

# Automatic Computation for Pressure Controlled Intermittent Coronary Sinus Occlusion

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## Abstract

Pressure controlled intermittent coronary sinus occlusion (PICSO) has been found to substantially salvage ischemic myocardium. By elevating venous pressure two mechanisms are involved namely the distention of venous vessels inducing mechanotransduction as well as a redistribution of venous flow towards ischemic areas. Mechanotransduction in endothelial cells inducing changes in the ischemic heart inducing myocardial salvage as well as myocardial recovery is blunted by possible consequences of myocardial perfusion deficits by limiting coronary inflow.

To limit these severe side effects we have evaluated a new mathematical model to describe the Increase (Inflation) and decrease (deflation) in coronary Sinus pressure (CSP) following pressure controlled intermittent coronary sinus occlusion (PICSO) and release. The model is evaluated and compared on the basis of dogs, pigs and sheep. The model consists of two parts with three parameter double exponential function for each, and it was fitted by using the non-linear least squares algorithms. The new model was used in implementation of automatic computing module which is responsible to compute the following quantities for Inflation and Deflation:

1. Systolic and diastolic plateau.
2. Rise-Time of systolic and diastolic plateau.
3. The mean integral of the CSP (Area under the curve).
4. Number of heart beats impact in inflation and deflation periods.
5. Driving the slope of CSP

Corresponding quantities for various coronary sinus balloon inflation and deflation cycles were computed with ranging from cycles being as short as 5sec/3sec (inflation/deflation ratio) to cycles as long as 12sec/8sec.

**Keywords:** *coronary sinus pressure (CSP), pressure controlled intermittent coronary sinus occlusion (PICSO) and Left Anterior Descending Artery (LAD).*

## 1. Introduction

Pressure controlled intermittent coronary Sinus occlusion PICSO has been proposed and investigated as a new technique in interventional cardiology and cardiac surgery to salvage ischemic areas of the myocardium.

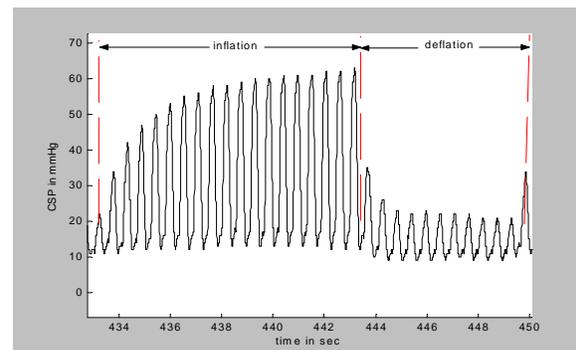


Fig. 1 One PICSO with Inflation and deflation time 10/6 sec

Because the beneficial effect of this intervention appears to be closely linked to an optimal timing of coronary venous pressure elevation (i.e. to define the therapeutic range of salvage and severe side effects induced by prolonged increase in coronary resistance), a new mathematical model has been developed in order to put the estimation of occlusion and release times on a quantitative basis. The model consists of two parts with three parameter double exponential function for each.

$$P_{csp}(t) = \begin{cases} A * \exp\{B*[1 - \exp(-C*t)] - 1\} & \text{when } 0 < t < T1 \\ D * \exp\{E*[1 - \exp(-\frac{F}{t})] - 1\} & \text{when } T1 \leq t < T2 \end{cases} \quad (1)$$

Where

$P_{csp}(t)$  = Coronary sinus pressure (mmHg)

$t$  = Time (s), measured from the start of occlusion

$A, D$  = fitting parameter in (mmHg)

$B, E$  = fitting parameter (dimensionless)

$C, F$  = Fitting parameter (1/s)

$T1$  = Time that mark the end of the CSP occlusion phase (s)

$T2$  = Time that mark the end of the CSP release phase (s)

The first part Eq. (1a) describes the rise of the CSP during the Inflation (occlusion) time.

$$P_{csp}(t) = A * \exp\{B*[1 - \exp(-C*t)] - 1\} \quad (1a)$$

As shown in the Fig. (1), systolic peaks incremented coincided with the time during the inflation period.

The second part Eq. (1b) describes the release of the CSP during the deflation (release) time.

$$P_{csp}(t) = D * \exp\{E*[1 - \exp(-\frac{F}{t})] - 1\} \quad (1b) \quad \text{As}$$

shown in the Fig. (1), the systolic peaks decremented coincided with the time during the deflation period.

The systolic and diastolic peaks were fitted with the nonlinear least square algorithms. Additionally a new module was implemented using Oracle DB and Matlab, which is responsible to compute automatically the quantities of the CSP.

## 2. Method

Since the mathematical model Eq. (1a and 1b) together with both sets of three fitted parameters ( $A, B, C$  and  $D, E, F$ ) represent the envelope curve (systolic and diastolic, respectively), it is now possible to express the height of the CSP plateau as well as the time taken to reach the plateau in terms of fitted parameters.

### 2.1 Inflation

The inflation haemodynamic quantities were calculated by using the Eq. (1a) which developed by Schreiner [W. Schreiner]

#### 2.1.1 CSP plateau and rise time

The highest value of  $P_{csp}(t)$  in Eq. (1a) is reached for  $t \rightarrow \infty$

$$P_{csp}(t = \infty) = A * \exp(B - 1)$$

Since a plateau is never actually reached (in mathematical terms) it is meaningful to consider the time it takes to reach, say, 90% of the predicted height of the plateau.

The systolic Plateau is 90% from the  $P_{csp}(t = \infty)$

$$\text{Systolic Plateau} = 0.9 * A * \exp(B - 1) \quad (2)$$

The Diastolic Plateau was calculated exactly as the Systolic.

The rise time will be

$$\text{Rise Time} = (1/C) * \ln(-B / \ln(0.9)) \quad (3)$$

The diastolic plateau and rise time was calculated exactly as the systolic plateau.

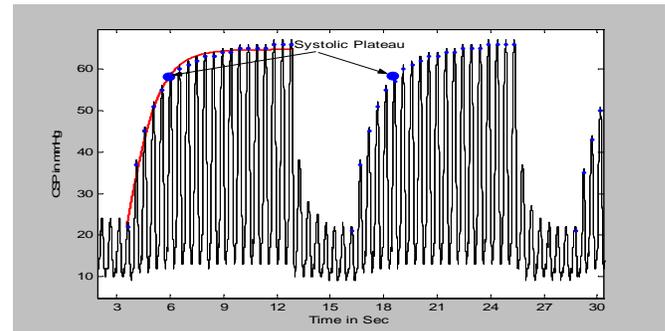


Fig. 2 Systolic Plateau of CSP during the inflation, the solid curve represents the fitted three parameter model functions, and the circle represents the systolic plateau

#### 2.1.2 Driving the slope of the CSP

The first derivative gives an estimate for the maximal slope in terms of the fitted parameters

$$dp/dt = A * B * C * \exp(B * (1 - \exp(-C * t)) - C * t) \quad (4)$$

### 2.2 Deflation

The deflation was calculated by using Eq. (1b)

#### 2.2.1 CSP plateau and rise time

The lowest value of  $P_{csp}(t)$  in Eq. (1b) is reached for  $t \rightarrow \infty$

$$P_{csp}(t = \infty) = D * \exp(-1)$$

Since a plateau is never actually reached (in mathematical terms) it is meaningful to consider the systolic Plateau is 110% of the predicted lowest of the plateau.

The systolic plateau is 110% from the  $P_{csp}(t = \infty)$

$$\text{Systolic Plateau} = 1.1 * D * \exp(-1) \quad (5)$$

The rise time will be

$$\text{Rise Time} = -F / \ln(1 - \ln(1.1) / E) \quad (6)$$

The diastolic plateau and rise time was calculated exactly as the systolic plateau.

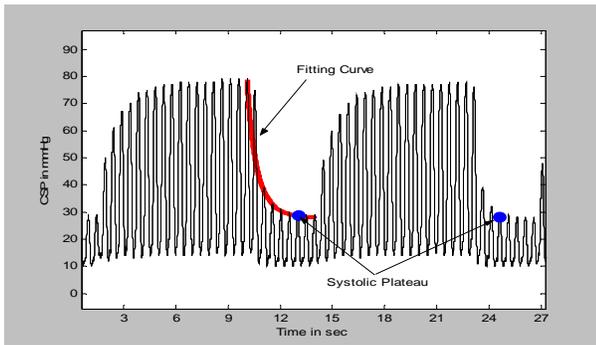


Fig. 3 Systolic Plateau of CSP during the deflation, the solid curve represents the fitted three parameter model functions, and the circle represents the systolic plateau.

### 2.2.2 Driving the slope of the CSP

The first derivative gives an estimate for the maximal slope in terms of the fitted parameters

$$dp/dt = (1/t^2) D * E * F * \exp(1 - \exp(-F/t)) * E - F/t - 1 \quad (7)$$

## 3. Results

The module computes automatically the haemodynamic quantities of the CSP in Multi-cycle, first finding the systolic and peaks for deflation and inflation then making the fitting curve and finding the plateau, rise-time, slope of CSP, mean integral, and the number of heart beats.

The model parameters and the derived quantities will change with time. For any diagnostic value it is essential to establish ranges which can be used as reference intervals for the normal state. The following results comprise a preliminary investigation of the spread of the derived quantities observed during PICSO.

### 3.1 Systolic and diastolic plateau

The Automatic computation module computes the systolic and diastolic plateau of the CSP for inflation and deflation periods. The plateau of coronary sinus pressure during LAD occlusion and after LAD reopening for thirteen animals (sheep, dogs and pigs) was computed with this module.

Fig. (4) shows the change of the systolic and diastolic plateau of the CSP during the inflation period.

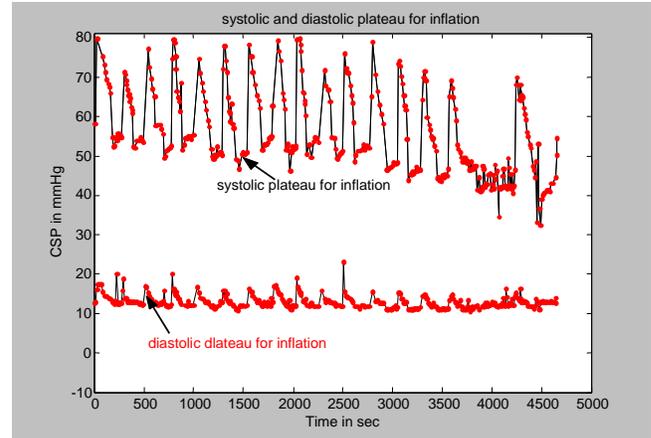


Fig. 4 Systolic and diastolic plateau during the inflation period

Statistical result of changing the systolic plateau during the inflation period depending on the occluded or opened LAD is illustrated in Fig. (5).

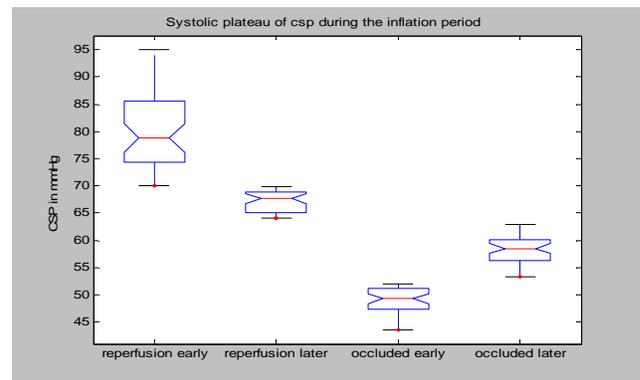


Fig. 5 Systolic pressure changes in dependence of LAD during the inflation period

The systolic plateau of the CSP will reached  $79.0445 \pm 5.00$  mmHg by reperfusion early (LAD opened), and  $67.7547 \pm 3.00$  mmHg by reperfusion late (LAD opened) and  $49.22 \pm 2.2$  by occluded early (LAD occluded) and  $57.3559 \pm 2.50$  mmHg by occluded late (LAD occluded).

### 3.2 Automatic computation of rise and release time

According to the definition, the rise/release time is the time it takes for the CSP to reach its plateau (systolic or diastolic), which can be reached after a prolonged occlusion or release.

Fig. 6 demonstrates the different rise times needed to reach the systolic and diastolic plateau in accordance with the LAD occlusion status. During the inflation period the

systolic plateau can be achieved very fast when LAD is respond.

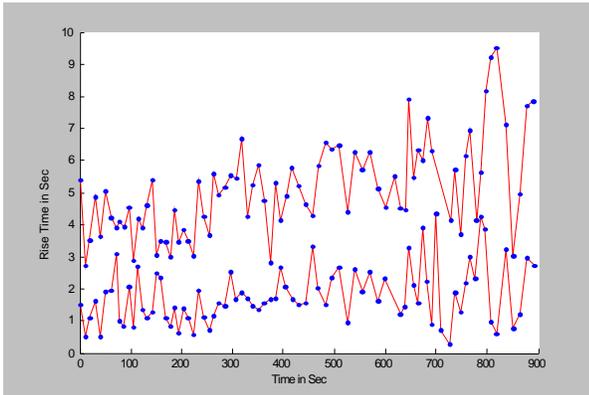


Fig. 6 Rise time for systolic and diastolic plateau of the CSP during the inflation period.

Different rise times during the inflation period depending on the occluded or opened LAD for systolic plateau is illustrated in Fig. (7). The systolic plateau will reach in  $5.13 \pm 1.00$  sec by reperfusion early and in  $5.31 \pm 1.00$  sec by reperfusion late and in  $5.89 \pm 1.20$  sec by occluded early and in  $5.80 \pm 1.10$  sec by occluded late. One/two-way ANOVA was to prove the significance of the obvious difference between the LAD status concerning rise times confirmed that the significance is evident ( $p < 0.0083$ ).

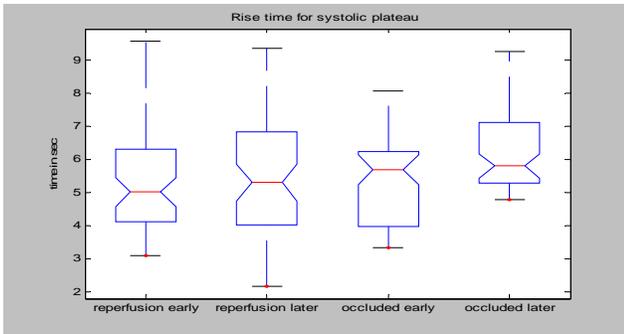


Fig. 7 Rise time of systolic plateau changes in dependence of LAD during the inflation period

### 3.3 Relations between derived quantities

Predicted plateau, rise times, mean Integral of CSP, number of heart beat per PICSO cycle and CSP slope ( $dp/dt$ ) are calculated from the fitting parameters and may be called the ‘derived quantities’. Whereas the parameters themselves are not directly accessible to physiological interpretation, the derived quantities are deliberately constructed to resemble intuitive criteria. Table 1 shows example of the hemodynamic quantities results from the automatic computation module during 3 minutes.

Table 1: Hemodynamic quantities result of the automatic computation module

Time in sec	Systolic plateau in mmHg	Rise time in sec	Mean integra in mmHg*sec	Heart rate beat / PICSO
0	55.4058	5.3956	228.0981	11
10.7925	55.3366	2.7313	116.5783	11
20.4862	54.3164	3.5208	142.2453	11
30.1731	57.8244	4.8766	204.5571	11
40.4861	54.3931	3.6464	147.5295	11
50.8025	55.9441	5.0325	205.9031	8
60.5261	54.404	4.2341	168.1017	11
70.7459	58.0824	3.8995	171.2134	6
78.275	56.7913	4.1195	174.6481	9
87.4225	57.6111	3.9438	164.7809	8
95.9406	55.3845	4.5537	178.9085	11
105.6809	51.6218	2.8945	111.9028	9
114.199	54.5463	4.1925	162.3834	11
123.3299	51.9723	3.8938	150.6698	11
131.9346	53.565	4.5921	181.1066	9
141.0488	53.9653	5.4086	215.2864	9
150.8257	52.0763	3.0519	119.6574	10
159.3938	52.8	3.4808	134.7787	12
168.5546	51.454	3.4619	133.1845	12
177.7121	50.2843	3.0083	113.2353	10
186.197	51.9618	4.4532	168.9303	10

## 4. Conclusion

The principal goal of this work was to build a robust mathematical model that could accurately and reliably calculate the rise and release of coronary sinus pressure (CSP) during inflation (rise) and deflation (release) periods. Such a model should be a useful tool that could substitute for time-consuming visual inspection of CSP data during heart operations or other surgeries, when time constraints can affect patient outcomes. Currently, during heart surgeries, clinicians must constantly recalibrate CSP data using this visual inspection, making calculations cumbersome and often inaccurate. Further-more, physiological reactions in heart patients change among individuals, and even within the same individual under different conditions. Thus, any reliable model must be able to accommodate such changes and to operate PICSO under optimal conditions.

To date, no mathematical model has been developed to predict or describe the relationship of inflation and deflation of the CSP. Schreiner (86) developed a model, which describes the rise of CSP, but without a model that also accounts for the release of the CSP. Without the other half of the model, calculating the CSP has been a matter of guesswork. To solve this problem, we developed a new mathematical model that efficiently describes the rise and the release of the CSP. Under normal

experimental conditions, one will always find common features that can be exploited. The CSP plateau is such a feature: while the height, the time to reach the plateau, and the maximum slope may vary, nevertheless a plateau is always reached, and this allowed us to identify features that could be incorporated into the model to make it both feasible for necessary physiologic adaptations and stable and robust for calculations.

Our model had to meet the following requirements:

- i. It had to be derived from the minimum number of fitting parameters.
- ii. It had to estimate the occlusion and release times on a quantitative basis.

The model consists of two equations, each having three parameters of double exponential functions. The CSP was expressed in terms of these fitted parameters, three for inflation and three for deflation. The systolic rise time can be used as a calculated parameter for the closed loop regulation of PISCO. The automatic computing module (computer module) calculates and computes several hemodynamic quantities, such as systolic and diastolic plateau, rise time, heart rate per cycle and the mean integral of CSP. This work has a number of implications for bioinformatics. It provides a new mathematical model that describes the increment and decrement of the CSP during individual PISCO cycles.

## 5. References

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