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OCA PAD INITIATION - PROJECT HEADER INFORMATION

08/01/88

Active

Project #: E-25-M62
Center # : Q5459-0A0

Cost share #:
Center shr #:

Rev #: 0
OCA file #:
Work type : RES
Document : GRANT
Contract entity: GIT

Contract#: 5 R29 HL39437-02
Prime #:

Mod #:

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Subprojects ? : N
Main project #:
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Project unit:
Project director(s):
KU D N

ME

ME

Unit code: 02.010.126

Sponsor/division names: DHHS/PHS/NIH
Sponsor/division codes: 108

/ NATL INSTITUTES OF HEALTH
/ 001

Award period: 880801 to 890731 (performance) 891031 (reports)

Sponsor amount	New this change	Total to date
Contract value	94,481.00	94,481.00
Funded	94,481.00	94,481.00
Cost sharing amount		0.00

Does subcontracting plan apply?: N

Title: HUMAN ATHEROSCLEROSIS: ROLE OF PULSATILE FLOW

PROJECT ADMINISTRATION DATA

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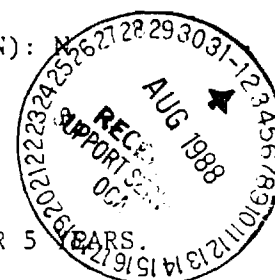
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Security class (U,C,S,TS) :
 Defense priority rating :
 Equipment title vests with: Sponsor

ONR resident rep. is ACO (Y/N):
supplemental sheet
GIT X

Administrative comments -

INITIATION. 2ND YEAR OF CONTINUING GRANT RECOMMENDED FOR SUPPORT FOR 5



GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

NOTICE OF PROJECT CLOSEOUT

Closeout Notice Date 07/27/90

Project No. E-25-M62_____ Center No. Q5459-OA0_____

Project Director KU D N_____ School/Lab MECH ENGR_____

Sponsor DHHS/PHS/NIH/NATL INSTITUTES OF HEALTH_____

Contract/Grant No. 5 R29 HL39437-02_____ Contract Entity GIT_

Prime Contract No. _____

Title HUMAN ATHEROSCLEROSIS: ROLE OF PULSATILE FLOW_____

Effective Completion Date 890731 (Performance) 891031 (Reports)

Closeout Actions Required:	Y/N	Date Submitted
Final Invoice or Copy of Final Invoice	Y	900323
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 Management	Y
Research Security Services	N
Reports Coordinator (OCA)	Y
GTRC	N
Project File	Y
Other _____	N
_____	N

E-25-2062

SECTION IV PROGRESS REPORT SUMMARY		GRANT NUMBER R29H239437	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR		PERIOD COVERED BY THIS REPORT	
APPLICANT ORGANIZATION		FROM 8/1/89	THROUGH 7/31/90
TITLE OF PROJECT (Repeat title shown in item 1 on first page)			
(SEE INSTRUCTIONS)			

1. Summary of plans for next year of support.

Specific Aims. 1. To quantify the pulsatile flow field for simulated rest conditions in an in vitro model of the human abdominal aorta.

2. To quantify the location and extent of early human atheroma in the abdominal aorta.

Methods. In general, the methods for achieving the goals are not changed from the original grant proposal. Several refinements have allowed us to produce much more accurate modelling of in vivo hemodynamics. New magnetic resonance imaging (MRI) are being developed which may become a major tool in future studies. The morphologic measurements should be easier to obtain and display due to new computer techniques which we have implemented.

The hemodynamic environment in the abdominal aorta is dominated by geometry and branch flow division for steady flow. For pulsatile flow, the unsteady characteristics of in-vivo aortic blood flow must also be modelled. A glass blown aorta model has been constructed based on the average measurements of 55 bi-planar angiograms and 10 pressure perfusion fixed cadaver specimens. The model dimensions were scaled up by 10% over in-vivo measurements to give an entrance diameter of 25.4 mm.

The flow system is a constantly recirculating type with water as the working fluid. Pulsatile flow is produced using an adaptation of the flapper nozzle valve, the design of which is presently being patented. Immediately following the valve, there is an entrance length of 100 diameters to allow the fluid to develop and reduce any disturbances caused by the valve. The outflows from each vessel are controlled using precision needle valves. A capacitance bottle is inserted in the outflow system of the iliac arteries to simulate the capacitance of the lower limbs. The flow through the aorta and iliac arteries is measured using Transonic Systems cannulating flow probes.

The mean and peak flow rates for the model are scaled to insure dynamic similarity to the in-vivo state. For resting conditions, the Reynolds number is 500. In order to simulate the time dependant flow characteristics of the in-vivo hemodynamics, the model heart rate must be scaled according to the non-dimesional Womersley parameter, $\alpha = (d/2)(\omega/\nu)^{1/2}$ which represents the ratio of unsteady to viscous effects. For typical resting and post-prandial conditions, α is 16. Under exercise conditions, α increases to 23.

One important aspect of pulsatile flow in the abdominal aorta is the difference between the flow waveforms in the suprarenal and infrarenal aorta. In the suprarenal aorta, the flow remains positive throughout the cardiac cycle, indicating that it feeds a low resistance vascular bed such as the kidneys. However, in the infrarenal aorta, there is a negative flow phase in late systole, followed by slow, forward flow in diastole. This triphasic flow is caused by the high peripheral resistance in combination with the capacitance of the arteries to the lower limbs. The triphasic waveform in the infrarenal aorta has duplicated for these

experiments.

Thus, we have been able to achieve an accurate simulation of pulsatile aortic hemodynamics in a laboratory model where we can reproducibly control the flow conditions. The next set of studies are designed to quantify the three-dimensional flow field in the abdominal aortic segment. The hemodynamic measurements will be based primarily on the pulsed Doppler ultrasound (PDU). We have obtained the Hartley PD-112 Variable Width 20 MHz Pulsed Doppler instrument and have been gaining experience in a simple pipe flow test system.

This test system has enabled us to develop additional software for the more accurate Doppler shift frequency detection parameters as described in the original proposal. It is anticipated that this system will provide excellent quantitative results. Additionally, we have been developing a new quantitative technique for velocity measurements based on magnetic resonance imaging (MRI). If successful, the MRI will provide an excellent complementary tool for verification of our results *in vivo*.

Morphology studies will be performed in collaboration with Drs. Seymour Glagov and Christopher K. Zarins at the University of Chicago. Over ten aortas have been harvested from cadavers under pressure perfusion fixation. The arteries will be sectioned for histologic evaluation and quantitation as described in the original grant application. We have added the capability to produce three-dimensional reconstructed images of the sections which will aid us in the correlation of plaque location to specific hemodynamic variables on a point-by-point basis.

2. Results.

The objective of this year's studies were to explore the influence of adding pulsatility to the flow model of the human abdominal aorta. To produce the physiological pulsatile waveform, we designed a new dynamic valve which is presently being patented. The combination of distal impedances from the renal and iliac arteries are known to affect the pulsatile flow waveforms in the infrarenal aorta. Physiologically, the aorta can experience a large increase in flow when comparing rest and exercise conditions. The flow visualization technique used for this experiment was dye injection. A video tape has been compiled for distribution as a demonstration of the complex, three-dimensional character of aortic hemodynamics.

Rest Conditions. Flow visualization of pulsatile aortic flow delineated clear flow differences between the thoracic and abdominal aortic sections. In the suprarenal aorta, the flow was relatively undisturbed throughout the cardiac cycle and exhibited a laminar type pattern which accelerated and decelerated regularly. In contrast, flow in the infrarenal segment was highly complex with regions of complicated vortex formation and transient separation. The relatively undisturbed streaks of dye changed into large vortices as the dye passes the renal orifices.

During systolic acceleration, flow patterns throughout the aorta exhibited no secondary flow. As the primary flow began to decelerate after peak systole, two vortices appeared at the level of the renal orifices. At the aortic bifurcation, the dye was seen to form a horseshoe

vortex. During flow deceleration, the strong vortex created two symmetric regions of flow reversal at the postero-lateral walls of the common iliac arteries. The horseshoe vortex would be expected to create relatively large circumferential shearing stresses along the outer walls of this bifurcation.

A region of transient separation was seen along the posterior wall of the aorta. A long, thin region of persistent dye extended from the renals to the iliacs, ending in a horseshoe pattern at the aortic bifurcation. The transient separation region exhibited an oscillating "to and fro" behavior, moving slightly forward during early systole and strongly reversing toward end-systole. The residence time of dye in this region was approximately eight cardiac cycles before clearing, as compared to the quick flushing of the anterior mainstream with each pulse.

Postprandial Conditions. The resulting increase in flow to the superior mesenteric artery created a new region of oscillatory flow along the anterior wall of the infrarenal segment. The flow patterns elsewhere in the abdominal aorta were not markedly altered.

Exercise Conditions. Exercise conditions were modelled through a large decrease in distal resistance to the legs and a 100% increase in cardiac output. Flow increased approximately 600% to the iliac arteries with a large increase in proportional flow to the legs. The dye patterns throughout the model showed a dramatic change. Even though the Reynolds number increased, flow laminarized throughout the infrarenal aorta. No vortices formed near the renal or SMA orifices at any point in the cardiac cycle. In comparison with the flows at rest, the separation regions and secondary flow vortices were greatly diminished. A very thin region of dye collection could be detected along the posterior curve of the infrarenal aorta extending from the level of the celiac orifice to the bifurcation. This persistent dye streak divided and continued laterally into the common iliacs. The residence time of dye in this thin region was between two and four cycles.

The introduction of pulsatility created a separation region which was oscillatory in character, with dye reversing strongly along the posterior wall throughout the entire infrarenal aorta after peak systole. The fluid residence time along the posterior wall could be estimated at eight cardiac cycles. Pulsatile flow additionally caused an augmentation of the secondary flow formations near the renal orifices and at origins of the iliacs. Exercise pulsatile conditions produced laminarization of the flow and greatly diminished the area subject to oscillatory reverse flow. The residence time decreased to less than four cycles of an increased pulse rate. Thus, absolute dye residence time was decreased by about one-fourth.

Relationship to atherosclerosis. An association appears to be present in our model of the human abdominal aorta between the hemodynamic conditions of low mean, oscillatory wall shear stress and high residence time and infrarenal atherosclerosis. While strongly implying that the posterior wall is the initial site of atherogenesis in the infrarenal aorta, this conclusion cannot be made without detailed correlation with morphologic measurements. It is interesting to note that the distribution of raised lesions in aortas obtained from young

individuals with traumatic accidents are located in the same posterior area of high residence time as predicted from our model (Cornhill - PDAY study).

Unsteady flow is inherently complicated and flow visualization is extremely useful in forming a physical feel for the complex fluid mechanics. A more complete description, however, will require quantitative measurements. These quantitative velocity measurements should aid in defining exactly which hemodynamic factors most strongly contribute to the localization of atherosclerotic plaque in the human aorta.

3. No human studies are proposed.

4. No vertebrate animal studies are involved.

5. Publications.

1. Holenstein, R., and Ku, D.N., "Reverse flow in the major infrarenal vessels - a capacitive phenomenon," Biorheology, 25;835-842, 1988.
2. Ku, D.N., Glagov, S., Moore, J.E., and Zarins, C.K., "Flow patterns in the abdominal aorta under simulated postprandial and exercise conditions," J. Vascular Surgery, 9;309-316, 1989.
3. Glagov, S., Zarins, C.K., Giddens, D.P. and Ku, D.N. "Hemodynamics and atherosclerosis: Insights and perspectives gained from studies of human arteries." Arch Path Lab Med, 112;1018-1031, 1988.
4. Zarins, C.K., Glagov, S., Giddens, D.P., and Ku, D.N. "Hemodynamic factors and atherosclerotic change in the aorta," in Aortic Surgery: New Diagnostic and Operative Techniques, (J.J. Bergan and J.S.T. Yao Eds.) Chicago: W.B. Saunders Co. (1988) pp. 17-26.
5. Moore, J.E. and Ku, D.N. "Pulsatile flow visualization of the abdominal aorta." Arteriosclerosis, in submission, 1989.
6. Moore, J.E. "Steady and pulsatile flow visualization in the human abdominal aorta. M.S. Thesis, Georgia Institute of Technology, Atlanta, GA 1988.
7. Binns, R.L. and Ku, D.N., "The effect of stenosis on wall oscillation in an "ideal" latex collapsible tube model: A possible mechanism of stroke and transient ischemic attack," The Society for Vascular Surgery, Chicago, p. 40, June 1988.
8. Moore, J.E., and Ku, D.N., "Steady and pulsatile flow visualization in the abdominal aorta," World Congress on Medical Physics and Biomedical Engineering, San Antonio, August 1988, p. 379.
9. Moore, J.E., and Ku, D.N. Pulsatile flow visualization in the abdominal aorta. FASEB, 615-1, 1989.