A NEW CORONARY MODEL FOR MRI PERFUSION STUDIES

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Abstract: **This paper proposes a modified Windkessel model applied to the coronary circulation and first pass imaging techniques. A compartmental description of the blood flow is used. The compartments taken into account are the arteries, capillaries, lymphatic and venous systems, extravascular /extracellular and cellular domains. In addition the model includes mass transport by blood flow between compartments.**
The predictions of the model are presented in the simple case of first pass output concentration curves obtained with MR contrast agent in a non-beating blood perfused pig heart. The first results are obtained for low and high input flows in a normal heart. The last one is a simulation of an ischemic heart behavior.
The results are in a good agreement with the experimental data from the normal heart and with the characteristic behavior of the microcirculation in the ischemic heart.
In conclusion this method which integrates both pressure-flow-volume and mass transport models would be well adapted for the modelisation of perfusion imaging studies.
Keywords: **Windkessel, Coronary circulation, Capillaries, Resistances, Compliances, Non-beating heart, MRI data.**

I. INTRODUCTION

The aim of this paper is the development of a clinically oriented lumped-parameter model of the coronary system. It is based on a modified nonlinear Windkessel model [5, 9] and takes into account the mass transport effects. A compartment schema is used. Each compartment is characterized by both mechanical parameters to represent blood flows and mass transport. The initial data is the input flow and the resulting variables are flux, flow and pressure for each compartment.

In the literature, several authors developed pressure-flow-volume models of the cardiovascular system (Rideout [9], Clark [5], Snyder [10]). Other ones, have been interested by modelling the mass transport of tracers and other matters such as water, oxygen, protein, see Bassingthwaighte [1]. These models are generally characterized by black box behavior and are not able to identify normal from abnormal cases.

The first aim of the present model is to discriminate between normal from abnormal myocardial micro-circulation behavior for a given indicator by using MR intravascular perfusion images [2, 3, 8]. Then, the pressure-flow-volume relations are combined with those of mass transport between compartments. In the present study, a linear case is presented and the results obtained are compared to MRI data for blood perfused non-beating pig hearts.

This model will be used later to identify, for an individual case, the coronary circulation parameters. It can be easily adapted to another system such as the lung circulation. The non linearity of arteries and capillaries resistances can be taken into account easily. In the present study, a linear case is presented and the results obtained are compared to MRI data for non-beating pig hearts.

II. THE MODEL

We use a compartmental diagram of an open circuit to simulate the coronary circulation system of a non-beating pig heart with a constant input flow Q_a, see the figure 1. We assume arteries, veins and capillaries to be made up of cylindrical vessels with linearly elastic walls. Then, blood and fluid may be regarded as incompressible fluids with simple Newtonian characteristics. The pressure is considered to be uniform in the cross-sectional area of the vessel. And, we assume that the resistance R to flow is given approximately by the Poiseuille law. The compliance C of a vessel is defined by the slope of pressure versus volume curve. This parameter can be regarded as a constant for limited range of positive transmural pressure.

Each compartment is then characterized by physical parameters such as resistances to flow or to diffusion and compliances. The principal compartments taken into account in this diagram are the coronary artery, capillaries, lymphatic and venous systems, cellular and extravascular/extracellular domains. A given compartment is characterized by three equations which calculate the flow, the pressure and the relation between flow/diffusion and pressure. For example, the following equations characterize the first compartment representing the coronary artery.

Flow equation: $$\frac{\partial V_a}{\partial t} = Q_a - Q_c \qquad (1)$$

Pressure equation: $$P_e = \frac{V_e - V_{e0}}{C_e} \qquad (2)$$

$$PTM_a = \frac{V_a - V_{a0}}{C_a} \qquad (3)$$

$$P_a = PTM_a + P_e \qquad (4)$$

Pressure-flow equation: $$Q_a = \frac{P_{ao} - P_a}{R_a} \qquad (5)$$

Where:

- V_a, V_e, V_{a0} and V_{e0} are respectively the actual and initial [5] blood volumes in the coronary artery and the extravascular/extracellular domain;
- PTM_a is the aortic transmural pressure;
- Q_a and Q_c are respectively the blood flow in the coronary artery and the coronary capillary;
- P_{ao}, P_a and P_e are respectively the aortic pressure, the arterial coronary pressure and the extravascular/ extracellular domain pressure;
- R_a is the resistance to flow in the coronary artery;

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Abstract

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- C_a and C_e are respectively the compliance in the coronary artery and in the extravascular/extracellular domain.

Ordinary differential equations of the compartment volumes (V_a, V_c, V_v, V_{at}, V_e, V_{cell}) are then derived:

$$\begin{cases} \frac{\partial V_a}{\partial t} = Q_a - Q_c \\ \frac{\partial V_c}{\partial t} = Q_c - Q_v \\ \frac{\partial V_v}{\partial t} = Q_v - Q_{cs} \\ \frac{\partial V_{at}}{\partial t} = Q_{cs} + Q_{lym} - Q_{at} \\ \frac{\partial V_e}{\partial t} = Q_{cap} - Q_{cell} - Q_{lym} + \frac{P_{myo} - P_e}{R_{myo}} \\ \frac{\partial V_{cell}}{\partial t} = Q_{cell} \end{cases} \quad (6)$$

with: $Q_{cap} = Q_c - Q_v$ (7)

We denote by Q_i the longitudinal or transversal flow (diffusion) in the i^{th} compartment.

The Ordinary Differential Equation (ODE) system (6) depends on the resistances and compliances, which characterizes the model, see figure 1. These parameters connect pressures and volumes to flows. We denote by :

- R_a, R_c, R_v, R_{cs} and R_{at} the resistances to flow, respectively in, the coronary artery, the coronary capillary, the venous, the coronary sinus and the atrium;
- R_{cap} the transversal resistance from the capillary system to the extravascular domain;
- R_{cell} the transversal resistance from the extravascular /extracellular compartment to cellular one;
- R_{lym} lymphatic compartment resistance;
- R_{myo} mechanical resistance of the myocardial system around the capillaries;
- P_{myo} the myocardial pressure around the capillaries;
- P_e the extravascular/extracellular pressure;
- P_{pi} the osmotic pressure;
- P_{atm} the atmospheric pressure.

These ODE equations are solved by using a numerical code [6] based on Backward Differentiation Formula method (BDF) using Newton iteration.

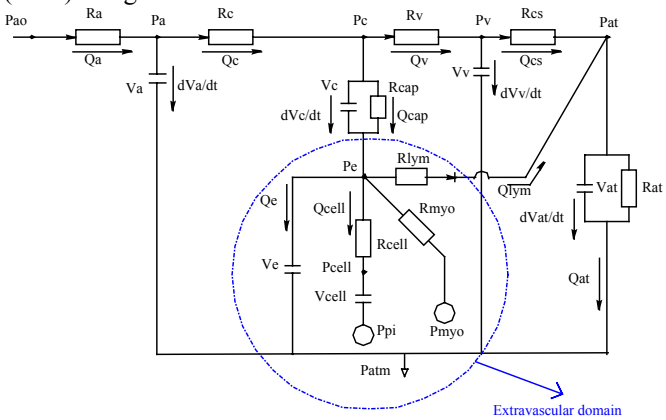

Fig. 1. Linear compartmental diagram of an open circuit representing coronary circulation of a non-beating heart.

III. Experimental Data

The experiments investigate the first-pass from intravascular MR contrast agent for blood perfused non-beating isolated pig hearts. The details of the preparation have been described elsewhere [2, 4]. Proximal left and right coronary arteries were isolated and selectively cannulated to avoid any leakage through the aortic valve. Both cannulas were connected to the same pump. The heart was perfused at controlled flow levels with a modified Krebs-Henseleit bicarbonate buffer [4], mixed with heparinized blood in a 4:1 proportion and 2,3 Butanedione monoxime (30 mmol/l). The perfusate was oxygenated and warmed at 38°C.

A constant quantity of 0.05 mmol of CMD-A2-Gd-DOTA [7] was injected into the perfusate. Ouput concentration curves were obtained by atrial blood sampling.

Figures 2 represents the experimental output concentrations curves. These results are obtained for a low and a high constant input flow (150 ml/mn and 400 ml/mn). The experimental output flow is given by:

$$Q_{output} = \frac{q}{\int_0^\infty C_{out}(t)dt} \quad (8)$$

where q is the quantity of contrast agent injected and $C_{out}(t)$ is the output concentration function. The output flow is determined by using gamma variate functions to fit experimental data. The output flow obtained for the low input one is 134.67 ml/mn. For the high input flow we obtain, 360.26 ml/mn.

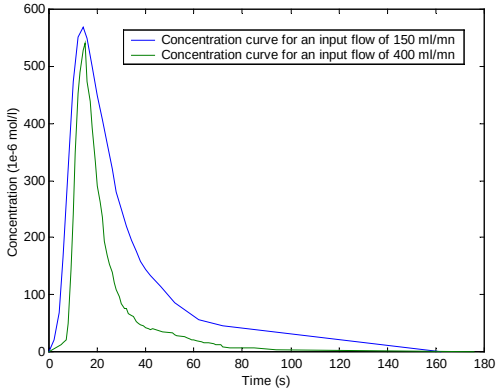

Fig. 2. Experimental curves for a low and a high input flow.

IV. Results and Discussion

A. Normal Heart

The results obtained from the theoretical model of a normal pig heart presented above for the low input flow (150 ml/ mn) are :

- the evolution of the different compartmental pressures, figure 3;
- the evolution of the different compartmental flows figure 4.

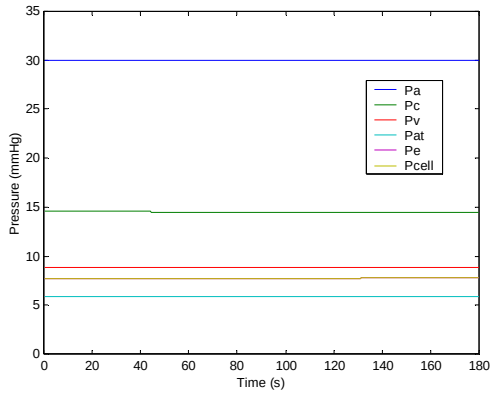

Fig. 3. Theoretical pressure curves of the different compartments for a low input flow.

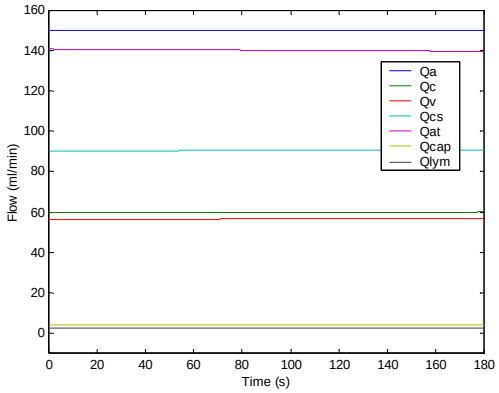

Fig. 4. Theoretical flow curves of the different compartments for a low input flow.

The results obtained from the theoretical model of a normal pig heart presented above, when we increase the flow from 150 ml/mn to 400 ml/mn (rest to stress), are :

- the evolution of the different compartmental pressures, figure 5;
- the evolution of the different compartmental flows, figure 6.

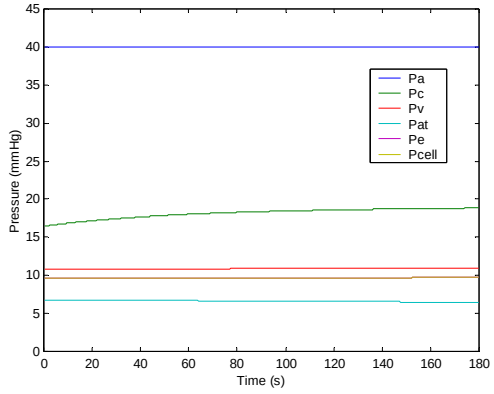

Fig. 5. Theoretical pressure curves of the different compartments for a high input flow.

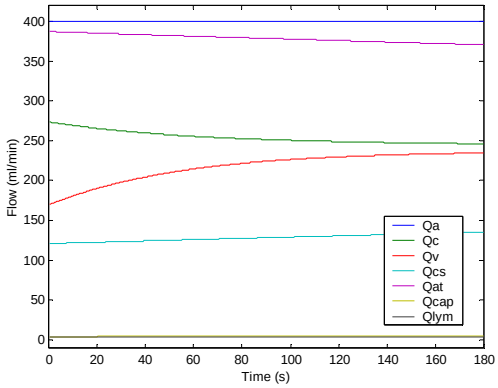

Fig. 6. Theoretical flow curves of the different compartments for a high input flow.

It can be shown that the predicted behavior of the heart, by the theoretical model, is in agreement with the expected physiological behavior. The pressure distribution in the principal branch present a good agreement with the physiological one. The theoretical output flow Q_{at}, for the low input one, is equal to 140.81 ml/mn, which represents a relative error of 4.56 % with the experimental value. For the high input flow the theoretical value is 378.58 ml/mn, the error is of 5.08 %. These results present a good agreement with the experimental data.

B. Ischemic Heart

Figures 7 and 8 represent the behavior of an ischemic heart. This behavior is obtained by increasing the different resistances of the theoretical model, in order to modelize ischemia. It is shown that the prediction is in agreement with the physiological behavior of such a heart. In fact, for a given constant input flow, we observe an increase of the pressures, and an important decrease of the flows. This matches some characteristics behaviors of an ischemic heart. For an input flow Q_a equal to 150 ml/mn the output flow Q_{at} is equal to 52.81 ml/mn. These predicted results allow to discriminate between normal and abnormal heart behavior.

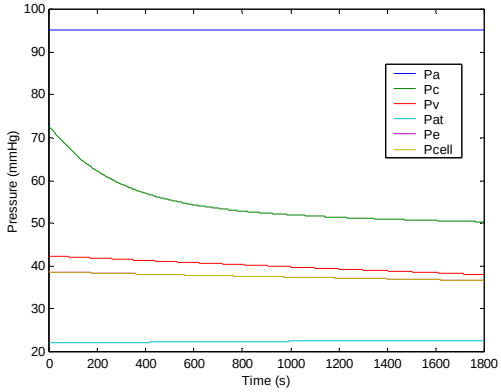

Fig. 7. Theoretical pressure curves of the different compartments for a low input flow.

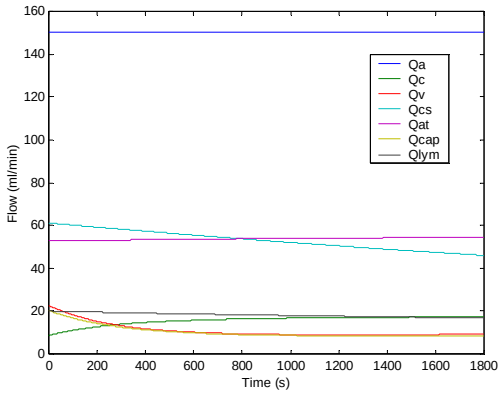

Fig. 8. Theoretical flow curves for a low input flow.

V. Conclusion

The presented model, based on a linear lumped schema, modelizes the behavior of the principal components of the coronary circulation system. It is based on a compartmental description of the blood flow in the heart. The compartments taken into account are the arteries, capillaries, lymphatic and venous systems, extravascular/extracellular and cellular domains.

Compared to other pressure-flow-volume models, the presented model includes as well mass transport by blood flow between compartments. The theoretical results obtained at two flow levels in a normal heart were compared to the experimental data with a good correlation. The third one presented is the prediction of an ischemic heart behavior. This last simulation has been obtained by increasing the resistances of the model, in order to modelize the spasm of the heart. Hence, for a given input flow, the model allows to discriminate between a normal from an abnormal heart, by comparing the theoretical and experimental output flows. As this is a non-beating heart the mechanical system can be considered as linear with constant resistances.

This model can be easily transformed to take into account mass transport by diffusion and nonlinear effect of coronary arterial behavior in the beating heart or pharmaceutical stimulations. It can also be adapted to another system such as the lung circulation.

In perspective, this model could be used to identify, for an individual case, the coronary circulation parameters. It can be easily adapted to other microcirculation systems such as cerebral, pulmonary or renal ones. The non linearity of arterial and capillaries resistances can be taken into account easily. Moreover, it can be applied to both global and regional perfusion measurements obtained by first-pass imaging techniques. As both flow and mass transports are included in the model, these predictions can be used to explore targeted effects of therapies in the post-ischemic heart.

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