GEORGIA INSTITUTE OF TECHNOLOGY — OFFICE OF CONTRACT ADMINISTRATION

PROJECT ADMINISTRATION DATA SHEET

[x] ORIGINAL [ ] REVISION NO. _____

Project No. E-16-D03 ~~E-16-618~~ DATE 10/15/81

Project Director: Don P. Giddens School/Lab Aerospace Engineering

Sponsor: DHHS/PHS/National Heart, Lung, and Blood Institute

Type Agreement: Grant No. 2 R01 HL 22635-03A1

Award Period: From 7/1/81 To 6/30/82 (Performance) ----- (Reports)

Sponsor Amount: $111,415 Contracted through:

Cost Sharing: $14,572 (E-16-357) GTRI/GIT

Title: Hemodynamics of Normal and Diseased Caratid Arteries

ADMINISTRATIVE DATA OCA Contact Leamon R. Scott

1) Sponsor Technical Contact:

Mr. Roger S. Powell
National Heart, Lung & Blood Institute
National Institute of Health
Bethesda, MD 20014
301-496-1586

2) Sponsor Admin/Contractual Matters:

Mrs. Lacey J. Durham
Grants Operations Branch
Division of Extramural Affairs
Nat'l Heart, Lung & Blood Institute
National Institute of Health
Bethesda, MD 20014
301-496-1586

Defense Priority Rating: N/A Security Classification: N/A

RESTRICTIONS

See Attached NIH 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 none proposed

COMMENTS:

Continuation of E-16-D02.

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GEORGIA INSTITUTE OF TECHNOLOGY OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT TERMINATION/CLOSEOUT SHEET

Date October 31, 1983

Project No. E-16-D03 School/~~Lab~~ Aerospace Engineering

Includes Subproject No.(s) _____

Project Director(s) Don P. Giddens ~~GTRI~~ / GIT

Sponsor DHES/PHS/National Heart, Lung and Blood Institute

Title "Hemodynamics of Normal and Diseased Carotid Arteries"

Effective Completion Date: 6/30/82 (Performance) _____ (Reports)

Grant/Contract Closeout Actions Remaining:

- [X] None
- [ ] Final Invoice or Final Fiscal Report
- [ ] Closing Documents
- [ ] Final Report of Inventions
- [ ] Govt. Property Inventory & Related Certificate
- [ ] Classified Material Certificate
- [ ] Other _____

Continues Project No. E-16-D02 Continued by Project No. E-16-D04

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PROGRESS REPORT

1. General Scientific Goals

The Long Range Objective and Specific Aims of our project remain the same as described in our last competitve grant application. They are as follows:

Long Range Objective

The long range objective of the proposed research is to develop methods of blood flow disturbance measurement and analysis which will be useful for the noninvasive detection of early stages of atherosclerosis in the carotid artery.

The research is based upon the hypothesis that the existence of atherosclerotic plaques in the region of the carotid bifurcation creates disturbances in the neighboring blood flow which, with proper mathematical treatment of pulsed Doppler ultrasound measurements of blood velocity, can be distinguished from normal flow patterns at a relatively early stage of plaque development.

A prerequisite for achieving this objective is a thorough knowledge of detailed hemodynamics for the normal carotid bifurcation and, consequently, a significant by-product of the research will be an increased understanding of basic carotid physiology.

Specific Aims

Achievement of the overall objective requires accomplishing the following specific aims.

1. Detailed measurements of blood velocity and of physiologic and pathologic flow disturbances in the neighborhood of the human carotid bifurcation will be performed at Piedmont Hospital with a pulsed Doppler ultrasound velocimeter which employs our improved phase-lock loop signal processing and with a multi-channel pulsed Doppler instrument on loan from Dr. Max Anliker of the Institut fur Biomedizinische Technik in Zurich, Switzerland. The purpose of this specific aim is to provide a hemodynamic description of normal and pathological flow fields in the human carotid.

2. Extensive flow field studies in models which are representative of normal and diseased carotid bifurcations will be performed with flow visualization and laser Doppler anemometer methods. The purpose of this specfic aim is to secure measurements under more controlled conditions and with greater accuracy than can be obtained in human subjects. The Principal Investigators are well aware of the limitations imposed in extrapolating the results of flow patterns in rigid anatomic models to the human carotid complex; but the variables are so numerous that it is impossible to interpret properly the findings in the latter case without recourse to measurements obtained under well-defined conditions. Also, it is known that the vessel geometry has a greater effect on local flow patterns than the elasticity of the neighboring walls.

3. Analysis methods will be developed to distinguish physiologic flow disturbances due to such factors as heart rate variability, respiration and geometry from disturbances created by stenoses. This is necessary to prevent attributing normal variations in hemodynamics to the presence of plaques.

4. The results of flow disturbance analysis will be compared with other clinical data from patients being studied in the Vascular Laboratory at Piedmont Hospital. The purpose here is to determine the sensitivity of our measurement and analysis methods in relation to other available methods and to define the role of flow disturbance analysis in the overall scheme of detection and quantification of atherosclerosis of the carotid vessels.

2. Studies Conducted to Achieve Specific Aims

Specific Aim #1. A multichannel, microprocessor-controlled pulsed Doppler ultrasound instrument was modified to allow for velocity profile measurements with 25 channels and turbulence velocity measurement with one of these channels. A series of patients and normals has been studied with the instrument and the data recorded on FM tape (5 normals and 15 patients suspected of carotid atherosclerosis). These data will serve as a data base for further development of signal analysis techniques. Descriptions of the instrumentation and current analysis methods have been presented at scientific meetings and manuscripts are in preparation (see list of publications). Analysis of these data is now in progress in consultation with Dr. Max Casty of the Institut fur Biomedizinische Technik in Zurich, and a manuscript reporting the findings of the initial analysis is in preparation.

Important Results to Date:

The "turbulence channel" gives reliable detection of coherent flow disturbances and of turbulent velocity fluctuations up to approximately 100 Hz.

- The curves describing the development of velocity disturbances during the cardiac cycle are a more sensitive indicator of disease than are disturbances averaged over the cycle.

- Using a "Disturbance Index" method for describing the level of flow disorder during the deceleration phase of systole discriminates between normal vessels and those patients whose disease has not yet caused flow reduction. Since we do not yet have a large patient population, however, it is premature to speculate on the sensitivity to detecting early lesions.

- Doppler ambiguity and system noise create a background or "apparent" disturbance level of approximately 2 cm/sec. Consequently, velocity disturbances cannot be reliably detected at present unless this threshold is exceeded.

- Physiologic disturbances, primarily caused by phase variations in triggering from the EKG due to heart rate variability, are significant in some instances.

Specific Aim #2. All steady flow model studies have been completed and manuscripts accepted for publication. Pulsatile flow studies in the bifurcation model are underway. A series of initial flow visualization experiments has been reported at a scientific meeting.

Important Results to Date on Pulsatile Flow:

- There are sufficient differences between the detailed steady flow results and the initial pulsatile flow visualization that it is necessary to proceed with extensive laser Doppler anemometer measurements of the pulsatile velocity field.

- Although no turbulence was seen for physiologic Reynolds numbers in steady flow, it appears that turbulence exists during a brief phase of the pulsatile flow cycle. This has important implication to the interpretation of clinical data.

- The separated flow region in the carotid sinus seen in steady conditions is likewise present for pulsatile flow. However, its size varies considerably during the cycle and the wall shear stress directions change strongly in magnitude and direction over most of the sinus region.

It is worth noting that at the recent NIH Workshop on Quantitative Evaluation of Atherosclerosis (at which the P.I. of this project was an invited participant) Dr. C.P.L. Wood reported that flow separation can be documented in the carotid sinus in a clinical setting using a multigate Doppler device. This agrees with our previous predictions based upon in vitro studies with our carotid model.

Specific Aim #3. Dr. R.I. Kitney, our consultant at Imperial College, has written a series of computer programs designed to answer specific questions concerning signal analysis problems. During the present grant year Dr. Kitney visited Georgia Tech twice for a total of four weeks, and Dr. Giddens visited Imperial College once for a total of two weeks. In fact, Dr. Kitney is presently at Georgia Tech implementing these programs on our central computer system and working on manuscript preparation.

Important Results to Date:

- Computer programs employing various filtering techniques, autoregressive spectrum analysis, and phase shift averaging methods have been completed and are now being applied to hot film anemometer velocity data obtained in the poststenotic region of the dog aorta.

- We have clearly demonstrated that combinations of low pass and high pass filtering do not accurately separate turbulent velocities from the underlying waveform. Rather, ensemble averaging techniques are required. This point has been a controversy in biofluid dynamics for several years.

- Physiologic variability is reduced remarkably by using a phase shift averaging method to account for heart rate variability. This has important implications in the treatment of clinical data since physiologic disturbances are frequently a problem.

- Two manuscripts are in preparation to document the techniques and results.

Specific Aim #4. We have not made any extensive comparisons where flow disturbance analysis has been correlated with other clincial data. Most of the present grant year has been spent in instrumentation development, collecting data and analyzing the flow disturbances. The clinical data are available on each of the patients studied, and the coming year will include the correlation with flow disturbance analysis, and we shall continue the collection of patient data.

IMPORTANT SERENDIPITOUS RESULT

Our experience with the hemodynamics of normal and diseased adult carotid arteries has led to the discovery of an apparently sensitive and powerful technique for early detection of patent ductus arteriosus in neonates. We have found that the carotid artery waveform is very sensitive to the presence of a patent ductus. By noninvasively measuring this waveform with pulsed Doppler ultrasound, we have been able to consistently detect ductus in a series of infants (15), and in all but one of these the carotid waveform alterations occurred prior to other clincial signs.

Although this work was not directly supported by the present grant, it was our familiarity with carotid hemodynamics which led to the finding. The technique is now being employed routinely by pediatric cardiologists at the Emory University Hospitals in an effort to fully evaluate its usefulness.

3. Specific Objectives for Coming Year

Specific Aim #1. We plan to complete the analysis of all existing human data on FM tape and to begin collecting new data on additional normals and patients. The analysis techniques will be modified to incorporate phase shift averaging to reduce physiologic variability. We will also examine analysis techniques which emphasize flow disturbance evolution, including energy specta determinations from the disturbance velocity and pattern recognition schemes for the underlying waveform.

Specific Aim #2. We plan to complete the laser Doppler anemometer velocity measurements in our carotid bifurcation model under pulsatile flow conditions. This will aid in the interpretation of the clinical data and will have relevance to the problem of atherogensis in the carotid bifurcation.

Specific Aim #3. We plan to complete the evaluation of the phase shift averaging program using human data. Additionally, we plan to examine the accuracy and usefulness of estimation of velocity disturbance energy spectra by means of autoregressive (AR) spectrum estimates. Initial indications are that the evolution of velocity disturbance energy specta during the cardiac cycle is a sensitve indicator of the presence of stenoses, and these evolutionary specta are likely to be estimated better by AR methods than by FFT methods. The AR approach may offer an entirely new technique for analyzing the changing frequency content of disturbed blood flows.

Specific Aim #4. The clinical data on patients whose Doppler carotid studies are already on tape will be compared with the flow disturbance analysis methods. As new patient data are obtained, this comparison will be continued with the objective of developing stenoses classification criteria based upon flow disturbances.

4. Research Involving Human Subjects

a. There have been no changes in the protocols involving human subjects since the last competitive review, nor do we anticipate any changes for the coming year.

b. The protocols were evaluated by our Human Subjects Committee at Georgia Tech. This committee has been requested to send an updated letter of approval.