PROJECT ADMINISTRATION DATA SHEET

Project No. E-16-645 (subproject is E-23-625/Vito/ESM)       DATE 4/1/82
Project Director: Don P. Giddens  School/Lab 4/1/82 A E
Sponsor: National Science Foundation; Washington, D. C.

Type Agreement: Amend 02 to Grant MEA-7921551 (formerly CME-7921551)
Award Period: From 2/15/82 To 3/31/83 (Performance) (Reports)
Sponsor Amount: $127,936 (Amend 02 only) *
Cost Sharing: $15,643 (E-16-372)

Title: Role of Fluid Mechanics in the Genesis, Proliferation and Detection of Atherosclerosis

ADMINISTRATIVE DATA

1) Sponsor Technical Contact:
   George K. Lea
   National Science Foundation
   Fluid Mechanics Program
   Mechanical & Engineering Group
   Civil & Mechanical Engineering
   Washington, D. C. 20550
   202-357-9542

Defense Priority Rating: N/A

2) Sponsor Admin/Contractual Matters:
   Terry J. Pacovsky
   National Science Foundation
   Division of Grants & Contracts
   Award Accountability Branch
   Washington, D. C. 20550
   202-357-9626

Security Classification: N/A

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 S500 or 125% of approved proposal budget category.

Equipment: Title vests with GIT

COMMENTS:
Continuation of E-16-664. New Project number assigned due to change in O.H. computation.

* $123,077 in E-16-645 and $4,859 in E-23-625.
Date: 8/2/84

Project No. E-16-645

Includes Subproject No.(s) E-23-625 /Vito/ESM

Project Director(s) Don P. Giddens

Sponsor National Science Foundation

Title "Role of Fluid Mechanics in the Genesis, Proliferation and Detection of Atherosclerosis"

Effective Completion Date: 10/31/83

Grant/Contract Closeout Actions Remaining:

☑ None

☑ Final Report of Inventions if positive

☑ Govt. Property Inventory & Related Certificate if positive

☑ Closing Documents

☑ Classified Material Certificate

☑ Other

Continues Project No. E-16-664

Continued by Project No.

COPIES TO:

Project Director
Research Administrative Network
Research Property Management
Accounting
Procurement/EES Supply Services
Research Security Services
Reports Coordinator (OCA)
Legal Services

Library
GTRI
Research Communications (2)
Project File
Other I. Newton
The research program was designed to determine which fluid dynamic factors relate to the development of atherosclerotic lesions in animal models and in human subjects by correlating various possible factors with lesion localization in specific arteries. Research methods combined both engineering and biological scientific personnel and techniques. Fluid dynamic studies in models of the human carotid bifurcation and of vessels with localized constrictions were performed at the Georgia Institute of Technology using laser Doppler anemometry to measure the velocity field. Animal studies were carried out using pulsed Doppler ultrasound to measure blood velocities in vivo. For the biological studies at the University of Chicago Medical School, constrictions were placed on the aortas of cynomolgus monkeys which were then fed an atherogenic diet for six months, after which the pattern of lesion development was examined morphologically. Investigations were also performed on excised carotid bifurcations from fresh cadavers, and the intimal and medial thicknesses were measured as a function of location within the vessels. The pathologic and fluid dynamic findings were then correlated. Results show that high wall shear and turbulence, both postulated in the literature as causative hemodynamic factors, are not causes of atherogenesis in either the animal model or the human carotid vessels. Rather, lesion development coincided with specific regions where wall shear was low in magnitude and/or where the direction of wall shear oscillated significantly during the heart cycle.
APPENDIX VII

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, Georgia 30332

2. NSF Program

3. NSF Award Number
   MEA - 7921551

4. Award Period
   From 2/15/80 To 10/31/83

5. Cumulative Award Amount
   $388,809

6. Project Title
   Role of Fluid Mechanics in the Genesis, Proliferation and Detection of Atherosclerosis

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

The research program was designed to determine which fluid dynamic factors relate to the development of atherosclerotic lesions in animal models and in human subjects by correlating various possible factors with lesion localization in specific arteries. Research methods combined both engineering and biological scientific personnel and techniques. Fluid dynamic studies in models of the human carotid bifurcation and of vessels with localized constrictions were performed at the Georgia Institute of Technology using laser Doppler anemometry to measure the velocity field. Animal studies were carried out using pulsed Doppler ultrasound to measure blood velocities in vivo. For the biological studies at the University of Chicago Medical School, constrictions were placed on the aortas of cynomolgus monkeys which were then fed an atherogenic diet for six months, after which the pattern of lesion development was examined morphologically. Investigations were also performed on excised carotid bifurcations from fresh cadavers, and the intimal and medial thicknesses were measured as a function of location within the vessels. The pathologic and fluid dynamic findings were then correlated. Results show that high wall shear and turbulence, both postulated in the literature as causative hemodynamic factors, are not causes of atherogenesis in either the animal model or the human carotid vessels. Rather, lesion development coincided with specific regions where wall shear was low in magnitude and/or where the direction of wall shear oscillated significantly during the heart cycle.

PART III—TECHNICAL INFORMATION (FOR PROGRAM MANAGEMENT USES)

1. ITEM (Check appropriate blocks)
   None
   Attached
   Previously Furnished
   To Be Furnished Separately To Program

   a. Abstracts of Theses
   b. Publication Citations
   c. Data on Scientific Collaborators
   d. Information on Inventions
   e. Technical Description of Project and Results
   f. Other (specify)

2. Principal Investigator/Project Director Name (Typed)
   Don P. Giddens

3. Principal Investigator/Project Director Signature

4. Date
   7/23/84

NSF Form 98A (3-83) Supersedes All Previous Editions

Form Approved OMB No. 3145-0058
ABSTRACT

AN EXPERIMENTAL INVESTIGATION OF STEADY FLOW AT AN ARTERIAL BIFURCATION

A PH.D. THESIS

BY

K. BALASUBRAMANIAN

The geometry of a typical adult human carotid bifurcation was established from a study of a large number of angiograms. A rigid model was constructed from glass and investigations were performed under steady flow conditions using dye injection and hydrogen bubbles. A second model was machined from plexiglas and employed in a series of laser Doppler anemometer measurements of velocity profiles within the bifurcation. Physiologic ranges of Reynolds numbers and flow division ratios were utilized in the experiments. The studies revealed a complex flow field in which flow separation and secondary flow patterns play an important role. The separation regions occurring at the outer regions of the branches are zones of low shear stress but are not regions of recirculation. The apex or flow divider neighborhood experiences relatively high wall shear stress while the side walls of the carotid sinus contain areas of moderate shear levels. Comparison with pathologic data for localization of atherosclerotic lesions indicates that zones susceptible to disease are areas which experience low shear stress while regions of relatively high shear are free of deposits.
ABSTRACT

AN EXPERIMENTAL INVESTIGATION OF STEADY AND PULSATILE FLOW THROUGH CONSTRICTED TUBES

A PH.D. THESIS

BY

S. A. AHMED

An experimental investigation of steady and pulsatile flow through axisymmetric contoured constrictions in a rigid tube has been conducted. The study was motivated by the problem of arterial stenoses occurring in certain cardiovascular diseases. Flow disturbances caused by the constriction have been shown to be an important feature of the flow, and their analysis may offer a diagnostic tool which could help in early detection of the disease.

Contoured constrictions with 25 percent, 50 percent and 75 percent area reductions were investigated. The steady flow experiments covered a range of Reynolds numbers from 500 to 2,000 while the pulsatile flow had an instantaneous Reynolds number varying from 200 to 1,000. The pulsatile upstream centerline velocity waveform was approximately sinusoidal with a frequency parameter of 7.5.

Investigations by flow visualization utilizing the hydrogen bubble technique demonstrated a complex flow field, particularly in the case of pulsating flow, consisting of a separated region downstream of the constriction, vortex shedding in the near distal region and turbulence in the far field.

Quantitative measurements of two velocity components made with a two-component laser Doppler velocimeter provided additional details of the development of velocity profiles, disturbance velocity profiles and wall shear stresses. Velocity measurements were conducted at numerous axial locations and radial positions.

The steady flow results show that the length of the laminar recirculation region increases with the Reynolds number and with the area reduction. Furthermore, the mean velocity profiles exhibit a jet-like character with large changes in velocity gradient. Downstream of the constriction, the flow field is dominated by vortex shedding which either breaks up into random fluctuations or decays deterministically due to viscosity effects, depending on the upstream conditions and stenosis geometry. Generally, disturbances are generated in the shear layer with a large fraction of the energy in the fluctuations being at lower frequencies. Nondimensional correlations were applied to the disturbance energy spectra.
The pulsatile flow is characterized by the lack of a stationary separated zone. Instead, there is a region of reverse flow which expands during systole and contracts during diastole. For high values of the frequency parameter, a strong vortex ring swirls into this region and is washed away during the next cycle. Flow disturbance analysis was applied to small intervals of the cycle to isolate the different fluid mechanics phenomena namely, starting coherent structure, vortex shedding and turbulence. The existence and interaction among these phenomena depend on the maximum Reynolds number, the frequency parameter and the degree of the constriction.

In general, the fundamental frequency of the velocity fluctuations increases with the degree of constriction at fixed axial location for both steady and pulsatile flows. However, it decreases farther downstream for the same occlusion.

Thus, the results of the present investigation have led to an extensive description of the flow field through a constricted tube with steady or pulsatile upstream flow conditions. The disturbances measured in the flow field are expected to help in the early detection of the initial formation of occlusions before becoming serious and clinically significant.
B. PUBLICATIONS

Papers and presentations listed in this section are directly related to the research areas of our present NSF Grant (February 15, 1980 - February 14, 1983). This listing does not include papers and presentations of the principals in other research areas.

A. Papers Published During NSF Grant Period and Related to NSF Research


10. L. J. D'Luna, V. L. Newhouse and D. P. Giddens: "In Vitro
Doppler Detection of Axisymmetric Stenoses from Transverse
Velocity Measurements," Journal of Biomechanics, Vol. 13, No. 9,

11. S. A. Ahmed and D. P. Giddens: "Velocity Measurements in Steady
Flow Through Axisymmetric Stenoses at Moderate Reynolds
505-578.

12. C. K. Zarins, R. A. Bomberger, K. E. Taylor, and S. Glagov;
"Artery Stenosis Inhibits Regression of Diet-induced

13. R. A. Bomberger, C. K. Zarins, and S. Glagov; "Medial Injury and
Hyperlipidemia in the Development of Aneurysms of

J. Dohrmann, "Increased Cerebral Blood Flow After External

15. R. A. Bomberger, C. K. Zarins, and S. Glagov; "Subcritical
Arterial Stenosis Enhances Distal Atherosclerosis," Resident

"Quantitation of Cells and Fibers in Histologic Sections of
Arterial Walls," In Connective Tissues in Arterial and Pulmonary
Disease, Ed. T. F. McDonald and A. B. Chandler, Springer-Verlag,
New York, pp. 57-93, 1981.

17. C. K. Zarins, R. A. Bomberger, and S. Glagov; "Local Effects of
Stenoses: Increased Flow Velocity Inhibits Atherogenesis,
Circulation 64 (Suppl. II): 221-227, 1981.

"Arterial Wall Disruption by Balloon Dilation: Quantitative
Comparison of Normal, Stenotic and Occluded Vessels," Surg.

19. C. K. Zarins and S. Glagov: "Aneurysms and Obstructive Plaques:
"Differing Local Responses to Atherosclerosis," Aneurysms:
Diagnosis and Treatment, Ed: John J. Bergan and James S. L. Yao,

20. C. K. Zarins, K. E. Taylor, R. A. Bomberger, and S. Glagov: "Do
Endothelial Injuries Predispose to Atherosclerosis?" Angio

21. A. G. Little and C. K. Zarins: "Abdominal Aortic Aneurysm and


B. Papers Presented During NSF Grant Period and Related to NSF Research


8. M. Casty and D. P. Giddens; "25 + 1 Channel Multigate Pulsed Doppler Instrument for Profile, Flow and Turbulence Analysis in Major Arteries," Annual Scientific Meeting of the American Institute of Ultrasound in Medicine, San Francisco, CA, August 1981. (Plenary Sessions)


E. TECHNICAL DESCRIPTION OF PROJECT AND RESULTS

1. Hemodynamics and Atherosclerosis in the Human Carotid Bifurcation

   In work accomplished in the laboratories of the School of Aerospace Engineering, the Georgia Institute of Technology, and the Departments of Surgery and Pathology, the University of Chicago, we have determined the following:

   a. Atherosclerotic lesions in the human carotid bifurcation do not localize in regions of relatively high, unidirectional wall shear stress.

   b. Although complex laminar secondary flow patterns occur in the normal carotid bifurcation, turbulence is not present until plaques are well-developed. Consequently, turbulence may influence the fate of established large plaques but can probably be ruled out as a direct initiating factor in atherosclerosis of the carotid artery.

   c. Plaques localize in regions of the carotid bifurcation which experience a low mean wall shear stress (outer wall of the sinus) and in regions where the wall shear stress vector changes direction significantly during the cardiac cycle (outer wall and, to a lesser degree, side walls of the sinus).

   d. Significant factors which affect flow patterns relative to (c) above are: branch angle, flow division ratio and flow pulse waveform.

   As a result of these findings, turbulence and high, unidirectional wall shear stress do not appear to be initiating factors of atherosclerosis in the human carotid bifurcations. Consequently, for future work we plan to concentrate upon investigating possible relationships between lesion localization and (i) specific characteristics of wall shear stress behavior and/or (ii) residence time of fluid elements near vessel wall sites susceptible to plaque development.

2. Stenotic Flows and Aortic Coarctations

   The Departments of Surgery and Pathology (Drs. C. K. Zarins and S. Glagov) have many years experience with the cynomolgus monkey as an experimental model for atherosclerosis. In work performed during the present NSF funding we have studied a series of 11 monkeys (9 with coarctations and 2 without) which were placed on an atherogenic diet with 2% cholesterol and 25% peanut oil for a period of six months. At the time of implanting the coarctation, several hemodynamic variables were measured to characterize flow, pressure and flow disturbances in the aorta. At the time of sacrifice these measurements were repeated and particular attention was given to obtaining pulsed Doppler
ultrasound measurements in the poststenotic regions, concentrating primarily upon characterizing the intensity of flow disturbances induced by the constriction. Although we have not yet completed all our analyses of these data, we have determined the following to date:

a. Hypertension per se was not a consistent factor in the development of atherosclerosis in the monkey aorta.

b. Inasmuch as the coarctation channel itself was consistently spared, relatively high levels of unidirectional wall shear stress were considered to exert an inhibitory effect on atherogenesis.

c. A good correlation between turbulence intensity and disease sparing existed for several vessel diameters distal to the coarctation. Further distally, this correlation deteriorated significantly. Consequently, although we are not prepared to conclude that turbulent flow inhibited atherosclerosis, we can state that turbulence did not play a contributory role in these experiments.

All hemodynamic data are recorded on FM tape, and we will be continuing the analysis and correlation with pathology over the next several months.

Additionally, we have completed a series of contoured stenoses with area reductions of 25, 50, and 75%. Steady flow experiments at Re = 500, 1000, and 2000 were performed as well as pulsatile experiments which employed a sinusoidal waveform with minimum and maximum Reynolds numbers of 200 and 1000 and a frequency parameter of $\omega = 7.5$. These latter values are similar to those of the monkey aorta. We have not completed our analysis of these experiments nor have we yet related them to the monkey coarctation studies. However, the following conclusions have been drawn to date:

a. Detailed velocity profiles in steady and pulsatile flows have been obtained noninvasively with the LDA method. Results cover a range of transitional flows and can be employed for comparison with laminar and turbulent computational fluid dynamic models.

b. Wall shear stresses have been measured in the stenotic field. Values of $\tau_w$ are maximum within the throat of the constriction. In steady flow the separated flow region contains areas of low $\tau_w$, but it also possesses areas for which the $\tau_w$ is comparable in magnitude, though opposite in direction, to the fully developed value far upstream.
c. The wall shear stress reaches a local maximum downstream of flow reattachment. However, this value is at most 2-3 times higher (when turbulence is present) than the upstream value, and it is an order of magnitude less than the maximum $w$ in the constriction throat.

d. Three distinct types of poststenotic disturbances can exist in pulsatile flow: (i) a coherent laminar structure associated with the acceleration phase of each cycle; (ii) laminar oscillations at discrete frequency arising from shed vortices; and (iii) turbulence.

Analysis of these data will continue over the next several months.