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Abstract

Methods for extraction of physiological information from ultrasonic measurements of pulsatile vascular dynamics from the fetal descending aorta are presented. The analysis is based on a simple dynamic volume balance model and geometric arguments. The ratio of vessel elasticity and the peripheral resistance may be identified on-line. The identified parameters may be utilized for on-line estimation of relative importance of chronotropic, inotropic, and vessel dependent causes to changes in blood flow. A new principle for real-time blood flow measurement based on ultrasonic data is presented.

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Mathematical notations

Measurements:

d_A Diameter measurement at site A [m]

d_B Diameter measurement at site B [m]

Modelling notations:

σ Vessel wall tension [N/m^2]

r Vessel radius (=1/2 inner-to-inner wall diameter) [m]

r_A Vessel radius at point A [m]

r_B Vessel radius at point B [m]

r_0 Vessel radius in asystolic equilibrium [m]

r_{0A} Equilibrium vessel radius at site A [m]

r_{0B} Equilibrium vessel radius at site B [m]

i Blood flow [m^3/s]

i_{in} Inflow of blood to a vessel segment [m^3/s]

i_{out} Outflow of blood from a vessel segment [m^3/s]

h Vessel wall thickness [m]

p Pressure [N/m^2]

E Young's module of elasticity [N/m^2]

R Total peripheral resistance [$(N/m^2)/(m^3/s)$]

V Volume [m^3]

ε Vessel wall strain [N/m^2]

L Length of vessel segment between measurement sites [m]

ϱ Density of blood [kg/m^3]

$f_\heartsuit$ Heart rate [Hz]

t Time [s]

INTRODUCTION

The significance of pulse wave propagation properties for cardivascular physiology was recognized early, see MacDonald [1]. It has recently become possible to study volume pulses in arterial vessels of the human fetus [2], [3], [4]. Ultrasonic equipment may thus be used for recording and measurement of the pulsatile motion of diameter in the fetal aorta.

Noninvasive measurements often give indirect information. The extraction of relevant physiological information from vessel diameter-time records is thus not self-evident [5], [6], [7], [8]. Therefore it may be necessary to make an interpretation via a mathematical model to obtain some desired information. Mathematical models are usually formulated in terms of variables (signals, states) and parameters (physiological constants). The purpose of the model is decisive in the choice between a simple function of time and more complicated static or dynamic models. Models of motion are in general dynamic because they handle situations where equilibria do not occur *in vivo*. Static models describe only equilibria or mean values and are therefore often unsatisfactory to interpret a physiological course of events. Descriptions by functions of time seldom give clues to physiological interpretation.

Mathematical models are useful for measurement interpretation only if they relate to measurable signals. However, also in a sparse model only a small fraction of the model variables are available for direct measurement - in our case the blood vessel diameter. It is often necessary to compute other variables by using unknown vessel model parameters such as elasticity and peripheral resistance. The model complexity therefore needs to be chosen with respect to the information contained in the measurements. Reversely, it is also critical that the measured signal really contains the desired information.

In this paper we study what can be obtained by physiological interpretation of the recordings of pulsatile motion of aorta. Our aim is to develop non-invasive methods for on-line estimation of blood flow and characteristics of circulation based on recording of the pulsatile motion of a blood vessel. We choose a dynamic flow balance model and formulate a simple model in terms of vessel wall elasticity, peripheral resistance and the vessel radius at asystolic equilibrium. It is assumed that no information is available concerning equlibrium vessel radius, vessel wall elasticity or peripheral resistance. Neither is the ejection volume from the heart nor the pressure of blood known. A

new principle for blood flow measurement is presented. A feasibility study is made to show that different causes to changes in blood flow such as peripheral resistance, vessel elasticity, chronotropic and inotropic effects can be monitored on-line via diameter measurements.

The paper therefore describes the kind of physiological information that may be extracted from the given diameter records.

MATERIALS AND METHODS

Instrumentation

The proposed methods were intended for use with an ultrasonic equipment for recordings of the pulsatile motion of the descending fetal aorta, see Gennser *et al* [2]. The diameter of the vessel was measured momentarily in two different transsectional planes simultaneously by echo following detectors. The length of the vessel segment between the measurement sites was denoted L [m].

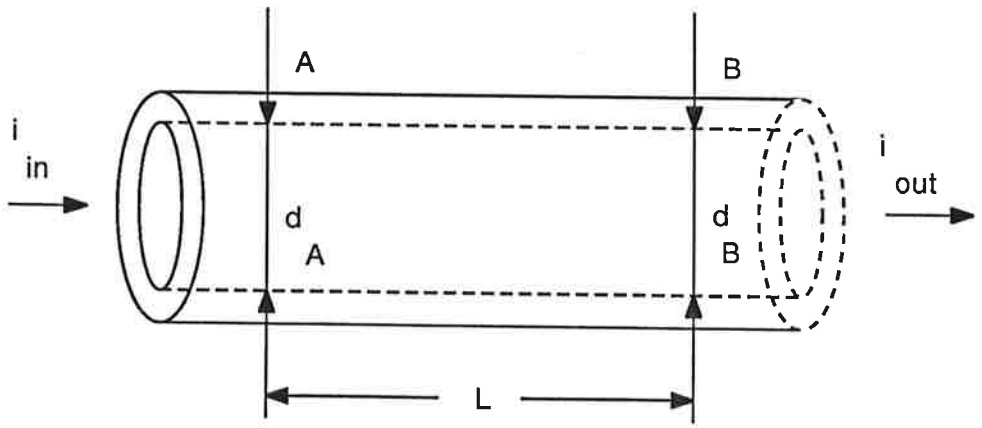

Figure 1. Segment of arterial vessel with two measurement sites A and B.

Mathematical models

A model of pulsatile motion has been formulated as a simple dynamic volume balance model determined by equations of blood pressure, total resistance to blood flow in the aorta, and the outflow of blood to peripheral tissues. The mathematical model is based on volume and force balances as well as geometric analysis. Modelling of wave

reflections, blood viscosity, and longitudinal vessel movements has been ignored. The following equations are fundamental:

ASSUMPTION 1:

The pressure p and the blood flow i are related as

$$p = Ri \tag{1}$$

where R denotes the peripheral resistance. □

ASSUMPTION 2:

The vessel wall tension σ and the strain ε are related as

$$\sigma = E\varepsilon \tag{2}$$

where E denotes Young's modulus of elasticity. □

ASSUMPTION 3:

The vessel has a circular section with vessel wall thickness h and radius r. □

The wall tension σ and the pressure p are related by a force equilibrium via an expression derived from assumptions 1-3.

$$p = \frac{h}{r}\sigma \tag{3}$$

This equation is often related to as Laplace's law. Elimination of vessel pressure p and wall tension σ gives a formula for the pressure's dependence on the vessel geometry.

$$i = \frac{Eh}{R}\left(\frac{1}{r_0} - \frac{1}{r}\right) \tag{4}$$

We need to describe the blood inflow i_{in} and the outflow i_{out} of a vessel segment in order to explain pulsatile motion.

ASSUMPTION 4:

The accumulated blood volume V in the vessel segment of length L [m] between the two measurement sites A and B of the ultrasound equipment is determined by the difference between inflow i_{in} and outflow i_{out} according to the volume balance differential equation:

$$\frac{dV}{dt} = i_{in}(t) - i_{out}(t) \tag{5}$$

□

Development of (5) according to appendix 1 gives an equation for the blood accumulation expressed in physiological parameters of the assumptions and the the measured signals

$$\frac{\pi L}{8}\frac{d}{dt}d_B^2(t) = -\frac{Eh}{R}\frac{1}{d_A(t)} + \frac{Eh}{R}\frac{1}{d_B(t)} + \frac{Eh}{R}\left(\frac{1}{2r_{0A}} - \frac{1}{2r_{0B}}\right) \tag{6}$$

Notice that (6) only contains physiological parameters and geometrical variables. The pulsatile motion thus follows a differential equation with parameters Eh/R, r_{0A}, and r_{0B}. The unknown parameters may then be estimated via measurements of $d_A(t)$ and $d_B(t)$.

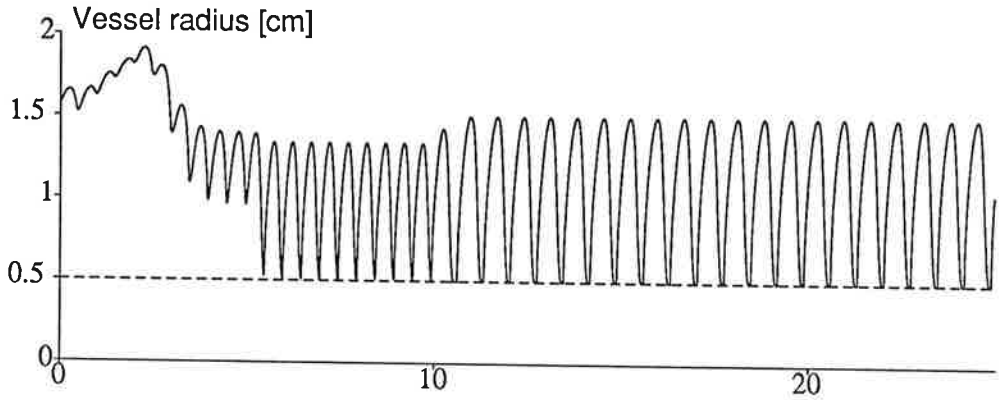

Figure 2. Simulated pulsatile variations of the vessel radius [cm] vs. time [s]. The dotted line denotes equilibrium radius r_0.

RESULTS

A new method to measure blood flow

The estimated parameter values may be utilized in a new method for measurement of blood flow. It is possible to calculate the blood flow at any time instant through the expression (4) if Eh/R and r_0 are known. A mathematical motivation is found in appendix 2. The principal steps of a blood flow estimation algorithm are as follows:

i. Estimate Eh/R and r_0 from the dynamics of (6) via least squares identification.

ii. Compute the blood flow via (4) and the diameter measurement.

$$i(t) = \frac{p(t)}{R} = \frac{\widehat{Eh}}{R}\left(\frac{1}{\widehat{r}_{0B}} - \frac{2}{d_B(t)}\right) \tag{7}$$

where Eh/R and r_0 are replaced by their estimated values.

iii. In the case of a noisy measurement it is preferable to replace d_B in (6) with a filtered value $\widehat{d}_B$ obtained from the following filter

$$\frac{\pi L}{8}\frac{d}{dt}\widehat{d}_B^2(t) = -\frac{Eh}{R}\frac{1}{d_A(t)} + \frac{Eh}{R}\frac{1}{\widehat{d}_B(t)} - k(\widehat{V}(t) - V_{AB}(t)) \tag{8}$$

with $\widehat{V}$ and V_{AB} as volumes contained in the vessel segments between the transsectional planes at the measurement sites.

$$\widehat{V}(t) = \frac{\pi L}{4}\widehat{d}_B^2(t) \tag{9}$$

$$V_{AB}(t) = \frac{\pi L}{12}(d_A^2(t) + d_B^2(t) + d_A(t)d_B(t)) \tag{10}$$

This is a Kalman type filter, see Jaswinski [9], based on the model (6) with a correction term to assure a matching between model and measurement of the vessel segment's blood volume. □

As an alternative to (7) it is possible to calculate the the stroke volume. This may be approximately determined by integration of the blood flow i_{in} over the time interval between two heart strokes.

Factor analysis in monitoring of blood flow

The blood flow may be monitored after on-line estimation of parameters Eh/R and r_0.

$$i = \frac{Eh}{R}\left(\frac{1}{r_0} - \frac{1}{r}\right) \tag{3}$$

The proposed method of analysis also allows a quantitative discrimination between the different causes to changes in blood flow. Comparisons are easy to make with respect to some reference state of blood flow i_{ref}, elasticity E_{ref} and peripheral resistance R_{ref} indicated by subscript 'ref'. Subscript '0' indicates equilibrium vessel radius. It may be natural to choose maximal flow of systole, minimal flow of diastole or a mean value as reference level together with representative values of peripheral resistance and elasticity.

$$i_{ref} = \frac{E_{ref}h}{R_{ref}} \cdot \left(\frac{1}{r_{0ref}} - \frac{1}{r_{ref}}\right) \tag{11}$$

A different blood flow i may be caused by changes in blood pressure and by changes in peripheral resistance. The relative change in blood flow is

$$\frac{i(t)}{i_{ref}(t)} = \frac{Eh/R}{E_{ref}h/R_{ref}} \cdot \frac{1/r_0 - 1/r(t)}{1/r_{0ref} - 1/r_{ref}(t)} \tag{12}$$

The blood vessel dependent relative change in blood flow due to changes in elasticity or peripheral resistance is determined via

$$\frac{Eh/R}{E_{ref}h/R_{ref}} \tag{13}$$

and the heart dependent change is

$$\frac{1/r_0 - 1/r(t)}{1/r_{0ref} - 1/r_{ref}(t)} = \frac{r_{ref}(t)}{r(t)} \cdot \frac{r_{0ref}}{r_0} \cdot \frac{r(t) - r_0}{r_{ref}(t) - r_{0ref}} \tag{14}$$

The chronotropic change is determined by the ratio

$$f_{\heartsuit 2}/f_{\heartsuit 1} \tag{15}$$

and the inotropic change is obtained from (14) as

$$\frac{r_{ref}(t)}{r(t)} \frac{r_{0ref}}{r_0} \frac{r(t) - r_0}{r_{ref}(t) - r_{0ref}} \frac{f_{\heartsuit 1}}{f_{\heartsuit 2}} \tag{16}$$

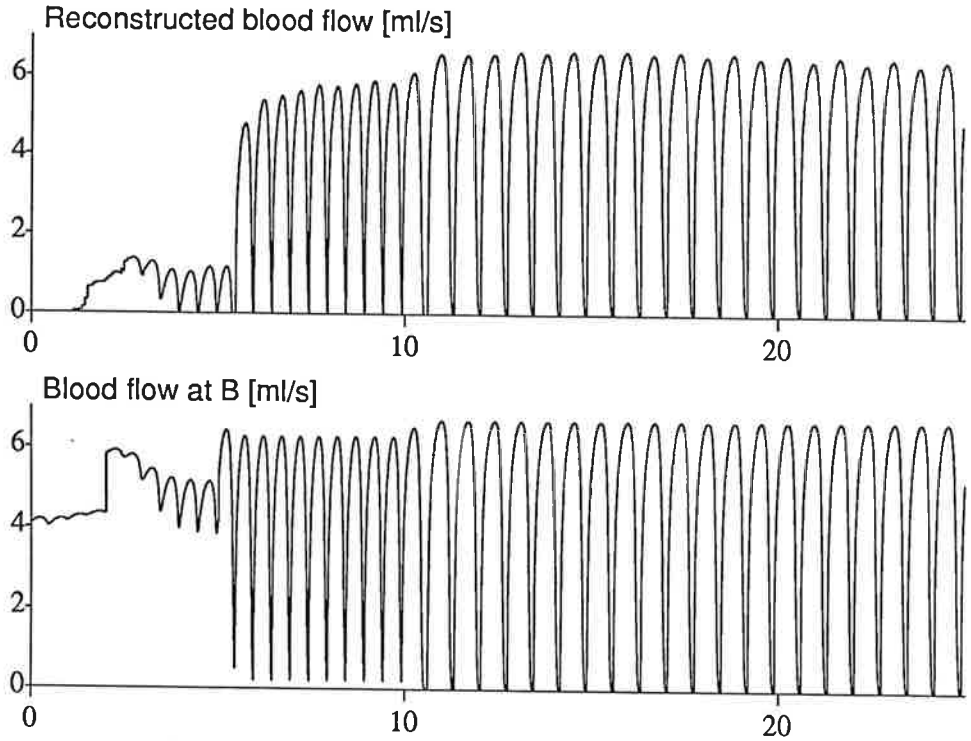

Figure 3. The estimated, 'reconstructed' blood flow (*upper*) computed via the mathematical model and with estimated parameter values. The simulated 'real' blood flow (*below*). All graphs vs. time [s].

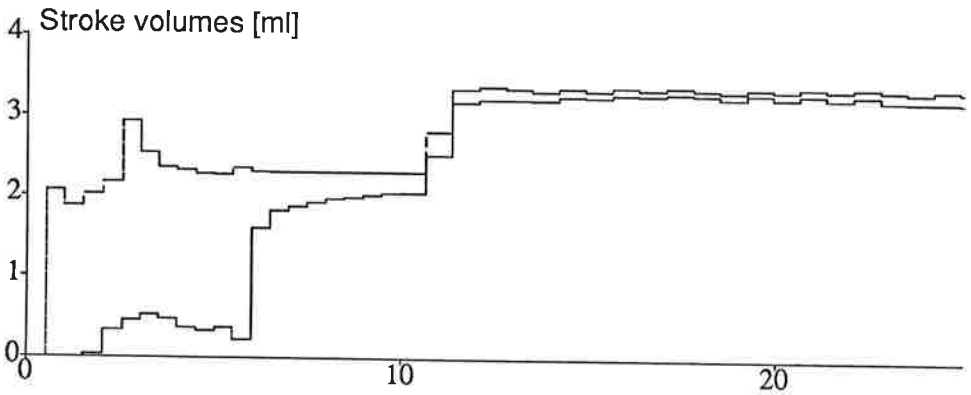

Figure 4. The estimated, 'reconstructed' stroke volume [ml] of blood flow (*lower trace*) computed via the mathematical model and with estimated parameter values. The simulated 'real' stroke volume of blood flow (*upper trace*). All graphs vs. time [s].

Simulation results

A simple model of pulsatile motion with computations and parameter estimations as presented above was simulated in Simnon [10]. The simulations were started with the following initial parameter settings:

- Heart rate $f_{\heartsuit} = 2$ [Hz]

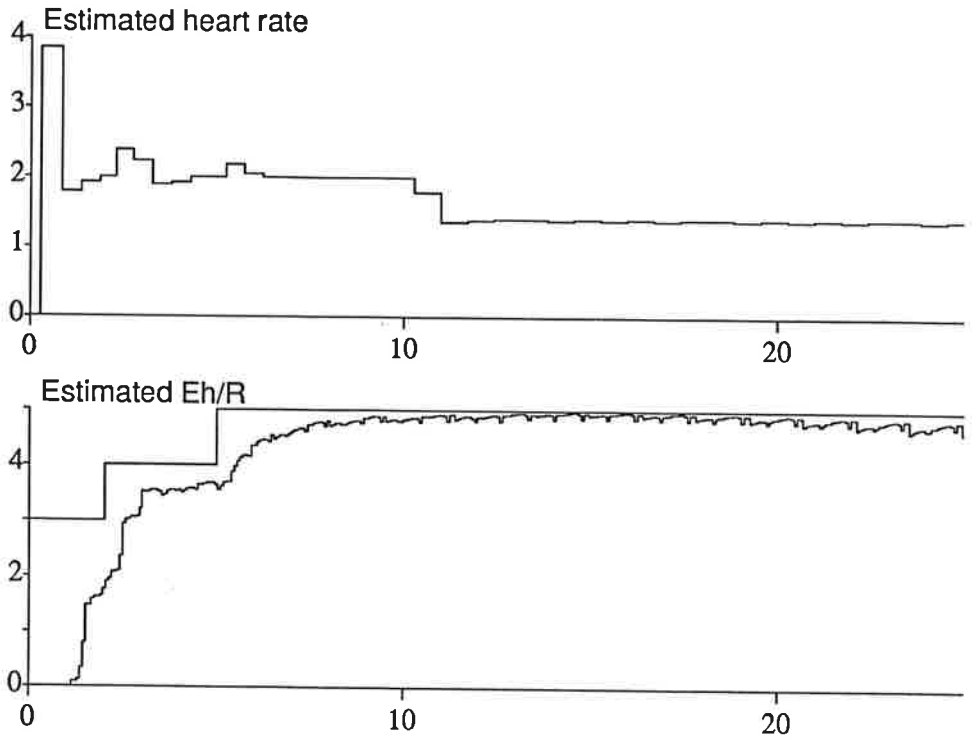

Figure 5. Estimated heart rate [Hz] vs. time [s] (*upper*). The 'true' value of Eh/R [10^{-5}. m^4/s] and the estimate $\widehat{Eh/R}$ vs. time [s] (*lower*).

- Vessel elasticity $Eh = 3.0 \cdot 10^3$ [N/m]
- Total peripheral resistance $R = 1.0 \cdot 10^8$ [Ns/m^5]

The simulation started at time 0 and the parameter estimation started one second later. Three rather drastic physiological events were simulated in the model namely:

1. The vessel elasticity E was increased from $3.0 \cdot 10^3$ [N/m] to $4.0 \cdot 10^3$ [N/m] at time 2 [s].
2. The total peripheral resistance R was decreased from $1.0 \cdot 10^8$ [Ns/m^5] to $0.8 \cdot 10^8$ [Ns/m^5] at time 5 [s].
3. The heart rate $f_\heartsuit$ was decreased 30% at time 10 [s] without any change in blood flow.

A simulation of the radial variations is shown in Figure 2. The proposed blood flow estimation algorithm was simulated (Figures 3,4). When Eh/R changed, the parameter estimation quickly reacted and caused a rapid self-recalibration of the blood flow measurement.

It was also shown to be possible to follow and discriminate quantitatively between

different causes to changes in pulsatile motion (Figure 5).

The estimation was made by a least squares method [11] to obtain both good accuracy and good tracking capability of the changing physiological parameters. The parameter estimates converged towards the correct parameter values and computations based on the estimated parameters gave reliable results. When noise affected the estimation, a systematic error appeared due to the properties of least squares estimation (Figure 5). The estimate of r_0 was more sensitive to noise than that of Eh/R. The noise dependent parameter errors then gave a bias in the blood flow estimation (Figure 4).

It is seen from the graphs that the estimated parametric values track the 'real' values so well that the estimated parameters may be used in a Kalman filter type algorithm [9] based on (4-6) for estimation of blood flow (Figure 3,4).

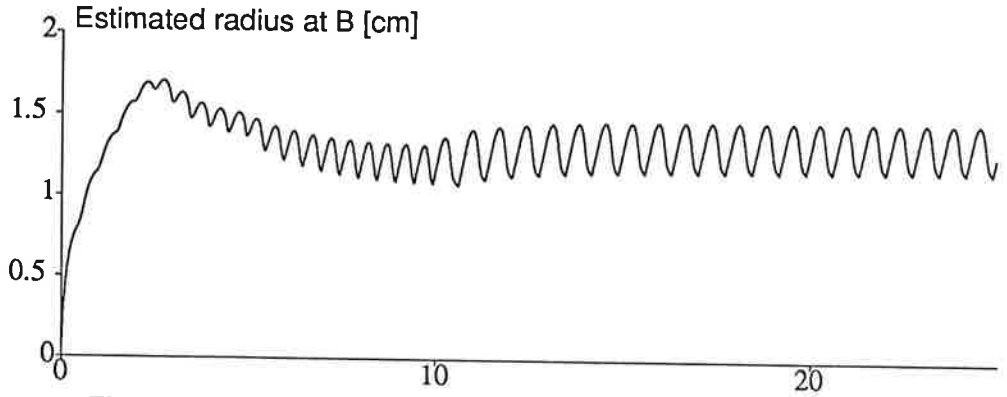

Figure 6. The simulated 'reconstructed' pulsatile radial motion [cm] at site B vs. time [s].

DISCUSSION

Pulsatile wave form patterns

The central problem is to decide what is the kind of information that can be extracted from the given measurements. The relationship of features such as pulse amplitude or relaxation velocity to a state of disease or to the physiological model parameters is certainly complex [8]. The geometric form of a recorded pulse is discussed elsewhere [7] and is well in agreement with the simulation results of assumptions 1-4. A qualitative investigation of the mathematical model (4-5) indicates dependence according to the table below. The following features may be extracted from the recordings of pulsatile motion as indicated in the following table:

	Wave form feature	**Dependence of:**
—	Base line drift	Eh, R, $f_{\heartsuit}$, p
—	Pulse amplitude	Eh, R, p
—	Pulse frequency	$f_{\heartsuit}$
—	Relaxation time constant	Eh, R

The quantitative relationships seem in general too difficult to allow direct extraction of parametric information from the wave form geometry. It is therefore motivated to proceed with model-based estimation of parameters.

Model complexity

Mathematical models are useful for measurement interpretation only if they relate to measurable signals. However, also in a sparse model only a small fraction of the model variables are available for direct measurement - in our case the blood vessel diameter. It is often necessary to compute other variables by using unknown vessel model parameters such as elasticity and peripheral resistance. The model complexity therefore needs to be chosen with respect to the information contained in the measurements.

The chosen model may be criticized to be too simplistic. An impedance model or a model based on a partial differential equation [1] might be suggested as alternatives. However, only two measurements with dynamic effects need explanation. The suggested model is chosen from the standpoint that it is helpful in the interpretation of

physiological measurements. A partial differential equation model is then more complex than what is motivated by the analysis of measurements.

We avoid the traditional impedance models by explicit modelling of the blood flow and volume balance (5). The model is then sufficient to explain the dynamic properties of vessel motion as observed in the measurements.

The low pass filter properties of the proposed model are compatible with the results reported by Anliker *et al.* [12]. They showed that the logarithm of the pulse amplitude along a blood vessel decreases linearly with the distance from the heart. This observation is in harmony with a model of cascaded low pass filters to represent the vessel segments. In our measurement situation we thus measure dynamics of one such segment.

Vessel elasticity and peripheral resistance

We have shown the parameter Eh/R and the equilibrium radius r_0 may be estimated from the measurements. It would be of physiological interest to know the blood vessel wall elasticity and the peripheral resistance. It is therefore natural to seek separate values of E, R, and h.

The vessel parameters Eh and R are unfortunately inseparable by identification and data analysis in the present test situation. Separation requires a pressure measurement or a force related measurement such as blood pressure p or vessel wall tension σ. Unfortunately, direct pressure measurements can not be performed on fetal subjects. Without a blood pressure measurement it is only possible to estimate the compound parameter Eh/R. Elastic effects and peripheral resistance effects are therefore inseparable in the present test situation. This means difficulties to separate between elasticity effects and peripheral resistance effects. The peripheral resistance R may therefore be calculated only in cases where it is reasonable to assume that the vessel elasticity Eh does not vary. The problem of separate identification of E and R is a standard problem of the same nature as in the following example:

EXAMPLE 1

Compare with the problem of a lowpass filter with input voltage V_1, output voltage V_2 and time constant RC.

$$V_2(s) = \frac{1}{1 + sRC} V_1(s) \tag{17}$$

Notice that R and C may not be estimated via measurements of the input voltage V_1 and the output voltage V_2. The time constant RC may however be estimated. A separate estimate of R or C requires a measurement of electrical current. □

Separation between elasticity effects and peripheral resistance effects is therefore not possible by a direct approach in a test situation with fetal subjects. A simultaneous recording of blood pressure p in e.g. *a. brachialis* may however be possible in adult subjects. The elasticity of a vessel may then be estimated by direct solutions of equations (1) and (7). Measurements of pressure waves would also allow calculation of Eh via the well-known Moens-Korteweg formula $c = \sqrt{Eh/2\varrho r_0}$ that relates pulse velocity with elasticity and blood density [1] (ch. 9). A calculation of the peripheral resistance R is then simple as a direct solution from estimated Eh/R and Eh. Such an approach would be of interest for investigation of arteriosclerosis but is not applicable in our test situation because pressure waves cannot be measured.

Changes in blood flow

The changes in blood flow may have different causes and the measurements may be used to monitor the relative importance of such different causes. The blood flow may change for heart dependent causes and blood vessel dependent causes: chronotropic and inotropic changes of the heart activity as well as changes of peripheral resistance and vessel elasticity. These primary physiological causes and their correspondence with the measurable quantities of the present experiment are given as follows:

Heart dependent increase of blood flow

Changes in pulse frequency is easy to measure in time records. A change in blood pressure is primarily reflected in a base line shift of the diameter records. Changes in blood flow due to heart frequency and blood pressure give the same reaction in a drifting base line of d_A or d_B. The two causes may be distinguished by monitoring the heart frequency in the recordings of blood vessel diameter. No change is expected in the vascular parameters Eh/R. This is verified by Okada [8] who found no effect of the heart rate on the transmission time.

Vessel dependent increase in blood flow

A changing peripheral resistance and a changing vessel elasticity are both reflected in changes of the monitored parameter Eh/R.

The close relation between the two parameters is not just a matter of measurement. A contraction of vessel wall muscle may be interpreted as an increased vessel wall elasticity within the monitored vessel segment and as an increase of the peripheral resistance downstream.

Further research

Noninvasive methods often give indirect information and such methods may sometimes be difficult to calibrate. An evaluation of the suggested method for clinical practice requires at least two more steps:

- A laboratory test with simultaneous measurements of blood flow and vessel diameter for determination of accuracy and sensitivity to measurement noise and modelling errors.
- A clinical test with comparison to other methods of blood flow measurement such as methods based on doppler shift analysis.

CONCLUSIONS

A new principle for blood flow measurement from ultrasonic measurements was presented. A simple volume balance model was formulated and the following features have been exploited to formulate the new, proposed measurement principle:

- Monitor blood flow via measurements of the vessel diameter and estimation of the unknown Eh/R. The blood flow is computed via the formula

$$i = \frac{\widehat{Eh}}{R}\left(\frac{1}{r_0} - \frac{1}{r}\right)$$

  where $\widehat{Eh/R}$ denotes the estimate of Eh/R.

The method is thus based on measurement of vessel diameter variations. It provides also quantitative on-line analysis of factors determinating the blood flow according to the following outlines:

- The measurement and the estimation allow separation between different causes to changes in blood flow.
  - A flow change due to a rise in pressure is characterized by a constant Eh/R and an increased vessel diameter and therefore a baseline shift in the recorded signal.
  - An increased blood flow due to decreased peripheral resistance is characterized by an increased Eh/R and a decreased vessel diameter.

The method was studied with simulation of the differential equations and it was found that the method works well also on noisy data.

APPENDIX 1

In this appendix is derived a mathematical model for pulsatile motion. The model is formulated in terms of blood pressure, peripheral resistance and vessel wall elasticity.

Force equilibria

Tangential force equilibrium

$$2 \cdot \sigma_\tau \cdot h \cdot \Delta x = p \cdot 2r \cdot \Delta x \Rightarrow \sigma_\tau = \frac{r}{h} p \qquad (A1.1)$$

The relation between stress and strain is given by Hookes lag

$$\sigma_\tau = E\varepsilon \qquad (A1.2)$$

The strain is determined by the relative change in vessel circumference

$$\varepsilon = \frac{2\pi(r - r_0)}{2\pi r_0} \qquad (A1.3)$$

The relation between the wall tension and the vessel pressure is given by

$$p = hE\frac{r - r_0}{r r_0} \qquad (A1.4)$$

$$\sigma_\tau = \frac{E}{r_0}(r - r_0) \qquad (A1.5)$$

The axial force equilibrium is

$$\sigma_a h \cdot 2\pi r = \pi r^2 \cdot p + Dynamic \quad pressure \qquad (A1.6)$$

and we ignore radial forces in the thin vessel wall.

Mass Balance

The differential equation to describe accumulation of volume and mass balance in a vessel segment is given by

$$\frac{d}{dt}V(t) = i_{in}(t) - i_{out}(t) \qquad (A1.7)$$

The inflow i_{in} is determined by the upstream activity of the heart and aorta. The outflow i_{out} depends on the blood pressure p and the peripheral resistance R according to the equation

$$i_{ut} = p \cdot \frac{1}{R} \qquad (A1.8)$$

The accumulated excess blood volume in a blood vessel segment of length L between the two markers of the ultrasonic equipment is given by

$$V(t) = (\pi r^2(t) - \pi r_0^2)L \qquad (A1.9)$$

and the accumulated mass is

$$m = \varrho \cdot V \qquad (A1.10)$$

The blood flow varies periodically and affects the accumulation of a blood volume in the vessel segment between the two markers according to the mass balance equation (A1.7). The geometric condition for blood volume gives

$$V = \pi L(r^2 - r_0^2) \Rightarrow \frac{dV}{dt} = \pi L \frac{d}{dt} r^2(t) \qquad (A1.11)$$

The outflow from the vessel segment at the marker B is determined by

$$i_{out} = \frac{p}{R} = \frac{1}{R}\frac{h}{r_B}\sigma = \frac{Eh}{R}(\frac{1}{r_0} - \frac{1}{r_B}) \qquad (A1.12)$$

An equation of inflow into the vessel segment at the marker point A is determined in the same way as

$$i_{in} = \frac{p}{R} = \frac{1}{R}\frac{h}{R}\sigma = \frac{Eh}{R}(\frac{1}{r_0} - \frac{1}{r_B}) \qquad (A1.13)$$

The flow balance equation may be reformulated into an equation for radial motion is given by

$$\pi L \frac{d}{dt} r^2 = \frac{Eh}{R}(\frac{1}{r_0} - \frac{1}{r_A(t)}) - \frac{Eh}{R}(\frac{1}{r_0} - \frac{1}{r_B(t)}) \qquad (A1.14)$$

Energy Balance

The force that is required to distend the vessel wall of a segment of length L is

$$F = \sigma_\tau \cdot h \cdot L \tag{A1.15}$$

The increase in circumference for an increase dr in vessel radius is

$$dx = 2\pi \cdot dr \tag{A1.16}$$

The work that is needed to distend the vessel wall is determined by

$$dW = F \cdot dx = \sigma_\tau hL \cdot 2\pi dr = 2\pi hL\sigma_\tau dr = p \cdot i_\heartsuit \cdot dt \tag{A1.17}$$

The vessel wall tension is

$$\sigma_\tau = \frac{E}{r_0}(r - r_0) \tag{A1.18}$$

The potential energy of the distended vessel wall is

$$W(t) - W(t_0) = \int_{r_0}^{r(t)} E\frac{r - r_0}{r_0} 2\pi hL dr = \cdots = \pi\frac{EhL}{r_0}(r(t) - r_0)^2 \tag{A1.19}$$

APPENDIX 2

Model of measurement in one point

The volume balance is determined by

$$\frac{d}{dt}V(t) = i_{in}(t) - i_{out}(t) \qquad (A2.1)$$

The relation between volume and radius

$$\frac{d}{dt}V(t) = \pi L \frac{d}{dt}[r^2(t)] \qquad (A2.2)$$

The relation between blood flow i, pressure p , and vessel radius r

$$i_{out}(t) = \frac{p(t)}{R} = \frac{Eh}{R}\frac{r(t) - r_0}{r(t)r_0} \qquad (A2.3)$$

A nonlinear equation for radial motion is therefore obtained as

$$\frac{d}{dt}r^2(t) = \frac{1}{\pi L}i_{in}(t) - \frac{E}{\pi LR}\frac{r(t) - r_0}{r(t)r_0} \qquad (A2.4)$$

A linearized equation is obtained as

$$\frac{d}{dt}r^2(t) = -\frac{hE}{2\pi LRr_0^3}[r^2(t) - r_0^2] + \frac{1}{\pi L}i_{in}(t) \qquad (A2.5)$$

Vessel radius dynamic with two measurements

Volume balance in the vessel segment upstream of A

$$\frac{d}{dt}V_A(t) = i_{in}(t) - i_A(t) \qquad (A2.6)$$

Volume balance in the vessel segment between A and B

$$\frac{d}{dt}V_B(t) = i_A(t) - i_B(t) \qquad (A2.7)$$

The relation between volume V and radius r gives

$$\frac{d}{dt}V_B(t) = \pi L_B \frac{d}{dt}[r_B^2(t)] \qquad (A2.8)$$

The relation between blood flow i, pressure p, and radius r assuming that Eh/R is approximately equal at the two measurement points

$$i_A = \frac{p_A}{R} = \frac{Eh}{R}\frac{r_A - r_{0A}}{r_A r_{0A}} \qquad i_B = \frac{p_B}{R} = \frac{Eh}{R}\frac{r_B - r_{0B}}{r_B r_{0B}} \qquad (A2.9)$$

Nonlinear equations are obtained as

$$\frac{d}{dt}r_A^2(t) = \frac{1}{\pi L_A}i_{in}(t) - \frac{Eh}{\pi L_A R}\frac{r_A(t) - r_{0A}}{r_A(t)r_{0A}} \tag{A2.10}$$

$$\frac{d}{dt}r_B^2(t) = \frac{Eh}{\pi L_A R}\frac{r_A(t) - r_{0A}}{r_A(t)r_{0A}} - \frac{Eh}{\pi L_B R}\frac{r_B(t) - r_{0B}}{r_B(t)r_{0B}} \tag{A2.11}$$

Linearized equations around the equilibrium

$$\frac{d}{dt}r_A^2(t) = -\frac{Eh}{2\pi L_A R r_{0A}^3}[r_A^2(t) - r_{0A}^2] + \frac{1}{\pi L_A}i_{in}(t) \tag{A2.12}$$

$$\frac{d}{dt}r_B^2(t) = \frac{Eh}{2\pi L_A R r_{0A}^3}[r_A^2(t) - r_{0A}^2] - \frac{Eh}{2\pi L_A R r_{0B}^3}[r_B^2(t) - r_{0B}^2] \tag{A2.13}$$

Statistical estimation of parameters

The variation in vessel radius is determined by the two equations

$$\frac{d}{dt}r_B^2(t) = -p_1 r_B^2(t) + p_2 r_A^2(t) + p_3 \tag{A2.14}$$

$$\frac{d}{dt}r_B^2(t) = -\alpha_1\frac{1}{r_A(t)} + \alpha_2\frac{1}{r_A(t)} + \alpha_3 \tag{A2.15}$$

Filtration of the left and right hand sides of the equations with a low pass filter $\lambda = 1/(1 + s\tau); s = d/dt$ gives a linear relation between measurable signals

$$r_B^2(t) = [1 - p_1\tau][\lambda(r_B^2(t))] + p_2\tau[\lambda(r_A^2(t))] + p_3\tau \tag{A2.16}$$

$$r_B^2(t) = \theta_1[\lambda(r_B^2(t))] + \theta_2[\lambda(r_A^2(t))] + \theta_3\tau \tag{A2.17}$$

and for the nonlinear equation

$$\frac{1}{\tau}\left[(1 - \lambda)r_B^2(t)\right] = \alpha_1\left[\lambda\frac{1}{r_A(t)}\right] + \alpha_2\left[\lambda\frac{1}{r_A(t)}\right] + \alpha_3 \tag{A2.18}$$

The signals on both left and right hand side are now possible to obtain by filtering. Implementation of low pass filtering makes the identification possible, see Johansson [11]. Estimation of $\theta_1, \theta_2, \theta_3$ is now possible with linear regression after sampling of filter r_A^2 and r_B^2. The parameters α_1, α_2, α_3, p_1, p_2, p_3 are computed by the least squares method.

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