

CORONARY AUTOREGULATION BASED ON OXYGEN FLOW: A MODEL OF OXYGEN SUPPLY TO CORONARY ARTERIOLAR SMOOTH MUSCLE IN INJURY AND ENDOTHELIAL DYSFUNCTION

N. Sheffer, M. Scheinowitz, O. Barnea

Department of Biomedical Engineering, Faculty of Engineering, Tel Aviv University, Tel Aviv, ISRAEL

Abstract - A multi-layers theoretical model of a coronary arteriolar smooth muscle was developed to elucidate the role of oxygen in the control of coronary blood flow. Both oxygen transport by diffusion and local tissue metabolism were considered. Oxygen partial pressure in all layers was calculated. The model suggests that in normal conditions, oxygen partial pressure reaches its minimal value in the media, where oxygen consumption is the greatest. When the smooth muscle is injured, its metabolic demands are increased in order to heal, resulting in a P_{O_2} decline. These results are in agreement with experimental results. The model also shows that increased myocardial oxygen partial pressure causes the arteriolar smooth muscle to contract in response to lack of oxygen. Decreased myocardial oxygen pressure results in expansion of the arteriole allowing greater coronary flow.

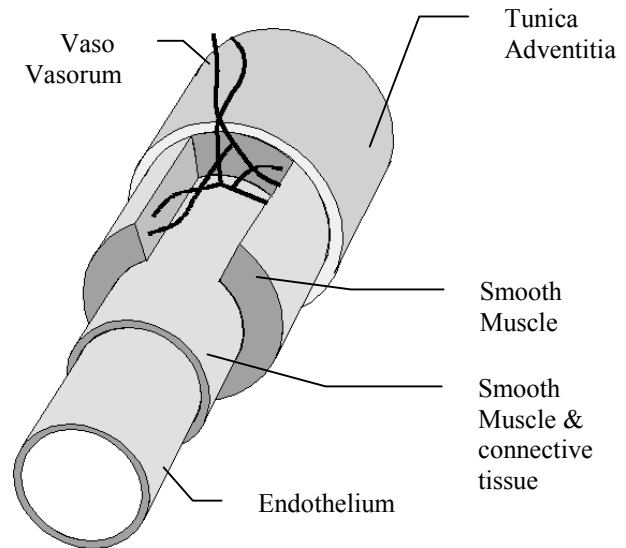


Fig. 1. Schematic diagram of the arteriole wall layers

I. INTRODUCTION

Experimental studies show that the arterial wall is oxygenated by two sources [Fig. 1]. The inner layer of the arteriolar smooth muscle receives oxygen directly from the vessel lumen, whereas the rest of the surrounding tissue is supplied by the vasa vasorum [1, 2,3]. The primary mechanism of oxygen supply is diffusion [3].

Previous theoretical models of oxygen supply to the arteriolar smooth muscle focused on O_2 and CO_2 transport between arterioles and surrounding tissue. However, no model accounts for both mass-transport through the inner layers of the arteriole and the supply by the vasa vasorum of the outer vessel layer. Furthermore, such a model was not specifically applied to the coronary bed.

In the study presented here, a model of O_2 supply to a coronary arteriolar smooth muscle was developed to calculate oxygen partial pressure in all layers of the arteriole wall in various states. Both oxygen transport by diffusion and local tissue metabolism were incorporated. Oxygen partial pressure in all layers was calculated.

II. METHODS

A theoretical model of O_2 supply to a coronary arteriolar smooth muscle was developed. The model consists of five cylindrical layers: a blood vessel lumen, an intima, a medial smooth muscle, an adventitial segment consisting of connective tissue component and a surrounding tissue. Experiments show that axial oxygen diffusion is very small in the perfused tissue along the arteriole [4]. Therefore, diffusion in the axial direction was neglected assuming it has only minor

Report Documentation Page

Report Date 25OCT2001	Report Type N/A	Dates Covered (from... to) -
Title and Subtitle Coronary Autoregulation Based on Oxygen Flow: A Model of Oxygen Supply to Coronary Arteriolar Smooth Muscle in Injury and Endothelial Dysfunction		Contract Number
		Grant Number
		Program Element Number
Author(s)	Project Number	
	Task Number	
	Work Unit Number	
Performing Organization Name(s) and Address(es) Department of Biomedical Engineering, Faculty of Engineering, Tel Aviv University, Tel Aviv, ISRAEL		Performing Organization Report Number
Sponsoring/Monitoring Agency Name(s) and Address(es) US Army Research, Development & Standardization Group (UK) PSC 802 Box 15 FPO AE 09499-1500		Sponsor/Monitor's Acronym(s)
		Sponsor/Monitor's Report Number(s)
Distribution/Availability Statement Approved for public release, distribution unlimited		
Supplementary Notes Papers from the 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 25-28 October 2001, held in Istanbul, Turkey. See also ADM001351 for entire conference on cd-rom.		
Abstract		
Subject Terms		
Report Classification unclassified	Classification of this page unclassified	
Classification of Abstract unclassified	Limitation of Abstract UU	
Number of Pages 3		

effect in comparison with radial oxygen diffusion. Both oxygen transport by diffusion and local tissue metabolism were considered.

Fig. 2 shows the basic structure of the three inner segments of the model and a sketch of the oxygen tension drop along the radial direction in two different metabolic states. The inner radius of the vessel is designated as R_i and the outer radius of the Intima as R_o . Oxygen partial pressure in the Intima and in the smooth muscle are designated as P_{In} and P_s , respectively.

Experimental observations show that oxygen unloading of erythrocytes during their motion along coronary arterioles is insignificant to the myocardial supply [5]. Also, Mean intra-myocardial partial pressure of varies in a small range and is determined by the interaction of different capillary diffusion fields [6, 7]. Thus, boundary conditions include oxygen partial pressure inside the inner layer that is equal to that in the blood, and at a distance away from the vessel partial pressure equals to the mean intramyocardial oxygen tension that is determined by capillary oxygen supply and myocardial consumption. Furthermore, partial pressures for the different layers had to match at the blood-smooth muscle wall, wall-adventitia, and adventitia-tissue boundaries. Also flow leaving one layer must be equal to the flow entering the next layer.

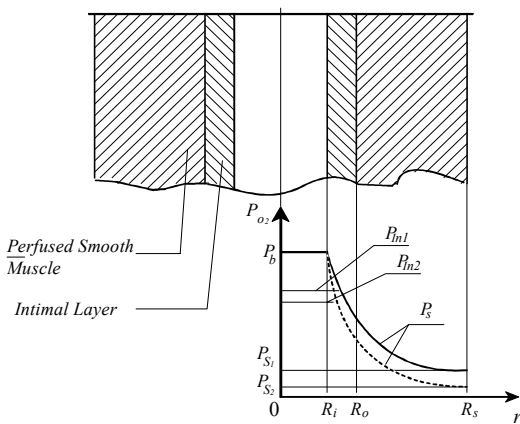


Fig. 2: A model of the arteriolar smooth muscle Oxygen distribution

The model was run in various states to study its behavior in normal and abnormal conditions. The sensitivity of oxygen availability in the smooth muscle to changes in intramyocardial pressure and in arterial blood P_{O_2} were examined.

III. RESULTS

Fig. 3 shows oxygen partial pressure drop as a function of the distance from the center line of the arteriolar lumen under normal conditions. The pressure reaches its minimum in the media-adventitia boundary. Then it increases until it reaches mean intramyocardial tension. This behavior exhibited by the model is similar to that found in experimental studies [8].

Fig. 4 shows oxygen partial pressure drop when the smooth muscle is damaged. In the particular example shown here metabolic demands were doubled in the smooth muscle layer to compensate for healing processes. This situation results in a P_{O_2} decline in comparison to partial pressure deviation under normal conditions.

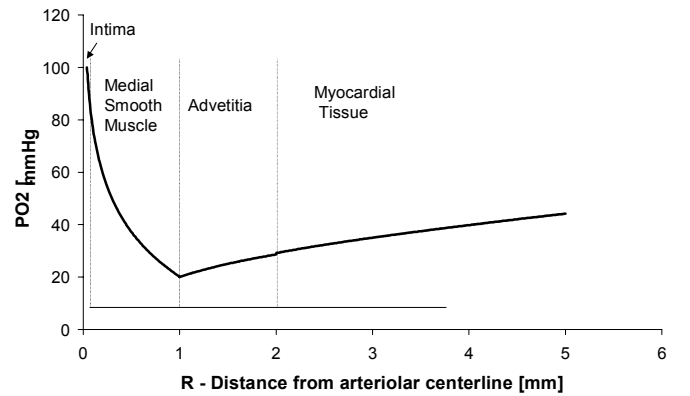


Fig 3. Oxygen partial pressure drop as a function of the distance from the center line of the arteriolar lumen

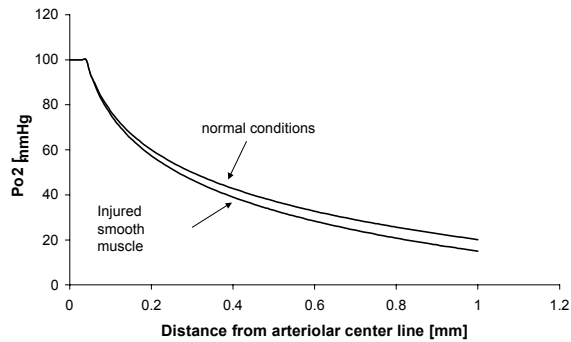


Fig. 4: Oxygen partial pressure drop for the Intima and the smooth muscle sections for healthy and injured still healing smooth muscle

IV. DISCUSSION

The model shows that in normal conditions, oxygen partial pressure reaches its minimal value in the media, where oxygen consumption is the greatest. Then partial pressure gradually increases until it reaches mean intramyocardial tension. When the smooth muscle is injured, its metabolic demands are increased in order to heal, resulting in a PO_2 decline. When the intimal endothelium is injured, less oxygen passes to the inner parts of the smooth muscle, hence leading to lower values of PO_2 at the media. These results are in agreement with experimental data obtained from peripheral arterioles in animals.

This model of arteriolar smooth muscle contraction as a function of oxygen availability was developed to be integrated into a comprehensive model of the coronary bed and a model of the heart to study cardiac autoregulatory mechanisms.

REFERENCES

1. Braunwald E. (Ed.) *Heart Disease: A Textbook of Cardiovascular Medicine*. W.B. Saunders Company, Philadelphia, 5th edition, 1997.
2. Gayeski, T.E.J., and Honig, C.R. Intracellular P_{O_2} in individual cardiac myocytes in dogs, cats, rabbits, ferrets and rats. *American Journal of Physiology*. 260:H522-H531, 1991.
3. Popel, A.S., Pittman, R.N., and Ellsworth, H.L. Rate of oxygen loss from arterioles in an order of magnitude higher than expected. *American Journal of Physiology*. 256:H921-H924, 1989.
4. Schacterle, R.S., Adams, J.M., and Ribando, R.J. A theoretical model of gas transport between arterioles and tissue. *Microvascular Research*. 41:210-228, 1991.
5. Honig, C.R., Gayeski, T.E.J. Precapillary O_2 loss and arteriovenous O_2 diffusion shunt are below limit of detection in myocardium. *Advances in Experimental Medicine and Biology* 247:591-599, 1989.
6. Honig, C.R., Gayeski, T.E.J. Comparison of intracellular P_{O_2} and conditions for blood-tissue O_2 transport in heart and working red skeletal muscle. *Advances in Experimental Medicine and Biology*. 215:309-321, 1987.
7. Clark, P.A., Kennedy, S.P., and Clark, A.Jr. Buffering of muscle tissue P_{O_2} levels by the superposition of oxygen field from many capillaries. *Advances in Experimental Medicine and Biology*. 248:165-174, 1989.
8. Kivisaari, J., Niinikoski, J. Oxygen tensions in healing anastomosis of rabbit aorta. *Surgery*. 78(2):165-175, 1975.