RICE UNIVERSITY

HYDRODYNAMIC CONSIDERATIONS
OF CORONARY BLOOD FLOW
WITH AND WITHOUT STENOSIS

by
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ABSTRACT

Hydrodynamic Considerations of Coronary Blood Flow With and Without Stenosis

by

Jean-Pierre Brugger

Coronary stenosis is one of the most common heart diseases. Though not much is known concerning the growth of the stenosis in the coronary arteries, it is nevertheless possible to study the effects of the stenosis on the blood flow, and thus to determine its influence on myocardial perfusion. In summary, this thesis is concerned with the effects of the stenosis on left coronary blood flow. To determine these effects it has been necessary in a first step to understand left coronary blood flow and its regulation. This is done by computing coronary blood flow as a function of the hydraulic power delivered by the heart. In a second step the hydrodynamic effects of the stenosis have been computed and experimentally tested in vitro.

It has been found that the resistance to the flow presented by the stenosis is a strong function of the percentage of stenosis, its inner radius and its length. Apparently the geometrical inlet shape of the stenosis is not an important factor. It has been shown also that for given conditions a 75% stenosis can present a high enough resistance to impede myocardial blood flow such as to lead to myocardial infarction. This is true even if the required blood supply is far from being excessive.
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To my son,

Simon
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NOMENCLATURE AND ABBREVIATIONS

A, A'  areas
a  proportionality constant between the velocity, C(t) and the frictional pressure drop along Δx (18)
C, c  mean velocities (m/s) (average over the section)
CBF  coronary blood flow (cc/min)
F  force (N)
HR  heart rate (BPM)
L, l  lengths (m)
m  \[ \frac{T_S}{T} \]
P  relative pressure (mmHg) (relative to the atmospheric pressure)
Q  mean flow (cc/s)
R  resistance (K) = (10³ \( \frac{\text{dyne/cm}^2}{\text{ml/s}} \))
T  period of one cardiac cycle (ms)
T_S  systolic time of one cardiac cycle (ms)
t  time (s)
V  volume (cc)
W  work (J)
\( \dot{W} \)  power (w)
Δx  distance between the two holes on the catheter used to measure the pressure difference (18) (cm)
ν  frequency (1/s)
η  percentage or efficiency
ρ  specific weight  1,06 gr/cm³
\( \mu \)  dynamic viscosity of the blood \( \approx 2.5 \) centipoises

\( \sigma \)  kinematic viscosity of the blood \( \approx 2.36 \) centistokes

\[ \text{time average} \{ ... = \frac{1}{(t_2 - t_1)} \int_{t_1}^{t_2} ... \, dt \} \]
I. INTRODUCTION

The heart is a four-chambered, two-sectioned pump which delivers needed blood supply to the pulmonary and systemic circulation by means of the right and left ventricles. As the right ventricle pumps blood from the right atrium to the pulmonary artery, the mean pressure in the right ventricle changes from approximately 4 mm Hg to 15 mm Hg. In comparison, the blood pressure in the left ventricle changes from approximately 5 mm Hg to 90 mm Hg as the left ventricle pumps blood from the left atrium to the aorta. Therefore, since both ventricles expel the same mean volume of blood, the work per stroke performed by the left ventricle is greater than the work per stroke performed by the right ventricle. The left ventricle maintains the proper blood flow to the systemic circulation by adjusting its output to meet the needs of the body. Thus, the left ventricle can be considered as being a hydraulic pump that can change its stroke volume and output pressure. However, this pump is very special in that it is able to provide its own fuel supply. It does this by receiving part of the expelled blood, which then perfuses the myocardium and delivers the necessary nutrients to the muscle fibers. If, for any reason, this nutrient supply is impeded or shunt off, the pump will no longer operate properly. One can see that to analyze the function of the heart, it is necessary to understand the coronary circulation which carries the
blood to the myocardium. The most common obstacle impeding myocardial blood flow in coronary patients is coronary stenosis. The study of this typical coronary diseases encounters numerous unanswered questions. One of these questions of great interest arose during discussions with both cardiologists and cardiovascular surgeons. The question was asked: "Why do some coronary patients with a determined magnitude of left coronary stenosis suffer from myocardial infarction during physical or emotional stress, whereas other patients with the same magnitude of stenosis, similarly located, do not suffer any symptoms of myocardial infarction?" The size, shape and location of the stenosis were diagnosed by an angiogram and checked post-mortem. There was no evidence that any geometrical changes of stenosis occurred before or after myocardial infarction. Could one possibly explain what was happening from fluid mechanical considerations? Was it possible that for given conditions the expected increase in CBF could not be achieved in the substenotic regions because of a sudden increase of the resistance presented by the stenosis, even if the substenotic region was completely vasodilated?

In regard to these questions, the object of this thesis research was to demonstrate that in vitro simulation of CBF at the level of the larger coronary arteries is possible and that it can be used to study the effect of coronary stenosis
on myocardial perfusion in the left ventricle. Only the left ventricle has been considered since it produces the most important part of the cardiac work. Further, a coronary obstruction in the left ventricular coronaries is more likely to produce cardiac failure.

Only the hydrodynamic aspects of the regulation of coronary blood flow (CBF) have been considered in this study. No attempt was made to solve the physiological problems inherent in the coronary circulation. However, it is important to fully understand the basic mechanism of CBF for two reasons: first, to analyze the important factors influencing CBF, and second, to define as accurately as possible the experimental range of parameters that must be taken into consideration. Anatomically, this study was concerned with the left aortic sinus which originates at the ostia that is situated 0.7 to 1 cm. above the root of the semilunar cusps, and with the left descending and circumflex coronary artery.

Even though CBF has been studied for over three hundred years*, (1,26) the subject is still not fully understood and remains highly controversial. Nevertheless, numerous

*see appendix (page 98)
authors describing CBF seem to agree on the following physical factors regulating the cyclic nature of the flow:

(a) The effective perfusion pressure (usually root aortic pressure minus right atrial pressure).

(b) The impedance to flow resulting from physical compression of the coronary vessels by myocardial contraction.

(c) The total peripheral resistance in the coronary system, which includes the small vessel resistance, which is added to the peripheral resistance. The peripheral vascular resistance depends on the effect of biochemical and neurogenic factors on the vascular wall.

As stated above, myocardial contraction during systole impedes systolic CBF. Some divergence of opinion appears as to whether or not CBF during systole is important. The most common assumption is that CBF occurs mainly during diastole (1,3). However, Gregg (26) has shown that systolic CBF can be important and that late instantaneous systolic flow can even exceed diastolic flow.

By taking into account the above described physical factors and by analyzing CBF recordings in the left coronary sinus (30) of a healthy human at rest, it has been found that left CBF could be fairly well reproduced by simulating heart contraction on the coronary vessels and by assuming that the coronary impedance during diastole was mainly resistive.

In summary, this thesis is concerned with the effects of stenosis on left CBF. To determine these effects it has
been necessary as a first step to understand left CBF and its regulation. This is done by computing CBF as a function of the hydraulic power delivered by the heart. In a second step the hydrodynamic effects of the stenosis have been computed and experimentally tested in vitro. The lumped in vitro system used to simulate CBF will be described in the chapter entitled Modelling. It has been found that the resistance to the flow, presented by the stenosis, is a strong function of the percentage of stenosis, its inner radius and its length. Apparently, the geometrical inlet shape of the stenosis is not an important factor. It has been shown also, that for given conditions, a 75% stenosis can present a high enough resistance to impede myocardial blood flow such as to lead to myocardial infarction, even if the required blood supply is far from being excessive.
II. CARDIAC POWER AND CBF

To facilitate the understanding of this chapter, it is important to clarify the following definitions:

(a) **Hydraulic work per stroke**

Hydraulic work is often defined in the literature as the work of the heart or as the mechanical work obtained by integrating the PV loop in the PV diagram over one cardiac cycle. The PV diagram is the diagram relating intraventricular volume to intraventricular pressure. These two variables concern only the fluid inside the ventricle and do not include either the volume or the pressure within the myocardium. Therefore, it seems to be more logical to define work done on the fluid over one cycle as the hydraulic work instead of mechanical work. One could be confused by "mechanical work" thinking that it is not only related to the pressure and volume in the cavity but is also related to work done within the myocardium.

(b) **Mechanical work**

Mechanical work will be taken here to mean only the mechanical work done by the muscle fibers within the myocardium. This work is in fact the strain energy in the myocardium. The mechanical work and the hydraulic work are not equal. Part of the mechanical work is lost due to interfascicular tension and blood viscosity (19).
It has been established (1, 15, 35, 40, 45) that left CBF is related to myocardial oxygen consumption and that myocardial oxygen consumption is directly proportional to myocardial energy consumption and, therefore, to mechanical work. Finally, mechanical work is related to the hydraulic work of the heart. In theory, CBF can be determined by computing either the mechanical or the hydraulic power delivered by the left ventricle.

In a first step, cardiac power and cardiac work will be defined. If one consider the PV diagram, it is known (40) that the cardiac work is defined as the surface integral or area of the PV loop. Introducing the above definition, this work is the hydraulic work done by the heart if one defines a control volume as being the volume containing the heart cavity and excluding the heart muscle itself. Thus, there is no work done during the isovolumic contraction between points 1 and 2 (Figure II) on the PV diagram.

From the physiologic point of view, the heart delivers strain energy (15, 19) not only during the isobaric ejection but also during the isovolumic contraction. This strain energy or mechanical work should be taken into account in any energy balance including the myocardium. If one wants to compute the mechanical work of the left ventricle, the control volume has to include the myocardium (where the myocardial strain energy during isovolumic contraction and
isobaric ejection have to be taken into account). The strain energy added to the different losses occurring in the myocardium, as described by Ghista (19) will give the total energy requirements of the left ventricle.

The determination of the stress-strain diagram of the human left ventricle, needed to determine mechanical efficiency leads to a complicated set of measurements and evaluations. For this reason, and also because of the fact that the hydraulic efficiency (usually defined in the literature as the mechanical efficiency) of a normal human is fairly constant, it was decided to relate oxygen consumption directly to the hydraulic work. If one wants a precise computation of the hydraulic efficiency by using a theory including the total energy balance of the left ventricle, it is possible to determine this efficiency through the utilization of the tension time index or velocity of contraction as described by Lichtlen, et al (35) or through the use of Ghista's theory (19), although both of these works are still theories not yet proven beyond doubt.
A. Hydraulic work and power

\[ V_1 \text{ = volume at time } t_1 \]
\[ V_2 \text{ = volume at time } t_2 \]
\[ dV = V_1 - V_2 \]
\[ C \text{ = mean velocity of the ejected fluid} \]
\[ \phi = \text{diameter of the duct} \]
\[ r = \text{radius of the exhaust duct} \]
\[ A = \pi r^2 \]

One can depict a mechanical analog of the left ventricle by a piston moving in a cylinder. A force \( F \) is applied to the piston. The ejected volume flows through the section \( A \) where section \( A \) simulates the section of the aortic root.
The elementary expression for the mechanical work (or hydraulic work) done by the piston on the fluid can be expressed as:

\[ dW = F \cdot dl \]  

1)

The force on the fluid can be expressed as:

\[ F = P_T \cdot S \]  

2)

\( P_T \) is the total pressure on the fluid side
\( S \) is the section of the piston.

Replacing equation 2 into equation 1:

\[ dW = P_T \cdot S \cdot dl \]

and with \( S \cdot dl = dV \)

\[ dW = P_T \cdot dV \]  

3)

The velocity reached in the section A for an incompressible fluid is:

\[ C = \sqrt{\frac{2(P_T - P)}{\rho}} \]  

4)

It is assumed that the velocity of the piston is negligible compared to the velocity of the fluid in the duct and that the process is isentropic.

That implies that the total pressure in the piston chamber is equal to the total pressure in the duct.

\( P_T \) can be obtained from equation 4:

\[ P_T = P + \rho \frac{C^2}{2} \]  

5)
Replacing equation 5 into equation 3 one obtains the hydraulic work:

\[ dW = P \cdot dV + \rho \frac{C^2}{2} \cdot dV \]

P and C are functions of time

\[ dW = P(t) \cdot dV + \rho \frac{C^2(t)}{2} \cdot dV \]  \hspace{1cm} (6)

\[ \Delta W(t) = \int_{V(t_1)}^{V(t_2)} P(t) \cdot dV + \rho \frac{C^2(t)}{2} \cdot dv \]

where \( dV = Q(t) \cdot dt \) and \( Q(t) = \) mean flow in section A (aortic flow)

\[ \Rightarrow \Delta W(t) = \int_{0}^{t} P(t) \cdot Q(t) \cdot dt + \int_{0}^{t} \rho \frac{C^2(t)}{2} \cdot Q(t) \cdot dt \] \hspace{1cm} (8)

\[ \Delta W = \int_{0}^{t} \{ P(t) \cdot Q(t) + \frac{\rho}{2A^2} \cdot Q^3(t) \} dt \]

where \( A = \pi r^2 \) and \( C = \frac{Q}{A} \)

Two important statements should be made in regard to hydraulic work:

(a) The total hydraulic work of the left ventricle is the integral over one cycle of the loop in the PV diagram (40) as shown in Figure II.

(b) The total hydraulic work of the left ventricle requiring energy uptake by the left myocardium concerns only the isobaric ejection (2 and 3 in Figure II) and isovolumic contraction (1 and 2 in Figure II) and does not include isovolumic relaxation nor passive or active filling of the left ventricle (40,45).
The total hydraulic work per unit time is the hydraulic power

\[ \dot{\hat{W}} = \frac{dW}{dt} = P(t)Q(t) + \frac{\rho}{2A^2} \cdot Q^3(t) \]  

10)

The total work per cycle is the power spent from 1 to 3 (Figure II) during the effective systolic time.

The mean hydraulic power over one cycle may be defined as:

\[ \bar{\hat{W}} = \frac{1}{T} \int_{0}^{mT} \frac{dW}{dt} \cdot dt \]  

11)

Replacing equation 10 into equation 11 one obtains:
\[
\dot{W} = \nu \int_{0}^{\frac{m}{v}} \{P(t) \cdot Q(t) + \rho \frac{Q^3(t)}{2A^2}\} \, dt
\]

where \( \nu = \frac{1}{T} \) = Heart rate in BPS (beats per second)

T is the period of one cardiac cycle

and \( m = \frac{T_s}{T} \)

Ts is the period of the systole in one cardiac cycle.

B. Power consumption of the left ventricle and diastolic CBF

The power is the work per unit time. Here the time unit is the cardiac cycle. The power consumption of the left ventricle is directly related to oxygen consumption (1,35,40,45). The oxygen supplied to the left ventricle is the oxidizer used to liberate the caloric energy. The pseudo-caloric energy of the \( O_2 \) is defined as \( \text{Eo}_2 \). \( \text{Eo}_2 \) has been empirically determined (45) and set to a constant value of \( 21 \times 10^6 \) Jm\(^{-3}\). The total \( O_2 \) brought to the myocardium is \( \text{CBF} \times (A-V \text{ O}_2 \text{ difference}) \), where \( \text{CBF} \) is the mean coronary blood flow averaged over one cycle (for the left ventricle), and \( A-V \text{ O}_2 \text{ difference} \) is the arterial-venous \( O_2 \) difference (aortic \( O_2 \) concentration - right sinus \( O_2 \) concentration). Several authors (40,45) have stated that the \( O_2 \) uptake by the myocardium is of the order of 70 to 75% of the arterial oxygen content and that this value remains constant for a wide range of CBF.

For simplification purposes, instead of taking the \( A-V \text{ O}_2 \)
difference, the aortic blood O\textsubscript{2} concentration V\textsubscript{O\textsubscript{2}}/V\textsubscript{b} has been multiplied by the per cent of extracted O\textsubscript{2}, \eta\textsubscript{c} as follows:

\[
\overline{\text{CBF}} \cdot (\text{A-V O}_2 \text{ difference}) = \overline{\text{CBF}} \cdot \frac{\text{V}_\text{O}_2}{\text{V}_\text{b}} \cdot \eta\textsubscript{c}
\]  

\[
\text{V}_\text{O}_2 = \text{volume of oxygen}
\]

\[
\text{V}_\text{b} = \text{volume of blood}
\]

The mean total power corresponding to the fuel consumption of the left ventricle is therefore:

\[
\overline{\dot{W}_T} = \overline{\text{CBF}} \cdot \text{Eo}_2 \cdot \frac{\text{V}_\text{O}_2}{\text{V}_\text{b}} \cdot \eta\textsubscript{c}
\]  

The hydraulic efficiency \eta\textsubscript{H} is defined as the per cent of total energy uptake converted into hydraulic work only. In equation form, the hydraulic efficiency is as follows:

\[
\eta\textsubscript{H} = \frac{\overline{\dot{W}}}{\overline{\dot{W}_T}}
\]  

If equation 14 is substituted into equation 15, the result is

\[
\eta\textsubscript{H} = \frac{\overline{\dot{W}}}{\eta\textsubscript{c} \cdot \frac{\text{V}_\text{O}_2}{\text{V}_\text{b}} \cdot \text{Eo}_2 \cdot \overline{\text{CBF}}}
\]  

The time average CBF over one cycle is therefore:

\[
\overline{\text{CBF}} = \frac{\overline{\dot{W}}}{\eta\textsubscript{H} \cdot \eta\textsubscript{c} \cdot \frac{\text{V}_\text{O}_2}{\text{V}_\text{b}} \cdot \text{Eo}_2}
\]  

Substituting equation 12 into equation 17 yields the following:
The preceding integral must be solved in order to undertake a parametric study of the CBF.

As a first approach, approximations have been made that would seem simplistic but that nevertheless give an idea as to the different important factors that influence CBF. These approximations are as follows:

(a) Most of the coronary blood flow occurs during diastole.

\[
\overline{\text{CBF}}_D = \frac{1}{1-m} \cdot \overline{\text{CBF}} \cdot \eta_D
\]

\(\eta_D\) is the percentage of CBF occurring during diastole

\(\eta_S\) is the percentage of CBF occurring during systole

\[
\eta_D = 1 - \eta_S
\]

where \(\eta_S\) may vary between 7 and 40% (45).

(b) Most of the blood flow to the left myocardium enters the left coronary sinus. The percentage of left CBF through the left coronary sinus is \(\eta_f\) and can be computed (15):

\[
\eta_f \approx 83\%
\]

(c) As a first approximation, the systolic pressure and the systolic flow are defined to be sinusoidal and in phase (Figure III).
\[ P = P_0 + \Delta P_S \cdot \sin \omega t \]  \hspace{1cm} 22) \\
\[ Q = Q_{\text{max}} \cdot \sin \omega t \]  \hspace{1cm} 23)

**FIGURE III. PRESSURE AND FLOW PATTERNS APPROXIMATED BY TWO SINES IN PHASE**

(see equations 22 & 23)

- \( P_0 \) = end diastolic aortic pressure
- \( \Delta P_S \) = peak to nadir systolic pressure
- \( Q_{\text{max}} \) = maximum root aortic flow

(d) Coronary blood flow is linearly related to the diastolic pressure (the coronary capillary bed acts as a simple resistance).

(e) It is further assumed that during diastole, quasi steady state conditions exist.
Using equations 22 and 23 the hydraulic power can be computed.

**Hydraulic power due to** $P(t) \cdot Q(t)$:

$$P(t) \cdot Q(t) = P_0 \cdot Q_{\text{max}} \cdot \sin(\frac{\pi m}{2})+ \Delta P_s \cdot Q_{\text{max}} \cdot \sin^2(\frac{\pi m}{2})$$  \ \ (24)

$$\int_0^m P(t) \cdot Q(t) = -P_0 \cdot Q_{\text{max}} \cdot \cos(\frac{\pi m}{2}) + \Delta P_s \cdot Q_{\text{max}}$$ \ \ (25)

**Hydraulic power due to** $Q^3$

$$Q^3(t) = Q_{\text{max}}^3 \cdot \sin^3(\frac{\pi m}{2}) = \frac{Q_{\text{max}}^3}{4} (3\sin(\frac{\pi m}{2}) - \sin^3(\frac{\pi m}{2}))$$ \ \ (26)

**Mean hydraulic power due to** $Q^3$

$$\int_0^m Q^3(t) \cdot dt = \frac{Q_{\text{max}}^3}{4} \left( -\frac{3m}{2\pi} \cdot \cos(\frac{\pi m}{2}) + \frac{m}{3\pi} \cdot \cos^3(\frac{\pi m}{2}) \right)$$ \ \ (27)

Therefore, the mean hydraulic power as defined in equation 11 is:

$$\int_0^m \{P(t) \cdot Q(t) + \frac{\rho}{2A^2} Q^3(t)\} \cdot dt = m(Q_{\text{max}} \cdot \left( \frac{2P_0 \cdot \Delta P_s}{\pi} + \frac{2}{3\pi A^2} Q_{\text{max}}^2 \right))$$ \ \ (28)

Finally, substituting equation 28 into equations 18 and 19, one can determine the mean diastolic CBF as follows:
\[
\overline{\text{CBF}}_D = \frac{m}{1-m} \cdot \frac{\eta_f \cdot \eta_D}{\eta_C} \cdot \frac{Q_{\text{max}} \left( \frac{2P_o}{\pi} + \frac{\Delta P_S}{2} + \frac{2}{3}\pi a^2 \frac{Q^2}{Q_{\text{max}}^2} \right)}{Eo_2 \cdot \frac{V_{O_2}}{V_b} \cdot \eta_H}
\]

C. Computation of the mean myocardial resistance during diastole and variation of the parameters contained in equation 29:

The mean driving pressure \( \overline{\Delta P}_D \) for \( \overline{\text{CBF}}_D \) is the mean diastolic aortic pressure \( \overline{P}_D \) minus the pressure in the right atrial sinus \( P_{\text{as}} \).

\[
\overline{\Delta P}_D = \overline{P}_D - P_{\text{as}}
\]

where

\[
\overline{P}_D = \frac{P_{\text{dicrotic notch}} + P_{\text{opening aortic valve}}}{2} = \frac{P_{d} + P_{o}}{2}
\]

The mean diastolic myocardial resistance is then:

\[
\overline{R}_D = \frac{\overline{\Delta P}_D}{\overline{\text{CBF}}_D}
\]

Introducing equations 31 and 29 into equation 32, one obtains

\[
\overline{R}_D = \frac{1-m}{2m} \cdot \frac{\eta_C}{\eta_f \cdot \eta_D} \cdot \frac{V_{O_2}}{V_b} \cdot \frac{Eo_2 \left( \frac{P_{d} + P_{o}}{2} - 2\overline{P}_{\text{as}} \right)}{Q_{\text{max}} \left( \frac{2P_o}{\pi} + \frac{\Delta P_S}{2} + \frac{2}{3}\pi a^2 \frac{Q^2}{Q_{\text{max}}^2} \right)}
\]

The preceding expression is heart-rate dependent through \( m \). Increase in heart rate corresponds to an increase in \( m \).

The values of \( m \) (for men) have been determined by Rushmer.
(45) and are given in Table I.

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<th>$m_m$</th>
<th>$m_{ul}$</th>
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<tr>
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</table>

**TABLE I** Minimum and maximum values of $m$ as a function of heart rate.

$m_m$ is the mean value of the ratio $T_s/T$

$m_{ul}$ is the upper limit of the ratio $T_s/T$

where $T_s$ is the systolic time and $T$ total time of the period

HR is in beats per minute (BPM)

These values are plotted in Figure IV.

CBF is strongly dependent on heart rate, but heart rate is not the true variable. One could imagine that for the same rate, it is possible to change the ratio of the systolic time to the total time and therefore change CBF (Figure IV). The influence of the other parameters are shown in Figure V. It is a non-dimensional diagram. The reference values have been
FIGURE IV CHANGE IN THE RATIO

\[ \frac{m}{1-m} \] VERSUS HEART RATE see Table I
FIGURE V  VARIATION OF THE NON DIMENSIONAL PARAMETERS CONTAINED IN THE EQUATION 29 AS A FUNCTION OF THE NON DIMENSIONAL CBF (see text)

EVERY CURVE REPRESENTS THE VARIATION OF ONE OF THE PARAMETERS WHILE ALL OTHER PARAMETERS ARE KEPT CONSTANT.
chosen as:

\[
\begin{align*}
HR_0 &= 60 \text{ BPM} \\
Q_{\max_0} &= 440 \text{ cc/s} \\
P_0 &= 80 \text{ mmHg} \\
\Delta P_{D_0} &= 50 \text{ mmHg} \\
\eta_{H_0} &= 20\% 
\end{align*}
\]

These values correspond to what could be measured in a resting individual (36). The non-dimensional quantities (*) are the calculated values divided by the reference value. As seen in Figure V the most important factors are obviously \(Q_{\max}, HR\) and \(\eta_H\). (A similar percentage increase in \(Q_{\max}, HR\) and \(\eta_H\) leads to a greater increase in CBF).

Going back to the literature (1,45), one can see that equation 29 contains the important parameters influencing CBF. However, one important empirical factor, that relating increase in \(O_2\) consumption to the velocity of contraction, does not appear explicitly in this equation. Furthermore, it is difficult from a clinical point of view to measure \(Q_{\max}\) in the aortic root of a healthy individual. For these reasons, a search was conducted for a procedure to estimate root aortic blood flow. Fry's theory (18,22,24,25) seems to give good results, at least for the region of interest here, that is during the systole.
D. Fry's theory (18)

This theory is based on the simplified Navier Stokes equations that relate axial aortic pressure gradient to the instantaneous blood velocity. Fry's expression for the instantaneous velocity is:

\[ C(t) = e^{-\frac{a}{\rho \cdot \Delta x \cdot t}} \left[ \frac{a}{\beta \cdot \Delta x \cdot t} \right] + Ke^{-\frac{a}{\rho \cdot \Delta x \cdot t}} \]  

(34)

The last term on the right hand side is a transient term that can be set equal to zero (18).

The following assumptions have been introduced in order to solve equation 34 for the purposes of the present investigation:

(a) One will be concerned only with the systolic aortic flow. The patient is assumed to have no valve disease and, therefore, zero flow at the end of diastole and zero flow at the closure of the aortic valve.

(b) The aortic pressure wave can be approximated by two cosines as illustrated in Figure VI. The first cosine has a period of 2\(m_1T\) and its amplitude is \(\Delta P_g\). The second cosine has a period of 2\(T^*\) and goes from the maximum systolic pressure to the dicrotic notch.

(c) By empirical determination \(\frac{\partial P}{\partial x} = \frac{1}{\rho} \frac{\partial P}{\partial t}\) this relation would be appropriate if there were no wave reflections. The quantity \(\rho\) is the velocity of the propagation of perturbation along the arterial wall.

*) see derivation of equation 34 in reference 18
From assumption (b) one can write:

\[
P(t) = P_0 + \frac{\Delta P_{\text{max}}}{2} \left(1 - \cos \frac{\pi}{m_1 T} t\right) \quad 0 \leq t \leq m_1 T
\]

\[35\]

\[
P(t) = P_0 + \frac{\Delta P_{\text{max}}}{2} \left\{1 - (1 - \alpha^*) \left(1 - \cos \frac{\pi}{T^*} (t - m_1 T) - \cos \frac{\pi}{T^*} (m - m_1 T)\right)\right\}
\]

\[
(1 - \cos \frac{\pi}{T^*} (m - m_1 T))
\]

\[36\]

\[m_1 T \leq t \leq m T\]

With assumption (c) equation 34 can be written:

\[
C(t) = \frac{e^{-\alpha \cdot t}}{\rho S} \left\{ \frac{\partial P}{\partial t} e^{\alpha \cdot t} dt \right\}_0^t
\]

\[37\]

where

\[
\alpha = \frac{a}{\rho \Delta x}
\]

\[38\]

By differentiating equations 35 and 36 with respect to time and then substituting in equation 37, one obtains:
\[ C(t) = C(m_1 T) - \frac{\Delta P_{\text{max}}}{2 \rho S} \cdot \frac{M}{\alpha^2 + M^2} \cdot (\alpha \sin M(T - m_1 T) + M^* \alpha \cos M(T - m_1 T)) \]

\[ C(t) = C(m_1 T) - \frac{\Delta P_{\text{max}}}{2 \rho S} \cdot \frac{M^* \alpha (m_1 - m)}{\alpha^2 + M^2} \cdot (\alpha \sin M^*(t - m_1 T) + M^*(t - m_1 T)) \]

\[ \Theta M^*(\alpha^2) \left( \frac{e^{\alpha m_1 T}}{e^{\alpha m T}} - \cos M^*(t - m_1 T) \right) \]

where

\[ M = \frac{\pi}{m_1 T} \]
\[ M^* = \frac{\pi}{T^*} \]

The value of \( \alpha \) is unknown and has to be computed such as the following boundary conditions are satisfied:

\[ C(t) = 0 \text{ at } t = 0 \]
\[ C(t) = 0 \text{ at } t = m_1 T \]

By using these boundary conditions, one finds the following relationship for \( \alpha \):

\[ \zeta (\alpha^2 + M^* \alpha) \left( \frac{e^{\alpha m_1 T}}{e^{\alpha m T}} - (\alpha^2 + M^2) \right) \{ \gamma (\alpha \delta + M^* \left( \frac{e^{\alpha m_1 T}}{e^{\alpha m T}} - \xi \right)) \} = 0 \]

where

\[ \zeta = \frac{\pi}{2 (m_1 T)^2} \]
\[ \gamma = \frac{(1 - \alpha)}{(1 - \cos \frac{\pi}{T^*} (m_1 - m_1 T) T^*)} \]
\[ \delta = \alpha \sin \frac{\pi}{T^*} (m_1 - m_1 T) \]
\[ \beta = \frac{\pi}{T^*} \cdot \gamma \]

\[ \xi = \cos \frac{\pi}{T^*} (m-m_1)T \]

Once \( \alpha \) is determined, it is easy to compute the instantaneous velocity and flow rate with equations 40 and 41. The results for two different sets of arbitrarily chosen values have been plotted in Figures VII and VIII.

The quantity \( M \) in equations 40 and 41 determines the rising time of the pressure curve and, therefore, represents the rising \( \frac{\partial P}{\partial t} \) or \( \frac{\partial C}{\partial t} \) which is related to the velocity of contraction of the left ventricle.

The amplitude of the aortic velocity is too low and has to be adapted experimentally by changing the value of \( S \) or by introducing a corrective factor. Nevertheless, one is able to compute \( Q^3(t) \) and \( P(t) \cdot Q(t) \) where \( Q(t) = f[P(t)] \) and undertake a parametrical study of the power equation 29. This study was not investigated further on the practical application of this equation. The interest was just to prove that if necessary, one could indeed come up with a substitution of \( Q^{\text{max}} \) the direct measurement of which is problematic.
\[ \Delta P_{\text{max}} \text{ [mmHg]} \]

**AORTIC PRESSURE**

- \( \text{HR} = 60 \text{ BPM} \)
- \( T = 1s \)
- \( T^* = 0.7s \)
- \( m_1 = 0.1909 \)
- \( m = 0.3 \)
- \( \alpha = 2.0170774 \)

**AORTIC VELOCITY**

**FIGURE VII**
AORTIC PRESSURE

\[ \Delta P_{\text{max}} \text{[mmHg]} \]

[Graph showing a curve with \( t \text{[ms]} \) on the x-axis and \( \Delta P_{\text{max}} \text{[mmHg]} \) on the y-axis.

HR = 60 BPM

AORTIC VELOCITY

\[ C \text{ m/s} \]

[Graph showing a curve with \( t \text{[ms]} \) on the x-axis and \( C \text{ m/s} \) on the y-axis.

HR = 60 BPM

- \( T = 1 \text{s} \)
- \( T^* = 0.7 \text{s} \)
- \( m_1 = 0.1 \)
- \( m = 0.3 \)
- \( \alpha = 4.9359471 \)

FIGURE VIII
III. MODELLING

The purpose of the lumped hydraulic model was to reproduce CBF patterns under various conditions that will later be defined. One must keep in mind that the two factors influencing the CBF cyclic patterns are the effective perfusion pressure and the myocardial resistance. This resistance, as stated in the Introduction, is divided into two types:

1. Myocardial resistance due to heart contraction.
2. Myocardial resistance due to the vascular bed adapting its resistance to the needed oxygen supply.

In the present model, for the first type of resistance it was assumed that the resistance depends only on the strength of myocardial muscle fiber contraction and does not depend on the state of vasodilation of the vascular bed. This is true also in vivo (45) except in the case of total myocardial vasoconstriction. The above statement holds as long as the total peripheral resistance is smaller than the resistance due to myocardial contraction.

The second type of resistance is entirely determined by the contraction state of the vessels. This resistance regulates the amount of flow admitted during diastole.

The model contains both kinds of resistances lumped into a single element. This element is described in Figure X. It
allows to change independently one from the other, the resistance during systole (first type of resistance) and the resistance during diastole (second type of resistance).

By varying these two resistances, one can adjust the mean CBF during systole and diastole to the desired value, for a constant driving pressure and a constant heart rate.

The ideal model would, of course, contain a feedback mechanism that could adapt the resistances and, therefore, the CBF as a function of heart rate, perfusion pressure and hydraulic work based on equation 29. Such a sophisticated stage of experimentation was not realized in the present study. The possibility of realizing such a model will be discussed later.

A. CBF without stenosis

A.1. Description of the in vitro Model for the simulation of CBF (see Figure IX)

The purpose of the primary loop (A) is to simulate the aortic pressure waveform. The five adaptable parameters are: driving pressure of the pump, rate and systolic time, compliance and lumped peripheral resistance.

The compliance was made out of a 0.020 inch medical grade silastic membrane surrounded by sponges and a metallic cylinder that limited the expansion of the silastic membrane. The
FIGURE IX
SCHEMA OF THE IN VITRO MODEL FOR THE SIMULATION OF CBF
- see legend next page -
LEGEND OF FIGURE IX

0          Return reservoir (right atrium)
1          Pulsatile pump (air driven)
2          Variable compliance
3          Resistance of the systemic circulation
4          Coronary loop connection
5          Electro-magnetic flowmeter
6 & 7      Pneumatic time-varying resistors
6' & 7'    Constant additional resistance ($R^+$)
8          Pressure transducer
9          Rotameter
10         Pneumatic driving console for elements 6 and 7
11         Pneumatic driving console for element 1
A          Primary loop
Ia         Left coronary sinus (3 mm of inner radius)
IIa        Left circumflex (1.5 mm of inner radius)
IIb        Left anterior descending (1.5 mm of inner radius)
I-II       Large coronary vessels (epicardial circulation)
II-III     Myocardium (endocardial circulation)
FIGURE X - TIME-VARYING RESISTORS. (ELEMENTS 6 & 7 IN FIGURE IX)

1. ACRYLIC BOXE
2. METAL MESH
3. POLYURETHANE MEMBRANE
4. RUBBER CORKS

A. CORONARY BLOOD FLOW INLET
B. CORONARY BLOOD FLOW OUTLET
C. CONNECTION TO THE AIR DRIVING SYSTEM (ELEMENT 10 IN FIGURE IX)
systemic resistance was obtained by squeezing the Tygon tubing forming the loop, between two plates. The coronary circulation starts at point 4 with 90-degree branching. The test section representing the lumped left coronary circulation is contained between station I and II. The first section, Ia, is the left aortic sinus and the second section, IIab, represents the anterior descending branch and the left circumflex branch. It is assumed that the flow through the two secondary branches is equal. The myocardial resistance and the resistance due to myocardial contraction is lumped into the two time-varying resistances 6 and 7. These time-varying resistors were made of acrylic boxes occluded by two rubber plugs containing a polyurethane membrane where expansion is limited by a metal mesh (as shown in Figure X). The boxes were air-driven with the same type of pneumatic drive as the ventricle. Rate and systolic time are identical to those of the ventricle, but it is possible to adjust the driving pressure in 10 (see Figure IX), to different values independently of the left ventricular driving pressure in 11 (see Figure IX). The shape of the pneumatic pressure in elements 6 and 7 is close to a square wave as shown in Figure XI. By adjusting the maximum pressure $P_{mm}$ (Figure XI) during systole, the effect of heart contraction on the CBF could be simulated. By adjusting the minimum pressure $P_{mm}$ (Figure XI) during diastole, myocardial resistance due to vasoconstriction or vasodilation could be simulated.
Because of the number of different variables, driving pressure ($\Delta P_D$) and heart rate (HR) were usually kept constant and these time-varying resistors were the only variable parameters controlling entirely the simulated myocardial blood flow.

It was possible to control CBF, under constant pressure head ($\approx 90$ mmHg) between 300 and 1000 cc/min. To obtain flows under 300 cc/min it was necessary to increase the total resistance by adding a complementary resistance in front of the pneumatic time-varying resistors. The Tygon tube leading to the time-varying resistors, was squeezed with a micrometric
screw. This was simply a constant additional resistance 6' and 7' \( (R^+) \) (see Figure IX). The coronary loop is finally completed by returning into the reservoir representing the right atrium where a constant pressure of 1.0 to 2.0 mmHg was maintained. The resistance of sections I-II due to frictional losses under laminar condition is of the order of 2K.

\[ K = 10^3 \cdot \frac{\text{dynes/cm}^2}{\text{ml/s}} \]

A.2. **Experimental procedure and experimental results of the loop without stenosis**

The experimentation conditions were:

(a) Constant aortic pressure and waveform. (130/80 mmHg)

(b) Constant return pressure in the reservoir. (1-2 mmHg)

(c) Constant rate and systolic time.

(d) The time-varying resistors and the additional resistance were adjusted in such a way to achieve mean coronary flows (CBF) of 100, 300, 500, 700 and 900 cc/min.

To establish the desired mean CBF one has to adjust the coronary flow during diastole and systole by looking at the recording (Figures XIV to XVIII). The pressure during systole \( P_{syst} \), in the time-varying resistors, is tuned in such a way as to achieve the minimum systolic flow possible, while assuming that the systolic flow cannot be negative. The pressure during diastole \( P_{dia} \) in the time-varying resistors, is then tuned to a value allowing the desired mean coronary flow. Furthermore,
by analyzing CBF patterns recorded on healthy humans (see Figure XII) one can assume that $\Delta P_D$ and $\overline{CBF}_D$ are linearly related and that steady state conditions prevail during diastole. These conditions are fairly well reproduced in the *in vitro* loop as it can be seen in Figure XIII. Thus, because of the linear relationship between diastolic pressure and flow, mean myocardial resistance $R_D$ will be defined as a function of mean diastolic driving pressure ($P_D$) and mean diastolic CBF ($\overline{CBF}_D$). This function, as shown in equation 32, is:

\[
\overline{R}_D = \frac{\Delta P_D}{\overline{CBF}_D} \text{ [K]}
\]
FIGURE XII

CORONARY BLOOD FLOW AND AORTIC PRESSURE.

THE CBF IS MESURED WITH AN ULTRASONIC DOPPLER SYSTEM ON A HEALTHY HUMAN (see reference 30)
FIGURE XIII  CORONARY BLOOD FLOW AND AORTIC PRESSURE

PATTERNS MEASURED IN THE IN VITRO LOOP DESCRIBED IN FIGURE IX
A.2a Experimental results of the loop without stenosis
FIGURE XIV

EXPERIMENTAL RESULTS

AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
FIGURE XV  EXPERIMENTAL RESULTS 2.
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
FIGURE XVI
EXPERIMENTAL RESULTS
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW

FIGURE XVII

EXPERIMENTAL RESULTS -A.-
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW

FIGURE XVIII

EXPERIMENTAL RESULTS

AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
HR = 80  \quad m = 0.45

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<th>CBF_D</th>
<th>%CBF_S</th>
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TABLE II  Summary of the experimental results of the loop without stenosis  
(see Figures XIV to XVIII)
No = number of the experimental result

$\overline{\text{CBF}}$ = total mean CBF (measured).

$\overline{\text{CBF}}_{DT} = \frac{\overline{\text{CBF}}}{(1-m)}$ = expected CBF during diastole assuming that there is no systolic flow (theoretically determined)

$\overline{\text{CBF}}_D$ = mean CBF during diastole (measured)

$\%\overline{\text{CBF}}_S = 1 - (1-m) \frac{\overline{\text{CBF}}_D}{\overline{\text{CBF}}}$ = % of systolic flow (theoretically determined)

$P_{SM}$ = maximum aortic pressure (measured)

$P_o$ = minimum aortic pressure (measured)

$\Delta P_s = P_{SM} - P_o$

$\overline{\Delta P}_D$ = mean driving pressure during diastole (measured)

$P_{mM}$ = mean maximum air pressure during systole in the time-varying resistors (measured)

$P_{mm}$ = mean minimum air pressure during diastole in the time-varying resistors (measured)

$\Delta P_m = P_{mM} - P_{mm}$

$R^+$ = utilization or not of the complementary resistance (see elements 6' and 7' in Figure IX)

$\overline{R}_D = \frac{\overline{\Delta P}_D}{\overline{\text{CBF}}_D}$ = mean myocardial resistance during diastole (theoretically determined)

flows are in cc/min

pressures are in mmHg

resistances are in $K = \frac{\text{dyne/cm}^2}{\text{ml/s}} \cdot 10^3$
B. CBF with stenosis

B.1. Description of the Model

Coronary blood flow with a stenosis in Section Ia and IIa was simulated. The lumped model can be viewed in two different ways:

(1) One can, as previously, consider that segment Ia represents the left coronary sinus and that IIa and IIb represent respectively the anterior descending branch and the left circumflex. The flow rate through both branches was assumed to be equal. Under these conditions, the stenosis would represent a stenosis of either the sinus, the left circumflex or the anterior descending coronary artery.

(2) One could also consider that the stenosis on IIa is a lumped model of all stenosis existing after the branching of the left circumflex and the anterior descending branch, and that IIb without stenosis is a lumped model of the normal blood flow to the myocardium. In this case, of course, it would not be possible to study the effect of one particular stenosis, but the resistance could be adapted in such a way to study the overall perfusion of the myocardium on healthy and diseased regions.

In this thesis, only the first description of the model will be taken into consideration.

The fundamental assumption now introduced, is that a
regional autoregulation of CBF exists. This means that the myocardium irrigated by the healthy or the stenosed branch will adapt its resistance by vasodilation to obtain the desired blood flow, and so the needed oxygen supply.

For instance, if a resistance is introduced by a stenosis, the myocardial vessels will have to dilate more to achieve the same total mean resistance than without the stenosis. Thus, while keeping the same driving pressure in both cases (with and without stenosis) the mean total resistance has to decrease to allow the needed blood supply. To reproduce this physiological adaptation the diastolic resistance in the time-varying resistors will be tuned to obtain the same mean CBF as the one obtained without stenosis.

B.2. Experimental procedure and experimental results with a 75% stenosis in IIa

(The inner radius of the vessel is 1.5 mm and the inner radius of the stenosis is 0.75 mm. The % of stenosis is the ratio of the sections).

The conditions described under (a), (b) and (c) for the case without stenosis also hold here.

(d) The stenosed branch IIa was clamped. Pressure and resistance were adapted such that the CBF through the healthy branch IIb was the same as in the preceding study without stenosis.

(e) The blood flow through IIa was established and the pressure readjusted to the same level as under (d).
(f) The pressure drop $\Delta P_{Dst}$ was measured across the stenosis.

Both time-varying resistors were driven by the same unit on the same airline. To drive them separately a third driving console coupled to the other two should be introduced. This unit being not available, the only possibility was to get the same resistance in both boxes. To decrease the resistance downstream of the stenosis, the driving line leading to the variable resistance was disconnected so that atmospheric pressure was reached on the outside of the polyurethane bag.
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
FIGURE XXI  EXPERIMENTAL RESULTS
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
FIGURE XXII  EXPERIMENTAL RESULTS
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
FIGURE XXIII

EXPERIMENTAL RESULTS 10

AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW

FIGURE XXIV
EXPERIMENTAL RESULTS .11.

AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW

\[ P_A \text{ [mm Hg]} \]

\[ CBF \text{ [ml/min]} \]

20 mm/sec

50 mm/sec
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW

FIGURE XXV
EXPERIMENTAL RESULTS
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
FIGURE XXVI  EXPERIMENTAL RESULTS -13-
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW

FIGURE XXVII
EXPERIMENTAL RESULTS

AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
Figure XXVIII
Experimental Results
Aortic Pressure and Total Left Coronary Flow
### TABLE III
Summary of the experimental results for 75% stenosis in IIa
(see Figures VI to XV)

<table>
<thead>
<tr>
<th>No</th>
<th>CBF</th>
<th>CBF_{IIb}</th>
<th>CBF_{DT_{IIb}}</th>
<th>CBF_{D_{IIb}}</th>
<th>CBF_{DT}</th>
<th>CBF_{D}</th>
<th>%CBF_{S}</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>IIb</td>
<td>50</td>
<td>50</td>
<td>90.91</td>
<td>60</td>
<td>90.91</td>
<td>60</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>275</td>
<td>50</td>
<td>90.91</td>
<td>60</td>
<td>500.00</td>
<td>290</td>
</tr>
<tr>
<td>8</td>
<td>IIb</td>
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<td>200</td>
<td>363.64</td>
<td>250</td>
<td>363.64</td>
<td>250</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>350</td>
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<td>363.64</td>
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</tr>
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<td>10</td>
<td>IIb</td>
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<td>350</td>
<td>454.55</td>
<td>350</td>
</tr>
<tr>
<td>11</td>
<td></td>
<td>450</td>
<td>250</td>
<td>454.55</td>
<td>350</td>
<td>818.18</td>
<td>500</td>
</tr>
<tr>
<td>12</td>
<td>*</td>
<td>500</td>
<td>250</td>
<td>454.55</td>
<td>350</td>
<td>909.09</td>
<td>540</td>
</tr>
<tr>
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<td>IIb</td>
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<td>350</td>
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<td>500</td>
<td>636.37</td>
<td>500</td>
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<td>350</td>
<td>636.36</td>
<td>500</td>
<td>909.09</td>
<td>730</td>
</tr>
<tr>
<td>15</td>
<td>*</td>
<td>600</td>
<td>350</td>
<td>636.36</td>
<td>500</td>
<td>1090.91</td>
<td>750</td>
</tr>
</tbody>
</table>

See explanations of the symbols contained in the table on page 63.
Second part of

TABLE III Summary of the experimental results for 75% stenosis in IIa
(see Figures VI to XV)

See explanations of the symbols contained in the table on page 63.
<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>number of the experimental result</td>
</tr>
<tr>
<td>CBF</td>
<td>total mean CBF (measured)</td>
</tr>
<tr>
<td>CBF_IIb</td>
<td>total mean CBF in branch IIb (measured) (see Figure IX)</td>
</tr>
<tr>
<td>(\frac{\text{CBF}}{(1-m)})</td>
<td>expected CBF in branch IIb assuming that there is no systolic flow (theoretically determined)</td>
</tr>
<tr>
<td>CBF_D</td>
<td>mean CBF in IIb during diastole (measured)</td>
</tr>
<tr>
<td>(\frac{\text{CBF}}{(1-m)})</td>
<td>expected CBF during diastole assuming that there is no systolic flow (theoretically determined)</td>
</tr>
<tr>
<td>CBF_D</td>
<td>mean CBF during diastole (measured)</td>
</tr>
<tr>
<td>(1 - (1-m) \frac{\text{CBF}}{\text{CBF_D}})</td>
<td>% of systolic flow (theoretically determined)</td>
</tr>
<tr>
<td>P_SM</td>
<td>maximum aortic pressure (measured)</td>
</tr>
<tr>
<td>P_o</td>
<td>minimum aortic pressure (measured)</td>
</tr>
<tr>
<td>(\Delta P_S)</td>
<td>(P_SM - P_o)</td>
</tr>
<tr>
<td>(\Delta P_D)</td>
<td>mean driving pressure during diastole (measured)</td>
</tr>
<tr>
<td>(\Delta P_{Dst})</td>
<td>mean pressure drop across the 75% stenosis in IIa (measured)</td>
</tr>
<tr>
<td>P_mM</td>
<td>mean maximum air pressure during systole in the time-varying resistors (measured)</td>
</tr>
<tr>
<td>P_mm</td>
<td>mean minimum air pressure during diastole in the time-varying resistors (measured)</td>
</tr>
<tr>
<td>(\Delta P_m)</td>
<td>(P_mM - P_mm)</td>
</tr>
<tr>
<td>R_R</td>
<td>utilization or not of the complementary resistance (see elements 6' and 7' in Figure IX)</td>
</tr>
<tr>
<td>(\frac{\Delta P_D}{\text{CBF_D}})</td>
<td>mean myocardial resistance during diastole (theoretically determined)</td>
</tr>
</tbody>
</table>
IIb = flow only through branch IIb with branch Ia clamped (see Figure IX)

* = time-varying pneumatic resistor 6, vent atmosphere (see Figure IX)

flows are in cc/min
pressures are in mmHg
resistances are in $K = \frac{\text{dyne/cm}^2}{\text{ml/s}} \cdot 10^3$
B.3. Experimental procedure and experimental results with a 75% stenosis in Ia

(The inner radius of the vessel is 3 mm and the inner radius of the stenosis is 1.5 mm. The % of stenosis is the ratio of the sections).

The previous conditions (a), (b) and (c) still held.

(d) The time-varying resistances were adapted in such a way as to achieve the same mean flow rate (CBF) as in the first experiment in the loop without stenosis.
Figure XXXI

Experimental Results

Aortic Pressure and Total Left Coronary Flow
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW

FIGURE XXXII
EXPERIMENTAL RESULTS 19
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW

FIGURE XXXIII  EXPERIMENTAL RESULTS -20-

P_{A} [mm Hg]

CBF [cc/min]

20 mm/sec  50 mm/sec
FIGURE XXXIV  EXPERIMENTAL RESULTS 21.
AORTIC PRESSURE AND TOTAL LEFT CORONARY FLOW
<table>
<thead>
<tr>
<th>No</th>
<th>CBF</th>
<th>CBF&lt;sub&gt;DT&lt;/sub&gt;</th>
<th>CBF&lt;sub&gt;D&lt;/sub&gt;</th>
<th>%CBF&lt;sub&gt;S&lt;/sub&gt;</th>
<th>ΔP&lt;sub&gt;DST&lt;/sub&gt;</th>
<th>P&lt;sub&gt;S&lt;/sub&gt;</th>
<th>ΔP&lt;sub&gt;S&lt;/sub&gt;</th>
<th>ΔP&lt;sub&gt;D&lt;/sub&gt;</th>
<th>P&lt;sub&gt;mm&lt;/sub&gt;</th>
<th>ΔP&lt;sub&gt;mm&lt;/sub&gt;</th>
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<th>R&lt;sub&gt;D&lt;/sub&gt;</th>
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<tr>
<td>16</td>
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<td>236.36</td>
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<td>0</td>
<td>130</td>
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<td>92</td>
<td>90</td>
<td>30</td>
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<td>130</td>
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<td>50</td>
<td>90</td>
<td>90</td>
<td>95</td>
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<td>1000.00</td>
<td>850</td>
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<td>20</td>
<td>130</td>
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<td>50</td>
<td>90</td>
<td>100</td>
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</tr>
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<td>19</td>
<td>730</td>
<td>1272.13</td>
<td>1000</td>
<td>21</td>
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<td>130</td>
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<td>90</td>
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<td>56</td>
</tr>
<tr>
<td>21</td>
<td>900</td>
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<td>45</td>
<td>190</td>
<td>146</td>
<td>54</td>
<td>150</td>
<td>145</td>
<td>130</td>
<td>15</td>
</tr>
</tbody>
</table>

**TABLE IV** Summary of the experimental results for 75% stenosis in Ia  
(see Figures XXIX to XXXIV)

See explanations of the symbols contained in the table on page 73.
\[ \text{No} = \text{number of the experimental result} \]

\[ \text{CBF} = \text{total mean CBF (measured)} \]

\[ \text{CBF}_{DT} = \frac{\text{CBF}}{1-m} = \text{expected CBF during diastole assuming that there is no systolic flow (theoretically determined)} \]

\[ \text{CBF}_D = \text{mean CBF during diastole (measured)} \]

\[ \%\text{CBF}_S = 1 - (1-m) \frac{\text{CBF}_D}{\text{CBF}} = \% \text{ of systolic flow (theoretically determined)} \]

\[ P_{SM} = \text{maximum aortic pressure (measured)} \]

\[ P_{O} = \text{minimum aortic pressure (measured)} \]

\[ \Delta P_S = P_{SM} - P_{O} \]

\[ \Delta P_D = \text{mean driving pressure during diastole (measured)} \]

\[ \Delta P_{DST} = \text{mean pressure drop across the 75\% stenosis in Ia (measured)} \]

\[ P_{mM} = \text{mean maximum air pressure during systole in the time-varying resistors (measured)} \]

\[ P_{mm} = \text{mean minimum air pressure during diastole in the time-varying resistors (measured)} \]

\[ \Delta P_m = P_{mM} - P_{mm} \]

\[ R^+ = \text{utilization or not of the complementary resistance (see elements 6' and 7' in Figure IX)} \]

\[ \bar{R}_D = \frac{\Delta P_D}{\text{CBF}_D} = \text{mean myocardial resistance during diastole (theoretically determined)} \]

flows are in cc/min

pressures are in mmHg

resistances are in \( K = \frac{\text{dyne/cm}^2}{\text{ml/s}} \cdot 10^3 \)
IV. EXPERIMENTAL RESULTS AND THEORETICAL CORRELATION

Table II shows that with the time-varying resistors and the constant clamping resistor $R^+$ to regulate low flows, the myocardial resistance can be widely changed. It was demonstrated before that the resistance of the section I-II was of the order of 2K, so that the range of myocardial resistance is between 42.45 and 4.46K, for a mean $\overline{CBF}$ of 100 cc/min to 900 cc/min, respectively (see Table II).

The average percentage of CBF during systole ($\%CBF_S$) was found to be 19.6% of the total flow (see Table II). For CBF up to 700 cc/min the average ($\%CBF_S$) was 16.25% and for 900 cc/min it was 33%, considerably above average. This is due to the fact that the minimum myocardial resistance is approximately 4K and that with a driving pressure $\overline{AP_D}$ of 90 mmHg, it is not possible to achieve diastolic flows exceeding 1100 cc/min (see Table II). To keep coronary systolic flow down, one should increase the driving pressure $\overline{AP_D}$ to increase $\overline{CBF_D}$. Thus it is seen that the maximum $\overline{CBF_D}$ is limited, at constant perfusion pressure, by the minimum myocardial resistance achieved at maximum vasodilation (see Figures XVIII and XXXIV).

Table II confirms that indeed if one increases the minimum myocardial resistance by introducing a stenosis, systolic $\overline{CBF}$ ($\overline{CBF}_S$) has to increase for the same driving pressure to
achieve the same mean CBF (see Figure XXIV).

To determine the resistance presented by the stenosis in IIa, \( \bar{R}_{Dst} \), the pressure drop across the stenosis was measured and the flow in IIa was determined by calculating the difference between the total mean CBF and the mean flow through section IIb (see Figure XXXV Curve 1 and Table V).

<table>
<thead>
<tr>
<th>No</th>
<th>( \overline{CBF}_D )</th>
<th>( \overline{CBF}<em>{D</em>{IIb}} )</th>
<th>( \overline{CBF}<em>{D</em>{IIa}} )</th>
<th>( \Delta P_{Dst} )</th>
<th>( \bar{R}_{Dst} )</th>
<th>( \bar{R}_D )</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>290</td>
<td>60</td>
<td>230</td>
<td>40</td>
<td>13.73</td>
<td>24.23</td>
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<td>9</td>
<td>400</td>
<td>250</td>
<td>150</td>
<td>25</td>
<td>13.16</td>
<td>17.76</td>
</tr>
<tr>
<td>11</td>
<td>500</td>
<td>350</td>
<td>150</td>
<td>26</td>
<td>13.69</td>
<td>13.89</td>
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<tr>
<td>12</td>
<td>540</td>
<td>350</td>
<td>190</td>
<td>38</td>
<td>15.79</td>
<td>12.57</td>
</tr>
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<td>14</td>
<td>730</td>
<td>500</td>
<td>230</td>
<td>40</td>
<td>13.73</td>
<td>9.63</td>
</tr>
<tr>
<td>15</td>
<td>750</td>
<td>500</td>
<td>250</td>
<td>50</td>
<td>15.79</td>
<td>9.37</td>
</tr>
</tbody>
</table>

**TABLE V** (see Table III) Resistance presented by the stenosis \( \bar{R}_{Dst} = \frac{\Delta P_{st}}{\overline{CBF}_{D_{IIa}}} \) in IIa.

(see explanations of the symbols contained in the table on page 63).

If one computes the resistance of the stenosis by the method described above, it is seen (Table V and Figure XXXV) that the resistance of the stenosis is constant for all flow rates. This is due to the fact that the flow through IIb does
FIGURE XXXV PRESSURE DROP VERSUS FLOW ACROSS THE STENOSIS WITH FLOW THROUGH THE STENOSED BRANCH $\Pi_a$ AND THE NON STENOSED BRANCH $\Pi_b$. 
not stay constant when the branch IIa is open or clamped. (Even if the driving pressure $\Delta P_D$ is readjusted). Therefore, the flow in IIa cannot be found by taking the difference between the measured total mean flow (flow through IIa and IIb) and the measured flow through IIb with IIa clamped. This difficulty appeared because it was not possible to measure separately the flow through IIa and IIb. To overcome this problem and thus to study the stenotic flow only, the flow in segment IIb was set to zero. The corresponding results are given in Table VI and plotted in Figure XXXVI curve 2.

<table>
<thead>
<tr>
<th>$\overline{CBF}_{IIa}$</th>
<th>$\overline{\Delta P}_{Dst}$</th>
<th>$\overline{R}_{Dst}$</th>
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</thead>
<tbody>
<tr>
<td>120</td>
<td>9</td>
<td>5.92</td>
</tr>
<tr>
<td>150</td>
<td>12</td>
<td>6.32</td>
</tr>
<tr>
<td>280</td>
<td>40</td>
<td>11.28</td>
</tr>
<tr>
<td>350</td>
<td>60</td>
<td>13.53</td>
</tr>
</tbody>
</table>

**TABLE VI** Mean resistance $\overline{R}_{Dst}$ presented by the stenosis in IIa during diastole (with flow through IIa only)

(see explanations of the symbols contained in the table on page 63).

For the pressure drop versus flow through the stenosis in Ia the results are given in Table VII and plotted in Figure XXXVII curve 1.
THE STENOSIS WITH FLOW THROUGH THE STENOSED BRANCH ONLY (IIa).

2. PRESSURE DROP VERSUS FLOW ACROSS THE STENOSIS WITH FLOW THROUGH THE STENOSED BRANCH ONLY (IIa).

3. PRESSURE DROP VERSUS FLOW OBTAINED BY APPLYING POISEUILLE'S LAW THROUGH THE STENOSIS.


<table>
<thead>
<tr>
<th>No</th>
<th>CBF</th>
<th>CBF&lt;sub&gt;D&lt;/sub&gt;</th>
<th>ΔP&lt;sub&gt;DST&lt;/sub&gt;</th>
<th>R&lt;sub&gt;DST&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>120</td>
<td>200</td>
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<td>0.00</td>
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<tr>
<td>17</td>
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<tr>
<td>19</td>
<td>730</td>
<td>1000</td>
<td>30</td>
<td>2.37</td>
</tr>
<tr>
<td>20</td>
<td>900</td>
<td>980</td>
<td>26</td>
<td>2.09</td>
</tr>
<tr>
<td>21</td>
<td>900</td>
<td>1250</td>
<td>45</td>
<td>2.84</td>
</tr>
</tbody>
</table>

**TABLE VII** Mean resistance $\overline{R}_{DST}$ presented by the stenosis in Ia during diastole.

(see explanations of the symbols contained in the table on page 73).

Obviously, flow and pressure drop through the stenosis are not linearly related, as it would be if one applies Poiseuille's law through the stenosis (see Figure XXXVI curve 3 and Figure XXXVII curve 2). Poiseuille's law can, therefore, not be applied to compute stenotic pressure drops.

The quadratic shape of curve 2 in Figure XXXVI and curve 1 in Figure XXXVII is not due to turbulent flow because the Reynold number in the stenosis remains below the critical value (2320) to flows up to 570 cc/min through IIa and flows up to 1140 cc/min through Ia.

The next part of the study will allow to theoretically determine the losses through a stenosis.
1. Pressure drop versus flow across the stenosis in $I_a$

2. Pressure drop versus flow by applying Poiseuille's law through the stenosis
A. Theoretical determination of the pressure drop through a stenosis

The total pressure drop through the stenosis is due to:

(1) Pressure drop due to the contraction.

(2) Pressure drop due to the fact that at the entrance of the stenosis, one does not have a fully-developed flow. The distance from the entrance until the flow reaches a fully-developed parabolic profile is called entrance length.

(3) Pressure drop due to frictional losses in the stenosis after the flow reaches a parabolic profile.
(4) Pressure drop due to sudden expansion. The total pressure drop $\Delta P_T$ may be expressed as the sum of the above individual pressure drop as follows:

$$\Delta P_T = \Delta P_1 + \Delta P_2 + \Delta P_3 + \Delta P_4$$  \hspace{1cm} (42)$$

The following equations can be found in any hydraulic book (48). They have been established for laminar flow and steady-state conditions. It was mentioned earlier that as a first approximation, one could assume that the steady-state conditions during diastole were achieved.

(1) The pressure drop due to the contraction may be expressed as:

$$\Delta P_1 = \rho \cdot \frac{A}{8} \cdot \cotg \frac{\varepsilon}{2} \cdot \{ 1 - \left(\frac{A_0}{A}\right)^2 \} \cdot \frac{c^2}{2}$$  \hspace{1cm} (43)$$

where $\lambda = \frac{64}{Re}$ for laminar flow

and $\varepsilon = \frac{\alpha}{2}$

(2) The pressure drop due to the entrance effect may be expressed as:

$$\Delta P_2 = 1.16 \rho \frac{c^2}{2}$$  \hspace{1cm} (44)$$

This is valid for the whole entrance length that is given by

$$\frac{x \sigma}{r^2 c} = 0.115 \Rightarrow \text{entrance length } x = 0.115 \frac{r^2 c}{\sigma}$$

(3) The pressure drop due to frictional losses may be expressed as:

$$\Delta P_3 = \frac{8}{\pi} Q \cdot \mu \cdot \frac{L}{r^4}$$  \hspace{1cm} (45)$$

where $Q = C \cdot A$ and $\mu = \text{dynamic viscosity}$
This pressure drop has to be included only if the length \( L \) of the stenosis is greater than the entrance length \( x \).

\[ (4) \quad \Delta P_4 = \rho \cdot C (c - C) \]

**Example**

The different pressure drops for a stenosis of 75% in section Ia at a flow rate of 300 cc/min. are estimated to be

\[ \Delta P_1 = 0.33 \text{ mmHg} \]
\[ \Delta P_2 = 35.29 \text{ mmHg} \]
\[ x \approx 7.8 \text{ cm} \]

The entrance length \( x \) being much greater than the length of the stenosis \( L \), \( \Delta P_3 \) has not to be taken into account,

\[ \Delta P_4 = 11.41 \text{ mmHg} \]

The total \( \Delta P_T \) is therefore:

\[ \Delta P_T = \Delta P_1 + \Delta P_2 + \Delta P_3 + \Delta P_4 \]
\[ \Delta P_T = 47.03 \text{ mmHg} \]

Theoretically determined \( \Delta P_T \) as a function of \( \text{CBF}_D \) using equations 42 through 46

The quantity \( \Delta P_1 \) being very small compared to \( \Delta P_2 \) and \( \Delta P_4 \), can be neglected and \( \Delta P_3 \) is not taken into account since \( x \) is much greater than \( L \) (see example above). The greatest
pressure drop is due to the entrance length effect ($\Delta P_2$). $\Delta P_2$, a function of $\frac{C_{BF}}{D}$ for a 75% stenosis in IIa, is plotted in Figure XXXIX curve 5 and for a 75% stenosis in Ia is plotted in Figure XXXX curve 4. If one adds the pressure drop $\Delta P_4$ due to sudden expansion to the pressure drop $\Delta P_2$ due to the entrance length effect, one obtains the total pressure drop across the stenosis. (For a 75% stenosis in IIa see curve 4 in Figure XXXIX and for a 75% stenosis in Ia see curve 3 in Figure XXXX). $\Delta P_4$ being very small compared to the total pressure drop, it implies that the precise inlet shape of the stenosis is not important.

The only important parameters describing the stenosis are:

(a) The per cent of the stenosis.

(b) The value of the inner radius of the stenosis.

(c) The length of the stenosis (for $x < L$).

One has at this point a very good agreement, for a 75% stenosis, between the theory and the experimental results (see Figures XXXXI and XXXXII), and it would be worthwhile verifying these results in vivo. It also confirms that the steady state assumptions made for the flow during diastole are indeed valid.
ACROSS THE STENOSIS IN $\Pi_a$ (FROM EQUATION 42)

4 TOTAL PRESSURE DROP $\Delta P_T$

5 PRESSURE DROP DUE TO THE ENTRANCE LENGTH EFFECT $\Delta P_2$
FIGURE XL - COMPUTED PRESSURE DROP VERSUS FLOW ACROSS THE STENOSIS IN I_a (FROM EQUATION 42)

3 TOTAL PRESSURE DROP $\Delta P_T$

4 PRESSURE DROP DUE TO THE ENTRANCE LENGTH EFFECT $\Delta P_2$
PRESSURE DROP VERSUS FLOW ACROSS THE STENOSIS IN IIα. SUMMARY OF THE FIGURES XXXV, XXXVI & XXXIX.
FIGURE XLII

PRESSURE DROP VERSUS FLOW ACROSS THE STENOSIS IN \( I_a \). SUMMARY OF THE FIGURES XXXVII & XL
B. Comparison between myocardial resistance and resistance of the stenosis

The mean resistance of the myocardium $\overline{R}_{DM}$ is the mean total resistance $\overline{R}_D$, measured in the loop without stenosis (see Table II), minus the mean resistance of the section I-II. The myocardial resistance in IIa is $\overline{R}_{DIIa} = 2 \cdot \overline{R}_{DM}$. This relation is true as long as one assumes that the flow is equal in both branches IIa and IIb. IIa and IIb being in parallel (see Figure IX) one can write:

$$\frac{1}{\overline{R}_{DM}} = \frac{1}{\overline{R}_{DIIa}} + \frac{1}{\overline{R}_{DIIb}} \quad 47)$$

$$\overline{R}_{DIIa} = \overline{R}_{DIIb} \text{ if } \overline{CBF}_{IIa} = \overline{CBF}_{IIb} \quad 48)$$

Thus for the non stenosed loop the resistance presented by the branch IIa ($\overline{R}_{DIIa}$), is obtained by replacing equation 48 into equation 47.

$$\overline{R}_{DM} = \frac{\overline{R}_{DIIa}}{2} \quad 49)$$

and:

$$\overline{R}_{DIIa} = 2 \cdot \overline{R}_{DM}$$

The values of $\overline{CBF}_D$ and $\overline{R}_D$ used to compute $\overline{R}_{DIIa}$, $\overline{R}_{DST}$, $\overline{R}_{DM}$, $\overline{R}_{DST}$ and $\overline{CBF}_{DIIa}$ are taken from Table II. $\overline{R}_{DST}$ and $\overline{R}_{DST}$ are theoretically determined with equation 42.

The myocardial resistance $\overline{R}_{DIIa}$ of the non stenosed sections IIa and III, and the resistance $\overline{R}_{DST}$ of the 75% stenosis
in IIa are given in Table VIII and plotted in Figure XXXXIII as a function of $\overline{\text{CBF}}_D$.

<table>
<thead>
<tr>
<th>No</th>
<th>$\overline{\text{CBF}}_{\text{IIa}}$</th>
<th>$\overline{\overline{R}}_{\text{IIa}}$</th>
<th>$\overline{\overline{R}}_{\text{DST}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>80</td>
<td>84.90</td>
<td>3.95</td>
</tr>
<tr>
<td>2</td>
<td>210</td>
<td>30.58</td>
<td>8.65</td>
</tr>
<tr>
<td>3</td>
<td>380</td>
<td>14.70</td>
<td>15.37</td>
</tr>
<tr>
<td>4</td>
<td>550</td>
<td>8.92</td>
<td>22.68</td>
</tr>
<tr>
<td>5</td>
<td>550</td>
<td>9.20</td>
<td>22.68</td>
</tr>
</tbody>
</table>

TABLE VIII Relation between myocardial resistance in IIa-III ($\overline{\overline{R}}_{\text{IIa}}$) and the calculated resistance of the stenosis in IIa ($\overline{\overline{R}}_{\text{DST}}$) as a function of the $\overline{\text{CBF}}_D$ in IIa ($\overline{\text{CBF}}_{\text{IIa}}$).

The myocardial resistance $\overline{\overline{R}}_D$ of the non stenosed loop, and the resistance $\overline{\overline{R}}_{\text{DST}}$ of the 75% stenosis in Ia are given in Table IX and plotted in Figure XXXXIII as a function of $\overline{\overline{R}}_D$.

<table>
<thead>
<tr>
<th>No</th>
<th>$\overline{\text{CBF}}_D$</th>
<th>$\overline{\overline{R}}_{\text{DM}}$</th>
<th>$\overline{\overline{R}}_{\text{DST}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>160</td>
<td>42.45</td>
<td>0.41</td>
</tr>
<tr>
<td>2</td>
<td>420</td>
<td>15.29</td>
<td>1.08</td>
</tr>
<tr>
<td>3</td>
<td>760</td>
<td>7.35</td>
<td>1.96</td>
</tr>
<tr>
<td>4</td>
<td>1100</td>
<td>4.46</td>
<td>2.83</td>
</tr>
<tr>
<td>5</td>
<td>1100</td>
<td>4.60</td>
<td>2.83</td>
</tr>
</tbody>
</table>

TABLE IX Relation between myocardial resistance in
II-III \( (R_{DM}) \) and the calculated resistance of the stenosis in Ia \( (R_{DST}) \) as a function of the CBF_D.

Curve 3 in Figure XLIII and curve 3 in Figure XLIV are the difference between the myocardial resistance without stenosis minus the resistance of the stenosis. As soon as this difference reaches a value equal to the minimal achievable myocardial resistance, the critical point would be reached. Below that point the adequate diastolic blood flow could not be delivered any longer and chances are that myocardial injury appears below the stenosed branch. (It is assumed that the patient does not develop any collateral circulation).
1. MYOCARDIAL RESISTANCE $R_{D_{IIa}}$ OF THE NON STENOSED SECTION $II_a III$

2. RESISTANCE OF THE 75% STENOSIS IN $II_a R_{D_{st}}$

3. $R_{D_{IIa}} - R_{D_{st}}$

4. MINIMUM ACHIEVABLE MYOCARDIAL RESISTANCE

Figure XLIII: Resistance Versus Flow

$R_K = \frac{\text{dynes/cm}^2}{\text{ml/s}}$
1. MYOCARDIAL RESISTANCE $R_{DM}$ OF THE NON-STENOSED LOOP

2. RESISTANCE OF THE 75% STENOSIS IN $I_g R_{DS}$

3. $R_{DM} - R_{DS}$

4. MINIMUM ACHIEVABLE MYOCARDIAL RESISTANCE

**Figure XLIV** RESISTANCE VERSUS FLOW [cc/min]
V. CONCLUSION

Apparently, there is not much connection between the theoretical determination of CBF and the modelling part of the study. Besides the previously cited reasons that led one to determine CBF as a function of cardiac work, it was shown that the evaluation of CBF as a function of the hydraulic power delivered by the left ventricle can be a very useful tool in modelling CBF.

As suggested in Chapter III, one could design a model in which CBF varies as a function of cardiac work, by solving equation 29 with an analogue computer. The model would basically be the same with the difference, that instead of addressing a hypothetical value to the time varying resistance, it would be determined by the hydraulic power computed on the basis of the aortic flow, aortic pressure, and heart rate. The computed value would be compared to the actual CBF and the resistance increased or decreased to match the calculated CBF.

The remaining values such as aortic compliance and resistance, oxygen concentration, $\eta_H$, $\eta_c$, $\eta_f$ and $\eta_D$ would be introduced as constants of different values, depending on the characteristics of the coronary patient, and then one could build a loop in which the diameters of the simulated coronaries in sections I-II is adapted to be the same as the
diameters of the patient's vessels, and finally, one could introduce the geometrically corresponding stenosis.

The experimentally-determined limit value below which the required $\text{CBF}$ cannot be achieved any longer should be below the limit value reached by the patient's $\text{CBF}$ because the model does not include any collateral simulation. If one still finds a good correlation between the CBF in the model and the CBF in the coronary patient or in the experimental animal, one could undertake a mathematical modelling of the problem, the advantage of which would be to allow a much wider and more complete parametrical study of CBF variations under various conditions. But, one can see that to simulate hydraulically CBF was an important step because it was the only way to study the behavior of stenotic flow and see if the equations valid for steady state conditions could be used to describe the problem. The hydraulic model also allows one to gain a better understanding of the physical factors limiting the control of CBF.

With the different lumped model, one could, for instance, simulate the perfusion through the different myocardial layers and, thus, determine the state of contraction and the pressures acting on the vessels in those different layers.

It is worthwhile to mention that one other function of the existing model would be to study the effects of intra-aortic balloon pumping on CBF. For the time being, the most
important improvements that have to be made are:

(a) To have the time-varying resistors driven by two separated driving units, so that each resistance could be adjusted separately.

(b) To use one flow meter per coronary vessel to control flow rate and the evolution of the flow pattern in each vessel.

(c) To introduce after the stenosis in branches IIa and IIb a variable compliance and a constant resistor adapted in such a way as to obtain a more physiological behavior of the downstream flow. In this case, the downstream flow was too much influenced by the behavior of the time-varying resistors.

Concerning the experimental study itself, the results obtained for a 75% stenosis should be confirmed by using stenosis of different lengths and different per cent of constriction. Finally, to answer the question raised in the Introduction, one can state on the basis of this work, that the pressure drop through the stenosis is an important function of flow (see figures XXXVI, XXXVII, curve 2,1) and that an increase in heart rate could, under specific conditions, lead to a lack of myocardial perfusion and therefore lead to myocardial infarction. One understands that the "specific conditions" vary from one case to another. It is easy to imagine that two different individuals under the same stress and work condition, with the same percentage of stenosis similarly situated, will not get the same pressure drop through the stenotic region, for several reasons:
(a) Even with the same percentage of stenosis, the diameter of the stenotic vessel can be different.

(b) The minimum achievable myocardial resistance may change.

(c) The values $\eta_C$, $\eta_f$, $\eta_D$ and $m$ can be combined differently from individual to individual (under the above specified conditions) and for a given combination the required blood flow may reach the limit value.

Those are part of the reasons that could explain why a certain percentage of patients reaches the critical state at which myocardial infarction occurs.

In conclusion, one can state that coronary blood flow with or without stenosis in the main coronary vessels can indeed be simulated in vitro, and if the results are to be corroborated through animal experimentation, one could use the hydraulic, or later on, the mathematical model, as a useful diagnostic tool to determine, in critical cases, if coronary surgery is needed.
APPENDIX

The subject here is not to write a complete historical survey on CBF, but rather to give a guideline to the reader that will allow him to find the necessary references to understand and to pursue this work.

Knowledge of regulation of CBF has already been summarized by Dr. Berne (3) and Dr. Gregg (26).

As mentioned in the introduction, CBF has been studied for over three hundred years. It was in 1645 that Harvey showed accurately that channels existed on the walls of the heart for its own nutrition. Later, in the 18th century, the existence of arterial anastomoses, the ventricular branches and the connections between the arteries and the heart cavities were shown. But until the 20th century, CBF and its regulation have not been well defined.

From now on, to simplify the reader's literature research, the information on the heart and its vascularization will be divided into three sections. Each section pertains to a different way of analysis of the myocardial vascularization and the heart activity.

(a) The static way, meaning the morphologic study of the myocardium by an injection technique, to obtain the casting of the coronaries, or by arteriography, or by a microsphere counting technique.
(b) The dynamic way, meaning the study of the CBF by a washout technique, by cineangiography, or by an electromagnetic flowmeter.

(c) The energetic way, meaning the study of the myocardial energetics by the control of the oxygen consumption, the metabolic exchanges and the hydraulic power delivered by the heart.

The publications, from the second half of the 20th century, taken into consideration, will be classified in one of these three sections.

(a) The static analysis

Using different injection techniques, the existence of anastomotic vessels (55) and the vascular communications between the coronary arteries (56) has been confirmed. Furthermore, with the help of these injection techniques, the anatomic study of the atrial coronary arteries has been undertaken on normal human hearts (31). In the meantime, through angiography and injection of microspheres, it has been possible to study the total and regional blood flow and the predominance in myocardial vascularization. Thus, it has been established that the right coronary arteries were predominant in 48% of the cases, balanced in 34% of the cases, and the left coronary arteries predominant in only 18% of the cases (47,54). This does not mean that in general, the right coronary flow is predominant, but simply states that the myocardial surface reached by the right coronary vessels is
Usually predominant. It already has been shown in the thesis that left CBF is in fact predominant in most of the analyzed subjects. Angiography is also used to understand and diagnose coronary arterial disease on man (10,11). Most of the microsphere techniques have been used to study flow distribution in conscious and anesthetized dogs (12,52). Epicardial and intramyocardial collateral circulations in dogs have been investigated by radioactive microspheres (5,6,9). The final result obtained, by superposition of angiography taken at different times, is already a "dynamic view" of the myocardial perfusion but does not describe the instantaneous behavior of the CBF, and, therefore, it is classified in the "static" section. On man where the dissection of the myocardium is not possible, techniques using, for instance, the rubidium and the coincidence counting method are used to determine myocardial blood flow in healthy and diseased state of the coronaries (8,92).

(b) The dynamic analysis

The washout method is probably the less "dynamic" method in this section. Nevertheless, this technique gives a good idea of the mean CBF with an accuracy below 20% of the real flow. Different kinds of dyes are usually used. One of the most common dyes is nitrous oxide (4,13,27). Another washout
technique, for instance, xenon injection, showed that average or total flow tends to be higher in patients with the severest degree of coronary arteriosclerosis (38).

The study of instantaneous and local CBF on man is realized by cineangiography. Cineangiography is less invasive than the electromagnetic flowmeter technique, but gives a good image of the blood flow in the main coronary arteries. Coronary heart disease and its progression is often investigated by selective coronary cinearteriography in catheterized patients (2,7).

The use of the electromagnetic flowmeter implies, as stated before, the possibility to reach the vessel in which the flow has to be measured. All of the chronic and most of the acute experiments are performed on animals (3,26). Dogs have been used to determine the regional myocardial blood flow during acute right ventricular systolic hypertension (16). But thanks to the development of cardiac bypass surgery, the electromagnetic flowmeter has also been applied to man, to measure flow and pressures in preinfarction syndromes (42), or in the syndrome of impeding myocardial infarction (21). The electromagnetic flowmeter has been set on fresh implanted vein grafts to determine the flow improvement due to the aorto-coronary bypass (15,51).
Good results have also been obtained for coronary flow measurements with the ultrasonic Doppler flowmeter system (30).

(c) The energetic analysis

All the methods described in the two sections above contribute to the investigation of the last section. As stated, in the introduction of the present thesis, the heart furnishes its own energetic supply. Therefore, the perfusion of the myocardium depends on the metabolic needs of the heart. These metabolic needs vary within a large number of parameters. The problem is to determine which are the most important parameters influencing the perfusion of the heart. It has been decided in this work to show the relation existing between myocardial blood flow, oxygen consumption and hydraulic work. Obviously, not every one agrees with this approach of the problem. Nevertheless, most of the experimentations made on man and animal showed that an important relation between CBF and hydraulic power does indeed exist. For instance, it has been established that chronic increase in the energy requirement of the hypertensive heart patients were met by an increase in the total oxygen consumption due to hypertrophy and that the efficiency of the failing heart was decreased (4). For healthy patients and patients with congestive heart failure, the effects of exercise on CBF is expressed by an increase in
oxygen consumption. But the increase in left ventricular work was found proportionally greater than the rise in left ventricular oxygen consumption. It has been concluded that efficiency of the myocardium was slightly increased with increased work (37). Furthermore, the importance of perfusion pressure, left ventricular work and oxygen consumption in determining myocardial blood flow has also been emphasized especially in coronary patients (35).

Animal experimentation on dogs showed that CBF was related to the following dynamic functions of the heart: cardiac work, cardiac output, cardiac rate and changes in mean arterial blood pressure. Again, it was found that the highest correlation was the one relating CBF and oxygen consumption (17). This was also confirmed in three other publications where it was demonstrated that a lack of oxygen induces an increase in CBF (29), that oxygen consumption is directly related to ventricular metabolism (44), and that nerve stimulation increases myocardial oxygen consumption and work (14).

Finally, it seems necessary to mention two interesting theories concerning the "energy section" that will have to be taken into consideration for further investigations in this field. Instead of relating oxygen consumption and CBF to the total hydraulic work, ventricular performance can be
deduced by analyzing the aortic flow and pressure patterns. This has been done on dogs where the principal effects of acute occlusion of the left circumflex appeared to be a reduction in peak ejection velocity, peak acceleration and stroke volume of the left ventricle. Large changes in left ventricular performance lead to ventricular fibrillation within minutes or hours after they occurred (4). The second interesting aspect is that myocardial flow is more closely related to lactate production than to oxygen uptake. It has been found that coronary flow and coronary oxygen extraction patterns did not distinguish patients with coronary artery diseases from normal subjects, either at rest or under stress. But the degree of lactate production usually bears a relation to the morphologic severity and the location of coronary arterial disease (7).
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