peripheral vessels and can be varied, thereby simulating different amounts of reflected wave energy from the periphery.

Table 30.1 Arterial parameters

Index	C_i Compliance $\left(\frac{\text{ml.}}{\text{mmHg}}\right)$	C_iD_i Damping timeconst. (msec)	L_i Inertia $\left(\frac{\text{mmHg}}{\text{ml.sec}^{-2}}10^{-3}\right)$	R_i Resistance $\left(\frac{\text{mmHg}}{\text{ml.sec}^{-1}}10^{-3}\right)$	Z_o Charact. impedance $\left(\frac{\text{mmHg}}{\text{ml.sec}^{-1}}10^{-3}\right)$		P_e External pressure
aac	$0{\cdot}23\,C_{ao}$	10	0·6	0·2	55	Ascending aorta	
aar	$0{\cdot}23\,C_{ao}$	7	0·8	0·2	65	Aortic arch	p_{th}
ad1	$0{\cdot}17\,C_{ao}$	5	1·3	0·4	95		
ad2	$0{\cdot}17\,C_{ao}$	5	1·3	0·4	95		
ad3	$0{\cdot}12\,C_{ao}$	5	2·1	0·8	140	Descending aorta	
ad4	$0{\cdot}08\,C_{ao}$	5	2·7	1·5	170		p_{ab}
ail	$0{\cdot}032\,C_{ao}$	5	5·0	6	370	Iliac arteries	
afe	$0{\cdot}030\,C_{ao}$	10	9·0	20	510	Femoral arteries	
aca	$0{\cdot}040\,C_{ao}$	10	6·0	10	380	Carotid subclavian arteries	0
aha	$0{\cdot}15+0{\cdot}17\,C_{ao}$	$330\,T_p$	13·0	40		Head and arm arteries	
aab	$0{\cdot}10+0{\cdot}11\,C_{ao}$	$100\,T_p$	6·0	10		Abdominal arteries	p_{ab}
alg	$0{\cdot}10+0{\cdot}11\,C_{ao}$	$150\,T_p$	13·0	40		Leg arteries	0
av	0·04	1	0·6*	0·2*		Aortic valve	
			same as *aac*			$V_{bak} = 2{\cdot}5$ ml.	

'Standard' values: $C_{ao} = 0{\cdot}87$ ml./mmHg, $T_p = 1$, $p_{ab} = 0$ mmHg and $p_{th} = -4$ mmHg.

tricular model

The input to the aortic model is generated by a left ventricular model. As a description of heart muscle function is of importance in evaluating heart performance, the ventricular model is based upon a muscle model, describing an average muscle fibre. This model, being a modified Hill muscle analogue,[4] has a characteristic force velocity curve, enabling us to use the parameters V_{max} and σ_{max} to define the contractile state of the model (Table 30.2). A model of the left ventricle describes the relation between the length, tension and velocity of this muscle model and the volume, pressure and flow of the ventricular model. This model is similar to that used by Beneken.[5]

Table 30.2 Model parameters changed

In the ventricular model
(*a*) V_m —myocardial volume
(*b*) T_{sys} —duration of active state
(*c*) V_{max}—maximum velocity of muscle contractile element
(*d*) σ_{max}—maximum active tension of muscle
(*e*) *EDV*—end diastolic volume
(*f*) *HR* —heart rate

In the arterial model
(*g*) G_p —total peripheral conductance (1/resistance)
(*h*) C_{ao} —aortic compliance
(*i*) T_p —peripheral damping

ılation of the model

In order to solve the equations describing this model, a computer is necessary. The model is built as a special purpose analogue computer as this means it is small enough for use at the bedside as well as in the laboratory. In building it we have taken care that operation of the model shall be simple and require only physiological insight. The output from the computer is displayed as time varying curves on a recorder or an oscilloscope.

The performance and characteristics of the model can be changed by changing its parameters. Because the problem of uniqueness (meaning that one set of parameters shall give only one solution) is important for interpreting the results, only a few parameters are changed at a time (see Table 30.2). All other parameters are given a fixed, constant value, described in ref. 1 and in Table 30.1. By changing the parameters, different cardiovascular states can be simulated. As described previously,[1] this model is capable of generating curves similar to those obtained from the human cardiovascular system. This makes it useful for educational purposes, as well as for simulating the effects of drugs and different disease states.[6]

ılating the individual patient

The basic idea behind simulating the individual patient is shown in Fig. 30.1. By making the same measurements in the model as in the human cardiovascular system, the difference between these measurements can be observed and the model parameters changed until a satisfactory match is achieved. Using this approach, the model parameters described in Table 30.2 can be estimated from the measurements, either manually or automatically. Because the parameters (*b*)–(*g*) (Table 30.2) change rapidly in a clinical situation, we use an

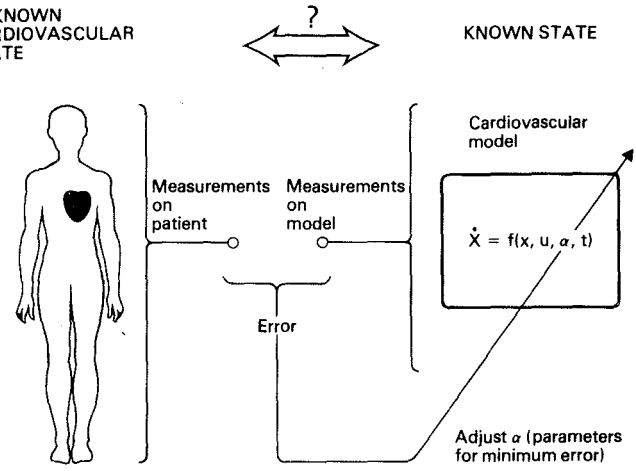


Figure 30.1.
The basic principle in this approach to parameter estimation. Analogous measurements are performed on both patient and model, the error between them adjusted until a satisfactory match is achieved.

automatic servosystem to update continuously these parameters. Parameter (*a*) and (*h*)–(*i*) are individually different, but change much more slowly, and a manual procedure is therefore used for the necessary alterations.

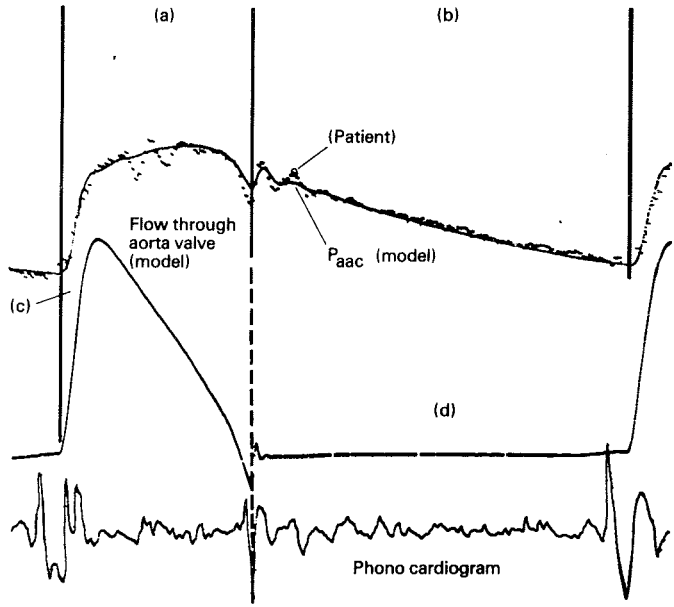
In principle, many measurements from the cardiovascular system can be used for estimating the model parameters. The choice of measurements to be used is critical, because they are important for the uniqueness of the solutions. It is, for instance, not possible to judge the filling of the left ventricle from pressure curves in the aorta, and therefore estimates of ventricular muscular parameters from the aortic pressure curve will not be unique (that is, more than one solution is possible).

At present we use the following measurements for simulating the individual cardiovascular system:

> Electrocardiogram (ECG), phonocardiogram (PCG), pressure pulse curve from the carotid and femoral artery (measured non-invasively), blood pressure curve and chest X-ray.

Ventricular systole

The ECG is used for starting the activation of the ventricular muscle model, thus ensuring the same heart rate in the model as in the patient. The ECG is used to adjust the length of the ventricular systole, T_{sys} (Table 30.2), so that the closure of the model aortic valve occurs simultaneously with the second heart sound in the patient. The pulse pressure curve is used for measuring the pulse transmission time between the carotid and femoral artery. This information is used later for estimating aortic compliance. The blood pressure in the aorta is measured with a catheter-manometer system, and the pressure curve is used to estimate heart parameters and peripheral conductance. In some instances pressure in the pulmonary artery and the left ventricle has been used for determining left ventricular filling. Chest X-ray is used to estimate myocardial volume, V_m.



re 30.2.
ılation strategy using measurements
CG, PCG and aortic pressure. This
sed for estimating V_{max} σ_{max} and
pheral conductance from the pressure
e. (a) Estimate σ_{max} for same mean
sure during ejection period. (b)
mate Rp for same mean pressure
ng non-ejection period. (c) Estimate
x for same mean pressure during first
sec of ejection. (d) Estimate $Tsys$
ortic valve closure (model) at second
t sound.

nparison of model with data

Figure 30.2 shows the simulation strategy. The pressure in the model is measured in a position analogous to the catheter position in the patient (in this case the ascending aorta). To minimise errors introduced by the measurement system, the pressure in the model is filtered through a model of the catheter-manometer system, where the damping and the resonant frequency can be changed. These parameters are altered until the oscillations in the aortic pressure curve, after the closure of the aortic valve, are identical with those measured (Fig. 30.2). In this study, the pressure difference between the patient and the model pressure curve is used as an error criterion. It is assumed that different portions of the pressure curve give information about different parameters of the system.

timation of parameters

The first 25 msec of ejection is used for estimating V_{max} of the left ventricular muscle model. σ_{max} is estimated from the pressure course during the ejection period, while G_p is estimated from the pressure course during diastole. A feedback servosystem controls the parameters until there is zero mean error over the intervals. The two remaining parameters to be estimated, namely T_d and C_{ao}, are adjusted manually. T_d of the peripheral arteries are changed until the form of the pressure curve has a best match with that measured in the patient, as judged by the model operator.

The pulse wave velocity in the aorta is dependent on compliance and inertia.[7] As already mentioned, the inertia is assumed to be constant, thus enabling calculation of the compliance ($\Delta V/\Delta P$, where ΔV and ΔP are incremental changes in volume and pressure respectively) from the pulse wave velocity in the aorta. This is done by adjusting the model aortic compliance until the pulse transmission

time between the carotid and the femoral artery in the model is identical with that of the patient. Given an identical pressure curve in the patient and in the model (zero error), the model stroke volume will be dependent on the aortic compliance. Thus, if the stroke volume is measured by an independent method in the patient, the model compliance can be estimated by determining the compliance value that gives identical stroke volumes in patient and model.

Results

This method has been used for studying the aortic dynamics in 29 persons between the age of 16 to 74 years. Using the compliance value calculated from the pulse transmission time, the model cardiac output was compared with one measured by an independent method (Fick, dye-or thermodilution), giving a correlation coefficient between the two of $r=0{\cdot}96$ and a regression line falling close to the line of identity.[8] Furthermore, the compliance values obtained by the pulse-transmission time were compared by those calculated from the stroke volume, giving a correlation coefficient of $r=0{\cdot}98$ between the 33 measurements that were performed.[9]

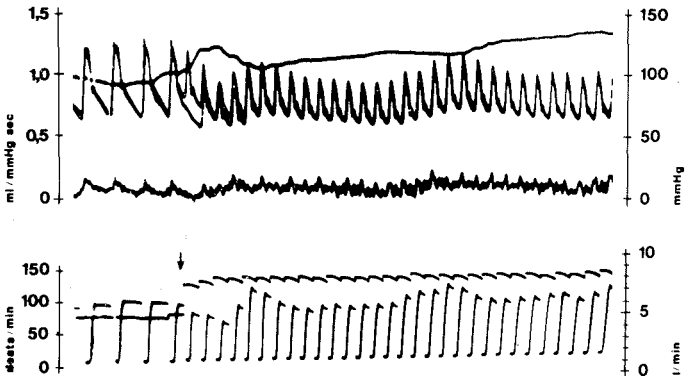


Figure 30.3.
Cardiovascular parameters estimated during right ventricular pacing. Pacing frequency 110 beats/min. From top to bottom can be seen patient and model aortic pressure superimposed, peripheral conductance, pulmonary artery pressure in patient, heart rate and cardiac output. The pacing starts at the time indicated by the arrow.

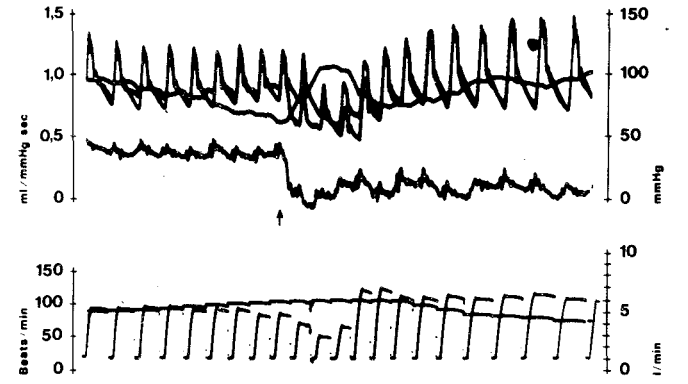
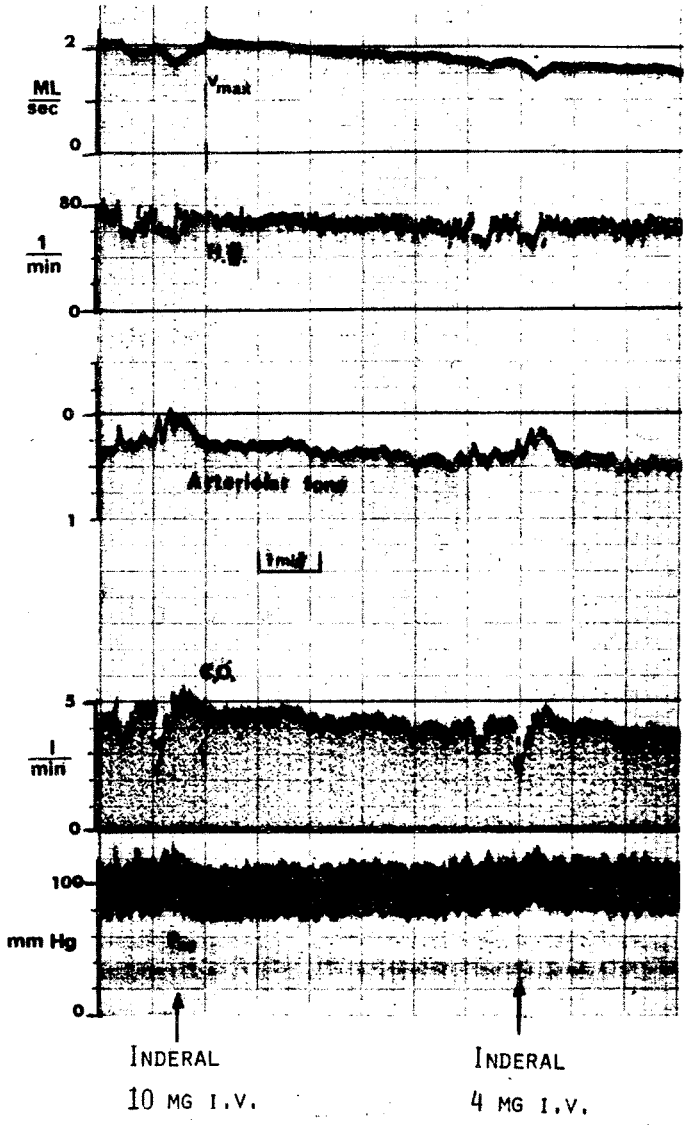


Figure 30.4.
Cardiovascular parameters estimated during the Valsalva manoeuvre. From top to bottom are patient and model aortic pressure curves superimposed, peripheral conductance, pulmonary artery pressure and heart rate. The height of the vertical bars at the bottom of the figure represent cardiac output.

tricular function

Taking pressure measurements from patients undergoing cardiac surgery, changes in left ventricular function could be simulated, giving aortic flow curves that were in close correlation with those measured simultaneously with an electro-magnetic flowmeter.[1] By this method, rapid changes in the cardiovascular state can be investigated. Figure 30.3 shows the changes in cardiac output and peripheral conductance following right ventricular pacing, and the changes in these parameters following the performance of a Valsalva manoeuvre can be seen from Fig. 30.4. The changes in the cardiovascular state following injection of a β-blocking agent is shown in Fig. 30.5, and the response to muscular exercise in Fig. 30.6.



30.5.
vascular parameters estimated
njection of propronolol (Inderal).
= max. velocity of contractile
t (muscle lengths/sec). *H.R.* =
rate. Peripheral conductance =
arteriolar tone. C.O. = cardiac
P_{ao} = patient aortic pressure.

Sources of error

The main question to be asked in using this sort of approach in analysing cardiovascular data, concerns the physiological relevance of the parameter estimates. Clearly this cannot be answered conclusively until more experience has been gained with the model but some preliminary remarks are valid. One source of error is that the physiological data on which the model is based are not correct. Obviously many assumptions and simplifications have to be made during the construction phase of the model. Furthermore, many

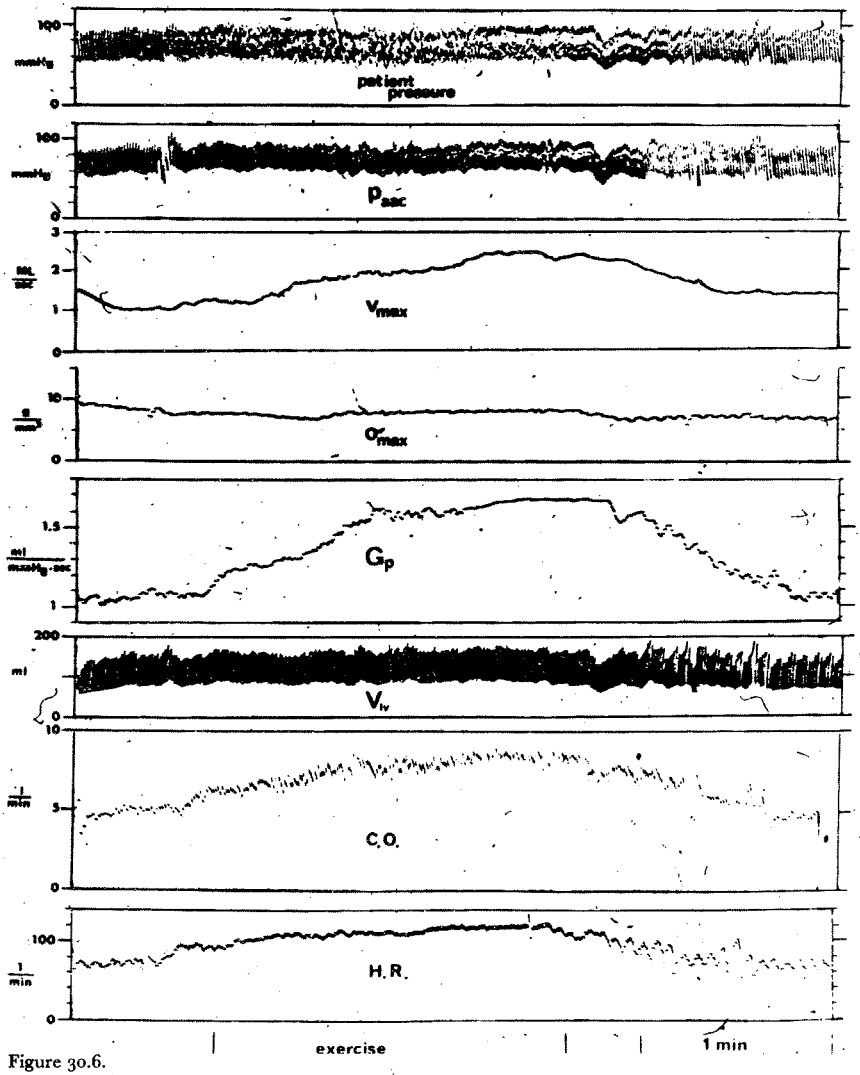


Figure 30.6.
Cardiovascular parameters estimated during exercise in the supine position. Load 400 kpm/min. Pressure is measured in the ascending aorta. *H.R.* = heart rate, *C.O.* = cardiac output, V_{lv} = model left ventricular volume, $G\rho$ = peripheral conductance, σ_{max} = max. tension of heart muscle fibre, V_{max} = max. velocity of contractile element (muscle lengths/sec), P_{asc} = pressure in model asc. aorta.

parameters not used in the estimation scheme, have to be given values based on the physiological insight of the model operator. Thus no proof of model uniqueness can be given, making it difficult to test the model rigorously. Similar to previous models,[10] this model is capable of simulating the behaviour of the human left ventricle and aorta with acceptable accuracy. Simulation of physiological experiments show that the model parameters obtained were in close correlation with those reported in the literature.[1] This makes the model a valuable tool for educational purposes and for studying the general function of the cardiovascular system. Since the aim is to simulate the cardiovascular system of individual subjects, the model must also be able to estimate quantitative correct parameters from measurements obtained in patients.

Using the foregoing method, we have investigated the arterial model and have concluded that aortic compliance can be estimated from pulse transmission time in the aorta. As the pulse wave velocity is dependent both on compliance and inertia, this conclusion is based on the assumption that the inertia, L_i, can be considered constant from person to person. At present there is no definite proof that this assumption is correct, but the data indicate that the compliance values calculated are accurate enough to permit an estimation of cardiac output from the aortic pressure curve.

If the compliance is calculated from the pulse transmission time, it is important that the measurements are performed accurately. An error of 10 msec in pulse transmission time, may introduce an error of approximately 15 per cent in the cardiac output determined. On the other hand, errors in ventricular parameters and in peripheral damping, T_p, do not significantly influence the estimates of cardiac output and peripheral conductance.[1]

In this study, a linear pressure-volume relationship is used in the model aorta. As the compliance values are dependent on pressure and decrease with increasing blood pressure, this can introduce an error, particularly in older patients and in patients experiencing large changes in blood pressure. Estimation of compliance, before and after lowering of blood pressure in eight severe hyptertensives, this non-linearity is significant,[11] and in these situations it is necessary to check the compliance values frequently, either by measurement of pulse transmission time or by an independent cardiac output determination.

By this method it seems possible to monitor cardiac output and peripheral conductance from the aortic pressure curve. Because these parameters change continuously, an automatic servo-system has to be employed. This offers the advantage that even quick changes in the cardiovascular state can be recorded. Figure 30.3 demonstrates the alteration following ventricular pacing. Immediately following the onset of pacing, the peripheral conductance starts to increase, but the mean cardiac output is kept nearly constant. Significant changes in cardiac output do not occur with right ventricular pacing unless the patient is suffering from heart disease.[12] As the immediate response to frequency changes appears to differ from that observed after several minutes of pacing,[13] continuous monitoring of the cardiovascular parameters might be of value. The Valsalva manoeuvre shown in Fig. 30.4, demonstrates that the model is able to

follow rapid changes in blood pressure. In the first few beats after the release of the intra-thoracic pressure, the diastolic pressure is higher in the model than in the patient, indicating an underestimation of peripheral conductance. Thus it is reasonable to assume that the change in peripheral conductance in the patient is even more rapid than shown here. In the normal subject, an overshoot in blood pressure occurs after the cessation of a Valsalva manoeuvre. This overshoot is absent in patients with congestive heart failure.[14] As the blood pressure overshoot will be determined by the relative magnitude of changes in cardiac output and peripheral conductance, the method described here can be of value for studying this effect in detail.

Congestive heart failure

Heart muscle function

There is considerable interest in finding methods that describe heart muscle function, and several methods based on left ventricular pressure curves have been proposed.[15] Using data from patients undergoing heart surgery, the model that we have described appears to be able to simulate ventricular function from ventricular pressure curves with reasonable accuracy.[1] If the pressure measurements are performed in the aorta, left ventricular filling is not known and this can introduce an error in the estimates of V_{max} and σ_{max}. Neither β-blockade, nor moderate exercise significantly change left ventricular filling.[16,17] The injection of propranolol seen in Fig. 30.5 is followed by a reduction in cardiac output, peripheral conductance and V_{max}, a reaction similar to that described in the literature.[16] Exercise in the supine position (Fig. 30.6) results in an increase in cardiac output and peripheral conductance. Interestingly enough, the V_{max} shows a marked increase, while σ_{max} does not change significantly. The estimated left ventricular volumes show very little change. This is in accordance with previous studies, where the cardiac output increase following mild exercise is mainly caused by an increase in heart rate and contractility.[15]

Model of hypothesis

One problem associated with conventional methods for calculating heart muscle parameters, is that changes in preload and afterload will introduce an error. This problem may be overcome by using the approach described in this chapter, because the model continuously adjusts itself to these changes. The model and the method presented here represent an effort to gain more information from cardiovascular data. This model may be regarded as an hypothesis, describing the behaviour of the cardiovascular system under certain assumptions. The experimental data obtained so far seem to support this hypothesis, although in no way conclusively. One advantage with this approach is that the hypothesis is described in quantitative terms, and therefore can be checked by experimental methods. Thus, while the hypothesis itself may be changed, or even wholly modified, it is hoped that this method will provide the basis for a better understanding of human cardiovascular physiology. New measurement techniques, for example transcutaneous measurement of aortic blood flow,[18] may be used to increase the accuracy of the parameters estimated.

KNOWLEDGEMENTS

The help of Ms. Elin Amundsen in investigating the patients and for preparing the figures is greatly appreciated. This work was supported by the Life Insurance Company, Forenede Liv A/S, Trondheim and the Norwegian Council on Cardiovascular Disease.

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USE OF A MODEL FOR SIMULATING INDIVIDUAL AORTIC DYNAMICS IN MAN

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THIS WORK WAS SUPPORTED BY THE LIFE INSURANCE COMPANY «FORENEDE LIV», TRONDHEIM AND THE NORWEGIAN COUNCIL ON CARDIOVASCULAR DISEASES

ABBREVIATED TITLE:

AORTIC DYNAMICS IN MAN

CORRESPONDANCE TO:

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Abstract.

A simulation model is suggested for the analysis of aortic dynamics in man. The aortic model consists of six segments and is part of a larger model of the closed-loop human circulation. The model is simulated on a special purpose analogue computer. Three parameters are employed to characterize the arterial system; peripheral resistance, aortic compliance and peripheral damping. Using a method for adapting the model to the individual patient, measurements of aortic pressure, cardiac output and pulse transmission time from 29 patients where used to test the validity of this approach. The model is able to simulate the pressure course along the aorta satisfactorily. The compliance calculated from the transmission properties of the aorta was compared with the compliance calculated from the stroke volume and pressure pulse. An adequate correlation ($r = 0.98$) was found between these two independent methods. The mean compliance of the total aorta was 0.6 ml/mm Hg at a mean pressure of 104 mm Hg. The compliance showed large individual variations and decreasing values with increasing age of the patient. It is concluded that the model enables simulation of the individual aorta.

Key words: Haemodynamics, Analogue computer model,
Pulse transmission time, Stroke volume,
Aortic volume elasticity, Aortic Compliance

Introduction

A model of the relation between pressure and flow along the aorta must describe both the shape and the propagation of the pulse waves. The dynamics of the system is complex and simplification is necessary for an analysis. A simple «Windkessel» or an elastic reservoir with a linear drain resistanse, describes the main features of the pressure pulse, and demonstrates how the pressure-time course is dependent upon stroke volume and aortic compliance (Frank, 1899). The compliance C_{ao} represents the elastic properties of the reservoir and is defined as $\Delta v / \Delta p$, where Δv and Δp are changes in volume and pressure respectively. This model does not describe the propagation of the pressue and flow pulses along the aorta. To do this, the aorta can be regarded as an elastic transmission tube and analyzed by transmission line theory.

A multisegment or multi- «Windkessel» model, where each segment is considered as an elastic reservoir and the transport of blood between two segments is governed by inertance and resistive effects, can be regarded as an approximation of a transmission line. This type of model is well suited for simulation studies with electrical (Noordergraaf et al., 1960) or electronic (Snyder et al., 1968) analogues, and was used in the present study. By adjusting model parameters, the model can be adapted to simulate the measurements from individual patients. The accuracy of this simulation can be studied by comparing simulated time courses of pressure along the aorta with measurements from patients. It is possible to use such a multisegment model to obtain estimates of aortic compliance. In this study e have compared compliance values, estimated from measurements of aortic pressure and stroke volume with those obtained from measurements of aortic transmission properties. This paper is based on material presented in a PhD-thesis by one of the authors (Aaslid 1974).

Material and Methods

1. Pressure measurements

Aortic pressure tracings were obtained from 29 patients without clinical signs of aortic regurgitation. There were 23 males and 6 females aged 16 to 74 years, hospitalised for various cardiovascular diseases. For further patient information, see Table 1. The pressures were measured in the upper part of the descending aorta, just below the left carotid artery in 17 patients, in the ascending aorta in 8 patients and in the femoral artery in 4 patients.

The patients were examined in the supine position. ECG electrodes were placed in a position giving a larger R-wave. A crystal microphone, Elema-Schonander type ENT 250C, was placed on the thorax in a position giving a clear second heart sound. Using the right or left femoral artery, a thin catheter was introduced and advanced to the desired position in the aorta under fluoroscopic control. The catheter was connected to a Statham P23D b transducer and continously flushed by a very slow saline drip. The zero-level of the transducer was at the anterior axillery line in the 4th intercostal space (Rokseth t al., 1960). A catheter was placed in the caval vein or the pulmonary artery via a brachial vein or the internal jugular vein. The pulse contour was recorded from the carotid and the femoral artery, using a pulse pick-up. All data were stored on magnetic tape, using a system described previously (Aaslid and Brubakk, 1971). This system uses a pulse duration modulation technique which enables recording of up to 8 channels on 1/4 inch magnetic tape.

2. Cardiac output determination

Cardiac output was measured by the Fick principle in 17 instances in 16 patients. The patients breathed through a mouthpiece into a Douglas bag for 3 minutes. In the middle of this period, blood was withdrawn from the aorta and the pulmonary artery and immediately analyzed for O_2 -saturation using an oximeter. The content of the Douglas bag was analyzed by a micro-Scholander apparatus.

Table 1
PATEIENT DATA

No	Sex	Age yrs.	Height cm	Weight kg	Rel.heart size ml/m^2	Diagnosis
1	M	16	181	76	—	Systolic murmur
2	M	20	181	91	270	Hypertension
3	M	27	173	68	440	Hypertension
4	M	32	176	75	—	Hypertension
5	M	36	190	75	—	Kidney cyst.
6	M	41	173	78	330	Hypertension
7	M	46	177	76	370	Hypertension/Hydronephrosis
8	M	47	170	74	—	Uremia
9	M	47	164	67	740	Cardiomyopathy
10	M	48	182	79	—	Hypertension
11	M	49	175	65	690	Mitral stenosis
12	M	57	166	86	460	Mitral insuff.
13	M	57	175	73	—	Aortic valve replacement
14	M	58	174	88	1200	Angina pectoris
15	M	58	169	79	650	Angina pectoris
16	M	59	170	70	—	Hypertension
17	M	59	184	91	610	Hypertension
18	M	59	177	85	425	Angina pectoris
19	M	60	163	82	500	Angina pectoris/Hypertension
20	M	60	171	69	380	Angina pectoris
21	M	64	170	65	—	Myocardial infarction
22	M	66	170	69	—	Myocardial infarction
23	M	78	171	73	835	Pulmonary hypertension
24	F	18	165	59	560	Cong. A-V block
25	F	40	168	53	350	Hypertension
26	F	44	163	68	500	Mitral stenosis
27	F	51	160	55	—	Myocard inf.
28	F	66	165	54	—	Renal tuberculosis
29	F	68	—	—	—	Mycocard.inf./Cardiogenic shock.

Cardiac output was determined by dye dilution technique in 9 instances in 9 patients. After obtaining blood for calibration of the densiometer, the base-line was recorded and 2 ml of 2.5 mg/ml soulution Cardiogreen were injected rapidly into the caval vein or the pulmonary artery and immediately flushed with 5—10 ml 0.9% NaCl. The blood was withdrawn from the aorta by a syringe-pump, type Atlas-Automatic 8008, at a rate of 30 cc/min, through the photocell of a Beckman Cardiodensitometer. After recording the curves, the densitometer was calibrated, using the same Cardiogreen solution as was injected into the patient. The cardiac output was estimated according to the method of Hyner (1962), using the integrator of the Beckman Cardiodensitometer. Thermodilution curves were obtained in 14 instances in 6 patients using the Devices Thermodilution Unit and the method described by Branthwaite and Bradley (1968).

To test the reproducability of the methods used for cardiac output measurement, paired determinations were performed in 17 instances using the dye-dilution method, in 13 instances using the thermo-dilution method and in 13 instances using the Fick method. Designating the first cardiac output value 100%, the second was 104.5% using the dye method (SD ± 8.5%), 99.5% using the thermodilution method (SD ± 9.8%) and 98.8% using the Fick method (SD ± 5.1%).

3. The model

In a simulation study, it is necessary to formulate the pressureflow relation of the aorta in mathematical terms. The aorta is divided into segments, and each segment is described by 2 differential equations. This simplification enables us only to simulate the pressure and flows at selected sites. The differential equations may be arrived at by starting from the Navier-Stokes equations and subsequently neglecting nonlinear terms (Rideout and Dick, 1967).

Let us consider two positions in the aorta with pressure P_0 and P_1 respectively. According to Fry (1967), the pressure gradient $P_0 - P_1$ is distributed among intertance and resistive terms:

$$P_0 - P_1 = L_1 \frac{dq_1}{dt} + Rq_1 \qquad (1)$$

where q_1 is flow between these points, dq_1/dt flow derivative with respect to time, L the inertance and R is viscous resistance. The rate of change of volume (dV_0/dt) within a section of the aorta is:

$$dV_0/dt = q_0 - q_1$$

where q_0 and q_1 are the flows into and out of the section respectively. The pressure P_0 is assumed to be a linear function of the volume and its rate of change:

$$P_0 = \left(\frac{1}{C} + D\right) V_0 \quad \frac{dV_0}{dt} \qquad (2)$$

where C is the compliance of the vessel segment and D is a coefficient related to vessel wall viscosity. A linear representation of the pressure-volume relationship seems resonable for the normal pressure range (Hallock and Benson, 1937). The equations describe the pressure-volume relationship of the aortic segment and in addition the transport of flow between two neighbouring segments. The aorta is divided into 6 segments as illustrated in Fig. 1. The abdominal arteries draining into the portal and the renal system are described as one segment. The carotid, iliac and femoral arteries are represented by single segments. The vessels beyond these segments are described by impedance approximations, possessing the same mathematical structure as that of the other segments, but the parameters L, R, C and D are not directly attributable to vessel dimension. These segments are referred to as terminating segments. The parameters used in this description are listed in Table 2. We have assumed constant inertances (L) and resistances (R) for all segments. The numerical values are based on the study by dePater (1966), and our experience with the model. The damping terms D·C, signifying the viscous properties of the wall, are constant for all segments except the terminating. The nummerical values of the latter, denoted T_p can be adjusted.

The compliance of the individual aortic and arterial segments are functions of the total aortic compliance, C_{ao}. In this model we have used a fixed elastic tapering of the aorta. The available measurements do not allow this tapering to be determined in individual subjects.

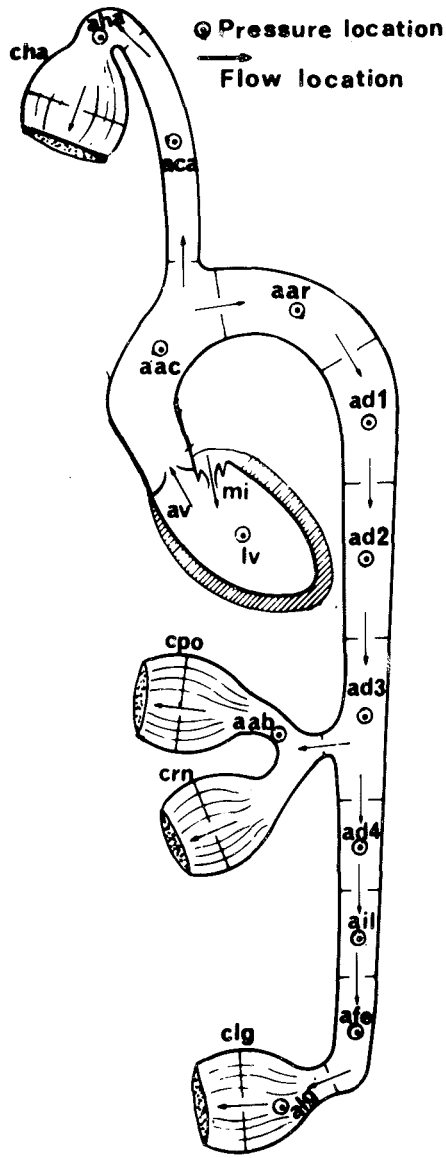

FIG 1. Model of the left ventricle and arterial system, showing the segmentation and the locations for measuring pressure and flow. Abbreviations: aac-ascending aorta, aar-aortic arch, adl-ad2-thoracic descending aorta, ad3-ad4-abdominal descending aorta, ail-iliac arteries, afe-femoral arteries, alg-leg arteries, aca-carotid arteries, aha-head and arm arteries, aab-abdominal arteries. The abbreviations with suffix c (cha, clg, crn, cpo) signify the peripheral resistances.

Table 2
AORTIC MODEL PARAMETERS

Aortic segment	C_i Compliance $\frac{ml}{mmHg}$	C_iD_i Damping timecourse msec	L_i Inertance $\frac{mmHg}{mlsec^{-2}} 10^{-3}$	R_i Resistance $\frac{mmHg}{mlsec^{-1}} 10^{-3}$		P_e External pressure
aac	0.23 C_{ao}	10	0.6	0.2	Ascending aorta	
aar	0.23 C_{ao}	7	0.8	0.2	Aortic arch	
adl	0.17 C_{ao}	5	1.3	0.4		P_{th}
-ad2	0.17 C_{ao}	5	1.3	0.4		
ad3	0.12 C_{ao}	5	2.1	0.8	Descending aorta	
ad4	0.8 C_{ao}	5	2.7	1.5		P_{ab}
ail	0.035 C_{ao}	5	5.0	6	Iliac arteries	
afe	0.035 C_{ao}	10	9.0	20	Femoral arteries	
aca	0.040 C_{ao}	10	6.0	10	Carotid subclavian	0
aha	0.15 + 0.17 C_{ao}	330 T_p	13.0	40	Head & arms arteries	
aab	0.10 + 0.11 C_{ao}	100 T_p	6.0	10	Abdominal arteries	P_{ab}
alg	0.10 + 0.11 C_{ao}	150 T_p	13.0	40	Leg Arteries	0

«Standard» values. C_{ao} = o.87 ml/mmHg, T_p = 1, P_{ab} = 0 mmHg and P_{th} = -4 mmHg

The peripheral resistances are represented as linear pressure-flow relationships where capillary flow is given by:

$$q_c = (P_a - P_v)/R_c \quad (3)$$

where P_a is arterial pressure (of terminating segment), P_v venous pressure (5 mm Hg in this study) and R_c is the peripheral resistance. The model has a fixed distribution of total peripheral resistance, Rp, on the 3 branches, with 25% of the cardiac output going to the head and arms, 10% to the legs and 65% to the abdominal region.

Although 24 differential equations and a number of constants are involved in this arterial description, only 3 parameters are used for characterizing the dynamic behaviour of the aorta: aortic compliance, C_{ao}, total peripheral resistance, R_p and peripheral damping, T_p.

The model of the left ventricle is necessary in order to simulate the input to the aortic model. This model, based on muscle mechanics, can generate a flow pulse into the ascending aorta and by varying the different parameters, like contractility, diastolic volume, ventricular size etc., this flow pulse can be changed individually. The model of the left ventricle is capable of generating flow pulses which are quite similar to electromagnetic flow curves measured in the ascending aorta. This is shown elsewhere (Aaslid, 1974). In this study we have not studied the function of the left ventricle in detail, but only the pressure and mean flow in the aorta.

These models are part of a closed loop model of the entire circulation and are simulated on a special purpose analogue computer. The complete model has been described in detail elsewhere (Aaslid, 1974). The outputs from this model are voltages that pulsate in real time, analogues to pressure and flow in the arterial system.

Using this model, it is possible to compare directly the model generated pressures with measurements obtained during catheterization. In order to minimise the dynamic errors in the pressure measurements, we observe the model outputs through a simple model of a catheter system. Thus similar distortions are introduced in both patient and model variables, and a comparison is possible.

4. Simulating the patient

Fig. 2 shows the main principle of this simulation. The R-wave of the ECG is detected and used to start the activation of the model left ventricle. Referring to Fig. 2, the sampled slightly noisly pressure course was obtained from the ascending aorta of the patient througt a catheter-manometer system. The continuous, smooth curve is generated by the cathetermanometer model connected to point aac (Fig. 1) analogues to the ascending aorta. The natural frequency and the damping of the catheter-manometer model are adjusted for each patient by observing the pressure course just after the occurence of a sharp undulation such as the upstroke, or the incisura. With underdamped catheters it is possible to obtain a satisfactory match on the basis of visual criteria. For further comparison it is necessary that the start and the end of left ventricular model ejection are synchronized with these events in the patient. The left ventricular model can be automatically controlled to achieve this end. The utstroke of the pressure course, and the incisure as well as the second heart sound, are used as criteria for controlling the start and duration of ejection respectively.

The actual course of the model pressure is the function of stroke volume (SV), peripheral resistance (R_p), peripheral damping (T_p) and aortic compliance (C_{ao}). The next step in the procedure is to find estimates of SV and R_p that result in mean and pulse pressures that match the observations. The heart cycle is first divided into 2 intervals «EP» — the ejection period and «NEP» — the non-ejection period. Then the parameters of the left ventricle are changed until the model pressure course during the EP is close to the measured one. The peripheral resistance is finally changed until the pressure course in patient and model is similar during the NEP.

We use as the criteria for satisfactory estimates of both SV and R_p that the error, defined as patient pressure minus model pressure, has a mean of zero during both these intervals.

A feedback servosystem which controls both SV and R_p to fulfill the mean criteria is relatively simple to build electronically and is used in the present application. In the model, the peripheral damping, T_p, influences the aortic pressure course through reflected wave-energy originating from the terminating seg-

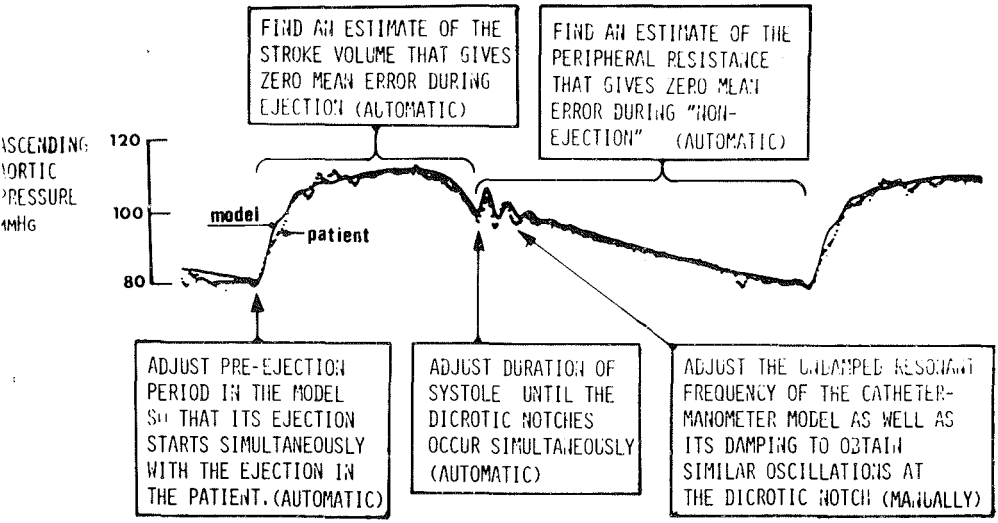

FIG. 2 Superimposed patient and model ascending aortic pressure demonstrating the main features of the simulation procedure.

ments. It is possible to adjust T_p to improve the curve fit. An example is shown in Fig. 3. In panel A, T_p is 0.5, and we observe an error in late ejection. If we increase T_p to 1.0, a more satisfactory match is obtaines as shown in panel B. Increasing T_p to 2.0 (panel C) again results in errors, seen as too steep diastolic slope. Although no thorough investigation of this phenomenon has been undertaken, it seems as though in Fig. 3A the reflected wave energy is smaller and in Fig. 3C larger in the model than in the patient. In the present study we choose T_p to satisfy a visual criteria of aortic pressure curvefit. After completing these procedures, the model now simulates the patient pressure-time course as can be seen in Fig. 2.

The next part of the simulation includes determination of the aortic compliance C_{ao}. For this porpose, two independent methods are used. The first one is based on the pulse transmission properities and the second on the volume storage effect of the aorta.

a) Estimation of C_{ao} (pulse)

The pulse wave velocity along the aorta is dependent on aortic compliance. By measuring the pressure pulse either invasively or non-invasively at two points along the aorta, the transmission time between these points can be compared to that between two analoque points in the model. By changing the aortic compliance in the model, a value can be found that gives pulse transmission times equal to those in the patient's aorta. This value for each individual patient is called C_{ao} (pulse).

Fig. 4 demonstrates how the C_{ao} (pulse) was calculated. Superimposed are the ascending aortic pressure and the femoral artery pulse from patient and model. Panel A shows a rather low value of model aortic compliance (C_{ao} = 0.55 ml/mm Hg), resulting in the femoral pulse occuring earlier in the model than in the patient, indicating a shorter pulse transmission time in the model. Panel C shows a higher value of compliance (C_{ao} = 0.94 ml/mm Hg), and in this case the femoral pulse occurs later in the model than in the patient caused by a longer pulse transmission time in the model. Panel B shows a value of C_{ao} = 0.72 ml/mm Hg which gives identical pulse transmission times in patient and model. This value is then termed C_{ao} (pulse) for this patient.

b) Estimation of C_{ao} (C. O.)

The cardiac output determination was not

utilized, nor even known to the operator at the time when C_{ao} (pulse) was estimated. It was therefore possible to use this information to obtain an independent estimate of C_{ao}. For a given pulse pressure, the cardiac output in the model (mean aortic flow), is dependent on aortic compliance. A satisfactory curvefit for EP and NEP does not give any information about the «correct compliance». The latter is the value of compliance that gives a cardiac output on the model identical with that measured in the patient with an independent method when aortic pressure in patient and model are matched by the procedure described above. In this part of the simulation, while the SV and R_p estimator servosystems were operating, the compliance values were changed until cardiac output in the patient (measured by an independent method) and model were identical. This value of compliance was designated C_{ao} (C. O.) for this patient. In this study the inertance to flow in the aorta is assumed to be constant. A change in inertance will influence the pulse wave velocity to a much larger degree than it influences the relationship between pulse pressure and stroke volume (see Discussion). As two independent methods of estimating aortic compliance have been used, it might be possible to correct the inertance parameters listed in Table I by multiplying them with the correction factor L_{ao} (corr) until C_{ao} (C·O) = C_{ao} (pulse). This correction factor is calculated as:

$$L_{ao}(\text{corr}) = \frac{C_{ao}(\text{pulse})}{C_{ao}(\text{C·O})}$$

A value for L_{ao} (corr) of 1 would signify that cardiac output as well as pulse transmission time are identical in patient and model. Consequently, the deviation of L_{ao} (corr) from unity signifies a difference in the estimaties of aortic compliance. After the simulation is completed, the aortic catheter is withdrawn and the aortic pressure curves at different positions along the aorta was compared with the model curve at analoque positions.

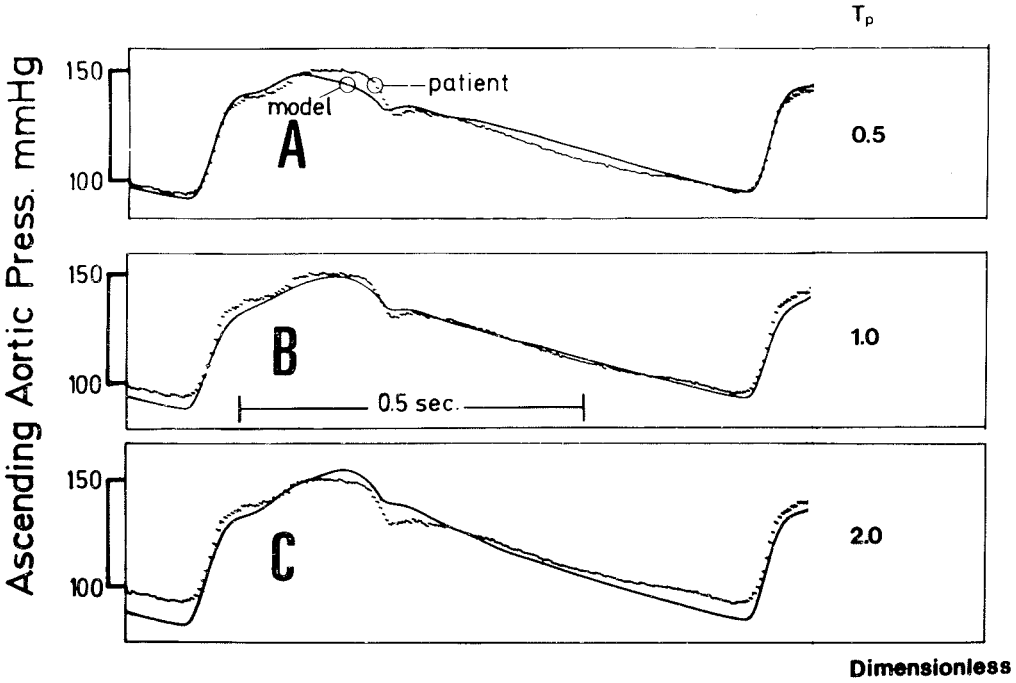

FIG. 3 Patient and model ascending aortic pressure at different values of peripheral damping, T_p.

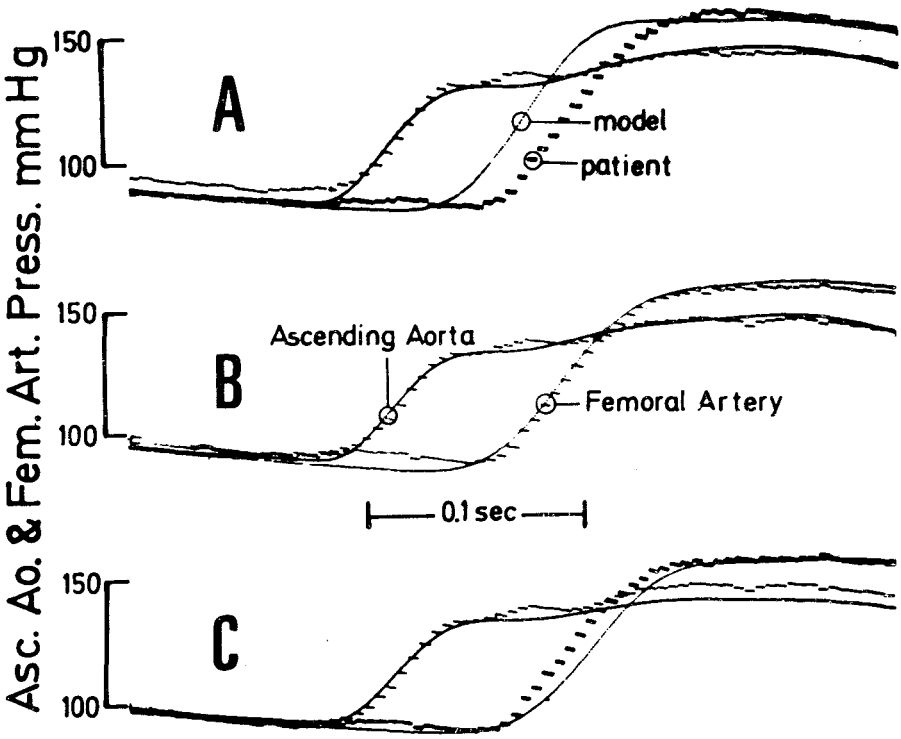

FIG. 4 Patient and model aortic ascending and femoral artery pressure at different values of aortic compliance in the model. In panel A the compliance is 0.55, in panel C 0.94 and in panel B 0.72 ml/ mm Hg.

Results

Two examples of transmission of the pressure pulse are illustrated in Fig. 5. The systolic wave shape changes from being relatively flatopped in the ascending aorta to a more triangular shape in the iliac arteries, and the systolic peak pressure increased as we proceed downstream. The simulated pressure curves show the same changes, indicating that the model is capable of generating pressure waveforms closely resembling the measured ones. Similar curvefits were obtained in all patients studied. The cardiac output was measured by an independent method in 41 instances. The results are compiled in Table 3. The comparison between the compliance calculated by pulse transmission time and the compliance calculated by cardiac output is shown in Fig. 6. Seven patients has atrial fibrillation with large variations in pressure and flow beat to beat. This makes compliance estimates based on transmission times rather inaccurate, and they have therefore been excluded from the statistical considerations. The mean difference for the remaining 33 measurements was 8% with a standard deviation of the difference beeing ± 5%. The correlation factor was 0.98. The estimates of the aortic compliance show large individual variations. Fig. 7 shows the C_{ao} pulse estimates relative to patient age. In this study the mean L_{ao} (corr) was 0.96 with a SD of ± 0.095. The correlation factors between L_{ao} (corr) and patient height, weight and body surface area are r = 0.09m r = -0.13 and r = -0.07 respectively, while the correlation factor between L_{ao} (corr) and mean blood pressure is r = 0.49 and between L_{ao} (corr) and patient age is r = 0.27.

TABLE 3
Results

No	Heart rate beats/min	Mean arterial Pressure mmHg	$C_{a\,(pulse)}$ ml/mm Hg	$C_{a\,(co)}$ ml/mm Hg	$L_{a\,(corr)}$	C. O. l/min
1	102	95	1.01	1.18	0.86	7.0
2	58	113	1.01	1.01	1.0	4.9
3	77	123	0.87	0.89	0.98	4.4
4	66	135	0.53	0.64	0.83	5.0
5	60	78	0.87	0.81	1.07	3.8
6	58	110	0.61	0.71	0.86	4.1
7	80	145	0.49	0.53	0.92	5.4
8	68	143	0.47	0.56	0.84	8.3
9	108	103	0.55	0.58	0.95	4.5
10	85	105	0.64	0.58	1.10	5.9
11	48	98	0.61	0.81	0.75	4.4*
12	71	95	0.81	0.89	0.91	5.4
12	110	90	0.55	0.59	0.93	4.1
13	100	88	0.30	0.31	0.97	2.6*
13	105	100	0.30	0.31	0.97	2.2*
13	100	95	0.30	0.33	0.91	2.0*
14	59	128	0.51	0.54	0.94	5.1
15	75	98	0.20	0.21	0.95	2.8
16	67	90	0.68	0.59	1.15	3.1
17	80	163	0.36	0.45	0.80	5.3*
18	66	103	0.55	0.61	0.90	4.2
19	62	125	0.45	0.45	1.0	5.2
20	69	113	0.43	0.46	0.96	4.3
21	78	100	0.47	0.50	0.94	3.4
21	75	100	0.47	0.52	0.90	3.0
21	79	100	0.47	0.45	1.04	2.7
22	100	100	0.32	0.29	1.10	3.4
22	85	88	0.32	0.32	1.0	2.8
22	84	83	0.32	0.30	1.07	2.5
22	115	75	0.51	0.57	0.88	1.7
23	65	113	0.41	0.32	1.08	3.7
23	65	105	0.41	0.50	0.82	5.1
24	34	65	1.52	1.96	0.76	5.8
24	56	93	1.52	1.62	0.94	9.7
25	98	153	0.47	0.43	1.09	6.2
26	80	115	0.53	0.37	1.43	3.5*
27	83	75	0.45	0.44	1.02	3.6
27	75	83	0.45	0.50	0.9	3.3
28	62	108	0.34	0.32	1.06	4.3
29	85	63	0.47	0.57	0.83	2.2*

* Atrial fibrillation

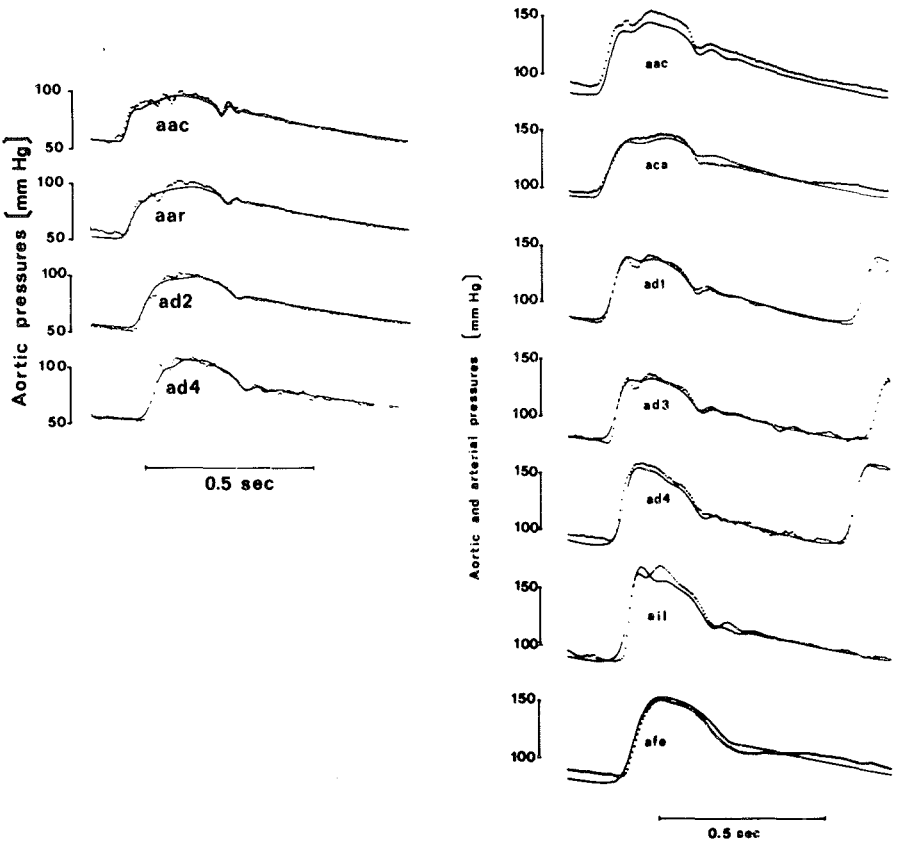

FIG. 5 Patient and model pressure along the aorta in two patients. The patient curves from the carotid and femoral artery are measured by external pulse-pick-ups. Abbreviations refer to segments in Fig. 1.

Discussion

This study shows that a relatively simple linear model is able to simulate pressure propagation along the human aorta with reasonable accuracy. Furthermore, the two independent methods of aortic compliance estimation correlate well. The segments distal to the aorta influences the pressure and flow waveforms considerably througt reflected energy as demonstrated in Fig. 3. Since the simulated pressure waveforms are quite similar or the measured ones, it appears that these reflections are of similar amplitude and phase in model and patient. This is, however, only indirect evidence for the impedance of the peripheral branches. Even large variations in T_p did not significantly influence the compliance estimates. In this study we have assumed fixed distribution of compliance on the various aortic segments. Although we may expect this to change from patient to patient, the correlation between the two estimates of aortic compliance indicates that the error due to this assumption is small.

We have assumed constant aortic inertance parameters in the present model. This assumption implies a constant ratio between the length and the crossectional area of an aortic segment and a constant velocity profile. The errors due to inappropriate inertance will influence the ratio between the independent estimates of the aortic compliance

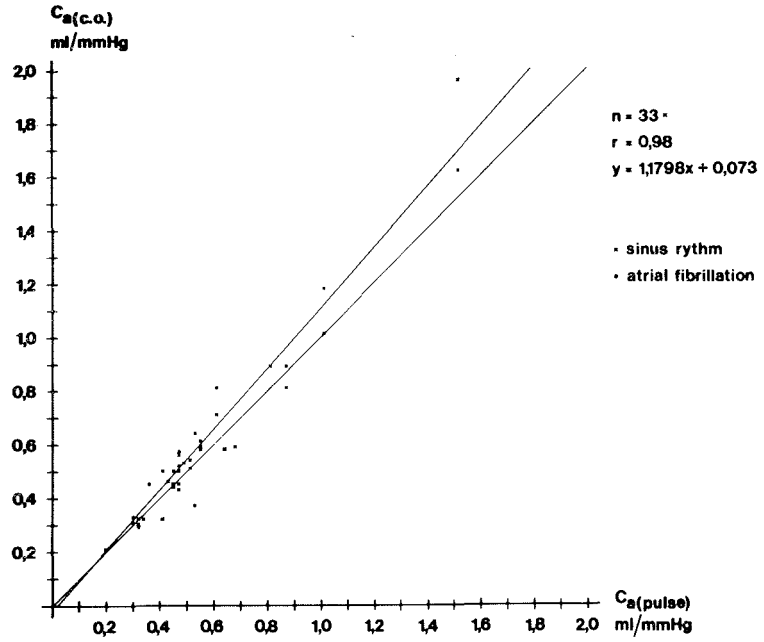

FIG. 6 Relationship between the compliance estimates. The measurements in patients with atrial fibrillation are not treated satistically.

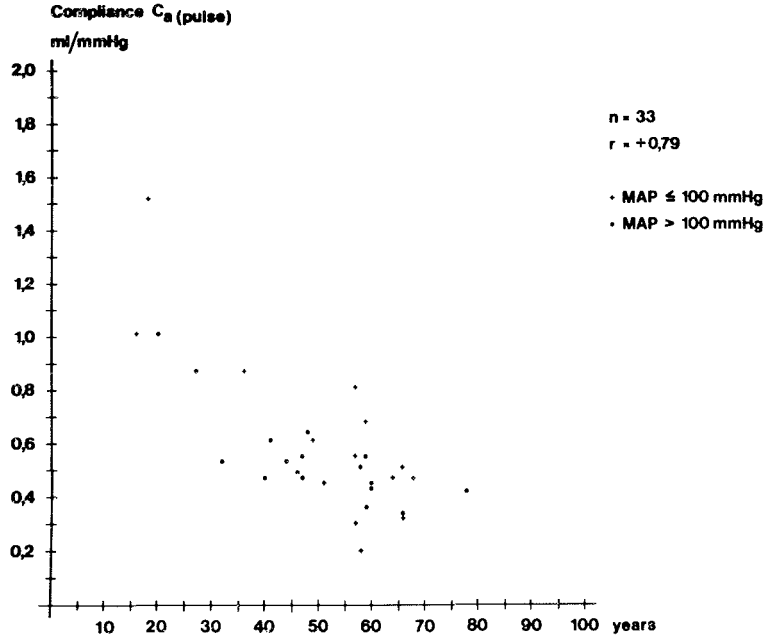

FIG. 7 Relationship between the estimate of aortic compliance and patient age.

$$\frac{C_{ao}(\text{pulse})}{C_{ao}(\text{C·O})}$$

As we find very low correlation between his ratio and the patient height (r = 0.09), weight (r = -0.13) and body surface area (r = -0.07), we have an indication that the assumption of constant intertance is reasonable for subjects of different sizes. We may, however, expect the aorta to dilate with increasing age and blood pressure. Then the assumption of a constant area/length ratio becomes questionable. An increased aortic radius (with fixed length) implies a decrease in the inertance parameters as predicted by the equation:

$$L_{ao} = 1.1 \cdot \rho \cdot \Delta z / \pi r^2 \qquad (4)$$

where ρ is blood density, z is segment length and r is aortic radius (Fry, 1967).

The wave velocity is dependent on the product of compliance and inertance (Wetterer und Kenner, 1968). Since, in a patient with dilated aorta, we assume an inertance that is larger than the real, we should expect that the pulse transmission time estimate of compliance will be smaller than the estimates based on stroke volume and pressure contour.

The pressure-volume-relation of the aorta may tend to be more nonlinear with increasing age and blood pressure. The pulse transmission time as used in the present estimation scheme is primarly dependent upon the aortic compliance at the diastolic pressure. In patients with considerable pulse pressure and nonlinear aortas, we can expect that aortic compliance as determined by the pulse transmission time is different from the aortic compliance as determined by the stroke volume-pressure contour method. The latter is more sensitive to the mean compliance over the pulse pressure range, which may be expected to be lower than the compliance at diastolic pressure. Thus in patient with nonlinear pressure-volume relations and increased pulse pressure, we should expect that the pulse transmission time estimate of C_{ao} is larger than the estimate based on the stroke volume and the pressure contour.

The error due to inertance variations and the errors due to nonlinearities change the compliance estimate in opposite directions. This may be the reason why a ralatively simple linear model with constant inertance parameters gives good correlation between the two independent estimates of aortic compliance. We find however, a distinct, if rather low, correlation between L_{ao} (corr) and blood pressure (r = 0.49) and age (r = 0.27), indicating that in most cases the errors due to nonlinearities are most prominent.

An additional explanation for the difference in the compliance estimates can also be found in the methods used for measuring pulse transmission time and cardiac output. Of the two, we expect the methods for cardiac output measurement to be the least reliable (except in patients with atrial fibrillation), as reproduceability better than ± 10% is difficult to achieve.

The calculation of a correction factor of inertance L_{ao} (corr) is based on the assumption that changes in inertance predominatly influences the compliance values calculated from pulse transmission time. Inertance will not influence the pressure-volume relationship in the aorta, but will influence the amplitude and shape of the pressure and flow curves and the amplitude of the reflected waves (Westerhof et al., 1977). These effects are, however, small in the aorta (Taylor 1964, O'Rourke and Tylor 1967), and therefore an estimate of stroke volume from the pressure curve is not significantly influenced by changes in L parameters. The ratio

$$\frac{C_{ao}(\text{pulse})}{C_{ao}(\text{C·O.})}$$

can accordingly be used for obtaining an estimate of aortic inertance on an individual basis.

To our knowledge no study on total aortic compliance in living man has been published. The reason for this is probably methodological, since such a study will require simultaneous measurement of pressure and volume along the whole course of the aorta.

Our results are therefore not directly comparable to those from other studies, (Greenfield and Patel, 1962, Simon und Meyer, 1958, Wagner und Kapal, 1952, Yaginuma et al., 1972) since they were done on short segments of the aorta or on aortas from cadavers. In a simulation study of the circulation, Hyndman (1973) uses the value of 0.7 ml/mm Hg for aortic compliance, and Guyton et al. (1973) use the value 1.1 ml/mm Hg.

None of the authors state how this value was calculated.

In a recent study, Yaginuma et al. (1972) measured pressure and volume in the ascending aorta in 25 patients. Calculating from their data, a mean compliance for this aortic segment is 0.30 ml/mm Hg at a mean pressure of 84 mm Hg. Greenfield and Patel (1962) measured pressure and diameter in the ascending aorta in 10 patients during heart surgery. Assuming a cylindrical shape of the aorta and no tapering, the compliance for a 70 cm length is 0.25 ml/mm Hg at a mean pressure of 100 mm Hg.

Wagner und Kapal (1952) measured the compliance in the thoracic aorta of 6 cadavers from persons 13 to 67 years of age, and found values of compliance ranging from 0.18 to 0.38 ml/mm Hg at 100 mm Hg pressure. Simon und Meyer (1958) measured total aortic compliance in 33 cadavers, finding values between 0.31 and 0.80 ml/mm Hg.

At a mean pressure of 104 mm Hg, we found values of compliance of 0.14 ml/mm Hg in the segment studied by Yaginuma et al., and 0.34 ml/mm Hg in the segment studies by Wagner und Kapal (aar, adl, and ad2, in Fig. 1). For the total aorta, the mean compliance was 0.6 ml/mm Hg in our study. These values are of similar magnitude as the ones found by the above mentioned authors. The patients studied by Yaginuma et al. were younger and had lower blood pressure than our patients, which could explain the higher observed values of compliance. There was considerable individual variation in aortic compliance in our study. The value tended to decrease with age, which could be explained as a loss of elastic wall material in the aorta with increasing age (Lansing, 1959).

Several simulated models of the arterial system have been presented over the past years (Beneken, 1965, Jager, 1965, Noordergraaaf, 1963, de Pater, 1966). In order to show that the model is sufficiently accurate, the output from the model must be compared with measurement data from the human aorta. Spencer et al. (1961) and recently Chang (1973) demonstrated reasonable waveshapes, while Sims (1970), was only moderately successful in simulating the aorta in the dog.

While our model, like many others, exhibited normal looking wavshapes, this is in itself no proof of physiological validity. After the simulation procedure as described in Fig. 2 had been completed in one position in the aorta, the pressure course in model and patient was similar along the rest of the aorta. This implies that the model is capable of simulating individual pressure courses in the patient studied. The pressure changed from being relatively flattopped in the ascending aorta to a more triangular shape in the femoral artery, and the pressure amplitude increased as the wave travelled downwards. As has been shown by Rideout and Sims (1969), this effect can be simulated both by impedance tapering in the linear system (as in this study) or by introducing small nonlineartities in the compliance. It seems reasonable to assume that both tapering and non-linearities are present in the real system, but our stydy gives no information about the relative magnitude of the two.

This study indicates that compliance of the aorta can be calculated from pulse transmission time. The concept of a constant relationship between wave speed and compliance is not new, and has in fact been used in several methods for calculating the cardiac output from central aortic pulse (Bramwell and Hill, 1922, Broemser und Ranke, 1933). When these methods have been compared with simultaneous measurements of cardiac output, the results have not always been encouraging. Our study suggests that this may be due to the methods used for calculating the cardiac output rather than using wrong compliance values.

There have been few attempts of adapting models to measurement data from human arterial systems. Wesseling et al. (1973) using ecternal pulse measurements from the arm artery, showed that the dynamic of pulse transmission could be simulated. The pulse from the brachial artery in one person was compared to the pulse in an analogue position on the model and after adjustment of the model to obtain a close curvefit, the resulting pulse in the «radial artery» on the model was compared to the measurement in the patient. The resulting curvefit was quite satisfactory. Using blood pressure curves from the renal artery in dogs and a simple model based on compliances, inertances and resistances, Rothe and Nash (1968) could simulate blood flow curves that closely resembled measured ones.

In order to judge the accuracy of a simula-

ɔn study, the results must be compares with ɔse obtained by an idependent method. Alt-ɔugh the model was used for both compli-ce estimates, the two values of compliance r each individual patient are based on two ffferent measurements and were calculated dependently. Furthermore, for calculating e pulse transmission time no model is necas-ry, but the described method greatly simpli-s the procedure.

The patients in the present study were quite heterogeneous with respect to age, blood pressure and cardiac output. Patients with normal as well as failing hearts were included. The correlation between the two independent methods of calculating compliance indicates that this type of model can simulate individual patients with reasonable accuracy.

Acknowledgement

The skilled technical assistance of Ms. Elin Amundsen is gratefully acknowledged.

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USE OF A SIMULATION MODEL FOR ESTIMATING CARDIAC OUTPUT FROM AORTIC PRESSURE CURVES

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THIS WORK WAS SUPPORTED BY THE LIFE INSURANCE COMPANY «FORENEDE LIV», TRONDHEIM AND THE NORWEGIAN COUNCIL ON CARDIOVASCULAR DISEANSES.

ABBREVIATED TITLE:
CARDIAC OUTPUT FROM AORTIC PRESSURE CURVES

CORRESPONDANCE TO:
ALF O. BRUBAKK,
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Abstract

A method for calculating cardiac output from aortic pressure curves is presented. The method is based on a simulation model of the human cardiovascular system. The aortic compliance is calculated from the pulse transmission time in the aorta.

The method has been tested against standard cardiac output measurements in 61 instances in 39 persons. 40 measurements have been performed at rest, while 21 have been performed during various changes in the cardiovascular state.

The mean difference between the pulse method and the standard cardiac output determination was found to be 9% with a standard error of the difference of 7%. The correlation coefficient was r = 0.96. The largest differences were found in patients suffering from atrial fibrilation, where changes in pressure in the aorta made compliance estimates based on pulse transmission time difficult.

Using a servosystem, the model is capable of following changes in the cardiovascular state whithin a few beats. This method should therefore be useful for calculating cardiac output in the intensive care situation.

Keywords: Aortic pressure curves, cardiac output, pulse transmission time, aortic compliance, intensive care.

Introduction

Measurement of cardiac output over long periods of time or during rapid changes in the cardiovascular state still remain a problem. The standard methods like indicator dilution or the Fick method, permit only intermettent measurements and are relatively complex to perform.

As there obviously is a relationship between arterial pressure and stroke volume, a large number of methods for calculating the stroke volume from the pressure pulse curve in the aorta has been presented over the last 40 years.

The early work of Frank (1930) regarded the aorta as a simple Windkessel with infinite length. As there is no reflections or drainage in such a system, the relationship between pressure and volume is defined solely by the elasticity of vessel wall.

This work was developed further and led to the conclusion that the stroke index in ml/m^2 was equal to the pulse pressure in mmHg (Hamilton, 1953) or that stroke volume could be calculated directly from the age and blood pressure of the subject (Starr et al., 1954).

Practical evaluation of these formulas led to the conclusion that they were highly unreliable (Brotmacher, 1957). The reason for this is that they do not take into consideration changes in systolic length, peripheral resistance and aortic distensibility, that occur from person to person or in one person during changes in the cardiovascular state.

Subsequent authors tried to improve the pulse contour method by taking some of these points into consideration.

Warner et al. (1953) calculated the stroke volume, SV, by the formula

$$SV = k \cdot P_{md}\left(1 + \frac{Sa}{D_a}\right) \qquad (1)$$

where P_{md} is end systolic mean distending pressure, S_a is systolic pressure area and D_a is diastolic pressure area. The calculation of P_{md} involves the assumption of a mean pulse transmission time in the aorta. The constant k, relating change in pressure to change in volume, is calculated from an idenpendent cardiac output measurement.

Using this formula, Warner et al. (1953) found excellent correlation between cardiac output calculated from this formula and cardiac output measured with the Fick method during exercise and body tilt in man.

Konchoukos et al. (1970) simplified this method further and proposed the formula for stroke volume.

$$SV = k \cdot P_{sa}(1 + T_s/T_d) \qquad (2)$$

where P_{sa} is area under the systolic part of the curve (above a horizontal line drawn from the end diastolic pressure) and T_s and T_d are duration of systole and diastole respectively. k is again relating change in volume to change in pressure, and was determined by a simultaneous measurement of pressure and flow at the start of the experiment.

They found excellent correlation between this method and electromagnetic flow measurement both at rest and during infusion of dextran, haemorrhage, pacing and occlusion of the caval vein in dogs. The correlation coefficient was signifcantly lowver during infusion of sympathomimetic drugs. In these cases the stroke volume was overestimated.

Their method was simplified still by Nichols, who omitted the term T_s/T_d (Nichols, 1973). k was determined as $1/Z_0$ where Z_0 was characteristic impedance, giving the equation

$$SV = 1/Z_0 \cdot P_{Sa} \qquad (3)$$

This formula was solved by a small computer (Wesseling et al., 1976). The results obtained indicated that the method was reliable even when symptomimetic amines were infused.

Starmer et al. (1973) have recently studied several of the methods presented here and conclude that the methods are unreliable when changes in the cardiovascular state occurs which influence the relationship between pressure and flow.

At a certain mean pressure, there is a constant relationship between the area under the systolic part of the pressure curve and the stroke volume. The factor of proportionality is determined by the elasticity of the vessel wall or the aortic compliance, $\Delta v/\Delta p$ (where Δv and Δp are incremental changes in volume

and pressure respectively).

Furthermore, in this case the peripheral resistance and the stroke volume vary inversly as predicted by the equation.

$$SV = \frac{MAP}{TPR} \quad (4)$$

where SV is stroke volume, MAP is mean arterial pressure and TPR is total peripheral resistance. In conditions of nearly steady state, where there are no larger changes in blood pressure and peripheral resistance, it is to be expected that the various methods described will give quite accurate estimates of stroke volume. If, however, the blood pressure, peripheral resistance, stroke volume and aortic compliance are changing, as is often the case when using these methods for continous monitoring, only methods capable of compensating for these changes will give correct results.

A method for calculating the stroke volume from the arterial pressure pulse must take the above mentioned points into consideration. Furthermore, is should be easy to use, depend on only one pressure measurement, preferably in a peripheral artery, and be able to follow even quick changes in the cardiovaskular state.

A method based on a simulation model of the aorta has been developed and the method has been tested against standard cardiac output measurement in 61 instances in 39 persons.

Methods

1. The model

The model is part of a closed loop model of the circulation, which have been described in detail elsewhere (Aaslid 1974). The model is simulated on a special purpose analogue computer.

A model of the aorta must describe its volume storage effect («Windkessel» function) as well as its transmission properties. Our description is based on a series of elastic reservoirs conected with rigid tubes. This lumped description allows the pressures and flows to be computed only at selected points, whith the «flow points» lying between the «Pressure points».

Each arterial segment is described by two differential equations. One describes the pressure as a linear function of the volume (de Pater, 1966). The pressure gradient determines the motion of fluid between two segments (Fry, 1959) and the volume of each segment is determined by integrating the difference between flow into and out of the segment.

The aorta consists of six segments. The illiac artery, the femoral artery and the carotid artery are each modelled as one segment since they represent aortic branches where pressure and flow pulses can easily be measured. The arteries to the head and arms, to the legs, and to the viscera are each modelled as one segment. The vessels beyond these locations are described as impedance approximations. The peripheral resistance is represented as a linear pressure flow relation.

The parameters used in the arterial model can be seen in Table I. The aortic inertances, L_i, resistances, R_i, and viscous dampings, D_i, for each segment are assumed to be constant, the numerical values being based on the study of de Pater (1966) and our experience with the model. The compliance of each segment is a fraction of the total aortic compliance, which can be varied. Elastic tapering of the aorta is assumed. The damping, T_p, controls the oscillatory input behaviour of the peripheral vessels and can be varied, thereby simulating different amounts of reflected wave energy from the periphery.

The input to the aortic model is generated by a left ventricular model. The ventricular model is based upon a mucle model, decribing an average muscle fiber. This model, being a modified Hill muscle analog (Grasser and Hill, 1924) has a characteristic force velocity curve, described by the contractile parameters V_{max} (maximum velocity of muscle contractile element) and σ_{max} (maximum active tension of muscle). A model of the left ventricle describes the relation between the length, tension and velocity of this muscle and the volume, pressure and flow of the ventricular model. This model is similar to the one used by Beneken (1965).

Table 1. Aortic model parameters.

Index	C_i Compliance $\frac{ml}{mmHg}$	C_iD_i Damping timeconst. msec	L_i Inertance $\frac{mmHg}{mlsec^{-2}} 10^{-3}$	R_i Resistance $\frac{mmHg}{mlsec^{-1}} 10^{-3}$	Z_o Charact. impedance $\frac{mmHg}{mlsec^{-1}} 10^{-3}$		p_e External pressure
aac	0.23 C_{ao}	10	0.6	0.2	55	Ascending aorta	p_{th}
aar	0.23 C_{ao}	7	0.8	0.2	65	Aortic arch	
ad1	0.17 C_{ao}	5	1.3	0.4	95	Descending aorta	
ad2	0.17 C_{ao}	5	1.3	0.4	95		
ad3	0.12 C_{ao}	5	2.1	0.8	140		p_{ab}
ad4	0.08 C_{ao}	5	2.7	1.5	170		
ail	0.032 C_{ao}	5	5.0	6	370	Iliac arteries	
afe	0.030 C_{ao}	10	9.0	20	510	Femoral arteries	0
aca	0.040 C_{ao}	10	6.0	10	380	Carotide subclavian arteries	
aha	0.15+0.17 C_{ao}	330T_p	13.0	40		Head & arms arteries	
aab	0.10+0.11 C_{ao}	100T_p	6.0	10		Abdominal arteries	p_{ab}
alg	0.10+0.11 C_{ao}	150T_p	13.0	40		Leg arteries	0
av	0.04	1	0.6* (same as aac)	0.2* (same as aac)		Aortic valve V_{bak} = 2.5 ml	

"Standard" values: C_{ao} = 0.87 ml/mmHg, T_p = 1, p_{ab} = 0 mmHg and p_{th} = -4 mmHg

2. Material

31 men and 8 women were investigated. Their age ranged from 16 to 78 years, with a mean age of 50 years. The patients were hospitalized for a variety of diseases of the cardiovascular system, as hypertension, myocardial infarction or heart conduction disturbances. None had clinical signs of aortic valvular insufficiency.

The measurements were performed during routine evaluation of their basic cardiovascular problems.

61 simultaneous measurements of carciac output and aortic pressure were performed. The aortic pressure was measured in the ascending aorta in 9 instances, in the descending aorta just below the branching of the left carotid artery in 40 instances and in the femoral artery in 12 instances. 40 measurements were performed at rest, while 3 measurements were performed during right ventricular pacing, 1 during exercise, 8 during hypotension induced by the drug Diazoxide and 9 during changes in left ventricular filling pressure by venesection using the method of Bradley et al. (1970).

The cardiac output was measured by the Fick method in 28 instances, with dye dilution in 19 instances and with the thermo dillution in 14 instances.

The patients were investigated in the supine position. Under fluoroscopy, a thin catheter was introduced from the femoral artery to the desired position in the aorta. The catheter was connected to a Statham P23Db pressure transducer and was continously flushed by a slow saline drip, using a system described previously (Aaslid and Brubakk, 1971). The zeroline was the crossing of the 4th rib with the forward axillary line (Rokseth et al., 1960).

The ECG was measured in a lead giving a large R-wave, usually lead II. The phonocardiogram was recorded using an Elema Schonander crystal microphone in a positiion where a clear second heart sound could be found.

Using a pulse-pick-up developed here and described previously (Aaslid and Brubakk, 1971), the carotid and the femoral pulse were recorded.

All data was recorded on magnetic tape, using a system previously described (Aaslid and Brubakk, 1971). This system is capable of recording up to 8 channels of analogue signals together with comentaries on 1/4 inch magnetic tape.

Cardiac output was measured by the Fick method by allowing the patient to breath into a Douglas bag for 3 min. In the middle of this period blood was collected from the pulmonary artery and the aorta and immediately analyzed for O_2- content using an oxymeter. The contents of the bag was analyzed by a micro-Scholander-apparatus.

For obtaining Dye-dilution curves, 5 mg Indio-syanin green was injected into the right atrium or the pulmonary artery. Arterial blood was continously withdrawn throught the cuvette of a Beckman Densitometer. Blood for calibration was obtained imediately prior to the injection of dye and calibration curves were recorded imediately afterwards, using the same batch of dye. Cardiac output was calculated by using the integrator on the Densitometer and the method of Hyner (1962) as described in the Densitometer manual.

Thermodilution curves were recorded using the Devices thermodilution instrument and the method of Branthwaithe and Bradley (1968). Cold saline was injected into the right atrium, using the jugular vein approach and the curves were recorded from a thermistor in the pulmonary artery.

3. Simulating the patient

The simulation were performed off-line, using the data on the magnetic tapes.

From the fluoroscopic examination, the position of the catheter tip in the patient aorta is known and hence the point were the aortic pressure was measured. The aortic pressure in the model is measured at an analogue position and the two curves are superimposed on an oscilloscope screen. As the pressure in the patient aorta is measured by means of a catheter-manometer system, distortions will occur, depending on the frequency response and damping of this system. To compensate for this, the pressures in the model aorta is filtered through a model of the measurement system, the characteristics of which may be changed as described below.

The activation of the left ventricular muscle model is triggered by the R-wave of the ECG from patient. The pre-ejection period in the

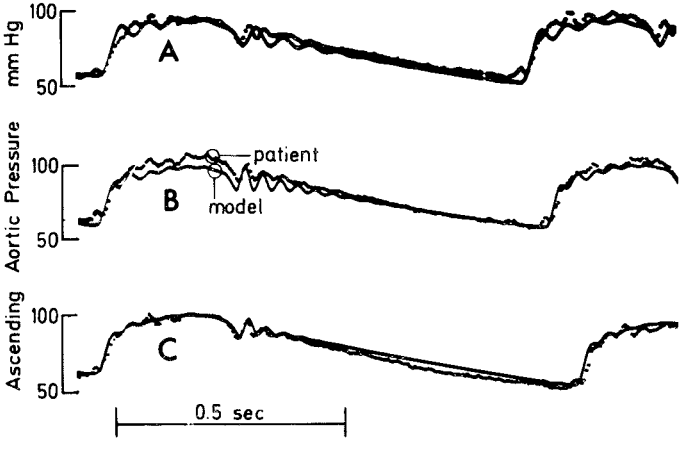
model is changed by changing the V_{max} in the muscle model until this period has the same length in the model as in he patient. Then the duration of systole in the model is changed until the closure of the aortic valve coincides in patient and model. This is either done by letting the model aortic valve closure be triggered by the first sharp deflections of the second heart sound or by manually changing the duration of systole until the incisura of the two aortic pressure curves coincide. The characteristics of the catheter manometer system are simulated by changing the frequency response and damping of the model catheter system until the sharp ondulations in the pressure curve after closure of the aortic valve are simular in patient and model. Fig. 1 shows the effect of changing the parameters of the measurement system. In A, the frequency response of the model catheter manometer system is too low, as judged from the higher frequencies present in the patient recording. In B, the frequency response is approximately similar, but the damping is too low. This has been corrected in C, giving close curvefit after the incisura of the pressure curves.

The model pressure course during left ventricular ejection is mainly dependant upon left ventricular end-diastolic volume, the value of σ max of the left ventricular muscle model and the compliance of the aortic vessel wall. As we were in this study only interested in the amount of blood ejected with each beat, the relative magnitude of the two ventricular parameters are not important. These two parameters are therefore changed intil the model and aortic pressure course are similar in model and patient during ejection. Fig. 2 shows the effect of changing the σ max of the left ventricular muscle model on the aortic pressure course during ejection. The left ventricular end diastolic pressure have been kept constant in this example.

The compliance, giving the factor of proportionality between pressure during ejection and stroke volume, is calculated from the pulse transmission time in the aorta as described below.

During diastole, the pressure decay will be determined by the peripheral resistance. The model peripheral resistance is therefore changed until the pressure course during diastole is similar patient and model. Fig. 3 shows the effect changing the peripheral resistance of the model on the diastolic pressure course in the aorta.

After these procedures have been completed, the model pressure course closely follows the one measured in the patient. We use as error criterion that the difference in pressure shall not be greater than ± 5mmHg during any part of the cardiac cycle.



σ_0 =	ξ =
17	0.15
26	0.10
26	0.19
Hz	diment.-less

FIG. 1. Influence of catheter parameters (frequency response and damping on aortic pressure time course in the model). For further explanation see text (page VI–7).

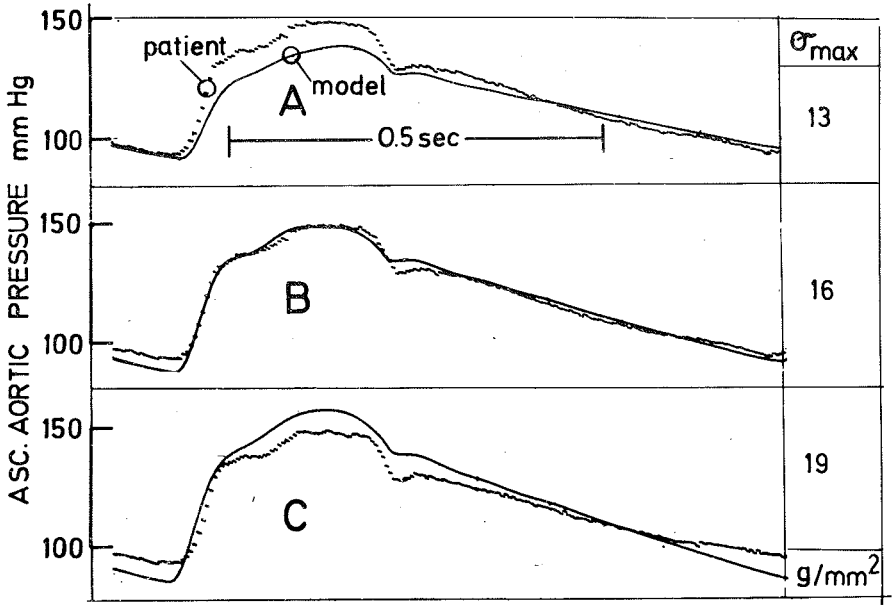


FIG. 2. Changes in model aortic pressure with different values for σ max (maximum active tention) of the left ventricular muscle model. From Panel A to C the value of σ max is increased, thereby increasing the model aortic pressure during ejection.

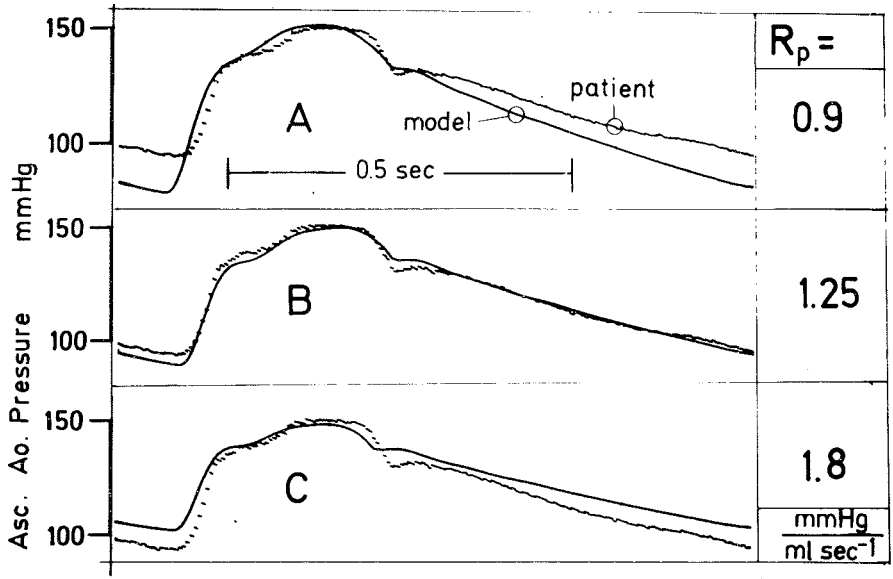


FIG. 3. Changes in the diastolic part of the model aortic pressure curve with different values of total peripheral resistance. The slope of the diastolic curve decreases as the peripheral resistance increases.

As the aim of this study is to develope a method wich permits measurement of cardiac output during changes in the cardiovascular state, an automatic servosystem has been developed which continously updates the estimates of σ max and peripheral resistance.

As previously mentioned, the aortic compliance will determine the relationship between the systolic part of the pressure curve and the stroke volume.

In this study, the aortic compliance is determined from the pulse transmission time from the aortic arch or the carotid artery to the femoral artery (see discussion). The compliance values in the model are changed until the transmission time between two analogues points model and patient is identical.

Fig. 4 shows the patient and model curves after the simulation procedure has been completed, showing the superimposed pressure curves as well as the superimposed pulse curved from the femoral and carotid artery.

The cardiac output from the model can now be compared to that measured by an independent method in the patient. As the human aorta has non-linear pressure-volume-caracteristics (see discussion) the transmission time must be checked when large changes in aortic pressure occurs and the compliance changed, if the transmission time is different in the patient and the model aorta.

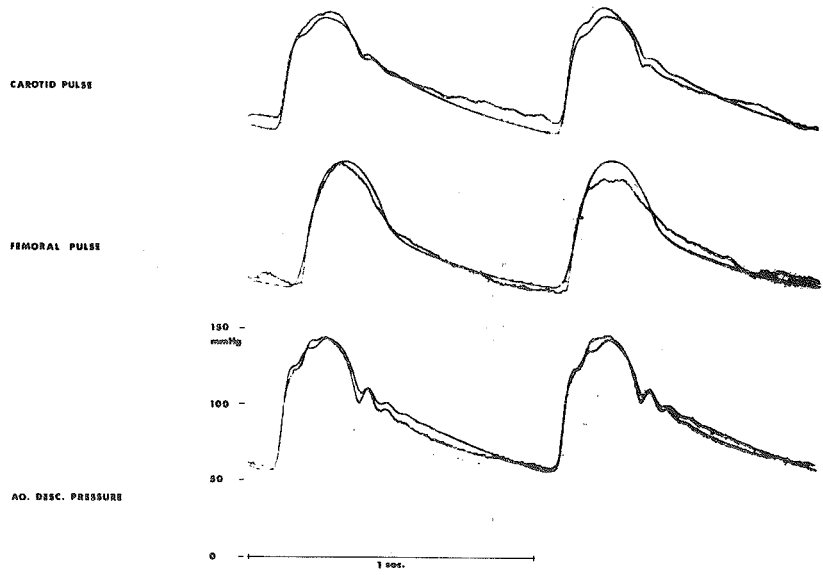


FIG. 4. Superimposed patient and model curves after completion of the simulation procedure as described in Methods. The carotid and femoral pulse in the patient is measured with external pulse pick-ups. The slightly noisy curves are the ones measured in the patient.

Results

Fig. 5 shows the comparisons between all measurements that were performed. The correlation coefficient is r = 0,96 and the regression line is close to the line of identity.

The results are compiled in Table 2. Some of the patients with atrial fibrillation showed quite large estimation errors, the largest being + 42%. The largest deviation found in the patients in sinus rythm was ± 16%, except for one patient with a very low heart rate of 34 beats/min. where the error was -22,5% (patient no. 3). It is to be pointed out that the estimation error was much lower in this patient during excercise.

The reason for the larger estimation errors in patients with aterial fibrillation is the large changes in blood pressure and flow from beat to beat, making an accurate measurement of pulse transmission time difficult. Furthermore,

TABLE 2

Measured hemodynamic variables and estimation error ($\frac{\text{Measured C.O.} - \text{Estimated C.O.}}{\text{Measured C.O.}} \cdot 100$) in the present study.

Patient No.	Sex	Age Years	Blood Pressure mmHg	Heart Rate Beats/min	Cardiac output l/min	Estimation Error %	Remarks
1.	F	55	125/75	80	5,9	+ 15,0	
		55	125/75	120	3,5	÷ 6,0	[P]
2.	F	66	170/80	53	3,1	÷ 13,0	
		66	175/80	78	3,1	÷ 3,1	[P]
3.	F	18	90/40	34	5,8	÷ 22,5	
		18	125/65	56	9,7	÷ 6,0	[E]
4.	F	44	150/80	80	3,5	+ 42,0	*
5.	F	51	100/50	83	3,6	+ 2,5	
		51	110/55	75	3,3	÷ 9,0	[V]
6.	F	40	190/115	98	6,2	+ 6,5	
7.	F	66	135/80	62	4,3	+ 7,0	
8.	F	60	250/170	100	2,7	÷ 11,0	
		60	135/90	96	3,3	÷ 6,0	[D]
9.	F	68	70/55	80—90	2,2	÷ 18,0	*
10.	M	63	170/80	72	4,2	÷ 7,0	
		63	165/80	100	4,7	÷ 6,0	[P]
11.	M	57	130/70	71	5,4	÷ 9,5	
12.	M	58	165/90	59	5,1	÷ 7,5	
13.	M	59	125/70	75	2,8	÷ 4,0	
14.	M	59	130/75	66	4,2	÷ 9,5	
15.	M	60	150/75	69	4,3	÷ 7,0	
16.	M	16	115/75	102	7,0	÷ 15,0	
17.	M	36	95/60	60	3,8	+ 8,0	
18.	M	47	175/110	68	8,3	÷ 16,0	
19.	M	47	120/85	108	4,5	÷ 4,5	
		47	110/70	110	4,1	÷ 7,5	
20.	M	48	130/80	85	5,9	÷ 10,0	[D]
21.	M	59	120/60	67	3,1	+ 16,0	
22.	M	78	150/75	65	3,7	+ 8,0	
		78	140/70	65	5,1	÷ 18,0	
23.	M	49	125/70	48	4,4	÷ 25,0	*
24.	M	59	200/125	80	5,3	÷ 19,0	*
25.	M	64	120/80	78	3,4	÷ 6,0	
		64	120/80	75	3,0	÷ 10,0	[V]
		64	115/85	79	2,7	+ 4,0	[V]
26.	M	66	120/80	100	3,4	+ 9,0	
		66	105/70	85	2,8	0	[V]
		66	100/65	84	2,5	+ 8,0	[V]
		66	85/65	115	1,7	÷ 12,0	[V]
27.	M	57	100/75	100	2,6	+ 4,0	*
		57	110/90	105	2,2	÷ 4,5	[V]
		57	105/85	100	2,0	÷ 10,0	[V]
28.	M	20	135/90	58	4,9	0	
29.	M	27	140/105	77	4,4	÷ 2,5	
30.	M	32	170/100	66	5,0	÷ 4,0	
31.	M	41	135/85	58	4,1	÷ 14,5	
32.	M	46	180/110	80	5,4	÷ 7,5	
33.	M	60	165/85	62	5,2	0	
34.	M	48	220/140	70	4,0	÷ 5,0	
		48	125/70	80	5,3	+ 2,0	[D]
35.	M	49	190/125	84	4,9	÷ 2,0	
		49	105/80	90	5,9	÷ 5,0	[D]
36.	M	60	215/160	84	6,4	÷ 1,5	
		60	150/70	100	7,9	+ 5,0	
		60	105/75	95	6,6	÷ 6,0	[D]
37.	M	32	155/105	56	6,7	+ 4,5	
		32	135/75	62	8,7	+ 8,0	[D]
38.	M	47	195/140	108	5,5	0	
		47	130/105	112	5,8	÷ 11,0	[D]
39.	M	50	225/130	72	7,4	+ 5,0	
		50	120/90	88	8,2	+ 5,0	[D]

P = Pacing, E = Exercise, D = Injection of Diazoxide, V = Volume change, * = atrial fibrillation

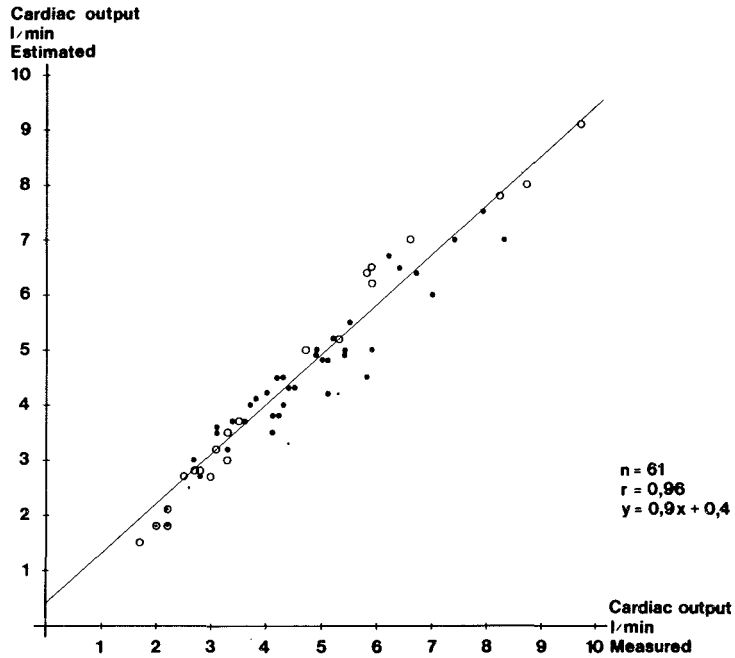


FIG. 5. The relation between cardiac output measured with a standard method and cardiac output estimated from the aortic pressure curve and the pulse transmission time in the aorta. The symbols are as follows:

- ● *Results from patients in sinus rythm at rest.*
- o *Results from patients in sinus rythm after interventions (Pacing, exercise, injection of Diazoxide, blood volume changes).*
- ● *Results from patients in atrial fibrillation at rest.*
- o *Results from patients in atrial fibrillation after interventions.*

he automatic servosystem is not capable of ollowing these rapid changes accurately. An xample of this can be seen in Fig. 6.

Although the automatic servosystem has a oo long time-constant to follow changes from eat to beat, the system is rapid enough to esti- nate changes over a few beats, as have been reviously shown (Brubakk and Aaslid, 1976).

Table 3 shows the correlations and standard eviations found in this study. The correlation oefficient for all measurements is 0.96, im- roving to 0,98 when patients with atrial fi- rillation are excluded. The cardiac output neasurements during interventions are treated ogether, as there is so few of the different ypes. The correlation coefficient for these neasurements is 0,99.

In this study the estimates of cardiac output vas compared with cardiac outputs measured vith an independent method. Fig. 7 demonstrates that the measurement procedure itself can change the cardovascular state and hence the cardiac output. Immediately after applying the face mask of the Douglas bag, the heart rate, blood pressure and cardiac output increase. The peripheral resistance also increases. The cardiac output was measured with the Dye method just before the measurement with the Fick method, veryfying the result of the simulation.

Discussion

Similar to many other methods presented previously, the method described in this paper appears to give values of cardiac output in close correlation with those measured with standard methods. The correlation is similar both at rest and during various interventions.

In order to judge these results, it is impor-

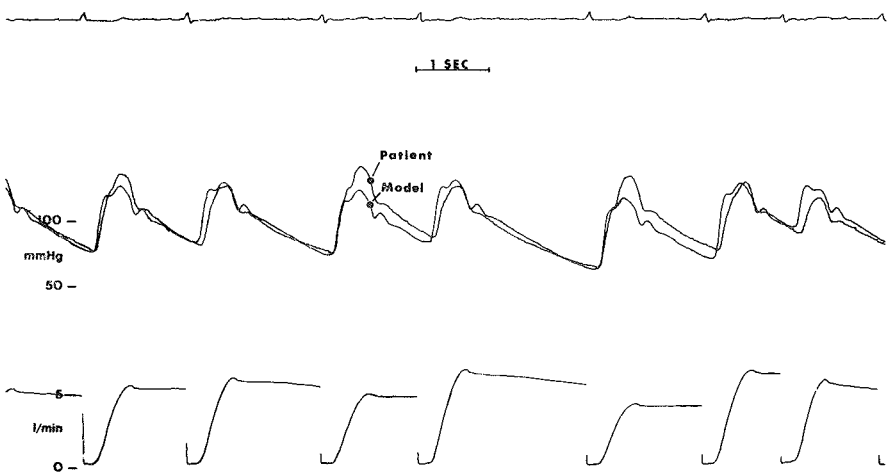


FIG. 6. Simulation of cardiac output in a patient with atrial fibrillation. From top to bottom can be seen ECG, patient and model aortic pressure curve superimposed and at the bottom cardiac output. The cardiac output integrator is reset at the beginning of systole. Not the beat-to-beat pressure changes in the patient, which the automatic servosystem does not manage to follow.

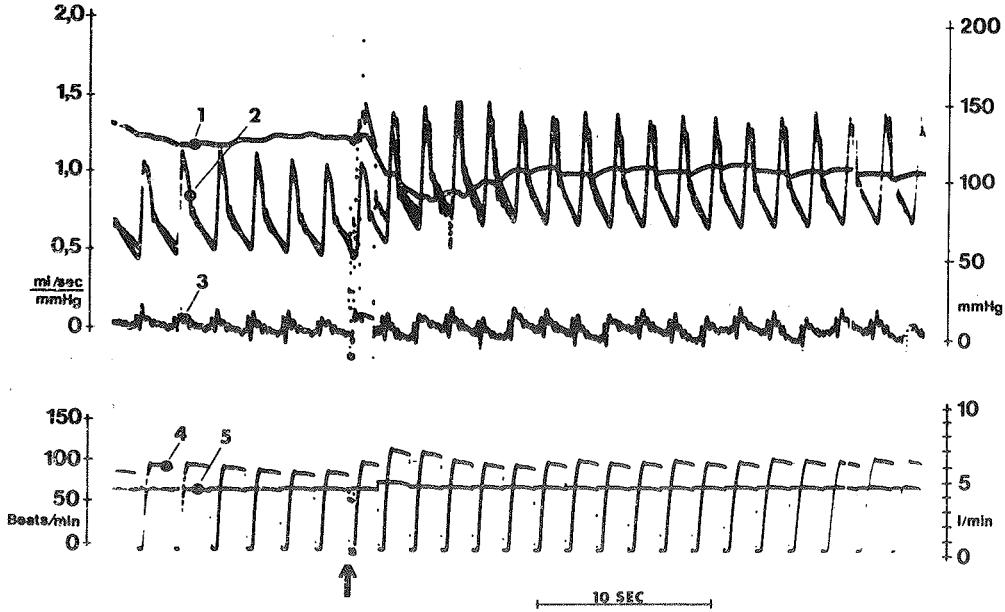


FIG. 7. Changes in the cardiovascular parameters during measurement of cardiac output with the Fick method. The different curves are denoted 1—5.

1. *Peripheral conductance* $\left(\frac{1}{\text{peripheral resistance}}\right)$
2. *Model and patient aortic pressure superimposed.*
3. *Pulmonary artery pressure in the patient.*
4. *Cardiac output.*
5. *Heart rate.The patient starts breathing into the Douglas bag at the time indicated by the arrow.*

tant to remember that the methods used for camparison also have their souce of error and do not measure «absolute» flow. Based on the work of McDonald (1974), it is reasonable to assume that no method used for cardiac output determination can give standard errors better than ± 5—10%.

It is interesting to observe the changes in cardiac output that occured when breathing into the moutpiece of the Douglas bag (Fig. 7). The model faithfylly reproduced this change in cardiac output.

In the methods that have previously been presented for measuring flow from the aortic pressure curve, elasticity of the wessel wall has either been assumed to be constant (Hamilton, 1953) or it is calculated by means of an independent methood of cardiac output determination (Warner et al., 1953, Kouchoukos et al., 1970, Nichols, 1973).

Several studies have demonstrated that wessel elasticity is highly variable from person to person and is dependent upon age and blood pressure (Wagner and Kapal, 1952, Greenfield and Patel, 1960, Brubakk and Aaslid, 1977).

Due to this variability, the methods based on a constant elasticity will be inaccurate. This is particularly the case when sympathomimetic drugs are given. Wiggers and Wegeira (1939) showed in dogs that administration of sympathomimetic drugs will decrease aortic diameter, while increasing distensibility., When calculating stroke volumes from the pressure pulse, a decrease in diameter will lead to an underestimation while an increase in distensibility will lead to an overestimation of stroke volume. As the stroke volumes are generally overestimated when giving sympathomimetic drugs (Kouchoukos et al., 1970), it seems reasonable to assume that the changes in distensibility influence the results more than changes in diameter.

The method based on calibration with an independent cardiac output measurement are more accurate, but have their practical limitations. The traditional cardiac output methods are rather time consuming and can only be performed intermittently. Due to the non-linearity of the aortic pressure-volume realionship, the vessel wall elasticity can change rather rapidly when large changes in blood pressure are encountered (unpublished observations) and simpler methods of calibration would be preferable. In this study, the compliance was calculated from the transmission time in the aorta.

The wave velocity, c, in the aorta is determined by the compliance, C, and the inertance, L, according to the formula

$$c = \frac{1}{\sqrt{L \cdot C}} \qquad (5)$$

(Wetterer und Kenner, 1968).

In our study the inertance is regarded as constant, allowing us to calculate the compliance from the pulse transmission time in the aorta.

The inertance is dependent upon arterial dimensions, according to the equation

$$L_i = k \frac{l}{a} \qquad (6)$$

where l is segment length and a is segment area (Fry, 1959). A constant inertance from person to person would indicate a constant relationship between segment length and area, or that the area and length change in an inverse relation. Our data does not permit the conclusion that the inertance really is constant, but the changes in inertance appear to be small enough to allow us to use the pulse transmission time to calculate compliance. Intertance changes may introduce an error when sypathomimetic drugs are used, but as previously pointed out, the diameter changes probably are of minor importance. Cibulsky et al. (1973), who calculated the cardiac output from aortic pressure curves in the dog, using a formula similar to the one used by Kouchoukos et al. (1970), noted the decreased accuracy of their method following the infusion of isoproterenol. They point out that the main source of error in their approach was the changes in pulse wave velocity following the injection of the drug.

In this paper, the shape of the diastolic pressure curve has been used to indicate total peripheral resistance. The validity of this approach has been confirmed by Bourgeois et al. (1976), who in dogs found a close correlation between the diastolic decay of the descending aortic pressure curve and the flow to the periphery during that beat.

This method of calculating compliance is critically dependent upont the accuracy of the pulse transmission time measurement. Simulations on the model demonstrate that errors of 10 msec in pulse transmission time will give an error of approximately 15% in the cardiac output estimate. The method is therefore diffi-

TABLE 3

Mean difference, standard error of the difference and correlation coefficient between the measured and estimated values of cardiac output.

	n	Mean Difference $\frac{\text{Measured C.O. - Estimated C.O.}}{\text{Measured C.O.}} \cdot 100$ %	Standard Error of the difference %	Correlation coefficient r
All Measurements	61	9	7	0,96
Atrial fibrillation	7	17,5	13	
Sinus rythm	54	7	5	0.98
At rest	33	7	5	0.98
Exercise	1			
Pacing	3			
Volume change	6	6,5	3	0,99
Hypotension	8			
	18			

cult to use when large changes in pressure and flow occur from beat to beat, as demonstrated in the patient with atrial fibrillation (Fig. 6).

The model described in this paper exhibits a linear pressure volume relationship in the aorta. Particularly in older patients this relationship is non linear and hence the compliance value will change when large changes in blood pressure occur. This is however, easy to check using the pulse transmission method. Use of a nonlinear model will greatly simplify this procedure and can make it possible to follow continously changes in cardiac output and peripheral resistance during blood pressure changes (unpublished observation).

The fluid-filled catheter-manometer system used for measuring aortic pressure in the patient will introduce dynamic errors. The dynamic characteristics of this system can be described by the undamped resonant frequency and a dampening factor (Gabe 1972). A pressure step can be applied before or after the actual measurement procedure to determine these characteristics. However, as the procedure for introducing catheters into the bloodstream considerably changes the dynamic characteristics of the system (unpublished observation), this method was not used in this study. The pressure in the model aorta was measured through a model of the catheter-manometer system, and the resonant frequency and damping of this model was changes until the oscillations in the pressure curve after the closure of the aortic valve was similar in patient and model. These oscillations are considered mainly originating from the catheter-manometer system.

The method presented in this paper allows the cardiac output to be computed continuously from the pressure curve. In most cases, use of a reference method for cardiac output determination is not needed. Changes in mean pressure and peripheral resistance are continuously followed, while changes in compliance can easily be measured and necessary corrections made. This method therefore seems well suited for use in intensive care situations. Even if changes in the cardiovascular state can no be followed from beat to beat when large changes in blood pressure occur, the method is rapid enough for most clinical purposes.

Although the results presented here indicate that the method can be used during differend types of intervention, the validity of this approach, particularly when using sympathomimetic drugs, must be investigated. In some of the patients the femoral artery was used for pressure measurements, indicating that more peripheral arteries than the aorta can be used for the calculations of cardiac output from the arterial pressure curve.

Acknowledgement

The help of Ms. Elin Amundsen in investigating the patients and for preparing the figures is greatly appreciated. Dr. R. D. Bradley of the Intensive Therapy Unit, St. Thomas Hospital, London is gratefully thanked for the permission to work in his laboratory and to use some of this measurement data. The collaboration of R. Aaslid, Ph. D. in this study is gratefully acknowledged.

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General Discussion

One purpose of this work was to develope clinical methods permitting measurement of blood flow in the aorta. Both methods presented in this thesis calculate flow indirectly. The method based on ultrasound (Papers I—III) calculates flow from the mean frequency of back-scattered ultrasound in the aortic blood stream. The method based on a model (Papers V—VI) calculate mean flow from the aortic pressure pulse and the pulse wave transmission time in the aorta. Both methods are based on certain assumptions that can introduce errors in the calculation of flow. The methods presented also enable calculation of aortic compliance (Paper V) and measurement of intraventricular blood flow velocities (Paper III).

Measurement of blood flow by the ultrasonic method

The instrument presented is capable of calculating instantaneous mean and maximum velocity of flow the frequency spectrum backscattered from the moving blood (Papers I and III). The mean and maximum frequency estimator used for this purpose was developed during the course of this work and is described in Papers II—III (see also ref. 47, 48). From the form of the mean and maximum frequency curve obtained, the approximate form of the spectrum can be deduced (Papers I and III). If the mean velocity of blood flow across a cross-section of a blood vessel is known, the instantaneous blood flow in that vessel can be calculated by multiplying the cross-sectional area with the recorded mean velocity.

In practical use, four problems are of importance.

- The angle between the ultrasonic beam and the blood stream
- The position of the sample volume of the ultrasonic beam in the thorax.
- The non-uniform illumination of the aortic cross-section
- The high-pass filtering of the received signal.

When measuring blood flow velocity in the ascending aorta transcutanously, the angle between the ultrasonic beam and the blood stream is unknown and the measured velocities will underestimate true velocities by a factor of cosine to this angle (Paper II). As judged from our results and from x-ray data, the exact position of the aorta shows individual differences, and the position must be determined in each subject if absolute values of blood flow velocity are to be determined.

Light (37) claims that absolute values of velocity can be measured in the aortic arch where the blood stream is thought to be nearly tagential to the ultrasonic beam. In one of the subjects studied by us (Fig. 13, Paper II), this is clearly the case, since the vessel lumen is nearly circular. However, recent published results from Light's group (49) as well as our own experience, indicate that this is an exception rather than the rule.

The doppler instrument employed in our study can be used as a continuous wave meter or in the pulsed mode (see introduction). For measurement of mean flow velocity inside the aorta, the pulsed mode must be used. The frequency shift of the ultrasonic beam reflected from moving blood is then measured inside a cylindrical sample volume of approximately 7,5 mm length and 20 mm diameter. This sample volume must lie entirely inside the vessel if true values of mean blood velocity is to be obtained. In our material (Paper II), the aortic diameter varied between 2,1 and 3,3 cm. If the ultrasonic beam is correctly aimed, it should be possible to place the sample volume entirely inside the vessel. This is, however, difficult to check transcutanously and the correct placing of the sample volume is therefore de-

pendent on operator ecperience and skill. When measuring aortic blood flow velocity from the suprasternal notch as shown in Fig. 4, Paper II, it is of importance to note that a position of sample volume must be sought that can give the maximum integral under the velocity curve. This is not always the position where the largest peak velocities can be recorded, as shown in Fig. 2.1, Paper I. Large peak velocities during part of systole have frequently been observed near the aortic velve, probably caused by jets of blood around and behind the valvular cusps.

The placement of the sample volume partly outside the aorta as well as the angle between the ultrasonic beam and the blood strem will cause an underestimation of mean velocity of blood flow in the vessel. The non-uniform illumination of the aortic cross-section, caused by the inhomogenities of the ultrasonic transducer field, and the high-pass filtering of the received signal will cause an overestimation of true velocity, as discussed in Paper II.

These are the resons why the method presented will only permit measurement of changes in blood flow. The ability to do this in a single patient is demonstrated in Fig. 2.2, Paper I and in Fig. 11, Paper II. In aortic insufficiency, the degree of requrgitation can perhaps be calculated. It is of importance to note the difference in velocity profile during systole the diastole, as shown in Fig. 4, Paper III. Because of this, an envelope around the spectrum, as proposed by others (36), will overestimate the amount of requrgitated blood. One assumption that has to be made, is that the aortic cross-sectional area is unchanged in systole and diastole. It is conceivable that the large blood volume pumped with each beat and the large pulse pressure can cause significant diameter changes in the aorta. In patients with small aortic insufficiencies, the amount of blood pumped is difficult to calculate, due to the effect to the high pass filtering of the received signal. Fig. 12 in Paper II demonstrate this, showing the velocity of blood flow going to zero before the end of diastole.

A method is proposed that permits measurement of absolute values for blood flow in the aortic arch. This method is basen on the scanning technique described in Paper II and the theoretical consideration discussed in Paper I. The method is independent of the angle between the ultrasonic beam and the blood stream and the inhomogentities of the ultrasonic beam. Furthermore, the method permits construction of velocity profiles across the vessel as shown in Fig. 14, Paper II.

Measurement of flow by the model method

The basic approach using models for studying cardiovascular function in man is discussed in Paper IV. The model developed is a closed loop model of the cardiovascular system with special emphasis on the left ventricle and the aorta. This model is capable of simulating the behaviour of the cardiovascular system in man with sufficient accuracy (50).

In this study the model has been used for calculating cardiac output from the aortic pressure curves (Paper VI). The basis for these calculations is a method for adapting the aortic pressure curve from the patient to those from the model (Papers IV and V) and the method for calculating aortic compliance discussed in Paper V.

In using this method for calculating cardiac output, the following problems must be considered:

— The method for pressure curve adaptation
— The accuracy of the compliance estimates
— The accuracy of the pressure measurements
— The accuracy of methods used for comparison
— The input impedance to the aorta

Since the location of the catheters in the patient's aorta was checked with fluoroscopy, the measurement of pressure at analogues positions in patient and model was assured. Furthermore, the activation of the left ventricular muscle model was triggered by the ECG from the patient, thus ensuring identical start of systole in patient and model.

In this simulation scheme, different parts of the pressure cruve have been considered to contain different informative values. The systole is considered going from the R-wave of the ECG to the incisura of the aortic pressure curve or to the second heart sound. Since these events probably occur about 10 msec. after the closure of the aortic valve (51), the length of systole is slightly overestimated with our method. Measurement of flow velocity will give a more accurate estimate of ejection time (51). The ventricular parameters described in Paper V are changed until the pressure course during systole is similar in patient and model.

The diastole is considered going from the ncisura of the aortic pressure pulse to the R-wave in the ECG from the next heart beat. The slope of the diastolic curve is regarded as a measure of total peripheral resistance (52). The effect of changing peripheral resistance in the model can be seen from Fig. 3, Paper VI. A lower value of peripheral resistance will increase the slope of the diastolic curve, while a higher resistance value will decrease this slope.

The pressure difference between the model and the patient pressure curve is considered the error criterion. As can be seen from several of the figures (Fig. 30.2, Paper IV, Fig. 4, Paper VI and Fig. 2, Paper V), this difference is less than ± 5 mmHg. An automatic servosystem continuously updates the ventricular parameters and the peripheral conductance, thus permitting calculation of cardiac output even when the state of the system is changing. The capabilities of the automatic servosystem can be seen from Fig. 30.3 and 30.4, Paper IV, demonstrating a time lag of under 5 sec. after the state of the system is changed. In atrial fibrillation where the pressure changes from beat to beat, this time constant is too long in order to follow these changes (Fig. 6, Paper V).

At a certain mean pressure, there is a constant realtionship between the area under the systolic part of the pressure curve and the stroke volume. This factor of proportionality is determined by the elasticity of the vessel wall or the aortic compliance (Δ v/ Δ p, where Δ v and Δ p are incremental changes in pressure and volume respectively).

The aortic compliance shows large individual variations and is dependent on age and blood pressure, as shown in Paper V and discussed in Paper VI. Thus, the vessel wall elasticity must be determined for each patient at each level of blood pressure. This can be done either by measuring the cardiac output with an independent method or by measuring the transmission time of the pressure pulse in the aorta. In Paper V these two methods for calculating aortic compliance have been compared, showing close correlation. Puls transmission time can be measured noninvasively by using pulse pick-ups on the carotid and femoral artery. Pulse transmission time was therefore used for calculating aortic compliance (Paper VI).

One of the assumptions made in using pulse transmission time for calculating aortic compliance, is that the inertance in the system can be considered constant, as the pulse wave velocity, c, is determined by

$$c = \frac{1}{\sqrt{L \cdot C}}$$

where L is inertance and C is compliance (53).

Our results seem to indicate that this is a reasonable approximation (Paper V).

The method is critically dependent on correct measurement of pulse transmission time, the principle of which is shown in Fig. 4, Paper V. An error of 10 msec. in pulse transmission time will give an error of approximatly 15% in the cardiac output determination. The mean error in the cardiac output estimates was 9% for all subjects studied in Paper VI, increasing to 17.5% in subjects showing atrial fibrillation. In single subjects, large errors were found, being + 42% in a patient with atrial fibrillation and -22.5 and -25% in two subjects in sinus rhytm. It is of interest to note that these subjects had slow heart rates, 34 and 48 beats pr. min. respectively, and that the error in estimated cardiac output was considerably reduced when the heart rate was increased in one of the subjects. The reason for this is not clear. An underestimation of compliance will occur if the inertance value is higher than assumed. Since the inertance is proportional to cross-sectional area (54), aortic dilatation caused by the large stroke volume might be an explanation. However, since the stroke volume was not significantly decreased in the one patient where the heart rate was increased, this does noe explain why the estimation error in cardiac output is smaller during right ventricular pacing. This last phenomenon could perhaps be explained by the fact that impedance to ejection, particularly the inertial part, is incresed at low frequencies (55).

It can therefore be suggested that inertance values must be calculated on an individual basis in patients with slow heart rates and large stroke volumes (Paper V).

The pressure in the aorta was measured via a cathetermanometer system. As has been pointed out in the introduction, it is difficult to obtain a satisfactory and reproducible frequency response of such a system when used in clinical practice. In order to overcome this

problem, the pressure in the model aorta was measured through a model of the catheter-manometer system, where the frequency response and damping could be changed so that the high frequency oscillations in the pressure curve resembled those recorded from the patient. An example of this can be seen in Fig. 1, Paper VI. The zero line and calibration of the system were frequently checked in order to compensate for drift and changes in position of the patient.

The cardiac output estimated by the model was compared to that measured by an independent method, using the Fick prinsiple, dye- or thermodilution. None of these methods measure absolute flow, but have been found to give results within ±5 to ±10% when checked with electromagnetic flowmeters or compared with each other (43) in serial measurements. Our own studies on reproducability gave similar results (Paper V).

One problem that has been illustrated in this study, is that the methods used for cardiac output determination can change the state of the cardiac vescular system considerably. This is demonstrated in Fig. 7, Paper VI, where the cardiac output and blood pressure increase when the patient starts breathing into the face mask of a Douglas bag.

The peripheral resistance is obtained by dividing the mean blood flow by the mean blood pressure. This procedure is only valid if the pressure and flow pulse curves are exactly similar in shape. In the aorta the flow and pressure pulses are not similar, indicating that the system is not solely resistive, but also contains inertial and elastic elements. The proper term for the resistance in these cases is impedance. The impedance is frequency dependent, but in the normal ascending aorta the frequency dependent part of the impedance is very low. This is the explanation why the energy cost of pumping blood is very low at any heart rate (56).

The input impedance describes the ratio of oscillatory pressure to flow out of the heart and is modified by reflection (57). In our study the pressure in the aorta was measured, and the ventricular parameters are changed to produce a model pressure curve similar to that measured in the patients aorta. In the model, a flow pulse (Fig. 30.2, Paper IV), can be observed in the aorta. The shape of this flow pulse is dependent on the ventricular parameters selected. No measurement of flow pulse was performed in this study, and consequently the input impedance is not known in the simulations presented here. However, since we consider only the area under the flow curve, i.e. stroke volume, this does not introduce an error.

A combination of the ultrasonic method (Paper II) and the model method (Paper VI) can make a check of input impedance possible. Furthermore, as the model makes estimation of changes in left ventricular muscle papmeters possible if the filling volume of the left ventricle does not change (Paper IV), model left ventricular muscle parameters could be compares with left ventricular function parameters derived from the velocity curve (58).

Aortic compliance

As shown in Paper V, the aortic compliance will increase with increasing age of the patient. This will change the form of the pressure pulses and thus augment impedance to ejection. Figs. 3a and 3b show flow and pressure pulses in the ascending aorta and illiac artery in the model at two different levels of compliance. The canges in the pressure and flow pulses as they travel away from the heart can clearly be seen. When the compliance decreases (Fig. 5b), the pulse pressure in the aorta increases. Furthermore, maximum flow in the ascending aorta appears long before maximum pressure is reached, thus increasing the impedance to ejection in late systole. It can also be seen that the pulse wave velocity in the aorta has increased, so that the reflected pressure wave will reach the aortic valve while it is still emptying, thus incrasing further the energy required for ejection. This is in accordance with the work if O'Rourke (59), observing considerable increase in pulsatile work of the left ventricle following stiffening of the aortic wall.

Thus. the calculation of aortic compliance might be of considerable interest. In hypertensive patients with stiff aortas, the load on the heart might still be considerable even when the diastolic pressure and preipheral resistance have been lowered with drugs.

Intraventricular blood flow

The function of the heart is dependent on an adequate function of the valvular appartus. Using utltrasound, blood flow velocity can be

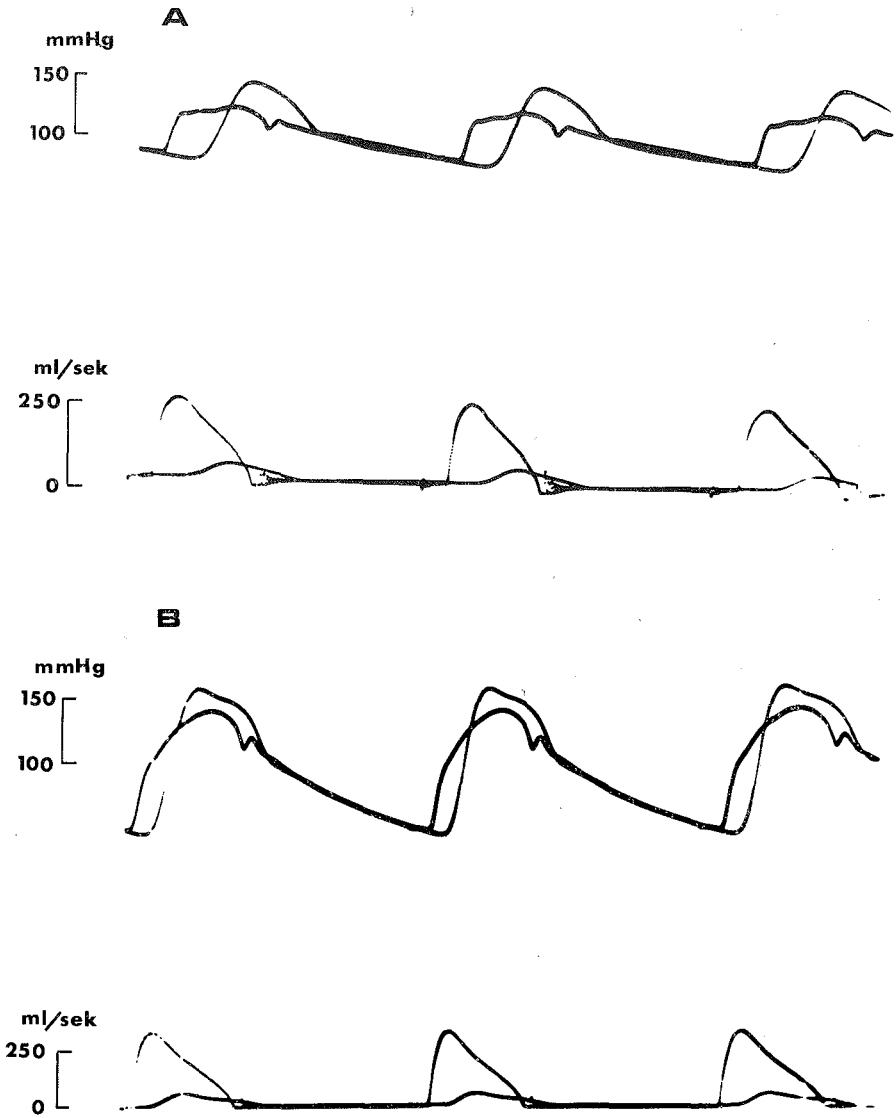

FIG. 3. Pressure and flow pulses in the aortic arch and the illiac artery of the model.
In A C_{ao} *= 1.21 mmHg/ml*
In B C_{ao} *= 0.41 mmHg/ml*

measured inside the heart, as demonstrated in Paper III. In this paper a method for determining the position of the sample volume is described. From the ECG, the timing of the velocity signal relative to the heart cycle can be estimated. Even if the position of the valves relative to the thoracic surface can vary from person to person, their relative position will be fairly constant. Thus, by using this anatomical knowledge as well as the form and direction of the velocity curve the blood flow in the different valve areas can be identified.

In valvular lesions, changes in the normal curve patterns can be found. In stenosis, the velocity of blood flo through the valve will incrase (Fig. 5, Paper III). In valvular insufficiency, velocities will appear during a period of a heart cycle when the valve is closed, as seen in Fig. 8, Paper III. Thus, the study of intraventricular blood flow might be of interest for diagnostic use particularly when combined valvular lesions are present.

The angle between the blood stream and the ultrasonic beam is unknown. The jet like flow thorugh the mitral valve is, however, directed towards the left anterior thoracic surface, making an approximation of the angle between the ultrasonic beam and blood stream of zero reasonable. From the maximum velocity present in the jet, the pressure drop across the valve can be calculated using the Bernoullis equation, assuming that viscous losses can be neglected (60, 61).

When stenosis are encountered, the doppler instrument must be used in the continuous mode, since the range-velocity product described in the introduction is exceeded. Thus, all velocities in the beam are measured. This does not introduce an error, however, since the maximum velocities encountered in the jet far exceed other velocities present.

Final comments

The two methods presented in this thesis differ in one important aspect. The ultrasonic method is a *measurement* method, enabling us to study flow patterns which have been difficult to record previously. The model method is a tool for *analyzing* cardiovascular data, with a far wider application than has been demonstrated here. Apart from its use as an educational tool, the model can be employed for analyzing experimental data and for simulating the cardiovascular behaviour in patients. This can be useful for studying the reaction of different patients to for instance drugs or right ventricular pacing.

A combination of the two methods might be the most fruitful avenue for further exploration. The accuracy of the doppler method for measuring beat-to-beat changes in aortic flow can be determined by comparing data from this method with the results obtained from the model. From the aortic velocity curve and the aortic pressure curve, the input impedance can be determined. This information can be used for improving the calculation of stroke volume from the aortic pressure curve.

Aortic flow velocity and acceleration are sensitive indicators of left ventricular performance (4). By using the model method, left ventricular muscle function can probably be determined under certain assumptions (Paper IV). Thus, a combination of data from the two methods can give new insight to the problem of judging left ventricular function in man.

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