GEORGIA INSTITUTE OF TECHNOLOGY — OFFICE OF CONTRACT ADMINISTRATION

PROJECT ADMINISTRATION DATA SHEET

[X] ORIGINAL [ ] REVISION NO. ____

Project No./(Center No.) E-25-699 (R6275-0A0) GTRC/~~GIT~~ DATE 3 / 17 / 87

Project Director: R. Nerem School/~~XXX~~ ME

Sponsor: National Science Foundation

Agreement No.: Grant No. ECE-8796223

Award Period: From 1/1/87 To 7/31/88 (Performance) 10/31/88 Reports

Sponsor Amount:	New With This Change	Total to Date
Contract Value: $		$ 17,500
Funded: $		$ 17,500

Cost Sharing No./(Center No.) E-25-340(F6275-0A0) Cost Sharing: $ 1,754

Title: "Coronary Fluid Dynamics"

ADMINISTRATIVE DATA

OCA Contact John B. Schonk X-4820

1) Sponsor Technical Contact:

A. Zelman
National Science Foundation
ENG/ECE
Washington DC 20550

2) Sponsor Issuing Office:

R.E. Hastings
National Science Foundation
DGC/ENG
202/357-9626

Military Security Classification: ____
(or) Company/Industrial Proprietary: ____

ONR Resident Rep. is ACO: ____ Yes X No
Defense Priority Rating: ____

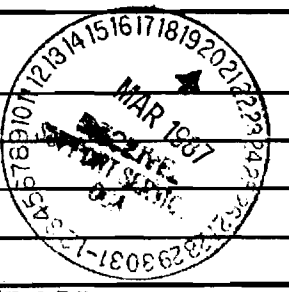
RESTRICTIONS

See Attached NSF Supplemental Information Sheet for Additional Requirements.

Travel: Foreign travel must have prior approval — Contact OCA in each case. Domestic travel requires sponsor approval where total will exceed greater of $500 or 125% of approved proposal budget category.

Equipment: Title vests with GIT

COMMENTS:



SPONSOR'S I.D. NO. 02.107.000.87.055

COPIES TO:

Project Director
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Other ____

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

NOTICE OF PROJECT CLOSEOUT

Closeout Notice Date 04/30/90

Project No. E-25-699 Center No. R6275-0A0

Project Director NEREM R M School/Lab ME

Sponsor NATL SCIENCE FOUNDATION/GENERAL

Contract/Grant No. EET-8796223 Contract Entity GTRC

Prime Contract No.

Title CORONARY FLUID DYNAMICS

Effective Completion Date 900131 (Performance) 900430 (Reports)

Closeout Actions Required:	Y/N	Date Submitted
Final Invoice or Copy of Final Invoice	N	
Final Report of Inventions and/or Subcontracts	N	
Government Property Inventory & Related Certificate	N	
Classified Material Certificate	N	
Release and Assignment	N	
Other	N	

Comments

Subproject Under Main Project No.

Continues Project No.

Distribution Required:

Project Director	Y
Administrative Network Representative	Y
GTRI Accounting/Grants and Contracts	Y
Procurement/Supply Services	Y
Research Property Managment	Y
Research Security Services	N
Reports Coordinator (OCA)	Y
GTRC	Y
Project File	Y
Other	N
	N

E-25-699

PROGRESS REPORT ON NSF GRANT EET-8796223
ENTITLED CORONARY FLUID DYNAMICS

Periods: December 1, 1986-November 30, 1987

Principal Investigators:
Robert M. Nerem
Murina J. Levesque

Work on this grant was initiated February 1986 at the University of Houston and has continued since late 1986 at the Georgia Institute of Technology. The effort has focused on obtaining a better understanding of the fluid dynamics of the coronary system in man as well as in animals. It is believed that this is important if we are to develop cardiovascular devices, e.g. synthetic vascular prostheses, as well as obtain a better understanding of diseased processes in man.

As part of the continued development of our coronary circulation computer model, which is for the left coronary arterial tree, the main emphasis during the past 12 months has been on developing an improved model of the intramyocardial microcirculation. This new improved model allows for the effects of intramycardial compression on the pressure-flow relationships in these small vessels. This intramyocardial model was first developed for a simplified coronary circulation system, and is now being implemented into a total, more complex model of the coronary circulation which includes finite branching effects. In addition, calculations of shear stress in the coronary circulation are being carried out in this finite branching model.

In a separate study, experiments have been carried out to investigate the effect of the left circumflex/left anterior descending coronary bifurcation angle on the detailed flow patterns in the coronary arteries. The shape of the velocity profile, including its degree of bluntness and skewness, and the wall shear stress distribution have been determined as a function of the bifurcation angle. These results are important in demonstrating the influence of coronary geometry on specific hemodynamic details. This influence is at times dramatic, and we believe is important in understanding the role of hemodynamics in atherosclerosis.

In addition, the collaborative effort with Professor Dieter Liepsch from Munich, Germany is continuing. In this effort, flow casts are being made from human coronary casts in order to study the detail flow characteristics in the human coronary circulation. Several casts have already been constructed, and flow experiments should commence during 1988. Travel associated with this international collaboration is being supported by NSF Travel Grant INT-8414953.

In addition to the above, work on Tasks D and E is being presently initiated. Although the move to Georgia Tech has involved some loss of time in our laboratory effort, this time was put to good use in the development of our computer models and in the analysis of data which had already been obtained. Overall, we believe that the move to Georgia Tech has greatly enhanced the effort on this grant.

Publications and presentations, since the time of the submission of the proposal which resulted in this grant and through November 30, 1987, are as follows.

Journal Articles and Proceedings

Altobelli, S.A. and Nerem, R.M., "An Experimental Study of Coronary Artery Fluid Mechanics," ASME Journal of Biomechanical Engineering, Vol. 107, No. 1, 1985, pp. 16-23.

Rooz, E., Wiesner, R.F., and Nerem, R.M., "Epicardial Coronary Blood Flow Including the Presence of Stenoses and Aorto-Coronary Bypasses". I: Model and Numerical Method, ASME J. Biomechanical Engineering, Vol. 107, No. 4, 1985, pp. 361-367.

Levesque, M.J., Liepsch, D., Moravec, S., and Nerem, R.M., "Correlation of Endothelial Cell Shape and Wall Shear Stress in a Stenosed Dog Aorta," Arteriosclerosis, Vol. 6, No. 2, 1986, pp. 220-229..

Nerem, R.M., Rooz, E., Wiesner, R.F., "A Method for Calculating Time-Dependent Coronary Blood Flow," Proceedings of the Henry Goldberg Workshop on Simulation and Imaging of the Cardiac System, eds. S. Sideman and R. Beyer, Martinus Nijhoff, Dordrecht, Netherlands, 1985, pp. 244-257.

Nerem, R.M., Wiesner, T.F., and Rooz, E., "A Parametric Analysis of Epicardial Coronary Blood Flow Including the Presence of Stenoses and Aorto-Coronary Bypasses," Proceedings of the Second Henry Goldberg Workshop on Simulation and Control of the Cardiac System, Volume II, eds. S. Sideman and R. Beyar, CRC Press, Inc., Boca Raton, Florida, 1987, pp. 155-168.

Wiesner, T.F., Rooz, E., and Nerem R.M., "Epidardial Coronary Blood Flow Including the Presence of Stenoses and Aorto-Coronary Bypasses. II: Experimental Comparison and Parametric Investigations," submitted for publication.

Holenstein, R. and Nerem, R.M., "Parametric Analysis of Flow in the Intramyocardial Circulation," submitted for publication.

Presentations and Abstracts

Nerem, R.M., Levesque, M.J., and Wiesner, T.F., "Dynamics of the Coronary Circulation," keynote lecture, Sessions on Cardiac Contraction and Coronary Circulation, Biomechanics Symposium, XIV International Conference on Medical and Biological Engineering, Espoo, Finland, August 11-16, 1985.

Wiesner, T.F. and Nerem, R.M., "Epicardial Coronary Blood Flow in the Presence of Stenoses and Aorto-Coronary Bypasses," American Society of Mechanical Engineers Winter Annual Meeting, Miami, FL, November 17-22, 1985.

Thai, B.N., Levesque, M.J., and Nerem, R.M., "Myocardial Blood Flow During Induced Aortic Hypertension in Dogs," 70th Annual Meeting of the Federation of American Societies for Experimental Biology, St. Louis, MO, April 13-18, 1986 (see Federation Proceedings, Vol. 45, No. 3, p. 398).

Nerem, R.M., Levesque, M.J., Sprague, E.A., and Schwartz, C.J., "Endothelial Cell Responses to Hemodynamic Shear Stress," Fifth International Conference on Mechanics in Medicine and Biology, Bologna, Italy, July 1-5, 1986.

Nerem, R.M., "Biologic Responses of Vascular Endothelium to Hemodynamic Shear Stresses," A Scientific Symposium on the Occasion of the 600th Anniversary of the University of Heidelberg and entitled The Pathobiology of Occlusive Arterial Disease, Heidelberg, Federal Republic of Germany, July 7-10, 1986.

Nerem, R.M., "Hemodynamics and the Arterial Wall," National Heart, Lung, and Blood Institute Workshop on Vascular Disease, Bethesda, MD, August 7-9, 1986.

Liepsch, D.W., Moravec, S., Levesque, M., and Nerem, R.M., "Laser-Doppler Velocity Measurements in a Stenosed Dog Aorta Model," 39th Annual Conference on Engineering in Medicine and Biology, Columbus, OH, September 13-16, 1986.

Nerem, R.M., Levesque, M.J., Holenstein, R., and Rabinovitz, R., "Fluid Mechanics of the Coronary Circulation," VII Nordic Meeting on Medical and Biological Engineering, Trondheim, Norway, June 28-July 1, 1987.

Rabinovitz, R.S., Levesque, M.J., Hastley, C.J. and Nerem, R.M., "Fluid Dynamics of the Left Main Coronary Bifurcation," 40th Annual Conference on Engineering in Medicine and Biology, Niagara Falls, NY., September 10-13, 1987.

Holenstein, R. and Nerem, R.M., "Parametric Analysis of Flow in the Intramyocardial Circulation, International Conference of the Cardiovascular System Dynamics Society, Osaka, Japan, October 4-7, 1987.

Nerem, R.M., Holenstein, R. and Levesque, M.J., "Fluid Mechanics of the Coronary Circulation," Chinese Third National Conference on Biomedical Engineering, Beijing, China, October 9-11, 1987.

Rabinovitz, R.S., Levesque, M.J., and Nerem, R.M., "Effects of Branching Angle on Wall Shear Stress in the Left Main Coronary Bifurcation," American Heart Association 60th Scientific Sessions, Anaheim, CA, November 16-19, 1987.

E-25-69

NATIONAL SCIENCE FOUNDATION Washington, D.C. 20550	FINAL PROJECT REPORT NSF FORM 98A	
PLEASE READ INSTRUCTIONS ON REVERSE BEFORE COMPLETING		
PART I—PROJECT IDENTIFICATION INFORMATION		
1. Institution and Address Georgia Institute of Technology Atlanta, GA 30332	2. NSF Program Biomedical Engineering and Aiding the Disabled	3. NSF Award Number EET-8796223
	4. Award Period From 1/1/87 To 1/31/90	5. Cumulative Award Amount $202,052
6. Project Title Coronary Fluid Dynamics		

PART II—SUMMARY OF COMPLETED PROJECT *(FOR PUBLIC USE)*

The goal of this project was to investigate the detailed fluid mechanic characteristics of coronary blood flow, including both spatial and temporal variations. These characteristics are believed to be important in the determination of the role of fluid dynamic phenomena in vascular disease processes and in the development of cardiovascular devices, e.g. hybrid vascular grafts for coronary bypass. Of particular interest has been the relationship of vascular geometry to flow characteristics. In this project it was demonstrated that the shape of the velocity profile and the distribution of wall shear stress in the main branching of the left main coronary artery is a direct function of the bifurcation angle, more specifically the turning angle of the flow experiences in moving into the left anterior descending and left circumflex coronary arteries. In a separate study carried out with Dr. Karl Perktold, it was shown that, although secondary flow velocities are small, they do influence the wall shear stress distribution. In addition, using a computer model of the left coronary circulation developed on the project, it has been demonstrated that the intramyocardial capacitance determines the nature of any back flow associated with the coronary flow waveform. It is these detailed characteristics of coronary flow which are believed to be important to our understanding the fluid dynamics of the system and to which this project has directly contributed.

PART III—TECHNICAL INFORMATION *(FOR PROGRAM MANAGEMENT USES)*

1. ITEM *(Check appropriate blocks)*	NONE	ATTACHED	PREVIOUSLY FURNISHED	TO BE FURNISHED SEPARATELY TO PROGRAM	
				Check (✓)	Approx. Date
a. Abstracts of Theses			X		
b. Publication Citations			X		
c. Data on Scientific Collaborators		X			
d. Information on Inventions		X			
e. Technical Description of Project and Results		X			
f. Other *(specify)*					

2. Principal Investigator/Project Director Name *(Typed)*	3. Principal Investigator/Project Director Signature	4. Date
Robert M. Nerem		April 16, 1990

Final Report

NSF Research Grant EET-8796223

Title: Coronary Fluid Dynamics

Principal Investigator: **Robert M. Nerem**
School of Mechanical Engineering
Georgia Institute of Technology
Atlanta, GA 30332-0405
(404) 894-2768

Amount: $202,052

Period: 1/1/87 - 1/31/90

Technical Report: This research effort was initiated at the University of Houston under NSF Research Grant ECE-8513922. The total three-year award was $269,686, with a start date of 2/1/86, and when the Principal Investigator relocated to Georgia Institute of Technology, the grant was transferred to Georgia Tech. The new grant number and the amount of the award transferred is as listed above.

The research effort has focused on obtaining a better understanding of the fluid dynamics of the coronary system in man as well as in animals. It is believed that this is important if we are to develop cardiovascular devices, e.g. hybrid vascular prostheses, as well as obtain a better understanding of disease processes.

As part of the continued development of our coronary circulation computer model, which is for the left coronary arterial tree, the main emphasis during the last 18 months of the project was on developing an improved model of the intramyocardial microcirculation. This new improved model allows for the effects on intramyocardial compression on the pressure-flow relationships in these small vessels. This intramyocardial model was first developed for a simplified coronary circulation system, and has been implemented into a total, more complete model of the coronary circulation which includes finite branching effects. In addition, calculations of shear stress in the coronary circulation were carried out in this finite branching model.

In a separate study, experiments were carried out to investigate the effect of the left circumflex/left anterior descending coronary bifurcation angle on the detailed flow patterns in the coronary arteries. The shape of the velocity profile, including its degree of bluntness and skewness, and the wall shear stress distribution were determined as a function of the bifurcation angle. These results are important in demonstrating the

influence of coronary geometry on specific hemodynamic details. This influence is at times dramatic, and we believe is important to understanding the role of hemodynamics in atherosclerosis.

In a separate study conducted in cooperation with Dr. Karl Perktold, University of Graz, Austria, numerical calculations of unsteady three-dimensional flow in a curved tube have been carried out. With a geometry and waveform simulating the left main coronary artery, it has been shown that, although the magnitude of secondary flow velocities is on the order of 2-3 percent, there still is an important effect on wall shear stress distribution.

In addition, a collaborative effort with Professor Dieter Liepsch from Munich, Germany is related to this grant. In this effort, flow casts were made from human coronary casts in order to study the detailed flow characteristics in the human coronary circulation. Several casts have already been constructed, and flow experiments commenced during 1989. Travel associated with this international collaboration was supported by a separate NSF Travel Grant.

It is the detailed characteristics of coronary flow, such as studied here, which are believed to be important to our understanding the fluid dynamics of the system.

Publications: Journal and proceeding publications and meeting presentations which have resulted from research on this grant are listed below.

Journal Articles and Proceedings

Altobelli, S.A. and Nerem, R.M., "An Experimental Study of Coronary Artery Fluid Mechanics," ASME J. Biomechanical Engineering, Vol. 107, No. 1, 1985, pp. 16-23.

Rooz, E., Wiesner, T.F., and Nerem, R.M., "Epicardial Coronary Blood Flow Including the Presence of Stenoses and Aorto-Coronary Bypasses." I: Model and Numerical Method, ASME J. Biomechanical Engineering,

Levesque, M.J., Liepsch, D., Moravec, S., and Nerem, R.M., "Correlation of Endothelial Cell Shape and Wall Shear Stress in a Stenosed Dog Aorta," Arteriosclerosis, Vol. 6, No. 2, 1986, pp. 220-229.

Nerem, R.M., Rooz, E., and Wiesner, T.F., "A Method for Calculating Time-Dependent Coronary Blood Flow," Proceedings of the Henry Goldberg Workshop on Simulation and Imaging of the Cardiac System, eds. S. Sideman and R. Beyer, Martinus Nijhoff, Dordrecht, Netherlands, 1985, pp. 244-257.

Nerem, R.M. and Levesque, M.J., "Fluid Mechanics in Atherosclerosis," Handbook of Bioengineering, eds. R. Skalak and S. Chien, McGraw-Hill, New York, pp. 21.1-21.22, 1987.

Nerem, R.M., Wiesner, T.F., and Rooz, E., "A Parametric Analysis of Epicardial Coronary Blood Flow Including the Presence of Stenoses and Aorto-Coronary Bypasses," Proceedings of the Second Henry Goldberg Workshop on Simulation and Control of the Cardiac System, Vol. II, eds. S. Sideman and R. Beyer, CRC Press, Inc., Boca Raton, Florida, 1987, pp. 155-168.

Nerem, R.M., "Endothelial Responses to Shear Stress: Implications in the Development of Endothelialized Vascular Grafts," Tissue Engineering, Proceedings of an NSF Workshop, UCLA Symposia on Molecular and Cellular Biology, New Series Vol. 104, eds. R. Skalak and C.F. Fox, Alan R. Liss, Inc., New York, NY, 1988, pp. 5-10.

Wiesner, T.F., Rooz, E., and Nerem, R.M. "Epicardial Coronary Blood Flow Including the Presence of Stenoses and Aorto-Coronary Bypasses. II: Experimental Comparison and Parametric Investigations," ASME J. Biomechanical Engineering, Vol. 110, No. 2, 1988, pp. 144-149.

Giddens, D.P. and Nerem, R.M., "Challenging Computational Problems in Cardiovascular Fluid Mechanics," Computational Methods in Bioengineering, BED-Vol. 9, eds. R.L. Spilker and B.R. Simon, American Society of Mechanical Engineers, New York, NY, 1988, pp. 21-28.

Nerem, R.M., "Vascular Endothelial Responses to Shear Stress," Blood Flow in Large Arteries: Applications to Atherogenesis and Clinical Medicine, Proceedings of the International Symposium on Biofluid Mechanics, held in Palm Springs, CA, April 27-19, 1988, ed. D. Liepsch, Karger, Basel, Switzerland, 1990, pp. 117-124.

Holenstein, R. and Nerem, R.M., "Parametric Analysis of Flow in the Intramyocardial Circulation," accepted for publication, Annals of Biomedical Engineering.

Presentations and Abstracts

Nerem, R.M., Levesque, M.J., and Wiesner, T.F., "Dynamics of the Coronary Circulation," keynote lecture, Sessions on Cardiac Contraction and Coronary Circulation, Biomechanics Symposium, XIV International Conference on Medical and Biological Engineering, Espoo, Finland, August 11-16, 1985.

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Thai, B.N., Levesque, M.J., and Nerem, R.M., "Myocardial Blood Flow During Induced Aortic Hypertension in Dogs," 70th Annual Meeting of the Federation of American Societies for Experimental Biology, St. Louis, MO, April 13-18, 1986 (see Federation Proceedings, Vol. 45, No. 3, p. 398).

Nerem, R.M., Levesque, M.J., Sprague, E.A., and Schwartz, C.J., "Endothelial Cell Responses to Hemodynamic Shear Stress," Fifth International Conference on Mechanics in Medicine and Biology, Bologna, Italy, July 1-5, 1986.

Nerem, R.M., "Biologic Responses of Vascular Endothelium to Hemodynamic Shear Stresses," A Scientific Symposium on the Occasion of the 600th Anniversary of the University of Heidelberg and entitled The Pathobiology of Occlusive Arterial Disease, Heidelberg, Federal Republic of Germany, July 7-10, 1986.

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Liepsch, D.W., Moravec, S., Levesque, M., and Nerem, R.M., "Laser-Doppler Velocity Measurements in a Stenosed Dog Aorta Model," 39th Annual Conference on Engineering in Medicine and Biology, Columbus, OH, September 13-16, 1986.

Nerem, R.M., Levesque, M.J., Holenstein, R., and Rabinovitz, R., "Fluid Mechanics of the Coronary Circulation," VII Nordic Meeting on Medical and Biological Engineering, Trondheim, Norway, June 28-July 1, 1987.

Rabinovitz, R.S., Levesque, M.J., Hartley, C.J., and Nerem, R.M., "Fluid Dynamics of the Left Main Coronary Bifurcation," 40th Annual Conference on Engineering in Medicine and Biology, Niagara Falls, NY, September 10-13, 1987.

Holenstein, R. and Nerem, R.M., "Parametric Analysis of Flow in the Intramyocardial Circulation, International Conference of the Cardiovascular System Dynamics Society, Osaka, Japan, October 4-7, 1987.

Nerem, R.M., Holenstein, R. and Levesque, M.J., "Fluid Mechanics of the Coronary Circulation," Chinese Third National Conference on Biomedical Engineering, Beijing, China, October 9-11, 1987.

Rabinovitz, R.S., Levesque, M.J., and Nerem, R.M., "Effects of Branching Angle on Wall Shear Stress in the Left Main Coronary Bifurcation," American Heart Association 60th Scientific Sessions, Anaheim, CA, November 16-19, 1987.

Rabinovitz, R., Hartley, C., Levesque, M., and Nerem, R., "Evaluation of Pulsed Doppler Measurements of Velocity Profiles," World Congress on Medical Physics and Biomedical Engineering, San Antonio, TX, August 7-13, 1988.

Olsmats, H., Holenstein, R., Seed, W., and Nerem, R., "Wall Shear Stress Calculations for Human Coronary Arteries," World Congress on Medical Physics and Biomedical Engineering, San Antonio, TX, August 7-13, 1988.

Nerem, R.M., "A Mammalian Cell's Response to a Fluid Flow Environment," plenary lecture at the 41st Annual Meeting of the Division of Fluid Dynamics, American Physical Society, Buffalo, NY, November 20-22, 1988.

Giddens, D.P. and Nerem, R.M., "Challenging Computational Problems in Cardiovascular Fluid Mechanics," invited lecture in Symposium on Computational Methods in Bioengineering, ASME Winter Annual Meeting, Chicago, IL, November 28-December 2, 1988.

Nerem, R.M., "Cellular Biomechanics and Atherosclerosis," plenary lecture at the 28th Annual Meeting of the Japanese Society for Medical Electronics and Biological Engineering, Osaka, Japan, May 23-25, 1989.

Scientific Collaborators: These are listed below.

M.J. Levesque, Ph.D. -- Senior Research Scientist
Peggy R. Girard, Ph.D. -- Senior Research Scientist
Stefan Schreck, Ph.D. -- Postdoctoral Research Associate
Rolf Holenstein, Ph.D. -- Postdoctoral Research Associate
Karl Perktold, Ph.D. -- University of Graz, Austria
Elkana Rooz, Ph.D. -- Visiting Scholar
Helene Olsmat -- Graduate Student
Raphael Rabinovitz -- Graduate Student
Theodore F. Wiesner -- Graduate Student
Bichlan N. Thai -- Graduate Student
Stephen A. Altobelli -- Graduate Student

Inventions: None